

**All**  
*of* **Us**

Research  
Priorities  
Workshop

Use Cases **s** Report

## Introduction

In March 2018, the National Institutes of Health's [All of Us Research Program](#) held a workshop with key stakeholders to identify research priorities that will capitalize on the program's one million or more participants and help ensure optimal value for advancing precision medicine. To drive this effort, *All of Us* collected substantial [public input](#) on the future design and content of the program.

The research community was asked to submit their ideas through a tool known as a “**use case**,” which outlines and describes a research question that the program can address using its unique platform. A use case also includes the following requirements: (1) the **datatypes** needed to answer the research question; (2) the **methods** to obtain the data types and to analyze the data; and (3) the **specifications** for using the methods. Together, these three requirements are considered a potential protocol element (PPE) that could be incorporated into future versions of the [All of Us protocol](#).

During the workshop, attendees used these ideas to generate hundreds of additional use cases and PPEs that cover a wide range of scientific areas, diseases, and conditions. Attendees identified 87 use cases they deemed “most important” to advancing precision medicine. In a separate process on day three, attendees identified 75 “game-changing” PPE that could have exceptionally significant impact on advancing precision medicine. Because these “game-changing” PPEs were created independently, only 7 coincidentally appear in the use cases (a total of 11 times).

This document contains a compiled and searchable list of the 1,110 uses cases collected both prior to and during the workshop, after removing duplicates. They are categorized into nine health conditions: (1) Cancer; (2) Cardio-respiratory and Blood; (3) Digestive, Renal, and Metabolic; (4) Health and Resilience; (5) Human Development and Aging; (6) Immunologic, Infections, and Inflammatory; (7) Mental Health and Addiction; (8) Musculoskeletal & Dental; and (9) Sensory, Pain, and Neurologic.

Within each health condition, the use cases are further organized by seven cross-cutting themes, which are disciplines and research areas that span across all the health conditions. Cross-cutting themes: (1) Environmental and Other Contextual Effects; (2) Genomics and Other –Omics; (3) Health Disparities, Health Care Quality, and Access; (4) Informatic, Methodologic, Ethical, Legal, and Statistical Research; (5) Mobile Health; (6) Risk Factors, Prevention, and Wellness; and (7) Therapeutic and Preventive Interventions. Each use case was also assigned a scientific category that reflects how the idea could advance precision medicine across a health/disease continuum.

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# Cancer

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RESEARCH PROGRAM | Precision  
Medicine  
Initiative

## Does use of thiazide diuretics raise endometrial cancer risk?

**Use Case ID** 194927

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

A 2009 article on the EDGE study found an increased risk of endometrial cancer in women who used thiazide diuretics. Fortuny et al., in “Risk of endometrial cancer in relation to medical conditions and medication use” (Cancer Epidemiol Biomarkers Prev 2009 May), recommend studying their findings further.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Thiazide diuretics use		
Endometrial cancer diagnosis		
Risk factors, self-assessment		
Clinical outcomes		

## Among patients who underwent partial mastectomy for treatment of ductal carcinoma in situ, what characteristics distinguish those who experience recurrence from those who do not?

**Use Case ID** 195128

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Follow people who had a partial mastectomy for DCIS and post-surgery treatments and actions, including physical factors, behavioral changes, diet changes, increases in exercise, stress reduction, and any change of geography. Follow them for up to 10 years to find patterns that reduce the return of the cancer.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Ductal Carcinoma In Situ (DCIS) diagnosis		
Relapse/recurrence		
Behavioral characteristics, self-assessment		
Diet, self-assessment		
Location data		

## Are participants who have been exposed to pesticides at higher risk of developing cancer?

**Use Case ID** 195834

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Study correlation between pesticides and cancer.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Electronic Health Record (EHR)	Every 3 years
Cancer information	Procedure codes	Every 3 years
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Pesticides exposure assessment results	Urine collection	Every 2 years
Clinical outcomes	Survey	Annually

## Do changes in a woman's mammographic breast density indicate a change in her risk of breast cancer?

**Use Case ID** 197750

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Breast cancer is the most common cancer in U.S. women. Breast density, usually measured from mammograms, is a strong risk factor for breast cancer and is correlated with many other risk factors, but it is unknown whether changes in breast density reflect changes in breast cancer risk. Importantly, breast density provides a measure of breast cancer risk during menopause when endogenous hormone levels are changing and breast tissue may be more susceptible to environmental exposures.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Breast cancer diagnosis	Electronic Health Record (EHR)	
Tumor characteristics	Tissue biopsy	Every 3 years
Lifestyle, self-assessment	PPI Survey (AOURP)	
Environmental samplings and exposure results	Urine collection	
Breast tissue sample	Formalin-fixed, paraffin-embedded (FFPE) blocks	

## ***Is there a relationship between exposure to indoor air pollution, particularly wood stove use, and development of breast cancer?***

**Use Case ID** 198168

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

It is known that indoor burning of fuel for heating or cooking releases carcinogens. Little is known about the impact of indoor air pollution from wood-burning stoves or fireplaces on breast cancer risk. We suggest collecting information on the use of indoor wood-burning stoves and/or wood-burning heat sources so that we can study the relationship between exposure to the resulting fine particle pollution and breast cancer. Outcome data would be collected through medical records.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Burning indoor fuel, chemical exposure assessment results	Survey	Annually
Breast cancer diagnosis	Electronic Health Record (EHR)	Annually
Family clinical outcomes	PPI Survey (AOURP)	Annually
Breast cancer screening information	Survey	Annually
Breast Imaging Reporting and Data System (BI-RADS)	Electronic Health Record (EHR)	Annually

## ***Is there a relationship between exposure to outdoor air pollution and development of breast cancer?***

**Use Case ID** 198174

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Previous research has suggested that women who live in areas with high levels of outdoor air pollution may have a higher risk of breast cancer. We suggest collecting data on participants' current and previous residence(s) and place(s) of work in order to link geographic location to existing air quality databases. Data collection would be facilitated through map features, allowing on-the-go geocoding. Outcome data would be collected through medical records and linkage to cancer registries.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Air quality assessment results		
Geocode data	Survey	
Breast cancer diagnosis	Electronic Health Record (EHR)	
Tumor characteristics	Electronic Health Record (EHR)	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually

## Do exposures to endocrine active compounds during puberty increase breast cancer risk?

**Use Case ID** 198445

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Emerging data suggest that exposure to toxicants during key life stages, such as puberty, alter breast development and influence cancer risk. A comprehensive measure of environmental exposures (e.g., air pollutants, parabens, phenols, pesticides) at puberty could link to future breast cancer-associated diagnoses (benign breast disease, atypical ductal hyperplasia, ductal carcinoma in situ, invasive breast cancer) identified through electronic health records.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Clinical diagnostic test	Annually
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Air quality assessment results		
Bisphenol A (BPA) levels		
Pesticides exposure assessment results		

## Are participants who have been exposed to pesticides at higher risk of developing cancer?

**Use Case ID** 198489

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Pesticides are commonly used inside and outside the home. Evidence from studies of farmers suggests that some pesticides are likely carcinogenic, but the impact of lower levels of exposure is less clear. By collecting information on pesticide exposure through surveys and analysis of carpet dust, we could evaluate the risk of cancer associated with low levels of pesticide exposure. Given their widespread use, even a small increase in risk could have a substantial public health impact.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pesticides exposure assessment results	Survey	Periodically
Cancer information	Electronic Health Record (EHR)	Annually
Pesticides exposure assessment results	Specimen collection	Baseline
Pesticides exposure assessment results		

## Does exposure to endocrine-disrupting compounds (EDCs) influence the effectiveness of treatments for hormone-associated cancers?

**Use Case ID** 198503

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Reduce Disease Impact

EDCs are widespread in consumer products, air, and drinking water. Cancer treatments (such as tamoxifen and aromatase inhibitors for breast cancers) depend on altering the body's hormone levels. All of Us could evaluate whether EDCs interfere with cancer treatments. This study would involve assessing EDC exposure in patients during treatment and evaluating hormonal outcomes and disease progression outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Bisphenol A (BPA) levels	Urine collection	At specified times anchored to the clinical event
Prescription medication\treatment	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Cancer outcomes		At specified times anchored to the clinical event
Pesticides exposure assessment results	Urine collection	At specified times anchored to the clinical event
Endocrine Disrupting Compounds (EDCs) levels	Urine collection	At specified times anchored to the clinical event

## Is there a strong correlation between geolocation (ZIP code) and the epigenetic expression of genes associated with cancer?

**Use Case ID** 1000769

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

ZIP code may be more important than genetic code, but does ZIP code (geolocation) have a direct influence on genetic expression via epigenetic modification?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Epigenomic/epigenetic markers	Blood draw	Annually
Immune biomarkers levels	Blood draw	Annually for 5 years
Nicotine metabolites levels	Blood draw	Annually for 5 years
Air quality assessment results		Continuous monitoring
Pesticides exposure assessment results	Blood draw	Periodically
Social environment	Interview	Periodically
Water quality assessment results	Environmental Protection Agency (EPA) air monitoring reports	Continuous monitoring
Psychological measures	Interview	Periodically
Small molecules and ion levels	Blood draw	Periodically

## Can the recommended frequency of cancer screening be tailored to individuals based on environmental monitoring?

**Use Case ID** 1000850

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Looking at environmental exposures/low penetrance genes/lifestyle.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environment	Geographic information system (GIS) code	Continuous monitoring
Environmental assessment results	Environmental Protection Agency (EPA) data	Continuous monitoring
Diet constitution assessment	Survey	Continuous monitoring
Air quality assessment results		Baseline
Water quality assessment results	Water purity test	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Annually

## How does a participant's physical and social environment relate to maintenance of health and prevention of disease over a lifetime?

**Use Case ID** 1000925 **Cross-Cutting Theme** Environmental and Other Contextual Effects

**Most Important** **Scientific Category** Maintain & Preserve Health

Environmental factors are known to impact an individual's ability to maintain and preserve health. Environmental exposures and factors such as food access, walkability, and air quality influence the development of cancer. These factors can be measured with population-based data collection and surveys (e.g., EPA reports, national surveys, etc.), surveys, specimen collection, and electronic monitoring/recording.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social environment	Survey	Annually
Biological Specimens	Blood draw	Baseline and at event
Environmental assessment results	Environmental Protection Agency (EPA) air monitoring reports	Annually
Environmental assessment results	Geospatial tracking	Continuous monitoring
Environmental assessment results	Personal air pollution monitor	Baseline and at event
Social environment	Electronic monitoring/recording	Continuous monitoring
Food security status	Survey	Annually
Food security status	Electronic monitoring/recording	Continuous monitoring
Location data	Survey	Baseline and at event
Location data	Electronic monitoring/recording	Continuous monitoring
Radiation exposure assessment results	Electronic monitoring/recording	Baseline and at event
Radiation exposure assessment results	Electronic Health Record (EHR)	Baseline and at event
Radiation exposure assessment results	Cell-free DNA sequencing	Baseline and at event
Biological Specimens	Environmental assessment	Baseline and at event
Environmental assessment results	Water purity test	Baseline and at event
Food security status	Geographic information system (GIS) code	Continuous monitoring
Location data	Geographic information system (GIS) code	Continuous monitoring
Location data	Survey	Continuous monitoring

## What genetic factors are associated with oral cancer (OC) and oropharyngeal cancer (OPC)?

**Use Case ID** 191744

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Tobacco and alcohol use and persistent oral infection with human papillomavirus (HPV) are risk factors for oral cancer (OC) and oropharyngeal cancer (OPC). CDC estimates that approximately 60% of OPC cases in the United States are caused by HPV types 16/18. Previous studies (GWAS) suggest genetic factors are associated with an increased risk of developing HPV-related OPCs. Assessing genetic factors in a large population could help to explain variances in susceptibility to OC and OPC.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Oral cancer diagnosis	Electronic Health Record (EHR)	Annually
Oropharyngeal cancer diagnosis	Electronic Health Record (EHR)	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually
Human Papilloma Virus (HPV) test results	Electronic Health Record (EHR)	Annually
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline

## What are the cancer outcomes for participants who lack a family history of cancer but who nevertheless have genetic markers related to Lynch syndrome and/or BRCA?

**Use Case ID** 194948

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

The goal of the study is to understand current practice for Lynch syndrome-related markers and BRCA1 and 2 related markers, where we have significant information from clinical settings, but imperfect information regarding interpretation in the general population. This would inform many future scenarios where a similar progression (from application in specific situations to broad use) would happen. We would gather qualitative data regarding patient and provider response to the info, and outcome.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Whole Genome Genotyping (WGG)	
Clinical outcomes	Procedure codes	Continuous monitoring
Behavioral characteristics, self-assessment	Natural language processing of notes	At specified times anchored to the clinical event
Treatment decisions	Interview	At specified times anchored to the clinical event

## Do cancer patients who receive targeted treatments based on sequencing of their tumors have better treatment outcomes than those who do not?

**Use Case ID** 194964

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Treat & Cure Disease

1. Divide “cancer” into multiple classes (e.g., breast, lung, pancreatic) and sequence tumors from 50 to 100 patients undergoing treatment. As with breast cancer, identify markers aligning with specific treatments and outcomes. 2. Perform the clinical trial. Use the deep sequencing as a diagnostic to aid in planning the treatment for a set of 50 to 100 patients for a given type of cancer. Track the outcomes: survival time, length of remission, effectiveness of treatment, etc. Use data to revise.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Tissue biopsy	At specified times anchored to the clinical event
Clinical outcomes	Physical exam	At specified times anchored to the clinical event
Cancer information		
Tumor biomarkers levels		
Outcomes		

## What genetic factors are associated with adenocarcinoma of the colon?

**Use Case ID** 195141

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Search for multigenerational histories of adenocarcinoma of the colon and look for genetic markers that would predict risk.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Colon cancer diagnosis	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Cancer information	Colonoscopy	At specified times anchored to the clinical event
Tumor Location		
Tumor biomarkers levels		

## Can an imbalance in tumor-promoting and tumor-inhibiting proteins be detected, leading to cancer detection?

**Use Case ID** 195179

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Classify all proteins as tumor suppressors/cell cycle inhibitors/cell cycle antagonists or tumor promoters/cell cycle agonists/cell cycle activators. Method 1: Take online cancer databases such as TCGA. Analyze for upregulation in oncogene/tumor promoter gene expression or inhibition of tumor suppressor gene expression. Method 2: Check PubMed for literature where oncogenic activity has been activated and tumor suppressing activity has been inhibited in tumors and metastases compared to controls.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
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## What is the etiology of lung cancer in never-smokers?

**Use Case ID** 196665

**Cross-Cutting Theme** Genomics and Other Omics

**Most Important**

**Scientific Category** Elucidate Disease Mechanisms

Incidence and mortality rates of lung cancer in never-smokers are high. Known risk factors only account for a small fraction of the cases. Methods to identify novel exogenous and endogenous processes of lung carcinogenesis: integrating genomics analyses of somatic mutational signatures, epidemiological and clinical data of risk factors and personal and family medical history, geocoded measures of residential exposures, detailed pathological record, and in vitro toxicological tests.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Tumor measurements (fresh frozen)	Tissue biopsy	At specified times anchored to the clinical event
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Genomic sequence data	Whole Genome Sequencing (WGS)	At specified times anchored to the clinical event
Clinical outcomes	Electronic Health Record (EHR)	Annually
Air quality assessment results		Continuous monitoring

## Can we identify diagnostic/prognostic biomarkers for cancer in participant biospecimens?

**Use Case ID** 198439

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

We developed a robust method to synthesize molecular libraries of non-biological molecular shapes ( $10^8$  variant molecules) and then down-selected individual ligands for diagnostics of disease states. We successfully applied the method to infectious and auto-immune diseases and have explored the utility of tumor-associated antigens (TAA) and TAA antibodies as cancer biomarkers. We propose to use our innovative method as a TAA biomarker diagnostic for differential diagnosis of multiple cancers.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Clinical diagnostic test	At specified times anchored to the clinical event
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Specified Biomarkers	Blood draw	At specified times anchored to the clinical event

## Are there blood markers (e.g., tumor proteins or circulating cell-free DNA) that can be used for cancer screening?

**Use Case ID** 198606

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

It is possible to detect protein biomarkers and circulating cell-free DNA from tumors in the blood. If All of Us collects and stores serial blood measures and links to medical records (or even cancer registries), we can start to ask whether there is the possibility that these biomarkers could be useful for cancer screening.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Tumor biomarkers levels	Blood draw	
Genomic analyses	Blood draw	
Cancer information	Blood draw	

## **What are the molecular characteristics of the tumors of participants diagnosed with cancer?**

**Use Case ID** 198652

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Treat & Cure Disease

In order to continue to move the field of cancer research forward, it will be imperative to collect detailed data on the molecular characterization of the tumors for All of Us participants who are diagnosed with cancer. Without these data (which cancer registries lack in completeness), cancer research within All of Us will be hampered. Stratification by these details will be extremely valuable for valid cancer studies within All of Us.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Tumor histological typing results		
Tumor biomarkers levels		
Cancer information		

## **What is the role of the gut microbiome in cancer incidence, treatment outcome, recurrence, and long-term survival?**

**Use Case ID** 1000707

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

The gut microbiome (GM) is hypothesized to play a role in development of several types of cancer, as well as with efficacy of cancer treatment. It is unknown whether the GM impacts cancer recurrence or survival or whether GM changes permanently after cancer treatment. It is also unknown whether the GM can be modified to reduce risk of cancer.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Gut microbiome sample	Stool sample	Annually or during clinical visits
Prescription medication\treatment	Survey	Baseline
Surgery event	Survey	Baseline

## What is the population frequency and penetrance of mutations in Lynch and BRCA-related genes for cancer subtypes?

**Use Case ID** 1000841      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

Much of the available data regarding mutation frequency and penetrance for hereditary cancer syndromes is derived from high-risk populations, which results in biased risk estimates. All of Us provides the opportunity to study this for a very broad range of conditions with a genetic basis.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Family clinical outcomes	PPI Survey (AOURP)	Every 5 years
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Cancer information	Electronic Health Record (EHR)	Periodically
Genomic analyses	Specimen collection	Baseline

## Can we use genomic, metabolomic, or other molecular strategies to identify cancer patients who are most likely to benefit from alternative treatments?

**Use Case ID** 1000945      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Reduce Disease Impact

Since heterogeneity in treatment responses exist, developing “omic” systems to identify those at risk of poorer outcomes could prompt alternative intervention/treatment strategies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Epigenomic/epigenetic markers	Clinical diagnostic test	Ongoing
Genomic instability assessment results		Baseline
Pharmacogenomics	Genomic testing	Baseline
Telomere length	Clinical diagnostic test	Baseline
Metabolomic profile	Biochemical assay	Ongoing
Microbiome sample	Genomic testing	Ongoing
Mitochondrial sequence	Genomic testing	Ongoing
Proteomic profile	Gas chromatography mass spectroscopy	Ongoing
Virome profile	Genomic testing	Baseline

## ***In what cases can a participant's genomic data predict their response to a given treatment?***

**Use Case ID** 1000989

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Treat & Cure Disease

Can pharmacogenomics predict the optimal treatment modality, method, dosage, etc.? Reuse retrospective large-scale clinical trial data (e.g., NCI trials) to more precisely model what worked, what not, why? Find a better cure? Can we use genetic/pharmacogenetic data combined with PRO data to inform selection of treatment and predict/prevent adverse events?

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Outcomes	Electronic Health Record (EHR)	Monthly
Pharmacogenomics	Genomic testing	Baseline
Prescription medication\treatment	Electronic Health Record (EHR)	Weekly
Side effects of prescription medication	Electronic Health Record (EHR)	Ad hoc
Side effects of prescription medication	Survey	Ad hoc
Outcomes	International Classification of Diseases (ICD) useage data	Monthly

## ***Is there a higher incidence of cancer in adulthood among participants who are survivors of pediatric cancer, compared with those who are not?***

**Use Case ID** 1001245

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Reduce Disease Impact

Looking at adverse effect of pediatric cancer survival on treatment affecting adult onset.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Clinical outcomes	Electronic Health Record (EHR)	Baseline
Patient-reported outcomes	Survey	Baseline
Genotyping data	Genomic testing	Baseline
Mental and psychosocial health, self-assessment	Interview	Baseline
Cancer outcomes	Electronic Health Record (EHR)	Annually

## What are the relative effects of genetically determined demographics versus socially determined demographics on cancer incidence and outcomes?

**Use Case ID** 192047

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

What, if any, are the differences in terms of cancer incidence and treatment outcomes for genetic demographics (biological sex, ethnicity) versus comparable self-reported demographics (gender, race, nationality)? The goal of this research would be to explore the relative contribution on disease, health, and outcome of genetically determined demographic characteristics versus personal, social, or culturally determined demographic characteristics.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer outcomes		
Cancer treatment/therapy		
Self-reported ancestry		
Genomic ancestry		

## What are the disparities in cancer incidence and cancer treatment outcomes among African and Caribbean immigrants, compared with the general population?

**Use Case ID** 195008

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

I would engage professional and scientific organizations that work with African and Caribbean immigrant issues, including the NIH-funded African Caribbean Cancer Consortium (AC3) and Caribbean Medical Providers Practicing Abroad (CMPPA), as well as federal agencies including NIMHD.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Annually
Cancer information	Electronic Health Record (EHR)	Annually
Sociodemographics		

## ***How does the use of concomitant medications alter the course of specific diseases and efficacy of treatment?***

**Use Case ID** 195184

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Treat & Cure Disease

Effect of concomitant medications on cancer chemotherapy and progression of autoimmune disease. Additional data collection would be needed in the initial design of the All of Us database. EMRs are incomplete in concomitant medications and many eliminate prior information with each update, so there is no historical information. This information would be useful to many studies.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Clinical outcomes	Survey	
Cancer information		
Autoimmune diseases diagnosis		
Cancer treatment/therapy		
Treatment effectiveness		

## ***What factors influence a participant's decision to undergo a specific course of treatment for cancer?***

**Use Case ID** 196129

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

The goal is finding out how patients make their decisions on cancer treatments. Cancer communication professionals will find the results helpful in determining where and how to provide accurate cancer information to the patients. Currently they only target the oncologists and rely on them to inform their patients. Going directly to the patients could provide more rational decisions by patients. Currently patients use social media.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Health literacy	Survey	
Patient education methods and content	Survey	
Technology Use	Survey	
Educational resources	Survey	

## ***Do disparities in environmental exposures contribute to racial disparities in triple negative breast cancer?***

**Use Case ID** 198448

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Elucidate Disease Mechanisms

Women of African, compared to European, ancestry in the U.S. are 2x–3x more likely to be diagnosed with triple negative breast cancer. The causes are unknown, but striking disparities in exposure to a number of potential carcinogens have been identified. Quantifying environmental exposures and linking to electronic health records for breast cancer–associated diagnoses would define the extent of disparities, chemical associations with cancer, and intervention targets.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Environmental samplings and exposure results	Clinical diagnostic test	Annually
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring

## ***Among tobacco users undergoing lung cancer screening, what factors affect receptiveness to smoking cessation interventions?***

**Use Case ID** 198688

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Lung cancer screening (LCS) may provide an opportunity to deliver smoking cessation treatments to particularly receptive individuals. Receiving LCS is associated with high risk perception and increased motivation to quit. Conversely, motivation to quit might be decreased for individuals with negative findings. Appropriately designed cessation interventions can increase and leverage LCS patients' motivation to quit smoking.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Tobacco/Nicotine Use	PPI Survey (AOURP)	Annually
Lung cancer diagnosis	Electronic Health Record (EHR)	Annually
Risk perception	Survey	Annually

## How does a participant's pattern of health service utilization (e.g., cancer screening) change after they enroll in the All of Us Research Program?

**Use Case ID** 1000785      **Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access  
**Most Important**      **Scientific Category** Maintain & Preserve Health

Little is known about how enrollment in a longitudinal study that gathers and returns large amounts of health information may change health service utilization and costs. This has relevance within the ongoing study and for future health system planning.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Health care participation	Electronic Health Record (EHR)	Periodically
Health care participation	Claims data	Periodic (approximately biweekly)
Health care cost	Claims data	Periodic (approximately biweekly)
Outcomes	Electronic Health Record (EHR)	Ad hoc

## Does the effectiveness of cancer treatment vary across race/ethnicity?

**Use Case ID** 1000832      **Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access  
**Scientific Category** Treat & Cure Disease

How effective are various cancer drugs across race/ethnicity?

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Sociodemographics	PPI Survey (AOURP)	Baseline
Cancer outcomes	Electronic Health Record (EHR)	Post-event or at least annually
Treatment data/specifics records	Electronic Health Record (EHR)	Ad hoc
Health insurance status	PPI Survey (AOURP)	Annually
Health insurance status	Electronic Health Record (EHR)	Annually
Cancer outcomes	Death records	Post-event or at least annually
Cancer outcomes	Imaging	Post-event or at least annually
Treatment data/specifics records	Prescription drug records	Post-discharge

## What are the most important factors relating to sociodemographic health disparities in cancer incidence?

**Use Case ID** 1000859

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

There is evidence that many socioeconomic and demographic characteristics contribute to disparities in the incidence of cancer of different types. Among these are education, income, race, geography, and ethnicity. It is difficult to determine what are the most of these because these factors are correlated. Because of All of Us's large sample size and deliberate oversampling of underserved populations, it affects the opportunity to dissect these contributors in more detail. These gradients may actually be due to tobacco use, childhood factors, and health care access, and stress may account for these factors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Home environment assessment results	Records	Ad hoc
Cancer information	Cancer registry	Annually
Behavioral risk factors for cancer	PPI Survey (AOURP)	Annually
Socioeconomic Status (SES)	PPI Survey (AOURP)	Baseline
Stress	PPI Survey (AOURP)	Annually
Heavy Metal Panel results		Baseline

## What is the financial burden experienced by cancer survivors?

**Use Case ID** 1000980

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

From the time of their diagnosis through cure and beyond, recurrence and end of life, persons with cancer experience many financial challenges due to costs of treatments and medications, loss of time at work, need to rely on caregivers in the home, who may also have to reduce time at work, or incur other expenses. We need to understand the extent of the financial burden and who experiences greater financial burden from cancer.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Financial status	Survey	Every 6 months
Health care cost		Continuous monitoring
Health care cost		Every 6 months
Cancer outcomes	Electronic Health Record (EHR)	Continuous monitoring
Symptoms	Survey	Every 6 months
Ability to perform activities of daily life (ADL) assessment results	Survey	Every 6 months
Health insurance status	PPI Survey (AOURP)	Every 6 months
Family relationships		Every 6 months
Ability to work	Survey	Every 6 months
Health care cost		Every 6 months

## What is the prevalence of mental health screening and treatment for patients undergoing cancer treatment?

**Use Case ID** 1001032

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

Do cancer patients get screened and treated per mental health factors (depression/anxiety)?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Clinical outcomes	Electronic Health Record (EHR)	Monthly
Mental health treatment	PPI Survey (AOURP)	Monthly
Mental health and behavior information	PPI Survey (AOURP)	Monthly
Health care cost		Monthly
Access to mental health care	PPI Survey (AOURP)	Annually

## How does recency of immigration influence cancer incidence, adjusting for detailed categories of race and ethnicity?

**Use Case ID** 1001048

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Elucidate Disease Mechanisms

Immigration status, race and ethnicity can be associated with cancer risk and outcomes. To elucidate how these factors influence the disease trajectory, research is needed to understand contextual factors that are most important (and potentially modifiable).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health literacy	Survey	Baseline
Sociodemographics	PPI Survey (AOURP)	Baseline
Medical Information	Electronic Health Record (EHR)	Annually
Social environment	Survey	Every 3 months
Social environment	Geographic information system (GIS) code	Every 3 months
Mental and psychosocial health, self-assessment	Survey	Every 3 months
Diet, self-assessment	Dietary assessment tool	Continuous monitoring
Specified Biomarkers	Clinical diagnostic test	Annually
Medical Information	Cancer registry	Annually

## What are the obstacles to identifying and screening relatives known to be at high risk of genetic disease?

**Use Case ID** 1001242

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

At-risk individuals/family members are not being identified who could benefit from this. Barriers may include psychosocial, economic, logistic, language, educational, or cultural (stigma). Assessing contributions of each of these would then guide implementation strategies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care participation	PPI Survey (AOURP)	Ongoing
Health literacy	Survey	Ongoing
Social environment	Survey	Ongoing
Mental and psychosocial health, self-assessment	Survey	Ongoing
Cancer information	Electronic Health Record (EHR)	Baseline

## Among participants diagnosed with cancer, what social factors are associated with treatment outcome?

**Use Case ID** 1001248

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Health care access and delivery are not equally available across our population. Is there a measurable impact of social factors on access and delivery and consequently on severity and outcome of treatment?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social environment	Survey	Continuously for 1 week every 6 months
Discrimination encounters	Diary/journal	Post-event or at least annually
Mental and psychosocial health, self-assessment	Diary/journal	Post-event or at least annually
Environment	Survey	Annually
Health care participation	PPI Survey (AOURP)	Annually
Personal Characteristics	Electronic Health Record (EHR)	Annually
Personal Characteristics	Survey	Every 2 years
Health care cost	Survey	Every 2 years
Health care participation	Electronic Health Record (EHR)	Annually
Outcomes	Survey	Annually

## Can a person's Web search activity help to predict cancer?

**Use Case ID** 1000696      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Most Important**      **Scientific Category** Detect Disease

Using search pattern algorithms to look for keywords related to preclinical symptoms which would help for early detection of disease.

Example: Screening for Pancreatic Adenocarcinoma using Signals from Web Search Logs: Feasibility Study and Results, Journal of Oncology Practice, 12.8, Aug 2016 Search tool: Hub of All Things

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Search query history	Social network mining	Continuous monitoring
Cancer information		

## How do cause-specific (cancer) and all-cause morbidity and mortality rates compare between All of Us participants and the general population/nonparticipants?

**Use Case ID** 1000738      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Scientific Category** Assess Risk

An understanding of the representativeness of the All of Us cause-specific (cancer) population relative to the cases in the general population is required to appropriately extrapolate findings.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Medical Information	Electronic Health Record (EHR)	Periodically
Health and phenotype data	Survey	Periodically
Medical Information	Cancer registry	Periodically
Death	Death records	Periodically
Health care cost		Periodically

## Can we generate a single, complete, and holistic medical record for each individual participant?

**Use Case ID** 1001010      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Scientific Category** Elucidate Disease Mechanisms

A single looking at interoperability of hospital data into a more pane of holistic medical record from cancer trajectory, from screening, detection, treatment, recurrence, survivorship/mortality.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Cancer treatment/therapy	Electronic Health Record (EHR)	Daily
Metadata	Records	Annually
Patient Engagement	Electronic Health Record (EHR)	Annually

## Can we develop and validate a machine learning approach to cancer treatment?

**Use Case ID** 1001062

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Elucidate Disease Mechanisms

Deep computing to generate hypothesis for domains in cancer outcomes, different treatments, therapeutic trajectory, QOL.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Personal Characteristics	Machine learning	Periodically

## What are the long-term outcomes of participants who are diagnosed with cancer?

**Use Case ID** 1001090

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Most Important Scientific Category** Maintain & Preserve Health

The validity of a prospective cohort to answer virtually any research question depends on attaining the following: (1) high rates of retention during follow-up and (2) complete outcome ascertainment during follow-up, thus reducing disease of interest (e.g., cancer) diagnosis and vital status. Being able to do passive follow-up for clinical outcomes through linkage is critical in addition to self-report and EHR.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Specified Biomarkers	Specimen collection	Ad hoc
Depression diagnosis	Actigraphy	Continuous monitoring
Social determinants of chronic disease	Survey	Continuous monitoring

## Are there critical points in the life course at which behavioral risk factors are particularly important for cancer prevention?

**Use Case ID** 1001250

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Maintain & Preserve Health

Modifiable risk factors vary over time or the life course. Longitudinal data with multiple opportunities to collect risk factor data would provide the opportunity to explore critical points in the life course for which risk factors play a role in cancer prevention or development. Model the impact of the behaviors over time in terms of maintaining health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Ongoing

## Is there an association between chronotype and cancer incidence?

**Use Case ID** 192183

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Assess Risk

Chronotype (bedtime and time of arising) is poorly captured in sleep questionnaires. Add activity monitor to track this important metric and relate it to disease endpoints.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Sleep behavior assessment results	Mobile monitor	
Health and phenotype data	Electronic Health Record (EHR)	

## Can mobile health technologies be used to reduce the wait time between primary physician referral and access to specialist care?

**Use Case ID** 195086

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

Mobile health platforms may be developed and validated to reduce patient wait times between primary care physician's referral and obtaining appropriate care from a specialist. The modalities may navigate the patient in the identification of a specialist, making appointment with the specialist(s), facilitate faster diagnostics and treatment decisions, increase access to needed care, improve patient adherence to treatment, and monitor quality of life while engaging the patient in the care continuum.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
	Mobile monitor	
Cancer outcomes		
Health care participation		
Treatment effectiveness		

## What is the best method for repeated biospecimen collection over time?

**Use Case ID** 198708

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Elucidate Disease Mechanisms

Currently, section 7.4 (Biospecimens) of the All of Us protocol does not emphasize "repeated collection over time." It may be useful to encourage experimentation with multiple methods to collect biospecimens (blood, urine) repeatedly over time, including "old" methods but also new technologies (perhaps wearable) and new methods for monitoring substances in the blood (like glucose can be monitored now). Like Galileo, we need a "better telescope" to observe biology. All of Us can help.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Blood sample characteristics		

## What adverse events are dose-limiting and potentially impact outcomes?

Use Case ID 1000716

Cross-Cutting Theme Mobile Health

Scientific Category Treat & Cure Disease

Description not provided.

Datatype	Method	Specification
Treatment data/specifics records	Electronic Health Record (EHR)	Weekly
Clinical outcomes	Electronic Health Record (EHR)	Post-event or at least annually
Patient-reported outcomes	Custom sensor/app	Weekly
Tumor characteristics	Electronic Health Record (EHR)	Post-event or at least annually
Perceived outcomes - patient		Post-event or at least annually

## How do modifiable lifestyle factors affect adverse breast cancer symptoms?

Use Case ID 1000756

Cross-Cutting Theme Mobile Health

Scientific Category Treat & Cure Disease

Do lifestyle factors (diet/exercise) affect treatment-related adverse symptoms for women with breast cancer?  
How does activity level impact level of side effects?

Datatype	Method	Specification
Treatment data/specifics records	Electronic Health Record (EHR)	Daily or weekly
Patient-reported outcomes	Mobile monitor	Weekly
Diet constitution assessment	Dietary assessment tool	Weekly or monthly
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Sleep assessments	Activity monitor	Continuous monitoring
Drug use/abuse, self-assessed	Diary/journal	Weekly or monthly
Stress	Diary/journal	Weekly or monthly

## What strategies are used by pediatric cancer survivors to manage the transition to adult care?

Use Case ID 1000757

Cross-Cutting Theme Mobile Health

Scientific Category Maintain & Preserve Health

Managing the transition from pediatric cancer care to adult care.

Datatype	Method	Specification
Health apps used	Survey	Baseline
Sociodemographics	PPI Survey (AOURP)	Baseline
Access to health care	Mobile monitor	Baseline
Personal EHR use	Electronic Health Record (EHR)	Baseline
Lifestyle, self-assessment	Activity monitor	Baseline

## Are mobile device data (e.g., fatigue/insomnia) prognostic for cancer diagnosis?

**Use Case ID** 1001045

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Reduce Disease Impact

Wearable devices and smartphones collect data relevant to cancer risk and symptoms after diagnosis. It might be useful to collect these data to assess whether these easily captured assessments are predictive of hard (diagnosis) and softer (symptom) end points.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Physical activity, self-assessment	Actigraphy	Continuous monitoring
Symptoms	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Symptoms	Survey	At specified times anchored to the clinical event
Cancer information	Pathology reports	Annually
Cancer information	Imaging	Annually
Cancer information	Blood draw	Annually
Cancer information	Electronic Health Record (EHR)	Annually

## Among cancer survivors, do those who use a mobile health device to track diet have greater change in nutrition behavior and/or increased time to recurrence than those who do not?

**Use Case ID** 1001209

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Other

At-home engagement and consumer behaviors and intervention through induced self-reporting (SMS, apps) crosses the digital divide. Can “upmarket” approaches toward healthy behaviors work?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mobile phone ownership	Mobile monitor	Continuous monitoring
Anthropometrics, whole body measurements	Electronic Health Record (EHR)	Periodically
Physical activity, self-assessment	Fitness tracker	Periodically

## What is the effect of ambient environmental air pollution on adverse health outcomes?

**Use Case ID** 191809

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Although exposure to air pollutants in the ambient (indoor and outdoor) environment is known to be associated with numerous adverse health outcomes (including cancer), the details of that association remain unclear. A key challenge for cancer studies is the lack of information on individual-level activities and other determinants of personal exposures over the lifetime; existing studies have had to rely on assumptions about time spent in microenvironments. Moreover, most data are from urban settings and underrepresent many racial and other population subgroups. The All of Us dataset could fill in the gap in this research question by providing more reliable data on individuals' lifetime exposures to ambient environmental air pollution.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Air quality assessment results		
Location data	Global Positioning System (GPS) monitoring	
Residence location		
Occupation Location		

## What are the underlying causes of different breast cancer subtypes?

**Use Case ID** 191820

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Breast cancer represents a major public health problem. In 2017, >250,000 women in the U.S. received a first diagnosis of invasive breast cancer and >60,000 of non-invasive breast cancer. This is a heterogeneous disease with respect to morphologic, molecular, and genomic features, defining subtypes with distinct etiology and clinical behavior. Understanding the causes of different subtypes is needed to improve risk assessment and inform precision prevention strategies for screening and primary prevention.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Breast cancer, metastatic	Electronic Health Record (EHR)	Every 3 months
Breast cancer, benign	Electronic Health Record (EHR)	Every 3 months
Breast cancer diagnosis	Electronic Health Record (EHR)	Every 3 months
Sociodemographics	PPI Survey (AOURP)	Every 3 years
Mammogram	Mammography	Every 3 years

## What are the metabolic features of people who develop cancer, compared with those who do not?

**Use Case ID** 191860

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Cancer is the second leading cause of death in the United States. Recent discoveries within cancer biology highlight that reprogrammed metabolism is a hallmark of cancer. Whether there are detectable metabolic perturbations that precede and/or predispose to development of cancer in individuals is not known, however. New metabolomics technologies make it possible to assay thousands of metabolites simultaneously and could be applied to blood samples to determine whether such prospective markers exist.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Diet, self-assessment	PPI Survey (AOURP)	
Metabolomic profile		

## Among participants with a genetic defect in the enzyme 22-hydroxylase, does childhood experience of abuse or trauma lead to increased risk of pituitary adenoma?

**Use Case ID** 194834

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

The emotional aftermath of abusive and traumatic experiences during childhood can yield consequences in adulthood. Some individuals develop illnesses while others remain unaffected. My personal experience as a clinical psychologist allows me to predict that patients carrying hereditary genetic mutations of the 22-hydroxylase enzyme are more susceptible to posttraumatic psychiatric disorders. Some of these patients will also develop pituitary adenomas as a result of chronic hyperstimulation of the hypothalamic-pituitary-adrenal (HPA) axis.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pituitary/hypophysis adenoma diagnosis	Electronic Health Record (EHR)	Baseline
Behavioral characteristics, self-assessment	Survey	Baseline
21-Hydroxylase Enzyme levels	Whole Genome Genotyping (WGG)	Baseline

## Does HSV infection increase prostate cancer incidence?

**Use Case ID** 195100

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Both genital HSV 2 infection and prostate cancer are prevalent diagnoses. The proposed study would answer the question of whether HSV genital infection in males increases the incidence of prostate cancer.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Herpes Simplex Virus type 2 (HSV-2) test results	Blood draw	At specified times anchored to the clinical event
Prostate cancer diagnosis		

## Among elderly participants, what factors distinguish those who have never had a cancer diagnosis from those who have?

**Use Case ID** 196120

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Identify the population of individuals who are 100 years old, half who may have had a cancer diagnosis and half with no cancer diagnosis in their lifetime. Survey those individuals as to their life experiences—medical history, employment history, lifestyle, exercise history, diet, etc. Individuals will provide a blood sample for complete genetic analysis. What genetic mutations are present which may cause cancer but did not? Look for which life factors may have prevented cancer from developing.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Cancer outcomes		
Genomic sequence data	Whole Genome Sequencing (WGS)	
Personal Characteristics		

## Among patients with autoimmune disease, what characteristics distinguish those who develop hematologic cancers from those who do not?

**Use Case ID** 196480

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Patients with autoimmune diseases have been found to be at a higher risk of certain types of cancers, particularly hematologic cancers. A recent study found that patients with Sjögren's were 11 times more likely to develop a hematologic cancer compared to patients without Sjögren's. The purpose of this study is to identify the pathogenic mechanisms leading to the development of blood and other cancers in patients with autoimmune diseases and better identify which patients are at risk.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Autoimmune diseases diagnosis		
Cancer information		

## ***Are the bacterial metabolites associated with participants' oral microbiomes more carcinogenic for participants who drink alcohol, compared to those who do not?***

**Use Case ID** 197067

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Oral bacteria are known to have both beneficial and detrimental effects on oral health, including carcinogenesis in the oral cavity. Since ethanol is a good organic solvent, oral bacterial enzymes and toxins may achieve greater exposure to the oral mucosa as a result of ethanol consumption, facilitating toxin access to intracellular processes. Subjects with different microbiome profiles and bacterial metabolites can be compared in vitro and in vivo for carcinogenicity.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Dental records	Every 3 months
Dental and oral data	Dental records	Every 3 months
Diet, self-assessment	Food diary	

## ***Among young women who do not smoke and do not use alcohol, what characteristics distinguish those who develop oral cancer from those who do not?***

**Use Case ID** 197483

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

There is an increasing incidence of oral cancer in younger patients who lack typical risk factors like smoking and alcohol use. While most head and neck squamous cell carcinoma is male-dominated, this “atypical” oral cancer seems to be equally distributed between males and females. Environmental factors (e.g., diet, medications, oral microbiome, etc.) and genetic/epigenetic factors should be studied in this atypical cohort to understand the emergence of this subtype.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Environmental samplings and exposure results	PPI Survey (AOURP)	
Genomic sequence data	Whole Genome Sequencing (WGS)	
Cancer outcomes	Electronic Health Record (EHR)	

## What factors influence a participant's decision to undergo screening for cancer?

**Use Case ID** 197744

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

Survey cancer patients and survivors and question what led them to seek care in the first place. Was it due to symptoms of disease or because screening or testing found cancer activity? The theory is that patients do not undergo screenings and testing until they become symptomatic and that many possible influences, including financial and cultural pressures, prevented them from doing so earlier. What can be done to encourage more people to seek screening?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	PPI Survey (AOURP)	Continuous monitoring
Cancer outcomes		
Health care participation		
Social determinants of health (SDH)		
Genotyping data	Genomic testing	Baseline
Psychological measures	Survey	Periodically
Access to health care	Global Positioning System (GPS) monitoring	Annually
Social determinants of health (SDH)	Global Positioning System (GPS) monitoring	Annually
Patient feedback	Electronic Health Record (EHR)	Annually
Social support	Survey	Monthly

## Can we develop and validate a machine learning approach to cancer diagnosis?

**Use Case ID** 198264

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The early detection of cancer has improved treatment outcomes and patient survival. Building precise risk prediction models can personalize cancer screening programs to one's need. The integration of variables capturing changes in lifestyle factors, exposure history, and molecular markers over time, together with the opportunity for passive surveillance through data linkage to electronic medical records and cancer registries, may be necessary to build such models.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Electronic Health Record (EHR)	
Lifestyle, self-assessment	PPI Survey (AOURP)	Every 2 years
Biological Specimens	Clinical diagnostic test	
Lifestyle, self-assessment	Mobile monitor	

## Is the incidence of cancer higher among participants who regularly use hair dye?

**Use Case ID** 198479

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Hair dyes are commonly used in today's society, but the long-term health effects are not known. Many hair dyes contain chemicals that are thought to be potentially carcinogenic. Studies have suggested that hair dyeing may be associated with an increased risk of lymphoma and possibly breast cancer; however, few prospective studies have been conducted. Given the extensive use of hair dyes, particularly among women, even a small increase in risk could have a substantial impact on public health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cosmetic use	Survey	Every 2 years
Cancer information	Electronic Health Record (EHR)	Annually
Disease endotypes results	Pathology reports	Annually

## Does psychosocial stress influence treatment outcomes in cancer, including time to recurrence?

**Use Case ID** 198633

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Treat & Cure Disease

In animal models, stress is a trigger for tumor growth and metastasis, yet we have not adequately addressed this question in human cancer patients or survivors. All of Us could longitudinally assess the biological experience of psychosocial stress (via a biomarker or wearable technology) at specified times in the cancer survivorship period and conduct an analysis of time to recurrence or time to death.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information		
Cancer treatment/therapy		
Stress	Mobile monitor	
Relapse/recurrence		
Death		

## ***Do stress-reducing activities or interventions influence cancer survivorship outcomes, including time to recurrence?***

**Use Case ID** 198636

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Treat & Cure Disease

Randomized trials could be set within All of Us to test these interventions at specific research sites.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Cancer information		
Cancer treatment/therapy		
Relapse/recurrence		
Death		
Behavioral characteristics, self-assessment		

## ***Is the microbiome of seminal fluid prognostic for risk of prostate cancer?***

**Use Case ID** 198654

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Prostate cancer has long been suspected to include an infectious etiology, although no agent has been identified. It is possible that one specific virus or bacterium is not significant, but rather the characteristics of the entire microbiota to which the prostate is exposed (e.g., the abundance and diversity of all microorganisms). This may be capturable by examining the seminal fluid microbiome.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Seminal fluid microbiome sample		
Prostate cancer diagnosis		

## ***Among participants with autoimmune disease, what factors distinguish those who develop lymphoma from those who do not?***

**Use Case ID** 198664

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Studies have shown that individuals with autoimmune diseases and other immune disorders are at increased the risk of developing lymphoma later in life, but the biological mechanisms are unclear. Better characterization of the risk, specific lymphoma subtypes involved, and the impact of treatment, along with an understanding of disease mechanisms, is critical for prevention of lymphoma in this highly susceptible population.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Cancer information	Electronic Health Record (EHR)	Annually
Autoimmune diseases diagnosis	Electronic Health Record (EHR)	Annually
Lymphoma diagnosis	Pathology reports	Annually
Treatment/Therapy	Electronic Health Record (EHR)	Annually
Genotyping data	Whole Genome Genotyping (WGG)	Baseline

## ***Among women referred for diagnostic breast biopsy, what histologic and radiologic factors distinguish those who are found to have high-risk breast precursor lesions from those whose biopsies are benign or preinvasive?***

**Use Case ID** 198677

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

In the U.S., about 1.6 million women a year undergo diagnostic breast biopsy. Although a history of breast biopsy is associated with increased breast cancer risk, the majority of biopsies range from benign to preinvasive disease. Characterization of breast biopsy tissues and breast imaging studies among women referred to diagnostic breast biopsy may facilitate the identification of histologic and radiologic biomarkers that relate to risk and progression of high-risk breast precursor lesions.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Breast tissue sample	Mammography	Annually
Breast cancer, benign	Clinical diagnostic test	Continuous monitoring
Breast cancer diagnosis	Clinical diagnostic test	Continuous monitoring
Breast cancer diagnosis	Electronic Health Record (EHR)	Annually

## What factors support successful cigarette smoking cessation among individuals who have been diagnosed with cancer?

**Use Case ID** 198679

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Cancer patients who smoke cigarettes have increased treatment toxicity and poorer prognosis compared with former or never-smokers. Only 50%–70% of patients who smoke at the time of diagnosis initially quit, and many later relapse to smoking. Research is needed to better understand how tobacco users who are diagnosed with cancer perceive the risks of tobacco use and the benefits of cessation, and to explore factors that support smoking cessation in these patients.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Tobacco/Nicotine Use	PPI Survey (AOURP)	Annually
Cancer information	Electronic Health Record (EHR)	Annually
Smoking cessation	PPI Survey (AOURP)	Annually
Sociodemographics	Electronic Health Record (EHR)	
Sociodemographics	PPI Survey (AOURP)	

## How does tobacco use reduce the efficacy or increase the morbidity of cancer treatment?

**Use Case ID** 198683

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Existing evidence does not adequately evaluate the effects with consideration of the patients' past history of tobacco use and the tobacco use during and after cancer treatment. The toxicity and expense of many cancer therapies warrant a better understanding of how concurrent tobacco use undermines efficacy or increases morbidity.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Tobacco/Nicotine Use	PPI Survey (AOURP)	Every 3 months
Cancer information	Electronic Health Record (EHR)	Baseline and annually
Side effects of treatment/therapy	Urine collection	
Clinical outcomes	Electronic Health Record (EHR)	

## What are the optimal type and dose of physical activity for cancer prevention?

**Use Case ID** 1000760

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Physical activity is associated with lower risk of various types of cancer, and more recent evidence supports time spent sitting is positively associated with cancer risk. The optimal dose and types of physical activity for cancer prevention are not well defined. By collecting more detailed data on bouts, types, intensity, and dose of activity and sitting patterns, more prescriptive physical activity recommendations can be made, including by sociodemographic factors (race/ethnicity, SES, gender, etc.).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Location data	Global Positioning System (GPS) monitoring	Continuous monitoring
Physical activity, self-assessment	Fitness tracker	Continuous monitoring
Physical activity, self-assessment	PPI Survey (AOURP)	Annually
Sedentary time	Diary/journal	Monthly

## Among cancer survivors, what factors reduce the risk of recurrence?

**Use Case ID** 1000770

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

What are the lifestyle behaviors that impact risk/risk reduction of breast cancer recurrence? What are the genetic characteristics that would predict breast cancer recurrence?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer outcomes	Electronic Health Record (EHR)	Annually
Genomic sequence data	Blood draw	Baseline
Behavioral characteristics, self-assessment	Survey	Monthly
Behavioral characteristics, self-assessment	Wearable electronics	Monthly
Environmental assessment results	Geographic information system (GIS) code	Annually
Tumor characteristics	Genomic testing	
Genomic sequence data	Cell-free DNA sequencing	

## What is the relationship between physical activity and cancer incidence and outcomes?

**Use Case ID** 1000797

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Little is known about how aspects of physical activity affect cancer risk and outcomes. Prospective collection of physical activity/exercise data linked to cancer and other disease outcomes data may lead to new approaches to risk detection/management.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	PPI Survey (AOURP)	Annually
Physical activity, self-assessment	Wearable electronics	Continuous monitoring
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline

## How does exposure to ambient pollution affect breast cancer risk, recurrence, and survival?

**Use Case ID** 1000815

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

A variety of ambient measures may be related to cancer risk. Air pollution is associated with lung cancer and may influence breast cancer risk. Some air pollutants and air toxins may be estrogenic. For example: PAH, NOx, metals are hormonally active. Metals such as lead, cadmium, and others are considered “metallo-shearers.” Conversely, green space and blue space (parks, forests, water) may positively affect well-being, exercise, and physical activity and prevent obesity, which then might reduce cancer risk. Challenges include interactions between these exposures such that being outdoors may increase exposure to pollution depending on location of green space.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Air quality assessment results		Annually
Cancer outcomes	Cancer registry	Periodically
Chemical exposure assessment results	Smartwatch	Continuous monitoring
Environmental assessment results	Environmental Protection Agency (EPA) data	Baseline
Sociodemographics	Fitness tracker	Continuous monitoring
Sociodemographics	PPI Survey (AOURP)	Periodically
Anthropometrics, whole body measurements	Electronic Health Record (EHR)	Annually
Anthropometrics, whole body measurements	Patient-reported outcome	Annually

## What is the relationship between early diagnosis of prostate cancer and clinical outcome?

**Use Case ID** 1000819

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

I.e., detecting prostate cancer earlier. Mitigate last-stage diagnosis in men.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mental and psychosocial health, self-assessment	Interview	Baseline
Sociodemographics	Electronic Health Record (EHR)	Pre- and post-treatment
Health care participation	Patient-reported outcome	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Periodically

## Is there a measurable association between common physiological measurements and cancer risk?

**Use Case ID** 1000827

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Little is known about how knowledge of common physiologic measures provides insights on cancer risk/outcomes. Prospective collection of physiologic data linked to cancer and other disease outcomes data may lead to new approaches to risk detection/management. This study could explore relationship to omic-based risk levels as well.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Glucose levels	Electronic Health Record (EHR)	Annually
Pulse	Wearable electronics	Continuous monitoring
Glucose levels	Clinical diagnostic test	During clinic visits
Glucose levels	Transcutaneous wearable	Continuous monitoring
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Medical Information	Cancer registry	Every 3 years

## What is the relationship between modifiable behavioral risk factors over the course of a lifetime and cancer risk/prevention?

**Use Case ID** 1001015      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Maintain & Preserve Health

Modifiable behavioral risk factors such as diet, physical activity, sleep, and tobacco use are known to influence health outcomes and maintenance across multiple diseases like cancer. Behavioral factors can be measures over the life course with survey, records, and wearables.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Every 3 months
Tobacco smoking	PPI Survey (AOURP)	Annually
Mental and psychosocial health, self-assessment	Survey	Annually
Diet, self-assessment	Food diary	Annually
Tobacco smoking	Saliva	Every 6 months
Tobacco smoking	Carbon monoxide (CO) monitor	Every 3 months
Alcohol Use	PPI Survey (AOURP)	Annually
Alcohol Use	Electronic monitoring/recording	Every 3 months
Alcohol Use	Specimen collection	Baseline
Nutritional supplement use	Survey	Every 3 months
Physical activity, self-assessment	Electronic monitoring/recording	Continuous monitoring
Sleep assessments	Electronic monitoring/recording	Continuous monitoring
Mental and psychosocial health, self-assessment	Clinical diagnostic test	Baseline and at event
Mental and psychosocial health, self-assessment	Electronic monitoring/recording	Periodically
Alcohol Use	Electronic Health Record (EHR)	Annually
Genotyping data		Every 5 years

## ***Does the pattern of physical activity, sleep, and sedentary behavior (24-hour sleep/activity cycle) engagement/accumulation across the life course influence the prevention and/or risk for cancer?***

**Use Case ID** 1001103

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Physical activity, sleep, and sedentary behavior are known, modifiable risk factors for cancer. Yet due to collection methods in the past, little is known regarding how the patterns of these behaviors affect cancer prevention and risk. For example, does the way in which you accumulate physical activity throughout the day matter? Are there critical time points across the life course where the pattern of sedentary behavior influences cancer risk? Note: This applies to multiple behavioral risk factors (e.g., diet).

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Physical activity, self-assessment	PPI Survey (AOURP)	Continuous monitoring
Physical activity, self-assessment	Wearable electronics	Continuous monitoring
Sedentary time	Survey	Continuous monitoring
Sedentary time	Wearable electronics	Continuous monitoring
Sleep assessments	Wearable electronics	Continuous monitoring
Sleep assessments	Survey	Continuous monitoring
Screen time	Survey	Continuous monitoring

## ***Can machine learning be used to improve the accuracy of screening mammography?***

**Use Case ID** 1001141

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

Description not provided.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Mammogram	Electronic Health Record (EHR)	Annually
Cancer information	Electronic Health Record (EHR)	Baseline
Cancer outcomes	Machine learning	Annually

## ***How does the natural history of disease (e.g., colon cancer) differ between cases detected via screening (pre-clinical) and those detected via symptomatic presentation (clinical)?***

**Use Case ID** 1001144

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Treat & Cure Disease

Overarching: How does early detection of disease alter natural history? Could be applied to many diseases.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Colon cancer diagnosis	Imaging	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Every 2 months
Quality of life	Survey	Monthly
Microbiome sample	Smart toilet	Baseline

## ***Do interventions to improve mental health/positivity affect treatment outcomes and long-term survival in cancer?***

**Use Case ID** 1001165

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

State of mental health likely influences outcomes in disease. Establishing effective strategies to improve mental health during cancer diagnosis and treatment could improve outcomes. Screening All of Us cancer patients in two cohorts. Those who engage/defer mental health strategies could define effective strategies.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Mental health treatment	Electronic Health Record (EHR)	Periodically
Social relationships	Electronic Health Record (EHR)	Periodically
Family relationships	Electronic Health Record (EHR)	Periodically

## What is the effect of diet and exercise on quality of life post-cancer treatment?

**Use Case ID** 1001173

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Many cancer patients experience decreased QOL during treatment. Could a change in diet and structured exercise program post-treatment impact QOL? Collection of surveys and data from wearables.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Diet, self-assessment	Diet history questionnaire	Baseline
Clinical outcomes	Survey	Baseline
Mental and psychosocial health, self-assessment	Survey	Baseline and at event
Physical activity, self-assessment	Activities Completed over Time in 24 Hours (ACT-24)	Baseline and at event
Cancer outcomes	Survey	Baseline

## What is the relationship between lifetime history of body weight/obesity and cancer? Are there differences across racial/ethnic populations?

**Use Case ID** 1001183

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Body fat percentage	Electronic Health Record (EHR)	Baseline and at event
Body fat percentage	Magnetic Resonance Imaging (MRI)	Baseline and at 5 years
Cancer outcomes	Electronic Health Record (EHR)	Annually

## What genetic and environmental factors are associated with non-syndromic cancers in patients younger than 40?

**Use Case ID** 1001199

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Tobacco smoking	PPI Survey (AOURP)	Baseline
Genotyping data	Whole Genome Genotyping (WGG)	Baseline
Pesticides exposure assessment results	Blood draw	Baseline
Heavy Metal Panel results	Blood draw	Baseline
Diet, self-assessment	PPI Survey (AOURP)	Baseline

## How does (short-term) physical activity and/or (long-term) physical fitness affect recovery from cancer treatment?

**Use Case ID** 1001237

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

There is variability in the speed and extent to which patients recover from cancer treatments. This is intended to discern whether patients with higher fitness recover better/faster and whether becoming more active in the short term improves recovery.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Electronic Health Record (EHR)	Pre- and post-treatment
Urinary tract infection (UTI) diagnosis	Clinical assessment	Pre- and post-treatment
Inflammation disorder diagnosis	Clinical assessment	Pre- and post-treatment
Sleep disorder information	Clinical assessment	Pre- and post-treatment
Radiation-related disease	Clinical assessment	Pre- and post-treatment
Ability to perform activities of daily life (ADL) assessment results	Clinical assessment	Pre- and post-treatment
Cardiopulmonary assessment	Clinical assessment	Pre- and post-treatment
Health care participation	Electronic Health Record (EHR)	Pre- and post-treatment
Treatment/Therapy	Electronic Health Record (EHR)	Pre- and post-treatment

## Does the performance of breast cancer screening depend on underlying breast cancer risk?

**Use Case ID** 1001239

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Breast cancer can be better stratified to identify which individuals might be best served with higher and lower screening frequencies and different screening modalities (mammography, tomosynthesis, and breast MRI). An observational study is needed to investigate multiple parameters of risk relative to the performance of breast cancer screening.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually for 5 years
Outcomes	Electronic Health Record (EHR)	Annually for 5 years
Family clinical outcomes	Electronic Health Record (EHR)	Annually for 5 years
Breast cancer screening information	Electronic Health Record (EHR)	Annually for 5 years
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline

## Among participants who develop cancer in adulthood, do survivors of pediatric cancer exhibit increased resistance to treatment and/or increased mortality?

**Use Case ID** 1001241

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Pediatric cancer post-treatment: resistance, early onset, mortality.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Exomic Sequencing (WES)	Baseline
Microbiome sample	Whole Genome Genotyping (WGG)	Pre- and post-treatment
Genotyping data		Pre- and post-treatment
Mental and psychosocial health, self-assessment	Patient-reported outcome	Daily
Cancer outcomes	Electronic Health Record (EHR)	Annually

## Can we define and validate a comprehensive risk profile for major cancer types and assess how an individual's risk changes over the lifetime?

**Use Case ID** 1001253

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

To understand the distribution of future cancer risk in All of Us and to elucidate the determinants of cancer risk for the major forms of cancer controlling for those factors. It is necessary to collect information about all the known risk factors for the major cancers. Change in these risk factors is essential, because risk changes with changes in behaviors and exposures.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Geospatial tracking	Annually
Risk factors, self-assessment	Survey	Annually
Cancer outcomes	Electronic Health Record (EHR)	Annually
Risk factors, self-assessment		Continuous monitoring

## Among participants with metabolic dysfunction, what factors distinguish those who develop cancer from those who do not?

**Use Case ID** 1001254

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Diabetes, obesity, insulin resistance, sleep disturbances, and other components of metabolic syndrome may increase risk for many cancers and influence outcomes following treatment. Understanding how these factors relate to cancer risk may be important for developing prevention strategies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Wearable electronics	Continuous monitoring
Biological Specimens	Clinical diagnostic test	Every 6 months
Diet, self-assessment	Smartwatch	Periodically
Clinical outcomes	Survey	Annually
Anthropometrics, whole body measurements	Clinical assessment	Annually
Prescription medication\treatment	Prescription drug records	Annually

## What is the association between newer-generation oral contraceptives and cancer risk?

**Use Case ID** 191851

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

Prior research studies have found that oral contraceptive (OC) use is associated with decreased risks of several cancers, and current use increases risk for breast cancer. However, most of these studies have been limited to women who used early-generation OCs, which contained higher estrogen concentrations and androgenic progestins compared to drugs used today. Although research suggests that newer drugs are still associated with early breast cancer risk, their influence on other cancers is largely unexplored. Differences in hormone formulations among the newer-generation OCs and their effects on cancer have also not yet been explored.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Hormonal contraceptive use	Survey	Baseline
Prescription medication\treatment	Survey	Every 3 years
Prescription medication\treatment	Electronic Health Record (EHR)	
Cancer information	Electronic Health Record (EHR)	

## What factors can help identify breast and prostate cancers that do not require aggressive treatment?

**Use Case ID** 192291

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

What factors can be looked at (e.g., markers, other tests) that could then be correlated with aggressiveness of a cancer?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer outcomes		
Sociodemographics		
Genomic analyses	Whole Genome Sequencing (WGS)	
Clinical outcomes		

## Among cancer patients who stop treatment after initially responding, what factors affect the time to recurrence?

**Use Case ID** 194348

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Cancer patients who have responded to therapy but then stopped therapy for various reasons (including side effects, cost, etc.) should be identified and then followed to determine if their cancer will reoccur. It will also be relevant to determine if the cancer again responds to therapy if the patients resume the treatment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes		Continuous monitoring
Clinical outcomes		At specified times anchored to the clinical event
Prescription medication\treatment	Electronic Health Record (EHR)	Continuous monitoring

## Among participants with rare diseases, including renal medullary carcinoma, what treatments lead to the best outcomes?

**Use Case ID** 194998

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

I have a cousin who is undergoing chemotherapy for renal medullary carcinoma, a cancer specific to patients with sickle cell. Aside from the fact that we need to discover a means of eradicating sickle cell from our planet, will the All of Us program be used to further research into the development of better treatment options for patients who develop this cancer? The pool of candidates is very small due to rarity of the incidence of the cancer.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Clinical diagnostic test	Continuous monitoring
Family clinical outcomes	Blood draw	Baseline
Perceived outcomes - patient	Whole Genome Sequencing (WGS)	
Sickle cell anemia diagnosis		
Renal medullary carcinoma diagnosis		

## What is the incidence and timing of thromboembolism after cancer diagnosis?

**Use Case ID** 196911

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Conduct research to understand the epidemiology of thromboembolism after cancer diagnosis and identify the contributing factors. Thromboembolism can cause treatment dilemma, as many anticancer treatments cause thrombocytopenia. Better understanding of the timing and risk factors can provide evidence-based management of cancer patients without the risks of life-threatening bleeding or thromboembolism. Possible risk factors include but are not limited to cancer type, anticancer therapy, and stress.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Prescription medication\treatment	Prescription drug records	At specified times anchored to the clinical event
Complete blood count (CBC)		At specified times anchored to the clinical event
Thromboembolism diagnosis	Clinical diagnostic test	At specified times anchored to the clinical event
Physical activity, self-assessment	Activity monitor	At specified times anchored to the clinical event

## Are microbial tumor characteristics predictive of cancer treatment effects and survival?

**Use Case ID** 197353

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Microbiota has been found in tumor tissues, and these communities are often found to differ from the neighboring healthy tissue. Current studies tend to be small and from single cancer centers. We propose collecting tumor samples for microbial analysis in conjunction with cancer treatment data to evaluate microbial characteristics that predict successful treatment. Comparisons can be made to evaluate microbial compositions that are associated with longer survival after cancer treatment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Microbiologic specimen evaluation	Tissue biopsy	At specified times anchored to the clinical event
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Cancer information	Electronic Health Record (EHR)	Continuous monitoring
Clinical outcomes	Death records	Continuous monitoring
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually

## Are participants with untreated pancreatitis at higher risk of developing pancreatic cancer?

**Use Case ID** 198524

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pancreatic cancer diagnosis	Electronic Health Record (EHR)	
Inflammation disorder diagnosis		

## Does the addition of nonselective beta-blockers to cancer therapy result in better treatment outcomes?

**Use Case ID** 198635

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Animal models are providing compelling evidence that activating the beta-adrenergic pathway (via stress) results in tumor growth and metastasis. Beta-blockers blunt this effect in animals. All of Us could design a randomized intervention trial to test this potential benefit in humans. An observational approach could also be taken with careful attention to pharmacoepidemiological principles and biases, such as confounding by indication.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information		
Cancer treatment/therapy		
Beta blocker use		
Clinical outcomes		
Sociodemographics		

## Can we develop and validate a risk model to guide treatment decisions for newly diagnosed prostate cancer?

**Use Case ID** 198659

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Although prostate cancer is the most common cancer among men in the U.S., many men have indolent tumors that are unlikely to cause death in a man's lifetime. Determining which prostate tumors are likely to lead to death is of critical clinical importance to prevent unnecessary treatment and unwanted side effects. Understanding factors related to disease etiology and progression and developing risk models are essential for personalized medicine and developing better treatment strategies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Electronic Health Record (EHR)	Annually
Cancer information	Pathology reports	Every 3 months
Prostate screening results	Electronic Health Record (EHR)	Annually
Genotyping data	Whole Genome Genotyping (WGG)	Baseline
Prostate-Specific Antigen (PSA) levels	Blood draw	At specified times anchored to the clinical event

## Does low-intensity physical activity reduce cancer risk?

**Use Case ID** 198704

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

We propose to investigate risk of developing cancer in a cohort of 100,000 All of Us participants using NCI's Activities Completed over Time in 24 Hours (ACT-24) recall system ([doi.org/10.1249/MSS.0000000000001428](https://doi.org/10.1249/MSS.0000000000001428)) and research-grade accelerometers. Cases of incident cancer will be captured via linkage to state cancer registries.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Activity monitor	Every 3 years
Physical activity, self-assessment	Activities Completed over Time in 24 Hours (ACT-24)	
Cancer information	Electronic Health Record (EHR)	Every 2 years

## How do changes in risk behaviors over long periods of time influence a person's lifetime cancer risk?

**Use Case ID** 1000737

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Other

Cancer develops over a long time period. Behavioral factors such as smoking, diet, and physical activity all contribute to risk and are correlated. Changes in these risk factors can influence risk profoundly. For example, stopping smoking reduces risk dramatically. To better understand known risk factors and study new ones, we need study participants who are willing and complete questionnaires frequently over years. This points to the need to understand study participants' motivations and what return of value the researchers can provide to keep study participants engaged long term and who are those who don't continue.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Motivation for research participation	PPI Survey (AOURP)	Every 2 years
Feelings about health research	PPI Survey (AOURP)	Every 2 years
Risk factors, self-assessment	PPI Survey (AOURP)	Every 6 months
Sociodemographics	PPI Survey (AOURP)	Baseline

## Are women with autoimmune diseases at decreased risk for cancer?

**Use Case ID** 1000782

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

Are women with autoimmune diseases at decreased risk for cancer? Do specific allergies correlate with immunotherapy efficacy?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lifestyle, self-assessment	PPI Survey (AOURP)	Baseline
Sociodemographics	PPI Survey (AOURP)	Baseline
Treatment/Therapy	Electronic Health Record (EHR)	Annually
Specified Biomarkers	Allergy testing	Every 4 years
Air quality assessment results		Continuous monitoring
Genomic analyses	Genomic testing	Baseline
Asthma diagnosis	PPI Survey (AOURP)	Annually

## Among participants who are actively being treated for cancer, what is the difference in severity of side effects between those who exercise and those who do not?

**Use Case ID** 1000884

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Exercise has demonstrated the benefits on the immune, neurologic, cardiovascular, metabolic, and musculoskeletal systems. There have been well-controlled RCTs documenting the efficacy of exercise to improve side effects during cancer treatment. However, the extent to which these benefits occur outside of an RCT is entirely unknown. This is a question of effectiveness.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Physical activity, self-assessment	Actigraphy	Continuous monitoring
Behavioral characteristics, self-assessment	Survey	Periodically
Physical activity, self-assessment	PPI Survey (AOURP)	Periodically
Cancer outcomes	Electronic Health Record (EHR)	Annually

## What is the optimal dose and type of exercise to reduce recurrence risk/increase survival after a cancer diagnosis?

**Use Case ID** 1000892

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Multiple mechanistic pathways have been proposed underlying the hypothesized role of exercise in reducing recurrence risk and increasing survival. Observational studies thus far have established a significant association of exercise and reduced recurrence and increased survival for a subset of hormonally related cancers. However, the relative contribution of modes of activity beyond aerobics and the optimal (minimally effective) dose for clinical impact remain to be elucidated.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	PPI Survey (AOURP)	Annually
Death	Death records	Annually
Relapse/recurrence	Biochemical assay	Annually
Relapse/recurrence	Imaging	Annually
Relapse/recurrence	Blood draw	Annually
Sensor data	Actigraphy	Annually
Sensor data	Activity monitor	Annually
Cancer outcomes	Electronic Health Record (EHR)	Annually

## What components of diet and nutrition correlate with positive treatment outcomes in cancer?

**Use Case ID** 1000957

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

Given that overall nutritional status can influence system(s) functional status, establish dietary components correlating positively with treatment outcomes. These components could then be used in pragmatic clinical (real-world) trials.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Per event
Diet, self-assessment	Food diary	Continuous monitoring
Health care cost	Survey	Periodically
Anthropometrics, whole body measurements	Electronic Health Record (EHR)	Periodically
Diseased, Missing, Filled Surface Score (DMFS)	Electronic Health Record (EHR)	Periodically
Bone density	Dual-energy X-ray Absorptiometry (DXA)	Periodically
Tumor characteristics	Clinical assessment	Periodically

## Can imaging be used to assess whether a cancer patient is responding to treatment early in the course of therapy?

**Use Case ID** 1001054

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Develop 4D precision imaging to assess the cancer treatment effectiveness and early responses.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer outcomes	Electronic Health Record (EHR)	Post-event or at least annually
Imaging	Electronic Health Record (EHR)	Post-event or at least annually

## Can data identify or predict the development of side effects or other health conditions during or post cancer treatment to provide therapeutic interventions?

Use Case ID 1001061

Cross-Cutting Theme Therapeutic and Preventive Interventions

Scientific Category Maintain & Preserve Health

The development of side effects can impact the preservation of health in cancer patients. Data collected on medical events or test procedures ordered can inform changes in health status of cancer patients/survivors.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Medical Information	Electronic Health Record (EHR)	Every 3 months
Prescription medication\ treatment	Electronic Health Record (EHR)	Every 3 months
Treatment data/specifics records	Electronic Health Record (EHR)	Every 3 months
Health care cost		Every 3 months
Patient-reported outcomes	Survey	Baseline and at event
Sleep assessments	Survey	Baseline and at event
Sleep assessments	Electronic monitoring/recording	Continuous monitoring
Weight	Survey	Baseline and at event
Weight	Electronic monitoring/recording	Continuous monitoring
Social determinants of health (SDH)	PPI Survey (AOURP)	Baseline and at event
Social determinants of health (SDH)	Electronic monitoring/recording	Periodically

## Among cancer patients, what psychosocial factors are most strongly associated with treatment adherence and outcomes?

Use Case ID 1001080

Cross-Cutting Theme Therapeutic and Preventive Interventions

Scientific Category Treat & Cure Disease

What psychosocial issues have the biggest impact on treatment adherence and outcomes?

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Cancer outcomes	Electronic Health Record (EHR)	Post-event or at least annually
Treatment data/specifics records	Electronic Health Record (EHR)	Post-event or at least annually
Psychological measures	Survey	Post-event or at least annually
Psychological measures	Electronic Health Record (EHR)	Post-event or at least annually
Adherence to treatment	Electronic Health Record (EHR)	Continuous monitoring
Adherence to treatment	Claims data	Continuous monitoring
Adherence to treatment	Mobile monitor	Continuous monitoring

# Cardiorespiratory and Blood

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## Does early lung function predict development of chronic obstructive pulmonary disease (COPD)?

**Use Case ID** 196851

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Population-based cohort study. Exposures: Smoking history, environmental exposure (home: cooking, environmental tobacco smoke, mold), geospatial pollution (PM 2.5, 10, etc.). Diet habits, DNA, family history, lung function measured over time (spirometry with and without bronchodilation), social determinants of health, and other sociodemographic characteristics. Collection of health symptoms and status (HRQoL, symptoms).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Chronic obstructive pulmonary disease (COPD) diagnosis	Spirometry	Annually
Behavioral characteristics, self-assessment	Survey	Annually
Health literacy	Survey	Annually
Depression diagnosis	PPI Survey (AOURP)	Annually
Diet, self-assessment	Food diary	Annually

## How do common environmental exposures impact cardiovascular (CV) outcomes?

**Use Case ID** 196871

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

We are constantly exposed to environmental exposures such as air pollution, allergens, and manmade chemicals. All of Us offers a unique opportunity to collect such exposures both passively (e.g., linking to local environmental data) and actively (e.g., using novel mHealth devices to measure new data from individual All of Us participants). These can be overlaid with behavioral, clinical, genomics, and biological data in All of Us to assess complex interplay and effects on cardiovascular and other health outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Air quality assessment results		
Allergens assessment results		

## Does adding environmental exposures at the primary residence to cardiovascular risk scores improve risk prediction?

**Use Case ID** 196906

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

The American College of Cardiology/American Heart Association Atherosclerotic Cardiovascular Disease risk score is a well-known and widely used risk score that provides 10-year risk estimates. However, this score does not account for environmental exposures as experienced at a person’s primary residence, many of which are strongly associated with cardiovascular disease. Using All of Us, we can evaluate whether measurements of environmental pollution at the home improve risk estimates.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results		Annually
Cardiopulmonary assessment	Electronic Health Record (EHR)	Annually
Residence location	PPI Survey (AOURP)	
Atherosclerotic Cardiovascular Disease (ASCVD) diagnosis	Electronic Health Record (EHR)	
Geocode data	Survey	

## In elderly with stable obstructive coronary disease, what factors predict long-term stability?

**Use Case ID** 196907

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Reduce Disease Impact

The number of elderly with heart disease is growing. All of Us can address key questions by following the clinical management and outcome of these patients—e.g., among elderly patients with recently diagnosed chronic stable obstructive coronary disease, what factors (comorbidity, genomics, socio/environmental, behavioral) predict long-term stability with medical management alone versus coronary revascularizations? And how does this vary by subgroups (race, sex, etc.)? Answers can inform future trials.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	
Prescription medication\treatment	Prescription drug records	
Angiogram	Angiography	
Cardiopulmonary assessment	Electronic Health Record (EHR)	

## What are the long-term pulmonary and cardiovascular consequences of premature birth from childhood into adulthood?

**Use Case ID** 197148

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

This study will enroll premature infants at the time of birth in order to follow the children in phases from birth to adulthood to test the central hypothesis that premature birth permanently impairs normal pulmonary and cardiovascular development, resulting in the development of common and rare cardiopulmonary conditions that reduce cardiopulmonary function throughout life. Phase I will study children from birth to 8 years of age, with subsequent phases to study older ages.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health and phenotype data	Electronic Health Record (EHR)	Annually
Blood pressure	Physical exam	Annually
Pulmonary assessment results	Clinical diagnostic test	
Ventricle function	Echocardiography	Every 2 years

## What factors promote and preserve ideal cardiovascular health across the lifespan?

**Use Case ID** 197392

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

Numerous studies have shown that cardiovascular health declines from childhood through adulthood. The preservation or promotion of ideal cardiovascular health is influenced by biological, environmental, and behavioral factors, including diet, physical activity, smoking status, body mass index, and biomedical indices such as blood glucose, blood pressure, and blood lipids.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Air quality assessment results		Annually
Diet, self-assessment	Biochemical assay	Annually
Behavioral characteristics, self-assessment	Survey	Upon enrollment and first obstetrical visit
Lipids panel results		Annually
Blood pressure		

## How do environmental chemicals influence comorbid chronic diseases?

**Use Case ID** 198500

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Two of the greatest public health challenges facing the U.S. today are obesity and asthma. These two comorbid conditions are also implicated in downstream disorders such as diabetes and CVD. There is evidence that environmental exposures contribute to a rapid increase in disease incidence. Using the All of Us cohort to understand how environmental exposures exacerbate the comorbidity between these conditions and subsequent disease progression will aid in developing intervention approaches for patients. \*\*\*

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Asthma diagnosis	Electronic Health Record (EHR)	Baseline
Obesity diagnosis	Electronic Health Record (EHR)	Annually
Diabetes diagnosis	Electronic Health Record (EHR)	Annually
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Air quality assessment results		Every 3 months

## How does environmental airborne exposures affect nasal symptoms and disease?

**Use Case ID** 198576

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Collect symptom diaries from individual across a range of exposures and correlate exposures with disease; determine if genetics, health characteristics, and demographic are associated with airway disease. Measure nasal inflammation and microbes in a subset of patients to determine mechanisms. Determine if genotype affects symptoms. Determine if there is an epigenetic signature of exposure in the nasal epithelium, and correlate that signature with symptoms and nasal inflammation.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Perceived outcomes - patient	Survey	Every 3 months
Clinical outcomes	Survey	At specified times anchored to the clinical event
Epigenomic/epigenetic markers	Genomic testing	Continuous monitoring
Air quality assessment results		

## What exposures impact the natural history of lung disease and its severity?

**Use Case ID** 198647

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

It is well known that the environment, behavior, and occupation play an important role in the development of lung diseases. We suggest tracking data on variables that can further elucidate these relationships, including detailed tobacco use histories (including products used), occupational exposures, and environmental exposures (including residential). This can help determine exposures that lead to development of fixed airway obstruction and are associated with increased severity of lung disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results		
Tobacco/Nicotine Use		
Lung disease information		
Clinical outcomes		

## What are the contributions of genetic, environmental, and dietary factors to peripheral atherosclerosis?

**Use Case ID** 198744

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Peripheral artery disease (PAD) affects about 13% of the population over 50 years of age and it is an important cause of morbidity and mortality. The ankle brachial index (ABI) is an inexpensive and noninvasive test used to screen for PAD, and an abnormal value is associated with increased cardiovascular events. Adding the collection of serial ABIs to the All of Us database will allow for numerous future studies aimed at defining the role of genetic and environmental factors in the development of PAD.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Blood pressure		
Genomic analyses	Whole Genome Genotyping (WGG)	
Diet, self-assessment	PPI Survey (AOURP)	
Lifestyle, self-assessment	PPI Survey (AOURP)	
Peripheral artery disease diagnosis		

## How do cleaning products at home and school impact development of asthma in children?

**Use Case ID** 198745

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

Description not provided.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Personal care product use	Survey	
Asthma attacks	Survey	
Asthma diagnosis		
Environmental samplings and exposure results		

## How does the home environment impact asthma development in children?

**Use Case ID** 198746

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

This study would look at aspects of the home environment, including cleaning products, address or block group for GIS mapping, proximity to roadways or certain agricultural or industrial facilities, pets, number of people living in the household, type of flooring, building structure, ventilation, type of heat, mold, and moisture level.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Asthma attacks		
Environmental samplings and exposure results	PPI Survey (AOURP)	
Air quality assessment results		
Geocode data		

## Does neighborhood-scale air quality affect the metabolome and health outcomes?

**Use Case ID** 198765

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Neighborhoods nominated for testing by underserved, understudied vulnerable persons with environmental injuries and illnesses, including toxicant-induced loss of tolerance (TILT), multiple chemical sensitivities, toxicant-induced encephalopathies, myalgic encephalomyelitis (ME), CFS, and asthma. Of particular concern on the neighborhood scale are pesticides and hydrophobic organic chemicals—especially those emitted in laundry exhaust—and their impact on the most vulnerable populations.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Air quality assessment results		
Environmental assessment results	Survey	
Metabolomic profile	Urine collection	
Residence location	PPI Survey (AOURP)	
Toxicant-induced loss of tolerance (TILT) diagnosis	Electronic Health Record (EHR)	

## Does real-time knowledge of air quality improve early detection of respiratory exacerbations?

**Use Case ID** 1001074

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Reduce Disease Impact

Can easily be A/B-tested with a mobile app.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Air quality assessment results		Daily
Asthma diagnosis	Electronic Health Record (EHR)	During clinic visits
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Annually
Access to health care	PPI Survey (AOURP)	Baseline
Air quality assessment results	Personal air pollution monitor	Daily

## Does access to green space correlate with heart, lung, blood, and sleep disease incidence?

**Use Case ID** 1001137

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Annually
Geocode data	Survey	Annually
Environmental assessment results	Survey	Annually
Location data	Wearable electronics	Annually
Behavioral characteristics, self-assessment	Survey	Ongoing
Physical activity, self-assessment	Wearable electronics	Ongoing
Physical activity, self-assessment	PPI Survey (AOURP)	Ongoing

## Does a person's environment influence the incidence or morbidity from respiratory and cardiovascular disease?

**Use Case ID** 1001243

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

The environmental determinants of most respiratory and cardiac diseases are largely understudied and unknown. Most data have focused on ambient or traffic-related air pollution exposure. After-exposures may contribute not just to respiratory and CVD but to many other diseases. They may also impact response to treatment. Examples of types of exposures: ambient air pollution; microbial; light; noise; toxicants inhaled, ingested, absorbed through skin, etc.; social interactions, proximity to pollution sources.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Location data	Global Positioning System (GPS) monitoring	Continuous monitoring
Cardiac outcomes	Electronic Health Record (EHR)	Annually
Lung disorders outcomes	Electronic Health Record (EHR)	Annually
Omics	Blood draw	Annually *GC
Occupational exposures assessment results	Occupational Exposure Matrix (OEM)	Annually

## Among asthma patients, what genes are associated with hypersensitivity to inhaled corticosteroids?

**Use Case ID** 192290      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Treat & Cure Disease

1) Bin asthma patients for hypersensitivity to inhaled corticosteroids (hypersensitivity: “dose-dependent slow but steady strangulation”). Improvement may be determined simultaneously, allowing complete characterization of response to treatment, according to drug, dosage, duration of treatment, etc. While this study is limited to inhaled corticosteroids, other drug treatments may be performed similarly. 2) Determine genetic differences: genes, alleles, expression, epigenetic status. 3) Correlate.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Asthma attacks		
Asthma treatment record		
Genomic analyses		
Epigenomic/epigenetic markers		
Side effects of prescription medication		

## Among participants with confirmed pollen allergy, what environmental exposures impact the incidence of asthma attacks?

**Use Case ID** 192317      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

A cohort of asthma patients (who believe they have a pollen allergy) would undergo genetic testing to identify genetic markers. Those patients would undergo blood and skin allergy testing to confirm the allergy, and then the patients would utilize a mobile monitor to track the weather and environmental exposures (especially pollen) that are causal to asthma incidences. With a more complete picture of pollen allergen impacts on patients, they would be able to limit the negative health outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Mobile monitor	Continuous monitoring
Asthma attacks		At specified times anchored to the clinical event
Allergies diagnoses	Skin allergy test	Baseline
Genotyping data	Whole Exomic Sequencing (WES)	Continuously for 1 week duration at 1 month, 6 months, and 1 year

## Using the AOURP longitudinal cohort, can a set of risk factors be identified creating a unified theory of atherosclerosis?

**Use Case ID** 195042

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Cardiovascular diseases, collectively the most common cause of death, disability, and health care expenditures in North America and Europe, are recognized as complex genetic and environmental phenotypes. While they can and traditionally have been studied individually, we believe that there are unified mediators of vascular injury and dysregulation. A “unified coronary arterial atherosclerosis theory” would better explain many of the associations that are regularly encountered.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes	Natural language processing of notes	Include child, teenager, early adult, adult, elderly
Genomic analyses	Blood draw	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Upon enrollment and first obstetrical visit
Cell-free nucleic acids levels	Blood draw	
Atherosclerotic Cardiovascular Disease (ASCVD) diagnosis		

## What are the genetic, comorbid risk factors and anticancer agents that contribute to heart failure after cancer therapy?

