Request for Information: NIH Precision Medicine Cohort - Strategies to Address Community Engagement and Health Disparities (NOT-OD-15-107)

An Executive Summary from the Precision Medicine Initiative Health Disparities and Community Engagement Working Group on the **Request for Information: NIH Precision Medicine Cohort - Strategies to Address Community Engagement and Health Disparities**

Overview

In January 2015, President Obama announced the launching of the precision medicine initiative (PMI) during his state of the union address. This new research endeavor would revolutionize how we improve health and disease, by taking into account a person's unique characteristics. To generate the knowledge to advance this research effort, NIH is seeking guidance on the creation of a national research cohort of 1 million or more Americans. This Request for information (RFI) solicited feedback to help guide the creation of a cohort that is reflective of the rich diversity of the U.S. The RFI specifically requested feedback on strategies and recommendations toward the development and implementation of effective community engagement strategies for the cohort, and ways to leverage the cohort's ability to conduct transformative research to address health disparities.

Responses:

69 responses (43 researchers, 14 patient advocates, 12 general public) from 44 cities across 23 U.S. states with 2 international respondents and 6 unspecified.

Community Engagement & Health Disparity Recommendations

Accessibility: In order to reach the medically underserved, historically underrepresented and socially disadvantaged populations, the science must be made accessible linguistically, culturally, and physically.

> *"Individuals and communities must be met where they are and where they live."*

Trust: The scientific community must first gain community trust by engaging with these communities as equal partners and making sure that they are being protected while contributing positively to science.

> *"Trust is particularly critical given the unfortunate legacy within medical research where participant rights have not been equally protected. Trust requires time and effort to develop, but is easily lost. It is usually less effective to create community partnerships and alliances at the time that research opportunities arise; it is much better to build on existing partnerships, going well beyond the needs of a single project."*

Education: Communities should be allowed to provide feedback on research initiatives while also being educated about the research being carried out.

> *"It will be necessary to educate people in simple terms that knowledge of the specific (genetic) background of individuals can lead to widely understood concepts, such as use of medications, risk for cancer and of chronic diseases such as diabetes, and how these familiar health challenges can be overcome through better knowledge using specific illustrations coming from communities of color or minority communities."*

Benefits: Clearly communicate the purpose, relevance and potential individual and communal benefits.

> *"Given the extensive volume of research that has been conducted with relatively little benefit for minority communities, and in some cases resulting in a widening of disparities, it will be critical to demonstrate that participation will realize benefits for all communities represented."*

Multi-Level Analysis of Health: "The Cohort" study design and research has the potential to illuminate the complex and interconnected web of biological, social, environmental and policy factors that lead to health disparities.

> *"Study the multiple determinants of health and their interactions (personal, social, economic, environmental factors) on disease risk, disease mechanism, and individual response to therapy."*

Novel Methods to gather and assess health disparities data: Emerging technology such as m-health and data sensors should be used to assess geographic, environmental and lifestyle impact on health.

“mHealth technologies and many of the hundreds of thousands of apps now available for tracking health and lifestyle data present exciting opportunities to gather data on geographic, environmental, and social determinants of health.”

NIH Precision Medicine Initiative

Overview of Public Input:
Responses to the NIH Request for Information

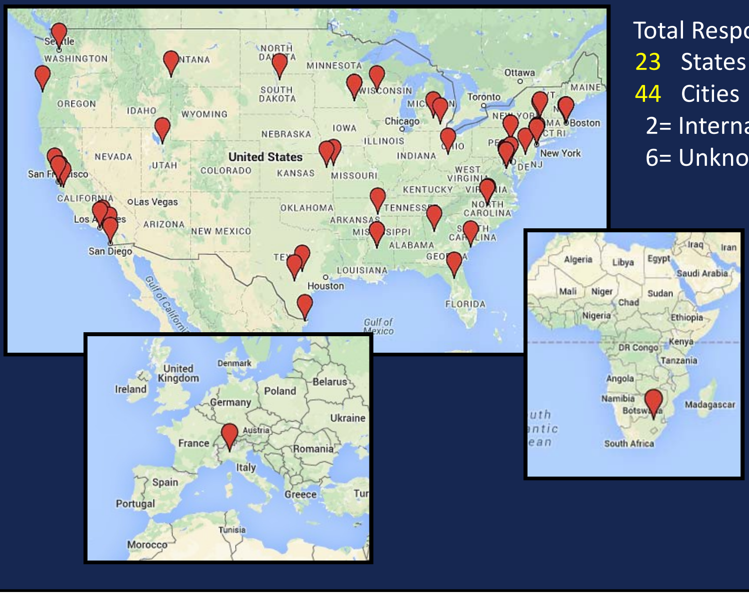
NIH Community Engagement Team

Co-chairs: Vence Bonham, J.D., and Regina James, M.D.
Members: Albert Avila, Ph.D., Paul Kimmel, M.D., Ebony Madden, Ph.D.,
Khara Ramos, Ph.D., Nishadi Rajapakse, Ph.D., Della White, Ph.D.

Workshop of the Precision Medicine Initiative Working Group
of the Advisory Committee to the NIH Director

July 1-2, 2015

RFI Responses



Total Responses N=69
23 States
44 Cities
2= International
6= Unknown

Community Engagement Strategies

Request for Information Questions
A.1. Factors and incentives for participation
A.2. Community engagement strategies and partnerships
A.3. Barriers to participation and strategies to address them
A.4. Ways to avoid stigmatization, manage unintended consequences of the PMI cohort
A.5. Safeguards to assure net positive potential of PMI

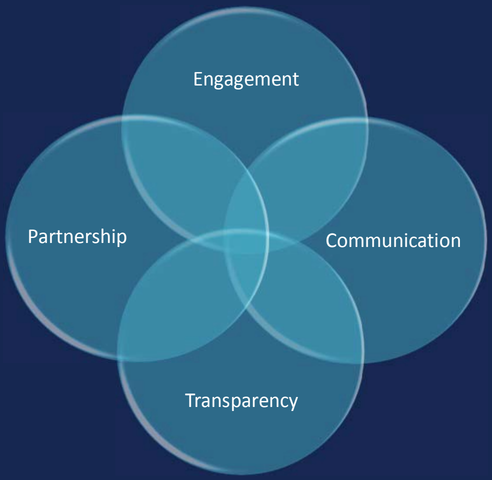
Common Themes

Community engagement strategies for a diverse sustained U.S. precision medicine cohort

Community Engagement Strategies

- Meaningful Engagement of Communities
- Continuous Communication
- Transparency
- Partnership
- Privacy Protections
- Education
- Remove Barriers of Participation
- Active Governance and Oversight
- Trust and Trustworthiness

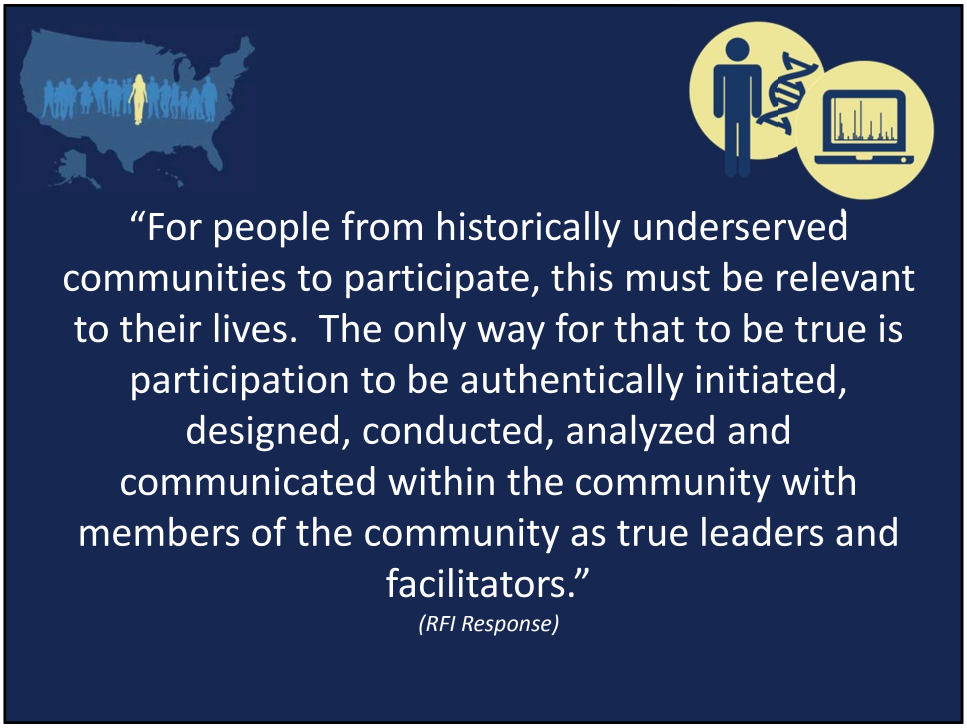
…meaningful involvement of community members from a very early stage in development of aims, procedures, analyses, communication of results.



Build national and local community action boards who will partner equitably with researchers.

The major component of reassurance of the positive benefits of this will be constant communication (including listening), education, and dialogue involving people who are respected and trusted by the community.

This project must operate with the highest level of transparency possible, including frequent project updates to key stakeholders.



“For people from historically underserved communities to participate, this must be relevant to their lives. The only way for that to be true is participation to be authentically initiated, designed, conducted, analyzed and communicated within the community with members of the community as true leaders and facilitators.”

(RFI Response)

Strategies to Address Barriers to Participation

“Ensure **materials are available at low literacy, in multiple languages, and in multiple mediums**. … develop additional strategies to educate and engage non English speaking participants and those with low general literacy

There will be **variation among communities** in terms of existence of electronic medical records, and access to various models of mobile phone **technology**. Consider alternate models for patient-entered data.

“Ensuring that structural factors such as coverage for transportation costs and childcare are covered by the research study could be a mechanism to **facilitate participation in research**

“Trust is particularly critical given the unfortunate legacy within medical research where participant rights have not been equally protected. Trust requires time and effort to develop, but is easily lost.”

(RFI Response)

Research Opportunities

Request for Information Questions
B.1. Priority health disparities research questions to be addressed by PMI
B.2. Opportunities to study various determinants of health
B.3. Obtaining new scientific knowledge
B.4. Novel methods for gathering data on health disparities
B.5. Novel ways to assess health disparities data

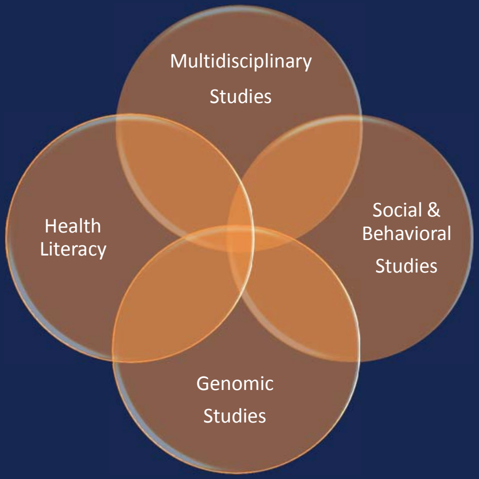
Common Themes

Health Disparities Research Opportunities

Research Opportunities

- Epigenetics Studies
- Environment Genetic Interaction Studies
- Genomics Studies
- Health Literacy Studies
- Research Participation and Health Services Research Studies
- Pharmacogenomics Studies
- Policy and Cost Studies
- Sex Differences Studies
- Multilevel Systems Studies (social, behavioral, economic, policy, environmental factors)

Study the multiple determinants of health and their interactions (personal, social, economic, environmental factors) on disease risk, disease mechanism, and individual response to therapy.