**Use Case ID** 196492

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Maintain & Preserve Health

Goals: To study the epidemiology of cardiovascular complications of cancer therapy in order to design prevention strategy and precision treatment of cancer patients while minimizing debilitating cardiovascular complications. Methods: Compare data on genetic, comorbid risk factors and anticancer agents used in association with cardiovascular complications after cancer therapy. Expected outcomes: This study will provide much-needed data on cardiovascular toxicity of anticancer agents.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Prescription medication\treatment	Prescription drug records	Continuous monitoring
Cardiovascular disease information	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Cardiopulmonary assessment	Clinical diagnostic test	At specified times anchored to the clinical event
Brain Natriuretic Protein (BNP) levels	Blood draw	At specified times anchored to the clinical event

## What individual differences in genes, environment, and lifestyles result in developing chronic obstructive pulmonary disease?

**Use Case ID** 196841

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

Use baseline data from individuals who do not have lung disease based on patient-reported physician diagnosis and electronic health records. In a random sample, obtain spirometry to confirm the absence of airflow limitation. We know there is some underdiagnosis, so this random sample will provide an estimate of the prevalence of underdiagnosis in the All of Us study and will identify groups more likely to have underdiagnosis.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Chronic obstructive pulmonary disease (COPD) diagnosis	Spirometry	Every 3 years
Tobacco smoking	PPI Survey (AOURP)	Annually
Physical measurements	Computed Tomography (CT) scan	
Occupation	PPI Survey (AOURP)	Annually
Genomic analyses		

## What are the molecular factors of heightened sensitivity to air pollution?

**Use Case ID** 196858

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Defining heightened sensitivity as an increased hazard ratio for an association between air pollution and a health outcome, identify subsets of the population based on molecular factors (e.g., genetic variants), hypermethylated regions, which are at increased risk of adverse cardiovascular or pulmonary events during high air pollution days.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results		
Residence location	PPI Survey (AOURP)	
Genomic analyses	DNA methylation array	
Clinical outcomes	International Classification of Diseases (ICD) usage data	

## What are the molecular subtypes of hypertension?

**Use Case ID** 196861

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Hypertension is a very common chronic disease that significantly increases risk of stroke and myocardial infarction. Though its clinical definition is simply based on blood pressure, its molecular etiology is quite complex and poorly understood. This project would seek to identify genetic, epigenetic (DNA methylation), and metabolomic “subtypes” of hypertension both in isolation and as clusters. These subtypes may be more etiologically homogeneous and help us better understand hypertension.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Genotyping (WGG)	Baseline
Epigenomic/epigenetic markers	DNA methylation array	Every 3 years
Metabolomic profile		
Clinical outcomes	International Classification of Diseases (ICD) usage data	
Prescription medication\ treatment	Prescription drug records	

## Can we develop more accurate and clinically relevant su-classification and phenotyping of heart failure?

**Use Case ID** 197140

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Treat & Cure Disease

Heart failure (HF), though relatively common in U.S. adults, can be thought of as a syndrome with many subtypes that require different treatments. All of Us provides a rich platform on which to collect more data (e.g., novel biomarkers and imaging studies) on HF patients. This, coupled with All of Us’ existing rich genomics, behavioral, and clinical data, can be analyzed to refine the phenotyping and sub-classification of heart failure, thereby informing future precision medicine trials in HF.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cardiac outcomes	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Brain Natriuretic Protein (BNP) levels	Blood draw	At specified times anchored to the clinical event
Genomic analyses	Blood draw	At specified times anchored to the clinical event
Cardiac outcomes	Echocardiography	

## What are the long-term cardiovascular effects of cancer therapy? Do childhood cancer survivors have reduced cardiac functions?

**Use Case ID** 197154

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Maintain & Preserve Health

To study adult cancer survivors who received cancer therapy during childhood. What are their cardiovascular functions compared to adults who did not receive cancer therapy? Reduction of cardiovascular functions after anticancer therapy may take years to develop. These undesirable complications can compromise quality of life or shorten life spans. This study will provide evidence-based guidelines for physicians to choose anticancer agents/protocols with better long-term outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Electronic Health Record (EHR)	Baseline
Prescription medication\treatment	Electronic Health Record (EHR)	Baseline
Cardiopulmonary assessment	Clinical diagnostic test	At specified times anchored to the clinical event
Cardiovascular disease information	Electronic Health Record (EHR)	Baseline
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline

## What are clinical characteristics and biomarkers that identify patients with chronic obstructive pulmonary disease (COPD) who are at high risk for disease progression?

**Use Case ID** 197155

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Disease progression should be characterized by COPD exacerbations or hospitalizations for respiratory insufficiency. It can also be characterized by changes in spirometry or chest radiographic (CT) evidence of progressive emphysema and/or airway inflammation. These characteristics should be correlated with smoking history, environmental exposures, pulmonary function, radiographic markers of disease, plasma protein biomarkers, RNA-Seq, and genomics.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Specified Biomarkers		
Chronic obstructive pulmonary disease (COPD) diagnosis	Electronic Health Record (EHR)	
Airway inflammation	Spirometry	
Airway inflammation	Computed Tomography (CT) scan	
Environmental samplings and exposure results		

## What are the genetic, epigenetic, and microbiome contributions to hypertension?

**Use Case ID** 198154

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

The goal would be to enhance our understanding of how social and environmental exposures, genomic factors, and gut microbiota interact to influence hypertension susceptibility and phenotype. This would require integrated analyses of genomic and other omics data, exposures, and phenotype data and could lead to insights that enable more targeted prevention and treatment. Inherent in this would be discovery of pathways that contribute to disparities in hypertension onset or treatment response.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Hypertension outcomes	Electronic Health Record (EHR)	
Genomic analyses	Blood draw	
Epigenomic/epigenetic markers	Blood draw	
Microbiome sample	Stool sample	
Sociodemographics	PPI Survey (AOURP)	

## What is the prevalence of hereditary hemochromatosis in the U.S. population?

**Use Case ID** 198338

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

Looking for the hereditary hemochromatosis gene (carriers, or people who have this recessive disease) in DNA sequencing and blood tests: testing ferritin, transferrin saturation, TIBC, and iron levels in patient blood labs; testing liver function in patient blood labs; testing chemical panel with glucose in patient blood labs; testing CBC in patient blood labs; and testing lipid panel (cholesterol, triglycerides, HDL, and LDL) in patient blood labs.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Whole Genome Genotyping (WGG)	Continuous monitoring
Genomic sequence data	Whole Exomic Sequencing (WES)	Continuous monitoring
Self-reported ancestry	Physical exam	Include child, teenager, early adult, adult, elderly
Genomic sequence data	Whole Genome Sequencing (WGS)	Continuous monitoring

## Can a vascular aging timeline be used to accurately predict cardiovascular events?

**Use Case ID** 198344

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Heart attack and stroke lead to more than half a million deaths in the United States annually. It is now possible to predict these cardiovascular events well in advance by using a number of biomarkers related to vascular structure and function. Collecting such noninvasive biomarkers as part of the All of Us cohort will allow us to fine-tune this timeline prediction.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
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## How do environmental exposures, behavior, and genetics, in combination, influence risk of atherosclerotic cardiovascular disease?

**Use Case ID** 198488

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Genetics can be the earlier risk predictor of common, heritable traits such as atherosclerotic cardiovascular disease (ASCVD). Longitudinal environmental exposures and behavioral practices subsequently modify risk. Uniform dense ascertainment of environmental exposures and behavior is feasible through wearable sensors. We and others are beginning to look at the comprehensive set of exposures that influence ASCVD risk.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Physical activity, self-assessment	Mobile monitor	Continuous monitoring
Genomic analyses	Whole Genome Genotyping (WGG)	
Sleep behavior assessment results	Mobile monitor	

## How do genetic and lifestyle factors contribute to cardiovascular diseases in adults with congenital heart disease?

**Use Case ID** 198603      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

An estimated 1.6 million American adults live with congenital heart disease (CHD), with this group growing at the rate of 40,000 to 50,000 people yearly. This sensitized population has a much higher risk of cardiovascular diseases. We will collect DNA samples and heart health data to detect how those factors contribute to their heart health. Identification of the risk factors will improve life quality and life span not only for people with CHD but also for the general population.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Mobile monitor	
Genomic sequence data	Whole Genome Sequencing (WGS)	
Lifestyle, self-assessment	PPI Survey (AOURP)	

## How do host genetics, metabolomic profile, and gut microbiome contribute to cardiovascular health?

**Use Case ID** 198611      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Elucidate Disease Mechanisms

The contribution of gut microbiome in the development of heart disease and its risk factors has significantly increased attention toward the connection between our gut and heart. Using systems biology approaches that combine genomic data, metabolomic profile with microbiota profile holds promise for developing a more integrated understanding of the relationship between microbes and their host, and to further our understanding of the pathogenesis and progression of cardiovascular diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Gut microbiome sample	Stool sample	*GC
Metabolomic profile	Clinical diagnostic test	
Genomic analyses		

## How do host genetics contribute to transfusion recipient health?

**Use Case ID** 198689      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Transfusion outcomes		
Genomic analyses		

## Can genomic analysis of diverse communities for familial hypercholesterolemia reduce disease impact of sudden cardiac events?

**Use Case ID** 1000709

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Reduce Disease Impact

See above. Could also include additional metrics for expansion (mediators/moderators).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually
Behavioral characteristics, self-assessment	Survey	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Specified Biomarkers	Blood draw	Annually
Stress	Survey	Annually
Discrimination encounters	Survey	Annually
C-Reactive Protein (CRP) levels	Blood draw	Annually
Inflammation disorder diagnosis	Blood draw	Annually
Hypercholesterolemia outcomes	Electronic Health Record (EHR)	Annually

## Is there a better risk predictor of chronic obstructive pulmonary disease (COPD) than what we have today?

**Use Case ID** 1000728

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Longitudinal study.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Whole genome sequence (WGS) data	Whole Genome Sequencing (WGS)	Baseline
Tobacco smoking	PPI Survey (AOURP)	Annually
Location data	Survey	Annually
Chronic obstructive pulmonary disease (COPD) diagnosis	International Classification of Diseases (ICD) usage data	Annually
Clinical outcomes	International Classification of Diseases (ICD) usage data	Annually

## Can acute cardiopulmonary events be predicted by changes in gut biome?

**Use Case ID** 1000744      **Cross-Cutting Theme** Genomics and Other Omics

**Most Important**      **Scientific Category** Assess Risk

Assess risk.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Microbiome sample	Stool sample	Every 6 months
Microbiome sample	Saliva	Every 6 months *GC
Cardiovascular event	International Classification of Diseases (ICD) usage data	Every 6 months

## What is the penetrance of variants for arrhythmia?

**Use Case ID** 1000762      **Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

This study can be applied to many diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Family clinical outcomes	PPI Survey (AOURP)	Annually
Genomic sequence data	Genomic testing	Baseline
Cardiovascular event	Electronic Health Record (EHR)	Annually

## What are the functional consequences of genetic variation in genes for known monogenic heart, lung, and blood disorders?

**Use Case ID** 1000778      **Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

There is a need to understand the functional consequences of variation across the genome. Cell lines in All of Us would provide an important resource for these studies, and for “in the future” potential therapeutics. This resource would be broadly applicable to all disease phenotypes. This also addresses important issues relevant to the relative dearth of genetic studies in underrepresented minorities.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health and phenotype data	Electronic Health Record (EHR)	
Health and phenotype data	Patient-reported outcome	
Family clinical outcomes	Electronic Health Record (EHR)	Baseline
Genotyping data	Genomic testing	Baseline
Genotyping data		
Cardiopulmonary assessment	Electronic Health Record (EHR)	Annually

## Can genomic analyses improve risk prediction and prevention of cardiac disease?

**Use Case ID** 1000838

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Lipids panel results	Blood draw	Periodically
Blood pressure	Blood pressure cuff	Periodically
Coronary Artery Disease (CAD) diagnosis	International Classification of Diseases (ICD) useage data	Annually
Weight	Physical exam	Periodically
Tobacco smoking	PPI Survey (AOURP)	Periodically
Cardiac outcomes	Electronic Health Record (EHR)	Annually

## Which variants of unknown significance (VUS) are common in the community and yet are not pathologic for inherited cardiac or pulmonary diseases such as primary ciliary dyskinesia (PCD)?

**Use Case ID** 1000969

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

This would look at the general population who do not have the inherited heart or lung diseases. There is no other data set of this size to rule out pathology of VUS.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Annually
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Pulmonary assessment results	Spirometry	Annually
Cardiopulmonary assessment	Electronic Health Record (EHR)	Annually

## What are the molecular mechanisms that underlie heterogeneity of bleeding risk while on anticoagulation medications?

**Use Case ID** 1000999

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

The underlying mechanisms of why some individuals bleed on prescription and OTC anticoagulation/antiplatelet meds is poorly understood.

<i><b>Datatype</b></i>	<i><b>Method</b></i>	<i><b>Specification</b></i>
Health and phenotype data	Electronic Health Record (EHR)	
Health and phenotype data	Patient-reported outcome	
Health and phenotype data	Pharmacy records	
Genotyping data	Whole Genome Sequencing (WGS)	
Epigenomic/epigenetic markers		
Proteomic profile		
Electrocardiogram (ECG/EKG) tracings	Wearable electronics	
Microbiome sample		
Health and phenotype data	Survey	

## What are the molecular mechanisms that mediate resiliency to the development of atherosclerosis?

**Use Case ID** 1001060

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

There are individuals who have a large burden of cardiovascular risk factors but who do not develop atherosclerotic diseases; the molecular mechanisms (genetic, epigenetic, microbiome, metabolic) are poorly understood. This concept is applicable to other diseases, but mechanisms may be different.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	Electronic Health Record (EHR)	
Sociodemographics	Patient-reported outcome	
Risk factors, self-assessment	Patient-reported outcome	
Risk factors, self-assessment	Electronic Health Record (EHR)	
Cardiopulmonary assessment	Patient-reported outcome	
Cardiopulmonary assessment	Electronic Health Record (EHR)	
	Patient-reported outcome	
	Electronic Health Record (EHR)	
Health behavior	Patient-reported outcome	
Health behavior	Electronic Health Record (EHR)	
Blood pressure	Patient-reported outcome	
Blood pressure	Electronic Health Record (EHR)	
Physical measurements	Patient-reported outcome	
Physical measurements	Electronic Health Record (EHR)	
Carotid Intima-media thickness (IMT) measurements	Electronic Health Record (EHR)	
Carotid Intima-media thickness (IMT) measurements	Echocardiography	
Omics	Whole Genome Sequencing (WGS)	Periodically
Methylation status		Periodically
Epigenomic/epigenetic markers		Periodically
Omics	RNA sequencing	
Metabolomic profile		
Proteomic profile		
Microbiome sample		
Antibody titres		
Socioeconomic Status (SES)		
Diet, self-assessment		
Physical activity, self-assessment	Global Positioning System (GPS) monitoring	
Neighborhood characteristics	Geographic information system (GIS) code	

## Are metabolomic or proteomic biomarkers from nontraditional matrices (hair, nails, etc.) better predictive markers of cardiovascular disease?

**Use Case ID** 1001106

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Matrices are more cumulative over time. Big data analysis and storage.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Metabolomic profile	Hair and nail clippings collection	Baseline
Proteomic profile	Hair and nail clippings collection	Baseline
Cardiovascular disease information	Electronic Health Record (EHR)	Annually

## Can we identify biologic mechanisms using comprehensive omic profiling and single-cell profiling in discarded clinical specimens?

**Use Case ID** 1001170

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Discarded clinical specimens coupled with advances in genomics/omics afford us an opportunity to study molecular mechanisms of atherosclerosis (and other diseases) and to understand molecular heterogeneity at a tissue level.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	RNA sequencing	
Metabolomic profile		
Physical measurements	Electronic Health Record (EHR)	
Sociodemographics	Patient-reported outcome	
Clinical outcomes	Patient-reported outcome	
Metabolomic profile		
Proteomic profile		

## Does heart catheterization provide a better long-term outcome?

**Use Case ID** 195595

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Detect Disease

Every year, more than 1 million heart catheterizations are performed in the United States alone. This study would aim to find if these procedures truly benefit the patient or if they are unnecessarily performed. In order to get accurate results, the study would need to take place over a 3- to 5-year time frame, comparing those who had the procedure and those who elected to forgo. The study would monitor the subjects' cardiac-related hospitalizations and whether recatheterization is required.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cardiovascular disease information	PPI Survey (AOURP)	Baseline
Heart catheterization	Survey	Annually
Cardiac-related hospitalization	Survey	Every 3 months
Perceived outcomes - patient	Survey	Baseline and annually
Perceived outcomes - surgeon	Survey	Baseline and annually

## What are the health care provider perceptions of high blood pressure screening for asymptomatic African-American teens?

**Use Case ID** 197004

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Detect Disease

Methods and tools used to determine a baseline blood pressure for African-American teens and to determine treatment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Blood pressure	Electronic Health Record (EHR)	Continuous monitoring
Self-reported ancestry	Electronic Health Record (EHR)	Continuous monitoring

## Identify and create a cohort of heart failure patients within All of Us to enable discovery and clinical research.

**Use Case ID** 197137

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Prevalence of heart failure (HF) in the U.S. has risen to ~6.1 million among those  $\geq 20$  years of age. All of Us provides a rich platform to identify HF patients through EHRs (including clinical laboratory and imaging reports) and claims data. The ability to follow and collect data prospectively in the patients, including ancillary studies of more surveys and imaging/biomarker collections, could advance discovery science and address several clinically relevant questions in different HF patient subgroups.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cardiopulmonary assessment	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Brain Natriuretic Protein (BNP) levels	Blood draw	
Cardiopulmonary assessment	Echocardiography	At specified times anchored to the clinical event
Clinical outcomes	Electronic Health Record (EHR)	

## What is the impact of treatment guidelines on patient outcomes?

**Use Case ID** 198642

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

There are guidelines/practice parameters for the treatment of lung diseases, and these evidence-based documents are updated regularly. However, it is unclear whether these guidelines are employed by practitioners and if so, what effects they have on patient care and outcomes. By collecting patient-reported information on their lung diseases, symptoms of their diseases, and treatments, it should be possible to determine how well these guidelines are followed and their impact on patient outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lung disease information		
Perceived outcomes - patient	Survey	
Treatment/Therapy		

## How can digital images be collected to assist with disease tracking and analysis?

**Use Case ID** 198648

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Detect Disease

Key to making this database even more useful to future researchers would be to determine how to make raw DICOM image files available for future analysis. This would allow CT images to be used to enhance the understanding of the development of lung and other diseases in future research.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Imaging	

## Should simple spirometry be the fifth vital sign in the elderly?

**Use Case ID** 198687

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

Both COPD and interstitial lung diseases (ILDs) such as interstitial pulmonary fibrosis (IPF) are diseases of aging and more common in the elderly. For these reasons, lung function should be obtained in the elderly at every visit. Research question: Does simple spirometry help us identify patients with lung disease early in the course of their disease?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pulmonary assessment results	Spirometry	Annually
Pulmonary assessment results	Survey	Annually
Chronic obstructive pulmonary disease (COPD) diagnosis	Electronic Health Record (EHR)	
Interstitial lung disease diagnoses	Electronic Health Record (EHR)	

## What factors contribute to the disparate respiratory and cardiovascular outcomes of infants born prematurely?

**Use Case ID** 198690

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Infants born at <28 weeks of gestation who survive can experience long-term impacts from subtle abnormalities in respiratory function to profound disability including asthma, early COPD, or long-term dependence on mechanical ventilation. It is unclear how maternal environmental exposures, geographic differences, social factors, or genetic predisposition in the pre-conceptional period or during pregnancy might contribute to this disparity in outcomes for premature infants.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pulmonary assessment results	Spirometry	Annually
Pulmonary assessment results	Survey	Annually
Genomic analyses	Blood draw	
Environmental samplings and exposure results	PPI Survey (AOURP)	
Sociodemographics	PPI Survey (AOURP)	

## Should intensive care unit (ICU) survivors of acute respiratory failure be routinely screened for post-intensive care syndrome?

**Use Case ID** 198700

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Detect Disease

Post-intensive care syndrome (PICS) is a series of health problems that occur in survivors of critical illness, such as acute respiratory failure requiring mechanical ventilation. However, patients are not routinely screened for PICS; after patients leave the ICU, physicians often are not aware of PICS and how it may affect patients and their recovery and return to function. Would routine screening for PICS and education of primary care providers lead to improvement in outcomes for PICS after hospital discharge?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Post-Intensive Care Syndrome (PICS) diagnosis	Survey	At specified times anchored to the clinical event
Post-Intensive Care Syndrome (PICS) diagnosis	Electronic Health Record (EHR)	At specified times anchored to the clinical event

## What is the impact of social determinants of health on blood pressure in diverse populations?

**Use Case ID** 1000878

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Stress	Survey	Annually
Socioeconomic Status (SES)	PPI Survey (AOURP)	Annually
Discrimination encounters	Survey	Annually
Mood patterns	Survey	Annually
Environment	Survey	Annually
Genomic analyses	DNA methylation array	Annually
Blood pressure	Blood pressure cuff	Annually
Body Mass Index (BMI)	Patient-reported outcome	Annually
Body Mass Index (BMI)	Electronic Health Record (EHR)	Annually
Genotyping data		
Geocode data	Geographic information system (GIS) code	Annually
Neighborhood characteristics	Geographic information system (GIS) code	Annually

## What are the factors that explain known gender differences in prevention of chronic obstructive pulmonary disease (COPD) in people with similar measures of lung function?

**Use Case ID** 1000963

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

Presentation includes symptoms, health care use, measures of lung function have different relationships to presentation in women than men. Health care provider social roles, access issues may all contribute.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pulmonary assessment results	Spirometry	Periodically
Blood gas levels	Clinical diagnostic test	
Body Mass Index (BMI)	Anthropometry	
Vision assessment results	Imaging	
Health care participation	Electronic Health Record (EHR)	
Health care participation	Patient-reported outcome	
Health care participation	Prescription drug records	
Clinical outcomes	Patient-reported outcome	
Clinical outcomes	Prescription drug records	
Trust in health care	Patient-reported outcome	
Trust in health care	Insurance records	
Trust in health care	Social network mining	
Pulmonary assessment results	Patient-reported outcome	
Pulmonary assessment results	Wearable electronics	
Pulmonary assessment results	Spirometry	
Health care participation	Social network mining	

## What factors contribute to the elevated risk for heart, lung, blood, and sleep conditions in rural communities?

**Use Case ID** 1001067

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Annually
Geocode data	Survey	Annually
Socioeconomic Status (SES)	PPI Survey (AOURP)	Annually
Geocode data	Electronic Health Record (EHR)	Annually
Specified Biomarkers	Genomic testing	Baseline
Environmental assessment results	Survey	Annually
Social networking use	Survey	Annually

## How can the understanding of “risk” be improved to drive behavioral modification and improved outcomes?

**Use Case ID** 1001104

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Current risk scoring tools have been developed without the benefit of genomics and cohort diversity available as part of All of Us. We propose developing a suite of improved health/risk scores, with emphasis on implementation by health care providers to better assess risk and encourage behavioral modification.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Genomic testing	
Clinical outcomes	Electronic Health Record (EHR)	
Prescription medication\treatment	Electronic Health Record (EHR)	
Risk factors, self-assessment		
Environment	Environmental Protection Agency (EPA) data	

## Can identifying and addressing barriers to early disease detection in disadvantaged socioeconomic populations decrease disease disparities?

**Use Case ID** 1001120

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Detect Disease

To include literacy level, rurality, social isolation (family, if elderly), and insurance.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cardiovascular disease information	Physical exam	Annually
Patient-reported outcomes	Patient-Reported Outcomes Measurement Information System (PROMIS)	Annually
Major Adverse Cardiovascular Events (MACE) diagnosis	National Death Index	Annually
Death	National Death Index	Annually
Credit score	Survey	Annually
Media use	Survey	Annually
Housing quality variables	Survey	Annually
Food security status	Survey	Annually
Diet, self-assessment	PPI Survey (AOURP)	Annually
Cardiovascular disease information	Electronic Health Record (EHR)	Annually
Cardiovascular disease information	PPI Survey (AOURP)	Annually
Major Adverse Cardiovascular Events (MACE) diagnosis	Electronic Health Record (EHR)	Annually
Death	Death records	Annually

## What are the causes and characteristics of sudden cardiac death among the general population?

**Use Case ID** 190195      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Scientific Category** Assess Risk

Sudden cardiac death (SCD) affects ~300,000 Americans annually. The majority of these deaths do not occur in those at high risk for SCD, but rather in the general population, where most are not known to have heart disease at the time of the event. A critical obstacle for study of risk stratification and prevention of SCD is the need for a very large cohort with comprehensive surveillance and a uniform definition of SCD that does not rely solely on death certificates, which may be inaccurate.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Sudden Cardiac Arrest (SCA) diagnosis	Electronic Health Record (EHR)	

## Can new insights into predicting cardiovascular disease be gained from combining genomic analysis and electrocardiography (ECG)?

**Use Case ID** 194974      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Scientific Category** Assess Risk

Electrocardiogram (ECG) is the most commonly used test to check on heart health and screen for heart disease. Medical standard 12-lead ECG holds a lot of information about the heart, which—together with genomic data—have the potential to predict which patients will develop coronary heart disease, myocardial infarction (MI), arrhythmia, stroke, and sudden cardiac death. With 1 million people’s ECG and genomic data, together with AI technology, it will be extremely powerful for cardiac health.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Echocardiograms	Echocardiography	Every 3 years
Genomic analyses		
Coronary Heart Disease (CHD) diagnosis		

## How many people in the U.S. have lymphedema, and are health care professionals diagnosing it?

**Use Case ID** 197558      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Scientific Category** Reduce Disease Impact

Lymphedema is underdiagnosed and underrecognized and can lead to recurrent bouts of cellulitis with hospitalizations, decreased functional abilities, chronic wounds, and diminished quality of life. Self-assessment of edema and quality-of-life surveys could be compared to the number of diagnoses made by health care professionals practicing in the same locations. This may help steer targeted educational campaigns aimed at early identification and training in treatment approaches.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lymphedema diagnosis	Survey	Annually
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Claims data	Annually
Quality of life	Survey	*GC
Lymphedema diagnosis	Electronic Health Record (EHR)	

## Can we create an image repository for scans performed as part of standard of care: chest CT scans, cardiac CT scans, echocardiograms?

**Use Case ID** 1001200      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Most Important Scientific Category** Detect Disease

Archival of the scans themselves for immediate and future data mining by researchers.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Computer Aided Tomography (CT/CAT) images	Computed Tomography (CT) scan	During clinic visits
Echocardiograms	Electrocardiogram (ECG/EKG)	During clinic visits

## Could the Precision Medicine Initiative help identify people with cardiovascular disease?

**Use Case ID** 196890

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Assess Risk

We will use non-invasive wearable monitoring sensors, similar to a Band-Aid on the wrist, that measure arterial wave forms at the radial artery in the wrist, providing information on the elasticity and function of cardiovascular system. The information will be uploaded to smartphones and correlated with age and known cardiovascular risk factors, allowing us to develop computational models to rapidly identify people at risk for vascular disease, stroke, and heart failure.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cardiopulmonary assessment		
Cardiopulmonary assessment	Mobile monitor	
Lifestyle, self-assessment	PPI Survey (AOURP)	

## Can mobile technologies be used to successfully empower heart failure patients to self-monitor and participate in disease management?

**Use Case ID** 198573

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Reduce Disease Impact

Management of heart failure involves attention to salt/fluid intake, control of blood pressure, and daily weight monitoring. Physical activity has been shown to reduce hospitalizations in patients with reduced cardiac function, and it may also play a role in diastolic heart failure. Recording data on home-measured parameters and linking them to cardiac outcomes will provide information on optimal methods for use of mobile health and how it can help decrease cardiac events.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Blood pressure	Clinical diagnostic test	
Cardiac outcomes	Electronic Health Record (EHR)	
Cardiac outcomes	Mobile monitor	

## Should routine screening of high-risk patients for sleep apnea be carried out using home sleep testing?

**Use Case ID** 198698

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

Sleep apnea is an extremely common problem, but there remain significant barriers to accessing care. Recent advances permit sleep testing in the home with monitors that can be mailed and remotely monitored PAP machines. Would use of annual home sleep testing and telemedicine in adults with BMI >35 enhance access to care, afford early detection and treatment of sleep apnea, and permit investigations into its heterogeneous causes and manifestations?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sleep quality assessment results	Survey	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually
Sleep quality assessment results	Activity monitor	Continuous monitoring
Sleep apnea diagnosis	Electronic Health Record (EHR)	

## Can mobile health technology monitor and track spirometry and detect acute decompensation in childhood asthma?

**Use Case ID** 198750

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

Acute exacerbation accounts for frequent and recurrent ER visits in children with asthma. Genetic susceptibility and interaction with factors such as infection/inflammation and exposure to environmental pollutants may contribute to acute decompensation. Predictive modeling using multiple data points, including genetic variants, environmental exposure, and self-monitored spirometry, may help with early detection and intervention, which will lead to reduced ER visits.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Blood draw	Baseline
Environmental samplings and exposure results	Personal air pollution monitor	Periodic (approximately biweekly)
Pulmonary assessment results	Mobile monitor	Periodic (approximately biweekly)
Allergens assessment results	Biochemical assay	Annually
Health care cost	Claims data	At specified times anchored to the clinical event

## How to accurately detect subclinical atrial fibrillation?

**Use Case ID** 1001188

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

Current mobile devices are not able to fully/accurately capture subclinical atrial fibrillation in the general population. Accurate detection is important so therapeutic and prevention measures (e.g., against embolic stroke) can be initiated.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Electrocardiogram (ECG/EKG) tracings	Mobile monitor	Continuous monitoring
Physical activity, self-assessment	Mobile monitor	Continuous monitoring
Physical activity, self-assessment	Patient-reported outcome	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Baseline and at event
Risk factors, self-assessment	Survey	Baseline and at event

## Can we identify factors that will allow better diagnosis and prediction of coagulation disorders?

**Use Case ID** 190200

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Undiagnosed hypocoagulation and unpredicted hypercoagulation contribute to considerable morbidity and mortality across the lifespan.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Outcomes	Electronic Health Record (EHR)	
Coagulation disorder diagnosis		
Coagulation disorder diagnosis		

## How does a woman's history of preeclampsia affect her future cardiovascular outcomes?

**Use Case ID** 192289

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

2 possible designs: 1) Enroll women diagnosed with preeclampsia (PEC) during current pregnancy and collect data (phenotype and biomarkers), follow up prospectively until cardiovascular events (acute coronary events, strokes, including cardiac surgery). 2) Ambidirectional design: enroll women with a PEC history now having cardiac surgery/cardiopulmonary bypass (CPB); collect biomarkers and clinical outcomes (phenotype after CPB) comparing CPB outcomes among women who had PEC versus those who did not.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes	Electronic Health Record (EHR)	
Cardiac outcomes		At specified times anchored to the clinical event
Cardiac outcomes		Continuous monitoring
Genomic analyses	Whole Exomic Sequencing (WES)	Baseline

## What genetic, dietary, environmental, and other factors are associated with sudden cardiac arrest?

**Use Case ID** 194465

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Each year sudden cardiac arrest (SCA) strikes >300,000 Americans, and ~90% die unless given CPR and/or an electric shock from an AED. While SCA is linked to some heart conditions, there is much to learn about the role of various genes, dietary factors, environmental toxins, some pharmaceuticals, and emotional stressors. It is recommended that a cohort of SCA survivors (with ICDs to prevent death) be included in the All of Us Program, since they often have recurrent SCA events.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sudden Cardiac Arrest (SCA) diagnosis	Electronic Health Record (EHR)	Every 3 months
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Diet, self-assessment	PPI Survey (AOURP)	Every 3 months
Environmental samplings and exposure results	PPI Survey (AOURP)	Every 3 months
Behavioral characteristics, self-assessment	Survey	Every 3 months

## What would you need to convince you to change your lifestyle if you learned that you have heart attack or stroke risk factors?

**Use Case ID** 194866

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Survey.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cardiac outcomes	Survey	Baseline
Lifestyle, self-assessment	PPI Survey (AOURP)	Baseline
Sociodemographics	PPI Survey (AOURP)	Baseline
Behavioral characteristics, self-assessment	Survey	Baseline
Lipids panel results	Electronic Health Record (EHR)	Baseline

## How can we increase the public's awareness of the signs of lung disease, with the goal of promoting earlier diagnosis and treatment?

**Use Case ID** 194931

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

Lung disease, particularly COPD, is the third largest killer among diseases in the United States, and fourth in the world. Nonetheless, the early signs of the diseases are subtle and slow to advance, leading to late diagnosis. Once diagnosed, there is a great reluctance to the lifestyle changes necessary to slow the advancement of the disorder. Smoking addiction, the stigma of smoking history, reluctance to show weakness and to be seen wearing a cannula, all contribute to the delay.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Patient education methods and content	Survey	
Clinical outcomes	Electronic Health Record (EHR)	
Chronic obstructive pulmonary disease (COPD) diagnosis	Electronic Health Record (EHR)	

## How does the pathobiology that underlies nonobstructive ischemic heart disease relate to the associated risks for acute coronary syndrome?

**Use Case ID** 196047

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

1. Genomic, proteomic, and metabolomic analyses of the NHLBI-sponsored WISE and other datasets to predict ACS, HF, etc. versus none subgroup. 2. Genomic, proteomic, and metabolomic analyses of the DoD-sponsored WARRIOR randomized controlled trial to predict responders versus non-responders.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Metabolic risk assessment result	Blood draw	Baseline and annually
Metabolomic profile	Blood draw	Baseline and annually
Proteomic profile	Blood draw	
Ischemic heart disease diagnosis		

## What hypertension medicine regimen is most effective in preventing common ancillary complications over time?

**Use Case ID** 196053

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Blood pressure and anti-hypertensive medication use will be collected at baseline through physical examination and medical history taking as well as from the EHR. Track blood pressure and changes in medication to examine different regimens and degrees of blood pressure control as predictors of vascular complications, while using continuing medical care to understand the role of potential comorbidities and medication effects, and leverage precision medicine approaches to hypertension treatment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Recreational drug use	Electronic Health Record (EHR)	During clinic visits
Blood pressure	Physical exam	During clinic visits
Clinical outcomes	International Classification of Diseases (ICD) usage data	At specified times anchored to the clinical event
Hypertension outcomes	Electronic Health Record (EHR)	At specified times anchored to the clinical event

## What are the interactions between diet, sleep, alcohol use, stress, and genetics that affect risk of depression?

**Use Case ID** 196414      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Elucidate Disease Mechanisms

Cardiovascular disease and depression are associated, but direction is unclear—or goes both ways (heart attack is a stressor triggering depression, depression leads to less exercise and increases CVD). Sleep disturbance is associated with alcohol and depression, with cause and effect unclear. Alcohol can increase depression risk, and vice versa. Increasing omega-3 versus omega-6 may be preventive for both depression and CVD. All of Us is longitudinal and over time, so these cause-effect relationships can be untangled.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Cardiovascular disease information		
Depression diagnosis		
Sleep assessments		
Stress		
Diet, self-assessment		

## Can we better determine which Sjögren’s mothers are at risk of having babies with fetal heart block and prevent its occurrence?

**Use Case ID** 196614      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Maintain & Preserve Health

It is known that the autoantibody SSA can lead to heart block in the fetuses of mothers with Sjögren’s and lupus. However, not everyone who is positive for SSA has a fetus with heart block. This study would focus on fine-tuning the risk factors for fetal heart-block to improve the odds of preventing its occurrence.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Autoimmune diseases diagnosis		
Autoimmune diseases diagnosis		
Risk factors, self-assessment		

## Does Asian-American ancestry correlate with cardiovascular risk factors?

**Use Case ID** 196848

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Most data from U.S. registries, EHR, death certificates, and cohort studies do not differentiate among Asian American subgroups (6 largest: Chinese, South Asian, Filipino, Vietnamese, Korean, and Japanese). Limited data to date suggests evidence of subgroup heterogeneity, including differences in prevalence of cardiovascular risk factors and diseases, which would be masked if subgroups are aggregated. All of Us deserves kudos for collecting this and is encouraged to target successful recruitment of these subgroups.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic ancestry	Survey	Baseline
Clinical outcomes	Electronic Health Record (EHR)	
Sociodemographics		
Cardiopulmonary assessment	Electronic Health Record (EHR)	

## How can we improve risk prediction of stroke and bleeding complications in Asian Americans with atrial fibrillation (AF)?

**Use Case ID** 196850

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Research in Asia versus findings in U.S. suggest risk of ischemic stroke and bleeding with oral anticoagulant may be higher in East Asian versus non-Asian AF patients. However, data is lacking in Asians living in the U.S. With its diversity goal, All of Us is expected to recruit a substantive number of Asian Americans. All of Us can be leveraged to see whether this finding extends to Asian Americans, who have different exposures (behavioral, social, environmental) than those in Asian countries.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Prescription medication\treatment	Prescription drug records	
Sociodemographics		
Genomic ancestry	Blood draw	

## How well do the ACC/AHA (American College of Cardiology/American Heart Association) Atherosclerotic Cardiovascular Disease (ASCVD) risk scores work in Asian Americans?

**Use Case ID** 196859

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The ASCVD risk scores were introduced by the American College of Cardiology (ACC) and American Heart Association (AHA) in 2013 to provide 10-year risk for use in blood cholesterol guidelines. Absence of Asian Americans in the cohorts that provided the data for developing the scores may limit its precision in these individuals. All of Us offers unique opportunity to collect CVD risk factors and outcomes in Asian Americans and heterogeneous subgroups and the ability to test current and create tailored risk scores.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Atherosclerotic Cardiovascular Disease (ASCVD) diagnosis	Electronic Health Record (EHR)	
Lipids panel results		
Blood pressure	Prescription drug records	
Sociodemographics		

## What is the association of cardiovascular risk factors on the development of vascular dementia?

**Use Case ID** 197149

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Recent findings from 15,744 black and white adults in the ARIC cohort study showed that several cardiovascular (CV) risk factors in middle age (smoking, diabetes, prehypertension, and hypertension) are linked to higher risk of dementia later in life and that blacks have higher rates of dementia than Whites have. All of Us offers an ability to evaluate differential associations of specific CV risk factors and their interactions with other factors on dementia risk among race/ethnic groups beyond blacks and whites.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Blood pressure	Physical exam	Every 3 months
Tobacco/Nicotine Use	PPI Survey (AOURP)	Every 3 months
Cardiac outcomes	Electronic Health Record (EHR)	Every 3 months
Lipids panel results		Annually
Dementia diagnosis	Cognitive test	Every 2 years

## Why are some people with multiple cardiovascular risk factors resistant to developing cardiovascular diseases?

**Use Case ID** 197170

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

People who smoke or have hypertension, diabetes, and hyperlipidemia are at increased risk of developing cardiovascular diseases (CVD). However, not all do, and it would be interesting to identify those who have CVD risk factors but remain free of CVD. Studying these people phenotypically, genomically, environmentally, and molecularly (via -omics) could provide great insight into novel mechanisms by which new treatments may be developed and tested in future trials.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Annually
Genomic analyses		
Metabolic risk assessment result	Blood draw	
Omics		
Physical activity, self-assessment	PPI Survey (AOURP)	

## What is the correlation between common blood pressure (BP) trajectories across the lifespan and cardiovascular outcomes?

**Use Case ID** 197172

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Following All of Us participants for decades could uncover common trajectories of BP across the lifespan and their associations with/impact on cardiovascular diseases (CVD). All of Us' size/diversity also enables precise measure of the associations by different subgroups (e.g., race, sex, social factors, presence of multiple risk factors). This could lead to refined risk predictions for CVD and further shed light on optimal timing for initiating and/or intensifying treatment based on one's BP pattern to date.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Blood pressure	Physical exam	Annually
Clinical outcomes		
Metabolic risk assessment result		Annually
Cardiopulmonary assessment		

## What is the correlation between body mass index (BMI) trajectories across the lifespan and cardiovascular outcomes?

**Use Case ID** 197174

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Following All of Us participants for decades could uncover common trajectories of body mass index (BMI) across the lifespan and their associations with/impact on cardiovascular diseases (CVD). All of Us' size/diversity also enables precise measure of the associations by different subgroups (e.g., race, sex, social factors, presence of multiple risk factors). The findings could further shed light on optimal timing for initiating and/or intensifying weight management treatment based on one's BMI pattern to date.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Weight	Physical exam	Annually
Height	Physical exam	Annually
Clinical outcomes	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Body Mass Index (BMI)	Physical exam	
Sociodemographics	PPI Survey (AOURP)	

## What are the health impacts of cannabis use in the U.S. population?

**Use Case ID** 197480

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Cannabis use is increasing with greater legalization; data on health consequences are limited. All of Us could enable a comprehensive study of health impacts of cannabis use. Sufficient questions to characterize past and current use of the range of cannabis products would need to be added. Health outcome data from questionnaires and medical record linkage already being collected could be used. Existing biospecimens could validate self-reported data on recent cannabis use in a subset.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cannabis use (detailed)	Survey	Periodically
Clinical outcomes	Electronic Health Record (EHR)	
Epigenomic/epigenetic markers	Blood draw	
Clinical outcomes		
Specified Biomarkers		

## What are the hereditary factors involved in venous thromboembolic disease?

**Use Case ID** 197548

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Research goals include creating improved prevention measures and treatments for venous thromboembolism.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Survey	At specified times anchored to the clinical event
Self-reported ancestry	PPI Survey (AOURP)	At specified times anchored to the clinical event

## How do metropolitan-level factors, including residential segregation, affect asthma?

**Use Case ID** 197557

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The prevalence of asthma is on the rise and is high for racial minorities. No attention has been paid to the impact of the variation in metropolitan-level characteristics on asthma, largely because of limited metropolitan variation in available data. Metropolitan-level residential segregation affects minority housing, and housing conditions are an important determinant of asthma. The All of Us project should collect asthma data from whites and racial minorities in at least 100 metropolitan areas.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Geocode data	Mobile monitor	
Asthma outcomes		

## What role do societal-level factors play in understanding heart disease?

**Use Case ID** 197737

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

There are strong areal relationships with the rate of heart disease. The All of Us design can help distinguish individual genetic risks and behaviors from the role of social factors. It is essential, however, that the data set include sufficient areal data and information (such as ZIP code and census tract) to support such analyses. The information that links to societal-level data needs to be collected repeatedly and be widely available. Privacy can be protected through data enclaves.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	Electronic Health Record (EHR)	Continuous monitoring
Geocode data		
Cardiovascular disease information		

## Why do factors exacerbate susceptibility to severe lower respiratory tract infections with common viruses?

**Use Case ID** 198122

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

This would be designed as a prospective observational cohort study of children (infants to 2-year-olds) with common seasonal respiratory viral illnesses (RSV, enterovirus/rhinovirus, human metapneumovirus, parainfluenza, influenza). Those with severe bronchiolitis/pneumonia requiring hospitalizations would then be compared to those who receive care as outpatients. The analysis would include clustering based on genetic variants, microbiome composition, and phenotypic characteristics.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Microbiome sample	Cheek swab	At specified times anchored to the clinical event
Microbiome sample	Stool sample	Baseline
Genomic sequence data	Whole Exomic Sequencing (WES)	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	
Respiratory viral illness diagnosis		

## What is the relationship between reproductive history and cardiovascular disease?

**Use Case ID** 198173

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Women with specific pregnancy complications, including poor fetal growth, preterm birth, and preeclampsia, may have an increased risk of later cardiovascular disease. Studies based on birth certificate data cannot include women with no births, through choice or infertility. A population-based study will allow inclusion of all women and provide data on all pregnancy outcomes, not just births. Postpartum interventions or health follow-up for women at high risk can decrease the incidence of CVD.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes	Survey	
Pregnancy complications	Electronic Health Record (EHR)	Annually
Blood pressure	Physical exam	Every 2 years
Prescription medication\treatment	Survey	Every 3 months
Tobacco/Nicotine Use	PPI Survey (AOURP)	Annually

## Can inclusion of erectile dysfunction (ED) assessment improve the prediction of cardiovascular disease (CVD)?

**Use Case ID** 198249

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

Recent epidemiological evidence shows ED is associated with CVD, suggesting ED may be a prodrome of CVD. We propose to assess associations between ED preceding CVD to confirm this association in the large and diverse All of Us cohort. Additionally, ED will be added to the existing Framingham risk prediction equation to determine if inclusion of ED improves the model.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Erectile dysfunction diagnosis	Electronic Health Record (EHR)	
Cardiovascular disease information	Electronic Health Record (EHR)	
Sociodemographics	Electronic Health Record (EHR)	
Social determinants of health (SDH)	PPI Survey (AOURP)	
Lipids panel results		

## Over long periods of time, what is the correlation between smoking and perceived quality of life?

**Use Case ID** 198405

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The correlation with specific disease states is well known, but it is likely that the nicotine addiction affects well-being and the perception of quality of life in many other ways.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Nicotine metabolites levels	Blood draw	Annually
Mental health outcomes	Survey	Annually
Quality of life		

## What are the predictors of transient ischemic attack (TIA)?

**Use Case ID** 198449

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

Transient ischemic attack (TIA) is a frequent precursor to debilitating conditions like stroke. Existing longitudinal cohort studies of TIA have limited applicability due to the relative rarity of TIA and the changing definitions of TIA over time. All of Us provides a unique opportunity to assess the incidence of TIA under modern medical practice in this longitudinal cohort. With All of Us's extensive data collection, we can assess predictors of incident TIA in the general population.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	International Classification of Diseases (ICD) usage data	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Prescription medication\treatment	Claims data	Continuous monitoring
Cardiovascular procedures	International Classification of Diseases (ICD) usage data	Continuous monitoring
Tobacco smoking	PPI Survey (AOURP)	Annually

## Can the recycling of influenza viruses explain changes in phenotypes of coronary heart disease (CHD) cases?

**Use Case ID** 198510

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

I proposed that the 1950s–1960s CHD deaths were associated with H1 and H2 influenza A reinfections of H3 influenza-primed individuals (born around 1890). After 1968, when the H3 influenza virus returned, high-serum cholesterol CHD cases declined, and a second atherogenic phenotype emerged (H3 reinfection of H1-primed cohorts born after 1900 and more after 1918?). Would CHD mortality with high serum cholesterol levels increase again as cohorts born after 1968 (H3) become reinfected with H1 viruses?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Inflammation biomarkers levels	Blood draw	At specified times anchored to the clinical event
Lipids panel results		Baseline and at event
Lipids panel results		
Influenza Virus test results		
Coronary Heart Disease (CHD) diagnosis	Electronic Health Record (EHR)	

## What are the risk factors for cardiovascular disease in survivors of childhood or adult malignancies?

**Use Case ID** 198572      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

Both children and adult survivors of malignancies have more cardiovascular risk factors than age/gender-matched controls. Once risk factors develop, the risk of cardiac events is potentiated at very high levels. Even patients with a remote history of radiation or anthracycline treatment have a much higher risk of cardiac events compared to those with no prior cancer history. The diagnosis and follow-up of CV risk factors and outcomes in this group would inform future trials.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Cancer treatment/therapy		
Cardiac outcomes		
Risk factors, self-assessment		

## What are the long-term consequences of deep vein thrombosis?

**Use Case ID** 198692      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Reduce Disease Impact

Description not provided.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Deep vein thrombosis diagnosis		
Clinical outcomes		

## What are the long-term consequences of anemia?

**Use Case ID** 198693      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Reduce Disease Impact

Description not provided.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Anemia diagnosis		
Clinical outcomes		

## What are the factors that affect the prediction and enhance the prevention of cardiac arrhythmias and sudden cardiac death?

**Use Case ID** 198695

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Development of prediction and prevention of cardiac arrhythmias is necessary. Routine 12-lead 10-second ECG is widely available and inexpensive. ECG can be also easily monitored via ECG patches. Study design: a prospective cohort. Routine 12-lead digital ECG at baseline, for measurement of electrophysiological phenomena. Outcomes: (1) genome: to study the biology behind electrophysiological substrates; (2) cardiac arrhythmias detected via ECG monitoring; (3) sudden cardiac death.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Whole genome sequence (WGS) data	Blood draw	Baseline
Electrocardiogram (ECG/EKG) tracings	Electrocardiogram (ECG/EKG)	Baseline
Sudden Cardiac Arrest (SCA) diagnosis	Autopsy	Baseline
Electrocardiogram (ECG/EKG) tracings	Electrocardiogram (ECG/EKG)	Periodic (approximately biweekly)

## What are the phenotypes and endotypes of asthma based on clinical and patient-reported data?

**Use Case ID** 198719

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Using clinical information obtained from patients (types of symptoms, severity of symptoms, exercise-related symptoms, day versus night symptoms, prednisone use, hospitalization, ED visit, etc.), determine if there is a relationship between these patient-reported symptoms and clinical data (FEV1, FeNO, peak flow, O2 saturation, etc.).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	
Asthma outcomes	Electronic Health Record (EHR)	
	Imaging	

## ***Does meeting sleep health goals (duration, consistency) reduce the incidence and morbidity of cardiovascular disease?***

**Use Case ID** 1000726      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Reduce Disease Impact

Describes core question: can fold in/expand to look at mediators and mechanisms: stress (EMA, survey); diet (survey, EMA); contextual information (light, screen time, noise); BP/HR (per monitor); intermediates (EHR, imaging—carotid U/S, CAC); biomarkers (CRP, IL-6).

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Behavioral characteristics, self-assessment	Survey	Annually
Sleep parameters	Wearable electronics	Continuous monitoring
Cardiac outcomes	Electronic Health Record (EHR)	Annually

## What are the environmental, behavioral, and genetic determinants of the maintenance of ideal body weight over the life course?

**Use Case ID** 1000759 **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important** **Scientific Category** Maintain & Preserve Health

Obesity is a worldwide epidemic contributing to nearly every adverse health outcome. Its etiology is multifactorial, with different drivers across individuals. Understanding how some manage to avoid obesity may allow us to develop individualized approaches. We propose a 5+ year study (including children) that makes measurements below to answer the above question.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Daily
Microbiome sample	Stool sample	Annually
Diet, self-assessment	Mobile monitor	Daily
Weight	Patient-reported outcome	Monthly
Physical activity, self-assessment	Wearable electronics	Daily
Physical activity, self-assessment	PPI Survey (AOURP)	Daily
Sleep assessments	Wearable electronics	Daily
Sleep quality assessment results	Wearable electronics	Daily
Epigenomic/epigenetic markers	Fat biopsy	Every 6 months
Weight	Physical exam	Monthly
Social environment	Geographic information system (GIS) code	Annually
Food security status	Geographic information system (GIS) code	Annually
Genomic analyses		
Metabolomic profile		
Clinical outcomes	Electronic Health Record (EHR)	
Sociodemographics	PPI Survey (AOURP)	
Anthropometrics, whole body measurements	Physical exam	

## What are omic and environmental factors affecting young adults that predict future chronic obstructive pulmonary disease (COPD)?

**Use Case ID** 1000787

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Follow up CAMP study.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Body Mass Index (BMI)	Physical exam	Annually
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Social environment	Survey	Annually
Body Mass Index (BMI)	Electronic Health Record (EHR)	Annually
Chronic obstructive pulmonary disease (COPD) diagnosis	Electronic Health Record (EHR)	Baseline
Pulmonary assessment results	Spirometry	Every 10 years

## What are the population-specific and trans-population genetic variants associated with risk of cardiomyopathy?

**Use Case ID** 1000795

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Need more genotype-phenotype data in non-European populations.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	
Blood pressure	Patient-reported outcome	
Blood pressure	Electronic Health Record (EHR)	
Echocardiograms	Echocardiography	
Cardiomyopathy type	Patient-reported outcome	
Cardiomyopathy type	Electronic Health Record (EHR)	
Sociodemographics	Patient-reported outcome	
Sociodemographics	Electronic Health Record (EHR)	
Blood pressure	Patient-reported outcome	Periodically
Epigenomic/epigenetic markers	DNA methylation array	
Discrimination encounters	Patient-reported outcome	
Health insurance status	Patient-reported outcome	
Adherence to prescription regimen	Patient-reported outcome	
Access to health care	Patient-reported outcome	
Access to health care	Electronic Health Record (EHR)	
Cardiopulmonary assessment	Machine learning	
Amyloid levels	Biochemical assay	

## What is the relative impact of different types of inhalational exposures (e.g., smoking, air particulate matter) on the maintenance of lung health?

**Use Case ID** 1000808

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

The air we breathe is a key determinant of maintenance lung health. We propose to deeply characterize All of Us participants for inhaled exposures and measures of lung health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Personal Characteristics	Survey	Baseline
Air quality assessment results		Baseline
Specified Biomarkers	Urine collection	Baseline
Occupation	PPI Survey (AOURP)	Baseline
Physical measurements	Spirometry	Every 3 months
Pulmonary assessment results	Physical exam	Annually

## What are the mechanisms that mediate heterogeneity of blood pressure?

**Use Case ID** 1000823

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

There is variability over time and in response to various influences (diet, stress, weight, physical activity).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Annually
Blood pressure	Wearable electronics	Continuous monitoring
Weight	Electronic Health Record (EHR)	Annually
Physical activity, self-assessment	Wearable electronics	Continuous monitoring
Stress	Survey	Annually
Aggression, self-assessment	Survey	Annually
Microbiome sample	Blood draw	Baseline
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Clinical outcomes	Survey	Annually
Clinical outcomes	Wearable electronics	Continuous monitoring
Pulmonary assessment results	Spirometry	Periodically

## What are the predictors of vulnerable plaque?

**Use Case ID** 1000843

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Family clinical outcomes	PPI Survey (AOURP)	Annually
Angiogram	Angiography	Annually
Omics	Blood draw	Baseline
Diet, self-assessment	Mobile monitor	Continuous monitoring
Geocode data	Survey	Annually
Myocardial Infarction diagnosis	Electronic Health Record (EHR)	Post-event or at least annually
Myocardial Infarction diagnosis	Clinical assessment	Post-event or at least annually

## What are novel risk factors for deep vein thrombosis?

**Use Case ID** 1000844

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Other

Longitudinal study looking for novel risk factors. \*Induced conditions (pregnancy, surgery, travel).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Tobacco smoking	PPI Survey (AOURP)	Annually
Diabetes diagnosis	Electronic Health Record (EHR)	Weekly
Diabetes diagnosis	International Classification of Diseases (ICD) usage data	Weekly
Whole genome sequence (WGS) data	Whole Genome Sequencing (WGS)	Baseline
Metabolomic profile		Annually
Epigenomic/epigenetic markers	DNA methylation array	Annually
Proteomic profile		Annually
Family clinical outcomes	PPI Survey (AOURP)	Baseline
Deep vein thrombosis diagnosis	Electronic Health Record (EHR)	Annually
Events		Post-event or at least annually

## Can we use lung CT scans from routine lung cancer screening to detect other cardiopulmonary diseases, direct therapies, and predict outcomes?

**Use Case ID** 1000863

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

CT scans would be collected as part of their routine/standard of care for lung screening, low-dose lung CT protocol. Need imaging repository.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Blood draw	Baseline
Pulmonary assessment results	Computed Tomography (CT) scan	Periodically
Coronary Artery Disease (CAD) diagnosis	Computed Tomography (CT) scan	Periodically
Coronary calcium scan results	Computed Tomography (CT) scan	Periodically
Epicardial adipose tissue assessment results	Computed Tomography (CT) scan	Periodically
Pulmonary fibrosis diagnosis	Computed Tomography (CT) scan	Periodically
Lung cancer diagnosis	Computed Tomography (CT) scan	Periodically
Bone density	Computed Tomography (CT) scan	Periodically
Muscle mass	Computed Tomography (CT) scan	Periodically
Echocardiograms	Echocardiography	Periodically
Death	Death records	Periodically
Death	National Death Index	Periodically

## What are the underlying mechanisms that mediate risk of cardiac arrhythmias and sudden cardiac death?

**Use Case ID** 1000882      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Elucidate Disease Mechanisms

The clinical and molecular mechanisms that mediate risk of cardiac arrhythmias and sudden cardiac death are not well understood, nor well integrated into comprehensive models of risk prevention. This issue is even more acute in underrepresented minorities.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	
Genotyping data	Whole Genome Sequencing (WGS)	
Proteomic profile		
Metabolomic profile		
Diet, self-assessment	Wearable electronics	Continuous monitoring
Chemical exposure assessment results	Mobile monitor	Continuous monitoring
Environment	Geographic information system (GIS) code	Annually
Echocardiograms	Echocardiography	Baseline
Magnetic resonance imaging (MRI) images	Cardiac Magnetic Resonance Imaging (MRI)	Baseline
Epigenomic/epigenetic markers	DNA methylation array	Baseline
Pulse	Wearable electronics	Continuous monitoring
Echocardiograms	Wearable electronics	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Annually
Clinical outcomes	Patient-reported outcome	Annually
Clinical outcomes	Echocardiography	Ad hoc
Clinical outcomes	Survey	Annually
Death		
Genomic analyses		Baseline
Diet, self-assessment	Food frequency test	Annually

## How does stress affect the ability to maintain optimal cardiovascular health?

**Use Case ID** 1000907      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Maintain & Preserve Health

Self-reported stress levels are a major risk factor for coronary heart disease and cardiometabolic disease. However, quantitation of stress is poorly done at present in population cohorts. We propose developing a suite of instruments to measure stress among participants in All of Us.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Personal Characteristics	Survey	Baseline
Cortisol levels	Saliva	Baseline
Mental and psychosocial health, self-assessment	Survey	Daily
Credit score	Survey	Baseline
Heart rate variability	Wearable electronics	Continuously for 5 years
Electrodermal activity measurements	Wearable electronics	Continuously for 5 years
Stress	Photograph	Baseline
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Dopamine levels	Saliva	Baseline
Dopamine levels	Sweat collection	Baseline
Androgens levels		Baseline
Androgens levels		Baseline
Adrenaline levels	Saliva	Baseline
Adrenaline levels	Sweat collection	Baseline
Hormone levels (non-steroidal)	Saliva	Baseline
Hormone levels (non-steroidal)	Sweat collection	Baseline
Sweat sample	Photograph	Baseline
Sleep assessments	Survey	Continuously for 5 years
Cardiopulmonary assessment	Electronic Health Record (EHR)	Annually

## How do we create novel subclassifications of cardiopulmonary disease?

**Use Case ID** 1000985

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

Cluster analysis (unbiased) needed. At least 100 variables needed. Encourage data types with low missingness.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Baseline
Pregnancy, smoking	Survey	Baseline
Genomic analyses	Genomic testing	Baseline
Pulmonary assessment results	Spirometry	Baseline
Pulmonary assessment results		Baseline
Ventricle function	Echocardiography	Baseline
Cardiopulmonary assessment	Computed Tomography (CT) scan	Baseline
Calcium levels	Computed Tomography (CT) scan	Baseline
Behavioral characteristics, self-assessment	Electronic Health Record (EHR)	Baseline
Behavioral characteristics, self-assessment	Patient-reported outcome	Baseline
Tobacco smoking	Electronic Health Record (EHR)	Baseline
Tobacco smoking	Patient-reported outcome	Baseline
Alcohol Use	Electronic Health Record (EHR)	Baseline
Alcohol Use	Patient-reported outcome	Baseline
Alcohol Use	PPI Survey (AOURP)	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Baseline

## What are the impacts of cannabis use on the incidence and morbidity of pulmonary and cardiovascular disease?

**Use Case ID** 1001021

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Cannabis increases as it is legalized in additional states. Thus more frequent assessment of use is warranted. Validation of reports of cannabis use/nonuse using biomarkers of THC would be important. Cannabis has potential impacts on many other health conditions, as noted in secondary conditions. (As a sub-question, within COPD and asthma, what is the impact of cannabis on shortness of breath?)

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Annually
Blood pressure	Blood pressure cuff	Every 2 years
Anthropometrics, whole body measurements	Spirometry	Every 2 years
Anthropometrics, whole body measurements	Anthropometry	Every 2 years
Cannabis use (detailed)	Survey	Annually
Clinical outcomes	Survey	Annually
Pulmonary assessment results	Clinical assessment	Annually
Sociodemographics	PPI Survey (AOURP)	Baseline

## Can mining of financial data predict risk of heart, lung, blood, and sleep conditions?

**Use Case ID** 1001064

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Will require the ability of participants to push financial data to All of Us ... a new "Sync for Science."

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Credit score	Survey	Annually
Cardiopulmonary assessment	International Classification of Diseases (ICD) usage data	Annually
Cardiopulmonary assessment	Electronic Health Record (EHR)	Annually

## Does genetic predisposition cardiopulmonary disease correlate with absence of other diseases, and are there pharmacological implications?

**Use Case ID** 1001118

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

I.e., cystic fibrosis/cholera, sickle cell disease/malaria, prostate cancer/severe asthma. Looking for things that have never previously been considered, using the large population.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Whole genome sequence (WGS) data	Blood draw	Baseline
Medical Information	Electronic Health Record (EHR)	Annually
Infectious agents	Electronic Health Record (EHR)	Annually
Prescription medication\treatment	Electronic Health Record (EHR)	Annually
Cardiac outcomes	Electronic Health Record (EHR)	Annually

## Can we use lung CT scans from routine lung cancer screening to detect other cardiopulmonary diseases, direct therapies, and predict outcomes?

**Use Case ID** 1001244

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

CT scans would be collected as part of their routine/standard of care for lung screening low-cost lung CT protocol. Need imaging repository (could also collect cardiac CT and echo done for standard). Need actual CT scans themselves, to allow researcher access to the images.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Coronary calcium scan results	Computed Tomography (CT) scan	Annually
Genotyping data	Genomic testing	Baseline
Pulmonary assessment results	Computed Tomography (CT) scan	Baseline
Pulmonary fibrosis diagnosis	Computed Tomography (CT) scan	Baseline
Muscle mass	Computed Tomography (CT) scan	Baseline

## **Reduce the incidence of sudden cardiac death by identifying individuals who benefit the most from the implantable defibrillator.**

**Use Case ID** 195002

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

The burden of sudden cardiac death remains high, accounting for more than 350,000 deaths in the U.S. annually. The implantable defibrillator remains the major primary prevention modality. However, in order for this important measure to stay sustainable from a health costs perspective, the criteria for selecting candidates most likely to benefit need to be improved significantly. It will be important to identify all use cases with implantable defibrillators to identify the ones who benefit the most.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Death	Death records	Every 3 months
Cardiac outcomes	Electronic Health Record (EHR)	Every 3 months
Health care cost	Electronic Health Record (EHR)	Every 3 months

## **What is the impact of persistent hypervolemia on development of hypertension and heart failure?**

**Use Case ID** 195098

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

It has been posited that hypertension is due to excess blood volume or vasoconstriction, but hypertension therapy trials have looked at specific doses of diuretic or vasodilator. The question to answer is: Does individualization of therapy for patient-specific hypertension improve outcomes and possibly avert onset of heart failure? Patients receiving treatment for hypertension could receive direct blood volume tests to ascertain appropriateness of therapy. Outcomes for all patients observed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Blood pressure	Electronic Health Record (EHR)	Annually
Hypertension outcomes	Electronic Health Record (EHR)	Annually
Blood volume	Blood volume test	Every 3 years
Heart failure event	Electronic Health Record (EHR)	

## What effect does exercise have on pain levels in individuals with sickle cell disease?

**Use Case ID** 195540

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Goal: determine the effect of regular and structured exercise on pain levels in individuals with sickle cell disease. Method: RCT with a group who perform at least 150 minutes a week of moderate physical activity (e.g., 30 minutes of weight lifting 5 days/week). Track daily pain levels using numeric pain rating scale from individuals in the exercise group and the control group. Can also track pain episodes and crises per individual, and include medication use in subject demographics. Time: minimum 8 weeks.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pain symptom diagnosis	Survey	Continuous monitoring
Physical activity, self-assessment	Activity monitor	Weekly
Sickle cell anemia diagnosis		

## How do drug and body chemistries affect the action of oral anticoagulants?

**Use Case ID** 195891

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

The study would seek to identify and prioritize drug-related factors (e.g., route of administration and dosage) and patient-related factors (e.g., blood cell count, creatinine clearance level, pharmacogenomic phenotype) that could enhance or mitigate the risk of harm from exposure to direct-acting oral anticoagulants.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Pharmacogenomics		Baseline
Perceived outcomes - patient	Survey	Every 3 months
Prescription medication\ treatment	Electronic Health Record (EHR)	Continuous monitoring
Oral anticoagulant	Blood draw	Every 3 months

## What is the natural progression of idiopathic pulmonary fibrosis (IPF) on chest CT?

**Use Case ID** 196391

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Detect Disease

IPF patients become aware of disease when becoming symptomatic with cough and dyspnea. By then, CT often shows advanced fibrosis. It is important to know how long the patient had changes on CT before becoming symptomatic and finding clues to predict progression versus stability—for example, the size of the pulmonary artery. This becomes more important now that the FDA has approved two medications that slow the progression of IPF and would likely be beneficial for patients with early disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pulmonary fibrosis diagnosis	Computed Tomography (CT) scan	
Cough diagnosis	Physical exam	
Dyspnea diagnosis		
Computer Aided Tomography (CT/CAT) images		

## Develop a Social Determinants of Health risk calculator for chronic disease development.

**Use Case ID** 196488

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

Which social determinants of health (SDH) or what combination carry the greatest risk for the development of top chronic diseases? Developing an SDH risk calculator can guide clinical practice, community resource allocation, and prevention efforts. Use evidence-based SDH variables to develop a predictive model for 10-year risk of developing the most common chronic diseases. Test model in a diverse sample.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social determinants of health (SDH)	Electronic Health Record (EHR)	Baseline
Social determinants of health (SDH)	PPI Survey (AOURP)	Baseline
Social determinants of health (SDH)	Mobile monitor	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring

## What is the role of stent grafts in the treatment of uncomplicated type B aortic dissection?

**Use Case ID** 196575

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

Evaluate mortality and major complications.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Aortic health	Imaging	Every 6 months
Health and phenotype data		

## Does utilization of the Leg Lymphedema Complexity Score (LLCS) reduce recurrent hospitalizations and episodes of leg cellulitis?

**Use Case ID** 197571

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Clinicians will be trained to use the LLCS via online learning and provided with access to free downloads of the tool. Developed in collaboration with national wound care, lymphedema, and vascular organizations, this tool includes practice guidelines and treatment recommendations. Complexity scores, tracked over time along with treatment interventions, are expected to correlate with reduced costs of recurrent hospitalizations and episodes of cellulitis and to improved quality of life.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lymphedema diagnosis	Physical exam	Every 6 months
Treatment decisions	Procedure codes	Every 6 months
Inflammation disorder diagnosis		At specified times anchored to the clinical event
Quality of life	Survey	Every 6 months
Adherence to treatment	Activity monitor	Continuous monitoring

## **Will using the guide to compression garment selection improve long-term management of edema and reduce venous ulcer recurrence?**

**Use Case ID** 197575

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

This guide is a collaborative effort between clinical experts, compression manufacturing companies, and individual users. The guide is intended to help clinicians understand parameters of compression garment engineering that influence effective edema management and to recommend the best compression for individuals. Functional outcomes, feedback from the users, and tracking ulcer recurrence will help refine the selection guide, improve design of compression garments, and reduce health care costs.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Edema diagnosis	Volumetric measurement	Weekly
Venous Leg Ulcer diagnosis	International Classification of Diseases (ICD) usage data	At specified times anchored to the clinical event
Adherence to treatment	Mobile monitor	Continuous monitoring
Patient feedback	Survey	Every 3 months

## **Are functional mobility, limb volume, and quality of life improved with a new, rehab-based approach to complete decongestive therapy (CDT) and lymphedema care?**

**Use Case ID** 197665

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

PTs/PTAs/OTs/COTAs will be certified in a new rehab-based approach to complete decongestive therapy for lymphedema management. Lymphedema complexity score, number and duration of visits, volumetric measurements, and functional outcomes will be correlated. We expect to find that patients with higher complexity scores will require more visits to achieve desired outcomes. We expect improvements in functional mobility, limb volume, and quality of life. These could also be compared to other approaches.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Treatment decisions	Electronic Health Record (EHR)	
Functional mobility assessment results	Clinical diagnostic test	Weekly
Muscle mass	Volumetric measurement	Weekly
Quality of life		
Complete Decongestive Therapy (CDT) use		

## **Do new manual lymphatic drainage (MLD) techniques reduce tissue inflammation, promote connective tissue remodeling, and lymph capillary regeneration?**

**Use Case ID** 197695

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Edema volume reduction has been used as a benchmark for showing improvements with lymphedema treatment, but equally important is the remodeling of skin and connective tissue to a more normalized state. This study aims to assess and track skin and subcutaneous tissue inflammation, connective tissue remodeling, and lymph capillary regeneration as a result of new manual lymphatic drainage techniques.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Connective tissue density & pliability	Calipers	Weekly
Dermal lymphatic drainage measurements	Near-infrared imaging	Every 3 months
Inflammation antigens levels		
Manual Lymphatic Drainage (MLD) use	Electronic Health Record (EHR)	Baseline

## **What are the consequences of different combinations of obstructive sleep apnea in terms of overall treatment?**

**Use Case ID** 198358

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Studies of OSA have so far focused on whether any one treatment (CPAP, dental appliances, hypoglossal stimulation, surgery, etc.) has an impact on outcomes. Physiologically, all that matters is whether the OSA is improved. Studies can be designed using as a metric whether any treatment (or combination) reduces the AHI or any other metric of severity of the OSA. This pooled data can then be related to any desired outcome—including symptomatic neurologic and cardiovascular consequences.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sleep behavior assessment results	Sleep study	Baseline and post-treatment
Sleep apnea diagnosis		
Treatment/Therapy		

## What is the long-term effectiveness of empagliflozin in a heterogeneous population with type 2 diabetes?

**Use Case ID** 198374

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Empagliflozin, a highly selective sodium-glucose cotransport 2 (SGLT2) inhibitor, has been shown to significantly reduce major adverse cardiovascular (CV) events and hospitalization for heart failure in patients with type 2 diabetes (T2DM) and established CV disease. The generalizability of this finding to lower-risk populations is unknown. We propose to compare cardiovascular outcomes in a more heterogeneous population of T2DM patients treated with SGLT2 inhibitors versus other antidiabetic agents.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Prescription medication\treatment	Electronic Health Record (EHR)	Continuous monitoring
Metabolic risk assessment result	Electronic Health Record (EHR)	
Albuminuria diagnoses	Urine collection	Every 6 months
Creatine levels	Urine collection	Every 6 months

## Can we identify potential treatments to reduce risk of stroke following a transient ischemic attack (TIA)?

**Use Case ID** 198451

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Transient ischemic attack (TIA) is a frequent precursor to stroke. Studies of modern treatments (e.g., carotid endarterectomy and carotid artery stenting) do not consider TIA as an indicator for treatment or which treatments may be more effective following a TIA. All of Us provides a unique opportunity not only to examine the interaction between TIA and treatment to prevent subsequent strokes but also to suggest characteristics of people who benefit most from each treatment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	International Classification of Diseases (ICD) usage data	Continuous monitoring
Cardiovascular procedures	Claims data	Continuous monitoring
Health and phenotype data	Electronic Health Record (EHR)	Continuous monitoring
Prescription medication\treatment	Claims data	Continuous monitoring
Tobacco smoking	International Classification of Diseases (ICD) usage data	Continuous monitoring

## What are the best acute management strategies for children with stroke?

**Use Case ID** 198588

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Key problem: While there is research and advances on treatment for adult stroke, acute stroke treatment for pediatrics has not been included. The TIPS trial (tPA in peds) was terminated due to lack of enrollment. Hence, there are no guidelines for treating acute stroke in children. Lack of timely medical intervention can result in more profound disabilities or death. Methods: Conduct research to identify safe and effective treatment for acute stroke in those age 18 years and younger.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Stroke, pediatric diagnosis	Pediatric Stroke Outcome Measure (PSOM)	Continuously for 1 week duration at 1 month, 6 months, and 1 year
Stroke, pediatric diagnosis	Pediatric National Institutes of Health Stroke Scale (PedNIHSS)	
Clinical outcomes		

## What are the factors that affect patient management of cardiovascular disease and comorbid conditions?

**Use Case ID** 1000829

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Incorporating the patient in the management of disease(s) and motivate optimal compliance with care plan.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Electronic Health Record (EHR)	Continuous monitoring
Behavioral characteristics, self-assessment	Survey	Periodically
Protein levels	Blood draw	Baseline, first trimester, monthly through delivery, and 1 year postpartum
Hormone levels (non-steroidal)	Blood draw	Baseline, first trimester, monthly through delivery, and 1 year postpartum
Small molecules and ion levels	Blood draw	Baseline, first trimester, monthly through delivery, and 1 year postpartum
Lipids panel results	Blood draw	Baseline, first trimester, monthly through delivery, and 1 year postpartum
Genotyping data	Genomic testing	Baseline
Medical Information	Survey	Periodically
Medical Information	Survey	Baseline and post-treatment
Medical Information	Electronic Health Record (EHR)	Continuous monitoring
Behavioral characteristics, self-assessment	Activity monitor	Periodically
Behavioral characteristics, self-assessment	Activity monitor	Baseline and post-treatment
Behavioral characteristics, self-assessment	Diary/journal	Baseline and post-treatment
Physical measurements	Electronic Health Record (EHR)	Baseline
Blood pressure	Blood pressure cuff	Baseline
Social determinants of health (SDH)	Electronic Health Record (EHR)	Baseline
Social determinants of health (SDH)	PPI Survey (AOURP)	Baseline
Social determinants of health (SDH)	Geospatial tracking	Baseline
Behavioral characteristics, self-assessment	Electronic Health Record (EHR)	Baseline
Behavioral characteristics, self-assessment	Survey	Baseline
Behavioral characteristics, self-assessment	Diary/journal	Baseline
Mental and psychosocial health, self-assessment	Survey	Baseline
Mental and psychosocial health, self-assessment	Health behavior mindset scale	Baseline
Mental and psychosocial health, self-assessment	Language comprehension assessment	Baseline

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mental and psychosocial health, self-assessment	Psychological test	Baseline
Mental and psychosocial health, self-assessment	Milestone Tracker mobile app	Baseline
Outcomes	Survey	Baseline
Outcomes	Health behavior mindset scale	Baseline
Outcomes	Language comprehension assessment	Baseline
Outcomes	Psychological test	Baseline
Outcomes	Milestone Tracker mobile app	Baseline
Symptoms	Survey	Baseline
Symptoms	Health behavior mindset scale	Baseline
Symptoms	Language comprehension assessment	Baseline
Symptoms	Psychological test	Baseline
Symptoms	Milestone Tracker mobile app	Baseline

## **How to increase survival and recovery among vulnerable populations diagnosed with pneumonia?**

**Use Case ID** 1000847

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pulmonary assessment results	Blood draw	Baseline and post-treatment
Pneumonia diagnosis	Blood draw	Baseline and post-treatment
Clinical outcomes	Electronic Health Record (EHR)	Baseline and post-treatment
Oral microbiome sample		Baseline and post-treatment
Environment	Survey	Baseline and post-treatment
Behavioral characteristics, self-assessment	Survey	Baseline and post-treatment
Hospitalization	Electronic Health Record (EHR)	Post-event or at least annually

## Does screening for and treatment of sleep apnea reduce incidence, morbidity, and mortality of heart failure in minority populations?

**Use Case ID** 1000861

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

Sample with oximetry subgroup based on risk factors for heart failure and sleep apnea; over-recruit minorities (oximetry - study screening test). Follow-up with clinical sleep evaluation.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Baseline
Sleep behavior assessment results	Survey	Baseline
Anthropometrics, whole body measurements	Physical exam	Baseline
Clinical outcomes	Survey	Baseline

## What are the socioeconomic, genetic, and environmental determinants of bronchodilator response?

**Use Case ID** 1000940

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Current medications as confounders. Genetic examples: B2AR, ADH5. Environment examples: smoke exposure.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Tobacco smoking	PPI Survey (AOURP)	Annually
Genotyping data	Whole Genome Genotyping (WGG)	Baseline
Prescription medication\ treatment	Electronic Health Record (EHR)	Annually
Pulmonary assessment results	Electronic Health Record (EHR)	Baseline
Tobacco smoking	Electronic Health Record (EHR)	Annually
Air quality assessment results		Annually
Socioeconomic Status (SES)	Geographic information system (GIS) code	Baseline
Socioeconomic Status (SES)	PPI Survey (AOURP)	Baseline
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Physical activity, self-assessment	PPI Survey (AOURP)	Periodically

## Does the timing of cardiovascular disease medications impact efficacy of treatment?

**Use Case ID** 1000953

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Timing = over the day.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Blood pressure	Electronic Health Record (EHR)	Annually
Body Mass Index (BMI)	Electronic Health Record (EHR)	Annually
Prescription medication\treatment	Survey	Annually
Clinical outcomes	Survey	Annually
Adherence to prescription regimen	Survey	Annually
Blood pressure	Clinical assessment	Annually
Heart rate variability	Electronic Health Record (EHR)	Annually
Heart rate variability	Clinical assessment	Annually
Blood pressure	Mobile monitor	Baseline
Blood sample characteristics	Blood draw	Annually
Body Mass Index (BMI)	Clinical assessment	Annually

## Does early detection of biofilm buildup on stents and other implants reduce cardiovascular disease complications?

**Use Case ID** 1000977

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Early detection of bacterial infections on stents and other implants.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cardiopulmonary assessment	Custom sensor/app	Continuous monitoring
Cardiopulmonary assessment	Blood draw	During clinic visits
Microbiome sample	Blood draw	During clinic visits
Adherence to prescription regimen	Electronic Health Record (EHR)	Annually

## What aspects of physical activity are associated with maintenance of cardiovascular health?

**Use Case ID** 1001006

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

We propose to deeply characterize physical activity patterns on the entire All of Us population. Physical activity is a key determinant of nearly all major adverse health conditions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Wearable electronics	Daily
Physical activity, self-assessment	PPI Survey (AOURP)	Daily
Cardiovascular fitness	Wearable electronics	Baseline
Level of functionality (disability) assessment results		Baseline
Blood sample characteristics	Biochemical assay	Baseline
Occupation parameters		Daily
Environment	Global Positioning System (GPS) monitoring	Daily

## Which decisions on treatment and prevention for atrial fibrillation provide the best survivability?

**Use Case ID** 1001009

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

AF is most common arrhythmia and associated with multiple comorbidities and mortality once it is developed. Multiple treatment options and diversity of response and outcomes. Identify correct treatment for patients who have developed AF using genomics, imaging, monitory, and looking for approaches for AF prevention.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Air quality assessment results		Annually
Prescription medication\treatment	Electronic Health Record (EHR)	Every 6 months
Omics	Whole Genome Sequencing (WGS)	Baseline
Metabolomic profile		Periodically
Proteomic profile		Periodically
Diet, self-assessment		Continuous monitoring
Physical activity, self-assessment		Continuous monitoring
Physical measurements	Electronic Health Record (EHR)	Baseline and at event
Physical measurements	Echocardiography	Baseline and at event
Atrial Fibrillation (AF) diagnosis	Electronic Health Record (EHR)	Every 6 months
Congestive Heart Failure (CHF) diagnosis	Electronic Health Record (EHR)	Every 6 months
Stroke diagnosis	Electronic Health Record (EHR)	Every 6 months
Dementia diagnosis	Electronic Health Record (EHR)	Every 6 months
Sudden Cardiac Arrest (SCA) diagnosis	Electronic Health Record (EHR)	Every 6 months
Cardiopulmonary assessment	Electrocardiogram (ECG/EKG)	Annually
Heart rate variability	Mobile monitor	Continuously for 5 years
Cardiopulmonary assessment	Echocardiography	Annually

## What are the subclinical determinants of cardiopulmonary disease for early detection and prevention?

**Use Case ID** 1001087

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Microbiome sample		
Proteomic profile		
Metabolomic profile		
Epigenomic/epigenetic markers	DNA methylation array	
Genomic analyses	Whole Genome Sequencing (WGS)	
Telomere length		
Medical Information	Electronic Health Record (EHR)	
Symptoms	Patient-reported outcome	
Retinal images	Imaging	
Magnetic resonance imaging (MRI) images	Magnetic Resonance Imaging (MRI)	
Cardiopulmonary assessment	Wearable electronics	
Symptoms	Electronic Health Record (EHR)	
Small molecules and ion levels		
Whole exomic sequence (WES) data		

## What factors influence adherence to treatment and healthy lifestyle recommendations?

**Use Case ID** 1001095

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Adherence to medical and lifestyle interventions may be key to achieving optimal responses/health. However, adherence can be very poor. Can include device compliance (e.g., CPAP). Factors that may influence adherence may vary across the many All of Us sites, providing opportunity to tease out effects of (1) drug/dosing regimens, including timing of medications and side effects and perceived benefits; (2) social support/digital prompts/feedback; (3) mood, stress, and sleepiness; (4) socioeconomic factors and environmental stressors; and (5) education/understanding.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Stress	Survey	Every 3 months
Quality of life	Survey	Annually
Socioeconomic Status (SES)	PPI Survey (AOURP)	Baseline
Clinical outcomes	Survey	Baseline
Social support	Survey	Baseline
Treatment data/specifics records	Electronic Health Record (EHR)	Annually
Treatment data/specifics records	Survey	Annually
Prescription medication\ treatment	Survey	Every 3 months
Side effects of prescription medication	Survey	Every 3 months
Perceived outcomes - patient	Survey	Annually
Side effects of prescription medication	Electronic Health Record (EHR)	Every 3 months
Mood patterns	Survey	Every 3 months
Level of functionality (disability) assessment results	Survey	Every 3 months
Sleep assessments	Survey	Every 3 months
Social support	Survey	Every 3 months
Health literacy	Survey	Every 3 months
Adherence to prescription regimen	Electronic Health Record (EHR)	Annually
Adherence to prescription regimen	Pharmacy records	Annually
Lifestyle, self-assessment	Mobile monitor	Annually
Access to health care	Electronic Health Record (EHR)	Every 2 years
Access to health care	Health care provider	Every 2 years

## How does frailty impact treatment decisions and management?

**Use Case ID** 1001132

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Frailty is multimorbidity at an advanced age. There are existing indices of frailty that use various inputs (disease, functional capacity, mental capacity, etc.). It has a major impact on the quality and quantity of life. This can be an important consideration in management decision at the level of the clinician, patient, and caregiver.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Frailty, self-assessment results	Frailty test	Annually
Cognitive assessments	Cognitive test	Annually
Level of functionality (disability) assessment results		Annually
Ability to perform activities of daily life (ADL) assessment results	Survey	
Medical Information	Electronic Health Record (EHR)	Periodically
Prescription medication\ treatment	Electronic Health Record (EHR)	Periodically
Housing quality variables	Survey	Periodically
Screen time	Mobile device, passive collection	Periodically
Disease endotypes results		

## Are results of randomized trials broadly applicable across sex, race, ethnicity, and age?

**Use Case ID** 1001155

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Guidelines dependent on RCTs that are often performed in select populations may lack diversity, and unknown, for all subgroups of population. Recommendations are appropriate for all subgroups of population.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Blood pressure	Blood pressure cuff	Every 6 months
Treatment/Therapy	Electronic Health Record (EHR)	Every 6 months
Treatment decisions	Electronic Health Record (EHR)	Every 6 months
Symptoms	Interview	Every 6 months
Weight	Physical exam	Every 6 months
Medical Information	Interview	Every 6 months
Medical Information	Electronic Health Record (EHR)	Every 6 months
Symptoms	Electronic Health Record (EHR)	Every 6 months
Quality of life	Survey	Every 6 months

## **What are the molecular mechanisms that underlie the relationships between psychosocial stress and heart disease?**

**Use Case ID** 1001187

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

Associations of mind-body activities with CVD are important and bi-directional. Evaluate psychosocial measures with molecular and biological observations in context of CVD.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health and phenotype data	Patient-reported outcome	
Mind-body exercise	Patient-reported outcome	
Cortisol levels	Saliva	
Health and phenotype data	Electronic Health Record (EHR)	
Stress	Survey	

# Digestive Renal and Metabolic

**All of Us** | The  
RESEARCH PROGRAM | Precision  
Medicine  
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## How is stress/anxiety related to gastrointestinal complications such as gastroesophageal reflux disease or irritable bowel syndrome?

**Use Case ID** 192318

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Gastrointestinal health information	Electronic Health Record (EHR)	
Stress	Survey	

## What are the risk and protective factors influencing incidence and prevalence of lower urinary tract symptoms?

**Use Case ID** 192397

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Emerging evidence suggests alterations in the urinary “biome” (microbiome, virome, and metabolome) contribute to LUTS conditions. The All of Us protocol provides a unique opportunity to collect urine specimens and link health information of the enrollees. The goals of a study would be to prospectively correlate LUTS with the urinary biome and assess changes in symptoms with changes in urinary markers, while controlling for additional medical outcomes (antibiotic exposure, diet, etc.).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Urinary biome sample	Urine collection	At specified times anchored to the clinical event
Diet, self-assessment	PPI Survey (AOURP)	Every 3 months
Lower Urinary Tract Symptoms (LUTS) record	Survey	Every 3 months
Clinical outcomes	Electronic Health Record (EHR)	Annually
Specified Biomarkers		At specified times anchored to the clinical event

## Do environmental exposures in the Ohio-Mississippi River basin explain obesity?

**Use Case ID** 195503

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

I think the root cause of the obesity epidemics in the Mid-South USA is linked to the nutrient pollution of the Ohio-Mississippi River basin, in particular the runoff of agricultural fertilizers (nutrient enrichment). These rivers run across the states most affected by obesity. I recommend to measure environmental exposures—chemical (e.g., phosphorus) and biological toxins (e.g., microcystin, cyanotoxins)—and measure their impact on the biology of populations most affected by obesity.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results		
Obesity diagnosis		
Location data		

## How does the effect of childhood trauma affect the self-management behaviors of type 1 diabetes in adults?

**Use Case ID** 197232

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

I would use the Childhood Adverse Events scale to identify those who have experienced childhood trauma and compare the findings with A1c and the SDSCA behaviors. Then I would conduct interviews with those who are open to further inquiry regarding how they believe that childhood trauma affects their glucose control on a daily basis.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Hemoglobin A1C (HbA1C) levels	Electronic Health Record (EHR)	Every 3 months
Adverse childhood experiences	Survey	Baseline
Diabetes outcomes	Survey	Baseline

## Do exposures to environmental chemicals during pregnancy affect epigenetic biomarkers of metabolic syndrome, obesity, and breast cancer?

**Use Case ID** 197749

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Obesity and breast cancer are leading causes of morbidity and mortality. Evidence strongly suggests that certain periods of life, including those during fetal development and pregnancy, influence risk of breast cancer later in life. Environmental chemicals may increase breast cancer risk—especially during pregnancy—by mimicking estrogen and other hormones. Epigenomic signatures present in the placenta uniquely capture the effects of endogenous and environmental exposures for both mother and baby.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Breast cancer diagnosis	Electronic Health Record (EHR)	
Placental tissue sample	Tissue biopsy	
Pregnancy characteristics	Survey	
Mammogram	Mammography	Every 3 years
Environmental samplings and exposure results	Urine collection	

## What are the clinical, environmental, and genetic factors in glomerular disease susceptibility and progression?

**Use Case ID** 198569

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Glomerular disorders represent the third most common cause of end-stage kidney disease, after diabetes and hypertension. Well-designed and adequately powered clinical, genetic, and environmental exposure studies are missing for most glomerular disease types. Using genetic and environmental variables combined with kidney-related structured electronic health record phenotype data captured by All of Us, we aim to identify new determinants of glomerular disease susceptibility and progression.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Geocode data	Electronic Health Record (EHR)	
Creatinine levels	Electronic Health Record (EHR)	
Protein levels	Urine collection	
Environment	Urine collection	Annually

## What environmental factors reduce metabolic and digestive disease impact?

**Use Case ID** 1000955

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Reduce Disease Impact

Description not provided.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Medical Information	Electronic Health Record (EHR)	Annually
Geocode data	Survey	Annually
Microbiome sample	Whole Genome Sequencing (WGS)	Annually
Diet, self-assessment	PPI Survey (AOURP)	Every 6 months
Medical Information	Electronic Health Record (EHR)	Every 6 months

## What effects do food deserts have on glucose control?

**Use Case ID** 1001123

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Detect Disease

Food deserts are defined as limited access to affordable, good-quality, fresh fruits, veggies, and nutritious food. The long-term effects on glucose control while living in a food desert are unknown and may provide meaningful insights into non-biologic factors influencing health, wellness, resilience, and QOL.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Personal Characteristics	Survey	Annually
Hemoglobin A1C (HbA1C) levels	Electronic Health Record (EHR)	Continuous monitoring
Location data	Geographic information system (GIS) code	Continuous monitoring
Personal Characteristics	PPI Survey (AOURP)	Annually
Social environment	PPI Survey (AOURP)	Annually
Sociodemographics	Electronic Health Record (EHR)	Annually
Food selection	Survey	Quarterly or Annually

## What is the association of pathogens with metabolic disease?

**Use Case ID** 1001130

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

Infections are thought to be associated with many chronic diseases, but the pathogens associated are not clear.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Hemoglobin A1C (HbA1C) levels	Plasma	Annually
Respiratory viral illness diagnosis	Blood draw	Periodically
Infectious agents	Blood draw	Periodically
Infectious agents	Stool sample	Per event
Virome profile	Blood draw	Per event

## What are the modifiable environmental risk factors for APOL1-associated kidney diseases?

**Use Case ID** 1001246

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

APOL1 susceptibility variants are found almost exclusively in individuals of African origin and account for virtually all of the disparity in risk for severe kidney disease. HIV is a known co-factor exploiting APOL1 susceptibility. What other factors explain this incomplete penetrance?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Air quality assessment results		Baseline
Residence location	Geospatial tracking	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Periodically
Diet, self-assessment	PPI Survey (AOURP)	Every 3 months

## What are the factors that influence biological age and its relationship to metabolic health?

**Use Case ID** 1001249

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

There are many instances in which biological age (as measured by DNA methylation) does not correlate with chronological age. We propose to examine all factors, such as environment and lifestyle and metabolic, that may influence biological age.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lifestyle, self-assessment	Mobile monitor	Continuous monitoring
Environment	Geographic information system (GIS) code	Continuous monitoring
Diet, self-assessment	Food diary	Every 3 months
Methylation status		Annually
Glucose levels	Blood draw	Annually
Lipids panel results	Plasma	Annually

## What is the role of nutrition in disease susceptibility or amelioration?

**Use Case ID** 1001255

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Reduce Disease Impact

NHANES has indicated a number of nutrients of concern that are being over- or under-consumed, based on DRIs. But many DRIs were based on small studies—are they valid? Does being “deficient” or in excess track with disease progression or susceptibility? Also, added sugar and fish have been implicated in many diseases and healthy aging, respectively.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Blood draw	Annually for 2 years
Diet constitution assessment	Wearable electronics	Annually for 5 years
Hydration assessment results	Mobile monitor	Every 3 months
Blood pressure	Blood pressure cuff	Every 3 months
Medical Information	Electronic Health Record (EHR)	Every 3 months
Sugar intake	Hair sample collection	Every 6 months

## Cytochrome P450 polymorphisms affect patient metabolism; would profiling CYP in large studies help predict patient outcomes?

**Use Case ID** 194796

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Establish CYP profiling as a standard part of data collection in all large studies, especially related to pain management, immunology, cardiovascular dysfunction, and pharmacology. Based upon existing research, it can be anticipated that CYP profiles and polymorphism data may partition certain studies' patient populations into groups with common outcomes (negative, positive, neutral). Regarding the opioid crisis alone, CYP awareness is of national importance, and can improve treatment/outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cytochrome P450 (CYP) phenotyping	Blood draw	Baseline
Clinical outcomes		
Pain symptom diagnosis		

## Are individuals with Down syndrome more likely to be overweight or obese? If so, why?

**Use Case ID** 195414

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Within the U.S. there are numerous people with Down syndrome. Most are overweight or obese. This research study would include finding out why individuals with Down's are overweight and if it is because of a predisposing factor that cannot be controlled, such as genetics or a modification made by the chromosomal editing. It will also look at what ways we can help those individuals with weight needs. Discovering how individuals with Down's feel about their weight and if it hurts them emotionally.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Whole Genome Genotyping (WGG)	At specified times anchored to the clinical event
Weight	Physical exam	Annually
Behavioral characteristics, self-assessment	Survey	Include child, teenager, early adult, adult, elderly
Physical activity, self-assessment	Mobile monitor	Annually

## Can we identify functional gene polymorphisms that create metabolic heterogeneity and thereby alter nutrition requirements?

**Use Case ID** 195520      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Other

By collecting information on dietary intake and genotype, identify people who have gene-related perturbations in metabolism that are revealed when they are challenged by diet. For example, a genetic signature in people causes them to have difficulty secreting VLDL (fat) from liver. This is apparent only in people consuming excess calories who are therefore producing hepatic triglyceride and their limitations in capacity to remove fat from liver becomes rate limiting.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	
Genotyping data	Blood draw	
Lipids panel results		

## Which genetic variants are associated with intentional weight loss in response to a lifestyle weight loss intervention?

**Use Case ID** 195838      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Maintain & Preserve Health

The prevalence of overweight and obesity is a worldwide epidemic. Genomic and genetic studies have advanced our knowledge through the identification of genes and susceptibility alleles that increase risk for obesity. However, it is unclear whether these variants also contribute to weight loss, as the genetic determinants of weight loss may differ. The identification of genetic predictors of intentional weight loss can improve treatment response and increase intervention efficacy.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Genotyping (WGG)	Baseline
Weight	Physical exam	At specified times anchored to the clinical event
Behavioral characteristics, self-assessment	Survey	

## What genetic biomarkers or other factors confer risk for development and progression of diabetic retinopathy?

**Use Case ID** 196590      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

Submitted by: NEI Collaborative Clinical Research Program Officers. Diabetes often leads to end-organ complications, one of which is diabetic retinopathy and vision loss. This has a significant impact on quality of life for the diabetic patient. Finding genetic determinants would be predictive for this outcome within the diabetic population and may potentially lead to therapeutic interventions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Whole Genome Genotyping (WGG)	Baseline
Prescription medication\treatment	Survey	Annually
Diet, self-assessment	PPI Survey (AOURP)	Continuous monitoring
Glucose levels	Blood draw	Continuous monitoring
Environmental samplings and exposure results	PPI Survey (AOURP)	At specified times anchored to the clinical event

## Can metabolite profiles improve disease prediction and management?

**Use Case ID** 196892      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Reduce Disease Impact

The window of opportunity for disease prevention in at-risk individuals may be before symptoms occur and blood/urine chemistries indicate a problem. Considering that one's metabolome reflects both genetic and environmental influences, could metabolite profiles be explored in the All of Us biospecimens and assessed as diagnostic tools?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Metabolomic profile	Blood draw	Continuous monitoring

## What changes involved in the progression of type 2 diabetes and development of complications are apparent at the pre-diabetic state or during the transition state?

**Use Case ID** 197380

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Changes involved in the progression of T2D and development of complications is apparent at the pre-DM state or during the transition to T2D or with complications. Conducting “omics,” including DNA methylation, metabolomics, and microbiome studies in blood, saliva, and fecal samples, allows us to validate interactions of metabolites to microbiota to epigenetic regulations.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually
Chemical exposure assessment results	Blood draw	Annually
Lipids panel results	Blood draw	Every 3 years
Microalbuminuria diagnosis	Blood draw	

## Do dietary and microbial-derived metabolites modulate body weight and contribute to overweight and obesity?

**Use Case ID** 198351

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Integrate multi-omic approaches (metabolomic, proteomic, inflammasome, and microbiome analyses) with dietary assessment and clinical data in a nested cohort study. Dietary and/or microbial metabolites may modulate body weight and may influence other comorbidities. A comprehensive analysis of inflammatory and metabolic biomarkers of oxidative stress, nutritional assessment, short-chain fatty acids, and other microbial metabolites may provide predictive markers of weight gain or obesity.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Anthropometrics, whole body measurements	Physical exam	Every 6 months for 5 Years
Diet, self-assessment	Automated Self-Administered 24-Hour (ASA24) dietary assessment	Every 6 months for 5 Years
Microbiologic specimen evaluation	Stool sample	
Metabolomic profile	Stool sample	Every 6 months for 5 Years
Bone density	Dual-energy X-ray Absorptiometry (DXA)	Every 6 months for 5 Years

## What are the microbiome-based factors that predict onset of inflammatory bowel disease?

**Use Case ID** 198509

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

Does the composition of the gut microbiome predispose an individual to inflammatory bowel disease? Multiple lines of evidence indicate that patterns of gut microbiota, detectable in stool samples, may predict onset and progression of inflammatory bowel disease. Early detection/intervention could dramatically improve outcomes. All of Us will likely enroll 40–400 healthy individuals who will be diagnosed with IBD during the study, offering an opportunity to directly address this.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Microbiome sample	Stool sample	Annually
Perceived outcomes - patient	Survey	Every 3 months
Irritable bowel syndrome (IBS) diagnosis	Electronic Health Record (EHR)	

## What are the biological, behavioral, and metabolic factors that predict response versus non-response to overactive bladder treatment?

**Use Case ID** 198570

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Treat & Cure Disease

One out of 6 adults in the U.S. (33 million) and one out of 10 worldwide (546 million) are affected by overactive bladder (OAB). Despite the high economic cost (\$82 billion by 2020), treatment response for OAB remains suboptimal. Using data from more than 1 million men and women, we will identify biological (e.g., genomics, ethnicity, medical history), behavioral (lifestyle), and metabolic factors (e.g., metabolic syndrome, obesity) that predict response versus non-response to clinical OAB treatments.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Overactive bladder diagnosis	Survey	Annually
Clinical outcomes	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Metabolic risk assessment result	Electronic Health Record (EHR)	Baseline
Lifestyle, self-assessment	PPI Survey (AOURP)	Baseline
Genomic analyses	Blood draw	Baseline

## Do genomic, epigenetic, and metabolomic characteristics explain the excess risk of type 2 diabetes (T2D) in Asian-Americans?

**Use Case ID** 198578

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

California data shows T2D prevalence is higher among Pacific Islanders, Filipinos, and South Asians, compared to Latinos, African-Americans, and Native Americans; further, Chinese, Japanese, and Koreans in California have a 50% higher risk of T2D compared to Whites. High-throughput technologies, including metabolomics and genomics, could provide valuable insight regarding the etiology of T2D disease mechanisms, as well as novel predictive biomarkers.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Diabetes type II diagnosis	Blood draw	Every 3 years
Epigenomic/epigenetic markers	Genomic testing	
Genomic ancestry	Genomic testing	

## Are there sensitive and specific biomarkers to assess isolated post-challenge hyperglycemia in Hawaiians and Asian-Americans?

**Use Case ID** 198580

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

Asian-Americans have the highest prevalence (51%) of undiagnosed type 2 diabetes (T2D), and half of Asian-Americans and Native Hawaiians with newly diagnosed T2D have isolated post-challenge hyperglycemia (iPCH). They might remain undiagnosed or experience delayed T2D if screening practices are limited to glycosylated hemoglobin and fasting plasma glucose measures. Identification of novel biomarkers to identify individuals at risk for iPCH would enhance early T2D diagnosis and management.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Isolated Post-Challenge Hyperglycemia (iPCH) diagnosis	Oral glucose tolerance test	Every 3 years
Specified Biomarkers	Blood draw	

## A genetic variation in CREBRF promotes fat storage in Samoans; are there effective interventions for those with this variant?

**Use Case ID** 198582      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Reduce Disease Impact

Obesity prevalence among Samoan Americans, including Samoan children on the U.S. mainland, are higher compared to other ethnic groups. A genetic variation promoting fat storage was observed among Samoans, but effective interventions to reduce the risk of obesity-related health outcomes among Samoans and perhaps other Pacific Islanders and Native Hawaiians with this variant require development and evaluation.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Obesity diagnosis		
Genomic analyses		

## What are the genetic, environmental, and behavioral contributions to diabetic neuropathy?

**Use Case ID** 198599      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

Peripheral neuropathy is common in persons with diabetes and those over 40 and can be measured with validated claims data. The main disease risk factors, other than hyperglycemia, are unknown. We propose a first-in-kind study to simultaneously address how behavioral (diet, exercise, sleep), environmental (air quality, food access), and genetic factors influence the development of neuropathy and whether these factors promote metabolic changes that contribute to neuropathy.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Bisphosphonate levels	Claims data	Continuous monitoring
Behavioral characteristics, self-assessment	Survey	Annually
Environmental samplings and exposure results	Personal air pollution monitor	Annually
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Metabolic risk assessment result	Blood draw	Annually

## Can molecular diagnosis of monogenic forms of digestive, renal, and metabolic disease improve treatment and prevention in themselves and family?

**Use Case ID** 1000713      **Cross-Cutting Theme** Genomics and Other Omics  
**Most Important**      **Scientific Category** Treat & Cure Disease

A small percentage (1%–3%) of adult onset common diseases (e.g., diabetes, cardiovascular diseases, neurological diseases, etc.) have monogenic causes that are underdiagnosed and mistreated. Molecular diagnosis and cascade screening of family members would enable precision medicine for improved treatment and prevention of many diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Annually
Genotyping data	Genomic testing	
Family relationships	Survey	Annually
Physical activity, self-assessment	PPI Survey (AOURP)	Every 3 months for 1 year
Health care cost	Claims data	Annually

## Can a risk profile that includes genetic and other factors better explain and predict type 2 diabetes?

**Use Case ID** 1000774      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

Genetics and other factors are a major contributor to metabolic diseases such as diabetes. Our ability to predict diabetes from genetics is poor. The ability to combine genetic information with other information may lead to better prediction, aka AHA heart risk scores.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environment	Geographic information system (GIS) code	Annually
Metabolomic profile		Annually
Metabolomic profile	Whole Genome Genotyping (WGG)	Annually
Epigenomic/epigenetic markers	Whole Genome Genotyping (WGG)	Annually
Behavioral characteristics, self-assessment	Mobile monitor	Continuous monitoring

## Why do some people with high genetic risk do not develop diabetes?

**Use Case ID** 1000788

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Maintain & Preserve Health

Forms of diabetes are associated with genetic variance (MODY, possibly high complex disease risk scores). What are the protective factors (genetic, environmental, and lifestyles) associated with not developing the disease? Having this information can inform prevention therapy.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Metabolomic profile		Annually
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Glucose levels		Annually
Anthropometrics, whole body measurements	Physical exam	Annually
Behavioral characteristics, self-assessment	Mobile monitor	Continuous monitoring
Environment	Personal air pollution monitor	Annually
Clinical outcomes	Mobile monitor	Continuous monitoring

## How does the urinary and gut microbiome impact risk for APOL1 and other inherited kidney diseases?

**Use Case ID** 1000900

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Many common complex genetic diseases do not manifest in all who inherit risk variants. This proposal assesses interactions between the urinary and gut microbe on risk for developing inherited kidney diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Relapse/recurrence	Biochemical assay	Annually
Clinical outcomes	Electronic Health Record (EHR)	Every 10 years
Virome profile	Stool sample	Every 10 years
Diet, self-assessment	Food diary	Every 10 years
Nutritional supplement use	Survey	Every 10 years
Microbiome sample	Stool sample	Every 10 years
Renal disease information	Clinical assessment	Annually
Genotyping data		Baseline

## Does beer drinking impact colonic microbiome?

**Use Case ID** 1000908      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Other

Microbiome in the GI tract may be affected by dietary choices such as fruit, vegetables, and yogurt. Knowledge of the effect of alcoholic beverages, especially beer and wine, or changes in colonic microbiome are unknown.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Diet, self-assessment	Food diary	Daily
Microbiome sample	Stool sample	Weekly

## Can genomic analysis be used to estimate the frequency of specific genetic mutations in the population?

**Use Case ID** 1000962      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Detect Disease

There are 30 million Americans with a rare disease in the U.S., inclusive of an estimated 7,000 different diseases. Rare diseases are hard to diagnose, with the average patient requiring 5 years to diagnosis. Can artificial intelligence/machine teaching/informatics strategies identify true prevalence, speed diagnosis, provide decision support and spawn new therapeutic interventions?

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Family clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Health and phenotype data	Electronic Health Record (EHR)	Annually

## In children, what are the environmental predictors of metabolic syndrome, and how are they mediated by epigenetics?

**Use Case ID** 1001107      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

Big data. Mixture analysis problem. Pre-pubertal assessment with ongoing follow-up.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Epigenomic/epigenetic markers	Blood draw	Baseline
Physical measurements	Electronic Health Record (EHR)	Annually
Chemical exposure assessment results	Wearable electronics	Continuously for 1 week quarterly
Household exposures assessment results	PPI Survey (AOURP)	Annually
Anthropometrics, whole body measurements	Tanner scale	Annually
Diet, self-assessment	Dietary assessment tool	Every 3 months

## Is a culturally-adapted version of the Diabetes Prevention Program (DPP) more effective than a non-standard version in preventing new diabetes diagnoses?

**Use Case ID** 192323

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Goals: To address the health disparities related to type 2 diabetes among racial/ethnic minorities by identifying best practices for cultural adaptation of health behavior interventions and pilot-testing evidence-based interventions with these populations. Methods: Community-based participatory research. Testing concordance of race/ethnicity of facilitators and participants. Outcomes: Increased minority participation and ownership in research that improves group and community health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Hemoglobin A1C (HbA1C) levels	Electronic Health Record (EHR)	Continuous monitoring
Diet, self-assessment	Food diary	Continuous monitoring
Weight		Continuous monitoring
Diabetes type II diagnosis		Continuous monitoring
Sociodemographics		

## What are key communication gaps in chronic kidney disease care between physicians and patients who belong to underserved groups?

**Use Case ID** 197506

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

This would be a mixed-methods study. The qualitative section would involve interviews to ascertain gaps in chronic kidney disease communication (likely risk assessment in CKD progression, information about dialysis options, mental health, advance care planning). This would be followed by surveys of patient-reported measures of communication, such as CAT (Communication Assessment Tool; <https://www.ncbi.nlm.nih.gov/pubmed/17574367>).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Perceived outcomes - patient	Survey	Baseline
Perceived outcomes - patient	Interview	

## Can we identify the reasons why women from multiple ethnicities do not seek help for lower urinary tract symptoms?

**Use Case ID** 198658

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Focus group, semistructured interviews; survey expected outcomes: individual- and system-level.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Perceived outcomes - patient	Survey	Include child, teenager, early adult, adult, elderly
Behavioral characteristics, self-assessment	Survey	
Sociodemographics		Include child, teenager, early adult, adult, elderly
Lower Urinary Tract Symptoms (LUTS) record		

## What are the best diagnostic tests and thresholds for defining type 2 diabetes in Asian-Americans?

**Use Case ID** 198736

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Detect Disease

Traditionally, occurrence of microvascular disease (retinopathy) has been used to define the glucose threshold by which diabetes should be defined. But these studies have come from mostly white/European/Middle Eastern populations. Do all ethnic groups have similar thresholds for diagnosis? Are certain diagnostic tests better for making the diagnosis of diabetes than others in select race/ethnic groups? The pathophysiology of type 2 diabetes may differ, and we need to define subtypes of T2DM.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Glucose levels		
Glucose levels		Every 2 years
Hemoglobin A1C (HbA1C) levels		

## Why is gestational diabetes (GDM) risk highest among select Asian-Americans despite the absence of preconceptional obesity?

**Use Case ID** 198770

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

Gestational diabetes prevalence is higher among Asian Indians, Filipinos, Southeast Asians, and Chinese compared with White, Black, and Hispanic parturients, despite the absence of preconceptional obesity. Dissecting the etiology of elevated GDM risk in these Asian-American subgroups and evaluating effective interventions (other than weight management) to prevent GDM and reduce future risk of type 2 diabetes are urgently needed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy characteristics	Electronic Health Record (EHR)	
Gestational Diabetes Mellitus (GDM) diagnosis	Blood draw	
Genotyping data	Blood draw	

## Can foot amputation be prevented in diabetics with AI-powered diagnosis?

**Use Case ID** 198778

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Foot amputation is a major problem in diabetics in the South Asia. A small blister or ulcer in the foot can develop into a major complication where the foot/toe needs to be amputated. Due to lack of sensation in the foot, most of the time the injuries are unnoticed. An AI-powered solution that involves sensors and certain preliminary tests to prematurely detect the risk of foot amputation in diabetics at an earlier stage would contribute a lot to reduce complications that might occur.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diabetes diagnosis	Electronic Health Record (EHR)	Continuous monitoring
Hemoglobin A1C (HbA1C) levels	Blood draw	At specified times anchored to the clinical event
Diabetes outcomes	Custom sensor/app	Continuous monitoring

## What genetic and environmental risk factors contribute to racial or ethnic disparities in risk for type 2 diabetes?

**Use Case ID** 1000733      **Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access  
**Most Important**      **Scientific Category** Elucidate Disease Mechanisms

Major health disparities exist in prevalence of T2 diabetes cross the U.S., and both genetic and environmental factors contribute to risk. Using existing GWAS data to define genetic risk scores to assess specific environmental risk factors that modify risk for T2D (and this can further include syndrome X, adiposity, etc.). Comparison of genetic risk across population groups could also be performed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Every 2 years
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Family clinical outcomes	Genomic testing	Baseline
Physical activity, self-assessment	Mobile monitor	Every 2 years
Environmental assessment results	Geospatial tracking	Every 2 years
Blood sample characteristics	Blood draw	Baseline
Diabetes type II diagnosis	Clinical assessment	Annually

## What combination of care providers (Home health, social networks health care, social work) leads to the best outcomes for persons with diabetes?

**Use Case ID** 1000810      **Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access  
**Most Important**      **Scientific Category** Other

Who else is providing care to the individual, and how does that impact disease severity?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Access to health care	Electronic Health Record (EHR)	Continuous monitoring
Access to health care	PPI Survey (AOURP)	Annually
Glucose levels	Electronic Health Record (EHR)	Annually
Prescription medication\ treatment	Claims data	Annually

## What are the impacts of the gender transition process on metabolic health outcomes?

**Use Case ID** 1000846

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

The metabolic impacts of transitions between gender are currently unknown. The All of Us study has potential to include sufficient numbers of participants engaged in this process to fully assess the immediate and long-term effects of transition on metabolic health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Electronic Health Record (EHR)	Continuous monitoring
Metabolic risk assessment result	Blood draw	Every 6 months
Weight	Physical exam	Annually
Androgens levels		Every 6 months
Gender transition	Electronic Health Record (EHR)	During clinic visits

## What is the prevalence of reporting typed sexual orientation and gender identity, and do these change over time?

**Use Case ID** 1000927

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Most Important Scientific Category** Other

Limited data on prevalence of sexual orientation and gender identity in the U.S. population. Do these differ by age, race/ethnicity, environment (region, urban/rural, etc.)? Do these change over time?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Sexual orientation	PPI Survey (AOURP)	Annually
Gender identity	PPI Survey (AOURP)	Annually

## What is the impact of childhood trauma on diabetes self-management behaviors and outcomes among individuals?

**Use Case ID** 1001056

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

Trauma patients' physiological and mental health. These will impact how individuals practice self-management behaviors that have short- and long-term health outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Anthropometrics, whole body measurements	Electronic Health Record (EHR)	Annually
Social environment	Survey	Baseline
Trauma events	Survey	Annually
Blood sample characteristics	Electronic Health Record (EHR)	Annually
Medical Information	Electronic Health Record (EHR)	Continuous monitoring
Depression diagnosis	PPI Survey (AOURP)	Annually
Mental and psychosocial health, self-assessment	Mobile monitor	Continuous monitoring
Depression diagnosis	Electronic Health Record (EHR)	Baseline

## What is the prevalence of reporting type of sexual orientation and gender identity, and do these change over time?

**Use Case ID** 1001139

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

Limited data on prevalence of a sexual orientation and gender identity in the U.S. population. Do these differ by age, race, ethnicity or not (urban, rural, etc.)? Do these change over time?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Sexual orientation	PPI Survey (AOURP)	Annually
Gender identity	PPI Survey (AOURP)	Annually

## Is there a difference in diabetes incidence and complication of diabetes in immigrant versus natively born populations?

**Use Case ID** 1001140

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Where one is born and lives plays a role in diabetes disparities (for example, Native American in U.S. versus Mexico). How does diabetes incidence change when immigrating to the U.S.?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Diabetes diagnosis	Electronic Health Record (EHR)	Continuous monitoring
Medical Information	Electronic Health Record (EHR)	Continuous monitoring
Specified Biomarkers	Electronic Health Record (EHR)	Continuous monitoring
Prescription medication\ treatment	Claims data	Continuous monitoring

## Does the frequency of visits to a primary care doctor delay the risk of conversion from pre-DM to DM?

**Use Case ID** 1001152

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Access to care through visits to primary care may help and delay the progression of pre-diabetes via improved behaviors and medication management. However, understanding factors that affect access are needed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Glucose levels	Blood draw	Annually
Health care participation	Electronic Health Record (EHR)	Continuous monitoring
Location data	Geographic information system (GIS) code	Continuous monitoring
Health literacy	Survey	Baseline
Health care cost	Survey	Annually
Gestational Diabetes Mellitus (GDM) diagnosis	Clinical assessment	Monthly

## What are the effects of cross-sex hormones in the development of obesity and metabolic syndrome in non-cisgender people?

**Use Case ID** 1001158

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Detect Disease

Some non-cisgender (e.g., transgender, gender non-conforming) people take exogenous hormones as part of their medical transition. The effects of these cross-sex hormones on the development of obesity/metabolic syndrome is unknown.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Hormone levels (non-steroidal)	Electronic Health Record (EHR)	Annually
Specified Biomarkers	Electronic Health Record (EHR)	Continuous monitoring
Physical measurements	Electronic Health Record (EHR)	Continuous monitoring
Sex at birth	PPI Survey (AOURP)	Baseline
Physical measurements	PPI Survey (AOURP)	Annually
Hormone therapy	Electronic Health Record (EHR)	Annually

## What is the optimal travel time and distance to medical care for control of metabolic disease?

**Use Case ID** 1001205

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Treat & Cure Disease

Travel impedance can reduce patient willingness to seek routine care and may also reduce time/attention during visit, thus reducing knowledge of medical instructions. The threshold for adverse event outcomes is not known.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Location data	Geographic information system (GIS) code	Annually
Mental and psychosocial health, self-assessment	Survey	Annually
Health and phenotype data	Survey	Annually
Location data	Survey	Annually
Metabolic disease diagnoses	Electronic Health Record (EHR)	Annually

## How can modern data science methods be utilized to detect the latent structure of metabolic syndrome in at-risk populations?

**Use Case ID** 198504

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Detect Disease

This project will use innovative data science methods to detect metabolic syndrome, as part of personalized medicine, to mitigate confusion about what criteria are salient when diagnosing an individual with metabolic syndrome. Data required would be on variables related to diabetes/metabolic syndrome (triglycerides, metabolic risk profile, HbA1c). The result of this project will be population-specific descriptions of criteria useful for diagnosing patients at risk of metabolic syndrome.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Hemoglobin A1C (HbA1C) levels	Blood draw	Baseline
Lipids panel results		Baseline
Metabolic risk assessment result	Blood (EDTA)	

## Can we identify subtypes of diabetes?

**Use Case ID** 1000946

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Elucidate Disease Mechanisms

Diabetes and hyperglycemia are not a uniform phenotype. Can we create subtypes based on molecular, physiological, or other characteristics? Is All of Us the best study, or would this be better addressed in an existing larger cohort of diabetes?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diabetes diagnosis	Electronic Health Record (EHR)	Continuous monitoring
Genotyping data	Whole Genome Genotyping (WGG)	Baseline
Biological Specimens	Clinical diagnostic test	Every 10 years
Medical Information	Electronic Health Record (EHR)	Baseline
Behavioral characteristics, self-assessment	Electronic Health Record (EHR)	Baseline
Anthropometrics, whole body measurements	Electronic Health Record (EHR)	Baseline
Prescription medication\ treatment	Prescription drug records	Baseline
Omics	Specimen collection	Baseline

## Can we build an AI predictor of health disparities in diabetes?

**Use Case ID** 1001076

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Assess Risk

Who is a population that is underserved or might have health disparities? It is difficult to identify populations or recruit individuals of underserved populations in diabetes—can we build informatics tools to identify these people for recruitment?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Personal Characteristics	Survey	Annually
Geocode data	Survey	Annually
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Diabetes diagnosis	Clinical diagnostic test	Continuous monitoring
Specified Biomarkers	Electronic Health Record (EHR)	Continuous monitoring
Health care participation	PPI Survey (AOURP)	Annually

## Do self-reported nocturia episodes correlate with actual nighttime visits to the toilet, and what is the natural history of nocturia?

**Use Case ID** 195836

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Reduce Disease Impact

Nocturia is highly prevalent and has significant impact on quality of life. Therapeutic interventions often reduce nocturia episodes by less than one episode per night and rely on self-reported data to quantify efficacy. This study will identify a cohort with nocturia and compare self-reported nocturia to actual nighttime visits to the toilet as recorded by wearable technology, and will follow over time. We hypothesize that self-report may not be a reliable measure of nighttime voiding episodes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Nocturia diagnosis	Mobile monitor	
Nocturia diagnosis	Survey	
Treatment/Therapy	Electronic Health Record (EHR)	
Sleep quality assessment results	Mobile monitor	
Quality of life	Survey	*GC

## Can an app that measures diet correlate to a 24-hour urinary sodium test result?

**Use Case ID** 1000779

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Assess Risk

High sodium intake correlates with hypertension (D5 cardiovascular/risks associated); 24-hour urine collections are burdensome to complete; mobile dietary tracking app may be a viable substitute to the 24-hour urinary sodium test and improve medical management.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Blood pressure	Electronic Health Record (EHR)	Continuous monitoring
Diet, self-assessment	Mobile monitor	Continuous monitoring
Creatine levels	Electronic Health Record (EHR)	Continuous monitoring

## Can we develop a mobile technology to evaluate the findings of a urinalysis dipstick and assess the risk of disease?

**Use Case ID** 1001031

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Assess Risk

Urinalysis is an easy, cheap assessment that can be done at home by multiple individuals. Being able to transmit the results of urinalysis via mobile technology can be useful in diagnosing albuminuria, kidney disease, urinary tract infections. A visual or biochemical assessment that can be measured at home.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Every 3 months
Medical Information	Electronic Health Record (EHR)	Every 6 months
Small molecules and ion levels	Electronic Health Record (EHR)	Annually
Anthropometrics, whole body measurements	Physical exam	Annually
Cardiovascular disease information	Clinical assessment	Every 3 months

## Does sleep or other lifestyle behaviors impact metabolic health?

**Use Case ID** 1001086

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Maintain & Preserve Health

It is known that lifestyle behaviors affect diabetes, but details are not known. It is also not known if this varies across racial/ethnic groups.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Medical Information	Biochemical assay	Annually
Physical activity, self-assessment	Mobile monitor	Continuous monitoring
Mental and psychosocial health, self-assessment	Survey	Continuous monitoring
Environment	Social network mining	Continuous monitoring
Personal Characteristics	Survey	Continuous monitoring
Diabetes diagnosis	Electronic Health Record (EHR)	Continuous monitoring

## What is the impact of fluid intake on health?

**Use Case ID** 195117

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

There is a fluid intake range that is healthy. Below this level predisposes to urinary tract infections, urinary stone formation, changes in the gut and urinary micro biome, and results in generalized symptoms of well-being. Fluid intake above a healthy threshold predisposes to lower urinary tract symptoms, sleep interruptions, and may affect symptoms of well-being.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Fluid intake	Beverage Intake Questionnaire (BEVQ-15)	Annually
Urination frequency	Urination diary	Annually
Health and phenotype data	Electronic Health Record (EHR)	Annually
Urinary biome sample	Urine collection	Annually

## Does formula use in babies result in obesity in those individuals in adulthood?

**Use Case ID** 195121

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Background: I have heard of a theory that the abundance of food/nutrition in infant stages alters how the individual metabolizes food later in life. As a mother, I have observed my babies working harder when nursing compared to when being bottle fed. This may indicate that formula-fed babies drink more (abundance) and that may change how they eat and the volume and storage of fat. Trace both sets of individuals (obese vs. healthy weight range) retrospectively to see if they were given formula as infants.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Weight	Survey	Include child, teenager, early adult, adult, elderly
Body Mass Index (BMI)	Electronic Health Record (EHR)	Baseline
Infant formula use	Survey	

## Can we use precision nutrition to create microbiomes to ameliorate healthy gut to eliminate gastrointestinal disorders and use of antibiotics?

**Use Case ID** 195277

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Treat & Cure Disease

Use food sensitivity testing: blood, saliva, stool samples. Track food, stool types, and compare to food sensitivities. Eliminate sensitive foods from diet and track. Determine additions to diet to rebuild healthy microbiomes in the gut (e.g., supplements, vitamins, probiotics or stool transplants, eliminate use of antibiotics). The goal would be to create individualized nutritional plans to improve gut health, lose weight, and decrease use of antibiotics to treat GI disorders/disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Blood draw	
Microbiome sample		
Food intolerance diagnosis	Saliva	
Gastrointestinal health information		

## Does congenital sarcosinemia reduce the risk of depression?

**Use Case ID** 195325

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Congenital sarcosinemia is a rare metabolic condition characterized by elevated levels of sarcosine in the blood and bodily fluids caused by an enzyme defect. It appears to be essentially harmless. Sarcosine has recently shown promise as an atypical antidepressant with no apparent side effects and a higher rate of efficacy than citalopram. A simple study would involve using a database of known sarcosinemia patients, asking whether they have been depressed, and comparing with matched controls.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Depression diagnosis	PPI Survey (AOURP)	Baseline
Sarcosinemia diagnosis	Survey	Baseline

## Does a diet high in carbohydrates contribute to obesity and diabetes?

**Use Case ID** 195499

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The typical American diet, defined by high quantities of processed carbohydrates, and not high fat, has led to an obesity epidemic in the United States and to skyrocketing diabetes. I propose to analyze the number of carbohydrate grams consumed in two test groups, the typical American diet (control) and test subjects who identify themselves as “keto” or “low carb” to confirm that a low-carbohydrate diet is the key to weight control and diabetes control.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Food diary	Continuous monitoring
Weight	Physical exam	Baseline
Health and phenotype data	Electronic Health Record (EHR)	

## What types of data might be useful in helping to improve recommendations on nutrient intakes for an individual?

**Use Case ID** 195701

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

If specific nutrients are linked to specific disease/health outcomes, then to what extent (if any) is ancestry, sex, age, weight, physical activity, dietary patterns (and supplement use), and/or zip code (environmental stressors) expected to impact an individual's physiological needs/requirements for a specific nutrient(s)? Consider the use of regression models to determine which factors (in synergy and/or in isolation) show the greatest association to health outcomes and nutritional status.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	
Clinical outcomes	Electronic Health Record (EHR)	
Environmental samplings and exposure results	PPI Survey (AOURP)	
Sociodemographics	PPI Survey (AOURP)	
Geocode data	Survey	

## Are stomach ulcers only related to stress, or can it be caused by oral bacteria?

**Use Case ID** 195798

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

A study would be done on patients who had ulcers in the past and patients who currently have ulcers. We would analyze the size and severity of the ulcer, while observing the patient's oral hygiene by taking samples of saliva and checking for plaque and tarter build-up. Different stress factors would be measured by a questionnaire and by physical examinations. All factors would be measured to test their relations with stomach ulcers.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Dental and oral data	Dental records	Include child, teenager, early adult, adult, elderly
Stress	Survey	
Ulcer diagnosis	Electronic Health Record (EHR)	

## Does weight gain negate the beneficial effects of eating healthy foods?

**Use Case ID** 195912

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Adult weight gain and obesity increase risks of chronic diseases. The effects of a positive energy balance could outweigh any beneficial effects of foods associated with reduced health risks such as vegetables, whole grains, and omega-3 fatty acids. In subsets of adults who are either gaining weight or maintaining weight over time, does the impact of diet quality on health risks differ? Diet could be quantified by various diet indices such as the Healthy Eating Score or an Inflammatory Index.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Every 2 years
Weight	Physical exam	Annually
Hemoglobin A1C (HbA1C) levels	Blood draw	Every 2 years
C-Reactive Protein (CRP) levels	Blood (EDTA)	Every 2 years
Cancer information	Electronic Health Record (EHR)	Every 2 years

## How well do recipients of weight-loss surgery believe they were informed of the risks and restrictions the surgery poses?

**Use Case ID** 196494

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

WLS poses a variety of risks as well as a very specific set of restrictions: initially a highly restricted diet that relaxes over time. These risks/restrictions carry with them an emotional and sociocultural cost that is difficult to convey. I propose juxtaposing provider expectations of patient knowledge about risks and restrictions with patient reflections on the nuanced meaning of same. What do patients wish they'd known before surgery and how can this be provided to future patients?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Perceived outcomes - patient	Survey	At specified times anchored to the clinical event
Perceived outcomes - surgeon	Survey	At specified times anchored to the clinical event
Diet, self-assessment	Food diary	Periodic (approximately biweekly)
Perceived outcomes - patient		At specified times anchored to the clinical event
Perceived outcomes - patient		

## What characteristics are associated with maintenance of increased water intake in persons with urinary stone disease?

**Use Case ID** 196586

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Increased water intake reduces stone recurrence, but maintaining increased intake is challenging. Via the EHR and qualitative/quantitative methods, we will identify person and intervention characteristics associated with maintenance of increased intake to determine factors that facilitate intervention success and/or enable targeted interventions. Findings may provide insights into strategies for maintenance of behavior change that could be adapted in other conditions and/or behaviors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Urinary Stone Disease diagnosis	Electronic Health Record (EHR)	
Fluid intake	Mobile monitor	
Fluid intake		
Social determinants of health (SDH)	PPI Survey (AOURP)	
Geocode data	Survey	

## How do fluctuations in HbA1c impact long-term health outcomes? What are the primary causes of these fluctuations?

**Use Case ID** 197063

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

A longitudinal survey design to correlate HbA1c fluctuations over time to clinical outcomes in patients with type 2 diabetes. Literature demonstrates that most patients' A1c moves in and out of control over time. This proposal seeks to correlate these fluctuations with clinical outcomes and identify contributing factors to changes in A1c levels. By identifying these factors, education and support mechanisms can be developed to help patients maintain A1c levels.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Hemoglobin A1C (HbA1C) levels	Blood draw	Every 3 months
Weight	Survey	Periodic (approximately biweekly)
Diet, self-assessment	Food diary	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Annually
Depression diagnosis	PPI Survey (AOURP)	Every 3 months

## Can we identify potential causes of and best treatments for genital lichen sclerosis?

**Use Case ID** 197296

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Follow sufficient numbers of individuals, examine predisposing factors, examine biopsy results if data collection allows, and compare trajectories of different treatment courses. Examine how pregnancy and menopause influence symptoms for females (many note that symptoms improve during pregnancy—why is this?).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genital lichen sclerosis diagnosis	Electronic Health Record (EHR)	
Treatment effectiveness		
Pregnancy characteristics		
Menopause information		

## Is there an association between the human oral and fecal microbiota and chronic disease risk, such as cancer and diabetes?

**Use Case ID** 197351

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

There is a growing appreciation for the importance of the human microbiota to disease. However, it is unknown whether microbial changes occur before disease development or due to the disease. We propose collecting oral and fecal samples at baseline with additional sampling as feasible. We would assess whether baseline microbial factors or microbial changes between baseline and one year are associated with risk of adverse health outcomes such as cancer, diabetes, and overall mortality.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Microbiologic specimen evaluation	Stool sample	Annually
Health and phenotype data	Electronic Health Record (EHR)	Continuous monitoring
Cancer information	Electronic Health Record (EHR)	Continuous monitoring
Clinical outcomes	Death records	Continuous monitoring
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually

## ***Is the human oral and fecal microbiota associated with chronic disease risk factors, such as obesity and metabolic syndrome?***

**Use Case ID** 197352

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The human microbiota has been found to be associated with a number of health conditions, such as obesity. However, these studies have been relatively small and from convenience samples. It is important to understand how the human microbiota impacts these chronic disease risk factors in order to prevent future disease development. We propose collecting oral and fecal samples to determine associations with many chronic disease risk factors such as obesity, fatty liver disease, and smoking.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Microbiologic specimen evaluation	Stool sample	Annually
Health and phenotype data	Electronic Health Record (EHR)	Continuous monitoring
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually
Microbiologic specimen evaluation	Saliva	

## ***How can we improve dietary intake assessment methods?***

**Use Case ID** 197535

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Other

Currently, nutrition assessment focuses on self-reports, which has numerous measurement errors, including self-reported bias and recall bias. To accurately associate dietary intakes with nutritional status and chronic disease risk, objective measures of nutrient intakes are needed. Both recovery and predictive biomarkers offer promise, as well as emerging technologies. Research that would leverage All of Us participants for dietary and nutrient assessments is needed.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Diet, self-assessment	PPI Survey (AOURP)	

## What types of physical activity are associated with an increase or decrease in the risk of urinary symptoms in older adults?

**Use Case ID** 197725

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Lower urinary tract symptoms (LUTS; e.g., incontinence, overactive bladder, slow urinary stream) negatively affect the quality of life of many individuals as they age, yet some people never experience LUTS. Different types of physical activity (e.g., walking versus heavy lifting) may protect against or increase the risk of LUTS. We propose to identify people >65 years old with and without LUTS and identify how physical activities performed for work/recreation over time may be associated with LUTS.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lower Urinary Tract Symptoms (LUTS) record	Survey	Baseline
Physical activity, self-assessment	PPI Survey (AOURP)	Baseline
Quality of life	Survey	Baseline
Lifestyle, self-assessment	PPI Survey (AOURP)	Baseline

## What factors are associated with albuminuric and non-albuminuric diabetic kidney disease and with the estimated glomerular filtration rate reduction over time?

**Use Case ID** 198157

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Diabetic kidney disease (DKD) is the leading cause of end-stage renal disease (ESRD), the most serious and expensive stage of chronic kidney disease (CKD). Pre-ESRD stages of CKD are also associated with significant health care burden. DKD can progress to ESRD with or without albuminuria. Better understanding of risk factors attributable to the development of albuminuric and non-albuminuric DKD and to their progression to ESRD will help identify interventions to improve the management of DKD.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Creatinine levels	Blood draw	Continuous monitoring
Microalbuminuria diagnosis	Urine collection	Continuous monitoring
Sociodemographics	PPI Survey (AOURP)	Continuous monitoring
Prescription medication\ treatment	Prescription drug records	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring

## **What characteristics are associated with urinary stone recurrence in persons with prior episodes of urinary stone disease?**

**Use Case ID** 198245

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Urinary stone disease is burdensome and costly and frequently recurs. Via the EHR and qualitative/quantitative methods, we will identify person and intervention characteristics associated with urinary stone recurrence. Factors associated with recurrence may provide potential treatment targets for preventing stone recurrence.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Urinary Stone Disease diagnosis	Electronic Health Record (EHR)	
Fluid intake	Mobile monitor	
Urine acidity	Clinical diagnostic test	
Social determinants of health (SDH)	PPI Survey (AOURP)	
Urinary stone type	Electronic Health Record (EHR)	

## **What is the long-term impact of consumption of organic foods on health outcomes?**

**Use Case ID** 198473

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Organic foods are thought to be healthier than conventional foods because of the limited exposure to pesticides and other chemicals. Few studies have examined the long-term health effects of organic foods. By collecting information on organic food consumption and comparing those who tend to consume more organic foods (e.g., organic fruits/vegetables) with those who consume less, we could evaluate the impact of organic food consumption on the incidence of diseases, such as cancer and Parkinson's disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Organic diet	Survey	Every 2 years
Cancer information	Electronic Health Record (EHR)	
Parkinson's Disease diagnosis	Electronic Health Record (EHR)	
Pesticides exposure assessment results	Survey	

## Why assess diet and dietary supplements in the population?

**Use Case ID** 198476

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

More than half of U.S. adults and one-third of children take at least one dietary supplement. Combined with intakes of foods, total nutrient intake can be estimated and linked to health outcomes in etiologic research. Such population data can inform guidance, such as the Dietary Guidelines for Americans and Dietary Reference Intakes. Supplements may be warranted for subgroups where nutritional requirements may not be met through diet alone. ODS's recommendation: 2–4 dietary recalls and 1 FFQ per year.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Food diary	Annually
Sociodemographics	PPI Survey (AOURP)	Baseline
Weight	Physical exam	Annually
Vitamin D levels	Blood draw	Baseline
Physical activity, self-assessment	PPI Survey (AOURP)	Annually

## What are the biological, environmental, and behavioral factors associated with the longitudinal trends of interstitial cystitis?

**Use Case ID** 198571

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Interstitial cystitis (IC) is defined by the hallmark symptoms of chronic pelvic or bladder pain, often accompanied by urgency or frequency of urination. Using data from more than 1 million men and women, we will examine the natural history and longitudinal trends of IC symptoms over 10 years in a diverse population that is traditionally underrepresented in IC research. We will also examine the biological, environmental, and behavioral factors associated with the longitudinal trends of IC symptoms.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Interstitial cystitis	Survey	Annually
Pain symptom diagnosis	Survey	Annually
Environmental samplings and exposure results	Mobile monitor	Continuously for 1 week duration at 1 month, 6 months, and 1 year
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually
Sociodemographics	PPI Survey (AOURP)	Baseline

## What are the biological and behavioral factors that predict mesh complications after sling for stress urinary incontinence?

**Use Case ID** 198602

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Stress urinary incontinence (SUI) is prevalent among women, yet the standard of care treatment—midurethral mesh sling—can lead to devastating mesh complications (dyspareunia that precludes sex, chronic pelvic pain, infection). Using national data, we will identify biological (e.g., genomics, vaginal and urinary microbiome, race, comorbidities, metabolic syndrome) and behavioral (e.g., smoking, physical activity) factors that predict mesh complications after midurethral sling treatments for SUI.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Baseline and annually
Urinary biome sample	Urine collection	At specified times anchored to the clinical event
Genomic sequence data	Blood draw	At specified times anchored to the clinical event
Physical activity, self-assessment	Mobile monitor	Continuously for 1 week duration at 1 month, 6 months, and 1 year
Metabolic risk assessment result	Survey	Baseline

## Are the risk factors of friction/shear forces being adequately addressed in people with diabetes, to protect skin integrity?

**Use Case ID** 198613

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Diabetes places people at risk for problems with skin integrity and complications that can risk the patient's limbs and life. Friction and shear forces are known extrinsic factors in pressure injuries and diabetic foot wounds, but they are not consistently addressed as part of the treatment plan. This can contribute to complications and a higher cost of care. Better understanding of this gap in treatment may allow increased access to known therapeutic interventions that reduce these factors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\ treatment	Electronic Health Record (EHR)	Annually
Treatment/Therapy (other than Drug use)	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Outcomes	Survey	At specified times anchored to the clinical event

## What is the relationship between urinary urgency symptoms and heart failure?

**Use Case ID** 198661

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

Longitudinal study of newly diagnosed heart failure in adult men and women; sex difference in prevalence, incidence, and severity; progression of urinary symptoms; urinary urgency, severity; fatigue; and toileting behaviors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cardiovascular disease information	Blood draw	Every 3 months
Clinical outcomes	Physical exam	
Fatigue symptom	Survey	Every 3 months
Urination frequency		

## Is there a correlation between different transit mode use and body mass index?

**Use Case ID** 198667

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Goal: To determine whether transit mode choice and travel time is associated with BMI and health status, identify 3 neighborhoods with similar average incomes but different transport options and select a random sample of households from each neighborhood. One adult provides info on transit choice, travel time, destination distance, BMI, and health status. Expected outcome: Among similar income levels, adults who drive less have lower BMI and fewer health conditions than those who drive.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Travel choice	Smartphone-based ecological momentary assessment	Continuous monitoring
Weight	Survey	Baseline
Lifestyle, self-assessment	PPI Survey (AOURP)	Baseline
Health and phenotype data	Electronic Health Record (EHR)	
Body Mass Index (BMI)	Electronic Health Record (EHR)	

## Can we understand the pathogenesis of lipedema so as to differentiate between obesity and lymphedema?

**Use Case ID** 198764

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

Lipedema is an underdiagnosed or misdiagnosed adipose disorder that is often mistaken for obesity or lymphedema. It is estimated that 1 out of 9 adult females suffer from this fat disorder that is marked by an abnormal deposition of fat in the lower body that is resistant to diet and exercise. Research into the pathogenesis of lipedema would lead to better diagnostic methods and treatment modalities. Genetics are thought to play a role, as are estrogen and inflammation of SAT.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Physical exam	Every 3 months
Estradiol (E2) levels	Blood draw	Every 3 months

## What are the key genotypic, environmental, and other characteristics that define various types of diabetes mellitus?

**Use Case ID** 1000747

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important Scientific Category** Detect Disease

DM is a large public health problem. Current classification are inadequate to identify persons with DM and the spectrum of disease including the development of DM related complications (e.g., vascular, neuropathy,

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Metabolic risk assessment result	Electronic Health Record (EHR)	Continuous monitoring
Risk factors, self-assessment	Electronic Health Record (EHR)	Continuous monitoring
Physical measurements	Electronic Health Record (EHR)	Continuous monitoring
Genomic sequence data	Genomic testing	Baseline
Family clinical outcomes	PPI Survey (AOURP)	Annually
Clinical outcomes	PPI Survey (AOURP)	Annually
Physical activity, self-assessment	PPI Survey (AOURP)	Annually
Social determinants of health (SDH)	Imaging	Annually
Visceral adipose tissue distribution	Imaging	Every 3 years
Environment	Electronic Health Record (EHR)	Annually
Prescription medication\treatment	Claims data	Continuous monitoring

## What are the biological, medical, genetic, environmental, and behavioral factors associated with sexual dysfunction in males and females?

**Use Case ID** 1000786

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Sexual dysfunction is common yet poorly understood. Data are needed on risk factors (see above) and may differ by sex, race/ethnicity.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Clinical outcomes	Survey	Annually

## What urinary or vaginal microbiome characteristics are associated with onset or change in lower urinary tract symptoms?

**Use Case ID** 1000804

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

LUTS (urinary incontinence, frequency, urgency, dysuria, UTIs) are common in women and men and increase with age. Is there an association with urinary and vaginal (women) microbiomes and LUTS? Does it change over time (for example, with menopause in women)? Is it affected by genetics?

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Urinary biome sample		Annually
Lower Urinary Tract Symptoms (LUTS) record	Survey	Annually
Vaginal microbiome sample		Annually
Urinary tract infection (UTI) diagnosis	Urine collection	Annually
Urinary Stone Disease diagnosis	Urine collection	Annually

## How does metabolic disease change with age?

**Use Case ID** 1000839

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

When does it start? How does it progress? Focus on metabolic syndrome.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Anthropometrics, whole body measurements	Patient-reported outcome	Annually
Metabolic risk assessment result	Electronic Health Record (EHR)	Daily
Inflammation biomarkers levels	Clinical diagnostic test	Every 10 years
Diet, self-assessment	Custom sensor/app	Every 10 years
Health care participation	PPI Survey (AOURP)	Every 10 years
Lifestyle, self-assessment	PPI Survey (AOURP)	Every 10 years

## Can the estimated glomerular filtration (GFR) rate be optimized for all individuals using genetic determinants?

**Use Case ID** 1000852

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Current GFR estimators are based on broad racial categorizations. Can they be updated to reflect the racial diversity of the U.S.?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Creatine levels	Electronic Health Record (EHR)	Continuous monitoring
Sociodemographics	Electronic Health Record (EHR)	Annually
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring

## What is the association between urinary incontinence, overactive bladder, sleep disturbance, and falling or fracture?

**Use Case ID** 1000868      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

Urinary incontinence (UI) and sleep disturbance are common and increase with age. UI is a strong risk factor for falling and fracture (increases with age). Data are needed on the association of these three conditions and whether treating/improving UI and sleep quality decreases falling and fracture.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lower Urinary Tract Symptoms (LUTS) record	Survey	Annually
Sleep quality assessment results	Survey	Annually
Incontinence diagnosis	Electronic Health Record (EHR)	Annually
Overactive bladder diagnosis	Electronic Health Record (EHR)	Annually
Fall Events	Electronic Health Record (EHR)	Annually

## What are genetic factors predicting diabetes?

**Use Case ID** 1000870      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Maintain & Preserve Health

Nucleic acid sequence controls expression; understanding sequence—one piece of disease risk assessments.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Genomic testing	Baseline
Epigenomic/epigenetic markers	Genomic testing	Baseline
Family clinical outcomes	Interview	Periodically
Diabetes diagnosis	Electronic Health Record (EHR)	Periodically

## What is the predictive factors for progression of cyst growth in kidney disease?

**Use Case ID** 1000877      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

Kidney disease such as PKD can be a lifelong disease with impact on family members. Predictive factors would help understanding the outcome and maintain QOL and decision-making for dialysis versus transplant.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Specified Biomarkers	Blood draw	Annually
Personal Characteristics	Survey	Annually
Physical measurements	Electronic Health Record (EHR)	Annually
Genotyping data	Whole Genome Sequencing (WGS)	Annually
Sonogram	Ultrasound	Annually

## What are other health conditions' and treatment effects' impact on development and complications of diabetes?

**Use Case ID** 1000893      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

Look for interaction effects of other disease and treatment on outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care cost	Claims data	Annually
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Personal Characteristics	Electronic Health Record (EHR)	Every 3 months
Mobile phone ownership	Electronic monitoring/recording	Daily

## Can self-reported diet assessments be adopted to an artificial intelligence (AI) platform using the Alexa app and NDSR diet assessment program converted to a verbal format?

**Use Case ID** 1000929      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Most Important**      **Scientific Category** Assess Risk

Accurate dietary assessment is crucial to understanding the role of diet in development and nonpharmacologic treatment of chronic disease. Multiple 24-hour records are the preferred approach but limited due to burden, expense, and complexity. Conversion of NDSR (University of Minnesota) to a verbal format using an AI approach such as the Alexa app could permit participants to simply convey their dietary intake with this approach to capture more detailed, quantified, and specific intake with validated methodology combined with modern technology.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet constitution assessment	Activities Completed over Time in 24 Hours (ACT-24)	Continuous monitoring
Behavioral characteristics, self-assessment	Survey	Continuous monitoring
Metabolic risk assessment result	Specimen collection	Annually
Nutritional supplement use	Survey	Daily
Diet, self-assessment	Nutrition Data System for Research (NDSR) program	Annually

## What are largest environment and lifestyle factors predicting diabetes and complications?

**Use Case ID** 1000941

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Onset of diabetes and outcomes vary—what is the impact of environment and lifestyle?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Annually
Physical activity, self-assessment	Wearable electronics	Periodically
Diabetes outcomes	Electronic Health Record (EHR)	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually
Environment	Survey	Annually

## Can nontraditional behavioral factors reliably predict development of weight gain and obesity?

**Use Case ID** 1000952

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Nontraditional risk factors (see PPEs) are difficult to measure in large cohort studies. These NTBRFs can add to the predictors of developing overweight and obesity.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	PPI Survey (AOURP)	Annually
Diet, self-assessment	Food Acquisition and Purchase Survey (FoodAPS)	Annually
Body Mass Index (BMI)	Physical exam	Annually

## What is the major risk distinguishing normal weight diabetes from obese diabetes?

**Use Case ID** 1000987

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Both individuals that are of normal weight or obese develop diabetes. We will try to understand the genetic, environmental, behavioral and sociodemographic factors that determine diabetes risk in normal-weight or obese individuals.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Every 3 months
Medical Information	Electronic Health Record (EHR)	Annually
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Personal Characteristics	Survey	Annually
Personal Characteristics	Electronic monitoring/recording	Every 3 months
Medical Information	Clinical assessment	Annually

## How can one predict individuals that will have the greatest benefit from lifestyle interventions?

**Use Case ID** 1001001

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

The general population is interested in understanding which specific lifestyle changes they can make which can impact their health and wellness. If one could identify biomarkers associated with response to lifestyle choices, it would be easier to identify personalized approaches to decision-making and commitment to lifestyle changes. We support the potential to identify both positive and negative predictors of long-term benefit to the individual.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Annually
Environment	Survey	Annually
Personal Characteristics	Electronic Health Record (EHR)	Annually
Physical measurements	Biochemical assay	Annually
Genotyping data	Whole Genome Genotyping (WGG)	Annually
Specified Biomarkers	Electronic Health Record (EHR)	Annually

## What are the biological, genetic, environmental contributors and factors associated with lower urinary tract symptoms?

**Use Case ID** 1001012

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lower Urinary Tract Symptoms (LUTS) record	Survey	Annually
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Microbiome sample	Urine collection	Annually
Urinary biome sample	Urine collection	Baseline
Environment	Clinical diagnostic test	Annually
Anthropometrics, whole body measurements	Survey	Baseline

## Among individuals who have a high genetic susceptibility to obesity, what are the behavioral and environmental factors that distinguish normal-weight from obese?

**Use Case ID** 1001016

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**

**Scientific Category** Assess Risk

Not everyone who has high genetic risk becomes obese; some become obese, some individuals remain of normal weight. The question we want to answer is why and how the individual copes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Annually
Specified Biomarkers	Blood draw	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Anthropometrics, whole body measurements	Electronic Health Record (EHR)	Annually

## What is the association of body composition, physical activity, diet composition to urinary incontinence and lower urinary tract symptoms in women?

**Use Case ID** 1001047

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

A strong risk factor for UI is BMI. Does body composition, diet, and exercise contribute to risk of developing or worsening UI and LUTS? Is this mediated by age, genetics, medical comorbidities (like DM, CAD, etc.)? By the type of UI (stress, other)?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Annually
Physical activity, self-assessment	PPI Survey (AOURP)	Annually
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Lower Urinary Tract Symptoms (LUTS) record	Survey	Annually
Anthropometrics, whole body measurements	Clinical assessment	Annually
Movement assessments	Clinical assessment	Annually

## Can pediatric obesity be prevented from starting in utero by restricted weight gain in pregnant women who are overweight or obese preconception?

**Use Case ID** 1001105

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

It is well known that children born to mothers with OW/OB are at increased risk of developing OW/OB themselves, and this risk is even greater (>85%) when both parents have OB/OW. Can maternal diet and lifestyle intervention to reduce GWG by adopting recommended diet and physical activity goals help reduce risk or subsequent OW/OB in offspring, and can using mobile technology help behaviorally to track maternal lifestyles—but also nutritionally in regard to achieving diet quality and energy density—to facilitate improved maternal/fetal outcomes?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Daily
Anthropometrics, whole body measurements	Electronic Health Record (EHR)	Daily
Pregnancy outcomes	Electronic Health Record (EHR)	Annually
Adverse life events	Electronic Health Record (EHR)	Annually
Anthropometrics, fetal	Physical exam	Daily
Genotyping data	Whole Genome Genotyping (WGG)	Baseline

## How do we elucidate presence of non-diabetic kidney disease in people with type 2 diabetes and chronic kidney disease?

**Use Case ID** 1001145      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Detect Disease

In patients with DM2 and CKD, diabetic nephropathy is common. However, a subset of these patients may have kidney disease that is not caused by diabetes but appears similar using current biochemical assays. Elucidation of the kidney disease diagnosis required kidney biopsy, which is increasingly risky, burdensome, and expensive.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Blood sample characteristics	Electronic Health Record (EHR)	Continuous monitoring
Prescription medication\treatment	Electronic Health Record (EHR)	Continuous monitoring

## How do complications of pregnancy predict later maternal health?

**Use Case ID** 1001150      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Most Important**      **Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy complications	Electronic Health Record (EHR)	Every 3 months
Metabolic disease diagnoses	Electronic Health Record (EHR)	Ongoing post-pregnancy
Cardiopulmonary assessment	Electronic Health Record (EHR)	Ongoing post-pregnancy
Pregnancy outcomes	Survey	Baseline
Anthropometrics, whole body measurements	Wearable electronics	Continuous monitoring
Pregnancy outcomes		Periodically during pregnancy
Gestational Diabetes Mellitus (GDM) diagnosis	Clinical assessment	Periodically during pregnancy

## Are there other methodologies to better assess the outcomes of gestational diabetes of the mother?

**Use Case ID** 1001151      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Elucidate Disease Mechanisms

Women with gestational diabetes are at a higher risk for diabetes pre-birth. We propose to study the natural history of [unreadable “slycomic hismetrois”] in a mom’s past pregnancy.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Glucose levels	Blood draw	Continuous monitoring
Diet, self-assessment	PPI Survey (AOURP)	Monthly
Breast feeding use	Survey	Monthly
Gestational Diabetes Mellitus (GDM) diagnosis	Clinical assessment	Monthly
Diabetes outcomes	Survey	Post-pregnancy

## Are there other methodologies to better assess the outcomes of gestational diabetes on the infant?

**Use Case ID** 1001156      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Elucidate Disease Mechanisms

Children whose mothers have gestational diabetes are at a higher risk of developing the disease later in life. We propose to study the national history of potential [unreadable] disorders in the children.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Breast feeding use	Survey	Monthly
Infant formula use	Survey	Monthly
Pregnancy outcomes	Survey	Post-pregnancy

## What is the natural history of glucose metabolism during pregnancy?

**Use Case ID** 1001163      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Other

There is scant information on normal glucose metabolism during pregnancy. We propose to study glucose patterns in pregnant women from conception to birth.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Diet, self-assessment	PPI Survey (AOURP)	Monthly
Physical activity, self-assessment	PPI Survey (AOURP)	Monthly
Glucose levels	Blood draw	Monthly

## Do social networks impact individual health behaviors?

**Use Case ID** 1001166

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Social networks may allow visible sharing of information on health, diet, well-being, and exercise. This may drive healthier living measurable by improved dietary intake and fitness levels, or social networks may keep individuals connected and psychologically stable, improving well-being.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Community participation outcome	Survey	Every 3 months
Mental health outcomes	Survey	Every 3 months
Diet, self-assessment	Mobile monitor	Every 3 months
Diet, self-assessment	PPI Survey (AOURP)	Every 3 months
Physical activity, self-assessment	PPI Survey (AOURP)	Every 3 months

## Do fluctuations over time in blood biomarkers predict the onset of digestive renal and metabolic diseases?

**Use Case ID** 1001217

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Individual variations in biomarkers may be due to a breakdown in homeostatic mechanism, a harbinger of disease, offering opportunity to identify individuals at risk for disease for targeted prevention strategies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Specified Biomarkers	Blood draw	Every 3 months
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Personal Characteristics	Survey	Every 3 months
Metabolic disease diagnoses	Electronic Health Record (EHR)	Every 3 months
Renal disease information	Electronic Health Record (EHR)	Every 3 months
Gastrointestinal health information	Electronic Health Record (EHR)	Every 3 months

## Is including urinary incontinence and overactive bladder (OAB) measure in FRAX score more predictive of fracturing in older people?

**Use Case ID** 1001232

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

One of the strongest risk factors for falling and fracture in older women. Would adding the pressure of urinary incontinence (specifically urgency) and urinary frequency, urgency in case the predefine volume of the commonly used FRAX for tx risk asses.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Movement assessments		Annually
Anthropometrics, whole body measurements		Annually
Cognitive assessments		Annually
Overactive bladder diagnosis	Prescription drug records	Annually
Lower Urinary Tract Symptoms (LUTS) record	Survey	Annually

## What are factors that contribute to cultural or genetic ancestry difference in diabetes incidence and prevalence?

**Use Case ID** 1001235

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Diabetes (type 1 and 2) incidence and prevalence is increasing in the U.S. Much of this increase is in populations without current genetic risk. Understanding the new risk factors may suggest specific therapies that can be impactful in these individuals and others.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Personal Characteristics	Survey	Baseline
Treatment data/specifics records	Survey	Annually
Genomic analyses	Whole Genome Sequencing (WGS)	Annually
Environment	Geographic information system (GIS) code	Annually
Behavioral characteristics, self-assessment	Survey	Annually

## Can predictors of an individual's response to drug therapy be used effectively to design precision prevention strategies for people of risk?

**Use Case ID** 1001259

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

People respond to different drugs differently. Perhaps signatures exist early.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Epigenomic/epigenetic markers	Plasma	Annually
Treatment effectiveness	Electronic Health Record (EHR)	Continuous monitoring
Prescription medication\treatment	Electronic Health Record (EHR)	Continuous monitoring
Adherence to prescription regimen	Survey	Monthly

## Among women with urinary incontinence, what characteristics distinguish those who respond to midurethral sling surgery from those who do not?

**Use Case ID** 192241

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Midurethral sling surgery (MuSS) outcomes are inconsistent. We lack knowledge of outcome moderators. This study will identify a prospective subcohort of women age 18+ with incident successful and unsuccessful MuSS. Hypothesized moderators of MuSS outcome spanning the social ecological model (e.g., urinary microbiome, comorbidities, BMI, physical activity, race, occupation, income) will be compared across those with successful and unsuccessful MuSS outcome to identify determinants of MuSS success.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Midurethral sling surgery	Electronic Health Record (EHR)	
Perceived outcomes - surgeon	Electronic Health Record (EHR)	
Perceived outcomes - patient	Survey	
Physical activity, self-assessment	Activity monitor	
Occupation	PPI Survey (AOURP)	

## **Does midurethral sling surgery (MuSS) for stress urinary incontinence (SUI) improve a patient's metabolic risk profile?**

**Use Case ID** 192313

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

SUI may contribute to reduced physical activity and poorer adherence to diuretics, thereby increasing metabolic risk profile. This study will identify a prospective subcohort of women age 18+ with incident MuSS to compare metabolic risk profile before and after successful surgery. We hypothesize successful MuSS will decrease need to urinate during day, increase level of physical activity, and reduce metabolic risk. Patient perceived surgical outcome will serve as a proxy for success of MuSS.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Midurethral sling surgery	Electronic Health Record (EHR)	
Metabolic risk assessment result	Electronic Health Record (EHR)	Baseline and annually
Urination frequency	Survey	
Perceived outcomes - patient		
Physical activity, self-assessment	Activity monitor	

## **Does surgery to relieve obstruction from benign prostate enlargement (BPE) improve a patient's metabolic risk profile (MRP)?**

**Use Case ID** 192314

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Frequent and urgent urination secondary to obstruction from prostate enlargement may reduce physical activity and adherence to diuretics, thereby increasing metabolic risk profile. This study will identify a prospective subcohort of men with incident surgery to relieve bladder outlet obstruction (BOO). We hypothesize relief of LUTS will decrease need to urinate, increase level of physical activity, and reduce MRP. Patient perceived surgical outcome will serve as a proxy for success.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Bladder outlet obstruction (BOO) surgery	Electronic Health Record (EHR)	
Metabolic risk assessment result	Electronic Health Record (EHR)	
Perceived outcomes - patient		
Physical activity, self-assessment	Activity monitor	
Urination frequency	Survey	

## Is there an interaction between gut biome and brainwaves and health issues?

**Use Case ID** 194894

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Other

Having successfully used music with the level of brain waves included within the recording for sleep for more than 20 years, I am fascinated by the importance of these two areas which have not been widely published. Gut importance has implications for various health issues, brain waves as well.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Gut microbiome sample	Stool sample	*GC
Brain wave activity data	Physical exam	
Health and phenotype data		

## Can chronic conditions such as diabetes be improved through non-medication methods?

**Use Case ID** 195561

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

There is a lot of controversy on whether a disease can be treated based primarily on a change of diet. With this study, I would test the theory with participants from various groups to determine if the condition could be improved through diet and also determine if medication is needed for improvement.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Glucose levels	Blood draw	Every 3 months
Diet, self-assessment	Food diary	Periodic (approximately biweekly)
Blood pressure	Physical exam	Every 3 months

## What factors predict successful long-term weight loss maintenance?

**Use Case ID** 195640

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

More than 60% of U.S. adults are classified as overweight/obese. Treatments to promote long-term weight loss (e.g., behavioral, pharmacological, surgical) are often not successful and result in high variability across individuals. Measurement of potential predictors from multiple domains (behavioral, biological, environmental, and psychosocial) can help identify the factors that best predict success in response to intentional weight loss and guide development of individualized strategies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment		
Weight		
Mental and psychosocial health, self-assessment		
Environment		

## Can increasing physical activity be used as a strategy to improve dietary intake and weight loss?

**Use Case ID** 195787

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Though it is well recognized that obesity results from a complex and multifactorial etiology, dietary intake plays a central and essential role in its development—one cannot become obese without eating. Certain dietary patterns have been associated with greater risk for weight gain and metabolic disease, but much less is known about how dietary intake changes through the process of becoming physically active or how exercise intensity and duration may influence dietary preferences.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Activity monitor	Continuously for 1 week duration at 1 month, 6 months, and 1 year
Diet, self-assessment	Smartphone-based ecological momentary assessment	Continuously for 1 week duration at 1 month, 6 months, and 1 year
Metabolic risk assessment result	Blood (EDTA)	Continuously for 1 week duration at 1 month, 6 months, and 1 year
Genomic sequence data	Blood (EDTA)	Baseline
Weight	Physical exam	Continuously for 1 week duration at 1 month, 6 months, and 1 year

## ***In overactive bladder, does pharmacogenomics influence individual response to antimuscarinic and beta-agonist bladder medication?***

**Use Case ID** 195831

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Overactive bladder is highly prevalent with significant impact on quality of life. Medications are utilized despite variable efficacy, high side effect burden, and poor persistence on therapy. This study will identify an overactive bladder cohort who have been prescribed antimuscarinic or beta-agonist medication to relieve symptoms. We hypothesize relief of symptoms will be based on the individual's pharmacogenomics. Personalized prescribing will permit better utilization of health care resources.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Overactive bladder diagnosis	Survey	At specified times anchored to the clinical event
Treatment/Therapy	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Outcomes	Survey	At specified times anchored to the clinical event
Pharmacogenomics	Whole Genome Sequencing (WGS)	At specified times anchored to the clinical event
Side effects of prescription medication	Electronic Health Record (EHR)	

## ***Can we develop a self-help regimen for leaky gut that aids in establishing a healthy gut?***

**Use Case ID** 196103

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

1. Questionnaire to assess for leaky gut. 2. Lab tests to assess for abnormal intestinal flora. 3. Serum lab tests to assess for inflammation in body. 4. Dietary and nutritional supplement protocol to follow to establish healthy gut microbiome. 5. Correlate positive leaky gut diagnosis with other medical disorders present in the subject.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Leaky gut syndrome diagnosis		
Microbiome sample	Stool sample	
Inflammation biomarkers levels	Blood draw	
Diet, self-assessment		
Clinical outcomes		

## Does habitual holding of urine eventually lead to symptoms of urinary urgency?

**Use Case ID** 196563

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

Patients who present with urinary urgency often report that earlier in life they were able to hold their urine for long periods of time. Voiding diaries collected over time, perhaps yearly, could be used to answer this question. The results of this study could be used for patient counseling for prevention of urinary urgency and urge urinary incontinence.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Number of daytime urinations	Survey	Annually
Clinical outcomes	Survey	Annually

## How do outcomes compare for individuals with urinary tract infection treated with and without antibiotics?

**Use Case ID** 196587

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Antibiotics have long been the standard of care for treatment of urinary tract infections (UTI). However, UTIs may be successfully managed without antibiotics, thereby reducing unnecessary contributions to antibiotic resistance. We proposed to compare outcomes (e.g., pyelonephritis, sepsis, GI distress/diarrhea) in individuals with UTIs treated with and without antibiotics, controlling for potential confounders (infection severity, patient age, comorbidities, other medications, etc.).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Urinary tract infection (UTI) diagnosis	Electronic Health Record (EHR)	
Prescription medication\ treatment	Electronic Health Record (EHR)	
Pyelonephritis diagnosis	Electronic Health Record (EHR)	
Infection diagnoses		
Diarrhea diagnosis	Survey	

## Do specific diabetes drugs increase the risk of peripheral artery disease, diabetic foot ulcers, or amputation?

**Use Case ID** 197223

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

A major advance in diabetes treatment is the finding that specific glucose-lowering drugs reduce the risk of cardiovascular disease. The results were tempered by the increased risk of amputations for the groups that received the SGLT2 inhibitor, canagliflozin. The generalizability of this finding is unknown. An understanding of the association of specific diabetes drugs with lower-extremity complications will allow a better assessment of the risks and benefits for individual patients.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Prescription drug records	Every 3 months
Diabetic Foot Ulcer (DFU) diagnosis	Electronic Health Record (EHR)	Every 3 months
Peripheral artery disease diagnosis	Electronic Health Record (EHR)	Every 3 months
Amputation procedure	Procedure codes	Every 3 months
Hemoglobin A1C (HbA1C) levels	Electronic Health Record (EHR)	Every 3 months

## What are options for diabetic patients not on metformin trying to maintain a blood glucose level <7%?

**Use Case ID** 197319

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Background: Many large studies on diabetic patients' progression to complications are done with patients on metformin treatment, but many patients do not tolerate metformin or discontinue due to a feeling of lethargy. Goals: To do a non-metformin-centric study with other treatment, lifestyle, and dietary changes. Methods: Study a cohort of diabetics who have not taken metformin but are managing their blood glucose close to normal levels. Treatment: Guidelines will be developed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Metabolic risk assessment result	Biochemical assay	Periodic (approximately biweekly)
Fatigue symptom	Survey	Periodic (approximately biweekly)
Prescription medication\treatment	Prescription drug records	Continuous monitoring
Diet, self-assessment	Activity monitor	Weekly
Hemoglobin A1C (HbA1C) levels	Blood draw	Every 3 months

## Does long-term menstrual suppression through hormonal birth control have health effects?

**Use Case ID** 197337

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

Females who do not experience menstruation or who experience reduced frequency of menstruation due to hormonal birth control would be compared with females who experience menstruation and do not take hormones. Potential outcomes to compare include bone density, cancer, mental illness, and mortality. This would help people make informed decisions about hormone use.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Hormonal contraceptive use	Survey	
Menstruation pattern	Survey	
Clinical outcomes	Electronic Health Record (EHR)	

## What factors cause interstitial cystitis? What treatment options work best based on genetics?

**Use Case ID** 197389

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Clinical diagnostic test	Continuous monitoring
Genomic analyses	Smartphone-based ecological momentary assessment	
Interstitial cystitis		
Outcomes		

## Is FGF23 a therapeutic target for improving cardiovascular outcomes in dialysis patients?

**Use Case ID** 197530

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

FGF23 is a proven independent marker of progression of CKD and cardiovascular outcomes in CKD. FGF23 secretion is an adaptive response to phosphorus retention in CKD. FGF23 levels can be lowered by Sensipar and Renvela for example, but these meds have other effects. If we administer the monoclonal Ab KRN23 to a group of dialysis patients and a placebo to another group, the only parameter that should be affected is the FGF23 level. Measuring CV events and deaths in both groups should answer this.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Weekly
Fibroblast growth factor 23 (FGF23)	Blood draw	Weekly
Monoclonal Ab KRN23		

## Could adding fecal sampling to the All of Us campaign help resolve the role of the gut microbiome in complex disease risk?

**Use Case ID** 198143

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Other

The simple addition of fecal sample for the use of gut microbiome taxonomical assessment could prove a valuable resource for testing hypotheses about the gut flora as a target of and contributor to myriad human health and disease states. Fecal sample collection is non-invasive, and gut bacterial lab methods are becoming increasingly refined and high-throughput.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Gut microbiome sample	Stool sample	*GC

## What role do the pathomechanics of physical activity play in the formation and healing of diabetic foot ulcers?

**Use Case ID** 198454

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Although the presence of a relationship between physical activity and diabetic foot ulcers is widely accepted, there is limited understanding of this relationship. Most studies to date have included sample sizes of fewer than 100 participants and monitored physical activity for less than 6 months (often for a period of only several weeks). This prospective longitudinal study will evaluate the association of physical activity with the formation and subsequent healing of diabetic foot ulcers.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Physical activity, self-assessment	PPI Survey (AOURP)	Every 3 months
Diabetic Foot Ulcer (DFU) diagnosis	Electronic Health Record (EHR)	Weekly
	Survey	Every 3 months

## Will the clinical use of predictive glycation and oxidation biomarkers improve diabetes care and prevent long-term complications?

**Use Case ID** 198474

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Since diabetic complications occur in those who show more glycative and oxidative stress, we have validated their predictive power in groundbreaking outcome trials to create diagnostic blood tests for clinical use. To study the clinical efficacy and utility of these tests, we will identify those at high risk (HR) before DKD and CVD are apparent. Primary endpoints are achievement of rigorous glycemic and proposed treatment goals in HR. Long-term goals are improved prevention of complications.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Glycation levels	Blood (EDTA)	
Hemoglobin A1C (HbA1C) levels	Blood (EDTA)	Every 3 months
Prescription medication\treatment	Prescription drug records	Every 3 months
Lifestyle, self-assessment	Electronic Health Record (EHR)	Every 3 months
Diabetes outcomes	Clinical diagnostic test	Annually

## **Why do Asian-Americans accumulate excess visceral adipose tissue (VAT), and what interventions are effective in non-obese?**

**Use Case ID** 198581

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

Asian-Americans accumulate excess visceral adipose tissue (VAT) despite the absence of general obesity. Chinese, Filipino, and South Asians in the U.S. have more VAT compared to African-Americans. The determinants of excess VAT accumulation in normal-weight adults are unclear, and effective interventions to reduce excess VAT accumulation in normal-weight Asian-Americans are urgently needed to reduce adverse metabolic health outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Metabolic risk assessment result		
Visceral adipose tissue distribution	Physical exam	
Outcomes		

## **To what extent do gut permeability and dysbiosis affect systemic health?**

**Use Case ID** 198596

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

There is a plethora of preliminary data connecting intestinal permeability to chronic inflammatory diseases. More work is needed in this area to determine causal mechanisms. Doing so could help in developing interventions and other targets in reducing chronic illnesses and improve quality of life.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Inflammation biomarkers levels	Blood draw	
Dysbiosis diagnosis	Electronic Health Record (EHR)	

## What factors predict response to lifestyle modification and bladder training in adults with symptoms of overactive bladder (OAB)?

**Use Case ID** 198643

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Lifestyle (e.g., diet) modification and bladder retraining (LMBR) are effective for many but not all persons with OAB symptoms (urinary urgency, frequency, and incontinence). We will identify determinants of successful LMBR in a prospective cohort of adults with OAB symptoms treated with LMBR by comparing hypothesized moderators of LMBR spanning medical and social ecological models (e.g., self-efficacy, race, occupation, SES, education) across those with and without reduced OAB symptoms post-LMBR.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Mobile monitor	Pre- and post-treatment
Perceived outcomes - patient	Survey	Pre- and post-treatment
Fluid intake	Survey	
Number of daytime urinations	Survey	
Urination frequency	Survey	Baseline and post-treatment

## What characteristics predict response to pelvic floor muscle training (PFMT) in women with stress urinary incontinence (SUI)?

**Use Case ID** 198651

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

PFMT, or “Kegels,” are the first-line treatment for women with SUI, but they are inconsistently effective. Study will identify determinants of success with PFMT in a prospective subcohort of women aged 18+ with SUI. Hypothesized moderators of PFMT outcome spanning the medical and social ecological model (e.g., self-efficacy, BMI, physical activity, race, occupation, socioeconomic status, education, PFM strength) will be compared across those who are successful and unsuccessful at reducing SUI.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health and phenotype data	Electronic Health Record (EHR)	Baseline and post-treatment
Pelvic floor muscle strength	Ultrasound	
Physical activity, self-assessment	PPI Survey (AOURP)	
Stress urinary incontinence diagnosis	Electronic Health Record (EHR)	
Perceived outcomes - patient	Survey	Pre- and post-treatment

## How do we predict individual responses to various anti-obesity therapies?

**Use Case ID** 1000825

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

The diseases of obesity, spanning a spectrum of mild (overweight) to life-threatening, are associated with more than 200 comorbidities as well as quality of life and social impairment. Classical evidence suggests that there are numerous subtypes that vary in a clinical presentation, behavior, comorbidities, progression patterns, and response to therapy. Variable response to preventative strategies is thus inferred but not proven.

Understanding the genetic, biological, environmental, behavioral, and developmental contributors to this variability/heterogeneity will accelerate effective strategies to and impact of obesity.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Treatment/Therapy	Electronic Health Record (EHR)	Annually
Patient feedback	Survey	Annually
Personal Characteristics	Survey	Annually
Physical measurements	Physical exam	Annually
Genotyping data	Blood draw	Annually

## What controls progression and lack of progression in individuals with risk of diabetes (type 1 and type 2)?

**Use Case ID** 1000854

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Most Important Scientific Category** Maintain & Preserve Health

Diabetes impacts >10% of the U.S. population, and people with known risk factors do not all progress to disease. This gives the opportunity to identify potential interventions that can impact disease incidence in the general population. Elite non-progressors, for both disease diagnosis and complications, can be used to impact those with disease and in general.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Personal Characteristics	Survey	Annually
Genotyping data	Specimen collection	Annually
Blood sample characteristics	Specimen collection	Annually
Personal Characteristics	Electronic Health Record (EHR)	Annually
Diabetes outcomes	Electrocardiogram (ECG/EKG)	Annually

## What factors decrease the impact of lower urinary tract symptoms?

**Use Case ID** 1000873

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

50% prevalence—high impact on QOL for a large fraction of the population. Includes urinary incontinence, bladder pain, overactive bladder, nocturia, BPH.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lower Urinary Tract Symptoms (LUTS) record	Survey	Periodically
Whole genome sequence (WGS) data	Whole Genome Sequencing (WGS)	Baseline
Over-the-counter (OTC) medication Use	Survey	Periodically
Prescription medication\treatment	Electronic Health Record (EHR)	Daily
Clinical outcomes	Survey	Daily
Diet, self-assessment	PPI Survey (AOURP)	Periodically

## What is the impact of polypharmacy over-the-counter medication and nutritional scope on chronic disease patients?

**Use Case ID** 1001066

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

The medications, prescription and nonprescription, that people take influence the course of disease and have side effects and drug interactions. Similarly, nutritional supplements and dietary components are important. Therefore, it is important to capture these data.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Every 3 months
Medical Information	Electronic Health Record (EHR)	Every 3 months
Prescription medication\treatment	Claims data	Every 3 months
Prescription medication\treatment	Survey	Every 3 months
Genotyping data	Whole Genome Sequencing (WGS)	Every 3 months
Over-the-counter (OTC) medication Use	Survey	Every 3 months

## ***In newly diagnosed patients with T2DM, do targeted educational text messages about diabetes management and complications prevent neuropathy, retinopathy, and nephropathy?***

**Use Case ID** 1001136

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Detect Disease

DM2 can cause numerous complications, especially retinopathy, neuropathy, and nephropathy. Part of this is a result of inadequate patient education about the risks and needed annual preventative exams—annual eye exam, foot exams, albuminuria testing.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Diabetes type II diagnosis	Electronic Health Record (EHR)	Continuous monitoring
Diabetes outcomes	Electronic Health Record (EHR)	Continuous monitoring
Specified Biomarkers	Electronic Health Record (EHR)	Continuous monitoring
Personal Characteristics	Claims data	Continuous monitoring
Nephropathy diagnosis	Electronic Health Record (EHR)	Continuous monitoring
Neuropathy diagnosis	Electronic Health Record (EHR)	Continuous monitoring
Retinopathy diagnosis	Electronic Health Record (EHR)	Continuous monitoring

## ***Does the normalization of 25-OH vitamin D reduce the development or delay onset of a cardiovascular event including hypertension?***

**Use Case ID** 1001146

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Other

Low vitamin D levels have been associated with a wide range of diseases, including cardiovascular disease, bone health, and cancer.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Prescription medication\treatment	Claims data	Continuous monitoring
Vitamin D levels	Blood draw	Every 6 months
Hormone levels (non-steroidal)	Blood draw	Every 6 months
Blood pressure	Electronic Health Record (EHR)	Every 3 months
Small molecules and ion levels	Blood draw	Every 6 months
Cardiopulmonary assessment	Electronic Health Record (EHR)	Continuous monitoring

## What effects do cross-sex hormones have on globular filtration rate?

**Use Case ID** 1001168

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

Data are limited on transgender health. Specifically, we do not know how many cross-sex hormones affect 9FR in transgender normal [verge OFRor].