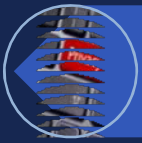
What new health literacy approaches will be necessary to ensure that patients and families understand precision medicine? Will these vary within subpopulations?

Critical to include careful, valid, and robust measures of social factors across the life course including socioeconomic, psychosocial, and environmental conditions.

What are the genetic and environmental factors across the lifespan that influence the development of disparities in risk and incidence or progression of hypertension, chronic kidney disease, and other chronic diseases?

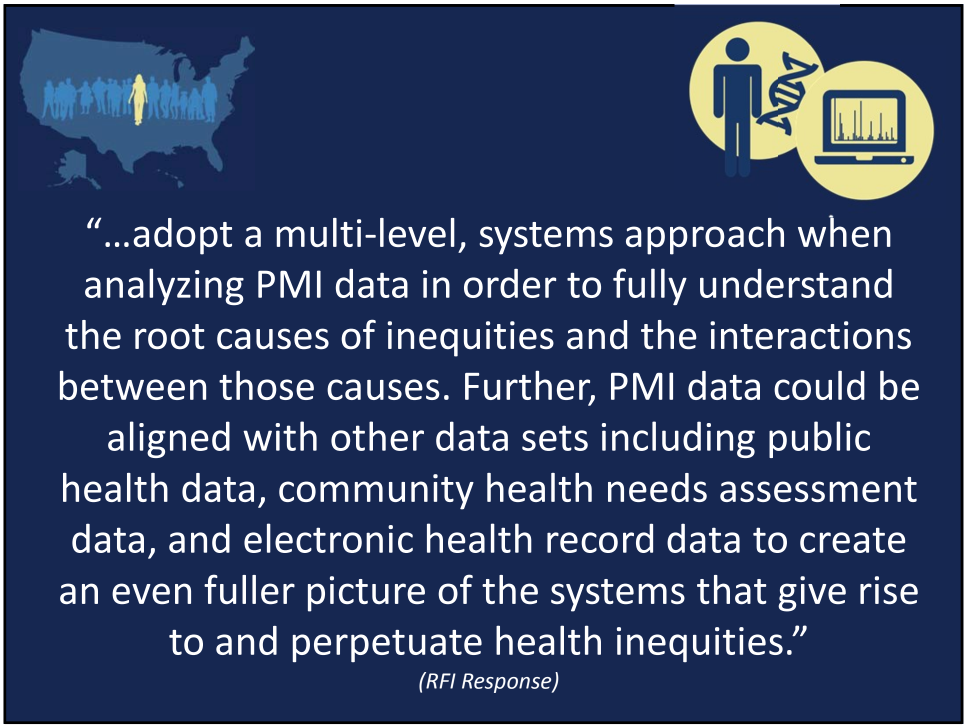
Research Opportunities

“PMI must include **sex and race/ethnicity differences** as key elements when developing research questions.



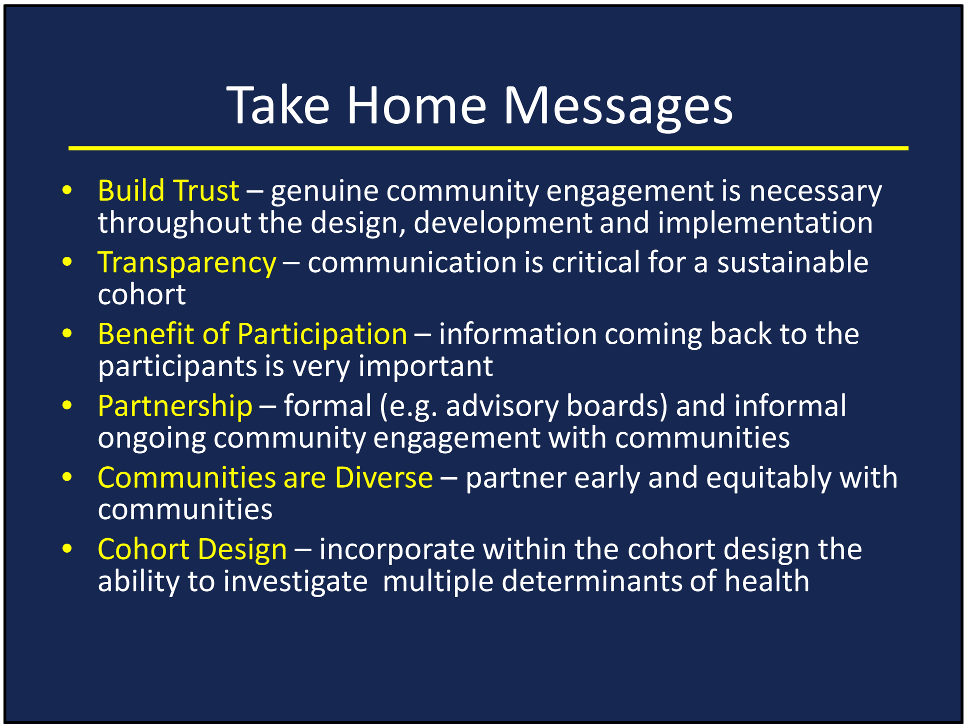
The PMI cohort provides an **opportunity to identify and test strategies to overcome study participation barriers**.

The PMI cohort provides an **opportunity to examine the neighborhood factors** that contribute to health disparities.



"…adopt a multi-level, systems approach when analyzing PMI data in order to fully understand the root causes of inequities and the interactions between those causes. Further, PMI data could be aligned with other data sets including public health data, community health needs assessment data, and electronic health record data to create an even fuller picture of the systems that give rise to and perpetuate health inequities."

(RFI Response)



Take Home Messages

- Build Trust – genuine community engagement is necessary throughout the design, development and implementation
- Transparency – communication is critical for a sustainable cohort
- Benefit of Participation – information coming back to the participants is very important
- Partnership – formal (e.g. advisory boards) and informal ongoing community engagement with communities
- Communities are Diverse – partner early and equitably with communities
- Cohort Design – incorporate within the cohort design the ability to investigate multiple determinants of health

Acknowledgements

- Regina James, M.D., NICHD and NIMHD
- Albert Avila, Ph.D., NIDA
- Paul Kimmel, M.D., NIDDK
- Ebony Madden, Ph.D., NHGRI
- Khara Ramos, Ph.D., NINDS
- Nishadi Rajapakse, Ph.D., NIMHD
- Della White, Ph.D., NICHD
- Joel Adu-Brimpong, B.S., NHGRI *(Intern)*

Question 1. The factors and incentives that would enable participation or make it more likely for people historically underrepresented in research to participate, including examples of successful models of recruiting and retaining participants from communities historically underrepresented in research

Obs	Q1A
1	Engage with trusted local community leaders (e.g., from not-for-profit organizations; religious institutions; tribes), gain their trust, train and employ individuals from the local community to conduct recruitment.
2	Don't ask this question to researchers, but instead ask the people who have been historically underrepresented in research what factors and incentives they consider to be important. The more this can happen directly between NIH and these communities--i.e., not filtered through investigators at local universities or local health care plans or local centers--the better.
3	Since 2004 we have been recruiting door-to-door, and then following at 5 and now 10 years a randomized, community-based Mexican-American health disparity cohort in South Texas. It now numbers about 3,500 and success in recruitment is over 70%. We have published over 40 papers describing the health of our population based on our cohort sample. We believe that our success is related to several factors: 1. Our recruitment team is drawn from the community we study and is known and trusted. The bilingual team members who recruit our participants had no previous experience but we trained them specifically in cohort procedures including administration of questionnaires, clinical examinations, data collection and venesection, and they all now perform to GCP standards. We have minimal staff turnover in a highly committed team most of whom have been working with us for 10 years or more 2. We created a Community Advisory Board when we started the cohort recruitment. It is over 10 years old and meets 4 times per year. We provide feedback from our research and solicit advice on dissemination, design and conduct of the projects. 3. We also have extensive intervention and prevention programs throughout our community many of them operated by community health workers and community volunteers and nonprofits. Success is due to trust within the community and the ability of our larger program to feedback health information and programs. 4. Since 70% of the participants have no health insurance of any kind, the most important incentive is provision of results (e.g. EKG, laboratory work), a small
4	The most effective strategy that enables Marshfield Clinic Research Foundation (MCRF) to engage the community and be successful in recruiting and retaining participants is trust. Marshfield Clinic Health Systems (MCHS) is committed to the provision of needed medical and health services to individuals regardless of their ability to pay for those services. A large percentage of current MCHS patients are low income and come from geographically isolated (rural) areas. The commitment to provide services has been expressed in a wide range of programs and initiatives implemented with the specific intent of aiding socially and economically disadvantaged populations, especially those with annual incomes below 200% of federal poverty levels. Family Health Center of Marshfield (FHC), a public health service §330 community health center, has partnered and been integrated with MCHS and Marshfield Clinic for more than 40 years in the vision to eliminate disparities in access and utilization of beneficial health services among socially and economically disadvantaged populations in its service area. MCHS’s commitment to providing an integrated healthcare environment to its rural communities has fostered trust. The second most effective strategy has been to listen to the voice of our research participants through focus groups, questionnaires, regular communication and advisory groups. These strategies have been used in many successful recruiting models aimed at retaining participants. The most visible is the Personalized Medicine Research Project (PMRP) recruiting 20,000 individuals and the NCI-sponsored Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial recruiting 17,000 participants.

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5	The AAMC encourages the NIH to ensure participants from historically underrepresented groups are engaged in all steps of the research cycle, including dissemination of research findings. Community input can be used to identify appropriate methods and measures, to clarify how groups and potential participants understand and perceive difficult scientific concepts, and to identify barriers to research participation and strategies to overcome them. We commend the NIH on the steps taken to increasing research participation among underrepresented groups, and recommend working with minority community organizations, respected leaders, and advocacy groups to continue the education process and report back the results from research studies. As the NIH continues to modify its community engagement strategies, AAMC also suggests comprehensive evaluation of the new engagement strategies to measure their effectiveness. Precision medicine is inherently complex and can be difficult for the general population to understand. Literature suggests that lack of familiarity with scientific concepts is a barrier to participation among racial/ethnic minorities. The AAMC suggests that the NIH, in collaboration with sub-populations it wishes to reach, prepare project-specific educational modules to help participants better understand the study purpose, time commitment, and logistics of participation. Additionally, we encourage the NIH to develop additional strategies to educate and engage non-English speaking participants and those with low general literacy.