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Hormone levels (non-steroidal)	Prescription drug records	Annually
Gender identity	PPI Survey (AOURP)	Baseline
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline

## Does stress incontinence alter the metabolic risk profile?

**Use Case ID** 1001177

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Stress incontinence surgery may allow men and women to be more active without leaking urine or having symptoms. As a result, they may see improved metabolic consequences.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	PPI Survey (AOURP)	Annually
Anthropometrics, whole body measurements	Survey	Annually
Treatment effectiveness	Survey	Post-discharge
Metabolic risk assessment result	Electronic Health Record (EHR)	Annually
Treatment/Therapy	Electronic Health Record (EHR)	Annually
Incontinence diagnosis	Electronic Health Record (EHR)	Annually

## Can we determine the optimal time to start dialysis based on disease, diet, lifestyle, genetics, and environment?

**Use Case ID** 1001216      **Cross-Cutting Theme** Therapeutic and Preventive Interventions  
**Most Important**      **Scientific Category** Treat & Cure Disease

Initiation of dialysis varies from person to person and is currently based on metabolic factor and symptoms. No ideal determination of optimal time to initiate dialysis exists. Incorporating lifestyle, genes, and environment into a predictive score for onset of dialysis in individuals and kidney failure becomes important.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environment	Geographic information system (GIS) code	Annually or with change in address
Diet, self-assessment	Food frequency test	Annually
Physical activity, self-assessment	Wearable electronics	Annually
Alcohol Use	PPI Survey (AOURP)	Annually
Waist circumference measurement	Physical exam	Annually
Genotyping data	Gene expression profiling	Baseline
Social determinants of health (SDH)	PPI Survey (AOURP)	Annually
Height	Physical exam	Annually

# Health and Resilience

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## Is there an increased incidence of disease among descendants of people who experienced toxic environmental exposures?

**Use Case ID** 192294

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Collect data pertaining to a person's ancestors. Where did they live? Where did they work? What did they do? A simple example of a possible correlation: Do the great-grandchildren of Pennsylvania coal miners who immigrated from Eastern Europe suffer from a higher incidence of lung cancers and lung disease even though they never smoked or have never been near a coal mine? Correlate disease to Superfund and Brownfield sites and subsequent generations after the exposure.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Self-reported ancestry	PPI Survey (AOURP)	Baseline
Family clinical outcomes	PPI Survey (AOURP)	Annually
Genomic analyses	Whole Genome Sequencing (WGS)	Every 2 years

## What aspects of pet ownership are associated with a person's health?

**Use Case ID** 194812

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

This could mostly be done by survey of pets in the household over time (number of pets, breed, age, etc.). Include whether pets are inside/outside, hours spent inside or outside, and health of the pet (getting at whether disease affects human/nonhuman).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Depression diagnosis	PPI Survey (AOURP)	Annually

## How do different food groups affect health?

**Use Case ID** 194865

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

Administer food diaries and assess the impact of food groups/categories, such as fruits, root vegetables, green leafy vegetables, all other vegetables, low-fat dairy, full-fat dairy, fish, white meat, red meat, processed meat, nuts and seeds, beans/legumes, whole grains made from flour (pasta, bread, pastries), intact whole grains (i.e., whole grain products not made from flour), refined grains, refined sugar, oils, etc. Also, get info on the cooking/processing method (e.g., frying, steaming).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Food diary	Periodic (approximately biweekly)

## How does the media we are exposed to affect our health?

**Use Case ID** 194942

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

I would have people track their media patterns. They could record this in a diary, or we could try to partner with Nielsen, or have people share their Netflix, etc. with us. Then we could monitor their health outcomes, with a focus on health behaviors like substance use (tobacco, alcohol, drugs), violence, eating and exercise behavior. We could also obtain data on indicators such as blood pressure. We would assess variables such as sociodemographics and other factors that might be confounders.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Media use	Smartphone-based ecological momentary assessment	
Tobacco smoking	Biochemical assay	Every 3 months
Lifestyle, self-assessment		
Physical activity, self-assessment		
Recreational drug use		

## Does occupational exposure to extreme heat increase the likelihood of serious injuries?

**Use Case ID** 195091

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Goal: Quantify a fuller range of heat-health risks to inform worker safety protocols as climate change increases the likelihood of extreme heat. Methods: Use a combination of worker's compensation data, surveys, and individual temperature and humidity sensors to associate heat exposure with severe injuries. Data collection could be limited to working hours or extended to non-work hours to capture heat exposure at home (e.g., housing for migrant farm workers may lack air conditioning).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environment	Survey	
Health and phenotype data	Claims data	
Sensor data	Mobile monitor	

## Do residential energy efficiency measures improve physical and mental health?

**Use Case ID** 195093

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

Goal: Identify and quantify health benefits of energy efficiency measures in single- or multi-family housing. Data tools: Resident surveys, air pollution monitors, temperature monitors, energy usage data from electric utilities. Expected outcomes: Previous qualitative and quantitative work suggests residents of more energy-efficient homes experience fewer cardiovascular symptoms (e.g., asthma attacks) and fewer exposures to unhealthy temperature extremes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environment		
Environmental samplings and exposure results		
Cardiopulmonary assessment		

## What neighborhood conditions promote health?

**Use Case ID** 195231

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

This project would examine contextual factors that may influence the health outcomes of individuals. Contextual factors include social environment factors (such as social cohesion, crime) and built environment factors (green space, mixed land use, access to healthy food and clinical services). These factors can help or hinder individuals from achieving or maintaining health. Outcomes of interest include obesity, diabetes, depression, and substance use, among others.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Smartphone-based ecological momentary assessment	Weekly
Clinical outcomes		
Environment		

## What are the effects of exposure to primary airborne and environmental insults?

**Use Case ID** 195323

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Other

Assessing and estimating exposure to primary airborne/environmental insults as was done 30 years after the fact in PM10/2.5 studies in Steubenville, OH. This was found to be a good model of next-day mortality. Expand this to include aldehydes, CO2, and diesel exhausts.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Air quality assessment results		Continuous monitoring
Environmental samplings and exposure results		

## How do environmental exposures and social factors interact to influence the risk of chronic disease?

**Use Case ID** 195656

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Hair and nail clippings collection	Annually
Air quality assessment results		
Heavy Metal Panel results	Urine collection	
Allergens assessment results	Physical exam	
Social determinants of health (SDH)		

## How does one's informational environment (e.g., Internet, social media, smartphones) impact physical health?

**Use Case ID** 195695

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Other

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Technology Use	Survey	
Clinical outcomes	Electronic Health Record (EHR)	
Education level attained	PPI Survey (AOURP)	

## How do exposures to multiple environmental stressors impact chronic disease risk?

**Use Case ID** 196381

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

The goal would be to examine the associations between multiple environmental stressors (air pollutants, temperature, etc.) on chronic disease risk, and how these associations are modified by inherent characteristics, lifestyle factors, and the built and natural environments. This would require current and historical residential/work addresses and appending environmental data. This would provide more information on how these factors interact in a wider range of individuals than previous studies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Geocode data	Survey	Post-event or at least annually
Air quality assessment results		Continuous monitoring
Environmental samplings and exposure results		
Environment		

## What factors prevent individuals with disabilities from seeking health promotion activities?

**Use Case ID** 196497

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Other

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Quality of life	Survey	Include child, teenager, early adult, adult, elderly
Behavioral characteristics, self-assessment	Activity monitor	
Behavioral characteristics, self-assessment	Food diary	

## What lifestyle factors (e.g., diet, physical activity) are associated with protection against environmental pollutants?

**Use Case ID** 196592

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Most research is devoted to understanding factors that increase disease risk. Here we specifically seek to find individuals who are healthy despite exposure to high levels of environmental pollutants (e.g., living in areas with elevated air pollution) and examine the lifestyle factors that may be protective. Protective lifestyle factors may be modifiable by the individual and may represent a means to improve environmental public health in the U.S.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	International Classification of Diseases (ICD) useage data	Every 3 months
Environmental samplings and exposure results		Every 3 months
Lifestyle, self-assessment	PPI Survey (AOURP)	Every 3 months
Residence location	PPI Survey (AOURP)	Every 3 months

## How do local, regional, state, and national retail food environments and policies affect diet and health?

**Use Case ID** 196629

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

Obesity and poor diet are threats to population health. The food environment and related policies may be major contributors. Longitudinal measures of food purchasing, diet, and health can be linked to environmental/policy data (e.g., community gardens, changes in convenience store offerings, fast food moratoriums, menu labeling, food taxes/subsidies) and used to identify health effects. Results can help prioritize multilevel preventive interventions. Submitted by Healthy Food Retail Working Group.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Geocode data	Survey	Annually
Diet, self-assessment	PPI Survey (AOURP)	Annually
Weight	Physical exam	Annually
Food purchasing information	Food Acquisition and Purchase Survey (FoodAPS)	Annually
Sociodemographics	PPI Survey (AOURP)	Annually

## What is the effect of the individual's family and community network on health status and health behaviors?

**Use Case ID** 196677

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

Focusing on the entire cohort, this study seeks to define inter-relationship linkages between the person (“ego”) and other associated participants (“alters”). Previous studies identified linkages through the specification of a family roster and alternate points of contact in the consent process. The relationship data produced would be available for network analysis to determine the impact of the social network on health behaviors, development of disease, and interplay with the environment.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Social relationships		
Family relationships		
Clinical outcomes	Electronic Health Record (EHR)	
Residence location	PPI Survey (AOURP)	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually

## What about our environment drives us to become healthy?

**Use Case ID** 196893

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

We are trained to conduct research to elucidate the causes of morbidity and mortality. A study designed to understand the cause of a given disease, however, is not the same as one designed to understand the root causes of health and quality of life. I suspect there is more to being healthy than riding a bike and eating green vegetables.... Let's work to find out and then apply that knowledge to design homes, schools, communities and cities around the idea of health.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Quality of life	Survey	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	
Environment		

## What is the relationship between adverse childhood experiences (ACEs) and resilience?

**Use Case ID** 196915

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

There is a growing epidemic in our nation that is impacting our schools, families, and communities. As explained by the Johns Hopkins Institute at All Children’s Hospital in St. Petersburg, Florida, left unattended, this syndrome, commonly referred to as adverse childhood experiences (ACEs) or childhood toxic stress, can lead to developmental delays, mental and health difficulties, and, in later life, earlier entries into the juvenile justice system.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Include child, teenager, early adult, adult, elderly
Adverse childhood experiences		
Clinical outcomes		

## What are the linkages between housing quality, household composition, and health outcomes?

**Use Case ID** 197447

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

Housing has been shown to be inextricably linked to well-being outcomes, but there are few data sets that contain good housing and housing quality (and neighborhood quality) and health outcomes. All of Us should collect housing data (see the American Housing Survey for a good basis of questions) as well as neighborhood-level variables that may impact health. Examine further sociodemographic variables, including family structure, to explore links between household composition, housing, and health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Housing quality variables	Survey	
Sociodemographics	PPI Survey (AOURP)	

## What are the effects of food additives and convenient foods on health status?

**Use Case ID** 198087

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Other

To find the reasons for increasing prevalence of degenerative diseases .To bring out awareness among the younger generations. To get the data about the knowledge and understanding of labeling.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Food diary	Continuous monitoring
Diet, self-assessment		Continuous monitoring
Degenerative diseases diagnoses	Electronic Health Record (EHR)	

## What aspects of the built environment, policies, and programs most effectively influence healthy lifestyle choices?

**Use Case ID** 198109

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Other

An improved understanding of the wide-ranging interplay of community design, programs, policies, worksite health, physician counseling, and other factors in influencing health behaviors and lifestyle choices is crucial to improving health outcomes. Methods could include data collection through wearable technology, validated self-reports, medical reimbursement, predictive analytics, and the unique insights from All of Us. ACSM applauds this pathway to health innovation.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Continuous monitoring
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Neighborhood characteristics	Survey	Baseline

## What are the combined environmental exposures that contribute to disease?

**Use Case ID** 198145

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Measure as many environmental chemical and nonchemical exposures as feasible using internal and external exposure monitoring technologies. Utilize different statistical approaches for evaluating the association of multiple exposures to biomarkers of disease. Statistical methods can also be used to identify common exposure combinations, which can be prioritized for further study in animal and in vitro models.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Urine collection	Continuous monitoring
Stress	Biochemical assay	Continuous monitoring
Specified Biomarkers	Biochemical assay	Continuous monitoring
Epigenomic/epigenetic markers	Biochemical assay	Continuous monitoring
Health and phenotype data	Electronic Health Record (EHR)	Annually

## Would the evaluation of environmental exposure history measured in deciduous teeth improve disease liability assessment?

**Use Case ID** 198146

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Sophisticated laboratory techniques can now extract levels of exposure to numerous trace organic and inorganic contaminants and medications in the layers of tooth enamel—giving timestamped exposure (temporal) sensitivity. This represents a massive step forward, because recall or chronic measurement of place and exposure is not necessary but is nevertheless important in defining exposure–outcome relationships. Participants can provide baby teeth or dentist-extracted teeth for analysis.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Dental and oral data	Dental records	
Environmental samplings and exposure results	PPI Survey (AOURP)	

## What are the long-term health outcomes of those exposed to contaminated water in Flint, Michigan?

**Use Case ID** 198169

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Other

The risks of lead exposure in children have been established by the scientific and medical communities. The 2014 drinking water crisis in Flint, Michigan, received much publicity; however, long-term impacts to the population exposed to the contaminated water need to be studied. We propose collecting data on those residents and following them over time to assess the long-term effects of lead exposure.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Residence location	PPI Survey (AOURP)	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Annually
Clinical outcomes	Electronic Health Record (EHR)	
Quality of life	Survey	Every 3 months
Heavy Metal Panel results		Baseline

## Is there an association between the use of household cleaning products and long-term health outcomes?

**Use Case ID** 198372

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Other

I would like to see this measure of sentiment correlated with use of cleaning products and general health, particularly microbiome health and the long-term effects of using sanitization products in households.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Autoimmune biomarkers levels	Blood draw	

## What are the health effects of sustained ambient exposure above state and federal health-based annual guideline concentrations?

**Use Case ID** 198386

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Other

For communities that have sustained (1+ years) ambient and community exposure levels above EPA and/or state environmental agency health-based annual guideline concentrations (e.g., U.S. v. Tonawanda Coke 10-CR-219-S, with increased residential neighborhood levels of PAHs and aldehydes). For these communities seeking research on the increased relative risk of rare disease outcomes, like leukemia, best served by the scale of All of Us, how can a recruitment and data collection site be requested?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	Every 2 years
Occupation	PPI Survey (AOURP)	
Prescription medication\treatment	Electronic Health Record (EHR)	Every 2 years
Clinical outcomes	Clinical diagnostic test	Every 2 years

## Is the measured biodiversity of the environment a person lives in associated with health outcomes?

**Use Case ID** 198404

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Biodiversity assessment results	Survey	
Clinical outcomes		

## Can exposome data from the All of Us Research Program be used to discover environment-disease associations?

**Use Case ID** 198486

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

The exposome has been defined as the totality of environmental exposures throughout the life course. Regardless of the definition, it is a tool for the untargeted, hypothesis-free discovery of associations between environmental exposures and disease outcomes. This is best applied to high-prevalence phenotypes that are likely to occur in the cohort, such as the conversion of metabolic syndrome to overt diabetes, where it can be nested as a case-control study.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Environmental Protection Agency (EPA) air monitoring reports	
Health and phenotype data	Electronic Health Record (EHR)	Continuous monitoring
Environmental samplings and exposure results	PPI Survey (AOURP)	Continuous monitoring
Inflammation biomarkers levels	Urine collection	Annually

## What factors cause some individuals to respond differently to environmental exposures than others?

**Use Case ID** 198507

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Some individuals are more susceptible or resistant to the health effects of certain environmental exposure for unknown reasons. It is likely that a combination of elements, such as genetic variation, microbiome differences, life stage, or the combined impact of multiple factors (such as diet), contributes to these differences. Mapping the multiple interactions between exposure and response requires the unprecedented power afforded by the All of Us cohort.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Environmental Protection Agency (EPA) air monitoring reports	Annually
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Microbiome sample	Stool sample	Every 3 months
Health and phenotype data	Electronic Health Record (EHR)	Annually
Diet, self-assessment	PPI Survey (AOURP)	At specified times anchored to the clinical event

## How does individual DNA repair capacity determine resilience against environmental exposures?

**Use Case ID** 198521

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Other

Environmental exposures can result in DNA damage, including mutations, altered DNA topology, and breaks, which can lead to multiple diseases. These lesions can be repaired by specialized enzymes in various DNA repair pathways; however, the efficiency of repair pathways can differ between individuals. Understanding these differences at the sequence level and how these differences might interplay with other cellular responses could provide insight into disease susceptibility.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Annually
Environmental samplings and exposure results	Blood draw	Annually
Genomic instability assessment results		At specified times anchored to the clinical event
Health and phenotype data	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Inflammation biomarkers levels	Blood draw	Annually

## How do early-life environmental and diet experiences predict disease in later life?

**Use Case ID** 1000700

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Potential for studying longitudinal birth cohort. Compare differential response to similar exposures to understand inherent/intrinsic protective mechanisms.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Environmental toxins exposure assessment results	Specimen collection	Every 6 months
Diet, self-assessment	PPI Survey (AOURP)	Every 6 months
Gut microbiome sample	Smart toilet	Every 6 months
Geocode data	Mobile monitor	Baseline

## How do music and sound environment affect emotion/stress regulation in people with chronic illnesses (e.g., dementia, schizophrenia)?

**Use Case ID** 1000880      **Cross-Cutting Theme** Environmental and Other Contextual Effects  
**Most Important**      **Scientific Category** Reduce Disease Impact

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental assessment results	Electronic monitoring/recording	Continuous monitoring
Mood patterns	Survey	Continuous monitoring
Behavioral characteristics, self-assessment	Patient-reported outcome	Daily
Physical measurements	Hearing test	Annually
Medical Information	International Classification of Diseases (ICD) usage data	Periodically
Prescription medication\treatment	Electronic Health Record (EHR)	Periodically

## How does diet/organic food reduce the impact of autoimmune/neurodegenerative diseases?

**Use Case ID** 1001049      **Cross-Cutting Theme** Environmental and Other Contextual Effects  
**Scientific Category** Reduce Disease Impact

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Personal Characteristics	Patient-reported outcome	Periodically
Microbiome sample	Stool sample	Periodically *GC
Personal Characteristics	Survey	Baseline
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	International Classification of Diseases (ICD) usage data	Periodically
Environmental samplings and exposure results	Dietary assessment tool	Continuous monitoring
Pesticides exposure assessment results	Dietary assessment tool	Continuously for 1 week every 6 months
Clinical outcomes	Mobile monitor	Continuous monitoring
Microbiome sample	Cheek swab	Periodically
Housing quality variables	Geographic information system (GIS) code	Baseline
Health care cost	Survey	Baseline
Symptoms	Mobile monitor	At specified times anchored to the clinical event

## How does having a support system affect treatment/cure?

**Use Case ID** 1001198

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Treat & Cure Disease

Support system is external to care team.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social support	Geospatial tracking	Continuous monitoring
Sociodemographics	PPI Survey (AOURP)	Annually
Technology Use	Mobile device	Monthly
Social environment	Survey	Continuous monitoring
Social environment	Social network mining	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring

## How does exposure to social stress affect an individual's ability to seek care, adhere to a prescription, and respond to a prescription?

**Use Case ID** 1001226

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Treat & Cure Disease

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Stress, occupational	Survey	Annually
Stress, occupational	Mobile device calendar	Annually
Stress, occupational	Survey	Baseline
Stress, occupational	Mobile device calendar	Baseline
Domestic obligations	Survey	Continuous monitoring
Domestic obligations	Mobile device calendar	Continuous monitoring
Discrimination encounters	Survey	Every 3 months
Genomic analyses	Genomic testing	Baseline
Socioeconomic Status (SES)	PPI Survey (AOURP)	Baseline
Socioeconomic Status (SES)	PPI Survey (AOURP)	Every 2 years
Socioeconomic Status (SES)	Records	Baseline
Socioeconomic Status (SES)	Records	Every 2 years
Sociodemographics	PPI Survey (AOURP)	Baseline
Geocode data	Survey	Baseline
Geocode data	Survey	Every 2 years
Geocode data	Mobile device	Baseline
Geocode data	Mobile device	Every 2 years
Geocode data	Geospatial tracking	Baseline
Geocode data	Geospatial tracking	Every 2 years
Personal Characteristics	Survey	Every 3 months
Sociodemographics	PPI Survey (AOURP)	Every 2 years
Prescription medication\treatment	Electronic Health Record (EHR)	Baseline
Prescription medication\treatment	Electronic Health Record (EHR)	Every 2 years

## Would a pharmacogenomics database that includes ethnicity data make precision medicine more feasible?

**Use Case ID** 195103      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Other

We all aspire for precision medicine, particularly when it comes to response to drugs, pharmacogenomics, cancer treatment, or heart disease, yet logistical and economic barriers still keep this far from universal application. The proposed study would answer whether precision medicine practice based on ethnicity is appropriate.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Blood draw	At specified times anchored to the clinical event
Clinical outcomes		
Sociodemographics		

## What disease risk variants are unique to naturalized citizens of recent African origin and enriched in African Americans?

**Use Case ID** 195659      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Other

To better understand variants relevant to African Americans and their disease risk, it would be helpful to have data on reference for African populations from the African ethnic groups with the greatest historical genetic contribution through the transatlantic slave trade. Naturalized U.S. citizens born in Africa would be more easily accessible to regional sequencing leaders (e.g., Houston has the largest Nigerian U.S. population and is near to the BCM sequencing center)

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	
Health and phenotype data		

## Is telomere length a determinant of disease susceptibility?

**Use Case ID** 198514

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Telomere length may influence the interplay between the combined effects of the environment and stress responses. For instance, a combination between psychosocial stress, chemical exposures, and windows of susceptibility could lead to altered homeostasis (a new “normal”). Uncovering how timing, allostatic loads, and physiology combined contribute to disease development and progression could be better understood with the power of numbers, age, race, etc. the All of Us cohort offers.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Telomere length	Blood draw	Annually
Omics	Blood draw	Annually *GC
Health and phenotype data	Electronic Health Record (EHR)	
Environmental samplings and exposure results	PPI Survey (AOURP)	At specified times anchored to the clinical event
Stress	Smartphone-based ecological momentary assessment	At specified times anchored to the clinical event

## How can the All of Us cohort help identify and understand genetic and epigenetic risk factors associated with disease?

**Use Case ID** 198705

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Combining genome-wide genetic/epigenetic variation and gene/protein expression with clinical, behavioral, imaging, environmental, and molecular data in the large and diverse All of Us cohort will enhance our understanding of disease risk factors and subtypes, relevant biological processes, and targeted treatments. Methods involved include genomic data generation, storage, and sharing; data integration, visualization, and interpretation; and return of results to participants and providers.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Epigenomic/epigenetic markers	Blood draw	Every 10 years
Environmental samplings and exposure results	PPI Survey (AOURP)	Continuous monitoring
Magnetic resonance imaging (MRI) images	Magnetic Resonance Imaging (MRI)	
Clinical outcomes	Electronic Health Record (EHR)	Every 5 years

## How do genomic, biological, environmental, and societal factors combine to contribute to disease risk?

**Use Case ID** 198715      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

Complex diseases are a result of a complex interplay of genetic, environmental, host, and societal factors operating over a prolonged time. Many factors associated with disease onset or progression have been elucidated using a siloed approach which fails to adequately assess interplay between factors. Longitudinal measures and more sophisticated analytical methods are needed to support comprehensive (e.g., systems or computational modeling) approaches to explore the combined contribution of factors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Epigenomic/epigenetic markers		
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Clinical outcomes	Electronic Health Record (EHR)	
Social determinants of health (SDH)	Mobile monitor	Annually

## What happens to high-risk people before and as they develop a disease? How do high-risk people who don't develop a disease differ?

**Use Case ID** 198717      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Elucidate Disease Mechanisms

We can identify people who are at high risk for many diseases. However, not all high-risk people develop the disease. This study would follow people in high-risk groups longitudinally and identify specific genomic, physiological, clinical, and exposure factors that are either predictive or protective of transition to disease. This should focus on a diverse set of people (ethnicity, gender/sex, age, SES, rural/urban, geographic location, etc.) and measure many factors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	
Clinical outcomes	Electronic Health Record (EHR)	
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Risk factors, self-assessment		
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months

## Do genomic data provide clinically useful information beyond the data gathered during standard clinical care?

**Use Case ID** 198721

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Other

1. A cohort of people with WGS and pharmacogenomic data from blood sample. Randomize half of to get data in easily available tissues: DNA sequence (for somatic variants and mosaicism), RNA expression, and epigenomic data. Compare health outcomes between both groups. 2. Assay all data types in a group and consider when genomics made a difference in their health care outcomes. For this approach we would need methods to estimate their health had the genomic data not been used.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Blood draw	
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
	Electronic Health Record (EHR)	

## What are the implications of rare deleterious variants in an unselected population?

**Use Case ID** 198756

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Characterize phenotypes of participants with rare deleterious variants of unknown significance discovered by deep sequencing through available surveys and EHR data or through recontact with additional studies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	
Health and phenotype data	Electronic Health Record (EHR)	
Personal Characteristics	Survey	

## What is the penetrance of known disease-associated rare variants for rare diseases, such as autoimmune polyglandular syndrome type 1?

**Use Case ID** 198757      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Other

The goal of this study is to ascertain clinical implications of rare variants associated with rare diseases such as autoimmune polyglandular syndrome type 1. Whole genome sequencing will discover variants known to cause disease, likely in individuals not carrying the diagnosis. Using existing phenotypes or potentially with recontact to participants, physiological impact of variants on health and disease can be understood.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	
Medical Information	Electronic Health Record (EHR)	
Quality of life	Survey	*GC

## What are the clinical implications of rare genetic variants predicted to be deleterious discovered in individuals not carrying the diagnosis?

**Use Case ID** 198758      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Maintain & Preserve Health

The goal of this study is to ascertain clinical implications of rare genetic variants predicted to be deleterious discovered in individuals not carrying the diagnosis. Using existing phenotypes or potentially with recontact to participants, physiological impact of variants on health and disease can be understood.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Whole Exomic Sequencing (WES)	
Medical Information	Electronic Health Record (EHR)	
Quality of life	Survey	GC

## How can we use data to predict underlying undiagnosed genetic conditions?

**Use Case ID** 198761      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Other

The goal of this study is to use existing data such as billing codes and laboratory values to predict the presence of a genetic condition before it is diagnosed by traditional medical practice.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health and phenotype data	Electronic Health Record (EHR)	
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	
Genomic sequence data	Whole Genome Sequencing (WGS)	

## Following exposure to environmental toxins, what genetic profiles (protective variants) are associated with health?

**Use Case ID** 1000702      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

Some individuals exposed to environmental toxins develop disease, while others remain healthy. Genetic variants may be protective.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Environmental toxins exposure assessment results	Specimen collection	Every 6 months
Metabolomic profile	Blood draw	Every 6 months
Geocode data	Mobile monitor	Continuous monitoring

## Among people with chronic stress, can we identify an omics signature?

**Use Case ID** 1000706      **Cross-Cutting Theme** Genomics and Other Omics  
**Most Important**      **Scientific Category** Reduce Disease Impact

Description not provided.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Stress	Survey	Annually
Physical measurements	Mobile monitor	Continuous monitoring
Behavioral characteristics, self-assessment	Survey	Periodically
Biological Specimens	Specimen collection	Annually
Genotyping data	Whole Genome Genotyping (WGG)	Baseline
Methylation status	DNA methylation array	Annually
Gut microbiome sample	Smart toilet	Monthly

## What factors allow one person to overcome substance abuse and another not to be able to do so?

**Use Case ID** 1000758

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Treat & Cure Disease

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Family clinical outcomes	PPI Survey (AOURP)	Baseline
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Social support	Survey	Every 3 months
Neighborhood characteristics	Survey	Every 3 months
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Adherence to treatment	Electronic Health Record (EHR)	Continuous monitoring
Drug use/abuse, self-assessed	Electronic Health Record (EHR)	Continuous monitoring
Alcohol Use	Electronic Health Record (EHR)	Continuous monitoring

## How does early life trauma interact with a genome to confer risk and resilience to cardiovascular risk behaviors?

**Use Case ID** 1000772

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Other

ACEs place individuals on a trajectory of health risk behaviors that lead to increased risk of cardiovascular disease. There may be genetic mechanisms that protect against risk after controlling for other social determinants of health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Adverse childhood experiences	Survey	Baseline
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Blood pressure	Electronic Health Record (EHR)	Annually
Health behavior	Electronic Health Record (EHR)	Annually

## What are the pharmacogenomic factors that predict response to treatment?

**Use Case ID** 1000905

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Treat & Cure Disease

Response to treatment includes beneficial and deleterious outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Electronic Health Record (EHR)	Annually
Genotyping data	Blood draw	Baseline
Side effects of prescription medication	Survey	Annually
Health and phenotype data	Electronic Health Record (EHR)	Annually
Hospitalization	Electronic Health Record (EHR)	Annually
Adherence to prescription regimen	Electronic Health Record (EHR)	Annually
Adherence to prescription regimen	Mobile monitor	Daily

## What is the relationship between intersectional underserved in biomedical research characteristics and health outcome disparities?

**Use Case ID** 190192

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Research on populations underserved in biomedical research (UBR) is often based on single UBR characteristics or combined age-race-ethnicity-sex groupings. However, there are population subgroups with particularly concerning constellations of UBR characteristics and very poor health status (e.g., persons without health insurance who live in rural Appalachia). All of Us can provide a more complete picture of the extent, magnitude, and determinants of disparities for these special groups.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics		
Genomic ancestry	Whole Genome Genotyping (WGG)	
Health care participation		
Healthy behaviors barriers, self-assessment		
Health literacy		

## Among people of color with multiple health conditions, how does health literacy affect outcomes?

**Use Case ID** 192272

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health literacy	Survey	Baseline
Quality of life	Smartphone-based ecological momentary assessment	Baseline
Clinical outcomes	Electronic Health Record (EHR)	

## Does access to appropriate specialty care impact patient outcomes across the lifespan?

**Use Case ID** 194369

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Economic and sociological drivers impact access to individualized specialty health care. This study would examine the role of age (pediatric, geriatric), gender, or ethnicity specialty expertise on patient outcomes. Demographic information would be combined with survey information about access to specialty medical care expertise. Outcomes would be determined by PPI and EHR, to include admissions, length of stay, disability status and impact on occupational status.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Include child, teenager, early adult, adult, elderly
Clinical outcomes	Physical exam	Annually
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Quality of life	Survey	*GC

## ***To what extent does the presence of a physical disability affect the quality of medical care and advice a person receives?***

**Use Case ID** 194375

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Create a definitional marker for disability (e.g., “a condition that is expected to be chronic that interferes with typical mobility, daily activities, or self-care”). Correlate the existence of a disability with answers to questions about access/service, such as: Are you able to see a doctor when you need to? Does your doctor recommend a regular exercise program for you? Was your last medical exam sufficiently thorough to evaluate your condition? (Note: Disabled people often get cursory exams.)

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Disability information		

## ***What is the relationship between gender and physical activity among Hispanic youths 13–20 years of age?***

**Use Case ID** 194821

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

The goals of the study will be to examine differences in gender as it relates to physical activity among Hispanic youths. Methods: conduct a survey or focus group to collect data.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	PPI Survey (AOURP)	Continuous monitoring
Personal Characteristics		

## ***How can the stigma associated with palliative care and hospice services be reduced?***

**Use Case ID** 195001

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

Conduct research amongst marginalized populations, many of which are not likely to make use of palliative care treatment and hospice services. For some, the idea of opting for palliative care is seen as a means of “giving up” on effective treatment and transitioning to hospice, however palliative care can be particularly effective once incorporated into standard care. How can we make PC a standard of care measure (as used in many other countries) while reducing its stigma of transition to hospice?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>

## **What are the personal characteristics associated with successful access to the health care system?**

**Use Case ID** 195500      **Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access  
**Scientific Category** Other

Key problem: There is much inequality in access to benefits of the health care system. Knowledge about the characteristics of people who receive what they consider good health care could help others modify behaviors in order to obtain better health care and also help modify the health care system to better serve more people. Proposed study: Ongoing survey of adults in the All of Us population to learn if they are satisfied with the health care they are able to obtain. Report findings annually.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Satisfaction with health care	Survey	

## **How do participants' health literacy (HL) levels compare with national estimates, and what is the role of HL in health outcomes?**

**Use Case ID** 197160      **Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access  
**Scientific Category** Other

Populations of limited health literacy have traditionally been underrepresented in genomic/genetic studies. We propose that All of Us participants complete brief baseline HL survey items as part of the participant-provided information (PPI; The Basics). HL measures can be analyzed in comparison with national estimates and in conjunction with other All of Us measures (e.g., uptake on genetic testing, behavioral outcomes, interests in return of sequencing results).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health literacy	Survey	
Motivation for study participation	Survey	

## Can All of Us be leveraged to advance research in social determinants of health (SDH) toward a personalized definition of SDH?

**Use Case ID** 197175

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

Healthy People (HP) 2020 defines social determinants of health (SDH) as “conditions in the environments in which people live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks.” All of Us can capture this data on its 1 million+ participants and address many unanswered questions, including “Can a more personalized definition of SHD be developed that takes into the account the HP2020 definition and other SHD elements?”

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results		
Clinical outcomes		
Geocode data		
Behavioral characteristics, self-assessment		
Sociodemographics		

## How does access to paid sick leave affect health and health care use?

**Use Case ID** 197519

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

Access to paid sick leave increases preventative care seeking and worker willingness and financial ability to avoid the workplace when ill. Expanding sick leave may reduce the spread of infectious diseases, including influenza. With such a large sample, the All of Us data will include residents of cities and states that require workers to give employees paid sick leave. Being able to track health behaviors, infectious disease incidence, and location will help assess the impact of these laws.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Occupation parameters	Survey	
Occupation Location	PPI Survey (AOURP)	
Clinical outcomes		

## What is the impact of food insecurity on disease management, health care utilization, and health outcomes?

**Use Case ID** 198271

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Complications of hypertension are common in poor populations. Strategies to improve blood pressure control rarely include social determinants associated with suboptimal hypertensive outcomes such as food insecurity. The All of Us program can provide data that will improve our understanding of the impact of food insecurity on disease management, health care utilization, and health outcomes of individuals living with chronic diseases like hypertension by collecting survey data on food insecurity.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Food security status	Survey	

## What is the impact of financial vulnerability and food insecurity on food selection and usage?

**Use Case ID** 198381

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

A controlled trial of vulnerable consumers would investigate their food selection and usage patterns in two settings: a grocery retail setting, where money is exchanged for food; and a pantry setting, where money is not exchanged. Groups of vulnerable consumers would be identified and asked to report the environments where they obtain and select food. Food preparation and diet quality would be measurable outcomes affected by the food environment and vulnerability status of participants.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Interview	At specified times anchored to the clinical event
Food selection	Survey	At specified times anchored to the clinical event
Food security status	Survey	Continuous monitoring
Food purchasing information	Survey	At specified times anchored to the clinical event

## Are minority data being considered enough for pharmaceutical drugs to be administered for chronic conditions?

**Use Case ID** 198471

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

To design this study, we would use the open FDA pharmacovigilance site to see how many side effects are reported by minorities from data available. We would also do literature reviews to examine commonly used drugs for chronic conditions common to minorities and examine/compare the number of samples with white counterparts to ensure we have adequate samples of minorities before drugs make it to market.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes		At specified times anchored to the clinical event
Sociodemographics	PPI Survey (AOURP)	

## What is the relationship between health insurance and health?

**Use Case ID** 198478

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Access to health care	PPI Survey (AOURP)	Every 3 months
Health care cost	Claims data	Weekly
Clinical outcomes	Death records	Every 3 months
Clinical outcomes	Procedure codes	Weekly
Health care cost		

## How does migrant selectivity affect health disparities at multiple levels of observation of a health system?

**Use Case ID** 198493

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

Health disparities remain persistently large across all categories of difference. Systemic explanations require linked observations across time and space and methodologies addressing uncertainty, open systems, and selectivity. Demographic data and demographic theories (e.g., cohort replacement, demographic transitions, and migrant selectivity) must be available to develop measures at all levels and develop the tools for assisting in the highest-quality interpretation of the All of Us data.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Health care participation	PPI Survey (AOURP)	Weekly
Stress	Blood draw	Continuous monitoring
Stress	Survey	Continuous monitoring

## What kinds of social interventions would most effectively reduce health disparities?

**Use Case ID** 198593

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

By crossing several kinds of data, also related to the social, demographic, educational, and economic conditions, All of Us is a unique opportunity to understand with unprecedented precision the role of the social determinants of health. In particular, it could disentangle the links among poor health, poor education, poor economic conditions, poor neighborhood, and unhealthy lifestyle and indicate which policies and social reforms would be most effective in terms of social and health equity.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Every 2 years
Health literacy	Survey	Every 2 years
Lifestyle, self-assessment	PPI Survey (AOURP)	Every 2 years
Socioeconomic Status (SES)	PPI Survey (AOURP)	Every 2 years
Stress	Survey	Every 2 years

## How can we assess the general population representativeness of the All of Us cohort?

**Use Case ID** 198594

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

1. Ensure that data linkage with population-based disease registries and large databases is possible, through inclusion in informed consent and collection of Social Security numbers. 2. Collect variables in the same categories as national surveys, allowing for assessment of representativeness based on demographics, SES, geography, and health outcomes. 3. Consider selecting a small subset of the cohort with formal probability sampling, allowing for formal re-weighting of the cohort.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Clinical outcomes	Survey	Every 2 years
Cancer information	Electronic Health Record (EHR)	Every 2 years
Geocode data	Survey	Every 2 years
Occupation	PPI Survey (AOURP)	Every 2 years

## How do health-, fitness-, and sickness-related expenses correlate with health outcomes?

**Use Case ID** 198710

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

With all feasible tools (diary, receipts, credit card records, third-party validation), record all expenses (real and in-kind), from self and all payers, related to personal health, fitness, and illness on a representative subset of cohort (ethnic, geographic, income, education, gender, age, etc.). Correlate with acute, intermediate, and longtime health outcomes, and track for a decade. Keep within the high-priority category of Guide NOT-OD-16-025 and consider collaborating with another agency.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care cost	Claims data	Periodic (approximately biweekly)
Clinical outcomes	Electronic Health Record (EHR)	Periodic (approximately biweekly)
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Periodic (approximately biweekly)
Clinical outcomes	Survey	Annually

## ***Within a healthy cohort, can genomic and social determinants be used to tailor preventive and primary care recommendations?***

**Use Case ID** 198716

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

This case study focuses on symptoms not identifiable as a “disease” or indication, and based on the risk factors captured in that subset’s data, identify what can be done with tailored prevention and primary care to prevent the symptoms from becoming syndromes. A participant subset with similar complaints, race/ethnicity, geographical factors, genetic, and SDH factors might sort out syndromes and treatment that are undiagnosed or untreated among underserved and vulnerable communities.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Genomic analyses		
Sociodemographics		
Clinical outcomes		

## ***Do diagnostic markers differ across racial and ethnic groups, and do they contribute to health disparities?***

**Use Case ID** 198762

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Treat & Cure Disease

The goal of this study is to research underlying causes of health disparities using existing data and novel data sources. For example, are diagnosis and treatment of diabetes different across ethnic groups, does A1c vary by G6PD genotype, and do follow-up and A1c target differ by diversity standards?

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Specified Biomarkers	Blood draw	
Outcomes	Electronic Health Record (EHR)	
Personal Characteristics	Survey	

## What are the barriers to disease detection?

**Use Case ID** 1000879

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Detect Disease

Social determinants of disease detection, access to health technology, health care, etc. Multiple outcomes including intermediary, such as having a smartphone.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Social environment	Survey	Annually
Health insurance status	PPI Survey (AOURP)	Annually
Movement assessments	Global Positioning System (GPS) monitoring	Continuous monitoring
Access to health care	PPI Survey (AOURP)	Annually
Socioeconomic Status (SES)	PPI Survey (AOURP)	Annually
Educational outcomes	Survey	Annually
Health literacy	Survey	Annually
Cultural attitude towards health/healthcare	Survey	Annually
Perceived outcomes - patient	Survey	Annually

## What factors make for a quality death?

**Use Case ID** 1001153

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

Death is the only certain outcome for all participants. To what extent does planning (e.g., advance directives and family discussion) lead to better quality of death?

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Death	Survey	At age 50 and every 5 years
Death quality	Interview	Post-event
Cause-of-death ascertainment	Death records	Continuous monitoring

## What interventions engage the substance use disorder populations successfully?

**Use Case ID** 1001247

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Treat & Cure Disease

Need to specify interventions and substance(s). Key terms: engage + successfully. All of Us should consider targeting recruitment of individuals with substance abuse disorders.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Pre- and post-treatment
Addiction-related information	Electronic Health Record (EHR)	Baseline
Treatment data/specifc records	Electronic Health Record (EHR)	Baseline
Treatment/Therapy (other than Drug use)	Electronic Health Record (EHR)	Periodically
Treatment data/specifc records	Interview	On Demand

## What is the most effective way to communicate an individual's genetic and non-genetic risk factors for a given condition?

**Use Case ID** 191717

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

Returning information to individuals about risk factors, both genetic and non-genetic, is an important component of personalized medicine for individuals, families, and communities. Understanding and quantifying how different types of information made available to participants are viewed, downloaded, shared, and lead to the taking of subsequent action could inform effective communication about risk to participants.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care participation	PPI Survey (AOURP)	Every 2 years
Lipids panel results		Annually
Health and phenotype data	Electronic Health Record (EHR)	Continuous monitoring
Genotyping data	Whole Genome Genotyping (WGG)	Baseline
Diet, self-assessment	PPI Survey (AOURP)	

## How do feelings about health research in the United States vary with race?

**Use Case ID** 192249

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

Especially given the negative history of past research efforts in the U.S. involving persons of color, use quantitative (survey) and qualitative methods (focus groups) to assess the disposition of racial and ethnic minority communities towards health research programs like All of Us.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Feelings about health research	Survey	Baseline
Sociodemographics		

## Can machine learning algorithms reliably identify distinct sub-populations and sub-phenotypes in a specific disease cohort?

**Use Case ID** 195114      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Most Important**      **Scientific Category** Elucidate Disease Mechanisms

Identify a cohort with a specific medical condition, intervention, and outcome and use heterogeneous patient measurements. Using a novel, soon-to-be-published machine learning platform that performs “X-rays” of cohorts, discover distinct sub-populations, their sub-phenotypes, and different outcome rates. The ability to discover distinct sub-populations characterized across many modalities would greatly advance the mathematical foundation for precision medicine for all diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Custom sensor/app	
Microbiome sample	Cheek swab	Baseline
Body temperature measurement	Electronic monitoring/recording	Continuous monitoring
Cognitive assessments	Imaging	Baseline
Pharmacogenomics	Whole Genome Genotyping (WGG)	Baseline
Prescription medication\treatment	Pharmacy records	
Clinical outcomes	Electronic Health Record (EHR)	
Depression diagnosis		Periodically

## Which observations of daily living are more effective in monitoring and improving a patient’s overall well-being?

**Use Case ID** 195163      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Scientific Category** Maintain & Preserve Health

Observations of daily living (ODL) are easily collected by patients or their families. They are dynamic, patient-generated data that improve decisions regarding health and well-being (for example, mood or sleep patterns). When integrated with medical data, ODLs help provide a holistic view of the patient. Other benefits include significantly expanding the time window and detail in which a patient recalls events, as well as introducing a pause in the busy day to reflect on their well-being.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Anthropometrics, whole body measurements	Physical exam	Weekly
Sleep parameters	Sleep journal	Weekly
Mood patterns	Mobile monitor	Weekly
Prescription medication\treatment	Mobile monitor	At specified times anchored to the clinical event
Perceived outcomes - patient	Mobile monitor	At specified times anchored to the clinical event

## How can disability caused by health conditions be measured in All of Us participants over time?

**Use Case ID** 195660

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

The shared goal of NIH and the participants is to reduce the burden of illness across conditions and segments of the population. How to capture burden of illness due to this variety of health conditions on an individual basis? A validated, standardized measure of disability would be extremely valuable to ascertain the impact of the various conditions on function in All of Us. Plan might be to assess the various, validated scales, then customize and pilot a scale for use in All of Us.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Disability assessment results	Survey	Annually
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Annually
Occupation	PPI Survey (AOURP)	Annually
Physical activity, self-assessment	Activity monitor	Every 3 months
Quality of life	Survey	Every 3 months

## What factors determine your willingness to share your electronic health record?

**Use Case ID** 196024

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

I propose to study what factors (demography, disease history, symptoms, genetics, environment) play a role in deciding to share your electronic health record (EHR). Using EHR for research leads to much faster acquisition of data, and All of Us offers a unique opportunity to study this further (similarly for electronic dental records).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	Electronic Health Record (EHR)	
Health care participation	PPI Survey (AOURP)	

## Who chooses to receive which types of individual-level data, and how does data receipt influence health care use/lifestyle behavior?

**Use Case ID** 196050

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

As individual-level data is returned, this could change health care utilization and lifestyle behaviors. From a methodological perspective, understanding these connections will show how behavior in the All of Us cohort is influenced by participation. From a health promotion perspective, data could contribute to intervention design. By investigating individual differences in data receipt choices, groups more likely to be left out of possible benefit conferred by information receipt could be identified.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Personal EHR use	AOURP Participant Portal	
Health care participation	Electronic Health Record (EHR)	Every 3 months
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Diet, self-assessment	Food diary	At specified times anchored to the clinical event
Sleep behavior assessment results	Activity monitor	Continuous monitoring

## What is the effect of health insurance on outcomes of major diseases?

**Use Case ID** 196068

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

Break down the level of insurance to five groups: uninsured, Medicaid, HMO style, Medicare, and private. Then compare the outcome in 10 common diseases and 5 rare diseases to see the influence of health insurance status on outcome. You can compare what treatments patients actually get based on insurance company. See if it makes a difference if patient gets the drugs the doctor prescribes when there is good insurance versus when an insurance company selects the medicine a patient needs to use.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Annually
Health care cost		Annually

## Can advancements in the treatment of one rare disease help make advances in the treatment of other rare diseases?

**Use Case ID** 196133

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

First, a computer program scans all rare diseases for commonalities and groups them as such. Then test current treatments of one rare disease on others.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Include child, teenager, early adult, adult, elderly
Perceived outcomes - patient	Survey	Continuous monitoring
Health literacy	Claims data	Continuous monitoring
Quality of life	Mobile monitor	Continuous monitoring

## How many researchers are utilizing participatory action research (PAR) in their methods?

**Use Case ID** 196477

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

Create a study with PAR/public participation. Identify states/cities where a high concentration of research is being conducted or areas targeted in response to natural disasters: Florida, Texas, Puerto Rico, California. Seek out community-based organizations to learn how studies and research have impacted communities in the past. Learn and listen to community members to understand how to conduct future research to minimize over-research. I highly recommend Tejasbarrios.org as a CBO.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Every 3 months
Quality of life		

## Can the All of Us database lead to an evidence-based approach to symptom assessment and response to treatment?

**Use Case ID** 196676

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Maintain & Preserve Health

Many outpatient visits are prompted by symptoms that cannot be tied to a disease-based explanation. The prescribed symptomatic therapy may be non-specific and ineffective, leading to repeat clinic visits. From the 1 million plus All of Us participants, can symptom-specific data be extracted with Natural Language Processing and analyzed in relation to clinical, demographic, environmental, and self-reported data, to achieve the overarching goal of more precise symptom assessment and treatment?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Natural language processing of notes	
Clinical outcomes	Electronic Health Record (EHR)	
Lifestyle, self-assessment	Natural language processing of notes	
Physical activity, self-assessment	Natural language processing of notes	
Quality of life	Natural language processing of notes	

## What are the most commonly cited motivations for participants to enroll in All of Us?

**Use Case ID** 197161

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

Identifying motivations and values that drive enrollment into the cohort is important for tailoring and optimizing accrual and sustained research participation. Including a baseline item such as the above can help the researchers (particularly communication experts) ascertain and track motivations for staying in the cohort. Examples of motivations may include family health history, scientific altruism, and specific health conditions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Motivation for study participation	Survey	

## How does genetic literacy influence and inform patient engagement, expectations, and health care utilization efforts?

**Use Case ID** 198117

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

Genetic literacy can be defined as one’s ability to understand concepts important to the use of personal genetic information. We propose that All of Us participants complete brief baseline survey items related to genetic literacy as part of the participant-provided information (PPI; The Basics). We would explore the association between genetic literacy and outcomes such as patient engagement in All of Us, expectations about participating in All of Us, and health care utilization.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health literacy	Survey	Baseline
Social support	AOURP Participant Portal	Continuous monitoring
Clinical outcomes	Survey	Annually
Perceived outcomes - patient	Survey	Baseline

## How can the All of Us Research Program most ethically motivate active participation in the cohort over many years?

**Use Case ID** 198128

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

The All of Us Research Program’s success depends on public trust, active participant involvement, and long-term support from all stakeholders. All of Us should support ethics and qualitative research on questions related to participant engagement and incentives, such as “What constitute ethically appropriate incentives? How can All of Us encourage participation of less engaged groups and individuals to ensure that the project does not disproportionately benefit highly motivated patients?”

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Motivation for study participation	Survey	Annually
Feelings about health research	Survey	Baseline
	Survey	Continuous monitoring

## What are best practices for engaging historically underrepresented groups in research?

**Use Case ID** 198137

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

Feedback from FQHCs and HPOs to determine reasons for enrolling, reasons for declining, and barriers to recruitment and retention, including but not limited to literacy level, digital divide, and perception of trust in government.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Patient Engagement	Survey	*GC

## What is the diagnosis concordance provided by classification models and traditional, physician-based diagnoses in clinical settings?

**Use Case ID** 198518

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Other

Classification models coupled with expert opinions are useful in clinical settings. Inappropriate use of these models can have negative outcomes. Variables related to metabolic syndrome would be required for a classification model to identify at-risk patients and test its use in a clinical setting. Comparison of recommended diagnosis derived by the model along with expert diagnosis and longitudinal patient tracking will provide a protocol for use of classification models in clinical settings.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Lipids panel results		Baseline
Metabolic risk assessment result	Blood (EDTA)	Baseline
Hemoglobin A1C (HbA1C) levels	Blood (EDTA)	Baseline

## What are the reasons for the minimal participation of urban community residents in longitudinal research?

**Use Case ID** 198702      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Scientific Category** Other

The purpose of this study is to understand reasons for minimal participation of urban community residents in longitudinal research. The study will also explore expectations of urban community residents as a result of participating in longitudinal research. The study will use a qualitative focus group approach with urban community residents in the Midwest.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health literacy	Survey	Baseline
Sociodemographics		
Location data		
Behavioral characteristics, self-assessment		

## How do different health conditions and treatments affect health-related quality of life (HRQOL)? How does HRQOL vary with other factors?

**Use Case ID** 198728      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Scientific Category** Other

Health-related quality of life (HRQOL) is a common metric for individual and population health and for comparing outcomes across health conditions. Utility-based HRQOL measures are used to estimate quality-adjusted life years for cost-effectiveness and other studies. Including utility-based HRQOL in regular All of Us data collections (baseline onward) will support myriad statistical, modeling, and evaluation studies by combining other All of Us data on patients, conditions (especially chronic), and treatments.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Quality of life	Survey	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Medical Information	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Treatment/Therapy	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Behavioral characteristics, self-assessment	Survey	Annually

## Can we build a model for resistance maintenance of health despite risk factor exposures?

**Use Case ID** 1000964

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Detect Disease

Transition to one program—detection early, presumptive, symptoms, systematic—healthy state for an intellectual; changes over time to detect disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Microbiome sample	Stool sample	Every 3 months
Patient-reported outcomes		Annually
Intestinal physiological measurements	Sensor (swallowed)	Continuous monitoring
Social networking use	Mobile device	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Ongoing
Credit score	Financial records, personal	Ongoing

## Can we build a predictive model of resilience from detected diseases back to health?

**Use Case ID** 1001000

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Detect Disease

Transition to/from disease state and health. Detection, early, presymptomatic, symptomatic, asymptomatic. Healthy state defined by individual/population. Data change across age group. Correlation between PRO/COA/AOL clinician-entered and self-reported and biomarker validation perception of health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Patient-reported outcomes		Annually
Social networking use	Mobile device	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Ongoing
Microbiome sample	Stool sample	Periodic (approximately biweekly)
Biological Specimens	Genomic testing	Periodic (approximately biweekly)
Health and phenotype data	Custom sensor/app	Continuous monitoring

## What is the best predictor of quality of life?

**Use Case ID** 1001008      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Most Important**      **Scientific Category** Assess Risk

The enormity of the data of All of Us will allow us, for the first time, to predict quality of life over time, and allow us to identify key factors that can inform interventions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environment	Survey	Annually
Quality of life	Survey	Annually
Dental/oral health information	Electronic Health Record (EHR)	Annually
Physical measurements	Electronic Health Record (EHR)	Annually
Lifestyle, self-assessment	Electronic Health Record (EHR)	Annually
Mental health and behavior information	Patient-Reported Outcomes Measurement Information System (PROMIS)	Annually
Sleep assessments	Electronic monitoring/recording	Continuous monitoring
Environment	Geographic information system (GIS) code	Continuous monitoring
Quality of life	Smartphone-based ecological momentary assessment	Continuous monitoring
Social environment	Social network mining	Periodically

## Can momentary assessment via mobile technology be used to characterize resiliency?

**Use Case ID** 1001169      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Scientific Category** Maintain & Preserve Health

Use cell phone to assess how you are feeling at the moment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Symptoms	Custom sensor/app	Continuous monitoring
Mood patterns	Mobile device	Continuous monitoring

## How can we partner with electronic medical record (EMR) payers/vendors to make EMRs more research-friendly and incorporate data not currently captured?

**Use Case ID** 1001222

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Assess Risk

Capture these data for machine-learning methods to identify individuals at risk for “readmission” or “adverse events.” Social data, family history (pedigree), genetic data, exposure data.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care cost	Financial records, personal	Monthly
Outcomes	Financial records, provider	Monthly
Genotyping data	Clinical diagnostic test	Baseline
Social determinants of health (SDH)	PPI Survey (AOURP)	Quarterly or Annually
Family clinical outcomes	Patient-reported outcome	Quarterly or Annually

## Can we detect a signal that represents a change in health status or transitions between health and disease?

**Use Case ID** 1001251

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Most Important** **Scientific Category** Detect Disease

Transition to/from. Detection—early/sx/asx. Healthy state for an individual changes over time. “Healthy state” defined by individual/population (data change across age groups, correlations between PRO/COA/QOL, clinician-entered, self-report and biomarker, perception of health).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Credit score	Financial records, personal	On Demand
Patient-reported outcomes		Annually
Microbiome sample	Stool sample	Every 3 months
Biological Specimens	Genomic testing	Periodically
Social networking use	Survey	Continuous monitoring

## **How can single accelerometers or smartphone-based measures of gross activity characterize voluntary and involuntary movements?**

**Use Case ID** 194550

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Other

Using either body-worn sensors, mobile devices, or other novel applications, the science of this small cohort study will focus on which data parameters are critical, which instruments are most appropriate, how much data is needed, from where on the body, and for how long in the measurement of movement. Ensuring that data are standard, that sensors are reliable in measuring the outcome of interest, and that approaches to data analysis are rigorous and reproducible are primary needs in the field.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Movement assessments	Smartphone-based ecological momentary assessment	Weekly
Gait assessment results	Walk test	Baseline
Physical activity, self-assessment	Mobile monitor	Weekly
Clinical outcomes	Electronic Health Record (EHR)	Baseline
Geocode data	Mobile monitor	Weekly

## **Can analysis of blood pressure and pulse rate data patterns lead to diagnosing current medical conditions or predicting future ones?**

**Use Case ID** 194754

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

Plan to collect blood pressure and pulse rate measurements multiple times per day. Initially, data could be collected from blood pressure monitor devices at home and moved over the Internet to the All of Us Data and Research Center (DRC). Later, blood pressure and pulse rate data could be collected and transferred in near real time from wearable wireless sensor devices.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Blood pressure	Mobile monitor	
Pulse	Mobile monitor	

## What are the characteristics of people who benefit from using health applications on mobile devices?

**Use Case ID** 195733

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Maintain & Preserve Health

We would assess the benefits of health apps on individuals' health on multiple survey and clinical diagnostic items and compare results between three groups. Group 1: no access to a smartphone; group 2: access to a smartphone, but no use of health apps; group 3: access to a smartphone and use of health apps. The goal of this data would be to better develop and design mHealth interventions to improve health outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mobile phone ownership	Survey	Annually
Health apps used	Survey	Annually
Behavioral characteristics, self-assessment	Survey	Annually
Health literacy	Survey	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually

## Does just providing Fitbits to individuals change and maintain any beneficial health behaviors, and will it result in improved health outcomes?

**Use Case ID** 196491

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Maintain & Preserve Health

Research is mixed on the effectiveness of mHealth interventions in changing and maintaining health behaviors. Does just providing Fitbits (without intervention) change and maintain any health behaviors? Does this lead to improved health outcomes (BMI, BP, lipids, etc.)? Provide Fitbits to a random sample (not a self-selected sample that may be motivated to change behaviors). Longitudinal comparison of those with/without Fitbits on health behavior change and maintenance and on health outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Mobile monitor	Continuous monitoring
Clinical outcomes	Physical exam	

## Could utilization of blockchain technology increase All of Us participant engagement and retention?

**Use Case ID** 197189

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Other

In “Power to the People: Data Citizens in Age of Precision Medicine,” solutions “may lie in embracing broader concept of autonomy empowers individuals to protect their interests by exercising meaningful rights of data citizenship.” Using distributed ledger technology (public or private) provides advanced privacy and security measures that data warehouses, gatekeepers of citizens’ genetic/genomic data, etc. would be remiss not to develop and deploy for use. Pilot with an HPO versus an HPO not using the tech.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Quality of life	Natural language processing of notes	Every 3 months
Behavioral characteristics, self-assessment	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Clinical outcomes	Claims data	At specified times anchored to the clinical event

## How can omic profiling technologies be used with wearable devices to predict disease occurrence?

**Use Case ID** 198604

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

With the sheer number of individuals that will be recruited for this program, this is an ideal cohort to test out the above hypothesis. Methods: Do a longitudinal study of the All of Us cohort using a variety of wearable devices (e.g., heart rate monitor, activity monitor, temperature monitor, SpO2 levels) and omics measurements (proteome, metabolome, genome, transcriptome, microbiome) to see if you can predict whether individuals are at high, medium, or low risk for developing a number of different diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical measurements	Mobile monitor	Continuous monitoring
Genomic analyses	Clinical diagnostic test	At specified times anchored to the clinical event
Metabolomic profile	Clinical diagnostic test	
Microbiome sample	Clinical diagnostic test	

## Can ubiquitous data from mobile devices be used to develop health and mental health behavior models?

**Use Case ID** 198640

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

Acquire sensor data from mobile phones (e.g., GPS, accelerometry, sound features, light, etc.) and other ubiquitous devices. Collect information on behaviors, psychological states, and environmental conditions through experiencing sampling or other data bases (e.g., weather, mapping services, etc.). Develop models that can use the passively collected data to estimate behaviors and psychological states related to the mental health and health conditions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Smartphone-based ecological momentary assessment	Continuous monitoring
Sensor data	Smartphone-based ecological momentary assessment	Continuous monitoring
Mental health and behavior information	PPI Survey (AOURP)	Every 3 months

## Could the development and refinement of novel GPS or GIS technologies better define community contextual exposures?

**Use Case ID** 198649

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Other

The built environment is only one contextual exposure of interest to investigators who study these factors in relation to disease (and even these function variably across rural and urban areas). New technology could assist in better clarifying a fuller scope of residential exposures, including what elements/exposures the All of Us participants actually come into contact with.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Location data	Custom sensor/app	
Chemical exposure assessment results		
Location data	Global Positioning System (GPS) monitoring	
Geocode data		

## Does access to mobile technology lead to increased resilience and better response to treatment?

**Use Case ID** 1000814

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Treat & Cure Disease

Technology may be advanced, and mobile will evolve to advance technology (i.e., implementable, wearable).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Technology Use	Mobile device	Continuous monitoring
Patient feedback	Survey	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually
Social environment	Survey	Annually

## What screening procedures can be used to maintain and preserve health using telehealth technology?

**Use Case ID** 1001236

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Maintain & Preserve Health

Using home health as a form of mobile health. Bringing technology to people without traditional medical home to motivate to seek preventive/diagnostic care.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Blood pressure	Electronic monitoring/recording	On Demand
Body temperature measurement	Electronic monitoring/recording	On Demand
Weight	Electronic monitoring/recording	On Demand
Imaging	Imaging	Periodically
Infectious agents	Whole Genome Genotyping (WGG)	Pre- and post-treatment
Clinical outcomes	Mobile monitor	Continuous monitoring
Location data	Geospatial tracking	Continuous monitoring

## What dietary factors affect an individual's susceptibility to chronic disease?

**Use Case ID** 192242

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

The top four causes of death in the U.S. are diet related, and many other troublesome diseases are affected by diet. It will be important, therefore, to capture nutritional status, food environment, and repeated 24-hour (ASA24s) dietary intakes along with measures that can validate dietary measures of public policy interest, including added sugar, energy, protein, sodium, iron, vitamins, dietary supplements, potassium, fruits and vegetables, and fish (for which validate measures exist).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Annually
Food selection	Clinical diagnostic test	Annually
Diet constitution assessment	Hair and nail clippings collection	

## Is body mass index a useful metric for determining an individual's health status?

**Use Case ID** 192271

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Monitor the health status over the course of five years from people who are within current "healthy" BMI ranges and people that are above and below the guidelines. It may be time to update these BMI ranges, based on empirical health outcome data.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Body Mass Index (BMI)	Physical exam	At specified times anchored to the clinical event
Lipids panel results		At specified times anchored to the clinical event
Fatigue symptom	Survey	
Cardiopulmonary assessment	Clinical diagnostic test	At specified times anchored to the clinical event

## What is the relationship between diet and incidence of disease?

**Use Case ID** 192288

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Would like to look at dietary features and compare with incidence of hypertension, diabetes, cancer, and Alzheimer's. What oil(s) people use? Whether they avoid gluten? Whether they eat moderate red meat? Whether they eat low-fat or fat-free food? Whether they eat cold breakfast cereal? How often they eat nitrate-containing meats (bacon, salami, etc.)? Are there any proven dietary correlations with Alzheimer's? The low-fat diet has resulted in a high-sugar diet in the U.S. Conflicting information results.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Every 3 months
Diabetes outcomes		
Hypertension outcomes		
Cancer outcomes		
Alzheimer's outcomes		

## What features of people's neighborhood environments predict healthy outcomes?

**Use Case ID** 194370

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

What features of people's environments—walkability, parks and greenspace, transit options, mixed use neighborhoods, etc.—predict healthy outcomes? For example, what neighborhood designs most encourage walking? Social connectivity? Safety? And how do those predict better cardiovascular health, mental health, life satisfaction, and life expectancy?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Neighborhood characteristics	Geospatial tracking	
Health and phenotype data		
Lifestyle, self-assessment		
Travel choice		
Social environment		

## What factors predict happiness, and to what extent does happiness predict good health?

**Use Case ID** 194371

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

What factors predict happiness, and to what extent does happiness predict good health? For instance, what are the roles of social networks (or conversely, loneliness)? Satisfying work? Religious faith? Wealth? Education? Discrimination?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Happiness measure	Survey	Annually
Social relationships		
Spirituality/Religion		
Sociodemographics		
Discrimination encounters		

## What role does perceived and/or factual evidence of love have on one's health and well-being?

**Use Case ID** 194507

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

What role does perceived and/or factual evidence of love of others, oneself, and received by others play in health/epidemiology? Goals and outcomes of methods would be to develop statistically reliable and valid longitudinal measures of the negative and beneficial manifestations of real or perceived love of oneself and love from others on personal health outcomes and on population-based epidemiology using a large random sample while controlling for bias among other biopsychosocial factors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Perceived outcomes - patient	Survey	Continuous monitoring
Behavioral characteristics, self-assessment	Clinical diagnostic test	Annually
Cortisol levels	Blood draw	Continuous monitoring
Behavioral characteristics, self-assessment	Activity monitor	Continuous monitoring
Clinical outcomes	Activity monitor	Continuous monitoring

## How does a lifelong adherence to healthy lifestyle habits affect the aging

**Use Case ID** 194810

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Goal: Show that a strict, lifelong adherence to a healthy lifestyle retards the aging process, enables you to avoid many common diseases, and allows you to greatly reduce health care costs. Method: Invite participants from all over the world to commit to following a healthy lifestyle regimen throughout life. Expected outcomes: Participants age more slowly, have fewer chronic diseases, and spend less on health care than the general population.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Food diary	Daily
Physical activity, self-assessment	Custom sensor/app	Daily
Sleep assessments	Sleep journal	
Eating disorders diagnosis	Diary/journal	Daily
Eating disorders diagnosis		Daily

## What are the long-term benefits of an enrollee's exercise routine?

**Use Case ID** 194823

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

This would be a long-term survey done on participants who would fill out a survey given to them quarterly with their self-reported answers. Over many years they would have their exercise routine tracked. The amount of exercise they do, the type of exercise they do, and the time they spend doing it would then be compared to the general public as far as the participants lengthening their lives and decreasing their cancer risk, diabetes, HTN, cardiovascular disease, and obesity rates.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	PPI Survey (AOURP)	Every 3 months
Cancer information	PPI Survey (AOURP)	
Obesity diagnosis	Survey	
Diabetes diagnosis	PPI Survey (AOURP)	
Cardiovascular disease information	PPI Survey (AOURP)	

## Does yoga contribute to fewer symptoms of chronic disease as well as long-term physical and mental health?

**Use Case ID** 194845

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

To follow yoga practitioners to see if they experience better physical and mental health in the long term. For those with a chronic disease, does it contribute positively to symptom management?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Annually
Yoga, activity	Activity monitor	Continuous monitoring
Mental health and behavior information		

## Why don't people change their health habits after they are diagnosed with conditions (e.g., high blood pressure or high cholesterol) that increase their risk for chronic diseases?

**Use Case ID** 194852

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Other

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lifestyle, self-assessment	Activity monitor	At specified times anchored to the clinical event
Health literacy	Survey	
Perceived outcomes - patient	Survey	

## Is weight change in men and women affected by age and chronic disease?

**Use Case ID** 194861

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

While it has been assumed that weight is changing with age, no contemporary population-based data exists to determine the magnitude of such change in different age groups for men and women. Using self-reported (and potentially spot-validated).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Weight		
Personal Characteristics		
Health and phenotype data		

## How does meal timing affect health?

**Use Case ID** 194864

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Collect data on the number of meals eaten per day, the times of those meals, estimated calories in each meal, when people go to sleep, and when people wake up. Then test for the health effects of (a) meal frequency, (b) the daily eating/fasting duration, and (c) the time of day that people eat (e.g., quantified as the midpoint of the eating period or at the 50% mark for caloric consumption during the daytime). You'll need to adjust for sleep duration and sleep timing, which are confounders.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Food diary	

## How does social support affect a person's health trajectory?

**Use Case ID** 195000

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important Scientific Category** Maintain & Preserve Health

Considering that the longest running health study (Harvard Men's Study) showed that the quality of relationships at age 50 is the biggest predictor of health at age 80, we realize we have less research than would be ideal into how the quality, quantity, and type of social support affects health. This is an excellent opportunity to fill that gap, simply by adding a module assessing quality, quantity, and type of social support as part of the ongoing study measures.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social support	Survey	Annually
Clinical outcomes		

## What is the relationship between spirituality and health outcomes?

**Use Case ID** 195099

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

A brief, simple non-denominational questionnaire during medical encounters about patients' spirituality and following major health outcomes over a 5-year period.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Stress	Electronic Health Record (EHR)	Annually
Spirituality/Religion		
Clinical outcomes		

## Does insufficient, disordered, or mistimed sleep cause physical or mental illness?

**Use Case ID** 195531

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The CDC calls insufficient sleep a “public health problem.” But sleep and circadian rhythms are oft-ignored—even derided—aspects of health. When you ask subjects about lifestyle, don’t stop at diet/exercise. Ask about sleep. When you ask about sleep, don’t stop at length/quality. Ask about circadian timing: when people sleep. Is timing dictated by their body clock or work/family demands? All of Us is an unprecedented opportunity to associate sleep deprivation and circadian mistiming with physical/mental illness.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sleep parameters	Survey	
Sleep quality assessment results	Survey	
Clinical outcomes	Electronic Health Record (EHR)	

## How is spirituality/religion functionally linked to physical and mental health?

**Use Case ID** 195675

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

The McLean Hospital/Harvard Medical School Spirituality and Mental Health Program (see <http://www.mcleanhospital.org/programs/spirituality-and-mental-health-program>) is developing a 6-item self-report survey measure to assess for positive and negative aspects of spiritual/religious life. Inclusion of the items in the All of Us protocol could facilitate powerful exploratory analyses to assess how this domain is related to health processes and outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Spirituality/Religion	Survey	Annually
Mental health and behavior information		
Health and phenotype data		

## Can men improve their health by better prioritizing disease prevention and wellness?

**Use Case ID** 196608

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Other

The top threats to men’s health are known, common, and often preventable. The goal of research in this area is to better explore male health promotion, screening, and treatment options. How can we increase self-management of chronic and other diseases among men? How do we help men to prioritize their health and plan for the eventualities of medical care? We can extract some of this information from the medical record.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Quality of life	Electronic Health Record (EHR)	
Health and phenotype data	Electronic Health Record (EHR)	
Health care participation		
Healthy behavior, self-assessment		

## What characteristics are associated with maintenance of long-term behavior change?

**Use Case ID** 196609

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Other

Some people have short-term success changing a behavior (e.g., to exercise more, get adequate sleep, or eat healthier). However, long-term maintenance is challenging. Why is it that some succeed, and some don’t? Is it possible that the secret to long-term success has less to do with what the behavior is (e.g., eating healthy) and more to do with personal attributes or mindsets? Thus, personal attributes/mindsets could be the common denominator among a variety of disease/condition settings.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Body Mass Index (BMI)	Electronic Health Record (EHR)	
Physical activity, self-assessment	PPI Survey (AOURP)	
Lifestyle, self-assessment	PPI Survey (AOURP)	
Depression diagnosis	PPI Survey (AOURP)	
Health issues, occupational	Survey	

## **What is the prevalence of cannabinoid use in All of Us, and what are self-reported reasons for use as well as its perceived effectiveness?**

**Use Case ID** 196670

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Other

The majority of U.S. states and D.C. have legalized cannabis to some extent; an increasing number of Americans are using cannabis products via medical prescription or self-selection, and data needed for understanding these facts from a health care and public health standpoint are sparse. Finding out how many people are using cannabinoids, which modalities, why, and any perceived effects in All of Us at study baseline and longitudinally would provide useful information for health professionals.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cannabis use	PPI Survey (AOURP)	Annually
Perceived outcomes - patient	Survey	

## **What is the effect of veganism on overall health?**

**Use Case ID** 196692

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

There is increasing evidence that a vegan diet promotes health in numerous ways. For example, due to the drastic reduction of meat and dairy consumption, people who follow a vegan diet are much less likely to develop several chronic diseases. To what extent does the diet play a role, and in what ways can people of different races and backgrounds in general benefit from the diet? Similarly, it would be interesting to study the effect of a plant-based diet on health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment		
Clinical outcomes		
Sociodemographics		

## How do fluctuations in weight impact long-term health outcomes? What are the primary causes of these fluctuations?

**Use Case ID** 197062

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

A longitudinal survey, to correlate weight fluctuations over time to clinical outcomes. Preliminary work from Japan suggests that fluctuations in weight are as detrimental as long-term obesity. This proposal seeks to validate these finding in the U.S., where rates of obesity are significantly higher, and identify factors that contribute to weight fluctuations. By identifying these factors, improved education and support mechanisms can be developed to help patients maintain weight loss over time.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Weight	Survey	Periodic (approximately biweekly)
Diet, self-assessment	Food diary	Continuous monitoring
Physical activity, self-assessment	PPI Survey (AOURP)	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Annually
Sociodemographics	PPI Survey (AOURP)	Baseline

## How does marijuana use affect other health indicators?

**Use Case ID** 197387

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Other

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cannabis use	PPI Survey (AOURP)	
Clinical outcomes	Electronic Health Record (EHR)	
Perceived outcomes - patient	Survey	

## How can precision medicine be most effectively used to influence lifestyle choices and behaviors, such as physical activity?

**Use Case ID** 198108

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

A transformative goal would be to use precision medicine to individualize and make far more effective dose-response interventions and prescriptions for physical activity and other health behaviors. Methods could include data collection through wearable technology, validated self-reports, other existing health data, and the unique insights from All of Us, especially related to sources and effects of lifestyle influence. ACSM applauds this pathway to health innovation.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Continuous monitoring
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Lifestyle, self-assessment		
Behavioral characteristics, self-assessment		

## What is the comparative and independent effectiveness of healthy lifestyle choices in preventing and treating diseases?

**Use Case ID** 198110

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Determine the lifestyle strategies and interventions that produce the most gains in prevention and treatment of diseases in a comparative and complementary context with pharmaceutical, surgical, and other approaches. Methods could include data collection through wearable technology, validated self-reports, comparative effectiveness data, medical reimbursement, predictive analytics, and the unique insights from All of Us. ACSM applauds this pathway to health innovation.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Continuous monitoring
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Lifestyle, self-assessment	PPI Survey (AOURP)	
Health care cost	Claims data	

## What active and healthy lifestyle interventions will most effectively reduce health disparities and increase health equity?

**Use Case ID** 198111

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Intentionally aim to ensure that All of Us insights extend to everyone, particularly regarding lifestyles and improved health for population segments of need and opportunity. Methods could include data collection through wearable technology, validated self-reports, comparative effectiveness data, medical reimbursement, predictive analytics, and the unique insights from All of Us. ACSM applauds this pathway to health innovation.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	
Behavioral characteristics, self-assessment	Survey	
Physical activity, self-assessment	Activity monitor	Continuous monitoring

## What biological, behavioral, and environmental factors influence functional and participation outcomes in disabled populations?

**Use Case ID** 198164

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

The prevalence of disabling conditions is increasing in the U.S., and yet we do not have a sufficient understanding of the factors that influence functional and participation outcomes in these populations. With the addition of self-reported measures along these lines, the NIH All of Us initiative could be a powerful tool to correlate demographic, biological, behavioral, and environmental data with functional and community participation outcome data to help answer these questions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Community participation outcome	Survey	Annually
Behavioral characteristics, self-assessment		
Environment		

## What are the associations between diet and health outcomes?

**Use Case ID** 198167

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Dietary intake is a complex and dynamic exposure known to affect health. To best assess foods, nutrients, dietary supplements, dietary patterns, and any latency in their relationship to disease, longitudinal collection every year of both long- and short-term dietary assessment instruments is necessary. To fully adjust for systematic error, replicated recovery and predictive biomarkers should be collected in a 10%–20% subset, coinciding with dietary data collection.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Dietary assessment tool	Every 3 months
Diet, self-assessment	Diet history questionnaire	Annually
Sodium levels	Urine collection	
Potassium levels	Urine collection	
Nitrogen levels	Urine collection	

## How do we define and measure health?

**Use Case ID** 198333

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Other

What does health mean these days? Health has two components: (1) mental and emotional happiness, which is harder to measure; and (2) biochemical health, which is measurable. Goals: Define health and then define measurements (markers) of health. Methods: Set forth the measurements of health, monitor and collect the dietary and biomarker data of people over time, record good/bad outcomes, and then relate them back to dietary intake. Expected outcome: Relate dietary intake to measurements of health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Mobile monitor	Continuous monitoring
Physical activity, self-assessment	Mobile monitor	Continuous monitoring
Clinical outcomes	Clinical diagnostic test	Every 3 months
Clinical outcomes	Mobile monitor	Annually

## Does a plant-based diet improve health and quality of life?

**Use Case ID** 198499

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Track and ask participants who follow a plant-based/vegan lifestyle every quarter or every 6 months. Additional data collection could include factors like blood tests, blood pressure, a questionnaire for chronic diseases, a food journal, etc.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Annually
Health and phenotype data		
Quality of life	Survey	*GC

## How does the social environment contribute to health behaviors and outcomes within intimate relationships?

**Use Case ID** 198523

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

There is insufficient knowledge about relationship-level factors in couples to adequately inform precision behavior change interventions. Existing interventions largely do not account for how the social environment contributes to lifestyle behaviors and that these behaviors are often done with others or in response to our relationships (i.e., couples). The All of Us cohort presents a unique opportunity to survey cohort participants and their partners to fill these knowledge gaps.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	
Relationship-level factors	Survey	
Sociodemographics	PPI Survey (AOURP)	

## Are patients' perceptions of their physician's warmth and competence related to the outcomes of their chronic illness?

**Use Case ID** 198563

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Treat & Cure Disease

Qualities of patient–provider relationships may be especially important for patient who suffer from chronic illness and see providers repeatedly. This study aims to (1) longitudinally measure chronically ill patients' perceptions of how warm and competent their physician was during their most recent visit and (2) test whether these patient perceptions are related to outcomes of treatment, both psychological (e.g., stress) and physical (e.g., recovery time for major surgery).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care interactions		Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually
Mental health outcomes	Survey	Annually
Quality of life	Survey	Annually

## What are the health benefits of mind-body exercises, such as Feldenkrais, tai chi, or yoga?

**Use Case ID** 198681

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Health benefits of mind-body exercises are underresearched compared with health benefits of aerobic exercises. Many people do not meet the current physical activity recommendations for maintaining health, in particular older adults and individuals with chronic health issues. Thus it is of high importance to facilitate the potential health effects of mind-body exercises. Funding for well-designed randomized controlled trials is needed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health and phenotype data		
Mind-body exercise	Survey	

## What is the estimated risk for common diseases (such as diabetes) based on genetic factors, dietary habits, and geolocalization data?