Question 1. The factors and incentives that would enable participation or make it more likely for people historically underrepresented in research to participate, including examples of successful models of recruiting and retaining participants from communities historically underrepresented in research

Obs	Q1A
6	We suggest that The Precision Medicine Initiative leverage the emergency department research infrastructure available within existing CTSI sites and other emergency departments. Each year there are an estimated 136 million emergency department visits across the country, and many of these are to centers that have active participant recruitment programs. Such programs exist in urban, suburban, and rural sites, and also stretch into the prehospital setting. These centers serve every population regardless of social construct or grouping. Access to communities is unrivaled. Patients presenting to the emergency department have a diverse range of symptoms and underlying illnesses. Patients of all ages, races, ethnicity, religious and economic backgrounds can be found in our nation's emergency departments. This diversity is not found in any other single healthcare venue. The nations' emergency departments offer an existing infrastructure with all the necessary tools for biological samples collection that could be used to recruit a strategically diverse population, continuously, 24 hours a day. For all these reasons, The Precision Medicine Initiative should heavily consider engaging the nation's emergency care research community as a point for biological sample collection and recruitment into the cohort.
7	Engaging historically underrepresented groups requires reducing or eliminating two broad categories of obstacles to their involvement: economic and social. For many underserved populations, economic obstacles begin with informational asymmetry -- a lack of knowledge that such opportunities to participate even exist -- and run through opportunity costs -- the tradeoff between participating in research as a volunteer and engaging in economic activity. Social obstacles include perceptions, perhaps rooted in historical realities, that participation in research is harmful or potentially harmful. For overcoming both information asymmetry and perceptions, social media will play an important role in reaching out to these populations. Identifying leaders in unnderrepresented communities with large followings on social media will enable rapidly reaching these communities while simultaneously deploying the trust of the leader to combat negative perceptions. For overcoming opportunity costs, it is critical to minimize opportunity costs: taking full advantage of mobile health technology and electronic health records to automatically and seamlessly reduce the ongoing and instantaneous burden of participation will be critical in engaging the economically disadvantaged participants that have traditionally not participated in research.
8	1. Our team blends pop culture, media, and public policy know-how to design and build innovative programs and platforms that link the real deeds and actions of the organizations we serve to positive outcomes for society. Our work product has engaged and enlisted broad numbers of previously uninvolved citizens in efforts to transform behaviors, public policy, and shift the status quo. For example, members of our group produced history's biggest live music, TV, web, and mobile events enlisting a global audience of 3 billion people in the fight against extreme poverty (Live 8) compelling the G8 nations to change debt policies in the developing world and doubling aid to US$50 billion to the world's poorest countries while spawning both the Make Poverty History and the One campaigns. Many of our other efforts have also achieved worldwide recognition like conceiving the world's first consumer device capable of multiple medical diagnosis (Qualcomm Tricorder X Prize), "greening" the first professional sports team (NFL's Philadelphia Eagles), collaborating to create television's defining charity event (American Idol Gives Back), implementing recycling in New York City, envisioning America's most successful youth voter registration organization (Rock The Vote), and developing an international online movement now in excess of 1.4 million people (Stop Global Warming.org).
9	We appreciate the opportunity to provide information on community engagement strategies to the NIH as it considers strategies for establishing a Precision Medicine Cohort. We applaud the transparency and thoughtfulness of NIH leadership and others involved in creating this Cohort, particularly the attention being given to community engagement and increasing involvement among underrepresented communities. Many biomedical research centers in the US have created community engagement infrastructure to engage local partners. Leveraging these existing structures will be critical to the success of the Cohort, as community engagement is inherently local and reflective of local values, needs, and relationships. We welcome the opportunity to partner with NIH and would be happy to share some of the strategies we use to engage the patients and communities we serve in discussions about biomedical research.
10	Lack of reliable access to health care will be a barrier to successful and long-term participation of those already underrepresented in research because they are underserved by our health care system. Should we consider forms of compensation to research participants, such reliable access to health care at participating hospitals, participant compensation, travel costs, costs associated with "wearables" and other devices that will track research participants' activity levels and diet?

Question 1. The factors and incentives that would enable participation or make it more likely for people historically underrepresented in research to participate, including examples of successful models of recruiting and retaining participants from communities historically underrepresented in research

Obs	Q1A
11	The precision medicine cohort needs materials transfer agreements that reflect a "Digital Human Being" - a new legal entity that is entitled to unique rights and protections.
12	
13	
14	• Incorporate community and patient and family engagement in education efforts and allow time for informed decision-making. Adopt individual/family/community awareness models. Individual's need awareness and informed opportunities to make informed decisions to participate in research. Awareness efforts should be trustworthy and address scientific, civic, and cultural literacy to help individuals anticipate their roles, rights, and risks as participants. Intentional efforts should be made to include community leaders and trained lay health advisors to facilitate engagement and participation in precision medicine. These concepts have been tested with promising success in the development of a minority recruitment registry (Project CONNECT) and community-based intervention, Community Bridges to Cancer Clinical Trials. Similar considerations should be considered to engage providers in precision medicine. • Retain contact with participants (between activities, after data collection) • Provide opportunities for investment (creation of a product) engagement in patient-centered questions and outcomes • Appoint a community PI; pair community/research investigators to strategize the research design and pragmatic issues in research design/implementation. Our institution has achieved success with Community Advisory Boards (CABs) and the Charrette Model. • Patient navigators to help participants get care for problems identified through participation in the study, long-term assistance • Ask/learn about what incentives would encourage participation in this type of research and consider all participation costs including transportation, parking, time lost from work, day care services, respite care
15	The HMO Research Network (HMORN) (soon to be the Health Care Systems Research Network - HCSRN) includes research centers embedded in 18 large not-for-profit healthcare systems in the U.S. serving a combined population of over 15 million members (ages 0-80+) in over 25 states. This represents about 1 in every 22 Americans. Several HMORN sites serve predominantly rural populations, and many include or collaborate with safety net and critical access hospitals caring for chronically underserved populations. The geographic diversity of the 18 HMORN sites also provides access to racial/ethnic populations underrepresented in most research, including people of African American, Asian/Pacific Islander, Native American, and Latino/Hispanic backgrounds. When examined across a number of sites combined, only half the members are non-Hispanic white. HMORN health plans also maintain substantial Medicare and Medicaid enrollments, as well as significant enrollment growth stimulated by the ACA. Increasing representativeness and engagement of underserved populations in research is an active area of HMORN research and they have developed successful models of recruiting and retaining health system members and research participants from these communities.
16	IMPLICATIONS of including Asian Americans in the cohort study: (1) In addition to the fact that the population is one of the fastest growing population in the US today with a potential of providing significant health data on the rapid changes in the health status of the US public, (2) it is it is ethnically, culturally, and linguistically diverse, (3) its gene pool is perhaps the widest of any population, (4) it originates in a wide range of physical environments (arctic , desert, tropical; mountainous, plains), (5) has wide and diverse lifestyles and spiritual beliefs that significantly impact activities of daily living and diets, and last bit not least, (6) a population that had shown resiliency in both acculturation as well as cross-color associations, including marriages.
17	Make it approachable and relate the effort to something that has been very successful. Organ donors. We routinely ask people from all areas of our society to sign up to be an organ donor. It is routine and understandable. We should now ask a similar question: will you be a data donor? This could be asked to occur at death, and then be explained to do so now. But by framing the request in the concept of being a donor it will become immediately relatable, and understood to be something of a sacrifice that helps the health of others.

Question 1. The factors and incentives that would enable participation or make it more likely for people historically underrepresented in research to participate, including examples of successful models of recruiting and retaining participants from communities historically underrepresented in research

Obs	Q1A
18	Access to healthcare and wellness programs should be universal and not depend on geographic or economic status or technology availability. Sustaining a universal approach to healthcare can be accomplished through community education and awareness programs, through mobile & wearable devices and technologies, and the collection of data for research. Outreach programs at community clinics, mobile health clinics, Federally Qualified Health Centers, local civic organizations and churches, etc. can be utilized to drive education and awareness to underrepresented populations. Providing free or low-cost devices and technologies to typically under-educated or less tech savvy populations incentivizes them to participate in prevention and rehabilitation programs for stroke, diabetes, and other diseases that occur frequently in these communities. Networks of healthcare providers and/or volunteers at community clinics, churches, and civic organizations and cross-generational family relationships can be leveraged to train, mentor, or assist less tech-savvy or physically disabled patients in technology usage. An example of a community health model is SOS Austin, a community health initiative that provides vital tools to everyone, no matter what age, gender, ethnicity, socio-economic background or community location. (http://www.strokefestival.org) The Nutrition Education Program at People's Community Clinic is dedicated to working intensively with patients as they develop the confidence to make long-lasting lifestyle changes that will improve their health. https://www.austinpcc.org/special-programs/nutrition/
19	A strategy for recruiting underrepresented participants in precision medicine research should have several key features. It should a) Be rooted in and build upon knowledge of the history, culture, socioeconomic conditions, politics, social networks, demographic trends, norms and values of the communities in which underrepresented participants live. b) Entail a broad based effort to establish relationships within, and build trust with these communities, relying on formal and informal leaders, community organizations, etc. Organizations that have established trust relationships with prospective participants should be identified and enlisted as collaborators. Coalitions—formed of individual leaders, community organizations, etc.—are important in developing support for, awareness of and shared commitment to precision medicine research. c) Deploy these relationships in a multilateral exchange about the purposes of precision medicine research, the value of that research for these communities, and the benefits, risks, and burdens that may accrue to individual participants. It should use these relationships to identify and clarify factors that may enable, impede or complicate participation by individuals and groups. d) Use multiple venues, methods and media to inform and educate individuals and groups. e) Meet, inform, engage, and recruit prospective participants in settings integral to their daily lives: schools; faith-based settings; organizations for both children and adults (e.g., Girl and Boy Scouts, Elks' and Moose Clubs, etc.); commercial venues; work settings; and clinics, hospitals, and physician offices. f) Specify the ways in which recruited participants will continue to be engaged in, and informed as research moves forward and continues to evolve.
20	Underrepresented communities tend to be vulnerable, and investigators and funding agencies proposing long-term studies in the community must develop trust with community members and leaders. Communities feel less than served by investigators and government-funded studies that appear to take their data and samples and disappear. Most studies that have included underrepresented communities and that have been successful for the long-term have included continued contact with the community including dissemination of results, input and feedback from the communities on proposed and ongoing studies, involvement of community health professionals in the research, and development of resources resulting from the studies that are returned back to the communities.

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Obs	Q1A
21	A. Participants should be actively and regularly updated and solicited for feedback. There should be a legitimate process for registering concern. B. Involve diverse communities and stakeholders in this planning process. C. Consider re-defining the structure of the program away from the traditional "researcher/participant" model, to a "researcher/citizen scientist" model, ensuring that participants are involved in all aspects of planning and implementation. D. Consider "snow ball" recruitment tactics where participants are encouraged to reach out to their networks and communities to help with recruitment. E. Contact the for-profit and academic genetic testing laboratories for input regarding the communities who may be the best candidates for prioritizing recruitment efforts. Often information about patients' ethnicity is collected and the laboratories may provide statistical information of demographic information of genetic testing consumers. F. Consider approaches that allow people to participate in portions of the PMI, such as an "opt-out" protocol that allows participants to only take part in research efforts they support. Genetic counselors are trained to describe testing options in a way that is clear to patients and participants, so consider partnering with trained counselors for this aspect of the program. G. Explaining to potential participants that testing can provide valuable information for families, not just individuals. Genetic counselors are specifically trained to discuss this aspect of genetic testing, so consider partnering with trained counselors for this aspect of the program. H. Provide culturally appropriate materials in the native language that may be accessible through social media or smart phones.
22	Language People, Inc. is a 27 year old language services company with a patent in the field of Video Conferencing and Video Interpreting and Video Medicine. We believe that the deaf and hard of hearing are significantly left out of the healthcare process to such an extent that they suffer severe hardships around their health.
23	This response is provided from the context of the Washington Heights Inwood Informatics Infrastructure Comparative Effectiveness Research (WICER) project (R01HS022961, R01HS019853). As part of the WICER community survey, Latinos were asked by a bilingual community health worker if they were willing to provide saliva and/or a dried blood spot for long-term storage and use for health-related research. They were also asked if they are willing to have their survey data linked with clinical data from the Clinical Data Warehouse of Columbia University Medical Center and to be contacted for future research by other researchers. We conducted a binomial logistic regression with consent for all purposes as the dependent variable. Predictor variables were: gender, age, education, marital status, Medicaid/Medicare status, immigrant status, and health literacy. In the sample of 2,271 Latinos who were primarily female and immigrant, the consent rates for data linkage, future research contact, and long-term storage and use of blood and salvia samples for health-related research purposes were 96.3%, 87.5%, and 53.2% respectively. Higher health literacy significantly increased the odds of consent in all three instances: data linkage (OR=1.14[1.06-1.24], p=.001), future research contact (OR=1.17 [1.04-1.31], p=.008), and long-term storage and use of biospecimens (OR=1.35[1.09-1.67], p=.006). Government insurance increased the odds of data linkage and biospecimen storage and use, but not research contact. Immigrant status also increased the odds of data linkage and male gender decreased the odds of consent for future research contact.
24	Trust is particularly critical given the unfortunate legacy within medical research where participant rights have not been equally protected. Trust requires time and effort to develop, but is easily lost. It is usually less effective to create community partnerships and alliances at the time that research opportunities arise; it is much better to build on existing partnerships, going well beyond the needs of a single project. There are many trusted entities within minority communities that could be engaged in recruitment efforts, (e.g. faith-based leaders, community health workers, unions, minority-run and focused business leaders, health care providers). All recruitment partnerships would need to be equipped to recruit and answer questions from those who trust them, and their time compensated. Relevance of research to one's community is also a critical part of efforts to engage diverse communities in research. Given the extensive volume of research that has been conducted with relatively little benefit for minority communities, and in some cases resulting in a widening of disparities, it will be critical to demonstrate that participation will realize benefits for all communities represented. Recruiting and retaining participants will also require researchers and clinicians to protect patients' privacy. At the same time, we must acknowledge and mitigate the risks, and address concerns of social and individual harm that could arise from research findings. This should also be balanced with including information in the consent regarding the benefits from any discoveries made.

Question 1. The factors and incentives that would enable participation or make it more likely for people historically underrepresented in research to participate, including examples of successful models of recruiting and retaining participants from communities historically underrepresented in research

Obs	Q1A
25	The Community Health Ambassadors Program (CHAP), co-created with community input and the Duke Cancer Institute' s Office of Health Equity and Disparities, provides a basic cancer and research/clinical trials training to members of the community. The program is modifiable to suit faith, business, and community organizations and essentially links people to services. Ambassadors are selected by faith, community, and business leaders and are trained at a one day, five-hour course that educates participants about cancer risk factors, symptoms, screenings, treatment, research, and clinical trials. Ambassadors, develop a team and implement awareness events and programming in the community and are directly linked to Patient Navigators (PNs) who help them both execute their programs and connect people to resources and services related to cancer screening, care, and research.
26	I would like to share a resource that may help in this effort. It is a document that was created between a partnership between the National Congress of American Indians and Montana State University on building research relationships with American Indian communities. The PDF can be accessed here and a description is below: http://www.ncai.org/resources/ncai_publications/walk-softly-and-listen-carefully-building-research-relationships-with-tribal-communities Increasingly, tribal leaders acknowledge that research is a key tool of tribal sovereignty in providing data and information to guide community planning, cross-community coordination, and program and policy development. Efforts to address longstanding issues, such as health disparities for American Indians and Alaska Natives (AI/AN), have increasingly used partnership research approaches. This document seeks to strengthen these partnerships by providing insight about how culture, sovereignty, and experience matter in research with Native communities. It features two cases of effective partnerships – Messengers for Health in Montana and RezRIDERS in New Mexico – and two vignettes including the reflections of a tribal community organizer and Native researcher. The appendix includes resources and an abridged annotated bibliography with information on research on Indigenous knowledge, research policies and protocols developed by Native communities, and insights on negotiating research relationships with Native communities.
27	1. Establish a consistent and sustainable presence in communities of interest that last beyond the collection of data a. Develop relationships with leadership of existing community based organizations - churches, community centers, local non-profits, etc. T b. Clearly communicate the request and BENEFIT TO THE COMMUNITY. For minority populations that have been victims of medical malpractice, abuse, exploitation, racism, etc. from the medical community, highlighting the positive effect clinical research on minorities can have on the ENTIRE population may not be a good strategy. It is reminiscent of past experimentation on racial minorities for the benefit of society as a whole, which was wrong (i.e. USPHS Syphilis Study, Johns Hopkins procedures on African Americans). Researchers should instead focus on possible benefits to individual communities (African Americans, Latinos, Native Americans, etc.). c. Ensure community relationships are RECIPROCAL. Support existing initiatives in communities of interest through technical assistance, financial support, and marketing. Learn the needs of communities, including health, financial, education, etc. and determine what goals of research align with existing needs. 2. Provide financial incentives to participants and community leaders An example of strategies to recruit and retain minority communities for clinical research. See Table 2: Moreno-John, Gina (11/01/2004). Ethnic Minority Older Adults Participating in Clinical Research. Developing Trust. Journal of aging and health. , 16 (5), p. 93S - 123S. (ISSN: 0898-2643)
28	As an organization that funds tens millions of dollars in research on maternal and child health every year, the March of Dimes is keenly aware of the challenges of recruiting historically underrepresented populations to participate in research. In our experience, the researchers we fund are most successful in this endeavor when they follow a handful of basic principles: • Approaching members of underrepresented communities in ways that are culturally sensitive in a language understood by the members of these communities; • Describing the purpose of the research in a way that's compelling to that group; • Partnering with organizations or entities that have direct ties to the populations in question; • Partnering with organization or entities that are trusted by the public; • Providing clear, understandable materials that are explicit about how the information will be collected and used, including how privacy will be protected.

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Obs	Q1A
29	There has to be protections such as the ones state in the Nagoya Protocol for human genome data and products from that data whether diagnostics, therapeutic or in synthetic biology for people of the Americas. Especially American Indians who have tribal sovereignty and international political/legal status because there is likely an abundance of novel variants at high frequency and much mechanistic information to be gleaned from their genomes. They are the poorest of the poor in every North and South American country and they have no great representation in law, governance, business or medicine that their voice and interests will be heard. Simply put, we do not trust "altruistic" endeavors based on resources from the Americas...because historically we have been left out on our land. The US has so far failed to adequately consult with tribal groups on this issue. To create incentive , you most go past individual rights to privacy an consent contained in GINA and protect communal rights.
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31	Hi there- I have a simple suggestion for this big question you are asking-- try community engagement through the arts. In addition to individual artists, there is an established network of private and governmental orgs from the NEA to SouthArts to local councils, etc. Artists are really good at diversity and communication, and they often have more flexible schedules. I live in rural South Carolina and know the arts community here very well-- and I know we're not the only historically un-represented artists by far. I do not have all the tools to put together an artist engagement program for precision medicine purposes, but am interested in contributing to one. I have been covering artists, healing and healthcare reform in a series I am writing for the Beaufort Gazette and Hilton Head Island Packet.
32	Factors -Understand the local context and realities - weak and non existent of community and involvement -Cultural and behavioural determinants to precision medicine utilisation - Fear, suspicions, anxiety and expectations to precision medicine opportunities (magic cure bullet) -Perceptions, involvement and the relationship between people and sources of information precision medicine - Structural factors including stigma and discrimination from affected families - Language and translational issues relating to the disease, informed consents and information - Lack or limited support structures for precision medicine alia - Weak leadership and governance programmes of communities and other government parastatals Incentives Outreach and awareness and education on genomic education and research enhancement, Health promotion and advocacy in precision medicine Recruitment and retention of minority participants strategies
33	We have shown that intergenerational volunteer programs placed in one's community, like the Experience Corps: Baltimore, can be attractive to minorities and low socioeconomic status groups at highest risk of health disparities and that the impact of this service on individuals' activity and health can be evaluated over repeated assessments using accelerometers, blood draws, and brain imaging (www.carlsonlab.org).
34	The "Precision Medicine" initiative will require the inclusion of racial and ethnic minorities in "Clinical Trials" to ensure the development of relevant treatments for diverse populations. To effectively reach these communities, and develop trusted relationships, the "Precision Medicine" initiative will need to employ A Broadcast to Broadband (B2B?) framework. B2B? is a two stage health communications model utilizing traditional broadcast, emerging alternate spectrum options, and Social, Local, Mobile (SoLoMo) apps to Engage, Educate and Empower (the 3E's) medically underserved communities by using an "Integrated Programmatic Marketing Strategy" (IMPS). The framework for the design, implementation, and quantitative evaluation of B2B's effectiveness is the Nielsen "3R SYSTEM"—REACH, RESONANCE, AND REACTION --the gold standard for analyzing and translating actionable data to enable better deployment, execution and optimization of persuasive multi-modality communications. Consequently, B2B? dramatically improves "Return on Marketing Investment" by allowing decision makers to more efficiently allocate resources and develop content based on quantitative measures of effectiveness. In addition to the efficient allocation of resources, the medically certified SoLoMo apps for smartphones, tablets and laptops can establish and sustain long term patient engagement with applications including: o Social networks for personal motivation and community support; o Location based services for improved patient awareness and access to community services; o Mobile apps for personal health monitoring, wellness, home health and chronic disease management. B2B? is a collaboration between the Cobb Institute of the National Medical Association (NMA), the National Association of