**Use Case ID** 198755

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Estimate risk for common disease or health outcomes based on known genetic factors combined with novel environmental data types such as proximity to food sources and pollution and laboratory measures of pollutant exposure. For example, what is the relative risk of genetic factors for diabetes compared with dietary habits and proximity to grocery stores?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Hemoglobin A1C (HbA1C) levels	Blood draw	At specified times anchored to the clinical event
Geocode data		
Genotyping data	Whole Genome Genotyping (WGG)	
Environment	Survey	

## What is the diversity of healthy profiles across diverse populations?

**Use Case ID** 198780

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Other

In addition to items mentioned in the protocol, 1) enroll subjects willing to make all their data (including genomic data, but minus other PHI) open consent, making data more accessible and avoiding many data management headaches; 2) collect microbiome samples and PBMCs and use Streck tubes for cell-free DNA and RNA; 3) questionnaires on food/nutrition and stress should be included; 4) freeze urine and plasma on dry ice ASAP; 5) ideally, also collect samples when people become ill.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Glucose levels	Mobile monitor	Annually
Microbiome sample	Stool sample	Annually
Diet, self-assessment	Food diary	Annually
Genomic analyses	Blood (Streck)	
Sociodemographics		

## How does receiving news of diagnosis affect your ability to receive care?

**Use Case ID** 1000693

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Treat & Cure Disease

How does an emotional impact affect ability to achieve treatment and engage as an active participant in a patient's care?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Electronic Health Record (EHR)	Continuous monitoring
Spirituality/Religion	Survey	Annually
Mental and psychosocial health, self-assessment	Survey	Periodically

## How do childhood adverse events influence health and emotional outcomes?

**Use Case ID** 1000771

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**

**Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Family relationships	Adverse Childhood Experiences (ACE) survey	Once for adults; annually for children
Educational outcomes	Academic records	Annually
Neighborhood characteristics	Mobile monitor	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually
Behavioral characteristics, self-assessment	Screening, Brief Intervention, and Referral to Treatment (SBIRT)	Annually
Personal Characteristics	Interview	Once for adults; annually for children

## How does perception of health affect health care use?

**Use Case ID** 1000821

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care participation	Electronic Health Record (EHR)	Annually
Health mindset	Survey	Every 2 years
Health and phenotype data	Interview	Annually
Health and phenotype data	Electronic Health Record (EHR)	Annually

## Why do people avoid health care?

**Use Case ID** 1000826      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Maintain & Preserve Health

What are the reasons people do not engage with or maintain relationships with health care entities? Does it matter in terms of health outcomes overall?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Access to health care	Claims data	Every 6 months
Motivation for study participation	Patient Activation Measure (PAM)	Every 6 months
Personal Characteristics	Survey	Every 6 months
Death	Claims data	Annually
Trust in health care	Survey	Every 2 years
Fear/hostility towards health care system	Survey	Annually

## How does daily stress affect the health span?

**Use Case ID** 1000849      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

While we know adverse events can predict longevity, effects are small. Daily stress can drive changes in biology implicated in disease and mortality, and may provide a better window into the effects of stress on health and what mitigates these effects. By “health span” we mean the healthy portion of the lifespan.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually
Stress	Survey	Annually
Stress	Diary/journal	Daily
Stress	Electronic monitoring/recording	Continuous monitoring
Death	Death records	Annually
Quality of life	Survey	Annually

## How do “lifestyle factors” in your social network impact your own health outcomes?

**Use Case ID** 1000923

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

E.g., substance abuse.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social determinants of health (SDH)	PPI Survey (AOURP)	Every 2 years
Social relationships	Survey	Every 2 years
Social relationships	Social network mining	Every 2 years
Health behavior	Survey	Every 2 years

## What are the protective factors that promote healthy aging and longevity?

**Use Case ID** 1000944

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**

**Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Nutritional supplement use	Patient-reported outcome	Monthly
Health behavior	Patient-reported outcome	Monthly
Environmental samplings and exposure results	Geospatial tracking	Continuous monitoring
Functional mobility assessment results	Walk test	
Omics	Genomic testing	Baseline
Diet, self-assessment	Patient-reported outcome	Monthly
Social relationships	Social network mining	Every 6 months
Social determinants of health (SDH)	PPI Survey (AOURP)	Annually
Bone density	Imaging	Every 5 years
Physical activity, self-assessment	Wearable electronics	Ongoing
Diet, self-assessment	Smart toilet	Monthly
Mind-body exercise	Patient-reported outcome	Monthly
Social relationships	Electronic monitoring/recording	Periodically
Social relationships	Social network mining	Periodically
Ability to perform activities of daily life (ADL) assessment results	Activities of Daily Living (ADL) assessment	Annually
Environmental samplings and exposure results	Custom sensor/app	Continuous monitoring

## How does exposure to childhood emotional trauma affect health and resilience (mental and physical well-being)?

**Use Case ID** 1001019

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Bullying, violence, emotional stress, trauma, poverty, food insecurity, relationship trauma/divorce, abuse—physical, sexual, emotional.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Food security status	Geospatial tracking	Every 6-12 months
Percent below poverty line by location	Geospatial tracking	Every 6-12 months
Emergency room (ER) visit	Electronic Health Record (EHR)	Every 6-12 months
Psychological measures	Electronic Health Record (EHR)	Every 6-12 months
Death	Death records	Every 6-12 months
Fatty liver disease diagnosis	Liver Function Test (LFT)	Every 6-12 months

## Can we molecularly and phenotypically subtype fatigue that impacts quality of life?

**Use Case ID** 1001115

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Do you have fatigue that negatively impacts your QOL? If yes, then questions regarding mode of onset, frequency, severity, duration, comorbid conditions, mitigating factors, etc.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sleep parameters	Mobile monitor	Daily
Fatigue symptom	Survey	Every 3 months
Depression diagnosis		Every 3 months
Depression diagnosis		Every 3 months
Depression diagnosis		Every 3 months
Omics	Gene expression profiling	Annually or during clinical visits
Metabolomic profile		Annually or during clinical visits
Proteomic profile		Annually or during clinical visits
Metabolomic profile	Wearable electronics	
Physical activity, steps/day	Wearable electronics	Daily
Gait speed	Wearable electronics	Daily
Physical activity, self-assessment	Wearable electronics	Daily
Sedentary time	Wearable electronics	Daily
C-Reactive Protein (CRP) levels	Enzyme-Linked ImmunoSorbent Assay (ELISA)	During clinic visits
Hemoglobin levels	Blood draw	During clinic visits

## What are the factors that influence vulnerability and resilience for opioid misuse in the face of chronic pain?

**Use Case ID** 1001257

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Opioid misuse is common in chronic pain. However, not all are equally vulnerable. Why?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Exomic Sequencing (WES)	Baseline
Pain symptom diagnosis	Survey	Annually
Opioid screen test results	Electronic Health Record (EHR)	Annually
Personal Characteristics	Survey	Baseline
Addiction-related information	Survey	Annually
Social environment	Electronic Health Record (EHR)	Annually

## Does the use of alternative therapies affect the development of complications from chronic disease?

**Use Case ID** 194425

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

Some individuals with chronic diseases eventually develop complications and sequelae. This study would address whether use of an alternative therapy would change or delay the development of these complications. This study would also address as the secondary objective whether the amount of medication required to address this chronic illness decreases over a period of time with the concomitant use of alternative therapies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Quality of life	Survey	*GC
Treatment/Therapy		
Prescription medication\treatment		

## Does the use of nutritional supplements reduce the burden of chronic illness?

**Use Case ID** 194426

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

In a chronic illness, whether the use of nutritional supplements in therapeutic quantities change the outcome of the illness and prevent complications, thus enabling individuals to lead a quality life. Also address the question whether these help in prevention of certain chronic ailments. This question will also address the issue of whether concomitant use of nutritional supplements decreases the overall pharmaceutical medications that the individual takes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Nutritional supplement use	Survey	
Prescription medication\ treatment	Prescription drug records	
Clinical outcomes	Electronic Health Record (EHR)	
Treatment effectiveness	Survey	

## How many participants in the All of Us Research Program use complementary and alternative medicine?

**Use Case ID** 194427

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Other

This survey will provide an idea about the number of people using nutritional supplements and alternative therapies, homeopathy, hypnotherapy, NLP, and yoga.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Perceived outcomes - patient	Survey	
Clinical outcomes	Electronic Health Record (EHR)	
Nutritional supplement use	Survey	

## To what extent does exercise modify manifestations of physical disability?

**Use Case ID** 194431

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Epidemiological study of exercise habits and outcomes in samples with physical disability.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Every 2 years
Disability information	PPI Survey (AOURP)	Every 2 years
Physical activity, self-assessment	PPI Survey (AOURP)	
Clinical outcomes	Physical exam	Every 2 years

## What is the role of medication adherence in evaluating drug response in precision medicine?

**Use Case ID** 195235

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

A goal of precision medicine is to predict which patients will have the best treatment response to medications. In order to evaluate treatment response, you must know adherence to the intervention. Measures of medication adherence should be included. Objective measures, such as pharmacy refill records or electronic monitors, can be used. Electronic monitors provide additional information about the date and time the medications were used.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Adherence to prescription regimen	Activity monitor	
Clinical outcomes		

## How do our diets and genomes interact to influence symptom risk, severity, and response to therapeutic interventions?

**Use Case ID** 196610

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Nutrigenomics studies are proposed to identify genome/nutrient interactions associated with symptom risk, severity, and variation in response to symptom management interventions to elucidate the molecular factors underlying the contribution of dietary behaviors to symptoms. Research will lead to development of genome-based dietary interventions aimed at preventing or alleviating symptoms, and reveal why individuals with seemingly similar symptoms respond differently to therapeutic interventions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Blood draw	
Diet, self-assessment	Electronic Health Record (EHR)	
Health and phenotype data		
Treatment/Therapy		
Clinical outcomes		

## Does collecting side effect data directly from patients improve compliance, personalized drug choice, and efficacy?

**Use Case ID** 196664

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

After a drug has been approved, big ADRs are reported to MEDRA, but smaller side effects are not usually reported. While some may be known and in the drug label, novel side effects may occur in populations not included in the original trials. Small effects may lead to discontinuation or poor compliance. Collecting better data about side effects and combining with genomic data could give improved pharmacogenomic prediction of side effects and allow for better selection of drugs for a patient.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Side effects of prescription medication	Smartphone-based ecological momentary assessment	Every 3 months
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Prescription medication\treatment	Prescription drug records	Every 3 months

## What are the effects of self-diagnosis and self-medication on the recovery or severity of any condition?

**Use Case ID** 197776

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Other

Goals: To study the impact of different free sources of information such as books, magazines, health blogs, and uploads on the disease status of an individual; to study the authenticity and reliability of abundance of free information available to today's generation; to find out the reasons for not approaching the right source of advice for their problems. Methods: Questionnaire, self-medication, and diagnosis statistics.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care cost	Survey	
Over-the-counter (OTC) medication Use	Survey	
Prescription medication\treatment	Survey	
Educational resources	Survey	
Clinical outcomes		

## Will improvements in the implementation of shared decision-making approaches in clinical practice positively affect health outcomes?

**Use Case ID** 198590

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Other

The shared decision-making (SDM) encounter provides a platform for sharing and discussing uncertainty, narrows the knowledge gap between patient and provider, empowers patients through involvement in the decision process, and promotes trust between patients and providers through transparency (Braddock CH., 2013). Improving implementation of SDM approaches into routine clinical practice may serve to reduce economic burden and improve health outcomes for patients.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Shared Decision Making (SDM) in health care		
Perceived outcomes - patient		
Perceived outcomes - patient		
Perceived outcomes - surgeon		

## Among people with chronic diseases, do integrative/complementary therapies reduce disease impact?

**Use Case ID** 1001162

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

What are social, environmental, and recreational exposures (e.g., creative arts, video gaming, clubs, robotics, dance, sports) that influence healthy social/emotional development (e.g., emotion regulation)? What is the role of complementary/integrative health therapies in disease/symptom management? Do early and ongoing life experiences (i.e., recreation, leisure, music training, etc.) influence (buffer) development of the management of disease?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social environment	Survey	Annually
Biological Specimens	Blood draw	Every 3 months
Symptoms	Patient-Reported Outcomes Measurement Information System (PROMIS)	Every 3 months
Biological Specimens	Saliva	Every 3 months
Quality of life	Patient-reported outcome	Every 3 months
Biological Specimens	Sensor (swallowed)	During clinic visits
Treatment/Therapy (other than Drug use)	Electronic Health Record (EHR)	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually

## How do therapies like chemotherapy, radiation treatment, and newer targeted treatment impact health/resilience?

**Use Case ID** 1001252      **Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Most Important**      **Scientific Category** Reduce Disease Impact

Although we have examined how our environmental stress and behaviors affect health/resilience, it would be interesting to explore the impact of therapies on health/resilience.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Functional mobility assessment results	Electronic monitoring/recording	Annually
Social relationships	Geospatial tracking	Annually
Social relationships	Survey	Annually
Patient-reported outcomes	Survey	Annually
Functional mobility assessment results	Patient-reported outcome	Annually
Functional mobility assessment results	Patient-reported outcome	During clinic visits
Functional mobility assessment results	Electronic monitoring/recording	During clinic visits
	Survey	Annually
	Geospatial tracking	Annually
Treatment/Therapy	Electronic Health Record (EHR)	During clinic visits
Clinical outcomes	Electronic Health Record (EHR)	During clinic visits
Behavioral characteristics, self-assessment	Survey	Post-event

# Human Development and Aging

**All of Us** | The  
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## Is it possible to measure the health impact of early family instability on subsequent health, using time in foster care system as a marker?

**Use Case ID** 194376

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Use one or more markers (e.g., experience in foster care system) to identify early family instability; then correlate that with markers for adolescent and adult health (e.g., chronic disease burden; frequency of hospitalization, use of medications, likelihood of having health insurance, quality of life self-reports).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Family relationships		
Prescription medication\treatment		
Health and phenotype data		
Quality of life	Survey	*GC
Family relationships		

## What microbiome characteristics of children exposed to antibiotics and different diets influence long-term health outcomes?

**Use Case ID** 194579

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Follow a subsample of all infants and children (<3 years of age) throughout childhood to obtain the following serial assessments: blood tests; medication history; neonatal, infant, and childhood health outcomes; and physical measurements and laboratory microbiologic evaluations of oral, skin, and vaginal specimens. Assessments and measures would be used along with health outcomes to determine associations and develop predictive models that could inform a “personalized microbiome growth curve.”

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Annually
Prescription medication\treatment	Electronic Health Record (EHR)	Annually
Microbiome sample		Annually
Genomic analyses	Whole Genome Sequencing (WGS)	Annually
Immune biomarkers levels	Blood draw	Annually

## What are the long-term effects and risks of opioid use disorder during pregnancy on maternal and child health?

Use Case ID 194666

Cross-Cutting Theme Environmental and Other Contextual Effects

Scientific Category Assess Risk

This study will focus on the entire cohort. The goal will be to determine the interaction of genomic, sociodemographic, physiologic, and environmental factors for the mother and child impacted by neonatal opioid withdrawal syndrome (NOWS) and their impact on treatment response, treatment outcome, health outcomes for the mother, and developmental outcomes for the child.

Datatype	Method	Specification
Depression diagnosis	PPI Survey (AOURP)	Annually
Opioid screen test results	Urine collection	Monthly
Treatment decisions	Electronic Health Record (EHR)	Annually
Side effects of Opium/Opioid	Blood draw	Annually for 5 years
Side effects of Opium/Opioid	Urine collection	Monthly

## Are there long-term health effects of fluoride in water and, if so, what are they?

Use Case ID 195148

Cross-Cutting Theme Environmental and Other Contextual Effects

Scientific Category Assess Risk

Fluoride has been associated with neurotoxicity in fetuses. How is this compound affecting the individual throughout their lifetime? Is it related to autism, Parkinson's, or other neurological diseases?

Datatype	Method	Specification
Environmental samplings and exposure results	Blood draw	Every 3 years
Neurological disease information	Cognitive test	Every 3 years
Fluoride levels	Water purity test	

## What predisposing conditions increase the risk of PCOS (polycystic ovary syndrome)?

**Use Case ID** 195232

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Analysis of conditions that increase the risk of PCOS, particularly genetics and environment, such as endocrine disruptors and diet/gut microbiology. PCOS can lead to many long-term health problems in women, such as type 2 diabetes, cardiovascular disease, depression, and hormone-related cancers. Identifying susceptible individuals would help to individualize treatment strategies. Additionally, research into the use of supplements (e.g., inositol) to alleviate PCOS symptoms may be beneficial.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Polycystic Ovary Syndrome (PCOS) diagnosis		
Environmental samplings and exposure results		
Genomic analyses		
Clinical outcomes		

## What are the functional mechanisms by which environmental exposures impact human health, and do they vary by age of exposure?

**Use Case ID** 195644

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Using biospecimens of persons of varying ages, characterize exposure to environmental chemicals and metals over time and conduct omics studies to identify the functional mechanism of observed health effects—gene expression, metabolomics, epigenetics, and genetic variants. Most importantly, have a plan for integrating the findings of these various studies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Chemical exposure assessment results	Blood (SST)	Annually
Clinical outcomes	Clinical diagnostic test	Annually
Clinical outcomes	Electronic Health Record (EHR)	Every 3 years
Prescription medication\ treatment	Prescription drug records	At specified times anchored to the clinical event
Alanine aminotransferase (ALT) levels	Blood (SST)	

## What is the population burden of fetal loss attributable to environmental exposures (alone or in mixtures)?

**Use Case ID** 195646

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Detect Disease

Characterize maternal and paternal individual exposure to environmental chemicals and metals using questionnaire data and environmental chemicals (as well as GIS for airborne and water exposures). Track fetal loss in different population strata. Determine the risk of fetal loss associated with single exposures and exposure mixtures, and then the population burden of fetal loss attributable to environmental exposures.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Chemical exposure assessment results	PPI Survey (AOURP)	
Pregnancy outcomes	Survey	

## What is the population shift in prevalence of chronic disease with past environmental exposures, especially in the elderly?

**Use Case ID** 195648

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Detect Disease

Careful and extensive characterization of lifetime environmental exposures and chronic disease phenotypes in the All of Us population; determination of genetic risk factors for various exposure and disease combinations; follow-up for chronic disease outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Chemical exposure assessment results	PPI Survey (AOURP)	
Clinical outcomes	Electronic Health Record (EHR)	

## Does a parent's passive radiation exposure increase the risk for a child to have a chromosome defect?

**Use Case ID** 196567

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Is there any correlation between nuclear exposure of a parent, through working in a nuclear facility or around radiation, and the diagnosis of chromosome defects in their biological offspring? This data could be collected utilizing existing patient records of children diagnosed with chromosome anomalies and surveying their parents' exposure to radiation through their military service and employment records.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes		
Genomic sequence data		
Environmental samplings and exposure results		

## What are the associations between the exposome and health?

**Use Case ID** 198502

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

To understand health effects of the exposome, exposure assessment in population-based research should include measures of all the exposures of an individual in a lifetime, including general external, specific external, and internal. Assessing the exposome requires multiple, repeated longitudinal and hierarchical exposure measurements with sufficient variability; standardized methodology and analysis; and capabilities for linkages among population-based studies, other datasets, and registries.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social support	Survey	Annually
Education level attained	PPI Survey (AOURP)	Annually
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Metabolic risk assessment result	Electronic Health Record (EHR)	Annually
Hormone levels (non-steroidal)	Electronic Health Record (EHR)	Annually

## How much do occupational exposures contribute to the burden of chronic disease (e.g., cancer, CVD) in U.S. adults?

**Use Case ID** 198662

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Most of us spend a lot of time at work. Workplace physical and chemical hazards as well as organizational attributes of the job can have a profound impact on health. While work-related acute injuries and illnesses may be easy to recognize, the effects of work on chronic disease are more difficult to assess. Collecting occupational history and exposure information from the All of Us cohort will help us better understand the contribution of occupational exposures to chronic disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Occupation Location	PPI Survey (AOURP)	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Environmental samplings and exposure results	PPI Survey (AOURP)	
Occupational environment assessment results	PPI Survey (AOURP)	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually

## What are the long-term effects of biopharmaceuticals (biologics) on children exposed in utero?

**Use Case ID** 198663

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Tens of millions of Americans are affected by autoimmune diseases; a majority of those affected are women. Biopharmaceuticals are prescribed even during pregnancy. It is assumed maternal health is monitored closely as it fetal health. However, what are the long-term effects on the child’s health, and how do biopharmaceuticals affect those children’s long-term disease risk profiles?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Treatment/Therapy		
Risk factors, self-assessment		
Autoimmune diseases diagnosis		

## Do contract and contingent (temporary) work arrangements affect worker health?

**Use Case ID** 198665

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

More than 90% of all job growth in the U.S. from 2005–2015 occurred in “alternative work arrangements” (e.g., part-time or contract work). This has provided flexible employment opportunities but negative effects on health. All of Us could look at how contract and contingent workers cope with job insecurity, lack of health and retirement benefits, and absence of job safety policies and training, and how these affect mental health, health behaviors, workplace injuries, and use of health care resources.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Occupation	PPI Survey (AOURP)	Annually
Occupation parameters	Survey	Annually
Health care participation	PPI Survey (AOURP)	Annually
Mental health outcomes	Survey	Annually
Health issues, occupational	Survey	Annually

## Do work conditions underlie disparities in maternal mortality, preterm birth, and breastfeeding?

**Use Case ID** 198672

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Over half of U.S. births occur to working women. A woman’s job dictates her ability to take leave for prenatal and postnatal care, to remain off work after the birth to heal and care for the baby, and to continue to breastfeed her baby through the first year of life. The All of Us study will allow researchers to determine what workplace factors are strengths and barriers to optimal health for both mother and baby, and which industries and occupations are the most urgent targets for change.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Occupation	PPI Survey (AOURP)	Annually
Occupation Location	PPI Survey (AOURP)	
Occupation parameters	Survey	
Pregnancy outcomes	Survey	Baseline and annually

## What lifestyle, diet, physical activity, and environmental factors contribute to healthy aging?

**Use Case ID** 198696

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Extensive epidemiological research suggests a causal relationship between diet, physical activity, and environmental factors and risk for, or protection from, a number of diseases, particularly diseases associated with aging. By examining the global health status of people 50 and over and variables such as epigenetics, diet, physical activity, and environmental exposure measurements, we aim to identify correlates of healthy aging.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Baseline
Lifestyle, self-assessment	PPI Survey (AOURP)	Baseline
Diet, self-assessment	PPI Survey (AOURP)	Baseline
Environmental samplings and exposure results	PPI Survey (AOURP)	Baseline
Quality of life	Survey	Baseline

## What parental environmental exposures are associated with de novo mutations in children?

**Use Case ID** 198701

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

“Why a genetic disease in my child?” Clinician Collins told parents, “She has a spontaneous DNA change.” Scientist Collins knows everything has a cause. Despite expectations, no environmental agent is a proven germ cell mutagen, neither radiation, A-bombs, nor chemotherapy. Design is sequencing family trios of either 1) a prospective cohort of survivors of mutagenic exposures (like for cancer) or 2) a retrospective group of persons with de novo mutations to examine parents’ environmental exposures.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Baseline
Environmental samplings and exposure results	PPI Survey (AOURP)	Baseline
Cancer information	Electronic Health Record (EHR)	Baseline
Self-reported ancestry	PPI Survey (AOURP)	Baseline

## Do systemic therapies used for cure or control of diseases like cancer, HIV, or diabetes alter aging phenotypes?

**Use Case ID** 198706

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Clinical evidence suggests that cancer survivors, people living with HIV/AIDS, and people with diabetes may age prematurely from treatment toxicity. The All of Us study could be used to study these observations over time by comparing aging trajectories and risk factors for individuals with and without systemic therapy use and investigate the mechanisms that cause alterations in the rate or way individuals age.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information		Include child, teenager, early adult, adult, elderly
Clinical outcomes		Periodically
Treatment decisions	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Specified Biomarkers		Periodically

## What are the environmental risk factors for fetal death/stillbirth?

**Use Case ID** 1000799

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Other

Mixture analysis issue. Also ethical issues to discuss. Preconsent, counseling, parent support. Can we pretest methods to preconsent for “difficult” decisions (autopsy, organ/tissue donation)? Issue of preconsent versus when the event occurs.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Geographic information system (GIS) code	Pre-pregnancy/during pregnancy
Chemical exposure assessment results	Autopsy	At birth
Metabolomic profile	Placental biopsy	At birth
Genomic analyses	Genomic testing	Baseline
Epigenomic/epigenetic markers	Blood draw	At birth
Pregnancy outcomes		At birth

## What environmental factors render vaccines ineffective?

**Use Case ID** 1000902

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Vaccine effectiveness is influenced by the environment, but the specifics are not well known. This study will examine which environmental factors are associated with vaccine effectiveness as well as the population breakthrough of vaccines due to the environment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Urine collection	Annually
Infectious agents	Electronic Health Record (EHR)	Annually
Antibody titres	Blood draw	Annually
Vaccination records	Electronic Health Record (EHR)	Annually
Environmental samplings and exposure results	Electronic Health Record (EHR)	Annually
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Environmental biomarkers assessment results	Urine collection	Annually

## What patterns of menstrual function predict PCOS?

**Use Case ID** 1000973      **Cross-Cutting Theme** Environmental and Other Contextual Effects

**Most Important**      **Scientific Category** Assess Risk

High rate of infertility, endometrial cancer, metabolic syndrome, diabetes. What are social determinants? Suggestion that early intervention may help. Suggestion of environmental influence.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Family clinical outcomes	PPI Survey (AOURP)	Baseline
Menstruation pattern	Mobile monitor	Continuous monitoring
Diet, self-assessment	PPI Survey (AOURP)	Every 2 months
Physical activity, self-assessment	Fitness tracker	Continuous monitoring
Stress	Survey	Annually
Epigenomic/epigenetic markers	Blood draw	Pre-menarche
Polycystic Ovary Syndrome (PCOS) diagnosis	Electronic Health Record (EHR)	Annually
Social determinants of health (SDH)	PPI Survey (AOURP)	Annually
Epigenomic/epigenetic markers	Blood draw	Post-menarche

## What is the attribution of gene versus environment in development of autism spectrum disorder?

**Use Case ID** 1001002      **Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Autism spectrum disorders (ASDs) are on the rise. There is more controversy as to how much is due to environmental, including fetal, versus genetic factors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes	Electronic Health Record (EHR)	Baseline
Genomic analyses	Tissue biopsy	Baseline
Pregnancy characteristics	Electronic Health Record (EHR)	During clinic visits
Autism Spectrum Disorders (ASD) diagnosis	Electronic Health Record (EHR)	Baseline
Environmental samplings and exposure results	Electronic Health Record (EHR)	During clinic visits

## What is the natural history of mosaicism (genomic and epigenomic) throughout development?

**Use Case ID** 1001055

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Compare repeated measures of mosaicism (somatic versus germinal cells) across the lifespan and its impact on development and aging. How do environmental exposures and other factors influence changes in mosaicism?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Tumor characteristics	Tissue biopsy	Every 5 years
Genomic sequence data	Whole Genome Sequencing (WGS)	Ad hoc
Environmental samplings and exposure results	Environmental assessment	Ad hoc
Methylation status		Ad hoc
Genomic analyses	Specimen collection	Ad hoc
Blood sample characteristics	Blood draw	Ad hoc
Telomere length	Blood draw	Ad hoc

## How do environmental and behavioral risk factors for asthma change across the lifespan for different asthma phenotypes?

**Use Case ID** 1001190

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Most Important Scientific Category** Assess Risk

This will be the first study of its kind to assess multiple risk factors (e.g., environment, behavior) on asthma phenotypes over the lifespan.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Air quality assessment results		Daily
IgE levels	Serum collection	Baseline
Chemical exposure, dust samples	Environmental assessment	Pregnancy then every 5 years
Dust samples, residential	Environmental assessment	Pregnancy then every 5 years
Microbiologic specimen evaluation	Environmental assessment	Pregnancy then every 5 years
Behavioral characteristics, self-assessment	Survey	Every 5 years

## Can we identify genetic markers that lead to early diagnosis of late-onset rare diseases?

**Use Case ID** 190194

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Most rare diseases, defined as those affecting fewer than 200,000 people, are genetic disorders with signs observable at birth or in childhood. However, a number have onset in adulthood (e.g., Huntington, Crohn, Charcot-Marie-Tooth, ALS, thyroid cancer). Of this subset, many have not been linked to a single genetic mutation or origin and, similarly, do not have an identified biomarker that allows for early diagnosis. Are there any genetic markers that can be identified as risk factors for development of adult-onset rare diseases?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data		
Health and phenotype data		
Specified Biomarkers		

## What is the genetic architecture of neurodevelopmental problems, and how does it relate to health disparities?

**Use Case ID** 194520

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

From a diverse sample of children in both clinical and non-clinical settings, investigate genetic contributions to a wide range of neurodevelopmental problems (NPs). Individual-variant and polygenic approaches can advance our understanding of the genetic overlap between, and specificity in, different types of NPs. In a large and diverse sample that includes different racial/ethnic and socioeconomic groups, these techniques can also advance our understanding of disparities in NPs.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Developmental milestones (medical)	Natural language processing of notes	At specified times anchored to the clinical event
Sociodemographics	Electronic Health Record (EHR)	Baseline
Environmental samplings and exposure results	PPI Survey (AOURP)	Every 3 years
Neurocognitive assessment results	Survey	

## What genetic markers predict consequences of pregnancy-associated hypertension and gestational diabetes for mothers and offspring?

**Use Case ID** 194538

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

This study will focus on women who are pregnant at enrollment or become pregnant during the study and the offspring of observed pregnancies. The information will help to define genetic and epigenetic predictors of long-term effects of common pregnancy complications.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Pregnancy outcomes	Electronic Health Record (EHR)	Annually
Blood pressure	Physical exam	
Anthropometrics, whole body measurements	Physical exam	Annually for 10 years
Cardiovascular disease information	Electronic Health Record (EHR)	Annually for 10 years

## What characteristics distinguish a healthy maternal pregnancy-microbiome from one that experienced microbial perturbations?

**Use Case ID** 194559

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

This study will focus on a subsample of all pregnant women and follow them throughout pregnancy to obtain serial assessments and measurements, including laboratory microbiologic evaluation testing of oral, skin, and vaginal specimens. Follow-up would end at delivery of the infant; serial pregnancies would be eligible to re-enroll. Assessments and measures would be used along with health outcomes to determine associations and develop predictive models.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes	Electronic Health Record (EHR)	Monthly
Prescription medication\ treatment	Electronic Health Record (EHR)	Monthly
Microbiome sample		
Genomic analyses	Whole Genome Sequencing (WGS)	Monthly
Immune biomarkers levels	Blood draw	Monthly

## What genetic and environmental risk factors contribute to the development of pelvic organ prolapse (POP) as females age?

**Use Case ID** 194581

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

This study will focus on the entire cohort (menarche through lifespan) to collect data on general health and wellbeing as well as detailed pregnancy and delivery histories. Activity level will be monitored, specifying any straining associated with either physical activity or occupation. Genetic/epigenetic factors, such as family history of POP or connective tissue disorders, will be obtained, as will data on other currently suspected risk factors (e.g., smoking, other environmental exposures).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pelvic organ prolapse diagnosis	Pelvic Organ Prolapse Quantification (POP-Q)	Annually
Pelvic organ prolapse diagnosis	Survey	Annually
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Physical activity, self-assessment	Mobile monitor	Every 3 months

## Why do some with a DNA germline mutation develop disease and others do not?

**Use Case ID** 194817

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

I would take siblings who have a germline mutation and do a complete genome. I'd look to see if there was a second mutation in the patient with disease that wasn't in the other. Or maybe something protective to the DNA mutation so it didn't turn into cancer that the healthy sibling had and the one with disease didn't have.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Cancer information		Baseline
Genomic ancestry	Whole Genome Genotyping (WGG)	Baseline
Genomic instability assessment results		

## Is having a BRCA1 or 2 mutation associated with fertility problems?

**Use Case ID** 195224

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Having a BRCA mutation can lead to earlier menopause, indicating that these women’s fertility windows could be altered. Survey women between age 30 and 45 to determine if there is a higher incidence in fertility problems (e.g., recurrent pregnancy loss, trouble conceiving, altered hormone levels) and/or at younger age in women who carry a mutation versus those who do not.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Genotyping data		Baseline
Genotyping data		Baseline
Pregnancy characteristics	Survey	

## What are the associations between genetics, environment, household, parenting time, and nutrition on early child development (ages 0–6)?

**Use Case ID** 196622

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Maintain & Preserve Health

Intensive data collection and analysis including genetic and epigenetic data over time, family history, physical environment (pollution, housing age, etc.), social environment (income, household, employment history, neighborhood, education resources, etc.), nutrition, parenting (preparedness, skills, family composition, generational support, etc.), early childhood stress, other exposures, demographics; to determine impact on early childhood development (ages 0–6) and long-term health and wellness.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Epigenomic/epigenetic markers	Blood draw	Every 3 months
Environmental samplings and exposure results	Mobile monitor	Continuous monitoring
Diet, self-assessment	Food diary	Continuous monitoring
Sociodemographics	PPI Survey (AOURP)	Annually
Personal Characteristics	Survey	Annually

## To what extent are treatment failures and readmissions linked to a failure to personalize medications and dosages?

**Use Case ID** 196679

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Reduce Disease Impact

Medicare penalizes hospitals that must readmit patients within 30 days. To what extent are those treatment failures linked to a failure to personalize medications and dosages? Metabolism and weight changes make the elderly more sensitive to dose variation. CYP phenotyping could be requested or incentivized as part of the readmission.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Prescription drug records	Baseline
Cytochrome P450 (CYP) phenotyping	Reaction phenotyping assay	
Prescription medication\treatment	Prescription drug records	

## How many unborn children have been identified as having spinal muscular atrophy due to carrier testing?

**Use Case ID** 198361

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

Evaluate records: whether carrier status was positive for the mother, then for the father, and then whether the unborn child was tested if carrier status was positive for both parents. Identify costs of testing and how many unborn children actually have SMA. Identify whether this information (carrier status) created a decision to terminate a pregnancy, helped parents prepare, or just created unwarranted fear. How often did genetic testing on unborn fetuses cause a complication with the pregnancy for a healthy unborn child?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Clinical diagnostic test	At specified times anchored to the clinical event
Genotyping data	Clinical diagnostic test	
Spinal Muscular Atrophy (SMA) diagnosis		
Specified Biomarkers		
Pregnancy characteristics		

## What are the genes associated with lactation, and how do the expression profiles change over time?

**Use Case ID** 198402

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Genotyping (WGG)	
Epigenomic/epigenetic markers	Blood draw	

## Are epigenetic aging clocks reliable predictors of morbidity/mortality, and are they able to be slowed or reversed?

**Use Case ID** 198442

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

An annual blood test with analysis of methylation sites from key epigenetic aging clocks (e.g., Horvath). Epigenetic aging clocks have already been shown to reliably predict age, time to death, all-cause mortality, cognitive function, immune function, CV disease, cancer, and more. They may also become a key tool to demonstrate the reversibility of disease risk through dietary and therapeutic regimens, as epigenetic states are thought to be reversible, and this is why annual monitoring is critical.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Epigenomic/epigenetic markers	Blood draw	Annually
Epigenomic/epigenetic markers		

## What are the implications of prenatal and early postnatal epigenetic changes for health disparities?

**Use Case ID** 198617

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Epigenomic/epigenetic markers		

## How does sex hormone binding globulin (SHBG) relate to health and disease at varying ages?

**Use Case ID** 198622

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

SHBG is a useful epidemiological marker of insulin sensitivity, cardiometabolic disease risk, and longevity. It has been most studied in older adult and aging populations. Its predictive value for the development of diabetes and heart disease is well developed for middle-aged and older adults. Examining its role as a biomarker in younger populations is of interest.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sex Hormone Binding Globulin (SHBG) levels	Blood draw	
Clinical outcomes		
Cardiovascular disease information		
Sociodemographics		

## What are the epigenetic changes associated with adverse childhood exposures (ACEs)?

**Use Case ID** 198638

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

This would ideally involve child participants from whom ACEs could be assessed and blood could be taken, and the children could be followed over time to evaluate the stability of the epigenetic results. These epigenetic markers could also be looked for in adults who experienced ACEs to evaluate potential persistence. Key would be identifying the physiologic impact of these epigenetic changes (e.g., dysregulated biological pathways).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Adverse childhood experiences	Survey	
Epigenomic/epigenetic markers	Blood draw	
Sociodemographics		

## What genetic, physiological, and environmental factors contribute to structural birth defects and functional defects?

**Use Case ID** 198653      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

Enroll sufficient numbers of pregnant women and offspring to study the genetic and nongenetic factors that contribute to human structural and functional defects and developmental disorders. Recruitment of sufficient pregnancies and pediatric cohorts is important to investigate the cause of birth defects and their long-term effects. A family-based approach will be effective in dissecting the genetic or nongenetic components in the formation of birth defects. (Submitted by the Teratology Society)

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Pregnancy characteristics		
Outcomes		
Environment		
Genomic analyses		
Mental and psychosocial health, self-assessment		

## How do genes influence anatomical variability?

**Use Case ID** 198718      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Elucidate Disease Mechanisms

We already know that things like hair color, eye color, height, and weight are strongly heritable. There is tremendous anatomical variability among the population, but we do NOT have a good understanding of genetic predictors of this variability. By integrating cross-sectional imaging data (e.g., CT) with All of Us and integrating advanced computer segmentation algorithms to help define normal anatomical structures, we can begin investigating links between our genes and the structure of our bodies.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Computer Aided Tomography (CT/CAT) images	Electronic Health Record (EHR)	
Genomic analyses	Blood draw	
Physical measurements	Electronic Health Record (EHR)	

## Does the human epigenome reflect exposure to environmental chemicals?

**Use Case ID** 198722

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

The human epigenome is altered by environmental pollutants, including particulate air pollution, bisphenol A, phthalates, metals, pesticides, dioxinlike compounds, and persistent organic pollutants. All of Us will be uniquely positioned to link exposure to environmental chemicals with alterations in the human epigenome. This will require refined measures of environmental exposure that—if measured in All of Us—will cause a quantum shift in the understanding of environmental disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Air quality assessment results		Every 3 years
Environment	DNA methylation array	
Bisphenol A (BPA) levels		
Environmental samplings and exposure results	Hair and nail clippings collection	
Whole genome sequence (WGS) data	Blood draw	

## What genetic changes are linked to the severity of Down syndrome-associated medical conditions?

**Use Case ID** 198749

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Genomic analyses	Whole Genome Sequencing (WGS)	Every 3 years
Neurocognitive assessment results	Neurocognitive test	At specified times anchored to the clinical event
Cardiac outcomes	Electronic Health Record (EHR)	

## What impact does pharmacogenomics have on real-world prescribing practices and medication use?

**Use Case ID** 198759      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Reduce Disease Impact

The goal of this study is to understand pharmacogenetic and other predictors of adverse effects of medications and therapeutic failure enabled by aggregation of claims data and pharmacy fill data from multiple sources over many years. For example, does treatment failure of proton pump inhibitors in genetic hypermetabolizers cause increased surgical procedures, and how do drugs interact in patients treated with multiple drugs with overlapping metabolism pathways?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pharmacogenomics	Blood draw	
Prescription medication\treatment	Electronic Health Record (EHR)	
Clinical outcomes	Electronic Health Record (EHR)	

## What genetic markers can be used to predict pregnancy complications such as gestational diabetes, hypertension (HTN), and prematurity?

**Use Case ID** 1000694      **Cross-Cutting Theme** Genomics and Other Omics  
**Most Important**      **Scientific Category** Reduce Disease Impact

Genetic variants are increasingly associated with pregnancy complications and outcomes that shape maternal health and program long-term fetal well-being, and will later become pregnant and the offspring of the observed pregnancies. This study will associate common and more rare variants and epigenetic modifications with common adverse pregnancy problems and later childhood trajectories.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes	Electronic Health Record (EHR)	Annually
Genomic analyses	Genomic testing	Baseline
Physical measurements	Blood draw	Periodically during pregnancy
Physical measurements	Electronic monitoring/recording	Annually
Physical measurements	Electronic Health Record (EHR)	Annually for 10 years

## What environmental-genetic factors lead to structural birth defects?

**Use Case ID** 1000721      **Cross-Cutting Theme** Genomics and Other Omics

**Most Important**      **Scientific Category** Assess Risk

Cleft lip/palate and neural tube defects.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Blood draw	Baseline
Epigenomic/epigenetic markers	Blood draw	Pre-pregnancy/post-pregnancy
Diet, self-assessment	PPI Survey (AOURP)	Early pregnancy
Chemical exposure assessment results	Blood draw	Early pregnancy
Environmental samplings and exposure results	Geographic information system (GIS) code	Annually
Birth defect diagnosis	Patient-reported outcome	At birth
Pregnancy outcomes		Annually
Genotyping data	Specimen collection	Baseline
Chemical exposure assessment results	Urine collection	Early pregnancy

## Can multi-omic profiling of a person reveal gene by environment determinants of physical health resilience across the lifespan?

**Use Case ID** 1000954      **Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Maintain & Preserve Health

Leverage multi-omic profiling to elucidate mechanisms underlying the variation in the natural history of health and well-being across the lifespan and resilience to environmental insult.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Omics	Genomic testing	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Annually
Social environment	Survey	Baseline
Chemical exposure assessment results	PPI Survey (AOURP)	

## Are there omic predictors of resilience and healthy aging across the lifespan, starting with preconception?

**Use Case ID** 1001018 **Cross-Cutting Theme** Genomics and Other Omics

**Most Important** **Scientific Category** Reduce Disease Impact

Measure the omic, social/behavioral, and environmental (exposome) factors contributing to health across the lifespan. Measures should start preconception in women and integrate family units when they are participants. Consider mix of genomic (mom, baby, and dad) and other omics (metabolomics, microbiome), though we prioritized genomic, environmental, and social and behavioral determinants of health factors. A key is adding family linkages to data collection.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Environmental samplings and exposure results	Wearable electronics	Continuous monitoring
Environmental toxins exposure assessment results	Blood draw	Every 5 years
Clinical outcomes	Survey	Pre-pregnancy/during pregnancy
Anthropometrics, newborn	Survey	At birth
Family clinical outcomes	AOURP Participant Portal	Baseline
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Environmental samplings and exposure results	Environmental Protection Agency (EPA) air monitoring reports	Annually
Environmental toxins exposure assessment results	Survey	Annually
Environmental toxins exposure assessment results	Geospatial tracking	Annually

## What are the genetic, epigenetic, and environmental factors that influence lifetime trajectory of obesity?

**Use Case ID** 1001142      **Cross-Cutting Theme** Genomics and Other Omics  
**Most Important**      **Scientific Category** Assess Risk

Drivers of obesity are largely unknown. How do these factors (e.g., epigenome, environment, diet, microbiome) change in their importance as risk factors for obesity phenotype?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Annually
Physical activity, self-assessment	PPI Survey (AOURP)	Every 3 months
Environmental samplings and exposure results	Urine collection	Annually
Genotyping data	Whole Genome Genotyping (WGG)	Baseline
Epigenomic/epigenetic markers	DNA methylation array	Every 5 years
Stress	Survey	Annually
Obesity diagnosis	Electronic Health Record (EHR)	Annually

## What are the polygenic variant patterns of early language impairments?

**Use Case ID** 1001164      **Cross-Cutting Theme** Genomics and Other Omics  
**Most Important**      **Scientific Category** Assess Risk

Could be ADD, dyslexia outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Epigenomic/epigenetic markers	Blood draw	Annually
Metabolomic profile	Blood draw	Annually *GC
Genomic sequence data	Blood draw	Baseline
Language cognition assessment results	Language comprehension assessment	At 6 months, 12 months, every 2-8 years after
Dyslexia diagnosis	Electronic Health Record (EHR)	At 6 months, 12 months, every 2-8 years after

## What are the genetic/epigenetic demographic characteristics that influence asthma phenotype over the lifespan?

**Use Case ID** 1001175      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

Little is known about the basics of the natural history of asthma over the life course. Most knowledge is derived from prevalence studies. Moreover, studies that have been based on cause definition of asthma, now specific phenotypes/endotypes are begging to be described. This study would be the first of its kind in understanding the patterns of asthma incidence, remission, and reoccurrence over the life course and associate these patterns with demographic genetic and epigenetic characteristics.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Airway inflammation	Serum collection	Every year <15, every 5 years after 15
Sociodemographics	PPI Survey (AOURP)	Every 5 years
Pulmonary assessment results	Electronic Health Record (EHR)	Every 3 months
Clinical outcomes	Survey	Annually
Epigenomic/epigenetic markers	Whole Genome Sequencing (WGS)	Baseline

## Can we use familial triads to understand genetic contribution and genetic susceptibility to environmentally induced autism phenotype?

**Use Case ID** 1001179      **Cross-Cutting Theme** Genomics and Other Omics  
**Most Important**      **Scientific Category** Elucidate Disease Mechanisms

The roles of genetics and the environment as drivers of autism risk are largely unknown. This will be the first study of its kind to assess triads (mother, father, child) for genetic and environmental contribution.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social relationships	Survey	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Environmental samplings and exposure results	Urine collection	Annually
Family relationships	AOURP Participant Portal	Baseline
Genotyping data	Whole Genome Sequencing (WGS)	Baseline

## Does genotype influence racial differences in children's responses to asthma medication?

**Use Case ID** 1001185      **Cross-Cutting Theme** Genomics and Other Omics  
**Most Important**      **Scientific Category** Treat & Cure Disease

There are significant differences in morbidity and mortality in minority children with asthma. Are differences in response to asthma medications influenced by the children's genotype and gene expression?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Genomic testing	Baseline
Prescription medication\treatment	Electronic Health Record (EHR)	Annually
Hospitalization	Electronic Health Record (EHR)	Every 3 months
Asthma diagnosis	Electronic Health Record (EHR)	Every 3 months
Genotyping data	RNA sequencing	Annually
IgE levels	Serum collection	Annually

## What are the molecular determinants of maintaining mobility?

**Use Case ID** 1001196      **Cross-Cutting Theme** Genomics and Other Omics  
**Most Important**      **Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Gait speed	Walk test	Ongoing
Gait speed	Survey	Ongoing
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline

## What are the genomic and environmental exposure contributions to fetal loss?

**Use Case ID** 1001202

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

This will be the first study of its kind to assess the role of the genome/epigenome and environmental contaminants as factors driving fetal loss.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes		Baseline
Pregnancy outcomes		Per event
Omics	Whole Genome Sequencing (WGS)	Baseline
Omics	DNA methylation array	Early pregnancy
Environmental samplings and exposure results	Specimen collection	Baseline
Environmental samplings and exposure results	Specimen collection	Early pregnancy
Pregnancy outcomes	Survey	Periodically
Pregnancy complications	Electronic Health Record (EHR)	Per event

## What are the unique factors associated with early onset obesity in different ethnic and racial groups?

**Use Case ID** 194552

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

This study will focus on women who are pregnant when they enroll or who become pregnant during the study, in order to follow their infants from birth to 8 years of age to determine trajectories of growth over time and identify genomic and epigenomic factors related to development of obesity. Critical to obtaining this information will be the review of electronic health records of providers who have the correct measuring tools and personnel to properly measure linear growth in children.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Anthropometrics, whole body measurements	Physical exam	During clinic visits
Microbiome sample	Stool sample	Annually
Glucose levels		
Diet, self-assessment	PPI Survey (AOURP)	Annually
Genomic analyses	Whole Exomic Sequencing (WES)	

## What is the best approach to improve language development in monolingual homes of Latino youths age 9–17 who are diagnosed as being moderate or severe language delayed?

**Use Case ID** 195109

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

One of the minority groups suffering for lack of services is Latinos and children that are later diagnosed with autism that is impacting language development. The goal of the research is to develop a questionnaire to identify at-risk populations and make it available through the platform. Access through current medical data, and outline specific requirements to develop the questionnaire. The outcome is to provide available information and develop more accurate diagnosed assessments.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Family clinical outcomes	PPI Survey (AOURP)	Continuous monitoring
Behavioral characteristics, self-assessment	Electronic Health Record (EHR)	Continuous monitoring
Health literacy	Survey	Periodic (approximately biweekly)
Clinical outcomes	Language comprehension assessment	Annually
Feelings about health research	Survey	Annually

## Would same-gender care increase the utilization of health care by men in the U.S.?

**Use Case ID** 195301

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

A study to produce evidence that men would increase their utilization of health care, if same-gender care was offered to them (especially for intimate care). If a male attendant was available, would more men seek help? Could health care be made more accessible (because more men would seek help, especially those with cultural sensitivities) and equitable (because men would be afforded the same option as women—i.e., women attendants for mammograms but no male attendants for male urology)?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care participation	PPI Survey (AOURP)	Baseline

## Do patient portals impact health care spending or health care outcomes?

**Use Case ID** 195311

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

I would like to do a longitudinal study of patients that utilize patient portals and those that do not. This would be a continuous assessment of the cost of health care, the number of tests given, outcomes, and overall health assessment for individuals of similar demographics and health statuses. Does the increase in availability of information cause a positive, negative, or unnecessary impact on the patient's health and the overall cost of treating the patient?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care cost	Claims data	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Quality of life	Survey	Every 3 months
Health literacy	Survey	Every 3 months
Technology Use	Survey	

## What are the common factors associated with an incompetent cervix for African American women compared to other races?

**Use Case ID** 195538

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

According to some research, although limited, African American women are twice as likely to have an incompetent cervix than white women. This condition subsequently leads to premature birth or a miscarriage. Many times this condition is silent and has no noticeable symptoms until it is too late. Could this be a genetic condition? More concrete information is needed in order to influence prevention and treatment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Incompetent cervix diagnosis	Electronic Health Record (EHR)	
Genomic sequence data	Whole Genome Sequencing (WGS)	

## Why is the U.S. newborn death rate higher than in other developed countries?

**Use Case ID** 195694

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Death records	Continuous monitoring
Pregnancy outcomes	Electronic Health Record (EHR)	Continuous monitoring
Social determinants of health (SDH)		Continuous monitoring
Sociodemographics	Activity monitor	At specified times anchored to the clinical event

## Can telemedicine provide quality care for chronic conditions?

**Use Case ID** 195734

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Treat & Cure Disease

There are a lot of unknowns when it comes to the quality of care via telemedicine. I would like to focus on patient outcomes as it relates to providing safe, reliable, and consistent results. The study could be implemented so that both subjective data and objective data are measured. Accessing EHR and implementing surveys of those patients who suffer from chronic conditions are two methods for collecting pertinent data. These should be measured weekly, or how otherwise instructed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Perceived outcomes - patient	Survey	Weekly
Clinical outcomes	Electronic Health Record (EHR)	At specified times anchored to the clinical event

## Does “race” as self-identified by patients meaningfully correlate with DNA?

**Use Case ID** 195777

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

Ask participants to self-identify “race” as they would be asked on many organizational forms, such as employment, school, and insurance forms. Examine whether DNA of participants correlates with their self-identified “race.” My theory is that “race” is a meaningless categorization of most people, but nevertheless people often use social categories without significant correlation with DNA. If true, then the All of Us data could encourage doctors and patients to avoid social categorizations of “race.”

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Self-reported ancestry	PPI Survey (AOURP)	Baseline
Genomic ancestry	Whole Genome Sequencing (WGS)	Baseline
Clinical outcomes	Autopsy	Baseline

## What social determinants and health/functional factors increase the risk of malnutrition for older adults?

**Use Case ID** 195817

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

It is important that the All of Us database includes a range of nutrition-related measures, which are used to help identify malnutrition risk. Additional measures of malnutrition-related characteristics are important for malnutrition diagnosis. Validated screening tools, such as the Malnutrition Screening Tool (MST), could be used regularly to collect this data, as well as linked surveys to capture demographic information and EHRs/exams to capture health/function.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Weight	Malnutrition screening tool	Every 3 months
Appetite	Malnutrition screening tool	Every 3 months
Sociodemographics	PPI Survey (AOURP)	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Baseline
Ability to perform activities of daily life (ADL) assessment results	Physical exam	Every 3 months

## What are social impacts on the developmental stage of children in primary school?

**Use Case ID** 195917

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

I would design a 7-year-long protocol study that would observe children's social developmental stages from various demographics from preschool to fifth grade. As we look at their food-nutrient intake; family social structure-dynamics environment; social interaction; extracurricular activities; and educational resources in order to see how to reduce disadvantaged youth while increasing child readiness.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Mobile monitor	Continuous monitoring
Diet, self-assessment	Food diary	Periodic (approximately biweekly)
Behavioral characteristics, self-assessment	Physical exam	Every 3 months
Quality of life	Survey	Continuously for 1 week duration at 1 month, 6 months, and 1 year
Lifestyle, self-assessment	Activity monitor	Annually

## What are the long-term health effects of adverse childhood experiences in racial/ethnic minority populations?

**Use Case ID** 196493

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Adverse childhood experiences (ACE; abuse, neglect) are not uncommon and are associated with increased risk of developing a range of chronic diseases in adulthood (e.g., cardiovascular, cancer). This has mainly been studied in white middle-class populations. Less is known whether ACEs similarly impact racial/ethnic minorities. Cross-sectional design with retrospective ACE report and longitudinal design for long-term follow-up of chronic disease development and/or progression.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Adverse childhood experiences	Adverse Childhood Experiences (ACE) survey	Every 2 years
Sociodemographics	Electronic Health Record (EHR)	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring

## What are the causes of maternal mortality in African American women?

**Use Case ID** 198200

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Coagulation disorder diagnosis		
Blood pressure	Electronic Health Record (EHR)	
Stress		
Sociodemographics		
Cardiac outcomes	Electronic Health Record (EHR)	

## What are the relative influences of race/ethnicity and geography (ZIP code) in chronic disease causation?

**Use Case ID** 198639

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

Data suggest that place of birth is important in chronic disease causation even after people move to new locations. Similarly, data abound regarding environmental exposure and chronic diseases. Understanding gene-environment interactions in the context of race/ethnicity is important for chronic disease causation and prevention. This study could use ZIP code-level data to stratify risk and track interventions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Geocode data	Survey	Annually
Environmental samplings and exposure results	Blood (EDTA)	Annually
Cardiopulmonary assessment	Clinical diagnostic test	Annually
Stress	Sleep journal	Annually
Diet, self-assessment	Food diary	Every 3 months

## How do the conversations between doctors and patients affect patient outcomes and future health care use?

**Use Case ID** 198773

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Research across sociology, psychology, and medicine have found that certain differences in the way doctors speak with patients can improve patient communication about presenting problems, increase patient satisfaction, and even enhance physiological responses to treatment. Collecting transcripts of conversations between patients and their doctors would provide a wealth of qualitative information that could be analyzed and used for a multitude of research questions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care interactions		
Perceived outcomes - patient	Survey	
Preventative care use	Electronic Health Record (EHR)	

## What are the long-term effects of childhood experiences?

**Use Case ID** 1000739

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Examine effects of adverse childhood experiences with focus on impact of various social determinants of health. Data can be collected pro- and retrospectively through parents or as adults. Psychometric measuring to make sure there is no bias.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Self-reported ancestry	PPI Survey (AOURP)	Baseline
Social determinants of health (SDH)	PPI Survey (AOURP)	Baseline
Trauma events	Survey	Annually
Social support	Survey	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Baseline

## Is health disparity in cardiovascular and metabolic disease related to health disparity in pregnancy outcomes?

**Use Case ID** 1000764

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Elucidate Disease Mechanisms

Health disparity exists in cardiovascular and metabolic diseases. The same candidates are impacted by pregnancy and are also associated with disparities in pregnancy.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Self-reported ancestry	PPI Survey (AOURP)	Baseline
Genomic analyses	Tissue biopsy	Baseline
Pregnancy outcomes	Electronic Health Record (EHR)	Baseline
Cardiovascular phenotype analysis results	Mobile monitor	During clinic visits
Metabolic risk assessment result	Mobile monitor	During clinic visits
Blood pressure	Blood pressure cuff	During clinic visits

## What factors can be used to predict infertility in women?

**Use Case ID** 1000961      **Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access  
**Most Important**      **Scientific Category** Assess Risk

Devastating for couples. Predictions of early ovarian aging are imperfect.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	PPI Survey (AOURP)	Baseline
Genotyping data	Blood draw	Baseline
Specified Biomarkers	Blood draw	Annually
Microbiome sample	Specimen collection	Annually
Fertility assessment results	Blood draw	Annually

## How does patient/provider communication affect outcomes, and what factors affect that communication?

**Use Case ID** 1001020      **Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access  
**Scientific Category** Reduce Disease Impact

A key component of health literacy is patient/provider communication. Key barriers include sensory impairment, culture, language, technology.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Electronic Health Record (EHR)	Every 3 months
Health and phenotype data	Electronic Health Record (EHR)	Annually
Patient feedback	Survey	Per event
Sensory assessments	Smartphone-based ecological momentary assessment	Annually
Language cognition assessment results	Survey	Baseline

## Does life course exposure to chronic stress result in premature aging as measured by short telomeres?

**Use Case ID** 1001072

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Body temperature measurement	Blood draw	Annually
Social determinants of health (SDH)	PPI Survey (AOURP)	Annually
Trauma events	Survey	Annually
Trauma events	Survey	Ongoing
Blood pressure	Wearable electronics	Ongoing
Stress	Survey	Ongoing
Telomere length	Genomic testing	Annually

## What are the contributors to racial disparities in pre-term birth?

**Use Case ID** 1001088

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Adverse life events	Survey	Baseline
Epigenomic/epigenetic markers	Blood draw	Baseline
Genomic analyses	Blood draw	Baseline
Environmental samplings and exposure results	Blood draw	Baseline
Socioeconomic Status (SES)	PPI Survey (AOURP)	Baseline
Health care participation	Electronic Health Record (EHR)	Baseline
Placental tissue sample		At birth
Genomic analyses	Placental biopsy	At birth

## Do rates of change in functioning of older adults vary by sociodemographic characteristics?

**Use Case ID** 1001101

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Rates of change in functioning (cognitive, physical, social) are known to differ by many characteristics, including race/ethnicity, SES, and demographic/ geographic characteristics. With a 1-millionperson sample, it will be possible to evaluate the influence of these characteristics on trajectories of change.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Access to health care	PPI Survey (AOURP)	Every 6 months
Genotyping data	Blood draw	Annually
Occupation	PPI Survey (AOURP)	Annually
Ability to perform activities of daily life (ADL) assessment results	Survey	Every 6 months
Cognitive assessments	Survey	Annually
Omics	Blood draw	Ad hoc
Clinical outcomes	Survey	Annually
Sociodemographics	PPI Survey (AOURP)	Baseline

## What are the most effective ancillary services to improve function and quality of life?

**Use Case ID** 1001218

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Most Important** **Scientific Category** Reduce Disease Impact

Across age groups—children and adults.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Annually
Health care participation	PPI Survey (AOURP)	Annually
Sociodemographics	Geospatial tracking	Annually
Quality of life	Survey	Annually
Functional mobility assessment results	Mobile monitor	Every 3 months
Family relationships	Survey	Annually

## Are rates of change in development and function for adults age 20–60 different by demographic characteristics?

**Use Case ID** 1001225      **Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access  
**Most Important**      **Scientific Category** Maintain & Preserve Health

Important for men; 20- to 60-year-olds are less likely have routine medical care without family history of disease, so methods to obtain information need to be mobile or sensor-based. Lots of lifestyle changes among this age group.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Occupation	PPI Survey (AOURP)	Annually
Clinical outcomes	Mobile monitor	Annually
Whole genome sequence (WGS) data	Whole Genome Sequencing (WGS)	Baseline
Cognitive assessments	Electronic Health Record (EHR)	Annually

## Is outdoor exercise beneficial or detrimental for residents of polluted areas?

**Use Case ID** 1001229      **Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access  
**Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Annually
Health care participation	Electronic Health Record (EHR)	Annually
Physical activity, self-assessment	PPI Survey (AOURP)	Weekly
Air quality assessment results		Daily
Clinical outcomes	Mobile monitor	Continuous monitoring
Location data	Geospatial tracking	Daily

## Can electronic health records (EHRs) be effectively utilized to facilitate clinical trials in pediatrics?

**Use Case ID** 194543

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Treat & Cure Disease

Use of EHRs in interventional trials is challenging due to lack of standardization and harmonization. There is a need to incorporate common data elements (developmental data, symptoms), establish linkages (event flags; real-time links for diagnosis, treatment, and adherence), enhance interoperability across vendor systems, standardize adverse event capture, develop identification for phenotypes or rare diseases, and streamline data collection.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	
Prescription medication\treatment	Electronic Health Record (EHR)	
Family relationships	Electronic Health Record (EHR)	

## What factors prevent U.S. women from successfully reaching the 2-year mark that the World Health Organization recommends for breastfeeding?

**Use Case ID** 195637

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Assess Risk

Breastfeeding moms should fill out a survey the day their baby is born and weekly after that, either until they fail or until they reach the 2-year mark. The survey will address pain, support, stress, physical obstacles, baby's abilities to suckle, and work-related obstacles to determine the root of U.S. failure.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pain symptom diagnosis	Survey	Weekly for 2 years
Stress	Survey	Weekly for 2 years
Emotional Support	Survey	
Physical obstacles data	Survey	Weekly for 2 years
Occupation-related obstacles	Survey	Weekly for 2 years

## Can we reasonably expand the inclusion/exclusion criteria related to age in diseases affecting older adults?

**Use Case ID** 198356      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Scientific Category** Detect Disease

Many clinical trials for diseases affecting primarily older adults (e.g., forms of arthritis or AML) have age cut-offs of 50–55 years of age. This both keeps older adults interested in a clinical trial from participating and possibly skews the results of studies. Research to determine the basis for such age limits could help to determine the validity of such restrictions.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Sociodemographics		
Feelings about health research		

## Can mobile health technologies, such as Fitbit or the Apple Watch, recapitulate known disease monitoring?

**Use Case ID** 198760      **Cross-Cutting Theme** Mobile Health  
**Scientific Category** Detect Disease

The goal of this study is to understand if mobile technologies can contribute clinically meaningful metrics. By analyzing mobile technology over time and comparing it with available clinical health records, supervised and unsupervised machine learning can be applied to understand the potential of this technology in clinical care and outcomes.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Clinical outcomes	Electronic monitoring/recording	
Clinical outcomes	Speech analysis app	
Clinical outcomes	Electronic Health Record (EHR)	

## What is the impact of sleep quality on healthy aging and independence?

**Use Case ID** 1000768      **Cross-Cutting Theme** Mobile Health  
**Scientific Category** Other

Description not provided.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Sleep pattern	Custom sensor/app	During clinic visits
Sleep behavior assessment results	Survey	Every 4 years
Daytime cognition assessment results	Cognitive test	Every 4 years
Fall Events	Survey	Every 3 months
Motor vehicle accidents	Motor vehicle/driving records	During clinic visits
Nicotine metabolites levels	Survey	Every 4 years

## Does acquisition of physical measures remotely in real time improve disease management in the elderly?

**Use Case ID** 1001201      **Cross-Cutting Theme** Mobile Health  
**Most Important**      **Scientific Category** Reduce Disease Impact

The elderly often face the challenge of limited mobility and functionality that impedes access to health care. Many areas are also lacking devices for gathering and providing health measure to caregivers remotely to better adjust treatment regimens and determine well-being. Data will be available to both the care team and elderly participants.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually
Functional mobility assessment results	Electronic Health Record (EHR)	Annually
Physical measurements	Mobile monitor	Continuous monitoring

## Are there preconception predictors of preterm birth?

**Use Case ID** 194461      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

Given the limited effects of current interventions to prevent preterm birth, it seems likely that the stage for adverse pregnancy outcomes is set even before the pregnancy begins. If enough reproductive-age women are enrolled, the All of Us cohort would be in a position to examine social, behavioral, medical, and biological/molecular predictors of preterm birth and its subtypes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy characteristics	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Environmental samplings and exposure results		
Epigenomic/epigenetic markers		
Stress		
Behavioral characteristics, self-assessment		

## What factors are involved in loss of fecundity in males and females?

**Use Case ID** 194544

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

This study will focus on the entire cohort across the reproductive lifespan (ages 12–55) collecting data on fertility (time to conception) and pregnancy loss. Additional data will include factors believed to be indicators of fertility as determined by questionnaire, blood tests, factors believed to negatively impact fertility, and genetic/epigenetic data that together may provide new targets for understanding oocyte depletion, worsening semen analyses, and pregnancy loss.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes	Electronic Health Record (EHR)	Annually
Pregnancy outcomes	Survey	Annually
Follicle-Stimulating Hormone (FSH) levels	Blood draw	Annually
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually

## How are sleep characteristics associated with pediatric developmental conditions, disorders, or chronic disease?

**Use Case ID** 194553

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

This study will focus on the entire cohort (infants to 19-year-olds) to provide health and behavior outcomes associated with sleep characteristics, including environmental and demographic factors. This information will help better define the development of sleep, help develop more precise strategies to target children with sleep characteristics predictive of poor health outcomes, and develop more precise strategies for children with chronic diseases or developmental disorders with sleep problems.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Mobile monitor	Continuous monitoring
Sleep quality assessment results	Survey	Annually
Family relationships	Survey	
Sleep disorder information	Electronic Health Record (EHR)	Annually
Developmental disorder information	Electronic Health Record (EHR)	Annually

## Does participation in K-12 sports outreach programs benefit individuals through adulthood?

**Use Case ID** 194857

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Longitudinal study, 13 years, from kindergarten through 12th grade, test whether providing the opportunities for professional sports training benefits children over a lifetime span as adults. Study may continue beyond 13 years, covering full lifespan up to 70 years and beyond. Possible benefits: disease reduction, longer lifespan, increased productivity in the workforce. Comparisons can be made with similar programs in other countries.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Educational outcomes		
Clinical outcomes		

## What is the role of maternal and paternal age in the risk for chronic disease and premature mortality in adult offspring?

**Use Case ID** 194946

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Personal Characteristics	Survey	
Clinical outcomes	Electronic Health Record (EHR)	

## What is the malnutrition risk for older adults?

**Use Case ID** 195816

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

It is important that the All of Us database includes a range of nutrition-related measures—not just diet and BMI—but other parameters, such as weight history and appetite history, which are used to help identify malnutrition risk. Additional measures of malnutrition-related characteristics are important for malnutrition diagnosis. Validated screening tools, such as the Malnutrition Screening Tool (MST), could be used regularly to collect this data.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Weight	Malnutrition screening tool	Every 3 months
Appetite	Malnutrition screening tool	Every 3 months
Sociodemographics		

## Is religiosity/spirituality protective against preterm birth?

**Use Case ID** 195896

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Assess religiosity as it may relate to social support to buffer stress, which could affect pregnancy length (number of weeks of gestation) and preterm birth rates.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes	Electronic Health Record (EHR)	
Spirituality/Religion	Survey	Upon enrollment and first obstetrical visit
Stress	Survey	
Epigenomic/epigenetic markers	Blood (EDTA)	At specified times anchored to the clinical event
Social support	Survey	At specified times anchored to the clinical event

## What are the effects of adverse childhood experiences (ACEs) over the lifespan?

**Use Case ID** 196589

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Much of what we know about ACEs is retrospective, yet we believe that there are developmental touch points and/or aspects of resilience that help or hinder the biologic stress that may or may not ensue after an adverse experience. Monitoring parent and child adversity and stress over time will clarify a much-needed field where we know that ACEs cause acceleration of physical, mental, and behavioral health problems in childhood as well as adult onset morbidities and mortality.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Stress	Survey	At specified times anchored to the clinical event
Adverse childhood experiences		
Clinical outcomes		

## How do maternal health complications affect the long-term health of women and outcomes in subsequent pregnancies?

**Use Case ID** 196909      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

Severe maternal morbidities are rare but increasing in the U.S., and the causes and long-term consequences are poorly understood. All of Us would provide a study population with enough participants, detail, and follow-up time to thoroughly investigate how complications during pregnancy, during delivery, and postpartum affect future health in women and their children to inform prevention of negative outcomes, such as cardiovascular disease and fetal loss in subsequent pregnancies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy complications	Electronic Health Record (EHR)	Annually
Prescription medication\ treatment	Prescription drug records	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually
Pregnancy outcomes	Electronic Health Record (EHR)	Annually

## What are the causes for unexplained male infertility?

**Use Case ID** 197390      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Elucidate Disease Mechanisms

I.e., male infertility not caused by varicocele or other known causes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Male fertility data	Survey	
Sociodemographics	PPI Survey (AOURP)	

## How do childhood chronic conditions influence adult health status and mortality?

**Use Case ID** 197450      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Elucidate Disease Mechanisms

Chronic health conditions have grown dramatically in prevalence among U.S. children and youth over the past half century—with much growth in high-prevalence, variable-severity conditions (asthma, obesity, mental health, and neurodevelopmental). How much does this growth, potentially in specific conditions, affect the rising rates of mid-life chronic conditions and the increasing mortality among working-age adults, especially males? Longitudinal data strategies are needed to address this question.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Asthma attacks	Electronic Health Record (EHR)	Weekly
Mental health and behavior information	PPI Survey (AOURP)	Baseline
Weight	Electronic Health Record (EHR)	Include child, teenager, early adult, adult, elderly

## **Does placing babies to sleep on their backs to sleep really reduce SIDS, and if so, how can we more effectively prevent plagiocephaly?**

**Use Case ID** 197528

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Since doctors have recommended that babies be placed on their backs to sleep to prevent SIDS, as many as 1 in 10 babies have developed plagiocephaly, or flat-head syndrome. (See Aliyah Mawji, “The Incidence of Positional Plagiocephaly: A Cohort Study.” *Pediatrics* 132:2; August 2013.) I would like to see more research into whether or not SIDS is actually reduced with back-sleeping. I would also like more in-depth education for new mothers on how to prevent plagiocephaly in their babies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sodium levels		
Nitrogen levels		

## **Are there age-related microbiota changes, and if so, what are their impacts on health, particularly chronic disease prevention, treatment, and progression?**

**Use Case ID** 198306

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The microbiome variations have been associated with health and disease status in cross-sectional studies. There is a need to examine these associations in a longitudinal fashion and to establish baseline changes in health and disease over a lifespan. All of Us together provides a game-changing amount of longitudinal data on enough individuals to begin to map the complex relationship between exposures (diet, antibiotics, pollutants), host (genetic background), and microbiome characteristics.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Microbiome sample	Stool sample	Annually
Microbially produced metabolites levels	Blood draw	
Air quality assessment results		
Methylation status	Blood draw	Annually

## How can we predict which women and couples would be at risk for preeclampsia/HELLP syndrome, and how can we prevent it?

**Use Case ID** 198385

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Preeclampsia/HELLP syndrome can be caused by many different underlying conditions. If we can determine who would be at risk (either the individual women and/or couples together), perhaps the disease can be prevented by testing their embryos before implantation (IVF) or by having women at risk take aspirin starting early in their pregnancy.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune biomarkers levels	Blood draw	Baseline
Allergens assessment results	Skin allergy test	Baseline
Blood pressure	Clinical diagnostic test	Periodic (approximately biweekly)
Protein levels	Urine collection	Periodic (approximately biweekly)

## Is douching associated with preterm birth?

**Use Case ID** 198477

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Douching may increase the risk of preterm birth. Douching alters the vaginal microbiome and may increase phthalate levels. Douching is a common practice among women of reproductive age. Data on douching practices in the 12 months prior to pregnancy, including products and frequency of use, would be collected in early pregnancy with the option of a self-collected vaginal swab to quantify vaginal dysbiosis. Pregnancy outcomes would be collected from the EHR.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Douching	Survey	Baseline
Pregnancy outcomes	Electronic Health Record (EHR)	Baseline
Vaginal microbiome sample	Vaginal swab	Baseline
Pregnancy characteristics	Survey	Baseline XXXX
Clinical outcomes	Survey	Baseline

## How do daily habits and routines influence the development of and progression of chronic conditions across the lifespan?

**Use Case ID** 198482

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

With web-based questionnaires, body-worn sensors, and lab tests, this study will (1) characterize the frequency and variety of meaningful daily activities, habits, and routines; physical activity; sedentary behavior; and physical, cognitive, and emotional health and well-being in a random sample of people of various age, race, socioeconomic status, and abilities and (2) examine relationships between daily activities and health to inform prevention and intervention for chronic health conditions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Every 3 years
Physical activity, self-assessment	Activity monitor	Every 3 years
Clinical outcomes	Electronic Health Record (EHR)	Every 3 years
Cognitive assessments	Survey	Every 3 years
Psychological measures	Survey	Every 3 years

## To what extent are adverse childhood experiences (ACEs) or trauma related to a wide range of adult diseases or premature death?

**Use Case ID** 198637

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Adverse childhood experiences (ACEs) can be retrospectively assessed in adults, ideally before the onset of the diseases under study. There are existing ACE instruments, or attempts to refine these instruments could be undertaken within All of Us.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Adverse childhood experiences	Survey	
Clinical outcomes		
Behavioral characteristics, self-assessment		
Epigenomic/epigenetic markers		

## How do pregnancy and delivery outcomes affect later-life health in women?

**Use Case ID** 198650

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Detailed pregnancy and obstetrical data collected longitudinally and analyzed either by: 1. Case-control study: Identify cases with adverse obstetrical outcomes and compare with matched controls without the adverse outcomes; follow for health status over the course of the study. 2. Assess the magnitude of risk conferred to women with adverse obstetrical outcomes on individual markers of cardiometabolic health using a multivariable logistic regression model.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes	Survey	Every 3 years
Cardiopulmonary assessment	Carotid intima-media thickness test (CIMT)	Every 5 years
Cardiac outcomes	Survey	Every 2 years
Metabolic risk assessment result	Blood draw	Every 3 years

## What is the cause for pregnancy complications?

**Use Case ID** 198655

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Enroll sufficient numbers of pregnant women and their offspring to study the causes of pregnancy complications, including preeclampsia, preterm birth, stillbirth, and intrauterine growth restriction. Target high-risk pregnancies such as those involving obesity, preexisting diabetes, and gestational diabetes. Follow up long-term effects and study genetic contributions in a family-based approach. Obtain maternal samples and placentas for possible mechanistic studies. (Submitted by the Teratology Society)

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy characteristics		
Gestational Diabetes Mellitus (GDM) diagnosis		
Outcomes		

## How do our mindsets about diet, exercise, and stress influence health behaviors and health outcomes?

**Use Case ID** 198737

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Research has shown that benefits of health behaviors such as diet, exercise, and stress depend not just on the behaviors themselves but on the mindsets people have about those behaviors (Crum, Achor, and Salovey, 2013; Zahrt and Crum, 2017; Turnwald, Boles, and Crum, 2017); however, large-scale databases have not yet included measures of mindset. The goal of this study is to use validated measures of exercise, stress, and diet mindsets to test the effect of mindsets on health behaviors and health outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health behavior	Health behavior mindset scale	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually
Blood pressure	Physical exam	Every 3 months
Behavioral characteristics, self-assessment	Survey	Every 3 months
Weight	Physical exam	Every 3 months

## Does conventional tampon use impact reproductive health differently from organic tampons or external menstrual products?

**Use Case ID** 198743

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

This study would compare those using conventional tampons to those using organic tampons or external menstrual products only and look at length of menstruation (number of days), pesticide metabolites, and pregnancy outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Menstrual product type	Survey	
Pesticides exposure assessment results	Urine collection	
Menstruation pattern	Survey	
Pregnancy outcomes	Survey	

## Are body fat and activity level related to pregnancy outcomes in normal- or high-BMI athletes with normal ovulatory function?

**Use Case ID** 198763

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The goal would be to examine how body fat, prepregnancy, and activity levels before and during pregnancy were related to pregnancy outcomes (e.g., miscarriage, full term, low birthweight, etc.) in athletes with a normal or high BMI and normal ovulatory function; prior studies focus solely on BMI, which is often an inaccurate measure for athletes. All of Us should collect data on body fat, preconception; physical activity levels before and during pregnancy; and pregnancy outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Body fat percentage		
Pregnancy characteristics	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Body Mass Index (BMI)	Physical exam	
Behavioral characteristics, self-assessment	Survey	
Sociodemographics	PPI Survey (AOURP)	

## What are the molecular mediators of wealth on successful aging?

**Use Case ID** 1000704

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Socioeconomic Status (SES)	PPI Survey (AOURP)	
Genomic analyses	Genomic testing	

## Is IVF technology a risk factor for adverse health outcomes of IVF-conceived children?

**Use Case ID** 1000718      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Most Important**      **Scientific Category** Assess Risk

2% of children are conceived through IVF. Association between IVF and lifelong health outcomes are largely unknown. Risk of imprinting disorders are increased in IVF children.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mode of conception	Electronic Health Record (EHR)	Baseline
Genomic analyses	Saliva	Baseline
Developmental milestones (medical)	Behavioral Risk Factor Surveillance System	Every 6 months
Family clinical outcomes	Electronic Health Record (EHR)	Per event

## What is the cause of labor?

**Use Case ID** 1000727      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

The cause of labor is unknown and a major cause of racial disparity. Preconception and prenatal factors that may include genetic, infectious, stress, and other influences must be ascertained. Preventing prematurity and the sequelae of prematurity would be informed by understanding the cause of labor.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Infection diagnoses	Cervical swab	Pre-pregnancy/during pregnancy
Environmental samplings and exposure results	Blood draw	Pre-pregnancy/during pregnancy
Infection diagnoses	Electronic Health Record (EHR)	Pre-pregnancy/during pregnancy
Pregnancy outcomes	Electronic Health Record (EHR)	Pre-pregnancy/during pregnancy
Genomic analyses	Genomic testing	Baseline
Pregnancy outcomes		At birth

## What are the determinants of loss of immune function with aging?

**Use Case ID** 1000743      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Maintain & Preserve Health

Most age-related diseases (cancer, heart disease, infection) are related to immune surveillance and response. Other risk factors for aging and age-related disease can vary with the immune aging environment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Bacterial infectious agent	Electronic Health Record (EHR)	Baseline
Fungal infectious agent	Electronic Health Record (EHR)	Baseline
Viral infectious agent	Electronic Health Record (EHR)	Baseline
Immunological assessments	Blood draw	Baseline
Immunological assessments	Electronic Health Record (EHR)	Baseline

## How does communication between health care providers and patients affect patient outcomes and future health care use?

**Use Case ID** 1000811      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Does the provider/patient relationship matter? All of Us offers a chance to evaluate whether the quality of the relationship influences proximal and distal health outcomes and whether the perception of relationship quality varies by generational cohort.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care provider standard of care	PPI Survey (AOURP)	Annually
Patient feedback	Survey	Annually
Clinical outcomes	Electronic Health Record (EHR)	During clinic visits
Patient Engagement	Survey	Annually
Sociodemographics	Electronic Health Record (EHR)	Baseline

## How does the placenta affect health resilience across the lifespan?

**Use Case ID** 1000822      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Elucidate Disease Mechanisms

The impact of placental function has not been studied in a diverse cohort and how it impacts development, resistance, and disease across the lifespan. All of Us has a unique opportunity to study a difficult-to-capture baseline sample across a diverse, longitudinal sample.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Placental tissue sample	Placental biopsy	At birth
Clinical outcomes	Electronic Health Record (EHR)	At birth
Whole genome sequence (WGS) data	Placental biopsy	At birth
Neonatal blood spot	Blood draw	Baseline

## What are the risk factors for readmission?

**Use Case ID** 1000834      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Examine various social determinants and genetic makeup/history that can affect readmission.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social determinants of health (SDH)	PPI Survey (AOURP)	Annually
Clinical outcomes	Survey	Annually
Pharmacogenomics	Genomic testing	Annually
Health care provider characteristics	PPI Survey (AOURP)	Annually
Social support	Geographic information system (GIS) code	Annually
Treatment decisions	Survey	Annually
Social support	Electronic Health Record (EHR)	Annually
Social support	Survey	Annually
Hospitalization	Electronic Health Record (EHR)	Annually

## To what extent are adverse childhood experiences (ACEs) and trauma related to cardiovascular disease in adulthood?

**Use Case ID** 1000842      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Most Important**      **Scientific Category** Assess Risk

Children who undergo adverse experiences are at risk for later life diseases. In this study, the first of its kind, we will examine interactive effects of genetics, epigenomics, and ACEs on cardiovascular disease later in life.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Adverse childhood experiences	Survey	Baseline
Diet, self-assessment	PPI Survey (AOURP)	Annually
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Cardiovascular disease information	Electronic Health Record (EHR)	Annually
Physical activity, self-assessment	Fitness tracker	Annually
Epigenomic/epigenetic markers	DNA methylation array	Annually
Perceived outcomes - patient	Short Form 36 (SF-36) health survey	Every 5 years

## What are the key factors leading to food allergy incidence and prevalence across the lifespan?

**Use Case ID** 1000883      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Most Important**      **Scientific Category** Assess Risk

Food allergy is on the rise and is one of the most requested topics for study in All of Us. This represents a huge burden on patients and families. This will be the first study of its kind to assess the role of demographics, genetics, microbiome, environmental contaminants, and diet influence on food allergy across the lifespan.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Microbiome sample	Specimen collection	Annually
Environmental samplings and exposure results	Urine collection	Annually
Diet, self-assessment	Diet history questionnaire	Periodically during pregnancy
Chemokine levels	Serum collection	Annually
Food allergy diagnosis	Electronic Health Record (EHR)	Annually

## How do age-related changes in microbiota impact health, and how does it affect treatment efficacy?

**Use Case ID** 1000967

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Changes in microbiome with age have been defined from birth to childhood but not into old age. There may be patterns of change that differ by age and health status and may influence subsequent disease and health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Microbiome sample	Stool sample	Every 5 years
Prescription medication\treatment	Electronic Health Record (EHR)	Ad hoc
Diet, self-assessment	Diet history questionnaire	Ad hoc
Functional mobility assessment results	Physical strength assessment	Ad hoc
Weight	Anthropometry	Ad hoc
Clinical outcomes	Electronic Health Record (EHR)	
Microbiome sample	Oral biofilm sample	Every 5 years
Functional mobility assessment results	Physical endurance assessment	Ad hoc

## How does preterm birth affect long-term health?

**Use Case ID** 1000995

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Preterm infants are at risk for adverse long-term outcomes. Which interventions in pregnancy and the neonatal period that improve long-term outcomes, including respiratory, neurologic, cardiovascular, are not well understood.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy characteristics	Electronic Health Record (EHR)	During clinic visits
Anthropometrics, newborn	Electronic Health Record (EHR)	At birth
Cardiopulmonary assessment	Electronic Health Record (EHR)	During clinic visits
Neurodevelopment milestones	Clinical assessment	Baseline

## What are predictors of successful aging?

**Use Case ID** 1001038

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Successful aging using the MacArthur Foundation definition. Absence of disease and maintenance of function across the lifespan.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Ability to perform activities of daily life (ADL) assessment results	Patient-reported outcome	Annually
Functional mobility assessment results	Patient-reported outcome	Annually
Cognitive assessments	Patient-reported outcome	Annually
Mechanical assistance	Electronic Health Record (EHR)	Annually
Sensory assessments	Physical exam	Annually

## What are the “norms” across the lifespan for biological and psychosocial milestones?

**Use Case ID** 1001053

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Specified Biomarkers	Electronic Health Record (EHR)	Annually
Hormone levels (non-steroidal)	Electronic Health Record (EHR)	Annually
Mental and psychosocial health, self-assessment	Neurocognitive test	Annually
Ability to perform activities of daily life (ADL) assessment results	Survey	Annually
Trauma events	Survey	Annually
Family relationships	Electronic Health Record (EHR)	Baseline
Mental and psychosocial health, self-assessment	Patient-Reported Outcomes Measurement Information System (PROMIS)	Annually

## What genetic, physiological, and environmental factors contribute to infertility in both men and women?

**Use Case ID** 1001063

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

1 in 6 couples trying to conceive have infertility. ~20% of infertile couples have idiopathic infertility.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Food diary	Daily
Genomic analyses	Saliva	Baseline
Hormone levels (non-steroidal)	Saliva	Daily
Seminal fluid microbiome sample	Specimen collection	Every 5 years
Sleep assessments	Sleep journal	Daily
Body temperature measurement	Wearable electronics	Continuous monitoring
Fertility assessment results	Blood draw	Baseline and at 5 years
Hormone levels (non-steroidal)	Saliva	Monthly

## What characteristics present in pregnancy are associated with development of asthma?

**Use Case ID** 1001084

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy, smoking	Survey	Baseline
Pregnancy, substance use	Survey	Baseline
Chemical exposure assessment results	Blood draw	Periodically during pregnancy *GC
Genomic analyses	Blood draw	Periodically during pregnancy
Epigenomic/epigenetic markers	Blood draw	Periodically during pregnancy
Education level attained	PPI Survey (AOURP)	At birth
Placental tissue sample		At birth
Socioeconomic Status (SES)	PPI Survey (AOURP)	At birth

## What are the preconception and prenatal omic and exposure determinants that predict healthy conception, pregnancy, birth, and early development?

**Use Case ID** 1001089

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Little is known about the mechanism by which parental factors during preconception influence fetal development, birth, and infant health and development. This requires recruitment of both partners. This study presents a unique opportunity to recruit and monitor both mothers and fathers for as long as 10 years prior to conception to measure environmental and omics data sets for analysis. This expands the vision of ECHO in several ways: (1) preconception data is more extensive, (2) recruitment of partners of All of Us participants, and (3) multi-omics profiling.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes	Electronic Health Record (EHR)	Annually
Behavioral characteristics, self-assessment	Survey	Annually
Environmental samplings and exposure results	Wearable electronics	Baseline, first trimester, monthly through delivery, and 1 year postpartum
Environmental samplings and exposure results	Geographic information system (GIS) code	Periodically
Sociodemographics	PPI Survey (AOURP)	Ad hoc
Proteomic profile	Specimen collection	Annually

## How does physical function in late life track from earlier life?

**Use Case ID** 1001128

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Function in old age depends on physiologic reserve, which is likely set down as early as conception and relates to achieving optimal development and varies tremendously with education and SES. Adults recruited into AoURP have a history of function and should be followed for function. No study has assessed function and its determinants across a life course.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Muscle tone measurement	Physical strength assessment	Ad hoc
Functional mobility assessment results	Patient-reported outcome	Ad hoc
Physical activity, self-assessment	Actigraphy	Ad hoc
Diet, self-assessment	Diary/journal	Ad hoc

## What are the determinants of loss of musculoskeletal mass and increased adiposity with aging?

**Use Case ID** 1001134      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Most Important**      **Scientific Category** Other

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical measurements	Anthropometry	Annually
Diet, self-assessment	Mobile monitor	Annually
Dental and oral data	Photograph	Annually
Skeletal mass	Urine collection	Annually
Obesity diagnosis	Anthropometry	Annually

## How does intergenerational obesity impact individual health outcomes?

**Use Case ID** 1001147      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Most Important**      **Scientific Category** Maintain & Preserve Health

50% of the U.S. population will be obese within two decades. Impact of parental obesity on offspring health outcomes are unknown. Two study populations: (1) All of Us participants for retrospective, and (2) enrolled participants trying to conceive.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Saliva	Baseline
Body Mass Index (BMI)	Electronic Health Record (EHR)	Baseline
Body Mass Index (BMI)	Anthropometry	Periodically during pregnancy
Physical measurements	Electronic Health Record (EHR)	Periodically during pregnancy
Socioeconomic Status (SES)	Electronic Health Record (EHR)	Periodically
Family clinical outcomes	Electronic Health Record (EHR)	Periodically
Adverse childhood experiences	Electronic Health Record (EHR)	Periodically
Obesity diagnosis	Electronic Health Record (EHR)	Annually

## What are the determinants of cognitive decline over the lifespan?

**Use Case ID** 1001154

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Body Mass Index (BMI)	Physical exam	Annually
Blood pressure	Blood pressure cuff	Annually
Sensory assessments	Physical exam	Annually
Waist circumference measurement	Physical exam	At age 50
Cognitive assessments	Neurocognitive test	During clinic visits
Waist circumference measurement	Physical exam	At age 50

## What genetic, physiological, and environmental factors contribute to the start and progression of bladder dysfunction, sexual dysfunction, and pelvic floor disorders?

**Use Case ID** 1001157

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important** **Scientific Category** Elucidate Disease Mechanisms

Prevalence of 50% for bladder and sexual dysfunction. Number 1 reason for early admission to assisted living facility. Top reason for decline of social activities in aging.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Stress hormones levels	Wearable electronics	Daily
Urination frequency	Diary/journal	Daily
Pelvic pain diagnosis	Diary/journal	Daily
Sexual function	Diary/journal	Weekly
Social determinants of health (SDH)	PPI Survey (AOURP)	Annually
Bladder dysfunction diagnosis	Electronic Health Record (EHR)	Annually
Pelvic floor disorders diagnosis	Electronic Health Record (EHR)	Annually

## What are the genomic factors that protect us from environmental exposures?

**Use Case ID** 1001160

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Throughout life, damage from environmental exposure, such as radiation, oxidation, etc., is repaired. Response to damage may vary with capacity for DNA repair and protect against cancer and aging.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Air quality assessment results		Annually
Immune biomarkers levels	Blood draw	Baseline
Cancer outcomes	Electronic Health Record (EHR)	Annually
Genomic instability assessment results		Baseline
Radiation exposure assessment results	Survey	Annually
Aging outcomes	Physical exam	Annually
Folate levels	Blood draw	Annually

## How does mode of child delivery affect long-term well-being of women?

**Use Case ID** 1001172

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Vaginal delivery increases risk of pelvic dysfunction, while Cesarean delivery increases risk of abdominal morbidity.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy characteristics	Electronic Health Record (EHR)	During clinic visits
Pregnancy outcomes	Survey	During clinic visits
Pelvic organ prolapse diagnosis	Mobile device	Baseline
Pregnancy outcomes		Baseline

## What is a healthy weight trajectory in late life?

**Use Case ID** 1001184      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Maintain & Preserve Health

It is common for adults to gain weight late in life, then lose weight at the end of life. Additionally, secular changes in the prevalence of obesity have confounded trends with aging. Comparisons between groups are confounded by weight history, dieting, and weight loss due to illness. Late life function is strongly influenced by late life obesity.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Anthropometrics, whole body measurements	Physical exam	Annually
Functional mobility assessment results	Physical strength assessment	Annually
Risk factors, self-assessment	Specimen collection	Annually
Developmental milestones (medical)	Patient-reported outcome	Annually
Weight	Dietary assessment tool	Annually
Functional mobility assessment results	Physical endurance assessment	Annually

## How do fetal and infant development impact long-term health outcomes, including rate of aging?

**Use Case ID** 1001191      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Epidemiological and lab data demonstrate that fetal and infant development influences later health (e.g., cardiovascular health, metabolic health, pulmonary health, aging, mental health). Mechanisms and interactions between genetic and environmental factors are not well understood. Recruit adults who are in prior studies. Recruit adults in All of Us as they have children. Query adults in All of Us about their past history.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Tissue biopsy	During clinic visits
Pregnancy characteristics	Electronic Health Record (EHR)	Baseline
Environmental samplings and exposure results	Environmental assessment	Annually or during clinical visits
Pregnancy outcomes	Electronic Health Record (EHR)	Baseline

## What are the determinants of autonomy across the lifespan?

**Use Case ID** 1001193 **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important** **Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Living independently	Survey	During clinic visits
Living independently	Short Physical Performance Battery (SPPB) protocol	During clinic visits
Cognitive assessments	Cognitive test	During clinic visits

## What are the determinants of urinary incontinence and how to avoid it?

**Use Case ID** 1001194 **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important** **Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Incontinence diagnosis	Survey	Annually
Incontinence diagnosis	Electronic Health Record (EHR)	Annually
Quality of life	Survey	Annually
Living independently	Survey	Annually

## How do stress, metabolic function, and inflammation from preconception through pregnancy influence preterm birth risk?

**Use Case ID** 1001197 **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important** **Scientific Category** Assess Risk

Drivers of preterm birth are largely unknown. This will be the first study of its kind to examine the roles of maternal stress, metabolic function, and inflammation on risk of preterm birth.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes	Blood draw	Pre-pregnancy/during pregnancy
Stress	Survey	Pre-pregnancy/during pregnancy
Inflammation biomarkers levels	Serum collection	Pre-pregnancy/during pregnancy
Metabolic risk assessment result	Electronic Health Record (EHR)	Pre-pregnancy/during pregnancy
Clinical outcomes	Electronic Health Record (EHR)	Pre-pregnancy/during pregnancy

## What is the effect of and mechanisms for the influence of wealth on recovery from medical issues and interventions?

**Use Case ID** 1001203      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Most Important**      **Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Functional mobility assessment results	Walk test	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Cognitive assessments	Cognitive test	Annually
Functional mobility assessment results	Walk test	Baseline and at event
Omics	Genomic testing	Baseline
Socioeconomic Status (SES)	PPI Survey (AOURP)	Annually

## Does the health of mother and father affect fetal development?

**Use Case ID** 1001206      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Most Important**      **Scientific Category** Maintain & Preserve Health

Maternal and paternal health is expected/known to be a key driver of healthy fetal development. Better understanding of the mechanisms can be attained through more informed data capture with respect to genetic, environmental, and lifestyle factors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Family relationships	Electronic Health Record (EHR)	Baseline
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Family clinical outcomes	PPI Survey (AOURP)	Baseline
Family clinical outcomes	PPI Survey (AOURP)	Annually
Developmental milestones (medical)	Electronic Health Record (EHR)	Ad hoc

## What are the risk factors associated with multimorbidity?

**Use Case ID** 1001211      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care cost	Medicaid/Medicare records	Baseline
Genomic instability assessment results	Immunosignature arrays	Baseline
Blood pressure	Blood pressure cuff	Baseline
Hospitalization	Electronic Health Record (EHR)	Ongoing
Gait speed	Walk test	During clinic visits
	Blood pressure cuff	Baseline

## How does stress impact disease reduction?

**Use Case ID** 1001219      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Reduce Disease Impact

Stressors—physical, environmental, social, work, etc.—adversely affect disease and disease response. Occupation and support networks are factors that have been less commonly measured and integrated into evaluations of health and disease and represent an opportunity for All of Us.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Occupation	PPI Survey (AOURP)	Baseline
Credit score	Survey	Annually
Environment	Geographic information system (GIS) code	Continuous monitoring
Family relationships	Survey	Baseline
Stress	Survey	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually
Social support	Survey	Annually

## Are rates of change in development and functioning among “youth” (age 0–18) different by demographic characteristics?

**Use Case ID** 1001221      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Most Important**      **Scientific Category** Maintain & Preserve Health

All of Us poses a good opportunity to understand how development differs among/across demographic groups. Among the challenges in this age band, self-reporting from infants and young kids is not possible, though this may be overcome by use of emerging technologies.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Developmental milestones (medical)	Clinical assessment	Ad hoc
Microbiome sample	Specimen collection	Ad hoc
Clinical outcomes	Patient-reported outcome	Ongoing
Family clinical outcomes	PPI Survey (AOURP)	Baseline
Genotyping data	Blood draw	Baseline

## What is the taxonomic structure of health-relevant lifestyle factors?

**Use Case ID** 1001233      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

With more than 1 million participants, All of Us poses a unique opportunity to evaluate the structure/ontology of phenotypes of BEHAVIOR. With smaller samples, it is only possible to study the relevance of one or a few specific behaviors for a health outcome, but All of Us can help to identify the constellation of relevant individual differences in behavior.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Behavioral characteristics, self-assessment	Survey	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually

## What impact does complementary medicine, acupuncture/herbs/nutritional supplements have on overall health?

**Use Case ID** 195833

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

Gather those people who have used complementary medicine as their primary medicine for at least 10 years. Compare percentage of use of prescription medicine, surgery, and death rate with those who have never used any form of complementary medicine. Or design a study more specifically for those with back pain, those with cancer, those with mental illness/depression, etc.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Complimentary medicine use	Survey	Include child, teenager, early adult, adult, elderly
Prescription medication\treatment	Prescription drug records	At specified times anchored to the clinical event
Perceived outcomes - patient	Survey	At specified times anchored to the clinical event
Depression diagnosis	PPI Survey (AOURP)	At specified times anchored to the clinical event
Cancer information	Electronic Health Record (EHR)	At specified times anchored to the clinical event

## Does palliative care initiated at the time of serious prenatal diagnosis affect outcomes for children and families?

**Use Case ID** 196983

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Outcomes of interest: decision-making by parents regarding pregnancy termination or continuation, fetal/newborn outcomes (survival, NICU intervention, pain), decision-making by parents after birth, coping by parents and siblings.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes		
Palliative care use		
Treatment decisions		

## What are the effects of bioidentical hormones on health, aging, and reproduction?

**Use Case ID** 198327

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

Review the use and dosages of bioidentical hormones prescribed and what the effects of them are. Include the study of natural desiccated thyroid versus Synthroid as well as bioidentical estrogen, progesterone, and testosterone. Understand what aspects of weight loss overall improved or decreased wellness, reproduction, and libido. Compare to synthetic use. Many studies have been done with the use of synthetic hormone replacement but not bioidenticals.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Coagulation disorder diagnosis		
Androgens levels		
Coagulation disorder diagnosis	Blood draw	
Glucocorticoid levels	Blood draw	
	Blood draw	

## Does trauma-informed care (TIC) improve health outcomes for individuals with a history of adverse childhood experiences (ACEs)?

**Use Case ID** 198401

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

A history of ACEs has been linked to numerous adverse physical and behavioral health conditions, many of them chronic. Individuals experiencing adversity (trauma) can be difficult to engage in preventative care or needed treatment. By creating safe and welcoming environments, policies, and practices, TIC is an approach to service delivery that seeks to improve engagement and satisfaction. Short-term outcomes likely reflect improved engagement, but do long-term outcomes include improved health?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Adverse childhood experiences	Adverse Childhood Experiences (ACE) survey	Baseline
Perceived outcomes - patient	Claims data	Every 3 months
Blood pressure	Clinical diagnostic test	
Glucocorticoid levels	Saliva	During clinic visits
Clinical outcomes		During clinic visits

## What are the most effective ways to reduce smoking and alcohol use in pregnant women?

**Use Case ID** 198657

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Survey pregnant women and their health professionals to determine levels of awareness about smoking, e-cigarettes, nicotine replacement products, and alcohol consumption. Determine when/if information is provided to pregnant women, evaluate the accuracy of the information, and assess its effectiveness. Cotinine measurements could be used as a surrogate for nicotine consumption. Alcohol use could be assessed by surveys and assessment of newborns.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy characteristics		
Tobacco smoking		
Alcohol Use		
Healthy behavior, self-assessment		

# Immunologic Infections and Inflammatory

**All of Us** | The  
RESEARCH PROGRAM | Precision  
Medicine  
Initiative

## **Can allergies predict the development of autoimmune or inflammatory disease? Does treatment reduce the risk?**

**Use Case ID** 194895

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Identify a group of participants with environmental/food allergies and ask if the allergies are well controlled. Use observational data over many years to determine the relative rate of development of autoimmune/inflammatory illness in participants whose allergies are/are not well controlled.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Survey	Every 3 years
Allergies diagnoses		
Autoimmune diseases diagnosis		

## **What is the role of persistent co-infections in health and disease?**

**Use Case ID** 195087

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

Co-infections can significantly alter disease risk, incidence, prevalence, aggressiveness, treatment response and outcomes, in addition to making it more difficult to manage and treat the diseases. Compare differences in host response to co-infections, disease risk, and treatment response to elucidate how the ubiquitous co-infections contribute to variations in disease incidence and outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Infection diagnoses		
Clinical outcomes		

## What are the criteria for environmental associated autoimmune diseases?

**Use Case ID** 195104

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

Goal: Survey patients with autoimmune diseases for information on occupational and other lifestyle exposures to factors associated with autoimmunity (smoking, silica dust, solvents, etc.). Build databases containing clinical parameters, blood tests, and exposure data to help identify putative diagnostic criteria. Compare with patients having idiopathic autoimmunity (i.e., lacking known risk exposures).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually
Autoimmune biomarkers levels	Clinical diagnostic test	Annually
Occupation	PPI Survey (AOURP)	Annually
Autoimmune diseases diagnosis	Electronic Health Record (EHR)	Annually

## What are the commonalities among autoimmune diseases?

**Use Case ID** 198112

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Goal: Survey patients with celiac disease, Hashimoto's, and other autoimmune diseases to evaluate lifestyle, environment, food, antibiotics, and previous stomach viruses to see what has triggered the onset of various autoimmune diseases. Is the similarity of the molecules that the body attacks significant (e.g., thyroid, gluten)? If left unaddressed, more autoimmune diseases can develop. What do people with autoimmune diseases have in common, and what are the possible links and triggers?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis	Survey	Include child, teenager, early adult, adult, elderly
Air quality assessment results		Every 2 years
Environmental samplings and exposure results	Urine collection	Every 2 years
Lifestyle, self-assessment	PPI Survey (AOURP)	Include child, teenager, early adult, adult, elderly
Diet, self-assessment	PPI Survey (AOURP)	Every 3 years

## What are the multi-level, immune-mediated, environmental exposure endotypes of environmental illnesses, asthma, and allergies?

**Use Case ID** 198343

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Focusing recruitment on communities with a disproportionate burden of environmental exposure (such as western New York), develop and test a multi-level model to ascertain the burden of environmental illness symptom clusters, asthma, and allergies attributable to environmental factors at the 1) community/neighborhood, 2) household, 3) personal, 4) internal body burden, and 5) inflammatory biomarker response levels over time. Ascertain how genetic variation mediates these relationships.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Clinical diagnostic test	Every 3 years
Air quality assessment results		Continuous monitoring
Pulmonary assessment results	Clinical diagnostic test	
Allergens assessment results	Skin allergy test	
Environmental assessment results	Survey	Annually

## What are the multi-level environmental exposure pathways of autoimmune inflammation/disease and reactive airway disease?

**Use Case ID** 198345

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Focusing recruitment on communities with a disproportionate burden of environmental exposures, develop and test a multi-level model to ascertain the burden of autoimmune inflammation, autoimmune disease, and reactive airway attributable to environmental factors at the 1) community/neighborhood, 2) household, 3) personal, 4) internal body burden, and 5) inflammatory biomarker response levels over time. Ascertain how genetic variation mediates these relationships.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis		
Environmental samplings and exposure results		
Inflammation biomarkers levels	Clinical diagnostic test	
Sociodemographics	PPI Survey (AOURP)	

## How can we use the All of Us platform to better understand exposures and/or biochemical signals that precede the onset of autoimmune disease?

**Use Case ID** 198508

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

One idea is to use the large NIH dataset in order to understand exposures/biochemical signals that precede the onset of autoimmune disease so that we can start to understand the pathogenesis/triggers that initiate the development of our diseases. Ultimately, this could lead to interventions that could identify those at high risk and prevent the onset of autoimmunity. Katherine Wysham, MD

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis		
Environmental samplings and exposure results		

## Does exposure to environmental chemicals, such as PFAS, affect the incidence of autoimmune diseases in young adults?

**Use Case ID** 198517

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

By prospectively assessing exposures to environmental chemicals, such as per- and polyfluoroalkyl substances (PFAS), All of Us could evaluate whether these exposures are contributing to the rising incidence of autoimmune diseases in young adults. Intermediate biological outcomes related to thyroid function, inflammation, and immune response could be assessed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Polyfluoroalkyl Substances (PFAS) levels	Blood draw	Every 3 years
Health and phenotype data	Electronic Health Record (EHR)	
Inflammation biomarkers levels	Blood draw	Every 3 years

## How do personal care products and processed foods impact the development of asthma and diabetes?

**Use Case ID** 198740

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Food diary	
Personal care product use		
Phthalate metabolites levels	Urine collection	
Food selection		

## Can the microbiome predict response to treatment for immune and/or inflammatory disease?

**Use Case ID** 1000958      **Cross-Cutting Theme** Environmental and Other Contextual Effects  
**Most Important**      **Scientific Category** Treat & Cure Disease

Evaluate the association between the microbiome profiles and responses to treatments in patients with immune-mediated diseases.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Prescription medication\treatment	Electronic Health Record (EHR)	Every 3 months
Bacterial 6S RNA	RNA sequencing	Every 3 months
Genomic sequence data	Quantitative Polymerase Chain Reaction (qPCR)	Every 3 months
Metabolomic profile	Serum collection	Every 3 months
Genomic sequence data		Every 3 months
Metabolomic profile	Stool sample	Every 3 months

## What are the environmental and socioeconomic factors that predict autoimmune disease severity and prognosis?

**Use Case ID** 1001068      **Cross-Cutting Theme** Environmental and Other Contextual Effects  
**Scientific Category** Assess Risk

External factors that predict disease severity and prognosis—not treatment response.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Prescription medication\treatment	Electronic Health Record (EHR)	During clinic visits
Location data	Interview	Annually for 10 years
Location data	Survey	Annually for 10 years
Occupational environment assessment results	Interview	Annually for 10 years
Occupational environment assessment results	PPI Survey (AOURP)	Annually for 10 years
Diet, self-assessment	Diet history questionnaire	Annually for 10 years
Social determinants of health (SDH)	PPI Survey (AOURP)	Annually for 10 years
Medical Information	Electronic Health Record (EHR)	During clinic visits
Medical Information	PPI Survey (AOURP)	Annually for 10 years
Autoimmune diseases diagnosis	Electronic Health Record (EHR)	Annually for 10 years

## How do inflammatory/infectious diseases contribute to social isolation and disease outcomes?

**Use Case ID** 1001117

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Reduce Disease Impact

Participants with selected inflammatory/infectious diseases are followed to determine their reported social isolation and their health/other outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Psychological measures	Survey	Periodically
Medical Information	Electronic Health Record (EHR)	Baseline
Disease severity assessment results	Electronic Health Record (EHR)	Periodically
Disease severity assessment results	Ecological momentary assessment (EMA)	Ongoing
Social isolation	PPI Survey (AOURP)	Baseline
Social isolation	Ecological momentary assessment (EMA)	Ongoing
Social support	Electronic Health Record (EHR)	Periodically
Death	National Death Index	Periodically
Health mindset	Short Form 36 (SF-36) health survey	Periodically

## What are the population genetics of genes that code for drug-metabolizing enzymes? Do any of these genes correlate with drug reactions?

**Use Case ID** 192293

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Treat & Cure Disease

1) Collect the genetics of drug-metabolizing enzymes from the genetic samples in the All of Us study. 2) Describe the population genetics of these specific genes. How many people are normal (extensive metabolizers, EMs)? How many have other profiles? How many genes is the “average person” abnormal for? 3) By collecting data for “allergies” (some of which are intolerances, not true allergies) and medication reactions requiring medical care, can we show that non-EMs are at higher risk?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Allergies diagnoses	PPI Survey (AOURP)	Every 3 years
Side effects of prescription medication	Survey	Every 3 years
Pharmacogenomics		

## **How can we translate knowledge about the microbiome into better ways to diagnose and treat autoimmune diseases?**

**Use Case ID** 196479

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Reduce Disease Impact

The scientific and medical communities are rapidly learning more about the human microbiome and the role it plays in our health, but there are still many gaps that need to be addressed. The purpose of this study would be to focus on identifying the relationship between the microbiome and a systemic disease state, helping to inform new methods for translating knowledge about the microbiome into better, more efficient ways to diagnose and treat Sjögren's and other autoimmune diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis		
Microbiome sample		
Clinical outcomes		

## **Are fibromyalgia, chronic fatigue syndrome, and Hashimoto's thyroiditis different manifestations of the same infectious disease?**

**Use Case ID** 197329

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

The study would require a technique/technology that could analyze genetic markers of differing tissues beyond blood, at a cellular level, to detect non-human microbes even when they are dormant. It would also be helpful to map the immune triggers and responses that may be causing differing symptoms' manifestation.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Tissue biopsy	
Infectious agents	Tissue biopsy	
Inflammation biomarkers levels	Blood draw	

## What is the pathogenesis of type 1 diabetes?

**Use Case ID** 197377

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Use a case-cohort study, identifying cases through the EHS system and confirming through a variety of clinical laboratory tests. We know little about the genetic basis of T1D in African-ancestry (non-white) populations or T1D with onset in adulthood. These data would also provide insights on the rates and types of complications that may differ between adult-onset T1D and childhood-onset T1D.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diseased, Missing, Filled Surface Score (DMFS)	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Genotyping data		Baseline
Hemoglobin A1C (HbA1C) levels	Blood draw	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually

## Are there unique biomarkers for acne vulgaris?

**Use Case ID** 198334

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Create a DNA database of individuals who suffer with acne, along with its subtypes such as “cystic acne-prone.” There could be further study of individuals with acne’s skin microbiome. The goal would be to understand the pathogenesis of acne vulgaris and create an antidote.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Microbiome sample	Clinical diagnostic test	

## How do genetics influence food allergies?

**Use Case ID** 198408

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Collect and analyze DNA information from blood samples, along with health records and survey responses to determine whether there is a genetic component to the following aspects of food allergies: 1. Predisposition to the development of allergies (who, at what age, to what degree of severity). 2. Triggers of allergic reactions. 3. Validity of allergy testing. 4. Response to treatment. 5. Predisposition to outgrow allergies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Blood draw	Baseline
Health and phenotype data	Electronic Health Record (EHR)	Every 2 years
Allergens assessment results	Electronic Health Record (EHR)	Include child, teenager, early adult, adult, elderly
Self-reported ancestry	PPI Survey (AOURP)	Baseline
Diet, self-assessment	PPI Survey (AOURP)	Every 2 years

## Does the efficacy of the flu vaccine depend on intrinsic, individual factors (e.g., physiological or genetic factors)?

**Use Case ID** 198608

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Treat & Cure Disease

We all know that the efficacy of the flu vaccine can vary from 10%–50% in the population. We also know that the flu virus mutates continuously and thus is an environmental factor that contributes to the lower efficacy of the flu vaccine. But why are there interindividual differential immune responses in those individuals that contract the flu (Influenza A or B), even after having received the flu vaccine, so that some individuals may not have a shortened or less severe disease phenotype?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Immune biomarkers levels	Blood draw	
Genotyping data	Whole Genome Genotyping (WGG)	
Treatment effectiveness		

## Can whole genome sequencing of women of childbearing age in the All of Us cohort with first-degree immunodeficiencies be used to target DNA editing to foster unaffected children?

**Use Case ID** 1001100      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Treat & Cure Disease

When a mother with a defined genetic cause of immunodeficiency is identified, consent for in vitro fertilization protocol would be obtained to perform ex vivo, CRISPR/Cas DNA editing.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Genomic instability assessment results		Baseline

## What are the social, environmental, and genetic determinants of epigenetics as related to inflammatory disease risk?

**Use Case ID** 1001143      **Cross-Cutting Theme** Genomics and Other Omics  
**Most Important**      **Scientific Category** Elucidate Disease Mechanisms

Measure methylation profiles, use All of Us data (SDH, environment/behaviors and WGS) to study predictors of inflammatory disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	DNA methylation array	Baseline
Genomic analyses	Whole Genome Genotyping (WGG)	Baseline
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Medical Information		Every 3 months
Medical Information	Electronic Health Record (EHR)	Every 3 months
Environment	Record of residence	Continuous monitoring
Diet constitution assessment	Dietary assessment tool	Continuous monitoring
Infection diagnoses	Electronic Health Record (EHR)	At specified times anchored to the clinical event

## Are changes in one's microbiome responsible for flares in inflammatory bowel disease (IBD)?

**Use Case ID** 1001178

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Targeting All of Us enrollees with IBD, determination of changes from baseline in intestinal bacterial microbiome will provide insight as to whether this triggers a clinical exacerbation (flare).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Gastrointestinal health information	Colonoscopy	Annually
Gastrointestinal health information	Magnetic Resonance Imaging (MRI)	At specified times anchored to the clinical event
Gastrointestinal health information	Electronic Health Record (EHR)	During clinic visits
Inflammation biomarkers levels	Enzyme-Linked ImmunoSorbent Assay (ELISA)	At specified times anchored to the clinical event
Gastrointestinal health information	Colonoscopy	At specified times anchored to the clinical event
Gut microbiome sample	Whole Genome Sequencing (WGS)	Baseline and post-treatment
Diet, self-assessment	Dietary assessment tool	Daily

## Can genomics identify asthmatics who do or don't respond to inhaled corticosteroids?

**Use Case ID** 1001207

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Treat & Cure Disease

Association of genetic variation, alone or in combination with transcriptomics/metabolomics, with asthma exacerbations in patients on inhaled corticosteroids.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Metabolomic profile	RNA sequencing	Annually for 10 years
Whole exomic sequence (WES) data	RNA sequencing	Annually for 10 years
Whole exomic sequence (WES) data	Serum collection	Annually for 10 years
Metabolomic profile	Serum collection	Annually for 10 years
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Asthma outcomes	Mobile monitor	At specified times anchored to the clinical event

## Can we develop better diagnostic testing for autoimmune diseases?

**Use Case ID** 195770

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Detect Disease

The process of diagnosis for autoimmune disease is often prolonged and difficult. Current testing (e.g., ANA test) is often not well-correlated with the disease status and can impede diagnosis. A longitudinal study could be done with this data set to look for other biomarkers that might be better correlated with disease state, facilitating early diagnosis.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Autoimmune biomarkers levels		

## Can we identify the reasons for overlapping disease manifestations across high-burden illnesses?

**Use Case ID** 196483

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

This study would focus on identifying the reasons why a range of high-burden diseases, including Sjögren's, fibromyalgia, and chronic fatigue syndrome, share overlapping disease characteristics. A better understanding of why this is would be greatly beneficial to a large group of patients with high-burden, costly illnesses, which often result in a decrease in quality of life and have negative economic implications.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Autoimmune diseases diagnosis		
Clinical outcomes		

## What is the health economics impact of congenital cytomegalovirus (CMV) infection?

**Use Case ID** 197469

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

Congenital cytomegalovirus (CMV) infection is the most common congenital infection and a common cause of neurodevelopmental disabilities, growth failure, hearing loss, and vision loss. Prevention of congenital CMV by vaccination was deemed a national priority for the 21st century by the Institute of Medicine in 2000. Information on the health economics of this common congenital infection is necessary to drive prevention through vaccine development and awareness through behavior modification.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health care cost	Claims data	Periodic (approximately biweekly)
Quality of life	Survey	Include child, teenager, early adult, adult, elderly
Health and phenotype data	Electronic Health Record (EHR)	Annually
Vision assessment results	Electronic Health Record (EHR)	Annually
Clinical outcomes	Death records	Baseline

## Can an AI chatbot help patients identify their disease risk and symptoms during an outbreak?

**Use Case ID** 198768

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Other

Whenever there is an outbreak of a pandemic disease, say swine flu, everyone gets alarmed and searches on the symptoms to check if they have actually got it. So a chatbot trained with AI to detect the key symptoms and guide the end user to identify if he or she is at risk or not would reduce the excitement among patients and also save general physicians time in effectively attending to only the actual patients.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Activity monitor	Continuous monitoring
Behavioral characteristics, self-assessment	Custom sensor/app	Continuous monitoring

## What is the relationship between social network (isolation) and inflammatory biomarkers?

**Use Case ID** 1000805

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Capture and categorize “social environment” for All of Us cohort and characterize “inflammation” to determine role of social determinants of health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social determinants of health (SDH)	PPI Survey (AOURP)	Annually
Behavioral characteristics, self-assessment	Survey	Annually
Behavioral characteristics, self-assessment	Psychological test	Annually
Inflammation biomarkers levels	Blood draw	Annually

## What is the relationship between ZIP code and inflammatory markers?

**Use Case ID** 1000848

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

Comprehensive sociodemographic assessments of All of Us enrollees by ZIP codes will be correlated to their levels of inflammatory markers and general health outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Inflammation disorder diagnosis	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Annually
Inflammation disorder diagnosis	Electronic Health Record (EHR)	Baseline
Health and phenotype data	Electronic Health Record (EHR)	Annually
Health and phenotype data	Survey	Annually
Social environment	Survey	Periodically
Air quality assessment results		Annually
Location data	Global Positioning System (GPS) monitoring	Annually

## What is the impact of provider characteristics on treatment outcomes in immunologic disease patients?

**Use Case ID** 1001059

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Treat & Cure Disease

The characteristics (age, gender, race, training, specialty) of the patient-identified primary provider impacts the outcome of the patient with immunologic diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Health care participation	PPI Survey (AOURP)	Annually for 10 years
Perceived outcomes - patient	Mobile monitor	Every 3 months

## What are the factors that impact variation in response to HIV antiretroviral treatment?

**Use Case ID** 1001149

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Factors—Adherence to medication (survey, blood)—Mental health (EHRs, PROs)—Substance use (blood, urine, hair, survey)—SES/food insecurity—Genetics (genomic testing, host or virus)—Health care insurance (survey, EHRs, CMS records)—Health care access (geocoding, survey).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Acquired Immunodeficiency Syndrome (AIDS) complications	Electronic Health Record (EHR)	Annually
Inflammation biomarkers levels	Blood draw	Periodically *GC
T-cells, CD4 counts	Electronic Health Record (EHR)	Periodically
Viral infectious agent	Electronic Health Record (EHR)	Periodically
Viral infectious agent	Genomic testing	Periodically
Acquired Immunodeficiency Syndrome (AIDS) complications	Survey	Annually
Inflammation biomarkers levels	Tissue biopsy	Periodically
Death	Death records	Per event

## Can mobile health applications decrease health disparities in disease outcomes for underrepresented in biomedical research populations?

**Use Case ID** 1001159

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Treat & Cure Disease

Apps to monitor health remotely, provide decision support, provide telemedicine, and connect with providers to improve health in UBRs. Use case: asthma.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Survey	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Location data	Geospatial tracking	Continuous monitoring
Risk factors, self-assessment	Survey	Continuous monitoring
Pulmonary assessment results	Peak flow meter	Periodically

## Do stress levels affect outcomes in inflammatory disease differently in racial/ethnic subgroups?

**Use Case ID** 1001167

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Treat & Cure Disease

Assess the association of stress levels by race/ethnic groups on patient and clinical outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mental and psychosocial health, self-assessment	Survey	Annually for 10 years
Hospitalization	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Emergency room (ER) visit	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Functional mobility assessment results	Mobile monitor	Continuous monitoring

## What are the socioeconomic determinants of vaccination rates?

**Use Case ID** 1001176

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Treat & Cure Disease

Evaluate the association of various socioeconomic variables (e.g., income, ZIP code, education level, employment status, family) on the compliance to vaccination recommendations (as per CDC recommendations).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Preventative care use	Electronic Health Record (EHR)	Annually
Preventative care use	Survey	Annually
Sociodemographics	PPI Survey (AOURP)	Annually

## For an individual with frequent canker sores, what risk factors predict the number of canker sore episodes per year?

**Use Case ID** 195096

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Assess Risk

Collect data on which relatives also suffer from canker sores and how many canker sores per year people have. In motivated people, get a diary of each episode (how long it took to treat), their diet, what toothpaste they use, flossing frequency, canker sores after injury versus from stress, and treatment used. Analyze what factors can predict severe disease (age, gender, genetics) in a sub-cohort of patients with severe canker sores (very frequent or very severe) and do a detailed analysis of genome.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Stress	Survey	
Family relationships	Survey	
Sociodemographics	PPI Survey (AOURP)	
Canker sores diagnosis	Survey	
Herpes Simplex Virus type 1 (HSV-1) test results	Electronic Health Record (EHR)	

## How are autoimmune diseases related to cancers, and can we share new knowledge across these two fields?

**Use Case ID** 195876      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Scientific Category** Other

Develop meta-analyses for autoimmune diseases and cancers that affect the greatest number of people. Through these analyses, develop hypotheses regarding similar infection routes and disease development. Identify common intervention protocols that could halt one or both kinds of disease. Involve expertise in both categories of disease so immediate sharing of knowledge will preclude withholding potential benefits to the vast number of Americans debilitated and dying from these diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis	Electronic Health Record (EHR)	Every 2 years
Cancer information	Electronic Health Record (EHR)	Every 2 years

## Can advanced methodologies used to predict rare events be applied to assess unexpected disease resistance?

**Use Case ID** 1001161      **Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research  
**Scientific Category** Detect Disease

Engineers can predict failure of an individual screw on a plane. Can we do the same in rare health care failures?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Family clinical outcomes	PPI Survey (AOURP)	Baseline
Genomic analyses	Genomic testing	Baseline
Location data	Global Positioning System (GPS) monitoring	Periodically
Clinical outcomes	Electronic Health Record (EHR)	Annually

## How can novel environmental exposure monitoring (via wearable technology) improve the discovery of exposure–disease outcomes?

**Use Case ID** 198142

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Reduce Disease Impact

Currently, environmental exposure monitoring measures classic or persistent chemical exposures but might fail to analyze newer chemicals. Many newer chemicals are high in production volume but are nevertheless not assessed in population or in study-targeted analyses but may, in fact, be associated with risk to human or animal health. New personal wearable silicone band monitoring devices, such as those designed Dr. Kim Anderson, could revolutionize exposure–disease outcome information.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Mobile monitor	

## Can we monitor drug adherence with mobile apps to improve HIV outcomes?

**Use Case ID** 1000719

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Treat & Cure Disease

Assess impact of monitoring drug adherence on HIV outcomes?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Human Immunodeficiency Virus (HIV) test results	Electronic Health Record (EHR)	Every 3 months
Adherence to prescription regimen	Mobile monitor	Daily
Hospitalization	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Clinical outcomes	Electronic Health Record (EHR)	At specified times anchored to the clinical event

## ***In patients with chronic symptoms (like pain or itch), can the All of Us platform be used to permit or help N-of-1 trials (the ultimate precision medicine)?***

**Use Case ID** 1000816

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Treat & Cure Disease

N-of-1 trials are a strong way to identify the right treatment for the right patient at the right time. But they are difficult to implement because of logistical issues, such as routine symptom measurement. The structure of the All of Us study will provide an infrastructure for these studies (e.g., for headache, sleep disturbances, other).

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Symptoms	PPI Survey (AOURP)	Periodically
Sleep assessments	PPI Survey (AOURP)	Periodic (approximately biweekly)
Functional mobility assessment results	PPI Survey (AOURP)	Periodically
Functional mobility assessment results	Mobile monitor	Periodically

## ***Does routine measurement of a participant's symptom severity improve his/her well-being?***

**Use Case ID** 1000986

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Reduce Disease Impact

Participant responds on mobile device about his/her experience of symptoms using brief validated measures.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Pain symptom diagnosis	PPI Survey (AOURP)	Continuous monitoring
Fatigue symptom	PPI Survey (AOURP)	Daily
Sleep behavior assessment results	Wearable electronics	Daily
Functional mobility assessment results	Wearable electronics	Daily
Functional mobility assessment results	Gross Motor Function Measure (GMFM)	Daily
Appetite	Food diary	Daily
Quality of life	PPI Survey (AOURP)	Periodically

## ***In HIV-Infected persons, can participant-reported symptom experience be used to manage HIV treatment effects?***

**Use Case ID** 1000994

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Reduce Disease Impact

Participants with HIV infection respond on mobile tools about their symptoms as the symptom occurs; their symptom information triggers feedback of self-care and caregiver/provider strategies for symptom management.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Fatigue symptom	Ecological momentary assessment (EMA)	Continuous monitoring
Sleep behavior assessment results	Ecological momentary assessment (EMA)	Continuous monitoring
Gastrointestinal health information	Ecological momentary assessment (EMA)	Continuous monitoring
Physical activity, self-assessment	Activity monitor	Periodically
Outcomes	Electronic Health Record (EHR)	Periodically
Adherence to treatment	PPI Survey (AOURP)	Periodically
Health and phenotype data	Short Form 36 (SF-36) health survey	Periodically

## ***Can daily spirometry tests using a mobile device better guide asthma management and reduce emergency department visits for pediatric asthma patients?***

**Use Case ID** 1001044

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Reduce Disease Impact

Results from daily spirometry that are collected via smartphone/mobile technology can be provided to primary care physicians and patient to better guide asthma management. Improved disease management will reduce use of the emergency department for asthma exacerbations.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Asthma diagnosis	Electronic Health Record (EHR)	Baseline
Asthma diagnosis	PPI Survey (AOURP)	Daily
Adherence to treatment	Survey	Daily
Adherence to treatment	Mobile monitor	Daily
Pulmonary assessment results	Spirometry	Daily
Mobile phone ownership	Survey	Baseline
Allergens assessment results	Environmental assessment	Weekly
Air quality assessment results		Weekly

## Do routine patient-reported experiences affect clinical outcomes?

**Use Case ID** 1001108

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Maintain & Preserve Health

Assess the impact of patient engagement (through reporting) on clinical outcomes for patients with immunologic diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Perceived outcomes - patient	Mobile monitor	Monthly
Patient education methods and content	Electronic Health Record (EHR)	Every 3 months
Immunologic disease information	Electronic Health Record (EHR)	Baseline

## Can we use mobile apps to monitor joint pain and swelling to improve inflammatory disease outcomes?

**Use Case ID** 1001109

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Treat & Cure Disease

Assess impact of collecting joint symptoms by mobile device on patient and clinical outcomes in patients with inflammatory arthritis.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Movement assessments	Mobile monitor	Continuous monitoring
Perceived outcomes - patient	Mobile monitor	Continuous monitoring
Education level attained	Mobile monitor	Every 3 months
Joint pain diagnosis	Mobile monitor	Continuous monitoring
Inflammation disorder diagnosis	Mobile monitor	Continuous monitoring

## Can the use of mobile health apps encourage the adoption of healthy lifestyle behaviors, reduce inflammation and infection, and improve health outcomes?

**Use Case ID** 1001135

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Maintain & Preserve Health

RCT in a subset who consent to educational feedback. Real-time assessment of risk factors with apps → immediate education module. Could be applied to a wide range of exposures (allergens → asthma, obesity → psoriasis, diet → gout, physical activity → joint pain). Could be studied in different UBR groups.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Behavioral characteristics, self-assessment	Survey	Continuous monitoring
Behavioral characteristics, self-assessment	Mobile monitor	Continuous monitoring
Physical measurements	Ecological momentary assessment (EMA)	Continuous monitoring
Physical measurements	Anthropometry	Continuous monitoring
Physical measurements	Actigraphy	Continuous monitoring
Physical measurements	Mobile monitor	Continuous monitoring
Location data	Geographic information system (GIS) code	Continuous monitoring
Inflammation biomarkers levels	Electronic Health Record (EHR)	Annually

## What are the risk factors for developing autoimmune disease?

**Use Case ID** 190196

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Many autoimmune diseases are characterized by the presence of autoantibodies, but these may be present long before disease starts. What triggers the transition from autoimmunity (the presence of the antibodies) to autoimmune disease is unknown, but it is likely to involve both environmental exposures and genetic susceptibility. What are the risk factors for the transition to disease? Are these modifiable? In which patients is the risk of transition sufficiently high that one would intervene?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune biomarkers levels	Blood draw	
Genomic sequence data	Whole Genome Sequencing (WGS)	

## What are the shared genetic factors underlying autoimmune disorders and their most common concurrent conditions?

**Use Case ID** 192136

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis	Electronic Health Record (EHR)	
Genomic analyses		
Disease endotypes results	Electronic Health Record (EHR)	

## What risk factors predispose children to sepsis, and what interventions are most effective for prevention and treatment?

**Use Case ID** 194555

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

This study will focus on the entire cohort of children (infants to 18-year-olds) and will identify those risk factors which predispose children to sepsis. The information will be used to create more precise strategies to identify individuals at highest risk of sepsis and to implement preventive or early treatment therapies that would improve outcomes. The study will also assess the use of adjunctive immunomodulatory therapies to inform their use with enhanced precision.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Infection diagnoses		
Neurodevelopment milestones	Clinical diagnostic test	
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Infection diagnoses	Electronic Health Record (EHR)	Annually
Physical activity, self-assessment	Mobile monitor	Continuous monitoring

## Does a gluten-free diet aid in management of symptoms of Hashimoto's disease?

Use Case ID 194846

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Do participants with Hashimoto's disease who follow a gluten-free diet experience better outcomes than those who follow a normal American diet?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune biomarkers levels	Clinical diagnostic test	Annually
Weight	Physical exam	Annually
Thyroid hormone levels	Blood draw	Annually
Perceived outcomes - patient	Survey	Every 3 months
Diet, self-assessment		

## Does having West Nile virus increase the risk of developing an autoimmune disease?

Use Case ID 194855

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Follow people who have had West Nile; see if they develop Factor V, Lewy body dementia. My husband was extremely healthy and active and then got West Nile. Then he was diagnosed with Factor V, needed amputation, and developed Lewy body. There has to be a connection.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis	Mobile monitor	Continuously for 1 week duration at 1 month, 6 months, and 1 year
Lewy body disease diagnosis	Mobile monitor	Continuous monitoring
West Nile Virus diagnosis		

## ***Has there been an increase in the incidence of shingles cases in adults; if so, is this increase associated with mental and physical stress?***

**Use Case ID** 195170

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

I would attempt to obtain numbers of shingles diagnosis in the year 1980, in an area of the U.S. with season, compare that by doing a current study of numbers of cases. Then I would begin to have physicians ask the question, “Did you recently go through a stressful event or were you exposed to very cold or hot temperatures, lack of sleep, or a stressful work environment?” The goal would be to determine if we are seeing an increase in shingles and, if so, is it due to modern stressful environments?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Quality of life	Physical exam	Continuous monitoring
Shingles diagnosis	Electronic Health Record (EHR)	
Stress	Survey	
Behavioral characteristics, self-assessment	Survey	

## ***Are recurrent urinary tract infections associated with high dietary intake of animal fat?***

**Use Case ID** 195835

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Recurrent urinary tract infections (rUTIs) are highly prevalent among women across the lifespan with significant impact on quality of life. Prevention strategies are utilized despite variable efficacy, high side effect burden, and increasing antibiotic resistance. This study will identify a cohort of women with rUTIs (>3/year) and inventory dietary intake. We hypothesize that moderate intake of animal fat and products with antibiotic exposure will be associated with increased risk of rUTIs.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Urinary tract infection (UTI) diagnosis	Electronic Health Record (EHR)	
Treatment/Therapy	Electronic Health Record (EHR)	
Diet, self-assessment	Food diary	
Travel itineraries	Survey	
Restaurant inventory	Survey	

## What is the relationship between pregnancy, childbirth, and postpartum immune system functioning and autoimmune disorders?

**Use Case ID** 196041

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Goals: To determine if women are more susceptible to infections and autoimmune diseases around the period of childbirth. To determine if infectious diseases like Lyme disease are a precipitating factor for other diseases like scleroderma. Participants: Females of childbearing age. Data: genetic, environmental, lab work, pain assessments, any factors that could moderate outcomes. Frequency of data: perhaps monthly, during pregnancy to 3 months afterward (may have to ask if this is too burdensome).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune biomarkers levels	Blood draw	At specified times anchored to the clinical event
Infectious agents	Blood draw	
Pregnancy characteristics	Electronic Health Record (EHR)	

## What are the genetic, epigenetic, and environmental factors of endometriosis, and how can they help identify its subtypes?

**Use Case ID** 196181

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Endometriosis is a systemic condition with a heavy burden on patients. It is estimated that 10% of women of reproductive age have endometriosis, but its etiology is still unknown. While it is accepted that endometriosis is a heterogeneous condition, what the exact subtypes of the disease are is still an open question.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Bisphenol A (BPA) levels	Smartphone-based ecological momentary assessment	
Epigenomic/epigenetic markers		
Genomic analyses		
Clinical outcomes	Electronic Health Record (EHR)	
Endometriosis diagnosis	Smartphone-based ecological momentary assessment	Continuously for 1 week duration at 1 month, 6 months, and 1 year

## What specific factors contribute to the reoccurrence of latent/dormant human viruses, such as herpes simplex, Epstein-Barr, and parvovirus?

**Use Case ID** 196300

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Comparisons of patients with autoimmune diseases and latent viruses with a control group having only one factor ensuring a statistically representative sample by gender, age, and race.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Autoimmune biomarkers levels	Serum collection	
Autoimmune diseases diagnosis	Electronic Health Record (EHR)	
Sociodemographics	PPI Survey (AOURP)	
Viral infectious agent	Electronic Health Record (EHR)	
Viral infectious agent	Serum collection	

## Can biomarker identification help improve diagnosis, identify risk factors, and better classify patients with autoimmune diseases?

**Use Case ID** 196478

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

For many autoimmune diseases, such as Sjögren's, a lack of clinical, hematological, and histological biomarkers has proven to be a hindrance to our understanding, management, and treatment of the disease. This study would focus on identifying such biomarkers in patients with autoimmune diseases to help improve diagnosis, better classify patients, and identify risk factors, and have the potential to show improvement with the use of a therapeutic to improve clinical trials.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Autoimmune diseases diagnosis		
Autoimmune biomarkers levels		
Specified Biomarkers		
Risk factors, self-assessment		

## Could the Precision Medicine Initiative determine who is at risk for preventable infectious diseases?

**Use Case ID** 196886      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

We will obtain a onetime blood measurement of immunity to preventable infectious diseases, such as measles, mumps, and human papillomavirus, in people who have been vaccinated. This will help identify people who do not respond strongly to certain vaccines, to identify at-risk populations for infectious diseases and HPV-associated cancers. The goal is to develop targeted vaccination and prevention strategies for infectious diseases and cancers.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Degenerative diseases diagnoses	Blood draw	
Treatment effectiveness	Clinical diagnostic test	

## What is the impact of low-level food allergies for sufferers of irritable bowel syndrome?

**Use Case ID** 198328      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Reduce Disease Impact

This study would require a sample of persons with identifiable low-grade food allergies. These would likely be identified via laboratory blood testing. Some participants should eliminate all dietary allergens, and others should continue to eat as usual. Questionnaires would be required to assess patient health. A possible blood test follow-up may assess the state of the allergens on an individual basis. Also suggest tracking hormonal changes in participants to find out if any patterns emerge.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Allergens assessment results	Blood draw	Annually
Diet, self-assessment	Food diary	Continuous monitoring
Quality of life	Survey	Every 3 months
Irritable bowel syndrome (IBS) diagnosis		
Hormone levels (non-steroidal)		

## Can we target tick preventers (e.g., permethrin) by tracking hikers interacting with disease-bearing tick habitats?

**Use Case ID** 198444

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Preventing Local Tickborne Disease Among Outdoor Hikers. Roberto Santamaria, Director, Nantucket Health Department; Peter A. Morrison, Nantucket Data Platform. We propose a generalizable use case to prevent tickborne disease nationwide. Target tick preventers like permethrin by tracking where hikers intersect disease-bearing tick habitats via cellphone “pings.” We use time-specific location data mirroring hiker concentrations, cross-analyzed with tick-borne disease incidence.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Activity monitor	Periodic (approximately biweekly)
Environmental samplings and exposure results		

## Does the timing of an individual’s first urinary tract infection correlate with the onset of other urinary tract disorders?

**Use Case ID** 198481

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Urinary tract infections are extremely common. For most adults, they are the first (sometimes the only) urinary tract disorder to present. By using participant recollection of UTI (most likely using the proxy measure of antibiotic prescription for UTI treatment), investigators may be able to assess associations between the timing/presence of first UTI correlate with timing of onset/presence of other urinary tract disorders. This may allow identification of a group at increased risk for LUTS.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Survey	Baseline
Urinary biome sample	Urine collection	
Urinary tract infection (UTI) diagnosis		
Lower Urinary Tract Symptoms (LUTS) record		

## How can we identify modifiable risk factors that could reduce the incidence of autoimmune disease?

**Use Case ID** 198501      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

Identification of modifiable risk factors that could reduce the incidence of autoimmune disease. (The analogy is with cancer research: For decades, the NCI's efforts focused primarily on treatment. Only when they started to fund research on preventable causes of cancer [e.g., smoking] did mortality really start to go down.) It's a bigger challenge in autoimmunity/rheumatology, since the risk factors are less obvious. Bryce A. Binstadt, M.D., Ph.D.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Rheumatoid factor levels		
Autoimmune diseases diagnosis		

## What is the scope of allergic reactions when using personal care products?

**Use Case ID** 198589      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

Objective: Determine the scope and severity of allergic reactions to the use of personal care products [1–10].  
Methods: All of Us participants will fill out a question on which personal care products (including brand) they use and the reactions that might ensue. The most commonly used products will be analyzed for chemical components. Follow-up studies will include toxicity studies of the chemical allergens.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Personal care product use	Survey	
Environmental samplings and exposure results	PPI Survey (AOURP)	

## How does chronic stress influence the persistence of oncogenic viruses or bacteria in otherwise healthy adults?

**Use Case ID** 198644

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Chronic stress has a significant suppressive impact on the immune system and would influence the risk of infection-associated cancers if high-risk infections are allowed to persist. In general populations and healthy adult populations, this question has not been addressed. It would involve serial measurement of oral or anogenital human papillomavirus, or even helicobacter pylori.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Stress	Mobile monitor	
Human Papilloma Virus (HPV) test results		Periodically
Helicobacter pylori test results	Metabolic risk profiling	Periodically
Sociodemographics		

## Can we personalize the prevention of rheumatoid arthritis?

**Use Case ID** 198709

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Modifiable risk factors interact with genes to predict rheumatoid arthritis (RA). Antibodies can be detected in pre-RA, up to 10 years before symptoms. Goal: Conduct RCT to reduce RA risk factors and delay/prevent RA onset. Methods: Find high-risk subjects (positive anti-CCP, high polygenetic risk score), monitor for early symptoms (mHealth), conduct RCT based on motivational interviewing/health coaching versus basic information, intervention to modify risk factors (smoking, obesity). Outcome: new onset inflammatory arthritis.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Blood draw	
Autoimmune biomarkers levels	Blood draw	Baseline
Pain symptom diagnosis	Mobile monitor	Every 3 months
Behavioral characteristics, self-assessment	Survey	Annually
Weight	Physical exam	

## How do inflammation and subclinical autoimmunity impact reproductive health?

**Use Case ID** 198724

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Preterm delivery is a serious problem. SLE and RA patients have increased pregnancy morbidity before diagnosis and their healthy sisters have increased rates of pregnancy complications. Therefore, preclinical autoimmunity or inflammation may affect pregnancy outcomes. Reproductive and family history, and rheumatic disease symptoms, would be collected and correlated with hsCRP levels and autoantibody production in a nested study to help reduce pregnancy risks and neonatal morbidity.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Coagulation disorder diagnosis		Every 2 years
C-Reactive Protein (CRP) levels	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Every 2 years
Autoimmune biomarkers levels	Neurocognitive test	
Self-reported ancestry	Electronic Health Record (EHR)	Baseline

## Can the All of Us platform be used to identify molecular pathways of autoimmune diseases as well as individuals at risk for these diseases?

**Use Case ID** 198726

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Autoimmune diseases afflict nearly 1 in 12 Americans, and many more have autoantibodies but no evidence of clinical disease. Recent work has identified biomarkers or clinical symptoms which associate with subsequent developing development of systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA), and NIH-funded prevention trials are underway. All of Us provides a unique opportunity to identify at-risk individuals through surveys and blood tests, and to identify molecular pathways of disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis	Electronic Health Record (EHR)	Baseline
Connective tissue disorder diagnoses	Survey	Every 2 years
C-Reactive Protein (CRP) levels	Blood draw	Every 3 years
Autoimmune biomarkers levels	Blood draw	Every 3 years
Environmental samplings and exposure results	PPI Survey (AOURP)	Baseline

## How do mindsets about illness and treatment affect inflammation biomarkers and treatment outcomes in patients with chronic illness?

**Use Case ID** 198738

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Half of all Americans are diagnosed with one or more chronic illnesses, like heart disease and cancer. Mindsets about these illnesses may have a profound impact on the diagnosis, progression, and treatment of these illnesses. This study aims to (1) understand the distribution of mindsets held by a diverse group of both healthy and chronically ill Americans, and (2) identify relationships between these mindsets, biomarkers of inflammatory processes, treatment outcomes, and quality of life.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health mindset	Health mindset scale	Annually
Health and phenotype data	Electronic Health Record (EHR)	Continuous monitoring
C-Reactive Protein (CRP) levels	Blood draw	Every 3 months
Quality of life	Survey	Every 3 months
Clinical outcomes	Survey	Every 3 months

## Are there certain commensal viruses that predispose individuals to autoimmune diseases?

**Use Case ID** 1000695

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The All of Us longitudinal tracking of development of autoimmune disease in the setting of virome determination will afford a case-control analysis of risk of AID with commensal viruses.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis	Electronic Health Record (EHR)	Periodically
Virome profile	Blood draw	Baseline and post-treatment
Autoimmune biomarkers levels	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Annually
Autoimmune biomarkers levels	Human leukocyte antigen (HLA) typing test	Annually
Virome profile	Stool sample	Baseline and post-treatment

## Is vitamin D level associated with the risk of immunologic, infectious, and inflammatory conditions?

**Use Case ID** 1000698

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Vitamin D levels	Blood draw	Annually
Diet, self-assessment	PPI Survey (AOURP)	Annually
Diet, self-assessment	PPI Survey (AOURP)	Daily
Intestinal physiological measurements	Sensor (swallowed)	Annually
Metabolomic profile	Stool sample	Annually
Specified Biomarkers	Hair sample collection	Annually
Medical Information	Electronic Health Record (EHR)	Annually
Medical Information	Electronic Health Record (EHR)	Every 3 months
Sociodemographics	PPI Survey (AOURP)	Annually

## Does infection with a neurotropic virus (e.g., HSV1) trigger and/or accelerate neurodegenerative disease (e.g., dementia or Alzheimer's)?

**Use Case ID** 1000712

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Longitudinal tracking of cognitive function to diagnose and monitor progression of dementia/Adz will be done in the All of Us cohort. For cases of new-onset and/or accelerated rate of progression, host immune response (antibody) to neurotropic viruses will be assessed in both archived (baseline enrollment) and serial blood samples.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Alzheimer's diagnosis	Electronic Health Record (EHR)	During clinic visits
Dementia diagnosis	Cognitive test	Every 6 months
Viral infectious agent	Reaction phenotyping assay	Baseline and post-treatment
Virome profile	Viral phage display arrays	Baseline and post-treatment
Virome profile	Immunosignature arrays	Baseline and post-treatment

## What aspects of the indigenous microbiome mediate colonization resistance against multidrug-resistant organisms?

**Use Case ID** 1000731

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Microbiome sample	Stool sample	Baseline
Microbiome sample	Skin sample	Baseline
Microbiome sample	Vaginal swab	Baseline
Antibiotic use	Electronic Health Record (EHR)	Every 3 months
Antibiotic use	Survey	Every 3 months
Drug-resistant infectious agent	Electronic Health Record (EHR)	Annually
Drug-resistant infection, carrier	Electronic Health Record (EHR)	Annually
Drug-resistant infectious agent	Nasal swab	Annually

## Does exercise reduce inflammatory markers and incidence of inflammatory diseases?

**Use Case ID** 1000749

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Physical activity, self-assessment	PPI Survey (AOURP)	Continuous monitoring
Physical activity, self-assessment	Custom sensor/app	Continuous monitoring
C-Reactive Protein (CRP) levels	Blood draw	Annually
Cytokines levels	Blood draw	Annually
Fat distribution	Physical exam	Annually
Fat distribution	Dual-energy X-ray Absorptiometry (DXA)	Annually
Statins	Electronic Health Record (EHR)	Every 3 months
Nonsteroidal Anti-inflammatory Drugs (NSAIDs)	Electronic Health Record (EHR)	Every 3 months
Over-the-counter (OTC) medication Use	Electronic Health Record (EHR)	Every 3 months
Outcomes	Electronic Health Record (EHR)	Every 3 months
Outcomes	Records	Every 3 months

## Does routine measurement of inflammatory disease patients' symptoms reduce health care costs and resources utilization?

**Use Case ID** 1000777      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Other

Assess impact of symptom measurement (from patients and providers) on cost/resource utilization in patients with inflammatory disease.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Perceived outcomes - patient	Mobile monitor	Monthly
Health care cost	Electronic Health Record (EHR)	Annually for 10 years

## Is migration to the United States associated with risk of inflammatory infectious diseases?

**Use Case ID** 1000789      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

Description not provided.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Medical Information	Electronic Health Record (EHR)	Every 3 months
Family clinical outcomes	PPI Survey (AOURP)	Annually
Sociodemographics	PPI Survey (AOURP)	Baseline
Location data	Survey	Annually
Racism encounters	Survey	Annually
Social relationships	Survey	Annually
Medical Information	Records	Every 3 months
Behavioral characteristics, self-assessment	Diet history questionnaire	Annually
Tobacco smoking	Smoking survey	Annually
Inflammation biomarkers levels	Blood draw	Every 3 months

## What is the role of the family in the development of asthma and infectious disease?

**Use Case ID** 1000818

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Household: defined as people you have lived with in the past year.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social relationships	Survey	Annually
Asthma diagnosis	PPI Survey (AOURP)	Annually
Infection diagnoses	Electronic Health Record (EHR)	Annually
Asthma diagnosis	Electronic Health Record (EHR)	Annually
Infection diagnoses	Survey	Annually
Household exposures assessment results	PPI Survey (AOURP)	Annually
Environment	Survey	Annually
Environment	Environmental assessment	Annually

## What is the relationship of selected putative biomarkers of inflammatory disease to outcomes?

**Use Case ID** 1000833

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

In participants with selected inflammatory diseases, new methodologic approaches will be developed to determine and better model the relationship between putative biomarkers and outcomes of disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Specimen collection	Baseline
Inflammation biomarkers levels	Specimen collection	Baseline
Imaging	Electronic Health Record (EHR)	Baseline
Treatment effectiveness	Electronic Health Record (EHR)	Periodically
Treatment effectiveness	Patient-reported outcome	Periodically
Health care interactions	Electronic Health Record (EHR)	Periodically
Clinical outcomes	National Death Index	Periodically
Clinical outcomes	Electronic Health Record (EHR)	Periodically

## What is the relationship between depression and inflammatory diseases over time?

**Use Case ID** 1000856

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Evolve the temporal relationship of depression numbers and inflammations.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mental health and behavior information	PPI Survey (AOURP)	Continuous monitoring
Appetite	Mobile monitor	Continuous monitoring
Sleep assessments	Sleep journal	Continuous monitoring
Sleep assessments	Survey	Continuous monitoring
Sleep assessments	Wearable electronics	Continuous monitoring
Inflammation biomarkers levels	Tissue biopsy	Periodically

## Can the All of Us platform identify high-risk individuals with genetic risk factors, antibodies, and behavioral factors for immune disease?

**Use Case ID** 1000918

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Risk factors, self-assessment	Whole Genome Genotyping (WGG)	Baseline
Epigenomic/epigenetic markers	Genomic testing	Baseline
Genomic analyses	Human leukocyte antigen (HLA) typing test	Baseline
Autoantibodies levels	Blood draw	Annually
Family clinical outcomes	PPI Survey (AOURP)	Annually
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Clinical outcomes	PPI Survey (AOURP)	Annually
Behavioral characteristics, self-assessment	Survey	Annually
Patient-reported outcomes		Annually

## What is the duration of protection from vaccines during longitudinal follow-up?

**Use Case ID** 1001036

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Vaccination records	Electronic Health Record (EHR)	Annually
Vaccination records	Survey	Annually
Immune biomarkers levels	Serum collection	Annually

## Is there a diet that reduces severity of inflammatory disease?

**Use Case ID** 1001052

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Association of diet with a variety of patient and clinical outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Hospitalization	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Functional mobility assessment results	Mobile monitor	Continuous monitoring
Food selection	Dietary assessment tool	Annually for 10 years
Food selection	Food diary	Annually for 10 years
Perceived outcomes - patient	Mobile monitor	Every 3 months
Nutritional supplement use	Dietary assessment tool	Annually for 10 years
Nutritional supplement use	Food diary	Annually for 10 years
Animal product intake	Dietary assessment tool	Annually for 10 years
Animal product intake	Food diary	Annually for 10 years

## Does perinatal exposure to vaginal and intestinal microbiome diversity predispose genetically susceptible infants to atopic and allergic diseases?

**Use Case ID** 1001081

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Enrolled pregnant women will have vaginal and intestinal microbiome diversity and complexity determined at the time of delivery. Neonatal microbiome will be determined at birth, 3 months, 6 months, 9 months, and 12 months along with genome (WGS). These infants will be tracked for development of atopy and food allergy to determine causal associations of microbiome characteristics with these allergic diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy characteristics	Electronic Health Record (EHR)	Baseline
Microbiome sample	Whole Genome Sequencing (WGS)	Baseline
Microbiome sample	Stool sample	Every 3 months for 1 year
Allergies diagnoses	Skin allergy test	Annually for 10 years
Asthma diagnosis	Electronic Health Record (EHR)	Annually for 10 years
Asthma diagnosis	Spirometry	Annually for 10 years
Breast milk sample	Dietary assessment tool	Every 6 months

## Is obesity related to flu vaccine immune response?

**Use Case ID** 1001083

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Influenza Virus test results	Electronic Health Record (EHR)	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Vaccination records	Electronic Health Record (EHR)	Annually
Vaccination records	Survey	Annually
Physical measurements	Physical exam	Annually
Immune biomarkers levels	Quantitative Polymerase Chain Reaction (qPCR)	Annually

## Can geolocation be used to prevent immunologic, infectious, and inflammatory diseases?

**Use Case ID** 1001097

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Outcomes	Electronic Health Record (EHR)	Every 3 months
Geocode data	Mobile device	Continuous monitoring
Geocode data	Survey	Continuous monitoring
Chemical exposure assessment results	Environmental assessment	Annually
Outcomes	Survey	Annually
Pesticides exposure assessment results	Urine collection	Baseline
Blue space assessment	Environmental assessment	Annually
Greenness assessment results	Environmental assessment	Annually
Neighborhood characteristics	Environmental assessment	Annually
Water quality assessment results	Environmental assessment	Annually
Radiation exposure assessment results	Environmental assessment	Annually

## How do we assess the risk of asymptomatic infection in disease outcomes?

**Use Case ID** 1001122

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Biospecimens and EHRs are used to detect asymptomatic or untreated infections, and the participants are followed for health and other outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Vaginal microbiome sample	Vaginal swab	Periodically
Virome profile	Blood draw	Periodically
Fungal infectious agent	Tissue biopsy	Periodically
Infectious agents	Blood draw	Periodically
Outcomes	Death records	Baseline

## Does unstructured, free-text entry from participants regarding their “hunches” about inflammatory triggers or treatments show significance across the All of Us cohort?

**Use Case ID** 1001148      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Most Important**      **Scientific Category** Maintain & Preserve Health

“When I drink herbal tea, I don’t see this symptom...” (anecdotal). “I’m pretty sure when I sleep less than 5 hours at night, I see a spike in my psoriasis...” (anecdotal). Need objective data to quantify exposures and outcomes/conclusions, with potential public health benefit in identifying novel exposure and outcome relationships.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Outcomes	Electronic Health Record (EHR)	Every 3 months
Sleep assessments	Actigraphy	Continuous monitoring
Perceived outcomes - patient	Survey	Periodically *GC
Imaging	Mobile device camera	Periodically
Inflammation biomarkers levels	Specimen collection	Periodically
Diet, self-assessment	PPI Survey (AOURP)	Periodically

## Does school education on STDs reduce incidence of infections?

**Use Case ID** 1001174      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Annually
Health behavior	Survey	Annually
Risk perception	Survey	Annually
Clinical outcomes	Survey	Annually
Self-efficacy	Survey	Annually
Infectious agents	Specimen collection	Annually

## What are the factors affecting successful treatment of Lyme disease?

**Use Case ID** 190198

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Gaps exist in Lyme epidemiology necessary for comparisons of symptoms and outcomes by genotype. A licensed vaccine was pulled due to low uptake, in part because there was a suggestion that individuals with certain HLA subtypes developed rheumatoid arthritis. Diagnostic uncertainty, diffuse symptoms, and a failure to notice tick bites (especially when bitten by larvae or nymphs) complicate identification of early disease. Early Lyme disease can be effectively treated with short-course doxycycline, but treatment of late-stage disease is often less effective.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lyme Disease diagnosis	Electronic Health Record (EHR)	
Clinical outcomes	Electronic Health Record (EHR)	
Prescription medication\treatment	Prescription drug records	
Treatment decisions		
Pharmacogenomics		

## Is isoniazid treatment for a positive purified protein derivative test associated with food intolerance and/or granuloma annulare?

**Use Case ID** 194639

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Is isoniazid treatment for +PPD associated with food intolerance and/or granuloma annulare?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Postpartum Mood Disorders (PPMD) diagnosis		
Isoniazid use		
Food intolerance diagnosis		
Inflammation disorder diagnosis		

## Can we treat Graves' disease and other autoimmune endocrine problems at the immune system level?

**Use Case ID** 195319

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Find out what antibodies cause the endocrinopathies and target them using a new system of tregitopes. This can also be use of checkpoint inhibitor medications that create endocrine immune problems, so using tregitope will block the immune response and then no target organ will be affected (endocrine organ).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Clinical diagnostic test	Continuous monitoring
Health care cost	Blood draw	Continuous monitoring
Stress	Clinical diagnostic test	Periodic (approximately biweekly)
Family clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Self-reported ancestry	Electronic Health Record (EHR)	Continuous monitoring

## Can we improve the identification and management of Sjögren's syndrome in children?

**Use Case ID** 196611

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Detect Disease

Children often present differently with Sjögren's when compared to adults, leading to delayed diagnosis and treatment. Additionally, awareness of Sjögren's in children among clinicians is low, which may further delay diagnosis and treatment. This study would focus on learning how to better identify, manage, and treat Sjögren's in this special population and how disease expression and pathways differ in children compared to adults.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis		
Medical Information		
Treatment/Therapy		

## How has the opioid abuse epidemic impacted hepatitis C incidence?

**Use Case ID** 196877

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Hepatitis C virus (HCV) is often transmitted through the use of shared injection drug paraphernalia. With the rise in opioid abuse, it is reasonable to expect a corresponding rise in HCV incidence. Current treatments can effectively cure HCV, making it more important than ever to identify those most at risk. Using data from this cohort, we can determine the current incidence of HCV and its association with opioid use and identify areas where incidence is highest to guide future interventions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Hepatitis diagnosis	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Every 3 months
Drug use/abuse, self-assessed	PPI Survey (AOURP)	Every 3 months
Location data	Survey	Every 3 months
Opioid screen test results	Urine collection	Every 3 months
Human Immunodeficiency Virus (HIV) test results	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Every 3 months

## How can human microbiome data be used to improve our understanding of the pathogenesis and treatment of infectious diseases?

**Use Case ID** 197457

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Precision microbiome engineering could be applied to vaccine delivery, immunology, drug-resistant infections, and post-surgical infections. Specific research questions regarding pathogenesis and treatment: What aspects of the indigenous microbiota mediate colonization resistance against *C. difficile*, as well as other multi-drug resistant organisms such as carbapenamase-producing gram-negative bacteria and vancomycin resistant enterococci? Determine optimal *C. difficile* treatment to prevent relapse.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes		
Microbiome sample	Clinical diagnostic test	
Infectious agents		

## ***Is functional medicine an efficacious approach to treating autoimmune disease?***

**Use Case ID** 198359

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Many autoimmune diseases, such as Sjögren's, RA, and psoriatic arthritis, utilize medications that have adverse side effects, which seriously compromise health or QOL without addressing the causation and cure of the diseases. Functional medicine claims to address the causes of illness and suggests ways to cure the disease, not just manage it. But what evidence exists that this is true? Can a research study compare the functional medicine approach with the current medicine approach?

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Autoimmune diseases diagnosis		
Treatment decisions		
Clinical outcomes		
Quality of life		

## ***What are the outcomes of pregnant and elderly patients with rheumatic diseases exposed to immunosuppressive medications?***

**Use Case ID** 198515

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

It is often the case that the true risks of our drugs remain unknown, especially for pregnant and elderly patients. If there was a cohort that was closely followed, we could see the long-term outcomes in patients exposed to these medications. Katherine Wysham, MD (American College of Rheumatology)

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Pregnancy outcomes		
Arthritis diagnosis		
Immunosuppressive drug use		

## Do metabolomic signatures predict novel treatment targets for diseases?

**Use Case ID** 1000705

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Comparing metabolomic profiles for a disease group versus a nondisease group can reveal common metabolomic characteristics that are unique to the disease group and may be candidate therapeutic targets.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Metabolomic profile	Blood draw	Annually for 10 years
Medical Information	Electronic Health Record (EHR)	Annually for 10 years
Prescription medication\treatment	Electronic Health Record (EHR)	Annually for 10 years
Symptoms	Clinical assessment	Annually for 10 years
Symptoms	Electronic Health Record (EHR)	Annually for 10 years

## How can we determine optimal antiretroviral treatment for aging people living with HIV?

**Use Case ID** 1000853

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Do older people require different treatments than younger people? If so, what are they?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Human Immunodeficiency Virus (HIV) test results	Blood draw	Annually for 10 years
Prescription medication\treatment	Survey	Baseline
Prescription medication\treatment	Electronic Health Record (EHR)	During clinic visits
Medical Information	Electronic Health Record (EHR)	During clinic visits
Patient-reported outcomes	Survey	Annually for 10 years
Side effects of treatment/therapy	Survey	Annually for 10 years

## Do blood virome level and diversity influence incidence and prognosis for inflammatory diseases?

**Use Case ID** 1000869

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

Commensal viruses circulating in blood—high levels and diversity may be important to health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Every 3 months
Virome profile	Blood draw	Annually
Medical Information	Survey	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually
Lifestyle, self-assessment	Interview	Annually
Clinical outcomes	Patient-Reported Outcomes Measurement Information System (PROMIS)	Annually
Outcomes	Death records	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Location data	Survey	Annually

## Can we design better immune-modulating clinical trials by leveraging next-generation, real-time biomarker determination?

**Use Case ID** 1000891

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Detect Disease

For patients/enrollees being considered for immunosuppression or immune-modulating therapies, randomization on the basis of real-time profiling of immune biomarkers will afford improved clinical trial design and interpretation of therapeutic response.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis	Electronic Health Record (EHR)	During clinic visits
Health and phenotype data	Electronic Health Record (EHR)	During clinic visits
Inflammation biomarkers levels	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Baseline and post-treatment
Autoimmune biomarkers levels	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Baseline and post-treatment

## Does vitamin D reduce pain in inflammatory disease?

**Use Case ID** 1000992

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Evaluate the association of serum vitamin D levels with levels of pain in patients with inflammatory disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Vitamin D, 25-hydroxy levels	Serum collection	Every 3 months
Pain symptom diagnosis	Mobile monitor	Weekly
Functional mobility assessment results	Mobile monitor	Continuous monitoring

## What are the long-term (downstream) outcomes of HIV pre-exposure prophylaxis on the individual?

**Use Case ID** 1001004

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Most Important**

**Scientific Category** Treat & Cure Disease

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cancer information	Electronic Health Record (EHR)	Periodically
Immune biomarkers levels	Blood draw	Periodically
Immune biomarkers levels	Urine collection	Periodically
Immune biomarkers levels	Tissue biopsy	Periodically
Bone health assessment results	Electronic Health Record (EHR)	Periodically
Bone health assessment results	Dual-energy X-ray Absorptiometry (DXA)	Periodically
Bone health assessment results	Survey	Periodically
Cancer information	PPI Survey (AOURP)	Periodically
Cancer information	Surveillance, Epidemiology, and End Results (SEER) program	Periodically
Cancer information	Blood draw	Periodically
Cancer information	Tissue biopsy	Periodically
Access to health care	PPI Survey (AOURP)	Periodically
Sexually transmitted infectious agent (not otherwise specified)	Blood draw	Periodically
Sexually transmitted infectious agent (not otherwise specified)	Tissue biopsy	Periodically
Sexually transmitted infectious agent (not otherwise specified)	Urine collection	Periodically
Sexually transmitted infectious agent (not otherwise specified)	Electronic Health Record (EHR)	Periodically
Sexually transmitted infectious agent (not otherwise specified)	Survey	Periodically
Drug-resistant infectious agent	Blood draw	Post-event or at least annually
Drug-resistant infectious agent	Electronic Health Record (EHR)	Post-event or at least annually

## Does a mobile tracking device help improve treatment adherence for immune and inflammatory diseases?

**Use Case ID** 1001092

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Does a mobile tracking device help improve treatment adherence for immune/inflammatory disease?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Electronic Health Record (EHR)	Every 3 months
Adherence to treatment	Survey	Every 3 months
Disease severity assessment results	Survey	Every 3 months
Medical Information	Electronic Health Record (EHR)	Baseline
Adherence to treatment	Mobile device	Ongoing

## Do the new HIV drug prevention (PREP) strategies prevent transmission?

**Use Case ID** 1001116

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

PREP—prevention for HIV → HIV yes/no → transmission ART—viral suppression → transmission. Do this in a subset of participants from HIV or STD clinics.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Risk factors, self-assessment	Survey	Annually
Adherence to treatment	Survey	Annually
Human Immunodeficiency Virus (HIV) test results	Electronic Health Record (EHR)	Annually
Family relationships		Periodically

## Is there a biomarker that can predict response to targeted immunospecific therapy?

**Use Case ID** 1001192

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Using observation of blood and genetic biomarkers to look for correlations with treatment outcome.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Pre-treatment
Perceived outcomes - patient	Survey	Pre- and post-treatment
Immune biomarkers levels	Blood draw	Pre- and post-treatment
Inflammation antigens levels	Immunosignature arrays	Pre- and post-treatment
Immune biomarkers levels	Immunosignature arrays	Pre- and post-treatment
Antibody titres	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Annually for 10 years
Immune biomarkers levels	Blood draw	Annually for 10 years
Antibody titres	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Pre- and post-treatment
Perceived outcomes - patient	Survey	Annually for 10 years
Clinical outcomes	Electronic Health Record (EHR)	Annually for 10 years
Clinical outcomes	Electronic Health Record (EHR)	Pre- and post-treatment

# Mental Health and Addiction

**All of Us** | The  
RESEARCH PROGRAM | Precision  
Medicine  
Initiative

## What are the effects of alcohol (and other drug) consumption on major somatic diseases and psychiatric disorders and their treatments?

**Use Case ID** 194843

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Alcohol affects nearly all major diseases. Failing to capture lifetime alcohol exposure will adversely affect the goals of All of Us. There are better questions about consumption that should be asked about previous year, typical year, and heaviest year. Questions should be asked about problems due to alcohol, and those should be focused on lifetime. Additional questions about other drugs should also be included.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Alcoholism diagnoses	PPI Survey (AOURP)	Every 2 years
Drug use/abuse, self-assessed	PPI Survey (AOURP)	Every 2 years
Alcohol Use	Mobile monitor	Annually

## Do the adverse emotions and/or perceptions of those with other deficiencies create unique PET scans?

**Use Case ID** 195119

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

It is well known that many deficiencies cause emotional problems, causing bad behavior. These emotional problems come from changed or reduced perception of self, others, environment, and the relation between each of these. Subjects are not hard to find. Many people take individual supplements of any one or more of thiamin, folate, B-12, magnesium, etc. and tell you they have to have the nutrient for a rational mind. Take PET scan with/without the nutrient deficiency.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Positron emission tomography (PET) images	Positron emission tomography (PET)	
Nutritional supplement use		
Mental health and behavior information		

## How can we better identify and assess environmental and genetic/physiological risk factors that lead to child/teen stress?

**Use Case ID** 195941

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Kids are exposed to tremendous pressure. This results in an unusual number of children and teenagers suffering from stress and depression, leading in some cases to devastating consequences. A study that could address to what level there are genetic predispositions to stress and depression and how they intersect with modern pressures, and that would involve school, children, and parents as cohorts, could provide better tools for parents and mentors to identify children at risk.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Stress	Clinical diagnostic test	Continuous monitoring
Depression diagnosis		
Genomic analyses		
Social determinants of health (SDH)		

## What health factors relate to positive and negative emotional bias?

**Use Case ID** 196572

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

When two faces are presented simultaneously, depressed people show a bias to look at the face with a negative expression. In contrast, older adults tend to look away from faces with negative expressions, consistent with the positivity effect seen in healthy older adults and their generally reduced negative affect. Little is known about how health helps shape these emotional biases. We also don't know how these biases typically change over time in people.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Smartphone-based ecological momentary assessment	Every 3 years
Blood pressure	Physical exam	
Diet, self-assessment		
Social determinants of health (SDH)		
Air quality assessment results		

## Is there a relationship between work-related injuries and opioid use (in either direction)?

**Use Case ID** 198673

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Workers in certain occupations might be more likely to use opioids if their first introduction to opioids follows a workplace illness or injury. Some of those same workers may abuse the drugs due to stressors at work. Also, workers using opioids might be more likely to injure themselves at work if they are less sensitive to pain and might be slower to react or less likely to notice dangerous workplace conditions. All of Us could help to better understand the relationship between opioid use and work.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Opioid use, prescribed	Prescription drug records	Annually
Opium/opioid addiction diagnoses	Electronic Health Record (EHR)	Annually
Opioid use, recreational	PPI Survey (AOURP)	Annually
Health care participation	PPI Survey (AOURP)	Annually

## How does serial/community context impact drug use trajectory?

**Use Case ID** 1000714

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Reduce Disease Impact

Follow from before adolescence through lifespan: transition from use to SUD, SUD to recovery, relapse.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Drug use/abuse, self-assessed	Patient-Reported Outcomes Measurement Information System (PROMIS)	Annually
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Patient-reported outcome	Annually
Outcomes	Patient-reported outcome	Annually
Social support	Patient-reported outcome	Annually
Social relationships	Patient-reported outcome	Annually

## What is the impact of neighborhood and built environment on drug and alcohol trajectories?

**Use Case ID** 1000753

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Reduce Disease Impact

Impact on recovery, relapse, transition from use to addiction—assess across lifespan, starting from preadolescence.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Food security status	Patient-reported outcome	Annually
Neighborhood characteristics	Patient-reported outcome	Annually
Geocode data	Patient-reported outcome	Annually
Environment	Geographic information system (GIS) code	Annually
Housing quality variables	Geographic information system (GIS) code	Annually
Physical activity, self-assessment	Patient-reported outcome	Annually

## What are downstream mental health and behavioral consequences of lifetime exposure to stress?

**Use Case ID** 1000790

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Detect Disease

Stress includes PTSD-qualifying events, life events that don't necessarily rise to the level of PTSD events (e.g., divorce, moving, losing a job), and perception of stress. Timing of stress over the course of childhood and adulthood is important (from history at the time of enrollment and forward), and developmental period in which stress occurred is an important feature.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cortisol levels	Saliva	Monthly
Stress	Patient-reported outcome	Annually
Stress	Smartphone-based ecological momentary assessment	Periodically
Mental health and behavior information	Patient-reported outcome	Baseline and post-treatment
Behavioral characteristics, self-assessment	Patient-reported outcome	Annually
Inflammation biomarkers levels	Blood draw	Baseline
Autonomic nervous system function	Wearable electronics	Continuous monitoring
Sociodemographics	Patient-reported outcome	Baseline

## Are there contextual or other factors that predict PTSD following trauma exposure?

**Use Case ID** 1000895      **Cross-Cutting Theme** Environmental and Other Contextual Effects  
**Most Important**      **Scientific Category** Assess Risk

Potential joint effort with MVP. Criminal justice data needed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Trauma events	Survey	Baseline
Biological Specimens	Blood draw	Per event
Family clinical outcomes	PPI Survey (AOURP)	Baseline
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Environment	Wearable electronics	Monthly
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Behavioral Risk Factor Surveillance System	Baseline

## How does the environment influence substance use and mental health outcomes?

**Use Case ID** 1001079      **Cross-Cutting Theme** Environmental and Other Contextual Effects  
**Scientific Category** Assess Risk

What environments at what developmental time points impact which outcomes?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Adverse life events	Survey	Annually for 10 years
Genomic sequence data	Whole Genome Sequencing (WGS)	Annually
Prenatal exposure assessment results	Placental biopsy	Every 3 months
Residence location	Geographic information system (GIS) code	Periodically
Air quality assessment results		Every 3 months for 1 year
Sleep assessments	Mobile monitor	Daily
Physical activity, self-assessment	Mobile monitor	Daily

## What genetic factors are associated with differences between siblings in susceptibility to addiction?

**Use Case ID** 192284

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Longitudinal study of children to track influences that protect from versus propel young people into substance use and dependence. In particular, why one individual may become addicted after only a few doses, while a sibling does not. Environmental factors would also play a role, but this would look specifically for differences in genetics between two siblings who had different addiction outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Addiction-related information	Survey	Annually
Genomic analyses		

## What genetic factors influence recreational use and abuse of alcohol and other drugs of abuse?

**Use Case ID** 194945

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Use standardized questions to examine both normal use of drugs and natural history of use and abuse (when started, how much, efforts to quit, used despite harmful consequences, etc.). Most health conditions are influenced by drug use, so not collecting this sort of data compromises the entire project. Must distinguish recreational from compulsive use.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Alcohol Use	PPI Survey (AOURP)	Every 2 years
Drug use/abuse, self-assessed	PPI Survey (AOURP)	Every 2 years
Genomic sequence data	Whole Genome Sequencing (WGS)	

## Could the Precision Medicine Initiative reduce social inequality?

**Use Case ID** 195120

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

The proposed study would identify microbial communities and metabolic profiles associated with stigmatized conditions such as idiopathic malodor or mental health. Working with systemic malodor/PATM community provides unprecedented opportunities to explore biomarkers of depression, social stress, diabetes, inflammatory diseases, dental, cardiovascular, and digestive health, exposure to antibiotics, lifestyle and dietary patterns, adverse childhood experiences, and social determinants of health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Microbiome sample	Blood draw	At specified times anchored to the clinical event
Diet, self-assessment	Food diary	
Perceived outcomes - patient	Survey	
Perceived outcomes - surgeon	Survey	
Metabolic risk assessment result	Biochemical assay	

## Do blood biomarkers predict mood transitions for peripartum mood disorder (PPMD)?

**Use Case ID** 195603

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Mood disorder in pregnant and postpartum women is common, often severe, but frequently undiagnosed and untreated, and largely understudied. I propose to augment the All of Us protocol for research into PPMD by adding collection of biospecimens for OMIC measurements at fixed times relative to pregnancy, and also when triggered by alerts of critical clinical mood state shifts as informed by wearable technology or computerized adaptive technology (CAT-MH by Robert Gibbons) self-report monitoring.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Depression diagnosis	Smartphone-based ecological momentary assessment	At specified times anchored to the clinical event
Genomic analyses	Whole Genome Genotyping (WGG)	Baseline
Metabolomic profile	Blood draw	At specified times anchored to the clinical event
Metabolomic profile	Urine collection	
Sociodemographics	Electronic Health Record (EHR)	Baseline

## Do individuals with diagnosed depression have a higher incidence of methylenetetrahydrofolate reductase (MTHFR) mutation?