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Obs	Q1A
35	I think you can make the case that the *entire* cohort could be from the deep south, where there is a great representation of African-Americans (with the most diversity of genetics, and with great diversity in environmentally-related outcomes). The statistics for the area south of Tennessee for smoking, cancer, and other environmentally-relevant health issues are also stunning. This would be a statement to the American people that we are going to boost up the area of our country that is in most need of help, and at the same time learn lessons that will help all Americans. I think you could add Florida and Texas in order to ensure Latino involvement. Why not have this cohort be HIGHLY enriched for those whose health needs the most attention?
36	The first and foremost barrier to enrollment is the lack of provisions in GINA. This act needs to be expanded to protect sale of life insurance, disability insurance, and long-term care insurance. In my experience enrolling research participants for Whole Genome Sequencing (WGS), I have found underrepresented populations to have an increased mistrust in both research and giving their information to "the government." Fears regarding government access to their DNA include privacy concerns, discrimination concerns, profiling, uses of material for criminal investigations, and paternity matters. Well-defined guidelines regarding the storage, sharing, and potential future usage of data will be required to earn the trust of these subpopulations, who have historically been either neglected or abused by researchers. Regarding research, there are those leery of research in general, and there exists a small population that fears experiments like cloning and genetic modification of their personal DNA for secretive research purposes, so education will be the key to success. All information presented to the public should clearly explain the intentions of the study, rights and responsibilities of the researchers, and it should clearly state how the information will not be used.
37	Booz Allen understands that inadequate representation of historically underrepresented groups in research studies limits the validity and generalizability of research. Booz Allen staff have experience managing health disparities studies. Through this work we identified a number of techniques for promoting participation among historically underrepresented groups: 1) Work with community advisory groups, and leaders to identify community ambassadors to assist with study recruitment and management and share culture with support staff; 2)Conduct initial surveys to identify incentives (e.g. both cash and non-cash incentives); 3) Develop tailored study communication and outreach tools that are culturally and linguistically appropriate. Booz Allen developed a VA mobile solution to aid with veteran-patient reported behavioral assessments. 4) Host study sessions in a centralized location and schedule sessions to accommodate participants' schedule. 5) Assess recruitment economic feasibility: plan for incentives and study time support (e.g. provide free meals or childcare for populations that may not participate in research due to household responsibilities). Several seminal research projects highlight how to successfully recruit and retain underrepresented groups: 1) Vietnamese REACH for Health Initiative (VRHI) Coalition: used a multimedia campaign; 2) The REACH 2010 Latino Health Project used telephone/face-to-face recruitment; 3) WISEWOMAN: used evaluation stakeholder group approach; 4) The Jackson Heart Study used mailings, door-to-door, and community events; 5) The Choctaw Nation Core Capacity Building Program used a website and events.
38	Many assume that financial incentives are key to recruitment and retention. However, while incentives are important, and perhaps more so to low-income participants, the research is mixed regarding the most effective methods of concretely incentivizing participants and therefore financial incentives should only be one piece to retain longitudinal study participation. Other effective methods include providing information to the respondent, managing expectations, frequency of contact, cultural competency of the staff, flexible scheduling, and retention events. Incorporating all of these should be considered in the initial design of this cohort. Motivational research has identified various factors, including expression of one's intrinsic values, protecting oneself from harm, developing social ties, and gaining knowledge, that affect an individual's decision to participate in research. It will be important to apply this motivational theory to the recruitment process; recognizing that individuals are motivated in different ways and adjusting the recruitment approach as needed. For oversampling purposes, NIH may consider utilizing the CDC NPCR to identify cancer patients for recruitment, as well as other disease registries whose members have high motivation to participate in research. Battelle has had success in recruiting diverse samples for population based studies through geographically based door-to-door, school based, and telephone recruitment efforts. This includes for the African American Eye Disease Study, the Los Angeles Latino Eye Study, and the Chinese American Eye Study which each aim to provide a better understanding of the biology of eye disease. Another successful study examined cultural influences of African Americans' decision to screen for co
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Obs	Q1A
41	When trying to contact individuals to invite their participation, use multi-methods; ex. email, phone calls and texts. Some people may not be comfortable with some of the current methods of participation and benefit from being contacted by multiple methods. Provide choices for how and if they want feedback; be prepared with resources and offer to make referrals as an incentive for participating. Offer a drawing for those participating to have the opportunity to win a fit-bit, athletic shoes or equipment, etc.
42	1) Accessibility: Consideration for dependent care, before/after working hours and on weekends, compensation, transportation, minimizing the time needed to participate in the research, ensure efficiency in process for performing research activities. 2) Appreciation/Hospitality: Ensure the research location is staffed by friendly, inviting, and personable people, and people most likely to connect well/appreciate the interests of the desired population. Offer magazines (in different languages), TV, coffee, juice, snacks, etc. while participating in study activities. Establish "meet and greet" encounters between with the actual investigative team and participants so participants can see who they will be interacting with if they elect to participate. Extend appreciation or send thank you cards to participants so they're more likely to help recruitment among their peers by feeling valued and speaking positively about their participation. Or offer a thank you breakfast/lunch, etc. once participation is complete. 3) Recruit patient champions – participants who have participated and are willing to be trained to recruit others. 4) Education. Offer education about diseases and the research 5) Focus groups: Before starting the project, conduct focus groups among those targeted for recruitment, and ask them what would help them decide to participate and what would discourage them from participating. 6) Recruit consultants/study staff specifically to plan, implement and evaluate recruitment initiatives (i.e., local recruitment representatives Example: http://www.ncbi.nlm.nih.gov/pubmed/16317982
43	Thank you for the opportunity to comment on this important issue. We have been studying how to locate, engage, and increase motivation for participation in medical research among under-represented groups for over 10 years. We focus on African American/Black and Latino populations. Of course a specific sampling plan depends on the geographical location and population of interest, but some general principles apply. For populations who may have competing priorities, or be wary or mistrustful, peer recruiters can be critical. These can be both trained, professional peer recruiters, or you can use a peer-to-peer recruitment method such as Respondent-driven sampling. Locating population members is step one. We use strategies informed by Motivational Interviewing to engage participants in studies. We have also developed intervention components to increase motivation to participate in clinical trials. We think that compensation is important but building trust and relationships is more important. Gwadz, M.V., et al. (2014). HIV-infected individuals who delay, decline, or discontinue antiretroviral therapy: Comparing clinic- and peer-recruited cohorts. Frontiers in Public Health, 2(81):1-14. DOI: 10.3389/fpubh.2014.00081, PMCID: PMC4100062. Gwadz, M.V., et al. (2014). ACT2 peer-driven intervention increases enrollment into HIV/AIDS medical studies among African-Americans/Blacks and Latinos/Hispanics: A cluster randomized controlled trial. AIDS and Behavior, 18(12): 2409-2422. DOI: 10.1007/s10461-014-0829-5. NIHMSID: NIHMS608760, Publ.ID: 2014-06-25_0001.pub
44	The American Cancer Society Cancer Action Network (ACS CAN) and the American Cancer Society (ACS) encourages the recruitment and participation of historically underrepresented research groups in the Precision Medicine Initiative. It is vitally important to engage community leaders and research study advocates in the entire process to help design appropriate models of recruiting and retaining study participants. These leaders and advocates can help with messaging why it is important that members of their communities should participate in research and can help to frame that messaging in relation to historical studies in which disadvantages communities were treated unfairly (e.g., Tuskegee). It is also critical that enrollment opportunities are made available in diverse communities, and in places frequently visited by community members (e.g., churches, schools, worksites, YMCA). All study materials must be appropriate for diverse study populations, and if necessary translated into multiple languages to assure that members from all cultural groups are represented. Finally, retention requires frequent contact through regular mail and through email to assure that study outcomes can be captured appropriately.

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Obs	Q1A
45	Factors and Incentives: • Engage community in the initial planning and all other aspects of the research process of the study; • Employ persons from communities where studies will be conducted • Insure equal partnership as a community/participant in the research which includes equal voting and decision-making opportunities (MOUS, contracts, etc) with specific actions to address violation or breach of either • Budgetary/fiscal sharing • Engage community in the initial planning and all other aspects of the research process of the study; • Employ persons from communities where studies will be conducted • Insure equal partnership as a community/participant in the research which includes equal voting and decision-making opportunities (MOUS, contracts, etc) with specific actions to address violation or breach of either • Budgetary/fiscal sharing • Transparency in all phases of the research • Cultural competence which according to the NIH: benefits consumers, stakeholders, and communities and supports positive health outcomes and is critical to reducing health disparities • Stipends to support travel to site • Easy access to site (preferably in or near community of residence • Opportunities to participate and advance the research through: presentations; manuscript development; planning sustainable research activities
46	Community partnership, trust, transparency and familiarity with research are perhaps the most significant factors in expanding underrepresented minority recruitment and sustaining minority participation in a nationwide 'cohort' study. The Jackson Heart Study (JHS) incorporated these elements to obtain optimal enrollment of 5,301 African Americans and maintain a 77% retention rate after 10 years. Although JHS focused on cardiovascular disease (CVD) in African Americans, the participant population was diverse in sex, age, socio-economic status (SES) and level of education. Before JHS, Jackson was selected as one of four sites for the Atherosclerosis Risk in Communities Study (ARIC), a longitudinal 'cohort' study to investigate the causes of atherosclerosis and progression in a diverse population. The Jackson community was already familiar with population research and the benefits to its community. JHS formed community and business partnerships to support the study's mission. A Partnership for Community Awareness and Health Education (PCAHE) approach, involving local residents in solving problems in each phase of the study, was implemented. PCAHE also included educational activities on healthy lifestyles and CVD, in addition to keeping the community well informed about the study's progress and outcomes. These outreach activities brought awareness and a sense of trust and transparency between JHS and the community. The San Diego Blood Bank (SDBB) and other blood centers across the nation have already established fruitful partnerships with their community and local businesses to support the blood centers' mission, saving lives with quality services in partnership with hospitals and research institutions within the community.
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48	The biggest barrier to participation by underserved populations is TRUST. The memory of Tuskegee is still fresh and serves to keep people reluctant to participate in clinical trials and registries which they feel might be used against them. Having this program instituted by President Obama is a healthy sign which hopefully will help to build their trust. Incentives like discounts on insurance or inclusion in some healthcare program would help to encourage people to join.
49	In the literature about chemical dependency, recruitment for studies has often drawn from populations that may not be well represented in other aspects of medicine, i.e., low SES, minority populations. Recruitment has often targeted these groups directly, through clinics and agencies that serve them, and usually offer some kind of monetary or other consumable reward for participation. Follow-up in these populations can be challenging, as they are often less stably housed, so provisions for this should be built into the plans. Additionally, the current opioid epidemic seems to be involving populations that traditionally have not been recruited for substance use research, i.e., more affluent, Caucasian, young people. Recruitment through high school and college campuses as well as at job fairs offering entry-level jobs might get to this group.

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Obs	Q1A
50	Ensuring that structural factors such as coverage for transportation costs and childcare are covered by the research study could be a mechanism to facilitate participation in research. Participants should be allowed to provide feedback to the research study (perhaps through a form of an exit interview). For example, participants could be anonymously surveyed at a later time point about what they liked and did not like about the research study, how they were treated by doctors and staff, etc. They could provide input to the nature of the questions presented on questionnaires that may be sensitive in nature (e.g., Were any of the questions in the X scale considered offensive?). For recruiting participants, it is important that there is a community presence among the research team. This could include efforts such as making presentations at the local church, participating at local food banks, distributing flyers and talking to participants at community organizations, going to clinics and setting up an informational booth about healthcare, etc. For retaining participants, it is important that they are made aware of research findings when they become available. Perhaps a research community blog, or a write up in a local magazine that community members read could be some ways of sharing information. These strategies should be outlined in the research study plan.
51	-Regular sharing of the data with the U.S. precision medicine cohort (mobile devices with app containing simple analytical tools). - Emphasis on diseases/condition/environmental and nutritional factors that disproportionately affect historically underrepresented communities
52	The Center for Health Equity and Community-Engaged Research at Mount Sinai has a library of successful engagement strategies to recruit patients to diverse studies, including diabetes prevention, genomics, cardiovascular disease, cancer, and maternal and child health. We regularly recruit patients historically underrepresented in research including through food pantries, churches, schools, social clubs, barbershops, and local organizations. We are happy to share our specific recruitment strategies with NIH.
53	Recruitiment and (especially) retention of participants for a long and difficult-to-understand medical research project is difficult even in the most engaged communities. “Gamification” is certainly one tactic that can make a difference; there are experts here. An even more important, basic strategy, and one which a frankly applies equally to the needs of researchers and any clinicians or technicians involved as to the needs of PMI participants, would be to employ interactive techniques for visualization and visual analytics. Reliance on tables, bar charts, pie charts, etc., would be ruinous to PMI participant engagement, given the data-intensity of the research. Excellent work in this area has been done by Ben Shneiderman, a renowned expert in human factors of computer use, at the Univ. of Maryland (https://www.cs.umd.edu/~ben/Shneiderman2013Improving.pdf); Shneiderman should definitely be consulted for the PMI. NIH has funded relevant work: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3046402/. A startup working in data visualization, Exaptive, Inc., has done highly innovative work in medical applications (Osher Center for Integrative Medicine, Harvard) and is, uniquely, building “apps” that could be used to enable PMI participants (and researchers) to design their own displays (http://www.boston.com/business/technology/innoeco/2013/12/cambridge-based_exaptive_wants.html). Established “big data” companies such as Tableau Software and Splunk, may have people who can speak to these topics as well. I would add that since large volumes of data will be integral to precision medicine in practice, the PMI risks being a “bridge to nowhere,” if it does not place heavy emphasis on data visualization and other cognitive issues. ==John L. Burch
54	In reading clinical studies, I’m surprised when information on the education, income, and employment status is not always provided. I think it would be very reasonable for NIH in progress reports ask for this data (in addition to race/ethnicity & gender) and if the sample does not have a sufficient proportion of impoverished participants, request information about how the investigators plan to address this. Certainly some studies avoid low income participants, view them as difficult populations, and do not have the training to work with vulnerable populations.

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Obs	Q1A
55	a. Ensure materials area available at low literacy, in multiple languages, and in multiple mediums. Do not require literacy for participation. b. Avoid the fate and reputation of much research, considered by communities to be "drive-by research" that leaves no impact on the communities where researchers recruit. c. Guarantee that all participants will have access to the precision medicine database, just as researchers do. d. Commit that all findings will be shared, specifically with every research participant, through regular updated communication in plain language (and multiple languages), and more broadly with the communities they come from. e. Work with community to determine the appropriate stipends for community partners leading these efforts and for participants. f. Offer stipends that recognize the time these efforts require. g. Build strategies and messages with community partners from the target groups and with communications experts. h. Make sure images of the study reflect the diversity of participants we should enroll. i Make this fun! It should be viewed as a party that can't be missed, and even better, as a team that they need to join, as they want it to win, and without each unique person, it cannot win. j. Send thank you, birthday and study anniversary cards. Go to patients. Make it easy. Have church Sundays, street fairs, and other events to engage populations. Have evening and weekend recruitment hours.Use lotteries to incentivize. k. Engage leaders of leading biobanks (such as Bottinger's BioMe at Mount Sinai) who have recruited diverse populations, with great success,
56	Aside from dollars: --Community education is an effective incentive to sustain participation. Focusing on the potential benefit participation to them personally. Suggesting the study benefits medicine and science in general is not enough incentive. --Information coming back to participants is very important, for example sending an update newsletter is an incentive --Inviting families to talk about decision to participate --Using a formal consultation process with tribal communities. Tribal organizations have consult groups who look at studies and consider participation. Federal agencies like CDC uses this formality and it seems to pay off in increasing acceptance --Respect is a factor --Building trust is a big factor!!
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58	•Analytic efforts of State DHHS and national CMS patient databases could be leveraged to identify patients meeting specific criteria for trials. Outreach could be performed via EMR alerts. •Additional incentives for minority engagement: assistance with enrollment for government-funded health insurance; breaks on premiums for healthy behaviors (i.e. wellness discounts), improved targeting for clinical research opportunities; transportation assistance. •Life science companies are pursuing stronger direct relationships with their customers. The PMI cohort should consider including broader consent options to enable underrepresented populations to access other programs offered directly from trial sponsors. •Community care centers could be financially incentivized to identify and recruit trial participants within certain zip codes, Medicaid coverage, etc. i. As outcomes tend to improve with trial participation, care could be paid for by life science companies instead of the state. Participants also benefit from additional education, which traditionally occurs during trials. •As the cohort is studied, the cost effectiveness of various interventions should be measured and broken out, in a de-identified way, to study if there are greater cost savings for underrepresented groups. Historically, these populations have higher healthcare costs because they wait longer to get care and present with more severe forms of disease. Overall cost savings may be greatest in this group. If earlier presentation can potentially break this cycle, results could be leveraged for further incentives to proactively enroll these underrepresented populations in healthcare services.
59	People from historically underrepresented communities are more likely to participate in research if they believe that they are included in the decision making and have a trusting relationship with the research team. The Jackson Heart Study successfully recruited 5301 African American Adults from the MSA of Jackson, MS. Since that time 15% are deceased, 5% are lost to follow-up, and 2% have refused to participate in ongoing study activities. The recruitment and retention strategies used by the JHS are described in by Wyatt et al (2003) and Fuqua et al (2005).
60	Rather than organizing PMI as a project dominated by the genomics "establishment" with the advice of the community, PMI should be organized as a partnership between government, the academic community and trusted representatives of groups making up the diversity of the US population. One successful model to consider is the Michigan Biotrust for Health, governed by a triumvirate of the component housing blood spots derived from Michigan's newborn screening program, a scientific board developing guidelines for approved research using this database, and a community values board addressing ethical and social issues. Other examples can be found in Europe and Australia, where genomics-related projects have a significant community component.

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Obs	Q1A
61	The offering of full health coverage for any participant in the cohort (below a certain income bracket) would be an enormous incentive exactly addressed to people from the most difficult social contexts and desperate situations. These are exactly the people that the Precision Medicine Initiative needs more than anyone else. They are probably the most touched people by extra genetic determinants of health, therefore they are the most interesting sample for the research. Yet they are probably the least studied people, because it so difficult to involve people living at the edge of society. Since these kinds of people are exactly what the cohort needs in order to achieve significant research results, and since they are exactly the people that might benefit mostly from this, their massive recruitment is essential. They should be involved with informative programs in the places they usually refer to (shelters, rehabilitation centers, but even simply public schools and gathering places in suburbs), and they must be incentivized with an immediate and evident benefit: the total free access to healthcare is the ideal thing. Or at least, significant facilities in the access to healthcare. “You share your health data with us, and we share our healthcare with you”, should be the principle. Such an incentive might be enough to potentially engage almost everyone below the poverty threshold: an extremely promising perspective for the Initiative.
62	Address language barriers Use low literacy materials Provide useful incentives Engage employers or community resources - ie send representatives to community gathering places such as food banks, Medicaid offices, community clinics
63	Lung Cancer Alliance is concerned that clinical trials have failed to adequately represent underserved populations that are disproportionately impacted by lung cancer. Recruitment must be specifically designed for these underserved communities with careful consideration given to cultural and financial impediments.
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66	For people from historically underserved communities to participate this must be relevant to their lives. The only way for that to be true is for the participation to be authentically initiated, designed, conducted, analyzed and communicated within the community with member of the community as true leaders and facilitators. Helicopter science will not succeed in this goal. It will also not work to take projects that are in the majority communities, led by scientists in those communities, to simply add a 'diverse arm'. Successful models can be seen in other fields - education and community organizing. There are a few examples in health, including the Southcentral Foundation System of Care - https://www.southcentralfoundation.com/nuka/. Another for the LGBTQ community is the PRIDE Study - http://www.pridestudy.org/TheTeam.html
67	There are already several existing successful models of studies that have recruited large cohorts of historically underrepresented people to participate in research involving collection of biological samples. A few of the several successful models from aging & health research include: 1) WHICAP (PI, Mayeux), in which a community-based cohort of older adults, originally recruited from lists of Medicare eligible residents obtained from CMS, are followed longitudinally. DNA, plasma, serum, MRI, and clinical measures are collected every 18 - 24 months. 2) Jackson heart study (PI: Mosely), a long-running community-based study of cardiovascular disease, and 3) and the National Survey of American Life (PI: Jackson) which included face-to-face interviews and biological sample collection from African American, Caribbean American, and non-Hispanic white individuals across the United States. These PIs and the institutions from which they are based had a previously established, proven track record of trust with the communities they were trying to recruit. Each of these studies created “ownership” by the community or populations they were targeting throughout development, recruitment, and follow-up. The faces and voices representing the study were people who are members of the communities targeted for recruitment. Travel to a medical center was not required, and most of these successful studies included interviews in the home or community-based sites. Incentives included cash reimbursement for participation and any travel costs. Many successful efforts of collecting biological samples have piggybacked/leveraged already successful recruitment for other work in communities of interest.
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Question 2A. Community engagement strategies and partnerships that can facilitate and integrate multiple perspectives at the community and individual level and account for diverse, social, religious, economic, and geographic settings