**Use Case ID** 196287

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Looking at individuals with diagnosed depression (any duration), is there a higher incidence of MTHFR mutations than in the general population? Methods would include offering a genetic test via cheek swab to look for MTHFR mutations. MTHFR mutation has been linked to depression but is not routinely tested for. If a mutation is found, a prescription for L-methyl folate can potentially alleviate depressive symptoms rapidly and may reduce the need for antidepressants.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Depression diagnosis	PPI Survey (AOURP)	Baseline
Genotyping data		Baseline

## Are different depression phenotypes associated with different prognoses after myocardial infarction (MI)?

**Use Case ID** 196487

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Treat & Cure Disease

Are there depression (MDD) phenotypes that have different genomic, biological, and psychological underpinnings, which we should be treating differently? Utilize an acute post-MI sample stratified by non-MDD, prior history of MDD, or new MDD. Then stratify all MDD by treated-success-MDD, treatment-resistant depression, and not treated. Examine mortality and cardiovascular event recurrence among non-MDD and MDD types, and potential epigenetic and biomarker mechanisms of these outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cardiac outcomes	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Depression diagnosis	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Epigenomic/epigenetic markers		
Biologic dysregulation biomarkers levels	Blood draw	At specified times anchored to the clinical event

## What are the common polymorphisms between psychiatric conditions and a predisposition to addiction?

**Use Case ID** 196922

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Screen a mental-health patient population suffering from depression who also exhibit addictive behavior, and test for certain common genotypes implicated in this association. Identify patients with these genotypes, and use caution when prescribing pain medication that can lead to addiction. The expected clinical outcome would be a decrease in incidence in the addiction spectrum.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Genotyping (WGG)	Baseline
Mental health outcomes	Clinical diagnostic test	Continuous monitoring
Recreational drug use	PPI Survey (AOURP)	Continuous monitoring
Recreational drug use	Electronic Health Record (EHR)	

## Is there a genetic basis for anorexia and other eating disorders?

**Use Case ID** 197242

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Eating disorders diagnosis	Electronic Health Record (EHR)	
Eating disorders diagnosis		
Genomic analyses	Blood draw	

## How do genetic variants influence outcomes (phenotypes) of interest to social scientists?

**Use Case ID** 198495

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

We are interested in phenotypes such as subjective well-being, depression, fertility, longevity, religiosity, personality (e.g., neuroticism), and economic preferences (e.g., risk tolerance). To increase sample sizes available for genome-wide studies of these phenotypes, the All of Us campaign should harmonize survey questions with other large genotyped datasets. Details regarding survey questions requested for harmonization are available at [http://ssgac.org/documents/Phenotypes\\_AoU.pdf](http://ssgac.org/documents/Phenotypes_AoU.pdf).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Genotyping (WGG)	
Sociodemographics	PPI Survey (AOURP)	
Mental health and behavior information	PPI Survey (AOURP)	
Behavioral characteristics, self-assessment	Survey	
Psychological measures	Survey	

## What are the phenotypic and genetic factors associated with behavioral addictions?

**Use Case ID** 198511

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Behavioral addictions (e.g., hair pulling, skin picking, gambling, internet addiction, etc.) are common chronic problems involving shared neural mechanisms (e.g., dopamine dysfunction) and repeated urges to engage in harmful acts. To enhance knowledge of underlying mechanisms and inform treatment development, we will identify phenotypic subtypes (i.e., comorbidity, affect, impulsivity, reward, sensory measures) using latent cluster analysis and correlate them with genetic markers of dopamine.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Mental health and behavior information	PPI Survey (AOURP)	Baseline
Behavioral characteristics, self-assessment	Survey	Baseline
Dopaminergic neurotransmitter pathway genes	Whole Genome Sequencing (WGS)	Baseline

## ***Is it possible to develop or optimize a noninvasive biomarker that can be used to measure the experience of stress in children and adults?***

**Use Case ID** 198631

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

The impact of psychosocial stress on child and adult health risk is increasingly appreciated. The measurement of this exposure is currently poor, and All of Us has the opportunity to develop or refine biomarkers that could help push this field of research forward in a valid way for the future. Such biomarkers could be a part of individual studies of stress and disease, and could also be used as a gold standard to develop and validate new and better surveys to measure stress.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Stress	Blood draw	
Stress	Hair and nail clippings collection	
Urinary biome sample	Urine collection	
Sweat sample		
Stress	Survey	

## ***What is the penetrance and prevalence of known neuropsychiatric genomic risk factors in the general population?***

**Use Case ID** 1000708

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Prevalence: How often are those risk factors seen? Penetrance: Of those with risk factors, how many express symptoms? Risk factor: single SNVs, CNVs, and polygenic risk scores. Complements" existing NIMH PGC resource by pulling data from nonascertained population.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Whole genome sequence (WGS) data	Whole Genome Sequencing (WGS)	
Genomic sequence data	Genomic testing	
Clinical outcomes	Electronic Health Record (EHR)	
Family relationships	Survey	
Mental health and behavior information	Electronic Health Record (EHR)	

## What genetic factors impact drug use trajectory?

**Use Case ID** 1000820

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Reduce Disease Impact

With focus on transition from drug use to SUD, SUD to recovery-, relapse.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Drug use/abuse, self-assessed	Electronic Health Record (EHR)	Annually
Drug use/abuse, self-assessed	Patient-reported outcome	Annually
Drug use/abuse, self-assessed	PPI Survey (AOURP)	Baseline
Chemical exposure assessment results	Patient-reported outcome	Baseline
Drug use/abuse, self-assessed	Electronic Health Record (EHR)	Baseline
Death	Death records	Baseline

## What genetic factors impact the alcohol use trajectory?

**Use Case ID** 1000836

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Reduce Disease Impact

With focus on 1) transition from use to disorder; 2) binge use; 3) AUD to recovery; 4) relapse. Must have 42 CFR Part 2 data with EHR.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Annually
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Alcohol Use	Patient-reported outcome	Annually
Family clinical outcomes	Patient-reported outcome	Annually
Pregnancy characteristics	Patient-reported outcome	Annually
Blood sample characteristics	Electronic Health Record (EHR)	Annually
Death	Death records	Annually

## Can we identify genes involved in the predisposition to alcohol and other drug use?

**Use Case ID** 1000845

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Need lifetime assessments of problem drinking and drugs use (not just from current use). Need access to 42 CFR Part 2 data with EHRs. Consider measures: AUDIT, SSAGA, CAGE or MMAST, FTND, CUDIT/SSAGA mini; DUDIT.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Alcohol Use (detailed)	PPI Survey (AOURP)	Baseline
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Survey	Baseline
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Recreational drug use	PPI Survey (AOURP)	Baseline

## What is the natural history of autism and other intellectual disabilities (e.g., fragile X syndrome)?

**Use Case ID** 1000876

**Cross-Cutting Theme** Genomics and Other Omics

**Most Important**

**Scientific Category** Assess Risk

(Related to use case numbers: 000219, 000478, 000588) Two subcohorts: 1. Birth cohorts (moms plus child) 2. Families with affected child (parents/unaffected sibling plus affected sibling). \*Important for how we recruit children into All of Us\*

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Family clinical outcomes	PPI Survey (AOURP)	
Mental health and behavior information	Patient-reported outcome	Baseline
Environment	Blood draw	
Treatment effectiveness	Survey	
Family relationships	Custom sensor/app	Continuous monitoring

## What are the prolonged physical effects of bisexual discrimination?

**Use Case ID** 195721

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

Study biphobia, bi-erasure, and lack of acceptance from the gay and lesbian community. Study how lack of community is detrimental.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Depression diagnosis	PPI Survey (AOURP)	Baseline
Addiction-related information	Survey	Baseline
Mental health outcomes	Survey	Baseline
Clinical outcomes	Survey	Baseline
Family relationships	Survey	Baseline

## What is the impact of time-varying, place-based social determinants of health measures on physical and mental health?

**Use Case ID** 198234

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

To answer important physical and mental health questions, we need to understand the trajectory of the individuals and the trajectories of the places they have lived (residential histories). If exposure equals space  $\times$  time (over the life course), we need data on the timing, sequence, and duration of residence in specific contexts (places). How we define/measure place is important for (retro)prospective work and will enable comparisons between movers and stayers and of the stayers in changing contexts.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Residence location	PPI Survey (AOURP)	Annually
Clinical outcomes	Electronic Health Record (EHR)	
Mental and psychosocial health, self-assessment	Survey	

## How do social disadvantage and chronic stress affect health and well-being in health disparity populations?

**Use Case ID** 198676

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Elucidate Disease Mechanisms

Chronic stress linked to social disadvantage—economic deprivation, exposure to racism and discrimination, etc.—contributes to health disparities. Social stressors vary across the life course, affecting disease risk, progression, and outcomes in disadvantaged groups. All of Us cohort data will shed light on mechanisms by which social disadvantage and chronic stress affect physiology, health behavior, and overall health, aiding the development of effective interventions to reduce health disparities.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Stress	Survey	Include child, teenager, early adult, adult, elderly
Behavioral characteristics, self-assessment	Smartphone-based ecological momentary assessment	Continuous monitoring
Environmental samplings and exposure results	Mobile monitor	Continuous monitoring
Epigenomic/epigenetic markers	Blood draw	Every 3 months
Racism encounters	Survey	

## What is the impact of economic stability on drug use trajectories?

**Use Case ID** 1000824

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Focus: use to addiction, addiction to recovery, relapse.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Drug use/abuse, self-assessed	Patient-reported outcome	Annually
Occupation	Patient-reported outcome	Annually
Food security status	Geospatial tracking	Annually
Housing quality variables	Patient-reported outcome	Annually
Geocode data	Geographic information system (GIS) code	Annually
Health care cost	Patient-reported outcome	Annually

## How does SGM (sexual and gender minority) status (including attraction and behaviors) impact suicidal ideation, planning, and suicide attempts across lifespan?

**Use Case ID** 1000966

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social relationships	Patient-reported outcome	Annually
Mental health and behavior information	Electronic Health Record (EHR)	Annually

## How does SGM (sexual and gender minority) status (including sexual attraction and behavior) impact mood disorders (depression and anxiety) across the lifespan?

**Use Case ID** 1001003

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Family relationships	Patient-reported outcome	Annually
Sex-specific measurements	Patient-reported outcome	Annually
Gender identity	Patient-reported outcome	Annually
Sex at birth	Patient-reported outcome	Annually
Sexual orientation	Patient-reported outcome	Annually

## What is the burden of stigma (racial, gender, sexual, etc.) on mental and physical health across the lifespan?

**Use Case ID** 1001078

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Elucidate Disease Mechanisms

Examine the impact of stigma/bias on mental and physical health, considering racial discrimination, institutional racism, gender bias, sexual orientation, and bias effects. Identify potential moderators, such as racial identity and awareness, gender (dys)identity and sexual orientation, and SES. Identify potential mediators, such as emotions, distress, physiological, (dys)regulation, and brain functioning.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mental health outcomes	Electronic Health Record (EHR)	Annually
Sociodemographics	Patient-reported outcome	Baseline
Gender identity	Patient-reported outcome	Every 5 years
Sexual orientation	Patient-reported outcome	Every 5 years
Self-reported ancestry	Patient-reported outcome	Annually
Discrimination encounters	Patient-reported outcome	Annually
Discrimination encounters	Patient-reported outcome	Every 5 years
Stress	Patient-reported outcome	Annually

## How can you assess mood and behavior in a nonverbal population?

**Use Case ID** 1001125

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

It is important to include the nonverbal autism spectrum disorder community and intellectual dysfunction community. Focus on getting medical records —> difficult population.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sleep quality assessment results	Wearable electronics	Continuous monitoring
Seizure diagnosis	Accelerometer	Continuous monitoring
Prescription medication\treatment	Pharmacy records	Annually
Mood patterns	Caregiver report	Daily
	Caregiver report	Daily
Diet, self-assessment	Caregiver report	Daily
Gastrointestinal health information	Caregiver report	Daily
Incontinence diagnosis	Caregiver report	Daily

## Can we define and validate novel assessment methodologies for mental disorders?

**Use Case ID** 192048

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Assess Risk

Assessment and treatment of mental disorders increasingly focus on neurocircuit-based abnormalities in functional domains such as emotion and cognition. There is a need for computational modeling to define and validate critical dimensions of psychopathology, using optimal behavioral tasks and patient-reported outcomes to develop refined diagnoses and outcome measures. Large samples are required for modeling analyses that converge on valid tasks with appropriate psychometric properties.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Smartphone-based ecological momentary assessment	Continuous monitoring
Passive monitoring behavior	Mobile monitor	Continuous monitoring

## How do psychiatric symptoms vary/cluster biologically within and between people over time?

**Use Case ID** 1001007

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Most Important**

**Scientific Category** Elucidate Disease Mechanisms

Contribute a deeper taxonomy of psychiatric illness. All of Us needed to help identify and validate these variables.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Behavioral characteristics, self-assessment	Patient-reported outcome	Annually
Specified Biomarkers	Magnetic Resonance Imaging (MRI)	Baseline
Sociodemographics	Patient-reported outcome	Baseline
Environment	Patient-reported outcome	Baseline

## **What is the role of communication technologies and social networks in mental and physical health outcomes?**

**Use Case ID** 197245

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Maintain & Preserve Health

Communication technologies allow for a better understanding of social networks, yet they are underutilized in the mental health context. All of Us provides an opportunity to consider how communication technologies can help promote physical and mental health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Technology Use	Survey	
Mental health outcomes	Psychological test	
Social networking use	Survey	

## **Is it possible to develop or optimize a noninvasive, wearable technology to measure the experience of stress in children and adults?**

**Use Case ID** 198629

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

The impact of psychosocial stress on child and adult health risk is increasingly appreciated. The measurement of this exposure is currently poor, and All of Us has the opportunity to develop or refine wearable technologies that could help push this field of research forward in a valid way for the future. Such technology could be a part of individual studies of stress and disease, and could also be used as a gold standard to develop and validate new and better surveys to measure stress.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Stress	Mobile monitor	
Stress	Survey	

## Can passively sensed data help identify psychotic relapse among participants with schizophrenia spectrum disorders?

**Use Case ID** 1000858

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

Combination of smartphone and sensor data.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Accelerometer	Continuous monitoring
Geocode data	Global Positioning System (GPS) monitoring	Continuous monitoring
Social environment	Natural language processing of notes	Continuous monitoring
Relapse/recurrence	Electronic Health Record (EHR)	Baseline
Family clinical outcomes	Interview	Weekly
Sleep assessments	Custom sensor/app	Continuous monitoring

## How does ongoing variation in stress/autonomic markers track mood or other symptom variation?

**Use Case ID** 1001051

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Elucidate Disease Mechanisms

Is it possible to measure autonomic activity continuously? Test how this predicts the time course of mood and mood disorders.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Baseline
Cortisol levels	Custom sensor/app	Continuous monitoring
Sacroiliac fixation diagnosis	Mobile monitor	Periodically
Autonomic nervous system function	Mobile monitor	Continuous monitoring

## ***Among previously opioid-naïve patients, what factors distinguish those who persist in opioid use after surgery from those who do not?***

**Use Case ID** 191971

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

The fundamental question in addiction research is why some people become addicted while others who are exposed to abused substances do not. There is an opportunity to answer this question for opioid addiction and respiratory depression in surgical patients. About 5% to 10% of surgical patients who are pain free and opioid naïve who are given opioids during and after surgery persist in opioid use 12 months after surgery, while in other surgical patients given opioids the use is a few days.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Opioid use, recreational	PPI Survey (AOURP)	Continuously for 1 week duration at 1 month, 6 months, and 1 year
Opioid use, prescribed	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Opioid screen test results	Urine collection	At specified times anchored to the clinical event

## ***Could ultrasounds on pregnant women be the cause of the rise of autism in children over the years?***

**Use Case ID** 194682

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Since ultrasounds came into use in the 1970s, autism has been on the rise. Originally used later in pregnancy and now very early in pregnancy. Before it was the norm, it was shown on a program that a drop of water on an ultrasound paddle would disintegrate immediately, so the concern was WHAT was it doing to the fetus's brain? A study could have a large group of women NOT have ultrasounds during their pregnancy and follow through to see if their children develop autism compared to women who had ultrasounds.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Pregnancy outcomes		
Autism Spectrum Disorders (ASD) diagnosis		
Sonogram		
Family clinical outcomes		

## What risk factors predispose patients treated for pain to misuse or abuse prescription drugs?

**Use Case ID** 194696

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Conduct an RCT to explore genetic and environmental risk factors associated with dose escalation leading to misuse or abuse of prescribed opioids. Use EHR and PDMP data to capture patient demographic, history, and treatment information. Goal is to determine if there are risk factors that predispose pain patients to opioid abuse.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Pain symptom diagnosis	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Depression diagnosis	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Addiction-related information	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Opioid screen test results	Electronic Health Record (EHR)	At specified times anchored to the clinical event

## Is the use of antidepressants/anxiety meds before and during pregnancy associated with increasing rates of autism?

**Use Case ID** 194822

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The potentially large number of pregnant women can be followed for at least 3 years until the children are determined to have or not have any developmental delay/problems or autism. Then the relationships between meds use prior to or during pregnancy can be linked to the outcomes. Alternatively, women with children who have developmental disorders can be surveyed for past use of antidepressant medication before or during pregnancy, and data can be analyzed in a large case-control type design.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Depression diagnosis	Electronic Health Record (EHR)	Baseline
Mental health outcomes	Survey	
Treatment/Therapy		
Autism Spectrum Disorders (ASD) diagnosis		
Pregnancy characteristics		

## Does pregnancy loss lead to an increased risk for anxiety and depression during/after subsequent pregnancies and deliveries?

**Use Case ID** 194854

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Follow women with pregnancy loss and screen for anxiety and depression during and after (each) pregnancy. Have a control group that has not experienced pregnancy loss and screen for anxiety and depression during and after (each) pregnancy. I would use separate instruments to screen for anxiety and depression.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pregnancy outcomes	Survey	
Depression diagnosis	Electronic Health Record (EHR)	
Stress	Survey	
Anxiety self-assessment	PPI Survey (AOURP)	

## How can perceived safety positively impact our lives, and what can we do to increase it?

**Use Case ID** 195663

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

One possible design for examining how perceived safety is associated with different facets of our lives is to include the P-SAFE scale (measuring different facets of safety such as perceived safety, fear of crime, neighborhood walkability) and examine its association/correlation with other measures included in the study (positive/negative life outcome, well-being, and other related measures). This will allow for future studies to build upon this knowledge with meaningful interventions on safety.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Quality of life	Survey	Annually
Physical activity, self-assessment	PPI Survey (AOURP)	Annually
Stress	Survey	Every 3 months
Depression diagnosis	PPI Survey (AOURP)	Every 3 months
Weight	Survey	Annually

## Are threat management resources predictive of long-term resilience, recovery from stressful events, and higher quality of life?

**Use Case ID** 195824

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Measure threat management resources (self-affirmation, optimism, self-compassion, social connections) early in study and then follow up to see how well these resources predict important health outcomes prospectively. Simple prospective design.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Optimism	Survey	Baseline
Self-affirmation tendencies	Survey	Baseline
Self-compassion	Survey	Baseline
Quality of life	Survey	Annually
Outcomes		

## How does having lesions in the frontal lobe of the brain affect the mental health of a multiple sclerosis (MS) patient?

**Use Case ID** 195923

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

MRI studies would be performed with each MS flare and annually. Patients with lesions in their frontal lobe would complete a questionnaire regarding their mental and emotional state. Caregivers would also complete the questionnaire with their observations of the MS patient. We would expect to see mood disorders and/or depression in MS patients who have lesions in their frontal lobe. Data would be collected for 5 years.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Brain magnetic resonance imaging (MRI) images	Electronic Health Record (EHR)	Post-event or at least annually
Frontal lobe lesion measurements	Electronic Health Record (EHR)	Post-event or at least annually
Psychological measures	Survey	
Family relationships	Survey	Weekly

## Could regular screening for up to a year after birth decrease postpartum depression?

**Use Case ID** 195945

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

I would select women who have just given birth or have children ranging from 3 months, 6 months, and 9 months to get a postpartum screening done every 3 months to see if they have any signs of postpartum depression. The outcome is to see what and how the mother is feeling in the different milestones of the child's life as well as their own. What effects does it have on both the mother and the child?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Postpartum Mood Disorders (PPMD) diagnosis		Every 3 months
Quality of life	Survey	Every 3 months for 1 year
Hormone levels (non-steroidal)	Saliva	

## Could requiring use of parental control filters for middle school students with cell phones improve mental health outcomes?

**Use Case ID** 195959

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Expected outcome: Restricting the unfettered access that many adolescents have to social media, pornography, graphic violence, and other adult themes could be expected to result in a decrease in symptoms of depression and/or anxiety. In addition, it would be expected that students with restricted Internet access would get more sleep at night and have improved social skills as a result of increased interaction.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Depression diagnosis	Clinical diagnostic test	At specified times anchored to the clinical event
Behavioral characteristics, self-assessment	Claims data	At specified times anchored to the clinical event
Cell-phone ownership	Survey	At specified times anchored to the clinical event
Sleep parameters	Survey	
Social determinants of health (SDH)	PPI Survey (AOURP)	

## ***Do febrile seizures in childhood represent a risk factor for dementia in later life?***

**Use Case ID** 196357

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Longitudinal study with cases identified in childhood (typically, before 5–6 years of age) with the presence of febrile seizures, followed over time for the diagnosis of dementia (including mild cognitive impairment). Genetic data and viral serologies also should be collected to identify causal/association data. Justification: Febrile seizures occur in 3% to 5% of the U.S. population (i.e., most common type of seizure). Changes in the temporal lobe are seen on MRIs and pathologically.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Febrile seizures diagnosis	Survey	At specified times anchored to the clinical event
Cognitive assessments	Cognitive test	At specified times anchored to the clinical event
Genomic analyses	Blood draw	Baseline
Viral infectious agent	Electronic Health Record (EHR)	At specified times anchored to the clinical event

## ***How can we better understand fatigue, depression, and cognitive dysfunction in Sjögren’s and other autoimmune diseases?***

**Use Case ID** 196485

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Autoimmune diseases, such as Sjögren’s, manifest themselves in a wide variety of ways in patients. However, a common thread in many of these diseases is fatigue, depression, and cognitive dysfunction, or “brain fog.” These physical and mental manifestations can have serious, debilitating consequences for those who suffer from them. A better understanding of the pathways of these manifestations will allow for a more informed approach to care and the ability to better address the symptoms.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis		
Fatigue symptom		
Depression diagnosis		
Cognitive assessments		

## **What is the effect of communication media consumption on health outcomes and behaviors?**

**Use Case ID** 197243

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

All of Us data on physical health, diet, fatigue, and work history will be combined with existing communication technology consumption data such as Pew or American Time Use Survey data, broadband and streaming access data, digital access and penetration data, or newly collected data on media consumption, including frequency and content, to determine the role of communication technology access and consumption on health outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lifestyle, self-assessment	Electronic Health Record (EHR)	Upon enrollment and first obstetrical visit
Media use	Smartphone-based ecological momentary assessment	

## **What mental health symptoms have an impact on end-of-life decision making?**

**Use Case ID** 198131

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

When people near the end of their lives, they face many challenging decisions. Mental health symptoms, such as depression and anxiety, could influence how people make those decisions. Research in this area could investigate how mental health symptoms influence decision making at the end of life and how interventions that address those symptoms might enhance decision making.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mental health and behavior information	PPI Survey (AOURP)	At specified times anchored to the clinical event
Treatment decisions	Survey	At specified times anchored to the clinical event

## What nutritional factors in pregnancy may increase the risk of having a child with autism?

**Use Case ID** 198384

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

I would call for a large study such as Framingham to study generations or look at the WH Study and study the results of these women as they relate to having children with autism. We have to find the cause of this condition. It is affecting too many families.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Diet, self-assessment		
Pregnancy characteristics		
Autism Spectrum Disorders (ASD) diagnosis		

## Can improvement in emotional health by using psychotherapy increase physical health while reducing risk factors of obesity?

**Use Case ID** 198546

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Treat & Cure Disease

Black Therapists Rock engages more than 19,000 psychotherapists who work with vulnerable populations. We have noticed a correlation of improved health outcomes in clients who have utilized Internal Family Systems (IFS), a psychotherapy model that focuses on healing the emotional wounds developed in childhood. We wish to expand upon this data by employing more therapists to use this model while advocating/recruiting participants for the All of Us program.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Depression diagnosis	Clinical diagnostic test	Every 3 months
Mental health and behavior information	Electronic Health Record (EHR)	Baseline
Weight	Electronic Health Record (EHR)	Continuous monitoring
Blood pressure	Physical exam	At specified times anchored to the clinical event
Behavioral characteristics, self-assessment	Survey	

## What psychological factors protect some lonely individuals from adverse health consequences?

**Use Case ID** 198561

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Measure the degree to which individuals who are lonely perceive their loneliness as beneficial—for instance, as an opportunity to develop themselves. Longitudinally, test whether these beliefs about the benefits of loneliness protect individuals from serious health consequences known to result from loneliness, such as increased vascular resistance, increased systolic blood pressure, increased HPA activity, altered immunity, and early mortality.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Loneliness	Survey	Annually
Attitude toward loneliness	Survey	Annually
Blood pressure	Electronic Health Record (EHR)	Annually
Autoimmune biomarkers levels	Blood draw	Annually
Behavioral characteristics, self-assessment	Survey	Annually

## How does marijuana usage impact opioid addiction and use?

**Use Case ID** 198607

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

To determine whether marijuana use influences opioid use, we will study marijuana use in a cohort of opiate users. Aim 1: To determine how marijuana use is associated with changes in opioid use. Aim 2: To determine whether and how marijuana use is associated with changes in HIV risk behavior, overdose, pain, and quality of life. Aim 3: To explore whether marijuana routes of administration are associated with frequency of opioid use among opioid injectors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Recreational drug use	PPI Survey (AOURP)	Every 3 months for 1 year
Opioid use, recreational	PPI Survey (AOURP)	Every 3 months for 1 year
Human Immunodeficiency Virus (HIV) test results	Survey	
Lifestyle, self-assessment	PPI Survey (AOURP)	

## What are the health consequences of long-term opioid use?

**Use Case ID** 198610

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

35 million people worldwide use opioids for medical and recreational use. The U.S. is experiencing an epidemic of drug overdoses. 63,600 people died from drug overdoses in 2016, a majority from opioids. Despite noted acute toxicity, little is known about the long-term health effects of chronic use. Limited existing data suggests possible associations with cancer and other diseases. If opioids do cause chronic disease, then the worldwide impact of opioids is far higher than currently appreciated.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\ treatment	Claims data	Periodic (approximately biweekly)
Drug use/abuse, self-assessed	PPI Survey (AOURP)	Annually
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Death records	Every 3 months
Cancer information	Electronic Health Record (EHR)	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually

## What is the health impact of changing tobacco and marijuana usage patterns in the United States?

**Use Case ID** 198616

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Tobacco products are responsible for more than 480,000 deaths per year in the United States. Nevertheless, tobacco usage patterns in the United States are changing rapidly. These patterns include a rising proportion of low-intensity and nondaily smokers and the emerging popularity of noncigarette tobacco products, including cigars, e-cigarettes, and water pipes. Marijuana is also becoming more popular. The impact of these emerging patterns on health is poorly understood.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Tobacco smoking	PPI Survey (AOURP)	Annually
Nicotine metabolites levels	Urine collection	Annually
Cancer information	Electronic Health Record (EHR)	Annually
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually

## What are the risks and protective factors for alcohol and other drug use disorders, as well as associated health outcomes?

**Use Case ID** 198684

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

More than 1 in 5 Americans meet lifetime criteria for alcohol use disorder, and 1 in 10 Americans meet lifetime criteria for a drug use disorder. Most individuals never seek treatment, and most reduce their alcohol or drug use in the absence of treatment. Research on the biological, psychological, and social risk factors for developing and recovering from alcohol/drug use disorders is critical. Annual assessments of DNAm, substance use, health, and biopsychosocial and environmental factors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Annually
Epigenomic/epigenetic markers	Blood draw	Annually
Opioid screen test results	Blood draw	Annually
Drug/drug metabolites levels	Blood draw	Annually
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Annually

## What is the impact of biological and psychological underpinnings of stress effects on mental health outcomes, including demographic factors?

**Use Case ID** 1000773

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Increasing interest in how stress gets “under the skin” and affects mental health outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Blood draw	Baseline
Specified Biomarkers	Blood draw	Annually
Behavioral characteristics, self-assessment	Patient-reported outcome	Annually
Sociodemographics	Patient-reported outcome	Baseline
Stress	Patient-reported outcome	Daily
Stress	Hair and nail clippings collection	Annually
Specified Biomarkers	Imaging	Annually
Specified Biomarkers	Specimen collection	Annually
Environment	Patient-reported outcome	Annually
Environment	Geospatial tracking	Annually
Behavioral characteristics, self-assessment	Electronic Health Record (EHR)	Annually
Physical activity, self-assessment	Patient-reported outcome	Annually
Physical activity, self-assessment	Electronic Health Record (EHR)	Annually

## What are the protective factors that prevent transition from suicidal ideation to behavior?

**Use Case ID** 1000783

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

How do we predict what is protective against suicidal behavior?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mental health and behavior information	PPI Survey (AOURP)	Baseline
Genomic analyses	Genomic testing	Every 4 years
Medical Information	Electronic Health Record (EHR)	Periodically
Mood patterns	Patient-reported outcome	Periodically
Social relationships	Mobile monitor	Continuous monitoring
Media use	Mobile monitor	Continuous monitoring

## Does impulsivity predict negative health outcomes including substance abuse, obesity, ADHD, criminality, low SES, educational attainment?

**Use Case ID** 1000812

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Personal Characteristics	Survey	Baseline
Behavioral characteristics, self-assessment	Custom sensor/app	Continuous monitoring
Outcomes	Electronic Health Record (EHR)	Annually
Social determinants of health (SDH)	PPI Survey (AOURP)	Annually
Technology Use	Mobile monitor	Baseline
	PPI Survey (AOURP)	Baseline

## What factors promote or protect against the transition from early alcohol/drug exposure to drug/alcohol disorder during adolescence?

**Use Case ID** 1000813      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Elucidate Disease Mechanisms

What factors determine the pathway toward addiction for adolescents?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Exomic Sequencing (WES)	Baseline
Immune biomarkers levels	Blood draw	Annually
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Annually
Metabolomic profile	Blood draw	Annually *GC
Behavioral characteristics, self-assessment	Patient-reported outcome	Continuous monitoring
Specified Biomarkers	Magnetic Resonance Imaging (MRI)	Annually
Neighborhood characteristics	Geospatial tracking	Annually

## What factors support resilience after traumatic events in childhood?

**Use Case ID** 1000830      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Maintain & Preserve Health

Which children exposed to adverse experiences thrive and why?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	Global Positioning System (GPS) monitoring	Continuous monitoring
Genomic analyses	Genomic testing	Baseline
Autonomic nervous system function	Custom sensor/app	Periodically
Food security status	Survey	Every 3 months
Mental health outcomes	Electronic Health Record (EHR)	Every 3 months
Health behavior	Wearable electronics	Periodically

## What factors contribute to successful adaptation to familial caregiving stress?

**Use Case ID** 1000851      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Maintain & Preserve Health

Caregiving across any health condition can create stress for individuals.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Genotyping (WGG)	Baseline
Health care participation	PPI Survey (AOURP)	Annually
Behavioral characteristics, self-assessment	Audio recordings	
Spirituality/Religion	Health mindset scale	Annually
Mental health outcomes	Electronic Health Record (EHR)	
Physical activity, self-assessment	Mobile monitor	
Mental and psychosocial health, self-assessment	Patient-reported outcome	

## Why do some opioid naive surgical patients exposed to opioids after surgery become persistent opioid users, while others do not?

**Use Case ID** 1000867      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Adherence to prescription regimen	Electronic Health Record (EHR)	
Opioid use, prescribed	Patient-reported outcome	
Metabolomic profile	Clinical diagnostic test	Baseline
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Baseline
Side effects of treatment/therapy	Patient-reported outcome	

## Are there premorbid and course biomarkers for serious mental illness?

**Use Case ID** 1000875      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Detect Disease

Could do high-risk screen and/or general population.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Biopsychosocial health	Mobile monitor	Annually
Psychological measures	Survey	Baseline
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Baseline
Environment	Geographic information system (GIS) code	Monthly
Drug use/abuse, self-assessed	PPI Survey (AOURP)	Baseline

## What are the convergent and divergent biological mechanisms between rare and common variant forms of developmental neuropsychiatric disorders?

**Use Case ID** 1000881      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Rare CNVs and structural genomic variants confer high risk for developmental neuropsychiatric disorders. Need a broader understanding at a variety of levels (genomic, environmental, etc.).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Genomic analyses	Whole Genome Sequencing (WGS)	Every 3 years
Behavioral characteristics, self-assessment	Survey	Annually
Brain magnetic resonance imaging (MRI) images	Imaging	Baseline
Environment	Blood draw	Baseline
Pregnancy characteristics	Survey	Baseline
Outcomes	Electronic Health Record (EHR)	Monthly
Health and phenotype data	Survey	Annually

## What are the factors that support healthy outcomes for people using marijuana?

**Use Case ID** 1000890

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

What factors influence and which people benefit from marijuana use?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Periodically
Genomic analyses	Whole Genome Sequencing (WGS)	Annually
Cannabis use (detailed)	Survey	Every 3 months
Behavioral characteristics, self-assessment	Mobile monitor	Every 3 months
Environmental samplings and exposure results	Wearable electronics	Periodically
Healthy behaviors barriers, self-assessment	Survey	Annually

## Can we use genomics to identify modifiable behavioral precursors of psychiatric and substance use disorders (SUDs)?

**Use Case ID** 1000911

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

This could interface with ABCD and other longitudinal childhood studies; would pertain to the future collection of children in All of Us.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Psychological measures	Survey	Annually

## How does mood disorder diagnosis impact behaviors related to HIV/HCV transmission and HIV/HCV status?

**Use Case ID** 1000913

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Immune response—as a measure of mood disorder physiological effects.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Annually
Immune biomarkers levels	Specimen collection	Annually
Human Immunodeficiency Virus (HIV) test results	Electronic Health Record (EHR)	Annually
Hepatitis diagnosis	Electronic Health Record (EHR)	Annually
Drug use/abuse, self-assessed	Patient-reported outcome	Annually
Social relationships	Patient-reported outcome	Annually
Social networking use	Smartphone-based ecological momentary assessment	Annually
Prescription medication\ treatment	Patient-reported outcome	Annually
Access to health care	Geographic information system (GIS) code	

## What are the long-term effects of medications on mental health and SUD?

**Use Case ID** 1000942

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Treat & Cure Disease

All of Us provides breadth and depth of information to get at this question.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Opioid use, prescribed	Prescription drug records	Monthly
Mental health outcomes	Electronic Health Record (EHR)	Annually
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Imaging	Baseline
Adverse life events	Wearable electronics	Annually
Metabolomic profile	Clinical diagnostic test	Baseline
Diet constitution assessment	Dietary assessment tool	Daily
Sleep behavior assessment results	Wearable electronics	Daily

## Can we identify factors involved in the course of alcohol use and problems?

**Use Case ID** 1000948

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Characterizing patterns of use over time will allow us to understand escalation of use and recovery. Can also predict onset of problems using retrospective algorithms.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Alcohol Use (detailed)	Custom sensor/app	Periodically
Accidents/Falls		Periodically
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Periodically
Genomic analyses	Whole Genome Sequencing (WGS)	Annually
Metabolomic profile	Clinical diagnostic test	Annually

## What are the factors that interrupt the development of depression/anxiety conditions after initial symptoms arise?

**Use Case ID** 1000959

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Many people have depressive symptoms or symptoms of anxiety at some point of their life. Only some of these develop mental health and/or substance use conditions. All of Us has the scale to help understand important contributing factors that can tell us why.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Geocode data	Mobile monitor	Continuous monitoring
Social networking use	Social network mining	Continuous monitoring
Mind-body exercise	Activities Completed over Time in 24 Hours (ACT-24)	Daily
Spirituality/Religion	Survey	Annually
Treatment/Therapy (other than Drug use)	Survey	Annually

## How do the symptoms of mood or compulsive disorders relate to brain mechanisms of reward, evaluation, and decision-making?

**Use Case ID** 1000981

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Dysfunction in the brain in terms of reward and decision making. Need to consider collecting online cognitive tasks.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Brain magnetic resonance imaging (MRI) images	Imaging	Baseline
Psychological measures	Survey	Annually
Behavioral characteristics, self-assessment	Cognitive test	Annually
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Cognitive assessments	Mobile monitor	Daily

## What are the factors that predict risk and resilience for anxiety, depression, and loneliness?

**Use Case ID** 1000988

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Loneliness	Health behavior mindset scale	
Anxiety self-assessment	Health behavior mindset scale	
Depression diagnosis	Health behavior mindset scale	
Clinical outcomes	Electronic Health Record (EHR)	
Passive monitoring behavior	Activity monitor	Continuous monitoring
Omics	Genomic testing	

## Can online activity-derived data help to detect psychosis?

**Use Case ID** 1000990      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important**      **Scientific Category** Detect Disease

Can collect overt postings, online traffic, network, search activity, time on websites.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social networking use	Social network mining	Daily
Cell-phone ownership	Mobile monitor	Continuous monitoring
Symptoms	Survey	Every 3 months
Arrest		Annually
Symptoms	Clinical assessment	Every 3 months
Media use	Diary/journal	Periodically

## Are developmental brain and behavioral trajectories that lead to mental illness influenced by in utero exposures?

**Use Case ID** 1001030      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Events during pregnancy (diet, psychosocial, environmental, drug, biological)—how do they affect brain trajectories, and are they natural targets for intervention?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Inflammation biomarkers levels	Blood draw	Monthly
Stress hormones levels	Blood draw	Monthly
Cognitive assessments	Magnetic Resonance Imaging (MRI)	Annually
Cognitive assessments	Ultrasound	Monthly
Psychological measures	Smartphone-based ecological momentary assessment	Annually
Cognitive assessments	Smartphone-based ecological momentary assessment	Annually
Epigenomic/epigenetic markers	Blood draw	Every 6 months
Breast milk sample	Specimen collection	Monthly

## Can measures of fear and stress response indicate who is at a higher risk of developing PTSD?

**Use Case ID** 1001238

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social networking use	Social network mining	Periodically
Fear response assessment results	Virtual reality	Every 3 months
Stress	Smartphone-based ecological momentary assessment	Weekly
Mobile device recordings	Mobile device camera	Weekly
Cortisol levels	Mobile monitor	Continuous monitoring

## Can sensor-generated data be used in predicting initiation, progression, and outcomes in mental health and substance abuse?

**Use Case ID** 1001240

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Other

Micro to macro: individual to community.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autonomic nervous system function	Wearable electronics	
Sleep apnea diagnosis		
Social networking use	Mobile device	
Air quality assessment results		
Light exposure assessment results	Mobile device	

## What factors prevent individuals from seeking specific treatment for alcohol use disorder?

**Use Case ID** 190193

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Alcohol use disorder (AUD) is a common problem with a significant public health impact. Despite available treatments of various types, fewer than 10% of individuals diagnosed with an AUD receive specific treatment for this disease. Identifying the factors that prevent individuals from seeking treatment could better improve access to treatment, thereby eliminating disease burden.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Alcohol Use (detailed)		
Alcoholism diagnoses		
Treatment decisions		

## What treatments are effective in reducing anxiety and increasing stress tolerance in high-functioning children with autism?

**Use Case ID** 194862

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

A cohort study of pre-teens with high functioning autism (formerly Asperger's) would collect data about pharmacological and behavioral therapies tried and obtain dose and duration of treatments. Survey data from parents would measure functioning and stress tolerance at age 10, 13, and 18.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Prescription drug records	At specified times anchored to the clinical event
Behavioral characteristics, self-assessment	Survey	At specified times anchored to the clinical event
Mental health outcomes	Survey	At specified times anchored to the clinical event
Stress	Survey	At specified times anchored to the clinical event

## Does regular exercise help to reduce/eliminate anxiety?

**Use Case ID** 195541

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

Regular exercise prevents and improves health issues ranging from physical, mental, and emotional. I would like to conduct an RCT over the course of a year for both males and females ranging from ages 20–35 to test how regular exercise affects an individual’s level of anxiety. There will be two groups, one that exercises regularly (experimental) while the other does not (control). A questionnaire will occur twice during the program, once at the beginning and then at the end to compare results.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Anxiety self-assessment	PPI Survey (AOURP)	At specified times anchored to the clinical event
Physical activity, self-assessment	Activity monitor	

## Which non-pharmacological interventions work in conjunction and in isolation with/from prescribed medications for mental health?

**Use Case ID** 196486

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Three-year longitudinal study that monitors individuals within specific age cohorts with diagnosed mental health disorders who are managing symptoms with medication and non-pharmacological interventions. Study goals would aim to identify effective and popular non-pharmacological methods that practitioners can prescribe their clients. Methods would include quarterly survey (both online and over the phone) data and diagnostic assessments. Outcomes would define a basis for future research.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Quality of life	Survey	Every 3 months
Stress	Clinical diagnostic test	Every 3 months
Depression diagnosis	Clinical diagnostic test	Every 3 months
Behavioral characteristics, self-assessment	Survey	Every 3 months
Mental health and behavior information	Electronic Health Record (EHR)	Annually

## How can we predict and prevent suicide and suicidal behavior?

**Use Case ID** 196913      **Cross-Cutting Theme** Therapeutic and Preventive Interventions  
**Most Important**      **Scientific Category** Maintain & Preserve Health

Suicide is a leading cause of death, and rates have not decreased in decades. Currently, there are no established risk factors that have demonstrated usefulness in predicting individual risk. The All of Us program is in a position to change this by leveraging the large and varied data that will be collected. Making progress in this area would be a major advance and could have a tremendous impact on the suffering that individuals and families now endure.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mental health and behavior information	Electronic Health Record (EHR)	Annually
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Annually
Death	Death records	

## Are teenagers who were exposed to SSRIs in utero more likely to experience psychiatric illnesses than those who were not exposed?

**Use Case ID** 197316      **Cross-Cutting Theme** Therapeutic and Preventive Interventions  
**Scientific Category** Elucidate Disease Mechanisms

Up to 8% of pregnant women take an antidepressant, but we do not understand the long-term effects on brain development and childhood mental illness. A cohort of young adults (16–21) would be assessed for psychiatric illness, in utero medication exposure would be recorded (with emphasis on antidepressants), and potential confounders such as intellectual/physical disability, adverse childhood experiences, family history, etc. would be recorded. Associations would be tested and future studies designed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mental health outcomes	Psychological test	
Prescription medication\treatment	Prescription drug records	
Pregnancy characteristics	Electronic Health Record (EHR)	

## What are the long-term effects of psychiatric medications on the people who take them?

**Use Case ID** 198390

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

A longitudinal study of people taking psychiatric medications for a period that is longer than what the FDA requires for testing efficacy and safety of psychotropic medications. Most people take medication for more than 6 months—in some cases for rest of their lives. Currently, there is limited information on the effects, efficacy, and side effects of medications like this on the general population, women, people of various ethnic and cultural backgrounds, and people of different ages. This study will help.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Side effects of prescription medication	Prescription drug records	Continuous monitoring
Mental health outcomes	Electronic Health Record (EHR)	Continuous monitoring
Behavioral characteristics, self-assessment	Electronic Health Record (EHR)	Continuous monitoring
Health and phenotype data	Electronic Health Record (EHR)	Continuous monitoring

## What is the impact of physical exercise on the development of postnatal depression?

**Use Case ID** 198753

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

Cohort study will be done by recruiting mothers at their first year after giving birth to their baby. The intervention can be both health center-oriented or home-based physical exercise coaching. Weekly Edinburgh Postnatal Depression Scale will be used to follow up on how their feelings and physical as well as emotional health are being improved. The result can be compared against previously conducted research on mothers or following up mothers in different places.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Continuous monitoring
Fatigue symptom	Survey	Continuous monitoring
Physical activity, self-assessment	PPI Survey (AOURP)	Continuous monitoring
Stress	Physical exam	Continuous monitoring
Depression diagnosis	PPI Survey (AOURP)	Continuous monitoring

## Can signaling pathways be causally related to gut-brain interactions in PTSD?

**Use Case ID** 198842

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

Studies suggest trauma is associated with alterations of the gut microbiota, and dysbiosis early in life could promote the development of PTSD later in life when subjects are re-exposed to traumatic events. This particularly applies to PTSD patients characterized by long-lasting low cortisol levels. This would consider the gut microbiota as a new biological factor mediating vulnerability versus resilience to stress and may suggest new targets in the treatment of PTSD.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Inflammation biomarkers levels	Blood draw	
Microbiome sample	Stool sample	
Stress	Survey	
Cortisol levels	Blood draw	
Post-Intensive Care Syndrome (PICS) diagnosis	Electronic Health Record (EHR)	

## What are the mechanisms that underlie the beneficial effects of exercise on mood, anxiety, and well-being, as well as the variation in response to exercise in terms of these effects in the population?

**Use Case ID** 1000740

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

Existing research indicates that exercise has positive effects on individuals' mental health, including decreased anxiety, and increased well-being and cognitive functioning. However, the mechanisms that underlie these effects are not understood, and individual variations in response to exercise are also poorly understood.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Electronic Health Record (EHR)	Annually
Behavioral characteristics, self-assessment	Patient-reported outcome	Annually
Prescription medication\treatment	Patient-reported outcome	Annually
Whole genome sequence (WGS) data	Genomic testing	Baseline
Mitochondrial sequence	Blood draw	Annually

## What are the genetic, behavioral, psychological, sociocultural, and environmental factors that predict treatment response for mental health and substance use disorders?

**Use Case ID** 1000860

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Need 42 CFR part 2 data with EHRs, individual factors, environmental factors; need scope and scale for big data analytics.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Methylation status	DNA methylation array	Baseline
Risk factors, self-assessment	Wearable electronics	Continuous monitoring
Social environment	Geographic information system (GIS) code	Continuous monitoring
Environmental assessment results	Geographic information system (GIS) code	Monthly
Health and phenotype data	Electronic Health Record (EHR)	Monthly
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Imaging	Ad hoc
Adherence to treatment	Claims data	Annually

## Can a transdermal alcohol measurement device predict morbidity and mortality among alcohol use disorder patients?

**Use Case ID** 1000874

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Measure blood alcohol and send signal to treating clinician and car lock when threshold is exceeded. Device worn continuously by AUD patients. Also sends signal to helper/monitor.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Alcohol Use	Custom sensor/app	Periodically
Accidents/Falls	Interview	Annually
Social support	Survey	Annually
Occupation-related obstacles	Survey	Annually
Treatment effectiveness	Survey	Annually
Clinical outcomes	Survey	Annually

## What are the long-term effects of psychiatric meds and psychological treatments?

**Use Case ID** 1000931

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

Treatment interventions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Genomic testing	Baseline
Prescription medication\treatment	Prescription drug records	Monthly
Biopsychosocial health	Survey	Monthly
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	International Classification of Diseases (ICD) useage data	Monthly

## What are the long-term effects of psychiatric medications and psychological treatments?

**Use Case ID** 1000996

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Long-term data collection at high(ish) frequency.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Metabolomic profile	Clinical diagnostic test	Baseline
Prescription medication\treatment	Patient-reported outcome	Monthly
Prescription medication\treatment	Electronic Health Record (EHR)	Monthly
Biopsychosocial health	Health behavior mindset scale	Monthly
Brain wave activity data	Electronic Health Record (EHR)	Baseline
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Imaging	Baseline

# Musculoskeletal and Dental

**All of Us** | The  
RESEARCH PROGRAM | Precision  
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## Does amoxicillin taken in infancy cause hypermineralization of the adult molars and sometimes incisors?

**Use Case ID** 197529      **Cross-Cutting Theme** Environmental and Other Contextual Effects  
**Scientific Category** Assess Risk

Dentists are seeing a rise in hypermineralization (discoloration and weakening of tooth enamel) in children’s permanent teeth. Some believe this is caused by taking amoxicillin in infancy. Is this the case, and if not, what is causing it?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Burning indoor fuel, chemical exposure assessment results	Dental records	
Prescription medication\ treatment		

## What are the social and environmental stressors that lead to changes in aging, as detected in bone mineral density?

**Use Case ID** 198406      **Cross-Cutting Theme** Environmental and Other Contextual Effects  
**Scientific Category** Assess Risk

Social and environmental factors (e.g., poverty, strain, environmental toxins) may affect the risk of premature aging as measured through bone density, and they may be linked to measures of inflammation. Data are needed on markers of inflammation, stress processes, bone density, subjective and objective environmental data, measures of social support and strain, detailed measures of socioeconomic status, measures of state and local social welfare policies, and exposure to food deserts.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Bone density	Dual-energy X-ray Absorptiometry (DXA)	Every 3 years
C-Reactive Protein (CRP) levels	Blood draw	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Clinical outcomes	Electronic Health Record (EHR)	Annually
Geocode data	Survey	Annually

## What environmental and genetic factors influence the development of osteoarthritis?

**Use Case ID** 198725

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Osteoarthritis (OA) is the most common cause of disability in the United States, and there are no available biomarkers or disease-modifying therapies for OA. Currently, we are unable to identify rapidly progressive OA patients at diagnosis. All of Us offers a unique opportunity to obtain clinical data and biospecimens, along with diet and exercise information, which associate with rapidly progressive OA to help foster development of novel therapies and improved outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Arthritis diagnosis		Annually
C-Reactive Protein (CRP) levels	Blood draw	Every 2 years
Body Mass Index (BMI)	Electronic Health Record (EHR)	Annually
Genomic analyses	Whole Genome Genotyping (WGG)	Baseline
Epigenomic/epigenetic markers	Reaction phenotyping assay	

## How do environmental exposures impact oral health?

**Use Case ID** 198741

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Dental and oral data		
Air quality assessment results		
Environmental samplings and exposure results		
Clinical outcomes		

## What are the benefits of using hypochlorous acid (HOCL) on skin conditions including vulvodynia and yeast infections?

**Use Case ID** 198748

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Treat & Cure Disease

HOCL is currently used in hospitals as a wound care agent. Several promising research studies have been done to suggest this molecule can do more than we currently know. Now that it is readily available, trials on patients with vulvodynia and/or chronic yeast infections could be conducted to confirm its healing properties for these specific conditions. It would be expected that patients would see noticeable symptom relief and reduced severity and occurrence of outbreaks.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Quality of life	Survey	At specified times anchored to the clinical event
Hypochlorous acid (HOCL)		
Vulvodynia diagnosis		
Infection diagnoses		

## What genetic and environmental risk factors contribute to adult dental decay?

**Use Case ID** 1000715

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Primary interest is gene–environment interactions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Omics	Blood draw	Baseline
Environment		Baseline
Fluoride levels		Baseline
Environment	Electronic Health Record (EHR)	Baseline
Location data	Electronic Health Record (EHR)	Baseline
Diet, self-assessment	Diary/journal	Baseline

## ***In what manner and which environmental factors act in concert with genetic factors to impact oral health?***

**Use Case ID** 1001069      **Cross-Cutting Theme** Environmental and Other Contextual Effects  
**Most Important**      **Scientific Category** Assess Risk

Oral health is influenced by numerous factors, including genetics and modifiers of genetic predispositions. By combining genetic, behavioral, and environmental information, it may be possible to answer the question of what genetic functions affecting oral health are impacted by risk-modifying environmental and behavioral factors.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Whole genome sequence (WGS) data	Blood draw	Baseline
Genomic sequence data	Blood draw	Baseline
Methylation status	Blood draw	Baseline
Whole genome sequence (WGS) data	Saliva	Annually
Genomic sequence data	Saliva	Annually
Methylation status	Saliva	Annually
Diet, self-assessment	Food diary	Annually
Diet, self-assessment	PPI Survey (AOURP)	Annually
blank	Geographic information system (GIS) code	Continuous monitoring

## ***What genetic factors are associated with aggressive periodontitis?***

**Use Case ID** 190201      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

Aggressive periodontitis (AgP) is a severe type of periodontal disease (PD) that affects younger patients (<30 years), with the highest prevalence in populations of African descent. Features include bone loss around teeth, familial aggregation, and altered neutrophil function. Unraveling the genetic architecture of AgP may help us understand the molecular mechanisms underlying AgP and chronic PD and could identify youth and young adults at risk for AgP.

<b><i>Datatype</i></b>	<b><i>Method</i></b>	<b><i>Specification</i></b>
Periodontal disease diagnosis	Dental records	Every 2 years
Dental billing procedure codes records	Claims data	Every 2 years
Tooth number	Dental records	Every 2 years
Lifestyle, self-assessment	PPI Survey (AOURP)	Every 2 years
Tobacco smoking	PPI Survey (AOURP)	Every 2 years

## What genes are associated with temporomandibular joint dysfunction (TMD) and its comorbid pain conditions?

**Use Case ID** 191745      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

Temporomandibular joint disorder (TMD) is a group of conditions that cause pain and dysfunction in the jaw joint and muscles that control jaw movement. The 2014 U.S. National Health Interview Survey reported 4.6% of adults reported pain in the face or jaw in the previous 3 months. TMD often overlaps with other pain disorders, including headache, low back pain, and chronic widespread pain. Identification of genes and gene products could allow development of new treatments for chronic pain.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Survey	Annually
Pain symptom diagnosis	Survey	Annually
blank	Survey	Annually

## What genetic factors and environmental factors are associated with dental caries?

**Use Case ID** 191750      **Cross-Cutting Theme** Genomics and Other Omics  
**Scientific Category** Assess Risk

Dental caries (cavities) is a condition that affects 90% of U.S. adults and is more severe in underserved populations. Caries is caused by a complex biofilm, and severity is influenced by dietary intake of sugars. Recent studies have identified caries-susceptibility alleles, some of which may be modified by fluoride use. However, more studies are needed in diverse populations. Understanding genetic factors influencing dental caries may improve caries prevention and treatment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diseased, Missing, Filled Surface Score (DMFS)	Dental records	Every 2 years
Genomic analyses	Survey	Every 2 years
Diet, self-assessment	PPI Survey (AOURP)	Every 2 years
blank	Survey	Every 2 years
blank	Electronic Health Record (EHR)	Every 2 years

## Are dural tears and spinal or cranial cerebrospinal fluid (CSF) leaks symptoms of heritable connective tissue disorders like Ehlers-Danlos syndrome (EDS)?

**Use Case ID** 192319

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

1. Identify patients with cerebrospinal fluid leak. 2. Examine genetic variants and gene expression and epigenetic status of respective genes. 3. Determine if there is a correlation of connective tissue disorder variants (e.g., Ehlers-Danlos syndrome) among CSF leakers.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Cerebrospinal fluid leak diagnosis		
Genomic analyses		
Epigenomic/epigenetic markers		
Ehlers-Danlos Syndrome diagnosis		

## What are the genetic, genomic, and environmental causes of cleft lip and palate?

**Use Case ID** 198352

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Orofacial clefts (OFCs) are the most common birth defects in the head and neck region, affecting one out of every 700 live births worldwide. These defects lead to significant financial, educational, medical, psychological, and cultural problems. All of Us provides an opportunity to investigate the genomes as well as understand the role of environmental factors. It will also help to understand the consequences of metabolic syndrome on craniofacial development leading to clefts.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Environment	Survey	Baseline
Genotyping data	Genomic testing	

## What genetic, general and oral health, and behavioral factors contribute to edentulism?

**Use Case ID** 198491

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Edentulism is the end product of years of poor oral health, with substantial personal, societal, and economic burden. Tracking the multiple factors contributing to this poor oral health outcome will be possible in the All of Us database and could lead to a much more detailed understanding of the genetic and behavioral risk factors involved, including chronic systemic health problems. This, in turn, may point to specific interventions to alleviate this debilitating condition.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Folate levels		
Transfusion outcomes	Dental records	
Health and phenotype data		

## What are the genomics of back pain?

**Use Case ID** 1000828

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Need to subset back pain by symptoms/location and demographics. Include contextual effects.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Accelerometer	Continuous monitoring
Sociodemographics	Patient-reported outcome	Baseline
Neighborhood characteristics	Geospatial tracking	Annually
Back pain diagnosis	Patient-reported outcome	Annually
Genomic analyses	Genomic testing	Annually
Accidents/Falls	Patient-reported outcome	Continuous monitoring
Biopsychosocial health	Patient-Reported Outcomes Measurement Information System (PROMIS)	Baseline

## What genetic and environmental factors contribute to aggressive periodontitis?

**Use Case ID** 1000949

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Focus is on gene and environment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Baseline
Omics	Specimen collection	Baseline
Dental and oral data	Dental/oral examination	Baseline
Medical Information	International Classification of Diseases (ICD) useage data	Baseline
Behavioral characteristics, self-assessment	Survey	Baseline
Health and phenotype data	Survey	Baseline

## Are there genetic factors that influence the risk of MSK deterioration with age or disease?

**Use Case ID** 1001005

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Bone, muscle.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Health and phenotype data	Imaging	Annually
Level of functionality (disability) assessment results	Wearable electronics	Daily
Grip strength	Grip assessment	Annually

## What are the gene and environmental predictors of fracture and osteoporosis risk?

**Use Case ID** 1001017      **Cross-Cutting Theme** Genomics and Other Omics  
**Most Important**      **Scientific Category** Assess Risk

Might be targeted to adults past peak bone mass.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Every 2 years
Physical activity, self-assessment	Wearable electronics	Daily
Genotyping data	Blood draw	Baseline
Prescription medication\ treatment	Electronic Health Record (EHR)	Annually
Health and phenotype data	Imaging	Annually
Nutritional supplement use	Electronic Health Record (EHR)	Every 2 years
Family clinical outcomes	Electronic Health Record (EHR)	Every 2 years
Bone density	Dual-energy X-ray Absorptiometry (DXA)	Annually
Health and phenotype data	X-ray imaging	Annually
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Annually
Cognitive assessments	Mini-Cog test	Annually

## What characteristics influence the biological basis and heterogeneity of dental caries and periodontal disease?

**Use Case ID** 1001098      **Cross-Cutting Theme** Genomics and Other Omics  
**Most Important**      **Scientific Category** Elucidate Disease Mechanisms

Investigate the salivary and biofilm (host and microbiome) factors underlying dental caries and periodontal disease via microbial taxonomy, function, gene expression, proteome, and metabolome analyses to identify biologically informed caries and periodontal disease taxonomies. This is a fundamental step to support precise phenotyping (biologically driven) and necessary for precision medicine.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Whole genome sequence (WGS) data	Blood draw	Baseline
Health and phenotype data	Imaging	Periodically
Health and phenotype data	X-ray imaging	Periodically
Periodontal disease diagnosis	Dental/oral examination	Periodically
Whole genome sequence (WGS) data	Saliva	Baseline
Diet, self-assessment	PPI Survey (AOURP)	Periodically
Tobacco smoking	PPI Survey (AOURP)	Periodically
Whole genome sequence (WGS) data	Oral biofilm sample	Periodically
Metabolomic profile	Oral biofilm sample	Periodically
Whole exomic sequence (WES) data	Oral biofilm sample	Periodically

## What are the gene and environmental interactions that drive primary Sjögren's, compared to systemic lupus, rheumatoid arthritis, and others?

**Use Case ID** 1001138

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Annually
Prescription medication\treatment	Electronic Health Record (EHR)	Annually
Genomic analyses	Genomic testing	Baseline
Autoantibodies levels	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Annually
Symptoms	Connective tissue disease questionnaire	Annually
Tumor characteristics	Electronic Health Record (EHR)	Annually
Environment	Survey	Annually
Environment	Wearable electronics	Annually
Environment		Annually

## Could vitamin D levels be used to prospectively identify patients at risk for bone fracture?

**Use Case ID** 195092

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Regular testing of vitamin D levels for patients over 50. Simple test that could save many from future bone fractures. Determine early if vitamin D supplement is needed while bone strength still has a chance to repair/increase. Learn how to build bone through exercise. Teach balance techniques to prevent falls. Huge health care savings.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Vitamin D levels	Blood draw	Every 3 years

## What are the physical benefits of adaptive fitness on physiological functioning and health outcomes?

**Use Case ID** 196863

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Options for persons with disabilities (who are not athletes) for daily exercise. Link studies of adaptive physical activity and exercise to functional outcomes in physical, emotional, social, community participation, and cognitive domains.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Biodiversity assessment results		
Outcomes		
Cognitive assessments		
Social determinants of health (SDH)		

## What is the impact of the payer on the outcome of patients with leg ulcers (including amputations) and race-related differences?

**Use Case ID** 198485

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Treat & Cure Disease

U.S. Wound Registry data confirm that outcomes for African Americans with lower-extremity wounds are worse than in whites, particularly for DFU outcomes, where amputation rates are higher. USWR data confirm use of advanced therapeutics in wound care is determined by payer. Whether a Medicare beneficiary has a secondary insurance determines if they get a cellular product, and use of all advanced therapeutics has changed with the rise of Medicare advantage plans. We do not know if this has changed outcomes.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Air quality assessment results		
Diabetic Foot Ulcer (DFU) diagnosis	Electronic Health Record (EHR)	
Treatment effectiveness	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Prescription medication\treatment	Prescription drug records	
Sociodemographics	PPI Survey (AOURP)	

## Are there certain factors that contribute to why an inordinate number of black women develop fibroid or dermoid cysts?

**Use Case ID** 198666

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Elucidate Disease Mechanisms

I would assemble a pool of Black females, beginning in their teenage years through their mid-30s or 40s, and track their lifestyle, nutritional habits, sexual activity/contraception, socioeconomic status, and genetics to determine if these variables contribute to Black women’s developing fibroid tumors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Clinical diagnostic test	Continuous monitoring
Sociodemographics		
Genotyping data		
Lifestyle, self-assessment		
Diet, self-assessment		

## Are conventional approaches to dental disease prevention effective in Native American populations?

**Use Case ID** 1000697

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Typical dental disease prevention programs were developed using a generalized approach. However, given the numerous factors that may impact dental health, it is unclear how effective they are among specific populations. Specifically, how effective are conventional approaches to dental disease prevention in Native American populations and, if there is a deviation from the general population, what are the factors that influence the efficacy? This information would be particularly beneficial as it pertains to Native American children.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Dental/oral health information	National Health and Nutrition Examination Survey (NHANES)	Every 2 years
Dental billing procedure codes records	Electronic Health Record (EHR)	During clinic visits
Diseased, Missing, Filled Surface Score (DMFS)	Dental/oral examination	Every 2 years
Omics	Blood draw	Baseline
Microbiome sample		Every 2 years

## Do disease detection rates differ in underserved populations based on social determinants?

**Use Case ID** 1000781

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

To determine whether there are underserved populations by contribution of social determinants to disease detection.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Environmental samplings and exposure results	Environmental Protection Agency (EPA) data	Annually
Environmental samplings and exposure results	Record of residence	Annually
Geocode data	Record of residence	Annually
Dental/oral health information	Survey	Baseline
Health care participation	PPI Survey (AOURP)	Baseline
Health literacy	Interview	Annually
Social support	Interview	Annually
Immigration status	Interview	Annually

## Does multidisciplinary care improve outcomes for children with oral clefts in the U.S. as it has been demonstrated elsewhere?

**Use Case ID** 1000960

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Children affected by oral clefts face a number of medical issues and potential complications beyond those typically addressed by dental and plastic surgeons. Numerous other specialists, such as speech pathologists, are often needed to address these problems. Studies from Europe suggest that multidisciplinary care featuring a team of healthcare providers improves outcomes for children with oral clefts. Is this finding generalizable and applicable in the U.S. population?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Baseline
Treatment/Therapy	Electronic Health Record (EHR)	Continuous monitoring
Speech quality measurements	Mobile monitor	Annually
Sensory assessments	Electronic Health Record (EHR)	Continuous monitoring
Mental and psychosocial health, self-assessment	Survey	Annually
Socioeconomic Status (SES)	Patient-reported outcome	Annually

## Does provision of dental insurance improve dental outcomes related to head and neck cancer after radiation treatment?

**Use Case ID** 1001014

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Dental caries increases dramatically after radiation for head and neck cancers. Patients often lose multiple teeth 2–4 years after therapy. What is oral/systemic impact, and would dental insurance reduce impact/improve QOL?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health insurance status	National Health and Nutrition Examination Survey (NHANES)	Annually for 10 years
Health insurance status	Behavioral Risk Factor Surveillance System	Annually for 10 years
Dental billing procedure codes records	Electronic Health Record (EHR)	Continuous monitoring
Oropharyngeal cancer diagnosis	Electronic Health Record (EHR)	Continuous monitoring
Cancer treatment/therapy	Electronic Health Record (EHR)	Continuous monitoring
Quality of life	Patient-reported outcome	Annually for 10 years
Quality of life	Patient-Reported Outcomes Measurement Information System (PROMIS)	Annually for 10 years
Gastrointestinal health information	Electronic Health Record (EHR)	Continuous monitoring

## Does dental insurance improve health and well-being, including employment status?

**Use Case ID** 1001033

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Primary focus is on patient-reported outcomes, including employment, QOL, self-rated health, tooth numbers/self-reported dental health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health insurance status	PPI Survey (AOURP)	Annually for 10 years
Dental and oral data	Survey	Annually for 10 years
Psychological measures	Survey	Annually for 10 years
Social determinants of health (SDH)	PPI Survey (AOURP)	Annually for 10 years
Treatment data/specifics records	Electronic Health Record (EHR)	Continuous monitoring

## What is the impact of insurance coverage on functional outcomes for PTS with musculoskeletal and dental conditions?

**Use Case ID** 1001112

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

This study will determine the impact of insurance coverage on the outcomes of musculoskeletal and dental disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical Oral Data	Dental records	Annually
Neighborhood characteristics	Medical Expenditure Panel Survey (MEPS)	Annually
Family clinical outcomes	Dental records	Annually
Patient-reported outcomes		Annually
Patient feedback	Patient-Reported Outcomes Measurement Information System (PROMIS)	Baseline and post-treatment

## Can resident tongue bacteria be an indicator for overall health?

**Use Case ID** 195601

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Maintain & Preserve Health

Shape and color of tongue are good indicators of overall health. Besides known tongue diseases, the role of dentures, tobacco use, and illicit drug and opioid abuse will be studied. Functions of resident tongue bacteria in periodontal diseases should be studied. Studies of resident bacteria and other tongue abnormalities are needed relating to overall health. Roles of tongue cancer in head and neck cancer also needs to be studied. Besides western treatments, traditional medicines and practices need to be tried.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Microbiome sample	Saliva	*GC
Oral cancer diagnosis		
Periodontal disease diagnosis		
Clinical outcomes		

## Are there clinically meaningful subgroups of low back pain (LBP) defined by lifestyle, clinical features, and/or genomics?

**Use Case ID** 197769

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Elucidate Disease Mechanisms

LBP is the #1 cause of years lived with disability worldwide (GBD 2016), yet little is known about its underlying mechanisms. In standard clinical care, people with very different presentations of LBP are treated the same. Longitudinal survey items related to LBP and data collection already planned by All of Us (surveys + physical measurements + EHRs + genomics) can be used to identify meaningful LBP subgroups that are connected to outcomes and the treatments most likely to work for specific people.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Back pain diagnosis	Survey	Annually
Genomic analyses	Whole Genome Genotyping (WGG)	Baseline
Pain symptom diagnosis	Survey	Annually
Clinical outcomes	Survey	Annually
Clinical outcomes	Electronic Health Record (EHR)	At specified times anchored to the clinical event

## Can we use an mHealth app to track rheumatoid arthritis (RA) symptoms and conduct pharmacogenetics analyses for biologic drugs?

**Use Case ID** 198703

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

Goals: to determine genetics of response to biologic drugs in RA. Methods: Define RA with EHR algorithm; use the mHealth app to record RA symptoms (RADAI), current/new meds plus adherence. Outcome: daily RA disease activity after drug start. Data: EHR meds, ESR, CRP; PPI confounders, demographics, smoking, exercise. Limitations of prior studies: small samples, no adherence or confounder info, sparse outcome data. Expected outcomes: PGx of drug response in RA, model for PGx in other chronic diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Mobile monitor	Daily
Genotyping data	Blood (EDTA)	
Prescription medication\treatment	Electronic Health Record (EHR)	Every 3 months
Sociodemographics	PPI Survey (AOURP)	
Behavioral characteristics, self-assessment	Survey	

## Can mobile app measurements of physical activity serve as early predictors of musculoskeletal functional decline?

**Use Case ID** 1000703      **Cross-Cutting Theme** Mobile Health  
**Most Important**      **Scientific Category** Assess Risk

Can participants take this information to clinicians to aid early detection and optimized interventions?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, steps/day	Mobile monitor	Daily
Sedentary time	Mobile monitor	Daily
Gait speed	Mobile monitor	Daily
Functional mobility assessment results		Daily
Medical Information	Electronic Health Record (EHR)	Annually
Prescription medication\treatment	Electronic Health Record (EHR)	Annually
Functional mobility assessment results	Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)	Every 6 months
Grip strength	Grip assessment	Every 6 months
Functional mobility assessment results	Jaw movement	Every 6 months
Inflammation disorder diagnosis		Annually
Pain symptom diagnosis	Survey	Annually
Pain Survey Score		Annually
Fatigue symptom	Survey	Annually

## Can sensors enhance medication compliance?

**Use Case ID** 1000855      **Cross-Cutting Theme** Mobile Health  
**Scientific Category** Treat & Cure Disease

Monitor levels of drugs. Electronic reminders to take meds.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Electronic Health Record (EHR)	Every 6 months
Drug/drug metabolites levels	Custom sensor/app	Daily
Electronic reminder use	Mobile monitor	Daily

## Can an intraoral sensing device improve detection, prevention, and management of oral disease?

**Use Case ID** 1000968

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

Can intraoral noninvasive connected sensing devices/sensors aid in the early detection, prevention, and management of oral disease, including dental caries, periodontal disease, and (oral) cancer?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Specified Biomarkers	Custom sensor/app	Continuous monitoring
Sleep pattern	Sleep survey	Baseline
Sleep pattern	Electronic Health Record (EHR)	Baseline
Dental/oral health information	Dental records	Continuous monitoring
Lifestyle, self-assessment	PPI Survey (AOURP)	Continuous monitoring
Dental health behavior assessment results	Survey	Continuous monitoring

## How can wearable technologies improve gait lead to improve PRO of function?

**Use Case ID** 1000998

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Maintain & Preserve Health

How can mobile devices or other wearable sensors be used to improve gait sufficiently to improve function in a patient in a meaningful way?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Body Mass Index (BMI)	Physical exam	Annually
Gait assessment results	Wearable electronics	Continuous monitoring
Level of functionality (disability) assessment results	Patient-Reported Outcomes Measurement Information System (PROMIS)	Daily
Level of functionality (disability) assessment results	3-item Pain intensity, interference with Enjoyment of life, and interference with General activity (PEG) survey	Daily
Level of functionality (disability) assessment results	Brief Pain Inventory (BPI)	Daily
Sociodemographics	PPI Survey (AOURP)	Every 2 years
Physical activity, self-assessment	Wearable electronics	Continuous monitoring

## Can sensors/mobile health apps improve or predict outcomes from joint replacement?

**Use Case ID** 1001058

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Reduce Disease Impact

Sensors to measure gait and activity apps that reinforce physical rehabilitation.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Accelerometer	Continuous monitoring
Pain symptom diagnosis	3-item Pain intensity, interference with Enjoyment of life, and interference with General activity (PEG) survey	Weekly
Joint replacement	Electronic Health Record (EHR)	Per event
Gait assessment results	Wearable electronics	Continuous monitoring

## Among people age 50 or older, what characteristics distinguish those who sustain bone fractures from those who do not?

**Use Case ID** 190202

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

This study will focus on the entire cohort age 50 or older and provide outcomes on bisphosphonate use and movement. The information will help to develop more precise strategies to target individuals who would benefit from bisphosphonates or other interventions for the prevention of bone fractures.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Diet, self-assessment	PPI Survey (AOURP)	Annually
Calcium levels		Every 3 months
Bone fracture diagnosis		
Bisphosphonate levels		

## What is an individual's ideal weight and muscle mass? Can we use this for individual health guidance?

**Use Case ID** 195312

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Critics of the BMI and other current methods note that these methods do not take into account a person's body type, muscle mass, sexual features (breasts), and upper limb length. I would use actual physical measurements of our population as well as surveys for sexual features to determine a realistic model of the individual ideal weight and categories of body types here in the U.S. These models could be advanced with health data to give muscle mass goals that will support a healthy metabolism.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Physical exam	At specified times anchored to the clinical event
Clinical outcomes	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Physical measurements	Physical exam	
Body Mass Index (BMI)	Physical exam	

## What is the effect of post-brushing rinsing behavior on dental caries?

**Use Case ID** 196938

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

The dental status of a group of school children of 9- to 12-year-olds will be recorded at baseline. They will randomly be divided into intervention and control groups. Both groups will be asked to brush their teeth under supervision once a day during school time. In the intervention group, the children will be asked not to rinse their mouth and just spit out, but in the control group, they will rinse their mouth. Differences in the caries levels of the two groups after 6 months will be analyzed and reported.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Dental and oral data	Dental records	
Behavioral characteristics, self-assessment		

## Is gait speed associated with health outcomes in a large, generalizable data set?

**Use Case ID** 197084

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Numerous controlled studies suggest gait speed is a marker of overall physical function and is predictive of a range of adverse events—including death. The All of Us data set provides a unique opportunity to explore relationships between gait speed, lifestyle factors, and health outcomes over time in a diverse, representative group of individuals. Insights gained could allow for more timely intervention by both patients and providers.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Gait assessment results	Physical exam	

## Can a trauma to the tailbone cause vulvodynia, and can it first be started with many yeast infections?

**Use Case ID** 197328

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Are there other women who have had this problem because of the conditions listed above?

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Stress		
Vulvodynia diagnosis		
Infection diagnoses		

## In diffuse idiopathic skeletal hyperostosis (DISH) calcifications, what causes ligaments to ossify, and how can we further expand treatment given that information?

**Use Case ID** 197758

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Findings answers may open doors to relieving the pain and misery of not only this disease but also many other related diseases. Research needs to be done to develop improved treatment options, and perhaps animal models can be used to understand mechanisms and to test new medicines. Outcomes from such research can lead to new therapies and methods to reverse the condition and at least halt the progression of this devastating disease.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Pain symptom diagnosis	Electronic Health Record (EHR)	Baseline
Pain symptom diagnosis	Survey	Weekly
Diet, self-assessment	PPI Survey (AOURP)	

## What alternative methods of measurement for height and weight will be used for those who cannot use standard normative measures?

**Use Case ID** 198166

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

This study will focus on individuals who cannot be measured in a standard way for height and weight. Specification of recumbent and head circumference measurements should be added for young children. The use of alternative systems for children, adolescents, and adults for measurement of height (e.g., ulnar length, arm wingspan, recumbent height) and measurement of weight that incorporates potential assistive devices and/or limb loss are of critical importance for inclusion of these individuals.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Anthropometrics, whole body measurements	Physical exam	Baseline
Height	Physical exam	Baseline
Mechanical assistance		
Mechanical assistance		Baseline
Mechanical assistance		Baseline

## What are the overall effects of sports, which promote physical activity but can also contribute to injuries, in America's health?

**Use Case ID** 198177

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Sports play a unique role as a platform for physical activity but can also increase the risk of injury. All of Us offers an opportunity to identify health benefits and risks of sports by population segment, sport, and level of play. A resulting "sports prescription for health" could be a powerful leap forward in improving health. Methods could include data on sports injuries, wearable technology, validated self-reports, and unique insights from All of Us. ACSM applauds this health innovation.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Health and phenotype data		

## Can relationships between systemic and oral health be identified via a longitudinal analysis?

**Use Case ID** 198492      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Maintain & Preserve Health

Evidence is beginning to accumulate that certain systemic and oral health conditions are related. For example, heart disease and chronic periodontitis are associated, although the reasons for this association remain unclear. The All of Us database, with its longitudinal design and large sample size, would be a powerful resource to discover additional systemic–oral health associations as well as determining causal relationships.

Datatype	Method	Specification
Dental and oral data		
Health and phenotype data		

## Is optimal musculoskeletal health associated with bladder health?

**Use Case ID** 198771      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Elucidate Disease Mechanisms

Musculoskeletal conditions, particularly low back pain, have been shown to be commonly associated with urinary incontinence throughout the female lifespan. We hypothesize that women with more musculoskeletal pain or injury history will have more LUTS. We postulate that both core muscle and pelvic floor muscle dysfunction contribute to this correlation. We propose to study this in a prospective observational study of women in multiple age groups.

Datatype	Method	Specification
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually
Lower Urinary Tract Symptoms (LUTS) record	Survey	
Musculoskeletal assessments	Physical exam	

## How does physical activity prevent joint pain?

**Use Case ID** 1000710      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Maintain & Preserve Health

Use multiple inputs.

Datatype	Method	Specification
Pain symptom diagnosis	Pain survey	Daily
Physical activity, self-assessment	Accelerometer	Continuous monitoring
Body Mass Index (BMI)	Physical exam	Annually
Self-reported ancestry	Patient-reported outcome	Baseline
Personal Characteristics	Survey	Baseline

## What are the risk factors for falls?

**Use Case ID** 1000720

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Might stratify analysis by age.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Annually
Medical Information	Electronic Health Record (EHR)	Annually
Prescription medication\treatment	Electronic Health Record (EHR)	Annually
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Fall Events	Accelerometer	Continuous monitoring
Sociodemographics	PPI Survey (AOURP)	Baseline
Vision assessment results	Physical exam	Annually
Physical activity, self-assessment	Activity monitor	Continuous monitoring
Geocode data	Record of residence	Annually

## What are the physical and environmental determinants of bone health?

**Use Case ID** 1000761

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Genes by environment. Open space access, gym access. Impact of wearing a Fitbit.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Body Mass Index (BMI)	Physical exam	Annually
Sociodemographics	Patient-reported outcome	Baseline
Physical activity, self-assessment	Accelerometer	Continuous monitoring
Bisphenol A (BPA) levels	Geospatial tracking	Continuous monitoring
Chemical exposure assessment results	Geospatial tracking	Continuous monitoring
Environmental assessment results	Geospatial tracking	Continuous monitoring
Location data	Geospatial tracking	Continuous monitoring
Architectural characteristics	Geospatial tracking	Continuous monitoring
Bone health assessment results	Dual-energy X-ray Absorptiometry (DXA)	Annually
Bone health assessment results	Custom sensor/app	Annually
Bone fracture diagnosis	Electronic Health Record (EHR)	Annually
Mental health and behavior information	Cognitive test	Annually
Whole genome sequence (WGS) data	Whole Genome Sequencing (WGS)	Baseline

## What factors prevent the trajectory of chronic musculoskeletal pain/conditions?

**Use Case ID** 1000780 **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important** **Scientific Category** Maintain & Preserve Health

A longitudinal study that examines risk factors for the trajectory of chronic musculoskeletal pain/conditions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Accelerometer	Continuous monitoring
Environmental samplings and exposure results	Mobile monitor	Continuous monitoring
Pain Survey Score	Patient-reported outcome	Daily
Pain Survey Score	Electronic monitoring/recording	Daily
Biopsychosocial health	Brief Symptom Inventory 18 (BSI 18)	Every 3 months
Air quality assessment results		Continuous monitoring
Allergens assessment results	Mobile monitor	Continuous monitoring
Chemical exposure assessment results	Mobile monitor	Continuous monitoring
Location data	Mobile monitor	Continuous monitoring
Pesticides exposure assessment results	Mobile monitor	Continuous monitoring
Sleep assessments	Patient-reported outcome	Continuous monitoring
Omics	Blood draw	Every 2-3 years
Biopsychosocial health	Stress survey	Every 3 months
Biopsychosocial health	Epworth Sleepiness Scale (ESS)	Every 3 months

## Which oral microbiome factors predispose (or protect) dental caries?

**Use Case ID** 1000939 **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Oral microbiome sample	Saliva	Annually
Diseased, Missing, Filled Surface Score (DMFS)	Dental records	Ad hoc
Orofacial pain diagnosis	Survey	Annually
Antibiotic use	Electronic Health Record (EHR)	Annually

## Do measurements of accelerated aging serve as surrogates of early mortality in underrepresented populations?

**Use Case ID** 1000951

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Can lifestyle changes slow biologic aging? Include accelerated muscle loss, joint pain, frailty, slowed walk, earlier osteoporosis, etc. Substudy (AI, HIS, AA, and age/gender/match EA).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Annually
Telomere length	Cell-free DNA sequencing	Baseline
Gait speed	Wearable electronics	Annually
Death	Death records	Annually
Death	PPI Survey (AOURP)	Annually
Death	Death records	Annually
Death	Survey	Annually

## Can sensors prevent anterior cruciate ligament (ACL) injuries?

**Use Case ID** 1000982

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Can sensors that detect landing reduce ACL injuries? Would require the development of app that reinforces good lower extremity alignment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Body Mass Index (BMI)	Physical exam	Annually
Sensor data	Wearable electronics	Continuous monitoring
Sociodemographics	Patient-reported outcome	Baseline
Anterior Cruciate Ligament (ACL) assessment results	Electronic Health Record (EHR)	During clinic visits
Anterior Cruciate Ligament (ACL) assessment results	Patient-reported outcome	During clinic visits
Physical activity, self-assessment	Patient-reported outcome	Annually

## What genetic factors modify the risk for dental caries?

**Use Case ID** 1001022

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Dental caries are thought to be influenced by multiple genetic and environmental risk factors. Through examination of personal and familial dental histories in combination with genetic analysis, it may be possible to identify the genetic risk factors that lead to the development and progression of dental caries in children and adults, which may be used to assess individual susceptibility and identify beneficial genetic risk modifiers.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Family clinical outcomes	PPI Survey (AOURP)	Annually
Whole genome sequence (WGS) data	Whole Genome Sequencing (WGS)	Baseline
Genomic analyses	Saliva	Baseline
Clinical Oral Data	Dental/oral examination	Annually
Dental outcomes	Dental records	Annually
Personal Characteristics	Electronic Health Record (EHR)	Baseline

## How can self-report of diet lead to weight loss to reduce arthritis?

**Use Case ID** 1001043

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

How diet influences microbiomes and metabolism and psychosocial.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Accelerometer	Continuous monitoring
Sociodemographics	Patient-reported outcome	Baseline
Diet, self-assessment	Patient-reported outcome	Daily
Body Mass Index (BMI)	Physical exam	Monthly
Joint pain diagnosis	Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)	Daily
Joint pain diagnosis	3-item Pain intensity, interference with Enjoyment of life, and interference with General activity (PEG) survey	Daily
Joint pain diagnosis	Patient-Reported Outcomes Measurement Information System (PROMIS)	Daily
Microbiome sample	Stool sample	Monthly
Microbiome sample	Saliva	Monthly
Mental health and behavior information	Patient-Reported Outcomes Measurement Information System (PROMIS)	Monthly
Metabolomic profile	Blood draw	Annually

\*GC

## What risk factors that influence the onset and trajectory of TMJ?

**Use Case ID** 1001065

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Risk factors including history of bruxism, dentition, and malocclusive conditions, injury.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pain symptom diagnosis	Pain intensity, interference with enjoyment of life, and interference with general activity (PEG) survey tool	Monthly
Biopsychosocial health	Brief Symptom Inventory 18 (BSI 18)	Monthly
Environment	Diary/journal	Monthly
Genomic analyses	Blood draw	Annually
Temporomandibular Disorders (TMD) diagnosis	Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) assessment	Annually

## What are the genetic and environmental determinants of carpal tunnel syndrome?

**Use Case ID** 1001070

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

What are the demographic risks?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Blood draw	Baseline
Health issues, occupational	Survey	Annually
Carpal tunnel syndrome diagnosis	Electronic Health Record (EHR)	Per event
Environmental assessment results	Geographic information system (GIS) code	Annually
Sociodemographics	PPI Survey (AOURP)	Every 2 years

## Are there connections between oral health and systemic disease, and can saliva be used to monitor both?

**Use Case ID** 1001073 **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Whole genome sequence (WGS) data	Blood draw	Baseline
Health and phenotype data	Electronic Health Record (EHR)	Continuous monitoring
Dental/oral health information	Electronic Health Record (EHR)	Continuous monitoring
Health and phenotype data	Patient-reported outcome	Continuous monitoring
Dental/oral health information	Patient-reported outcome	Continuous monitoring
Whole genome sequence (WGS) data	Saliva	Annually
Genomic analyses	RNA sequencing	Annually
Oral microbiome sample	Saliva	Annually
Sociodemographics	PPI Survey (AOURP)	Baseline and at event
Sociodemographics	Geographic information system (GIS) code	Baseline and at event
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually

## What are the causes and health consequences of decreased saliva flow?

**Use Case ID** 1001077 **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Decreased saliva flow can be a cause and consequence of many diseases. It also impacts quality of life.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Tooth number	Patient-reported outcome	Baseline
Mental and psychosocial health, self-assessment	Patient-reported outcome	Baseline
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Baseline
Whole genome sequence (WGS) data	Whole Genome Sequencing (WGS)	Baseline

## What factors drive the transition from acute to chronic pain?

**Use Case ID** 1001082 **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important** **Scientific Category** Assess Risk

E.g., genetics, environment, lifestyle choices, acute medical care, and non-adherence to clinical guidelines. Return of guidelines to acute pain patients to help them proactively manage their condition.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Blood draw	Baseline
Pain Survey Score		Continuous monitoring
Fatigue symptom	Survey	Continuous monitoring
Occupation	PPI Survey (AOURP)	Continuous monitoring
Pain Survey Score		Continuous monitoring
Prescription medication\ treatment	Survey	Continuous monitoring
Sociodemographics	Electronic Health Record (EHR)	Monthly
Health and phenotype data	Imaging	Monthly
Medical Information	Electronic Health Record (EHR)	Monthly
Level of functionality (disability) assessment results	Mobile monitor	Every 6 months
Geocode data	Survey	Baseline
Biopsychosocial health	Survey	Baseline
Biopsychosocial health	Brief Symptom Inventory 18 (BSI 18)	Baseline

## What are the long-term impacts of musculoskeletal birth defects from birth to adult, including prenatal/pregnancy outcomes?

**Use Case ID** 1001093 **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Most Important** **Scientific Category** Reduce Disease Impact

This study will determine the impact of congenital musculoskeletal birth defects on life quality. Genomic data and longitudinal follow-up will lead to a rich dataset.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Whole genome sequence (WGS) data	Blood draw	Baseline
Mental and psychosocial health, self-assessment	Survey	Annually
Quality of life	Survey	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Dental outcomes	Dental records	Annually
Family clinical outcomes	Dental records	Annually

## What genetic, environment, and lifestyle choices coalesce to drive autoimmune rheumatic disease development?

**Use Case ID** 1001096      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Most Important**      **Scientific Category** Assess Risk

Sub-study of women between 15 and 50? Return auto-antibody data to women, especially of childbearing age, to discuss with clinician.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environment	Survey	Annually
Family clinical outcomes	PPI Survey (AOURP)	Baseline
Genomic analyses	Genomic testing	Baseline
Environment	Geographic information system (GIS) code	Annually
Occupational environment assessment results	PPI Survey (AOURP)	Annually
Light exposure assessment results	Survey	Annually
Lifestyle, self-assessment	Custom sensor/app	Ad hoc
Medical Information	Clinical assessment	Ad hoc
Health and phenotype data	Imaging	Ad hoc
Family clinical outcomes	PPI Survey (AOURP)	Baseline and at 5 years
Sociodemographics	PPI Survey (AOURP)	Baseline and at 5 years
Autoantibodies levels	Clinical diagnostic test	Annually in high-risk individuals
Connective tissue disorder diagnoses	Survey	Annually in high-risk individuals

## What are the genetic/genomic and environmental risks of cleft lip and cleft palate?

**Use Case ID** 1001113      **Cross-Cutting Theme** Risk Factors, Prevention, and Wellness  
**Scientific Category** Assess Risk

Determine main effects and interactions effects of risk factors (genetics and environmental) leading to cleft lip and palate, as well as characterizing comorbidities.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Whole genome sequence (WGS) data	Blood draw	Baseline
Sociodemographics	Electronic Health Record (EHR)	Baseline
Diet, self-assessment	PPI Survey (AOURP)	Baseline
Lifestyle, self-assessment	PPI Survey (AOURP)	Baseline
Location data	Geographic information system (GIS) code	Baseline
Prenatal exposure assessment results	Survey	Baseline

## What are the risk factors for experiencing acute and/or chronic intraoral pain?

**Use Case ID** 1001114

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The perception and persistence of pain is unique to each individual and can be modified by a myriad of factors. Examination of self-reported and indirect pain measures in conjunction with environmental and physiologic factors may help identify risk factors for acute and/or chronic intraoral pain.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pain symptom diagnosis	Pain manikin	Baseline and at event
Pain Survey Score	Pain intensity, interference with enjoyment of life, and interference with general activity (PEG) survey tool	Baseline and at event
Pain Survey Score		Baseline and at event
Pain symptom diagnosis	Survey	Baseline and at event
Biopsychosocial health	Electronic Health Record (EHR)	Annually
Environmental samplings and exposure results	Dental/oral examination	Every 3 months
Environmental samplings and exposure results	Psychological test	Every 3 months
Environmental samplings and exposure results	Geographic information system (GIS) code	Every 3 months
Sleep assessments	Actigraphy	Every 3 months
Sleep assessments	Survey	Every 3 months
Fatigue symptom	Actigraphy	Every 3 months
Omics	Blood draw	Annually *GC

## Does auto-antibody positivity identify individuals at increased risk of a diverse array of health conditions, such as poor pregnancy outcomes, cardiovascular disease, thrombosis, and autoimmune disease?