Obs	Q2A
1	Engage with trusted local community leaders (e.g., not-for-profit organizations; religious institutions), gain their trust, train and employ individuals from the local community to conduct recruitment. Project management teams should include representation from the local community with equal authority to institutional researchers in the decision making processes.
2	This is more of a comment than a suggestion, but it seems this would depend on the specific aims and logistics of the PMI research. Does this question seek suggestions about including those perspectives in the planning of the research, or about continuing to obtain and act on those perspectives during the long-term research?
3	To achieve maximum participation in underserved communities the NIH should seek locations where there are existing strong community-based outreach programs or where they can be developed. These programs will require resources and support and need to be linked to an institution conducting research able to take responsibility for recruitment to the precision medicine cohort. In our case we have multiple programs in our community in schools to a communitywide campaign called your health matters (Tu Salud Si Cuenta). Our programs also include farmers' markets, community gardens, nutrition education programs conducted by community volunteers, and multiple sites for various physical activities again conducted by volunteers at schools and churches and other venues. We also work with federally qualified clinics and our local hospitals on numerous projects. Recognition of this in the past year was the award of the Robert Wood Johnson Culture of Health Award to our partner the City of Brownsville. We also worked extensively with our political leaders in the city and County commission and with other community leaders from business education and nonprofits. All of these programs include multiple ethnic, religious, gender, and age groups.
4	MCRF established a Community Advisory Committee for the PMRP bio bank. This active committee provides participant perspectives and guidance on how PMRP resources should be used. Yearly communication regarding PMRP activities is also distributed to PMRP participants to inform about research and discoveries. In addition, a survey has been distributed to PMRP minority participants to assess perceptions regarding genomic medicine. Through the engagement between MCHS and FHC, partnerships with job placement centers, home health organizations and patient advocacy groups have materialized to gain individual and community perspectives of low income and uninsured and disabled individuals. Marshfield Clinic recognized that improving the health of an entire community goes beyond doctor-patient visits when it created the Center for Community Outreach (CCO) in 1998. CCO partners with coalitions and others to promote quality of life and reduce the incidence of lifestyle related disease. Focus is placed on evidence-based strategies that address health priorities identified by Wisconsin's health plan, "Healthiest Wisconsin 2010: A Partnership Plan to Improve the Health of the Public." Staff provide education and training, technical assistance and consultation, and other resources to reduce the incidence and prevalence of alcohol, tobacco, and other drug abuse; promote healthy lifestyles, and contribute to community health education in the communities it serves. CCO staff promote and support local community coalition building to address community health needs. CCO community relationships can be leveraged effectively to disseminate information about Precision Medicine and to reach local disadvantaged populations more efficiently using grass-roots engagement.
5	Community engagement is important to develop PMI-specific education programs, appropriate measures and methods, and to tailor community-specific communication strategies to report back results. However, just as communities are heterogeneous, so too are the relationships between local community-based organizations (CBO) and the residents they engage. The AAMC encourages the NIH to identify appropriate community partnerships in recruiting participants to the PMI cohort by first understanding the characteristics of and the relationships between individual CBOs and their community members. By understanding the dynamics of how prospective partner CBOs interact with their community, the PMI can create appropriate partnerships and strategies that respectfully leverage and align with community values important to specific CBOs and their members. We commend the NIH for supporting the community engagement function of NCATS' CTSA program and suggest the PMI initiative avail itself of the community engagement expertise at those sites. Through partnerships with community organizations such as cultural centers, churches, and interest groups, education about the purpose of the PMI can be tailored and presented in a manner that provides deliverables the respective groups see as relevant and beneficial. In service of the mission of the PMI, an active effort must also be dedicated to reaching participants that are not a part of CBOs' membership. The AAMC urges the NIH to invest in sustained dialogue with individuals and community organizations to identify effective recruitment and engagement strategies that could benefit both PMI's enrollment targets as well as CBOs' membership building activities.

Question 2A. Community engagement strategies and partnerships that can facilitate and integrate multiple perspectives at the community and individual level and account for diverse, social, religious, economic, and geographic settings

Obs	Q2A
6	CDC data demonstrate that underrepresented minorities attend our nations' emergency departments at disproportionately higher rates than the population as a whole. The reasons that underrepresented minorities are over represented in this environment are extensive and complex, but it is clear that there is an interface between potential participants and the healthcare research system that does not exist elsewhere. Indeed the emergency department represents the sole source of contact with the healthcare system for many such patients. Moreover, emergency departments serve as vital community resources in touch with their local geographic base and are highly adept at adapting research protocols to the cultural and ethical sensitivities of their surrounding population. Patients who are systematically disadvantaged also frequently attend the emergency department for lack of access to other healthcare venues. Indeed the emergency department represents the sole source of contact with the healthcare system for many such patients. Thus, emergency departments are the only readily available site with large numbers of potential subjects from these populations. Moreover, emergency departments serve as vital community resources in touch with their local geographic base and are highly adept at adapting research protocols to the cultural and ethical sensitivities of their surrounding population.
7	An organic campaign to that systematically recruits community leaders first will be essential in bringing together a diverse cohort. When tapped correctly, the pervasiveness of social media makes it possible to spread messages with borrowed authority to a broad cross-section of society.
8	2. Imagine an authentic relationship between people and the products and services they choose. A relationship based upon shared values, interests, beliefs, a vision of healthy futures, and of the greater good. When we tell that story, it is the best that marketing can be. Today's consumers are seeking goods and services from trusted sources and trusted storytellers. The rise of technology has created a dramatic sea change in the relationship between commerce and consumers giving consumers the power to influence corporations/institutions and providing corporations/institutions with the ability to influence life. This shift allows trusted corporations and institutions interested in doing well by doing good to rise above by inspiring positive change in people's lives and in the world. There are now more mobile devices than humans on earth and mobile data networks are 30 times larger than the Internet was just 10 years ago. Additionally, were social media networks - now more than 1 billion strong - considered a separate country, social media would be 3rd largest nation on Earth. More than ever, our untethered borderless populace is looking into a future informed by imposing challenges to human health and the health of our planet. The aforementioned rise in technology, along with science and medicine are increasingly providing our populace with new and better tools to meet those challenges.
9	The Mayo Clinic Biobank recruits participants through clinics in Rochester, MN; Jacksonville, FL; and through a partnership with Mountain Park Health Center (MPHC) in Phoenix, AZ. Recognizing the sociocultural diversity of these communities, we established Community Advisory Boards (CABs) in each of these regions to engage patients and communities in discussions about the governance of our biobank. The memberships of these CABs are reflective of the unique regional and cultural traditions of each community. We engage our advisors on a regular basis, approximately 4-6 times per year, to ensure that our biobank is pursuing topics of concern to our supporting communities. We also engage our CABs on more general matters, including for example, our policies on the reporting of research results and communication plans. These community-engagement activities are supported by our institution and are viewed by leadership as an integral element of the repository's long-term sustainability. Without the strong support of our communities, the Mayo Clinic biobank could not be successful. Similarly robust strategies for promoting sustained community engagement will be essential to the success of the Precision Medicine Cohort. Although it may be possible to create new mechanisms for engaging community partners regarding the Cohort, we believe it would be far more efficient to work with established networks of community advisors who are already engaged in discussions about the use of biobank samples and familiar with the unique ethical and sociocultural issues raised by this type of research.
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11	Enable multiple perspectives by enabling patients to self-organize around their data with the ability to move their raw data to different trusted health data "registrars" in the event an entity had lost their trust.

Question 2A. Community engagement strategies and partnerships that can facilitate and integrate multiple perspectives at the community and individual level and account for diverse, social, religious, economic, and geographic settings

Obs	Q2A
12	The mission of the Personal Genetics Education Project (pgEd.org) is to raise awareness about the benefits that can come from knowing one's genome as well as the ethical, legal, and social implications of such knowledge. pgEd strives to make that awareness equally accessible across all segments of society regardless of socioeconomic, educational, ethnic, religious, or cultural background. pgEd has had great success and attributes much of that success to the unique way in which it engages its audience, highlighting the medical miracles coming from personalized genetics as well as the ethical, legal, and social implications. In some of the communities we visit the segments of society who are most vulnerable to discrimination fill the room. The goal is not to make it so that people want to avail themselves of genetic technology. It is simply to raise awareness so that everyone has a chance to make an informed decision about how they want to use their personal genome, whether they want to use information from their personal genome even as we all become very aware that there is tremendous diversity of opinion about personal genetics and we learn how to respect that diversity. It is this neutrality, separate from any research endeavor, and the willingness to engage on any topic that puts people at ease and rarely fails to capture attention, motivating individuals to seek information, express opinions, and, ultimately, become confident in their ability to bring genetics into their lives, if they so wish.
13	EngageUC is a NIH/NCATS-funded study to identify best practices for biorepository governance and consent. The study involves all 5 of the University of California (UC) medical center campuses. EngageUC works with researchers, regulators, and community members on governance and is using a randomized trial to provide evidence on best practices for consent. For community engagement, EngageUC has used a deliberative method to elicit Californians' recommendations for biorepository governance. Our approach included education and facilitated discussion. Participants were provided language-appropriate background materials about biorepository research; spoke with experts in the field; and then engaged each other in facilitated deliberations to arrive at recommendations for UC biorepository governance. This approach equips ordinary community members – not self-identified advocates – to express informed perspectives thus highlighting authentic community recommendations. EngageUC conducted deliberative events in LA and San Francisco (SF) with a total of approximately 50 people, who were a representative sample of Californians from those regions. Our events included diverse and underrepresented populations in California, including Spanish-speakers in LA and an oversample of Asian-Americans in SF. The vast majority of participants reported that they had a positive experience, learned a great deal, and had become more supportive of UC biorepository research. Many have since volunteered to participate in further research, advisory board, and governance activities. We recommend that deliberative methods be considered as an aspect of engagement strategies for the US Precision Medicine cohort.
14	• Make participation convenient to participants. For example, offer participation opportunities in easily accessible locations and times outside standard business hours. Engage key community stakeholders and offer alternate methods for assessment collection such as phone activated interactive voice response (IVR). • Compensation strategies should take into consideration participant costs (from place of work/home to participate in research studies, child care, parking fees, meal times) and reflect the potential profits from research findings. • Precision medicine should be visible in the communities. Collaborate and subcontract with organizations and businesses that serve underrepresented groups. Settings for community education efforts should include Historically Black Colleges and Universities (HBCUs), faith groups, social clubs, senior centers, and practice settings. • Investment in existing local/community infrastructure and organizations for efficiency and utilization of existing communication networks and familiar, trusted health workers. • Create clear messages and branding. Disseminate aggregate research findings in a timely manner via newsletter, websites, social media, and African American and Latino media sources. Evaluate internet accessibility and usability for targeted communities before developing recruitment strategies. The internet can be an efficient communication means for the populations for which it is accessible, usable, and affordable. To reach marginalized populations, for which this is not always the case, personal contacts through trusted community liaisons often are more effective means of reaching potential participants.

Question 2A. Community engagement strategies and partnerships that can facilitate and integrate multiple perspectives at the community and individual level and account for diverse, social, religious, economic, and geographic settings