**Use Case ID** 1001131

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Auto-antibodies (anti-CCP, anti-cardiolipins, anti-TPO), genetics of auto-antibody production and disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Genomic testing	Baseline
Autoantibodies levels	Blood draw	Every 2 years
Autoantibodies levels	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Every 2 years
Medical Information	Electronic Health Record (EHR)	Annually
Autoantibodies levels	Electronic Health Record (EHR)	Annually
C-Reactive Protein (CRP) levels	Blood draw	Annually
C-Reactive Protein (CRP) levels	Electronic Health Record (EHR)	Annually

## What are the effects on frequency and progression of dental caries in teeth adjacent to a fixed prosthesis?

**Use Case ID** 196937

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Dental and oral data	Dental records	

## What is the prevalence of Ehlers-Danlos syndrome in chronic pain patients?

**Use Case ID** 198462

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

Conduct the Brighton and Brighton screening tests on all pain patients to screen for Ehlers-Danlos. This is especially relevant for fibromyalgia and idiopathic joint pain groups who have not had a diagnosis yet. Goals would be to recognize that this is not a rare disease and hopefully start screening children to prevent long-term chronic pain and get answers to patients who have historically been neglected by physicians who don't believe there is a real physiological problem.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Ehlers-Danlos Syndrome diagnosis	Physical exam	Baseline
Pain symptom diagnosis	Physical exam	Baseline
Family relationships	Survey	Baseline
Clinical outcomes	Survey	Baseline

## Could a pre-operative bilateral sacroiliac joint (SIJ) injection for lumbar fusion candidates be a diagnostic tool to identify sacroiliac joint pain patients?

**Use Case ID** 198490

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Sacroiliac joint (SIJ) pain, an elusive generator of lower back pain (LBP), affects 10%–30% of lumbar patients with nonradicular pain. However, there is no diagnostic indicator that can be used as a reliable tool to screen SIJ pain. This prospective study uses a preoperative bilateral injection, targeting a goal to develop a diagnostic tool to screen the incidence of SIJ problems. Expected outcome(s) is this procedure will provide the necessary SIJ pain information to optimize surgical plans.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pain symptom diagnosis	Survey	Post-event
Perceived outcomes - patient	Diary/journal	Continuously for 1 day
Sacroiliac Joint (SIJ) pain diagnosis		

## How does global posture change as the population ages?

**Use Case ID** 198525

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

The development of an open access database of full-body images and global spine parameters will provide spine surgeons with normative data that can be used to guide clinical decision making and surgical planning. Furthermore, the database can be used by researchers to obtain control measurements for comparison in studies of various spine and potentially non-spine pathologies. Use survey questionnaires and EOS x-ray imaging.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Spino-pelvic parameters	X-ray imaging	Baseline
Back pain diagnosis	Survey	Baseline
Level of functionality (disability) assessment results		Baseline
Health and phenotype data	Survey	Baseline
Sociodemographics	PPI Survey (AOURP)	Baseline

## Does underreporting of myelopathic incidence in the general population result in misdiagnosis and insufficient myelopathy treatment?

**Use Case ID** 198539

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

The best cervical myelopathy outcomes rely on early recognition and treatment. Using questionnaires about past history, family history, and trauma history could better elucidate myelopathy and causes of cervical myelopathy. Use of Hoffman's testing in conjunction with imaging (MRI) can help determine incidences for sub-clinical myelopathy in the general population and the need for earlier intervention, clarify diagnosis, and develop better treatment plans.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Survey	At specified times anchored to the clinical event
Self-reported ancestry	PPI Survey (AOURP)	At specified times anchored to the clinical event
Quality of life	Survey	At specified times anchored to the clinical event
Cervical myelopathy diagnosis	Magnetic Resonance Imaging (MRI)	At specified times anchored to the clinical event
Cervical myelopathy diagnosis	Hoffman cervical test	At specified times anchored to the clinical event

## ***Is kyphoplasty for the first fracture an alternative to following a preventative plan in high-risk postmenopausal osteoporosis patients?***

**Use Case ID** 198605

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Postmenopausal osteoporosis (PMO) from dropping estrogen leads to bone loss. High-risk PMO women begin high-cost medical prevention plans 14 years before statistical fractures. However, due to demanding responsibility, 50% of patients abandoned preventative therapy by 7 years. We propose an option not to have preventative therapy and treat first fracture by minimally invasive kyphoplasty. The procedure would inject 2-4 cc of cement into risked vertebrae, and cost differences would be analyzed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Treatment/Therapy (other than Drug use)		
Magnetic resonance imaging (MRI) images	Magnetic Resonance Imaging (MRI)	
Outcomes		

## ***Does sacroiliac fixation in multilevel spinal fusion surgery increase the incidence of postoperative sacroiliac joint pain?***

**Use Case ID** 198615

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

Sacroiliac fixation for long construct adult scoliosis decreases instrumentation failure, reduces sacral stress fractures, and improves fusion rates. However, there is a potential increase of postoperative sacroiliac joint (SIJ) complications leading to continued vague pain with patients. This is a prospective study to track patients with multilevel fusions (T10-pelvis) and sacroiliac fixation long term. We will evaluate the incidence of postoperative SIJ complications of this cohort.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pain symptom diagnosis	Oswestry Disability Index (ODI)	Periodically
Sacroiliac Joint (SIJ) degeneration diagnosis	X-ray imaging	
Sacroiliac Joint (SIJ) pain diagnosis		
Sacroiliac fixation diagnosis		

## What are the effects of oral health and use of dental preventive services and treatments on overall well-being and underlying mechanisms?

**Use Case ID** 198674

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Dental and oral data		
Health and phenotype data		
Quality of life		

## How could sensors for posture improve chronic back pain?

**Use Case ID** 1000798

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Need sensors and app to detect poor posture and provide feedback to participants.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	Patient-reported outcome	Baseline
	Mobile monitor	Continuous monitoring
Back pain diagnosis		Monthly
Functional mobility assessment results	Patient-Reported Outcomes Measurement Information System (PROMIS)	Monthly

## What factors lead to the reduction of back pain?

**Use Case ID** 1000835      **Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Most Important**      **Scientific Category** Reduce Disease Impact

What risk factors predict treatment responses to conservative (noninvasive) treatments (including exercise) for back pain?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	Patient-reported outcome	Baseline
Physical measurements	Electronic Health Record (EHR)	During clinic visits
Pain symptom diagnosis		Daily
Pain symptom diagnosis	3-item Pain intensity, interference with Enjoyment of life, and interference with General activity (PEG) survey	Daily
Pain symptom diagnosis	Gracely Pain Intensity Scale	Daily
Biopsychosocial health	Patient-Reported Outcomes Measurement Information System (PROMIS)	Weekly
Treatment decisions	Electronic Health Record (EHR)	During clinic visits
Physical activity, self-assessment	Patient-reported outcome	During clinic visits
Physical activity, self-assessment	Electronic Health Record (EHR)	During clinic visits
Prescription medication\treatment	Electronic Health Record (EHR)	During clinic visits
Prescription medication\treatment	Patient-reported outcome	During clinic visits
Allergens assessment results	Patient-reported outcome	Weekly
Chemical exposure assessment results	Patient-reported outcome	Weekly
Adverse life events	Patient-reported outcome	Weekly
Biopsychosocial health	Activity monitor	Weekly
Biopsychosocial health	Survey	Weekly

## Does supplement use present in individuals who have musculoskeletal pain? If so, which?

**Use Case ID** 1000864

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Nutritional supplement use	Electronic Health Record (EHR)	Annually
Pain symptom diagnosis	Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)	Annually or during clinical visits
Pain symptom diagnosis	Visual Analogue Scale (VAS)	Annually or during clinical visits
Depression diagnosis	Beck Depression Inventory	Annually
Fatigue symptom	Fatigue survey	Annually
Sociodemographics	PPI Survey (AOURP)	Baseline
Physical activity, steps/day	Mobile monitor	Ad hoc
Gait speed	Mobile monitor	Ad hoc
Sedentary time	Mobile monitor	Ad hoc

## Do impaired sleep profiles contribute to poor treatment responses?

**Use Case ID** 1000887

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Poor treatment response may have a surrogate of medication change for a given condition (e.g., rheumatoid arthritis, OA, osteoporosis, etc.)

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Electronic Health Record (EHR)	Annually
Sleep parameters	Mobile monitor	Daily
Prescription medication\treatment	Electronic Health Record (EHR)	Quarterly or Annually
	Electronic Health Record (EHR)	Quarterly or Annually
Medical Information	Electronic Health Record (EHR)	Quarterly or Annually
Patient-reported outcomes		Ad hoc
Gait speed	Wearable electronics	Ad hoc
Physical activity, steps/day	Wearable electronics	Ad hoc

## What is the optimal frequency, intensity, and type of physical activity in order to ameliorate joint and muscle dysfunction?

**Use Case ID** 1000993

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

Dosing includes frequency, intensity, and type.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Wearable electronics	Daily
Physical activity, type	PPI Survey (AOURP)	Every 6 months
Physical activity, self-assessment	PPI Survey (AOURP)	Every 6 months
Functional mobility assessment results	Survey	Every 6 months
Physical measurements	Physical exam	Every 6 months
Physical Therapy (PT) use	Electronic Health Record (EHR)	Annually

## Do current treatments of musculoskeletal and oral diseases increase quality of life?

**Use Case ID** 1001094

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Determine whether or not patients feel better after treatment. Are we doing good things?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health and phenotype data	Electronic Health Record (EHR)	Annually
Dental and oral data	Electronic Health Record (EHR)	Annually
Quality of life	Survey	Annually

# Sensory Pain and Neurologic

**All of Us** | The  
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## Conduct research to determine if frontal lobe injury affects future mental health and/or increases the occurrence of autism.

**Use Case ID** 194656

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Frontal lobe injury diagnosis	Clinical diagnostic test	Include child, teenager, early adult, adult, elderly
Mental health outcomes	Clinical diagnostic test	Include child, teenager, early adult, adult, elderly
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Include child, teenager, early adult, adult, elderly
Behavioral characteristics, self-assessment	Survey	Every 3 months
Autism Spectrum Disorders (ASD) diagnosis	Electronic Health Record (EHR)	Include child, teenager, early adult, adult, elderly

## What are the genetic and environmental risk factors that contribute to the broader autism phenotype in adolescents and adults?

**Use Case ID** 194674

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

To study genotype–phenotype correlations, utilize measures targeting the Broader Autism Phenotype: social and communication scales (SRS), Connors Rating Scale for ADHD, ratings of depressive symptoms (PHQ-9), anxiety disorders, and adverse childhood experiences (ACEs) and traumatic life events. Children transitioning to adulthood during the study will have repeat assessment of function and mental health status at a later age to help determine the outcome of the transition.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Developmental milestones (self-reported)	Milestone Tracker mobile app	Every 2 years
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Autism Spectrum Disorders (ASD) diagnosis	Electronic Health Record (EHR)	Every 2 years
Environmental samplings and exposure results	PPI Survey (AOURP)	Every 2 years
Androgens levels		Every 2 years

## Does calcium propionate, a common preservative in tortillas and breads, cause headaches? Is it neurotoxic?

**Use Case ID** 194795

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Calcium propionate levels		
Diet, self-assessment		

## Is there an association between chemical exposures and neurological disease?

**Use Case ID** 194950

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Epidemiological studies and anecdotal reports suggest an association between certain neurological diseases (e.g., Parkinson's, Alzheimer's, ALS, various neurodevelopmental disorders) and chemical exposures (pesticides, metals, endocrine disruptors) via residential, occupational, and other activities. The study, using genetic information captured, could also possibly shed light on gene-environment interactions as well.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	PPI Survey (AOURP)	
Clinical outcomes	Survey	
Pesticides exposure assessment results	Survey	
Neurological disease information	Electronic Health Record (EHR)	

## What is the role of environmental and dietary factors in the incidence of chronic pain?

**Use Case ID** 195125

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Investigate the correlation between the incidence of reported pain and various social and biological characteristics. Investigate the correlation between the incidence of reported pain and dietary factors including foods and food additives such as dyes, preservatives, and other additives. Investigate the correlation between the incidence of reported pain and environmental exposures including pollution, pesticides, and the cyanide-based additives in road salt.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Environmental samplings and exposure results	PPI Survey (AOURP)	Daily
Diet, self-assessment	Food diary	Daily
Air quality assessment results		At specified times anchored to the clinical event
Pain symptom diagnosis	Smartphone-based ecological momentary assessment	Daily

## What exacerbates and causes circadian rhythm disorders (CRDs)?

**Use Case ID** 195571

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

People with CRDs are told, “Try harder to sleep/wake when society does.” But CRD people are held hostage by body clocks that defy control. CRDs derail education, employment, relationships, parenting, life. All of Us is about inclusivity and less-common conditions. What causes CRDs? Genetic mutations, light over/undersensitivity, faulty eye ipRGCs, impaired melatonin production/metabolism, faulty homeostatic sleep drive, environmental toxins, gut microbiota, etc.? Answers mean effective treatment, restored life.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sleep parameters	Survey	
Sleep quality assessment results	Survey	
Genomic analyses	Blood draw	
Lifestyle, self-assessment	PPI Survey (AOURP)	
Circadian Rhythm Disorders (CRD)	Electronic Health Record (EHR)	

## What is the role of neuroendocrine-immune system in cancer initiation, progression, and metastasis?

**Use Case ID** 195687

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Little is known about the nervous system's role in cancer. Interplay of neural and immune system pathways may play an important role in cancer.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>

## What causes a heightened or decreased sense of smell?

**Use Case ID** 196958

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Quality of life	Survey	At specified times anchored to the clinical event
Clinical outcomes	Blood draw	At specified times anchored to the clinical event
Air quality assessment results		At specified times anchored to the clinical event
Physical activity, self-assessment	Physical exam	At specified times anchored to the clinical event
Diet, self-assessment	Blood draw	At specified times anchored to the clinical event

## How does maternal anosmia influence the development and maintenance of mother–infant bonding?

**Use Case ID** 197066

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Reduce Disease Impact

Questionnaire-based study comparing congenitally anosmic mothers and offspring with matched controls measuring parental and child attachment; involvement; social, emotional, and psychological adjustment; stress; etc.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Anosmia diagnosis	Electronic Health Record (EHR)	
Family relationships	Survey	

## What are the environmental and genetic causal relationships in primary lateral sclerosis (PLS)?

**Use Case ID** 197318

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Epigenomic/epigenetic markers	Blood draw	Baseline
Environmental samplings and exposure results		
Health and phenotype data		
Lifestyle, self-assessment		

## What are common problems with wayfinding experienced by people with blindness or low vision?

**Use Case ID** 197366

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Reduce Disease Impact

A survey to identify problems experience in wayfinding, both indoors and outdoors. Correlate the extent of low vision with mobility.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Quality of life	Survey	Annually
Behavioral characteristics, self-assessment	Activity monitor	Continuous monitoring
Vision assessment results		

## Why are there fewer cases of Alzheimer's disease in India?

**Use Case ID** 197478

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Maintain & Preserve Health

To address this question, it is necessary to find a cohort group of some kind with parents/first-degree relatives diagnosed with Alzheimer's disease in the United States and India. After that, we will need to break the groups down into ethnicity, environmental factors, etc. We can then find the triggering or protective factors of this disease. These differences may be in terms of food habits, genetic markers, or the gut microbiome.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Self-reported ancestry		
Location data		
Alzheimer's diagnosis		
Environment		
Genotyping data		

## What are the characteristics of the virus that causes post-viral anosmia?

**Use Case ID** 197767

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Goal: To identify the virus that causes anosmia. Methods: Survey post-viral anosmics about the virus's onset, timing, characteristics, duration, symptoms, and treatment. Recruitment through Facebook groups, message boards, and specialists. A control group could be identified through medical records.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Survey	Baseline
Perceived outcomes - patient	Clinical diagnostic test	
Anosmia diagnosis	Electronic Health Record (EHR)	
Social networking use	Survey	
Outcomes	Electronic Health Record (EHR)	

## What are the biological, psychological, social, and environmental determinants of high-impact chronic pain?

**Use Case ID** 198141

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Detect Disease

Define the construct of “high-impact chronic pain” using available EHR and patient-reported data (e.g., questions developed by CDC and NHIS) and examine biological, psychological, and social/environmental variables as predictors and correlates of high-impact chronic pain. Within each domain (i.e., biological, psychological, social/environmental), consider the broadest array of constructs and measures, including genetic and other biomarkers, behavioral factors associated with pain, and employment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pain symptom diagnosis	Survey	Every 3 months
Behavioral characteristics, self-assessment	Survey	Every 3 months
Mental health and behavior information	Electronic Health Record (EHR)	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	Every 3 months
Health issues, occupational	Survey	Every 3 months

## How does aging affect people with neurodevelopmental disorders?

**Use Case ID** 198147

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Elucidate Disease Mechanisms

Many patients with neurodevelopmental disorders (e.g., autism, fragile X, Angelman syndrome, etc.) are adults. How aging-related cognitive and neurological declines affect these people is not fully clear. This study should involve families and caregivers in addition to clinicians. The impact of enriched environment and physical activities known to enhance adult neurogenesis and neuroplasticity in animal models should be assessed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment		Every 3 years
Blood pressure	Physical exam	Every 3 years

## What environmental exposures, including lifestyle factors, are common among migraine sufferers that can inform primary prevention?

**Use Case ID** 198170

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Reduce Disease Impact

Migraine sufferers are a diverse group of people, with different habits, triggers, and symptoms (other than the headache). A possible study design would be a retrospective and prospective, longitudinal review of the All of Us database to identify common denominators in the migraine-sufferer population, focusing on factors such as nutritional deficiencies and environmental exposures, to inform strategies that prevent the occurrence of migraines without drug treatments.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Migraine headache diagnosis	Electronic Health Record (EHR)	
Environment	Survey	
Diet, self-assessment	PPI Survey (AOURP)	

## How does exposure to pesticides across the lifespan impact one's risk of Parkinson's disease?

**Use Case ID** 198171

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Existing studies on a small scale have linked some pesticide exposure to neurologic outcomes. To investigate this on a national scale, we propose collection of occupational history on all participants. For those who worked or lived on a farm for more than one year, we would follow up with a detailed questionnaire on exposures, such as pesticides, and detailed use of personal protective equipment. Follow up on a control group as well. Outcome data would be collected through medical records.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pesticides exposure assessment results	Survey	
Parkinson's Disease diagnosis	Electronic Health Record (EHR)	Annually
Occupation	PPI Survey (AOURP)	Annually
Parkinson's disease symptoms	Electronic Health Record (EHR)	Every 3 months
Tobacco/Nicotine Use	PPI Survey (AOURP)	Annually

## What environmental and lifestyle factors affect the risk of developing a neurodegenerative disease?

**Use Case ID** 198699

**Cross-Cutting Theme** Environmental and Other Contextual Effects

**Scientific Category** Assess Risk

Extensive epidemiological research suggests a causal relationship between diet, physical activity, and environmental factors and risk for, or protection from, a number of diseases. By examining the potential connection between environmental factors and lifestyle factors, we aim to better understand their role in the development of neurodegenerative diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually
Diet, self-assessment	PPI Survey (AOURP)	Annually
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Neurological disease information	Electronic Health Record (EHR)	Annually

## What are the genetic and environmental factors that predispose a person to spina bifida?

**Use Case ID** 192277

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

It is unknown what tips an individual with genetic risk for the neural tube defect spina bifida (SB) to expression of the disease. Genome variant patterns conferring predisposition, epidemiological data, and dietary and lifestyle information would combine to illuminate the complex gene-environment interactions that underlie the disease. Information about maternal health and prenatal care would also be of interest. Biomarkers and genetic variation in folate metabolic pathway could study folate impact on SB expression. Prospective study of SB patient management could include renal, orthopedic, and neurosurgical intervention.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Folate levels	Biochemical assay	
Glucose levels		
Hemoglobin A1C (HbA1C) levels		Upon enrollment and first obstetrical visit
Diet, self-assessment	PPI Survey (AOURP)	Annually

## Which genetic pathways are commonly expressed in patients with arachnoiditis or low back pain with radiculopathy?

**Use Case ID** 192320

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

1. Identify patients with a diagnosis of arachnoiditis or low back pain with radiculopathy. 2. Examine genetic variants and gene expression and epigenetic status of respective genes. 3. Determine if there is a genetic relationship among respective patient community.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Back pain diagnosis		
Arachnoiditis diagnosis		
Radiculopathy diagnosis		
Genomic analyses		

## How do genetic factors of ADHD influence treatment strategies? Can they affect treatment success or the choice of therapy?

**Use Case ID** 194546

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Reduce Disease Impact

Screen school-age children for ADHD by testing, if feasible, or by electronic health record search. Perform WGS on children as the preferred strategy to identify new genetic associations and confirm previously reported genetic associations. If WGS is not possible, develop a marker panel and test children who have ADHD for known or suspected genetic factors. Follow children by periodic medical evaluations and school performance to develop “personalized” therapy based on the results.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Attention Deficit Hyperactivity Disorder (ADHD) diagnosis	Electronic Health Record (EHR)	Annually
Attention Deficit Hyperactivity Disorder (ADHD) Assessment	Clinical diagnostic test	Baseline
Attention Deficit Hyperactivity Disorder (ADHD) biomarkers	Blood draw	
Genomic analyses	Whole Genome Sequencing (WGS)	
Educational outcomes	Educational records	

## What are the genetic or environmental causes of Meniere's disease, and is there an inflammatory component?

**Use Case ID** 194940

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Meniere's disease diagnosis		
Inflammation disorder diagnosis		
Environment		
Genomic analyses		
Environmental samplings and exposure results		

## What are the underlying factors affecting narcolepsy?

**Use Case ID** 195127

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

The genetic makeup or the missing cells that cause narcolepsy and/or designer medications. If it is an autoimmune disorder, destruction of hypocretin.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune biomarkers levels	Human leukocyte antigen (HLA) typing test	Annually
Sleep quality assessment results	Sleep journal	Continuous monitoring
Genotyping data	Whole Exomic Sequencing (WES)	

## Is there a genetic or environmental component to the neural tube defect of epidermoid brain tumors or cysts?

**Use Case ID** 195774

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Look for genetic component to the epidermoid brain tumor that forms in the third to fifth week of pregnancy, a neural tube defect. An environmental study to study maternal/paternal health or environment contributes to neural tube defects and epidermoid cysts that cause much disability. Could any pharmaceutical agents shrink these tumors? Medical treatments to treat these tumors, as surgery is the only treatment. They are 0.2% to 0.5% of all brain tumors, are benign, and are very under-researched.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Whole Genome Genotyping (WGG)	
Environment	Survey	
Family relationships	Survey	
Clinical outcomes	Electronic Health Record (EHR)	
Genomic ancestry	Whole Genome Genotyping (WGG)	

## What genetic and environmental factors influence the progression of hearing loss (presbycusis) in aging adults?

**Use Case ID** 195949

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

NIDCD estimates that age-related hearing loss, or presbycusis, affects 1 in 3 individuals in the United States between 65 and 74 years old, and nearly half of those older than 75. Despite this large burden, few genetic risk factors have been identified, and it is unclear how genetics and environment interact to influence hearing loss susceptibility. I propose to measure hearing loss progression in the All of Us cohort, so that this topic can be studied and preventative treatments can be developed.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Hearing assessment results	Hearing test	Annually

## Are genes or modifiable factors a greater risk for migraine headaches?

**Use Case ID** 196354

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Longitudinal study of people suffering from migraines, to examine whether genetics or modifiable factors (e.g., obesity) have a greater association with development of headaches. Justification: Links between obesity and migraine are becoming more established, but a family history of migraines is one of the most powerful predictors of their appearance. Cross-sectional designs are limited in their ability to disentangle these powerful risk factors, but a longitudinal design would help sort this out.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Body Mass Index (BMI)	Electronic Health Record (EHR)	Annually
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Migraine headache diagnosis	Survey	
Family clinical outcomes	PPI Survey (AOURP)	

## Why do respiratory viruses lead to smell loss (anosmia) in some individuals but not others?

**Use Case ID** 196593

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Exome sequencing of self-identified viral anosmics versus congenital anosmics versus healthy match controls to identify candidate genes related to susceptibility.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Exomic Sequencing (WES)	Baseline
Olfaction assessment results	Clinical diagnostic test	Every 2 years
Viral infectious agent	Electronic Health Record (EHR)	

## Can we advance our understanding of epilepsy by developing new, data-driven tools for use in its diagnosis and treatment?

**Use Case ID** 196598

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Gather MRI, genetic, and basic clinical and behavioral data from all patients with epilepsy (conservatively 1% of the population). Data can then be analyzed using a machine learning approach to identify consistencies and differences among patients, which can then inform our understanding of epilepsy subtypes and subsequent treatment decisions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Brain magnetic resonance imaging (MRI) images	Magnetic Resonance Imaging (MRI)	Baseline
Genotyping data	Blood draw	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Every 2 years
Behavioral characteristics, self-assessment	Electronic Health Record (EHR)	Every 2 years
Depression diagnosis	Electronic Health Record (EHR)	Every 2 years

## Can GWAS identify the causes of variable expression and progression in Charcot-Marie-Tooth disease?

**Use Case ID** 196882

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Charcot-Marie-Tooth disease (CMT) is one of the most common inherited neurological disorders, affecting approximately 1 in 2,500 people in the United States. Since 1991, 90 different genes causing CMT subtypes have been identified, but the severity of the disease can vary even among families with the same genetic variant. Disease-modifying genes, epigenetics, mitochondrial involvement, exercise levels, diet, and environmental factors have all been suggested as possible causes of this variability.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Charcot-Marie-Tooth disease (CMT) diagnosis	Charcot-Marie-Tooth neuropathy score (CMTNS)	Include child, teenager, early adult, adult, elderly
Epigenomic/epigenetic markers		Include child, teenager, early adult, adult, elderly
Physical activity, self-assessment	PPI Survey (AOURP)	
Mitochondrial sequence	Blood draw	Baseline
Genomic sequence data	Whole Genome Sequencing (WGS)	

## What are the connections between comorbid brain disorders, such as epilepsy and bipolar disorder, and multiple sclerosis?

**Use Case ID** 197484

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Too many people have comorbid brain disorders. Not enough is known about each disease independently, what causes them, and what, if anything, contributes to resilience in those of us who do not suffer from them. Research on familial links, people with similar comorbid brain disorders, genetics that play into who gets these diseases, and how individuals react uniquely to medications can all lead us to a better understanding, treatment, and eventually a cure for all of them with the help of All of Us.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Include child, teenager, early adult, adult, elderly
Family clinical outcomes	PPI Survey (AOURP)	Baseline
Genomic analyses		
Neurological disease information		
Treatment/Therapy		

## What are the mechanisms underlying fatigue?

**Use Case ID** 198139

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Fatigue is a ubiquitous symptom commonly reported in people with acute and chronic illness. We do not know the specific underlying mechanisms of fatigue; some studies suggest inflammation, and the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system are implicated in fatigue. We propose longitudinal assessments of self-reported fatigue and inflammatory biomarkers monthly over 1 year to determine those underlying mechanisms of fatigue.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Inflammation biomarkers levels	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Every 3 months
Cortisol levels	Saliva	Monthly
Autonomic nervous system function	Heart rate recovery	
Fatigue symptom		

## **What is the basis for circadian timing, duration, and quality of sleep and vulnerability to develop sleep disorders?**

**Use Case ID** 198158

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Study would seek to characterize the etiological bases, including genetic, sociocultural, and environmental, for the circadian timing, duration, and quality of sleep and vulnerability to develop sleep disorders.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Circadian Rhythm Disorders (CRD)		
Sleep parameters		
Sociodemographics		
Genomic analyses		
Environmental assessment results		

## **What are the biomarkers of sleep sufficiency for use in safety for duty assessment and longer-term health indices?**

**Use Case ID** 198163

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

Biomarkers of sleep sufficiency need to be developed for use in safety for duty assessment and also for use as longer-term health indices.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sleep parameters		
Specified Biomarkers		
Clinical outcomes		

## What gene-environment interactions influence chronic eye disease outcomes?

**Use Case ID** 198380

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Leverage sample size to investigate genetic polymorphism and environment exposure (G\*E) interactions in chronic eye disease. Smaller studies are suggestive, yet few adequately powered studies exist. As chronic eye disease shares cardiovascular disease (CVD) risk factors, focusing on CVD G\*E interactions may identify novel risk factors and targets to reduce eye disease risk/burden. Potential examples include MTHFR polymorphisms and folate intake, as well as vitamin D pathway polymorphisms and sunlight.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Epigenomic/epigenetic markers	Blood draw	Baseline
Diet, self-assessment	Food diary	Annually
Vitamin D levels	Blood draw	Baseline

## What etiology factors contribute to the onset of seizures in late adulthood?

**Use Case ID** 198494

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

The incidence of seizures increases after the age of 50 years. With the increased life expectancy, seizures in older adults represent an emerging and important public health concern. Although cerebrovascular disease contributes to some cases, the etiology of these seizures in most patients is largely unknown. Metabolic factors are likely to contribute to risk in some patients, as diet changes can reduce the frequency of seizures for some. Epigenetic or genetic factors may also contribute to risk.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Seizure diagnosis	Electronic Health Record (EHR)	
Diet, self-assessment	PPI Survey (AOURP)	Every 2 years
Epigenomic/epigenetic markers	Blood draw	
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline XXXX

## What biomarkers are associated with the restorative/non-restorative sleep continuum?

**Use Case ID** 198597

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

Sleep participates in regulation of biological systems that support health. Sleep is experienced as restorative, and non-restorative sleep is associated with debilitating fatigue, experienced in many medical conditions. Questions are needed to assess subjective restorative quality of sleep (in the last months) together with questions about mental and physical health; sleep continuity, quality, and duration; and circadian timing. With these data, biomarkers of sleep sufficiency can be discovered.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Specified Biomarkers		
Sleep behavior assessment results		
Health and phenotype data		
Mental health and behavior information		

## Can a genomic score for risk of hearing loss be constructed and validated through longitudinal measures of hearing acuity across All of Us population?

**Use Case ID** 1000722

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Over 90 genes are associated with hearing loss, and it is unclear if a burden/GWAS analysis can identify persons with high or low risk. Assuming the development of polygenic/burden risk score (perhaps outside of All of Us), such a score could be validated through longitudinal testing of hearing acuity.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Blood draw	Baseline
Hearing assessment results	Mobile monitor	Periodically

## Can the microbiome be used to track disease?

**Use Case ID** 1000857

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

Gut microbiome has been implicated in numerous diseases impacting severity and manifestation. This may be a new avenue for treatment/detection.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Biological Specimens	Stool sample	Continuous monitoring
Biological Specimens	Smart toilet	Continuous monitoring
Health and phenotype data	Electronic Health Record (EHR)	Continuous monitoring
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Microbiome sample	Stool sample	Monthly
Environment	Global Positioning System (GPS) monitoring	Continuous monitoring
Diet, self-assessment	PPI Survey (AOURP)	Monthly

## Can cell-free DNA be used for early glioma detection?

**Use Case ID** 1000862

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Detect Disease

Glioma is usually detected only after symptoms develop at advanced stage. The All of Us population is expected to develop 10–20 cases of glioma, so it provides a good opportunity for detection.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Biological Specimens	Blood draw	Annually
Family clinical outcomes	PPI Survey (AOURP)	Per event
Whole genome sequence (WGS) data	Whole Genome Sequencing (WGS)	Per event
Biological Specimens	Blood draw	Baseline

## What is the prevalence of heterozygous mutations in SMA1?

**Use Case ID** 1000886

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Would perform in utero testing/treatment of spinal muscular atrophy and impairment in affected individuals. Informatics challenge! Could be expanded to other genes, but treatment is not available.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Spinal Muscular Atrophy (SMA) diagnosis	Blood draw	Baseline

## Are there genetic variants that contribute to sensory-sensitive subtypes of autism, and can they be used to target treatment?

**Use Case ID** 1001050

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Elucidate Disease Mechanisms

Assuming that there are genetic factors contributing to autism subtypes, important to include considerations of culture, gender, social dynamics that may influence ascertainment, diagnosis, and associations. Importance of sensitivity and stigma of ASD-neurovariability.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Annually
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Sensor data	Clinical assessment	Annually
Environmental samplings and exposure results	Ambient air monitoring	Baseline
Psychological measures	Electronic Health Record (EHR)	Annually
Prescription medication\treatment	Electronic Health Record (EHR)	Every 6 months

## Can patient knowledge or education of their own pharmacogenomic risk factors reduce the incidence of adverse drug events?

**Use Case ID** 1001091

**Cross-Cutting Theme** Genomics and Other Omics

**Scientific Category** Assess Risk

Genetic variants can modify one's ability to metabolize drugs, and these variants can be population-specific. Physician/provider knowledge and training is limited in pharmacogenomics. Population screening for generic/common drugs may not be cost effective, thus creating a need for individual patient knowledge.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Personal Characteristics	Survey	Baseline
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Prescription medication\treatment	Electronic Health Record (EHR)	Monthly
Side effects of prescription medication	Survey	Baseline
Patient education methods and content	Survey	Every 6 months

## What is the value of screening for cognitive impairment, including dementia, in the absence of a cognitive complaint?

**Use Case ID** 195190

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Detect Disease

The structure and scope of All of Us is such that it would be well positioned to address the following goals and approaches: Measure the benefit or detriment of identification of cognitive impairment on the family and health care provider decision making. Can a baseline healthy cognitive assessment serve as a baseline for future determination of meaningful change? Determine how to overcome financial, technical, and social barriers to detecting cognitive impairment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cognitive assessments	Cognitive test	Every 2 years

## How can cardio- and cerebrovascular health education and treatment be leveraged to improve brain health throughout life?

**Use Case ID** 195194

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Maintain & Preserve Health

Cardio- and cerebrovascular disease are linked to poor brain health outcomes, including dementia. To increase public health impact of this knowledge, better train care providers to identify and counter vascular risk and disease (e.g., hypertension, clots, diabetes, metabolic syndrome) in everyday care settings, and better educate patients on the importance of vascular health and related lifestyle decisions for brain health. Track brain outcomes to determine long-term impacts of these measures.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lifestyle, self-assessment	PPI Survey (AOURP)	Every 3 months
Blood pressure	Physical exam	Every 3 months
Health literacy	Survey	Every 3 months
Weight	Physical exam	Every 3 months
Glucose levels	Blood draw	Every 3 months

## How do experiences of racial discrimination relate to hypothalamic, pituitary, and adrenal (HPA) axis activity and the prevalence of chronic illnesses?

**Use Case ID** 195905

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Assess Risk

Instances of racial discrimination activate the HPA axis, and this chronic activation may be related to the disproportionate prevalence of chronic illnesses in members of racial minority groups. Some studies have found a blunted cortisol concentration in African Americans, compared to Caucasians. However, it's unknown whether all members of racial minority groups have a blunted cortisol concentration, and how it relates to instances of racial discrimination and occurrence of chronic illnesses.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Racial discrimination encounters	Survey	Annually
Cortisol levels	Saliva	Every 3 months
Clinical outcomes	Electronic Health Record (EHR)	Annually
Perceived outcomes - patient	Survey	

## Would access to eyeglasses improve the educational outcome for children in Title I schools?

**Use Case ID** 196942

**Cross-Cutting Theme** Health Disparities, Health Care Quality, and Access

**Scientific Category** Reduce Disease Impact

Regularly monitor children's vision from grades K to 12. Track those who use their glasses K-3.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Activity monitor	Include child, teenager, early adult, adult, elderly
Vision assessment results	Vision test	
Educational outcomes	Survey	

## Among people who sustain traumatic injury, what characteristics distinguish those who have optimal recovery from those who do not?

**Use Case ID** 190199

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Elucidate Disease Mechanisms

Injury to the musculoskeletal system or the central and peripheral nervous system or other conditions that cause disability are associated with significant morbidity. These injuries have substantial economic cost due to inability to work, high health care costs, and the need for long-term rehabilitation. Biomarkers of plasticity and contextual factors may predict functional outcome and guide prescription of the intensity of rehabilitation needed for optimal recovery.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Outcomes	Electronic Health Record (EHR)	
Specified Biomarkers	Blood draw	

## Are there patient characteristics that predict resilience to and coping strategies and treatments chosen for recurrent pain?

**Use Case ID** 195652

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Maintain & Preserve Health

Identify subsets of All of Us participants with chronic pain of various types. Administer questionnaire that asks in general about coping mechanisms, self-perceived pain tolerance, interference of pain disorder with function, child and adult exposures to adverse life experiences, history of depression/PTSD, drivers of decision of whether or not to treat an episode of pain, use of pharmacological therapies, use of non-pharmacological coping mechanisms and therapies.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pain symptom diagnosis	Survey	Baseline
Prescription medication\treatment	Survey	Baseline
Mental health outcomes	Survey	Baseline
Adverse life events	Survey	Baseline

## What combination of patient characteristics and intervention characteristics leads to the best outcomes for children with cerebral palsy?

**Use Case ID** 197772

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Reduce Disease Impact

Large-scale longitudinal observational study of patient characteristics and intervention characteristics gathered from electronic medical records analyzed using causal inference methodologies to determine the best interventions for each subgroup of children with cerebral palsy. Outcomes would be analyzed using measures across the ICF for body structure and function and activities and participation.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Movement assessments	Electronic Health Record (EHR)	Include child, teenager, early adult, adult, elderly
Cerebral Palsy (CP) diagnosis	Electronic Health Record (EHR)	Baseline
Treatment/Therapy (other than Drug use)	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Perceived outcomes - patient	Survey	Annually
Quality of life	Survey	Annually

## Is the use of fitness wearables associated with reduced risk of cognitive decline?

**Use Case ID** 1001013

**Cross-Cutting Theme** Informatic, Methodologic, Ethical, Legal, and Statistical Research

**Scientific Category** Maintain & Preserve Health

Individuals at risk of cognitive decline may be less active and less aware of the impact of physical activity on further decline. By either collecting data on whether or not the individual uses a wearable fitness tracker or providing a wearable, this study would determine whether use of a fitness tracker provides cognitive stimulation and increased physical activity and reduces risk of cognitive decline.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Wearable electronics	Ongoing
Patient Engagement	Wearable electronics	Daily
Physical activity, self-assessment	Mobile monitor	Continuous monitoring
Cognitive assessments	Interview	Periodically

## How do changes in sensory sensitivity correlate with development of chronic pain?

**Use Case ID** 195090

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Assess Risk

Understand how sensory sensitivity precedes development of chronic pain or sensitivity states (like itch bloating). Prospective study with smartphones repeated assessments of pain and symptom self-report (similar to PROMIS). Also include measures of visceral unpleasantness (nausea, photophobia, bloating). Determine if mood and neurological diagnosis, pregnancy, history of trauma, neighborhood, diet, social support, exercise, music tastes, and food preferences influence time course.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pain symptom diagnosis	Smartphone-based ecological momentary assessment	Every 3 months
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Prescription medication\treatment	Prescription drug records	Every 3 months
Depression diagnosis	PPI Survey (AOURP)	Every 3 months
Pain symptom diagnosis	Mobile monitor	Every 3 months

## Could the Precision Medicine Initiative enable artificial intelligence use in ophthalmology?

**Use Case ID** 196889

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

We will reach out to the public to upload eye images using smartphones and evaluate them, creating a large corpus of human eye images. A convolutional neural network will be trained to diagnose eye diseases and then used to remotely provide human-level prescreening and diagnosis to patients for easy and early detection and treatment. A few studies started building AI systems, but the available images are insufficient. The system will provide no-risk, early, and easy diagnosis.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Trauma Informed Care (TIC) implementation	Mobile monitor	

## What can be learned by inclusion of survey questions sensitive to sleep and circadian phenotypes?

**Use Case ID** 198159      **Cross-Cutting Theme** Mobile Health  
**Scientific Category** Assess Risk

There is a need to include survey questions sensitive to sleep and circadian phenotypes, which may be easily administered via smartphone applications.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Sleep assessments	Survey	

## What can we learn from wearables that capture sleep and circadian information?

**Use Case ID** 198162      **Cross-Cutting Theme** Mobile Health  
**Scientific Category** Detect Disease

Wearables that can capture sleep and circadian information—across the day/night and over time—should be included. Activity monitors, EEG, ECG, and oximetry measurement are increasingly accessible with miniaturization of technology. Consumer interest in many of these devices has accelerated development and driven costs down. Analysis of these data—perhaps using open platforms—holds promise for deriving quantitative measurements that predict health and disease.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Sleep parameters	Custom sensor/app	

## What are the voice, speech, and language digital biomarkers that predict the onset of Alzheimer's disease?

**Use Case ID** 198455      **Cross-Cutting Theme** Mobile Health  
**Scientific Category** Detect Disease

Description not provided.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Voice pattern	Smartphone-based ecological momentary assessment	Weekly

## **How are sleep, sedentary behavior, and physical activity related to one another and interactively related to health?**

**Use Case ID** 198498

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Maintain & Preserve Health

Sleep (quantity, quality, timing), sedentary behavior, and physical activity of various intensities affect each other and many health outcomes. Health conditions affect individuals' sleep and activity patterns. Capturing 24-hour device data repeatedly will allow exploration of multiple hypotheses about sleep, sedentary behavior, physical activity, and health. Longitudinal data will allow exploration of causality in both directions, as well as cross-sectional associations.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Activity monitor	For a week, at least monthly
Sleep parameters	Activity monitor	For a week, at least monthly
Sex Hormone Binding Globulin (SHBG) levels	Activity monitor	

## **How can mobile technology help us to understand the role of sleep patterns in health and behavioral outcomes?**

**Use Case ID** 198598

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Assess Risk

Participants will receive mobile technology (electronic diaries/accelerometers) for periodic monitoring of sleep/wake patterns to characterize relationships of sleep/circadian patterns on cardiometabolic health, incident diseases, and mood/QOL. Second, genetics and behavioral and environmental data will identify factors that influence sleep; characterize interrelationships of sleep, diet, and activity; and identify subgroups susceptible/resilient to the health/behavioral effects of insufficient sleep.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sleep parameters	Mobile monitor	Every 3 months
Clinical outcomes	Electronic Health Record (EHR)	Annually
Perceived outcomes - patient	Sleep journal	Every 3 months

## How to track migraines with wearables?

**Use Case ID** 1000701

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

Migraine is a common neurological condition treated with medication/lifestyle changes. Medications have frequent intolerable side effects. Risk factors may modify severity, and tracking would provide prevention strategies. Would also elucidate specific subtypes to potentially modify treatment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Migraine event log	Custom sensor/app	Per event
Environment	Mobile monitor	Continuous monitoring
Physical measurements	Smartwatch	Continuous monitoring
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Biological Specimens	Urine collection	At specified times anchored to the clinical event

## Can we use smartphone technology to provide cognitive assessments over lifespan and prior to neurodegenerative disease?

**Use Case ID** 1000776

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

We would like to identify early predictive signs in participants that are later diagnosed with dementia or neurocognitive disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Speech quality measurements	Smartphone-based ecological momentary assessment	Weekly
	Smartphone-based ecological momentary assessment	Daily
	Smartphone-based ecological momentary assessment	Weekly
Gait assessment results	Mobile monitor	Continuous monitoring
Social environment	Smartphone-based ecological momentary assessment	Continuous monitoring
Environmental samplings and exposure results	Global Positioning System (GPS) monitoring	Continuous monitoring

## Can we use wearables to detect or forecast seizures?

**Use Case ID** 1000784

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

Epilepsy is a common neurologic condition impacting over 3.4 million Americans. Less than 1 million do not have seizure control from their medications, and those that do are at risk of breakthrough seizures. Those with uncontrolled seizures are at risk of sudden death. Patients can experience loss of consciousness leading to injury (i.e., drowning, car accidents). A seizure that lasts less than 5 minutes is a medical emergency.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Wearable electronics	Daily
Environment	Wearable electronics	Continuous monitoring
Physical measurements	Wearable electronics	Continuous monitoring
Physical activity, self-assessment	Wearable electronics	Continuous monitoring
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Genomic analyses	Whole Genome Sequencing (WGS)	Annually

## Will better phenotyping improve the yield of genetic association studies?

**Use Case ID** 1000831

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Elucidate Disease Mechanisms

This applies to many diseases, but using Parkinson's as an example.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Gait assessment results	Mobile monitor	Continuous monitoring
Sleep assessments	Actigraphy	Continuous monitoring
Physical activity, self-assessment	Actigraphy	Continuous monitoring
Autonomic nervous system function	Actigraphy	Continuous monitoring
Neurocognitive assessment results	Smartphone-based ecological momentary assessment	Annually
Voice pattern	Smartphone-based ecological momentary assessment	
Muscle tone measurement	Electronic monitoring/recording	Continuous monitoring

## Does use of a mobile seizure detector reduce hospitalizations for seizures?

**Use Case ID** 1000837

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Assess Risk

Seizure disorders affect about 1 in 20 people. Seizures occur randomly and typically outside of a clinical setting. Patients typically have no warning prior to a seizure. Patient seizure diaries are historically inaccurate. For effective disease management, we could assess patient function under seizure medication usage.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Specimen collection	Baseline
Family clinical outcomes	Patient-reported outcome	Baseline
Health and phenotype data	Patient-reported outcome	Periodically
Physical activity, self-assessment	Wearable electronics	Continuous monitoring
Prescription medication\ treatment	Patient-reported outcome	Daily

## How data science can optimize technology to track disease progression for movement disorders?

**Use Case ID** 1000991

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Treat & Cure Disease

Motor sensors are becoming ubiquitous, and kinematic data is a key element in assessing sensory motor function. This information, from a large population, can be important for detection, monitoring of disease progression and recovery, and management of lifestyle (ADLs).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health and phenotype data	Electronic Health Record (EHR)	Periodically
Physical measurements	Wearable electronics	Continuous monitoring
Genotyping data	Genomic testing	Baseline
Environment	Electronic Health Record (EHR)	Periodically
Lifestyle, self-assessment	Custom sensor/app	Continuous monitoring

## How early can subtle motor changes predict development of gait disturbances?

**Use Case ID** 1001046

**Cross-Cutting Theme** Mobile Health

**Scientific Category** Detect Disease

Not enough is known about time-course of the development of gait disturbance. The All of Us population provides a broad sample.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Gait assessment results	Mobile monitor	Continuous monitoring
Gait assessment results	Electronic Health Record (EHR)	Every 3 months
	Mobile device camera	Weekly

## Do wearables predict functional decline in Parkinson's or detect pre-clinical disease?

Use Case ID 1001111

Cross-Cutting Theme Mobile Health

Scientific Category Detect Disease

Big data analysis/storage issues. IRB issues. Collect voice (probably not).

Datatype	Method	Specification
Physical activity, self-assessment	Wearable electronics	Continuous monitoring
Parkinson's Disease diagnosis	Wearable electronics	Continuous monitoring
Voice pattern	Wearable electronics	Daily
	Wearable electronics	Daily

## Can patterns of sleep/wake cycles, sleep apnea, and sleep movement detect pre-clinical dementia?

Use Case ID 1001171

Cross-Cutting Theme Mobile Health

Most Important

Scientific Category Detect Disease

Big data analysis/storage.

Datatype	Method	Specification
Cognitive assessments	Cognitive decline assessment game	Monthly
Sleep pattern	Wearable electronics	Continuous monitoring
Dementia diagnosis	Electronic Health Record (EHR)	Annually
Sleep quality assessment results	Survey	Daily

## What are the risk factors for comorbid health outcomes in persons with immobility caused by neurological injury or disease?

**Use Case ID** 194368

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

This would focus on incidence of health problems in the entire cohort to ask if loss of mobility or neurological impairment are separate risk factors. Demographic and pre-enrollment ICD codes will be obtained with the All of Us core dataset. Volunteers will be followed for 5 years with annual PPI, physical exams, and blood draws. ICD codes will be obtained at any clinical encounters. Principal component analysis will be used to define the primary risk factors associated with comorbidities.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Physical exam	Annually
Clinical outcomes	Clinical diagnostic test	
Metabolic risk assessment result	Blood draw	Annually
Lipids panel results	Blood draw	Annually
Quality of life	Survey	Annually

## What are the physical and chemical characteristics of amyloid plaques associated with Alzheimer's disease?

**Use Case ID** 194968

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Meaningful analysis requires harvesting of brain tissue, post mortem, of Alzheimer's patients, requiring informed consent from family members. Prepared slices or segments of amyloid plaque will be analyzed via 1) non-destructive testing that includes multi-frequency ultrasound scanning, multiple wavelength and chemi-fluorescence optical scanning, and SEM assessment and measurement; 2) destructive testing that includes mass spectrometry and gas chromatography. Scrutinize data for key character.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Mental health outcomes	Clinical diagnostic test	At specified times anchored to the clinical event
Biopsy results	Autopsy	
Amyloid plaque analysis results		

## What are the effects of long-term use of video games, handheld gaming devices, and cell phones on vision?

**Use Case ID** 195330

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Conduct research to identify the effects of long-term use of video games, handheld gaming devices, and cell phones on adult's and children's vision. Effects of long-term use of handheld devices could be causing permanent damage to adult's and children's vision. Does long-term use of handheld devices increase the risk of needing prescription glasses? Research may show a direct correlation to deterioration of vision in patients with frequent use of gaming devices.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Trauma Informed Care (TIC) implementation	Physical exam	Every 3 months
Self-reported ancestry	Electronic Health Record (EHR)	Every 3 months
Retinal function	Physical exam	Every 3 months

## What are the short- and long-term consequences of concussion?

**Use Case ID** 195661

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

The consequences of concussion on cognition, especially repeated concussion, is a major concern in the U.S. The ABCD research program is assessing the effects of concussion on behavioral health in children, but there are no other population studies of concussion effects. Obtaining information about index events and incorporating it into follow-up assessments of cognition and diagnosis of dementia would be extremely valuable, as the long-term effects in non-professional athletes are unknown.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Concussion diagnosis	PPI Survey (AOURP)	Every 3 years
Pain symptom diagnosis	Survey	Every 3 years
Fatigue symptom	Survey	Every 3 years
Cognitive assessments	Smartphone-based ecological momentary assessment	Every 3 years
Dementia diagnosis	Electronic Health Record (EHR)	Every 3 years

## Can we identify risk factors for age-related macular degeneration (AMD)?

**Use Case ID** 196289

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

From NEI Working Group on AMD: Use cohort with structural and functional phenotyping with genetic and EHRs to identify risk factors and their interactive effects for AMD development/progression. A subset could be identified based on AMD or family history of AMD (via EHRs), or presence of high-risk variants (via WGS), and could then be followed annually with fundus autofluorescence, OCT, dark adaptation. Additional data to collect would include AMD risk factors (hypertension, obesity, etc.).

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Clinical outcomes	Electronic Health Record (EHR)	Annually
Diet, self-assessment	Food diary	Annually
Vision assessment results	Vision test	Annually
Blood pressure	Physical exam	Annually

## What are the risk factors for developing epilepsy later in life?

**Use Case ID** 196358

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Initial data (e.g., demographic) and data that are noted routinely as part of health care maintenance (e.g., anthropomorphic factors, blood pressure, cholesterol, serum creatinine) could be collected longitudinally and then evaluated in terms of onset of epilepsy later in life. Justification: As the U.S. population ages, the incidence and prevalence of epilepsy is expected to increase, given the association of epilepsy with vascular risk factors and dementia.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Epilepsy seizure frequency	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Lipids panel results		Annually
Creatinine levels	Blood draw	Annually

## ***Is a history of localized provoked or generalized vulvodynia associated with lower urinary tract symptoms (LUTS)?***

**Use Case ID** 196481

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

8% of women may experience stigmatizing and debilitating chronic vulvar pain (vulvodynia) by age 40. Recurrent urogenital infections are associated with vulvodynia and women with vulvodynia may be at risk of LUTS. Vulvodynia patients fail to seek care and therefore we propose to ask women to report any period of pain during intercourse, tampon use, or at the time of a pelvic examination that lasted for at least 3 months or longer. We will assess, bi-directionally, its relation to bladder health.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Vulvar pain	Survey	Annually
Lower Urinary Tract Symptoms (LUTS) record	Survey	Annually
Urinary tract infection (UTI) diagnosis	Electronic Health Record (EHR)	

## ***What are the pathophysiologic factors associated with the development of vulvodynia?***

**Use Case ID** 196570

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

As many as 16% of women in the U.S. suffer from vulvodynia at some point in their lives. It affects women of all ages, races, and ethnic backgrounds. Yet, the exact cause of vulvodynia is unknown due to a lack of research. As a result, treatments used to treat this condition are the same ones used for other chronic pain conditions and there is little or no proof of their efficacy. Research on the cause of this condition is essential for developing treatments specifically for vulvodynia patients.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Vulvodynia diagnosis		
Vulvar pain		
Pathophysiologic assessment results		
Treatment effectiveness		

## What lifestyle choices can negate or reduce the risk of Alzheimer’s and other dementia in persons with genetic predisposition?

**Use Case ID** 197487

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

A study of lifestyles, including eating habits, exercise habits, where one lives, stress factors, mental health issues, and other health issues, in persons who may be predisposed to Alzheimer’s/dementia due to genetic markers or variants or family history.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Epigenomic/epigenetic markers	Blood draw	Baseline
Diet, self-assessment	Food diary	Continuous monitoring
Family clinical outcomes	PPI Survey (AOURP)	Baseline
Lifestyle, self-assessment	PPI Survey (AOURP)	Annually
Physical activity, self-assessment	Activity monitor	Continuous monitoring

## What are the social, biological, and behavioral factors that influence fatigue in adults and children?

**Use Case ID** 198138

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Fatigue is commonly reported as prodromal to acute and chronic illness. At this point, we do not understand the etiology of fatigue; it is often confused with sleepiness. Longitudinal assessments of self-reported symptoms (fatigue, sleep, pain, depression), comorbid conditions, physical activity, and biomarkers will be collected monthly over 1 year to allow us to assess potential temporal effects of fatigue on daytime and nighttime (sleep) activity patterns in adults and children.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Fatigue symptom	Enzyme-Linked ImmunoSorbent Assay (ELISA)	Every 3 months
Clinical outcomes		Annually
Fatigue symptom		Every 3 months
Sleep quality assessment results	Patient-Reported Outcomes Measurement Information System (PROMIS)	Every 3 months
Sleep behavior assessment results	Actigraphy	

## How does fatigue differ from excessive daytime sleepiness?

**Use Case ID** 198140

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

Fatigue and daytime sleepiness are commonly reported symptoms. While these are distinctly different concepts, they may share common etiologies and/or mechanisms. Longitudinal assessments of self-reported fatigue and daytime sleepiness, along with actigraphy (objective sleep measurements), may allow us to discern those similarities and/or differences between fatigue and excessive daytime sleepiness.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Fatigue symptom		
Daytime sleepiness assessment results		
Sleep behavior assessment results	Mobile monitor	Continuously for 1 week

## What are the neurodegenerative outcomes for people who develop hyposmia, anosmia, or chronic constipation?

**Use Case ID** 198149

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

These are frequent antecedents in neurodegenerative disease. They may, in themselves, be early biomarkers and/or demarcate a peripheral origin for the disease. However, their onset is not well understood, and they are not specific to neurodegenerative diseases. Understanding their natural history and co-association with other midlife/old-age symptoms coupled with omic data may help understand the role of these symptoms either as markers of disease or as aetiological players (e.g., microbiome).

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Anosmia diagnosis	Electronic Health Record (EHR)	
Neurological disease information	Electronic Health Record (EHR)	

## What midlife lifestyle factors make someone more or less likely to develop dementia with Lewy bodies?

**Use Case ID** 198150

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Exercise, socialization, cognitive training, education, dietary habits, and environmental exposures interacting with genetic profiles are suggested to raise the risk of Alzheimer’s dementia. Less is known about environmental, genetic, and epigenetic contributors to raising the risk of dementia with Lewy bodies. Large-scale data sets would allow first-of-its-kind enhanced profiling in multi-path analyses of key midlife factors (risk and protective) that contribute to occurrence of this disease.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lewy body disease diagnosis	Electronic Health Record (EHR)	
Diet, self-assessment	PPI Survey (AOURP)	
Environment	Survey	
Genomic analyses	Genomic testing	

## What are the outcomes for people who present with REM sleep behavior disorder (physically acting out dreams while asleep)?

**Use Case ID** 198152

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

REM sleep behavior disorder (RBD) can precede subsequent Lewy body disease by many years/decades. Thus, RBD could be a potent prodromal biomarker of future disease and allow for identification of an ideal target population for disease-modifying treatment. In-depth assessment of sleep behaviors in midlife as measured using a participant survey complemented by wearable devices technology could provide unparalleled information in identification of RBD and contributory environmental and genetic factors.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sleep behavior assessment results	Mobile monitor	
Sleep quality assessment results	Survey	
Genotyping data	Genomic testing	
Personal Characteristics	Survey	
Lewy body disease diagnosis	Electronic Health Record (EHR)	

## **What are the relationships between sleep, diet, physical activity, and stress, and how do they affect health outcomes?**

**Use Case ID** 198160

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

There is a need to understand the relationships among sleep, diet, physical activity, and stress on one another and health outcomes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sleep parameters		
Diet, self-assessment		
Physical activity, self-assessment		
Clinical outcomes		

## **What is the association between head injuries and loss of smell?**

**Use Case ID** 198250

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

The connection between head injury and loss of smell is well known. But are there levels of association between the two? For instance, could there be limited loss, or is loss permanent and total?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Perceived outcomes - patient	Clinical diagnostic test	At specified times anchored to the clinical event
Head Injury diagnosis		
Anosmia diagnosis		

## Can we identify modifiable factors involved with the transition of acute pain to chronic pain?

**Use Case ID** 198348

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Research is needed to evaluate the transition of pain from an acute episode to chronic pain, especially in prevalent and costly conditions such as back pain, joint pain, and headaches. The transition from acute to chronic pain may vary along physical, behavioral, and psychological factors. Prospective research is needed to identify these factors, especially factors that can be modified through existing interventions, both non-pharmacologic and pharmacologic.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Pain symptom diagnosis	Survey	Include child, teenager, early adult, adult, elderly
Pain symptom diagnosis	International Classification of Diseases (ICD) usage data	Include child, teenager, early adult, adult, elderly
Prescription medication\treatment	Prescription drug records	Include child, teenager, early adult, adult, elderly
Lifestyle, self-assessment	PPI Survey (AOURP)	Include child, teenager, early adult, adult, elderly
Depression diagnosis	Center for Epidemiologic Studies Depression Scale (CES-D)	Include child, teenager, early adult, adult, elderly

## Can measures of speech and language be pre-clinical predictors of neurological disease?

**Use Case ID** 198379

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

Complex brain networks are responsible for translating thoughts and ideas into sequences of movements that produce the sounds of speech. Any disturbance in these networks can lead to changes in how we speak and what we say. Evidence shows that subtle changes in speech are early harbingers of neurological disease. We propose to use the All of Us platform to validate this hypothesis on a large scale and to develop AI tools for early detection based on speech analytics.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Speech analysis app	Weekly
Clinical outcomes	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Behavioral characteristics, self-assessment	Mobile monitor	Annually

## What is the relationship between smoking, addiction propensity, and Parkinson's risk?

**Use Case ID** 198496

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Epidemiological data suggests a protective effect with smoking for the risk of Parkinson's disease (PD). Alternatively, smoking can simply be a sign of a predisposition to addictive behavior, which is the real protecting factor (risk aversion is also known to be associated with risk of PD). This is an important question, with community health implications as well as the potential to refine research directions. This would be a multivariate analysis of social history factors and ICDs.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Survey	Include child, teenager, early adult, adult, elderly
Tobacco smoking	PPI Survey (AOURP)	Baseline
Lifestyle, self-assessment	PPI Survey (AOURP)	Baseline
International Statistical Classification of Diseases and Related Health Problems (ICD) codes record	Electronic Health Record (EHR)	Baseline
Parkinson's Disease diagnosis		

## What can we learn by gathering information on pain and surveys of health as well as quantitative sensory testing?

**Use Case ID** 198513

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Information can be gathered via WOMAC, painDETECT, SF36, and MDHAQ. Anne-Marie Malfait, MD, PhD (American College of Rheumatology)

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Arthritis diagnosis		
Clinical outcomes	Multidimensional Health Assessment Questionnaire (MDHAQ)	
Pain symptom diagnosis	Quantitative Sensory Testing (QST)	

## What factors contribute to chronic back pain?

**Use Case ID** 198727

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Back pain is a common cause of disability in the U.S. All of Us provides a unique opportunity to assess measures of physical activity, diet, environmental factors, depression, and coping skills on prevention of the transition of acute back pain to chronic back pain. Participants can be provided with exercise and health information regarding these conditions, and the impact of racial/ethnic background on outcomes can be assessed. This is a timely study which could aid the opioid crisis fight.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Back pain diagnosis		
Diet, self-assessment		
Physical activity, self-assessment		
Environment		
Mental health and behavior information		

## Can we better identify early markers of Alzheimer's in adults with Down syndrome to improve access to treatment?

**Use Case ID** 198735

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Behavioral characteristics, self-assessment	Clinical diagnostic test	At specified times anchored to the clinical event
Clinical outcomes	Autopsy	Continuous monitoring
Mental health and behavior information	Clinical diagnostic test	At specified times anchored to the clinical event

## What behavioral factors and mechanism contribute to risk of neurological disorders?

**Use Case ID** 1000711

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Social networking use	Smartphone-based ecological momentary assessment	Continuous monitoring
Movement assessments	Smartphone-based ecological momentary assessment	Continuous monitoring
Diet, self-assessment	Mobile device camera	Continuous monitoring
Health and phenotype data	Electronic Health Record (EHR)	Periodically

## Can we identify biologic and objective corollaries of pain in the All of Us cohort?

**Use Case ID** 1000754

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Treat & Cure Disease

Since pain is so ubiquitous, due to variable causes, we need to identify common factors in acute and chronic pain. A better characterization of the pain spectra could lead to prevention, coping strategies, and potential interventions. This will allow us to identify alternative factors to allow us to crowdsource effective alternative pain treatments prior to medical intervention.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sociodemographics	PPI Survey (AOURP)	Baseline
Health and phenotype data	Electronic Health Record (EHR)	Periodically
Family clinical outcomes	PPI Survey (AOURP)	Baseline
Coping strategies, self-assessment	Survey	Periodically
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline

## Is trauma-induced loss of smell indicative of what TBI patients go on to develop neurogenerative disease?

**Use Case ID** 1000767

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Include children.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cognitive assessments	Wearable electronics	Annually
Head Injury diagnosis	Electronic Health Record (EHR)	Continuous monitoring
Head Injury diagnosis	Patient-reported outcome	Continuous monitoring
Anosmia diagnosis	Patient-reported outcome	Annually
Head Injury diagnosis	Electronic Health Record (EHR)	Annually
Gait assessment results	Accelerometer	Weekly
Patient Engagement	Interview	Annually
Brain wave activity data	Magnetic Resonance Imaging (MRI)	Annually for 5 years

## Among those with mild cognitive impairment (MCI), what factors contribute to disease progression?

**Use Case ID** 1000793

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Reduce Disease Impact

Assumes interventions for people with MCI may be able to prevent or delay progression of disease. Need for inclusion of diverse populations; disease trajectory varies across SES—URMs are at higher risk for rapid progression to dementia. Need to ensure family member and/or caregiver engagement.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Physical activity, self-assessment	Wearable electronics	Continuous monitoring
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Neurocognitive assessment results	Clinical assessment	Every 6 months
Neurocognitive assessment results	Wearable electronics	Monthly
Diet, self-assessment	Wearable electronics	Daily
Sensor data	Wearable electronics	Monthly

## How is the quality of sleep a risk factor for the development and progression of neurodegenerative diseases?

**Use Case ID** 1000817

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Quality of sleep has been identified as a risk factor for multiple neurodegenerative diseases. Monitoring sleep quality can potentially illuminate that connection and provide an opportunity for intervention.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sleep pattern	Custom sensor/app	Daily
Circadian Rhythm Disorders (CRD)	Custom sensor/app	Daily
Sleep assessments	Survey	Every 6 months
Quality of life	Survey	Every 6 months
Clinical outcomes	Electronic Health Record (EHR)	Annually

## What factors cause migraines, including severity differences?

**Use Case ID** 1000885

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health and phenotype data	Electronic Health Record (EHR)	Continuous monitoring
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Brain wave activity data	Magnetic Resonance Imaging (MRI)	Annually
Lifestyle, self-assessment	PPI Survey (AOURP)	Baseline and at event
Diet, self-assessment	Food diary	Ongoing
Light exposure assessment results	Survey	Periodically

## **How do genetics, ancestral origin, and ethnicity interact with socioeconomic status and access to care to influence blinding eye diseases and neurodegenerative diseases?**

**Use Case ID** 1000888

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Genetics and ancestral origin are known risk factors for blinding eye diseases and neurodegenerative diseases. Socioeconomic status and access to care also influence outcomes for these diseases. Yet the interaction between these intrinsic and extrinsic factors is unclear.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Personal Characteristics	Survey	Baseline
Socioeconomic Status (SES)	PPI Survey (AOURP)	Annually
Retinal images	Imaging	Annually
Neurocognitive assessment results	Survey	Annually

## **What modifiable factors influence transition from acute to chronic pain?**

**Use Case ID** 1000910

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Brain magnetic resonance imaging (MRI) images	Magnetic Resonance Imaging (MRI)	Baseline
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Psychological measures	Mobile monitor	Periodically
Prescription medication\ treatment	Electronic Health Record (EHR)	Periodically
Social networking use	Smartphone-based ecological momentary assessment	Periodically

## How do sleep patterns relate to overall health status?

**Use Case ID** 1000947

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

The relationship between sleep and health is profound and undercharacterized. The All of Us population provides an important platform for elucidating this relationship.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Sleep assessments	Wearable electronics	Daily
Physical activity, self-assessment	Wearable electronics	Continuous monitoring
Patient-reported outcomes	Wearable electronics	Daily
Sleep assessments	Electronic Health Record (EHR)	Every 3 months
Prescription medication\ treatment	Mobile monitor	Daily
Cognitive assessments	Wearable electronics	Daily

## What is the role of chronic inflammation in neurodegenerative disease presence and progress?

**Use Case ID** 1000950

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Chronic inflammation impacts brain health, cardiovascular health and function, cancer, and many other diseases and health conditions. Understanding the role of chronic inflammation in neurodegenerative diseases could allow for earlier intervention and better treatment. This is particularly important in our aging population.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Annually
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Inflammation biomarkers levels	Blood draw	Annually
Gut microbiome sample	Stool sample	Annually
Retinal images	Mobile device camera	Annually

## What are the determinants of chronic pain?

**Use Case ID** 1000965

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

A significant proportion of the population experiences chronic pain. All of Us provides an opportunity to identify patterns and risk factors for chronic pain and its management.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Sleep assessments	Wearable electronics	Continuous monitoring
Pain symptom diagnosis	Mobile monitor	Daily
Biological Specimens	Urine collection	Baseline and post-treatment
Autonomic nervous system function	Wearable electronics	Continuous monitoring
Psychological measures	Survey	Periodically

## What factors influence optimal recovery from TBI or stroke?

**Use Case ID** 1000970

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Other

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genotyping data	Whole Genome Sequencing (WGS)	Baseline
Brain magnetic resonance imaging (MRI) images	Electronic Health Record (EHR)	Periodically
Cognitive assessments	Mobile monitor	Periodically

## What are the future neurological conditions for those with hyperosmia, anosmia, and constipation?

**Use Case ID** 1000978

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

These conditions have been implicated in prodromal stages in different neurological diseases, such as Parkinson's and Alzheimer's. They could be used for early detection/screening.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Daily
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Health and phenotype data	Electronic Health Record (EHR)	Continuous monitoring
Brain magnetic resonance imaging (MRI) images	Magnetic Resonance Imaging (MRI)	Baseline and post-treatment
Physical measurements	Smell test	Monthly
Physical measurements	Wearable electroencephalogram (EEG)	Continuous monitoring
Physical measurements	Sensor (swallowed)	Monthly

## What factors affect the development of hearing disorders over time?

**Use Case ID** 1000997

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Treat & Cure Disease

Hearing loss can be attributed to multiple etiologies. Due to the nature of heterogeneity, data science will be a powerful tool to characterize and classify to provide insight into potential effective intervention.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lifestyle, self-assessment	PPI Survey (AOURP)	Baseline
Family clinical outcomes	PPI Survey (AOURP)	Baseline
	Mobile monitor	Continuous monitoring
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Prescription medication\ treatment	Electronic Health Record (EHR)	Continuous monitoring
Sensory assessments	Smartphone-based ecological momentary assessment	Continuous monitoring

## Among a population of individuals at high risk for blinding eye disease, can we identify novel risk factors protective against disease?

**Use Case ID** 1001075

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Known mutations exist for many blinding eye diseases. Some who carry these mutations never develop these diseases. Can we identify genetic, lifestyle, or environmental factors that are protective within this population?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lifestyle, self-assessment	PPI Survey (AOURP)	Baseline
Medical Information	Electronic Health Record (EHR)	Annually
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Environment	Survey	Annually
Socioeconomic Status (SES)	PPI Survey (AOURP)	Annually
Retinal images	Mobile monitor	Annually
Diet, self-assessment	Diary/journal	Continuous monitoring

## Among people at high risk for developing neurodegenerative diseases because of genetic risk factors, can we identify environment or lifestyle factors that prevent or delay disease onset?

**Use Case ID** 1001085

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Known genetic mutations exist for many neurodegenerative diseases. Some who carry these mutations never develop these diseases. Can we identify genetic, lifestyle, or environmental factors that are neuroprotective within this population?

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually
Medical Information	Clinical assessment	Annually
Lifestyle, self-assessment	Mobile monitor	Continuous monitoring
Diet, self-assessment	Diary/journal	Ongoing
Retinal images	Mobile monitor	Annually

## What environmental and sociodemographic factors or exposures are most likely to modify risk for chronic eye disease?

**Use Case ID** 1001099

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Air quality assessment results		Continuous monitoring
Personal Characteristics	Survey	Annually
Retinal images	Imaging	Annually
Diet, self-assessment	Diary/journal	Ongoing
Retinal function	Clinical assessment	Annually
Light exposure assessment results	Mobile monitor	Continuous monitoring

## How is eye health and vision impairment connected to systemic disease and quality of life?

**Use Case ID** 1001110

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Detect Disease

Eye health and vision impairment can be an indicator of systemic disease. While some of these relationships are known, many additional important relationships can be identified as new technologies improve disease understanding. We will also be able to quantify the extent of visual impairment and its impact on quality of life. This will allow us to develop adaptive technologies to address these gaps.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health and phenotype data	Electronic Health Record (EHR)	Annually
Quality of life	Survey	Annually
Retinal images	Imaging	Annually
Neurocognitive assessment results	Survey	Annually
Psychological measures	Survey	Annually
Vision assessment results	Clinical assessment	Annually
Vision assessment results	Survey	Annually

## What determinants are responsible for maintaining visual function over the lifespan?

**Use Case ID** 1001124

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Maintain & Preserve Health

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Vision assessment results	Patient-reported outcome	Annually
Vision assessment results	Mobile monitor	Annually
Retinal images	Mobile monitor	Every 2 years
Omics	Genomic testing	Baseline

## Can retinal imaging be used as a biomarker for neurodegenerative and systemic disease?

**Use Case ID** 1001234

**Cross-Cutting Theme** Risk Factors, Prevention, and Wellness

**Scientific Category** Assess Risk

Retinal imaging is a non-invasive method that can identify clinical features of a wide variety of systemic diseases, such as hypertension, diabetes, CVD risk factors, and potentially Parkinson's and AD. There is potential to capture mobile images with the potential to apply deep learning methods for analysis.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Cognitive assessments	Clinical assessment	Annually
Retinal images	Mobile device camera	Annually
Medical Information	Electronic Health Record (EHR)	Annually
Sleep quality assessment results	Survey	Annually
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline

## How can we suppress the brain circuits involved in auditory hallucinations?

**Use Case ID** 194401

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Utilize functional brain imaging techniques, or develop techniques to track the transmission of neural impulses, while individuals are experiencing auditory hallucinations in order to identify specific pathways for intervention and potential treatments.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Brain magnetic resonance imaging (MRI) images	Magnetic Resonance Imaging (MRI)	Pre-treatment

## Does a decrease in estrogen contribute to chronic pain of adhesions in post-hysterectomy patients?

**Use Case ID** 194788

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

The study would need to include patients with total hysterectomies who are on all forms of estrogen therapy along with those who are not. The case studies would need to include patients who have the common complaint of chronic abdominal pain that has been verified to have no other cause. The expected outcome is that estrogen therapy proves to be an integral factor in the improvement of chronic abdominal pain due to abdominal adhesions.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Total hysterectomy procedure	Electronic Health Record (EHR)	
Prescription medication\treatment	Electronic Health Record (EHR)	
Hormone therapy		
Abdominal adhesions diagnosis		

## Does the prescription drug Lovaza (4 gm omega-3) correlate with improved cognitive function?

**Use Case ID** 194838

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Compared with a matched control group in age and medical problems, does a group taking Lovaza prescription (4 gm dose of omega-3 purified fish oil) perform better on cognitive tests or other measures of brain function? Most importantly, is the effect stronger in those who carry the APOE-4 gene? (The various generics for Lovaza could be used instead of Lovaza.)

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	PPI Survey (AOURP)	Annually
Neurocognitive assessment results	Cognitive test	Annually
Prescription medication\treatment	Electronic Health Record (EHR)	

## Is there a correlation between statin use and neurodegenerative disorders?

**Use Case ID** 195097

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

Easily accessible from medical history and of a very large pool of subjects, trying to establish the effect of widespread statin use and rate of neurodegeneration. There is a tsunami of cognitive decline/dementia in the U.S. in addition to Parkinson's disease, and statin use is extremely prevalent. Establishing a positive or negative correlation would be useful in making decisions about statin use and taking measures to curb the growing problem of neurodegenerative diseases.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Treatment/Therapy		Continuous monitoring
Neurological disease information		
Dementia diagnosis		

## Can childhood loss of cognitive function caused by drug side effects be restored with neuro-rehabilitative therapies?

**Use Case ID** 195178

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Side effects of some medicines used alone or in combination with others (e.g., minocycline and birth control) may impact cognitive function in children or young adults. Questions to be answered could include, "What percentage of people taking these meds develop cognitive dysfunction?" "Is there a common factor in who develops this?" "Can function be restored using neuro-rehabilitation?" and "Can function of the brain be assessed using functional MRI?"

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Clinical outcomes	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Mental health outcomes	Clinical diagnostic test	At specified times anchored to the clinical event
Quality of life	Survey	*GC

## Does Alzheimer's disease progress faster with patients who do not take Alzheimer's medication versus patients who do?

**Use Case ID** 195890

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Conduct a study that compares individuals with Alzheimer's disease and track how rapidly they progress through each stage of Alzheimer's. One group would be people who take prescription Alzheimer's medication and the other group would be individuals who elected not to take Alzheimer's medication or chose other types of treatment (holistic, for example). The goal would be to see if medication was effective in slowing down the progression of the disease or if it actually increases progression.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Treatment/Therapy	Electronic Health Record (EHR)	Continuous monitoring
Alzheimer's diagnosis		

## Can we find better treatments for neuropathic numbness and pain in Sjögren's and other autoimmune diseases?

**Use Case ID** 196613

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Peripheral neuropathies are common in Sjögren's and related autoimmune diseases and can be a presenting symptom of Sjögren's. Burning pain and numbness in the extremities, trigeminal neuralgias, weakness, poor balance, and altered gait can occur. Symptoms can interfere greatly with quality of life and function. This study would focus on identifying better treatments to address these symptoms in Sjögren's and autoimmune disease patients.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Autoimmune diseases diagnosis		
Autoimmune diseases diagnosis		
Treatment/Therapy		

## What medications work best for people with epilepsy?

**Use Case ID** 196663

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Aim 1: Pharmacoepidemiology. Among people with epilepsy subtypes, what are the most commonly used medications? Aim 2: Comparative Effectiveness. For each epilepsy subtype, which medication works best? Aim 3: Pharmacogenetics. Within epilepsy subtypes, what genetic markers predict response to treatment? (Epilepsy subtypes might include new onset focal epilepsy, new onset generalized epilepsy, Dravet syndrome, Doose syndrome, refractory focal epilepsy, refractory generalized epilepsy, etc.)

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Treatment effectiveness		
Pharmacogenomics		
Disease endotypes results		

## Can we differentiate healthy neurological aging from incipient nervous system dysfunction by using smartphone apps?

**Use Case ID** 196668

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Detect Disease

Neurons are mostly non-renewing cells, and neurodegenerative diseases are often diagnosed after many have already died. This severely limits therapeutic efficacy. We propose accurate, convenient measures of broad neurological functions using developed smartphone apps to test whether derived subject-specific progression slopes can differentiate healthy aging from incipient neurological dysfunction. Such analysis may eventually serve as personalized results in clinical trials and broad medical practice.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Neurocognitive assessment results	Smartphone-based ecological momentary assessment	
Gait assessment results	Mobile monitor	Monthly

## How can we better address retinal damage related to the use of hydroxychloroquine?

**Use Case ID** 196847

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Retinal damage is a serious and feared side effect of hydroxychloroquine, a frequently prescribed treatment for Sjögren's and lupus patients. Though we have sensitive tests and guidelines for monitoring patients on the therapy, more information is needed on how we can reverse the potential progression of damage once it has been detected.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Retinal function		
Side effects of prescription medication		
Autoimmune diseases diagnosis		
Hydroxychloroquine use		

## How can we better treat tinnitus and hearing loss as a side effect of hydroxychloroquine and other medications?

**Use Case ID** 196852

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Treat & Cure Disease

Tinnitus and hearing loss can occur as side effects of hydroxychloroquine and other medications, which are frequently prescribed to treat symptoms of Sjögren's and lupus. This study would focus on identifying how we can reduce the risk of these hearing-related symptoms and investigate potential ways to restore full hearing.

<i>Datatype</i>	<i>Method</i>	<i>Specification</i>
Hearing assessment results		
Tinnitus diagnosis		
Side effects of prescription medication		
Autoimmune diseases diagnosis		
Hydroxychloroquine use		

## What is the natural history of ventilator dependence in children with severe neurologic impairment?

**Use Case ID** 196986

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

Survival, health care utilization, hospice utilization, cause of death, location of death.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Neurodevelopment milestones		
Health care participation		
Clinical outcomes		
Death		

## Do antidepressants interact with cognitive decline to increase the risk of falls that result in injury?

**Use Case ID** 197317

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Assess Risk

A retrospective analysis of longitudinal health data from the EHRs and self-reports of patients who are chronic users of antidepressants. Both antidepressants and cognitive decline are associated with falls and repeated falls, a major source of morbidity/mortality. Antidepressants are poorly studied in patients experiencing cognitive decline. The study would test for a synergistic interaction between the drug class and disease, possibly suggesting a clinical management strategy.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Prescription medication\treatment	Electronic Health Record (EHR)	Continuous monitoring
Clinical outcomes	Electronic Health Record (EHR)	Continuous monitoring
Mental health outcomes		Baseline
Accidents/Falls	Survey	Periodic (approximately biweekly)

## What neural circuits underlie orofacial pain?

**Use Case ID** 198387

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

Orofacial pain, especially when chronic, is a common reason patients seek dental care. Despite broad advances in knowledge of the neurobiological basis of pain at different levels of nervous system, there is relatively scarce knowledge about pain circuitry in the brain. Thus, it is urgent to explore brain neural circuit mechanisms underlying the pathogenesis of chronic orofacial pain and then create mechanism-based new strategies for orofacial pain treatment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Orofacial pain diagnosis	Survey	

## What are the best practices to optimize motor rehabilitation in children with stroke?

**Use Case ID** 198587

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Key Problem: More than 60% of children with strokes have permanent neurological deficits, the most common being hemiplegia. The impact of stroke on motor skills varies; therefore, it will not be responsive to one single curative treatment. Pediatric stroke requires a multidisciplinary approach to rehabilitation for optimal outcome. No standard of care exists for these children. Proposed Study: Assess and survey what multidisciplinary practices exist for rehabilitation of infants to 18-year-olds with motor impairment.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Perceived outcomes - patient	Survey	Every 3 months
Clinical outcomes	Electronic Health Record (EHR)	Every 3 months
Clinical outcomes	Gross Motor Function Measure (GMFM)	Every 3 months
Neurological disease information		

## Why do patients with myalgic encephalopathy (ME) or chronic fatigue syndrome (CFS) have post-exertional malaise (PEM) after physical or mental exertion?

**Use Case ID** 198634

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

Finding out what happens to the system that controls energy in a person with ME would allow for an intervention to be created that corrects the system that regulates energy. PEM is the hallmark symptom of this disease and must be researched so that an FDA treatment and/or cure can be realized.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Myalgic Encephalopathy (ME) diagnosis	Electronic Health Record (EHR)	At specified times anchored to the clinical event
Myalgic Encephalopathy (ME) diagnosis	Electronic Health Record (EHR)	
Post Exertion Malaise (PEM)	Electronic Health Record (EHR)	
Cortisol levels	Blood draw	

## What is the relationship between neurogenerative disorders and statin use?

**Use Case ID** 1000746

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

It is possible that reducing the risk of cerebrovascular disease will have an impact on the development and progression of neurodegenerative disease. By tracking when statins are started, dosing, and impact and its interplay with the diagnosis of neurodegenerative disease (and treatment). Other potential mediators to consider would be sociodemographics and genetic risk.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Medical Information	Electronic Health Record (EHR)	Annually
Prescription medication\treatment	Electronic Health Record (EHR)	Annually
Cognitive assessments	Wearable electronics	Annually
Sociodemographics	PPI Survey (AOURP)	Annually
Sociodemographics	Electronic Health Record (EHR)	Annually
Genotyping data		Baseline

## Can loss of cognitive function caused by drug side effects or medical event be restored with neurorehabilitative therapies?

**Use Case ID** 1000791

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Loss of cognitive function is pertinent to many medical conditions, including normal aging. Identifying factors present with loss of cognitive function may be a first step to identifying which neurorehabilitation therapies could be most beneficial.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Lifestyle, self-assessment	PPI Survey (AOURP)	Baseline
Health and phenotype data	Electronic Health Record (EHR)	Periodically
Prescription medication\treatment	Prescription drug records	Periodically

## What are the determinants of intraocular pressure?

**Use Case ID** 1000916

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Maintain & Preserve Health

Intraocular pressure is an important risk factor for glaucoma, a leading cause of blindness worldwide. Determinants of intraocular pressure could define new methods to control intraocular pressure and potentially treat glaucoma.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Health and phenotype data	Electronic Health Record (EHR)	Every 3 months for 1 year
Whole genome sequence (WGS) data	Whole Genome Sequencing (WGS)	Baseline
Prescription medication\treatment	Electronic Health Record (EHR)	Annually
Health and phenotype data	Electronic Health Record (EHR)	Annually
Environmental samplings and exposure results	PPI Survey (AOURP)	Annually

## How do we optimize pain management based on patient medical history, genetics, and other longitudinal information?

**Use Case ID** 1000956

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Pain management needs are unique for different populations, including people with disabilities.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic analyses	Whole Genome Sequencing (WGS)	Baseline
Pain symptom diagnosis	Survey	Monthly
Mental health and behavior information	Electronic Health Record (EHR)	Annually
Mental health and behavior information	PPI Survey (AOURP)	Monthly
Functional mobility assessment results	Survey	Monthly

## Can we advance our understanding of epilepsy by developing new data-driven tools from use on its diagnosis and treatment?

**Use Case ID** 1001011

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Elucidate Disease Mechanisms

Description not provided.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Genomic sequence data	Whole Genome Sequencing (WGS)	Baseline
Diet, self-assessment	PPI Survey (AOURP)	Weekly
Prescription medication\treatment	Electronic Health Record (EHR)	Annually
Brain magnetic resonance imaging (MRI) images	Magnetic Resonance Imaging (MRI)	Baseline
Seizure diagnosis	Mobile monitor	Continuous monitoring

## Can outcomes be improved for patients with movement disorders by providing tools to track activities of daily living?

**Use Case ID** 1001057

**Cross-Cutting Theme** Therapeutic and Preventive Interventions

**Scientific Category** Reduce Disease Impact

Tracking tools need to be accessible for all patients. Patients should be able to choose their preferred mode of tracking. Community outreach and engagement to teach participants. Emphasize that reporting activities benefit future generations and will not be shared with law enforcement or used for other purposes.

<b>Datatype</b>	<b>Method</b>	<b>Specification</b>
Diet, self-assessment	Mobile monitor	Daily
Psychological measures	Mobile monitor	Weekly
Perceived outcomes - patient	Mobile monitor	Daily
Personal Characteristics	Mobile monitor	Weekly
	Electronic Health Record (EHR)	Annually
Neuromotor testing results	Clinical assessment	Every 6 months