Obs	Q2A
15	The HMORN established a Patient Engagement in Research Special Interest Group (PER SIG) to address this specific issue. This SIG has grown to 60 members (including a community patient partner) who are actively interested in and contributing to the identification and development of best practices for community engagement, and improving skills and capacity for engagement throughout the network and within their own institutions. Using data gathered from SIG members currently engaging community members and patients in research, the PER SIG created a public access workbook (http://www.hmoresearchnetwork.org/en/Tools%20&%20Materials/Plan_Field/HMORNPatientEngagementWorkbook.pdf) outlining the logistical and other preparatory steps required for engagement in research, including identification and recruitment of community members; compensation, data sharing, and retention considerations; training of community partners and research team members; and monitoring and evaluation. The PER SIG also offers a consulting service to provide research teams with the knowledge, methods, and tools to meaningfully engage community partners on their research teams. Planned activities for the PER SIG include the compilation of templates, scripts, and other content resources for research teams and community partners to use in improving engagement practices and to facilitate the integration of community members into research teams, and the development of engagement metrics for assessing the impact of community engagement.
16	STRATEGIES for engaging Asian Americans and in the cohort study, including GATHERING genetic, environmental and lifestyle data: This is a relatively young population. With the exception of the offspring of the older generation Chinese who came under the Chinese Exclusion Act of 1882, most Asians (including Chinese) are newcomers to the US. The first large group of immigrants was Koreans (post-Korean War) and the next, Vietnamese and Cambodians (plus others), post- Vietnam War—the largest subset of new immigrants landed on US shores between 1980 and current times, most settling in small contiguous and regionally-defined communities proximal to large metro-areas (NY, Phila, SF, DC, Houston, Chicago, LA, Seattle, etc.). There is substantial behavioral and health data on these communities. Center for Asian Health at Temple University has developed a variety of strategies to engage Asian Americans in NIH/Other-funded research endeavors that included: (1) community-outreach projects coordinated by trained bilingual health coordinators (often members of engaged om communities); (2) leadership training programs; community-wide health education/awareness programs'; (3) use of CBPR, wherein communities are involved directly in all stages of research including translation and utilization of research results; (4) building of professional and lay partnership Center for Asian Health partnership have grown from about 10 to currently more than 300 partners); (5) training and engaging young researchers in the conduct of CBOR; and engaging local and regional in a variety of health-message propagation, etc….
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19	Community needs assessments are now routinely collected by charitable hospitals as to assess and address disparate health and social issues in the community. Qualitative methods, including focus groups and community conversations, are used to engage members of the community and specifically invite members of organizations representing a host of diverse populations. future funding announcements should also support quantitative assessment of capacity to expand these methods to the work under consideration.. Geisinger Health System in Pennsylvania has a ten year history of conducting community needs assessments that consist of community conversations at the individual level as well as at the organizational level. These community conversations allow the system to educate at the population and institutional level, allow the system to be educated at the provider, researcher and institutional level, and promote partnerships that engage patients and other community members. In addition, these conversations offer a basis for developing strategies and forming partnerships that can facilitate the integration of multiple perspectives at both the community and individual level. Although a variety of qualitative methods could play important roles in engagement strategies, consideration should be given to the design and conduct of deliberative engagement forums, which offer a targeted means for educating select communities and, on that basis, inviting their informed participation in precision medicine research. A solid (and growing) evidence base supports the use of deliberative techniques in efforts to enhance the participation of isolated, underrepresented communities in a range of initiatives, including policy development and public health.
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Question 2A. Community engagement strategies and partnerships that can facilitate and integrate multiple perspectives at the community and individual level and account for diverse, social, religious, economic, and geographic settings

Obs	Q2A
21	A. Depending on the community, datasets may be submitted in various formats, so it will be important to watch out for methods to standardize & harmonize. B. Efforts to educate members of religious communities on the benefits of genetic testing for preventive care will reduce barriers and extend the reach to target communities. For example, the sentiment that health is in God's hands, including preventive medicine may present a barrier in accepting participation in research trials or precision medicine. Consider researching how to address this barrier in a way that is respectful of religious beliefs. C. Work with organizations and/or researchers who already have established trust within their local community. D. Hire recruitment staff from within the targeted community. E. Interface with genetic counselors who work in public health and community outreach settings.
22	Language People Inc. has sister corporations called Deaf Nation Enterprises, Inc. and LP Connect, which are companies that provide outreach into the deaf and hard of hearing communities
23	WICER built upon the engagement strategies initiated by the Community Engagement Core Resource of the Irving Institute for Clinical and Translational Research which is partially funded by Columbia's CTSA.
24	While PM focuses on individual patients, the implementation may require large system-level changes that have their own level of complexity. Community engagement/benefit sharing in research may enable researchers and clinicians to better understand community priorities while empowering a community to address its own needs and inequities. A community perspective on issues such as harnessing information from social media and return of health information would be particularly important. Communities should take the lead in identifying incentives for engagement as well as determining how knowledge gained could effectively be disseminated in their respective communities (e.g., via faith-based communities, reading groups, newsletters). They should also be informed as to how biospecimens/data from their communities are being used for research. Community representatives should be represented on key decision-making committees (bioethics, access, etc.). It is critically important to recognize that the perspectives of patient advocacy groups are likely to differ significantly from those of under-represented communities, and it is critical to build the resource to ensure strong representation of both patients and the community voice. It is also important to develop a common understanding of the definition of "communities", and the range of areas in which diversity is of interest. For example, in addition to racial/ethnic diversity, diversity by socioeconomic status should be an important part of the PMI. Lower income groups are more likely to have interpersonal and environmental exposures that increase risk of disease, and are critically important to understand in the PM context.
25	The CHAP is a training, outreach and services program where faith and civic organization leaders develops a partnership with the DCI and selects two people within their organization to serve as health ambassadors in their organization. To date, there are 11 faith organizations trained that includes, African American, Asian and Latino faith serving institutions. The Ambassadors come to one-day training on how to build a health team, an outreach agenda, and engage people in their organization and the surrounding community to be aware and act upon the cancer information they need through the DCI Patient Navigation program. After training, each Ambassador team develops a year-long cancer awareness program and our PNs serve as the link to education, screening, and follow-up. Organizations work with DCI to develop cancer support programs in community settings.
26	
27	1. Include community members in the development of the study design and implementation 2. Recruit researchers that are reflective of the community 3. Recruit participants in low-income areas through WIC offices, food banks, hospitals, public transportation, grocery and convenience stores, parks, etc. - CLEARLY note financial incentives if any 4. Include transient populations by advertising in shelters and public spaces and by providing an easily accessible central location for data collection.
28	The March of Dimes urges the PMI to embrace the need to enlist many diverse partners in the recruitment process. The PMI should reach out across not just agencies, but federal departments to identify existing coalitions and partnerships that could be tapped to educate many sectors of the public. Entities like the Department of Housing and Urban Development or the Department of Agriculture may have reach into specific underserved communities the PMI wishes to reach. In addition, partners should have a degree of freedom in promoting the PMI. As a governmental effort, this initiative is susceptible to becoming bogged down in the federal government's traditional desire to control and approve every communication issued. The PMI should consider promoting a different communications model, perhaps one in which partners are given key principles or "talking points" that they are then encouraged to tailor appropriately to the various populations they serve.

Question 2A. Community engagement strategies and partnerships that can facilitate and integrate multiple perspectives at the community and individual level and account for diverse, social, religious, economic, and geographic settings

Obs	Q2A
29	There has to be protections such as the ones state in the Nagoya Protocol for human genome data and products from that data whether diagnostics, therapeutic or in synthetic biology for people of the Americas. Especially American Indians who have tribal sovereignty and international political/legal status because there is likely an abundance of novel variants at high frequency and much mechanistic information to be gleaned from their genomes. They are the poorest of the poor in every North and South American country and they have no great representation in law, governance, business or medicine that their voice and interests will be heard. Simply put, we do not trust "altruistic" endeavors based on resources from the Americas...because historically we have been left out on our land. The US has so far failed to adequately consult with tribal groups on this issue. To create incentive , you most go past individual rights to privacy an consent contained in GINA and protect communal rights.
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32	- Promoting community-based programmes - social mobilisation and participatory research through - Parent and household/community Involvement/Engagement - Schools, recreation places and churches Involvement/Engagement - Continuous two-way exchange based on multifacet forms of information communications - Individual and community empowerment and orientated program/project ownership - Involvement of local expertise to foster trust and sense of ownership between the community - Drama, TV/radio public announcements, controlled social media/blog, door-to-door health education campaigns with the local community/group - Leadership, wisdom and community encouragements - Support, care and assistance in other public health in private clinics, hospitals and ambulances - Network and social grouping, community and community leaders, - Community forums, faith-based and trade communities, - Fraternity organisations, voluntary and philanthropic organisations, - Ethnic groups, neighbourhood associations engagement
33	
34	N/A
35	I think you can make the case that the *entire* cohort could be from the deep south, where there is a great representation of African-Americans (with the most diversity of genetics, and with great diversity in environmentally-related outcomes). The statistics for the area south of Tennessee for smoking, cancer, and other environmentally-relevant health issues are also stunning. This would be a statement to the American people that we are going to boost up the area of our country that is in most need of help, and at the same time learn lessons that will help all Americans. I think you could add Florida and Texas in order to ensure Latino involvement. Why not have this cohort be HIGHLY enriched for those whose health needs the most attention?
36	Public education should be a key priority prior to the initiation of recruitment. Meeting with local community leaders and candidly explaining the purpose of this initiative and the potential uses for the data collected will be essential to gaining community buy-in. Transparency will be crucial to this initiative's success. Community representatives should be invited to the table to discuss both the design and potential future implications of the study: how participants will receive results, secondary findings, potential for cultural discrimination based on findings, limitations of GINA, implications for family planning, potential misunderstanding of risk rates, increased need to further promote healthy lifestyles despite reassuring results, etc. Identification of community-specific and/or population-specific will require thoughtful and tailored strategies that require those members to guide the process. Once education needs have been identified, the community leaders/members should continue to be engaged in tailoring the education materials to meet the needs of their community. The potential risks also have to be minimized, then the community-based work group should focus on the best ways to communicate to the community the benefits, both individual and general.

Question 2A. Community engagement strategies and partnerships that can facilitate and integrate multiple perspectives at the community and individual level and account for diverse, social, religious, economic, and geographic settings

Obs	Q2A
37	In 2003, Booz Allen aided in the stand-up and strategic plan for the National Center on Minority Health and Health Disparities (NCMHD); this, along with our staff's experience, support our understanding of working with diverse community characteristics to integrate multiple perspectives. Strategies include: 1) Develop suite of strategies for county/areas to choose from: In the National Children's Study, a pilot study of 10 counties was authorized to evaluate different methods to recruit pregnant women. Because of the diversity of these counties, a research team (RT) from each county developed recruitment strategies. For Baldwin County, support from public and civil leaders was necessary to encourage the recruitment of participants. The RT partnered with each of these organizations and groups (Board of Education, Chamber of Commerce, City Council, County Health Board, religious leaders, hospital leaders/physicians), and they in turn pledged support for the study. The groups announced support during local HS football games, annual health fair, jazz festival booths. All of these community engagement activities helped facilitate the successful recruitment of over 200 participants. 2) Partner with local academia, media, commercial and non-profit organizations. Booz Allen in collaboration with the Jimmy Carter Center, Georgia State University, Habitat for Humanity, and Morehouse School of Medicine invited 40 community leaders from local governmental agencies, non-profit organizations, and businesses with the goal of fostering collaborative initiatives that will further support the establishment of School Based Health Centers (SBHC). This interactive forum identified methodologies to engender school based health and behavioral health programs across
38	Building local partnerships with an aim to recruit the precision medicine cohort is also an opportunity to build local capacity to benefit community level public health. By working with local partners, the approach would create a win-win for the development of the cohort and for local partners. This would increase the credibility of the study and promote trust in the community. The study would be able to provide the community with technical assistance, knowledge and perhaps training opportunities in the process of educating the community about precision medicine and the importance of the cohort. We therefore suggest a two-prong engagement approach which includes local, grassroots organized efforts combined with a broad based, high profile public awareness campaign. The local effort should involve an assessment of the community in which the recruitment is taking place, engagement with diverse and respected local leaders, and outreach efforts targeted to the medical community. Individuals should hear positive messages about the study coming from multiple areas of their lives including from their doctor, their places of worship and their social supports (schools, work, friends, etc.). We also suggest that NIH develop a national, targeted, coordinated community awareness campaign supported by high level government officials, community leaders, and celebrities (First Lady, members of congress, movie stars, athletes) and are integrated into a variety of media (internet, radio, television, print, 24/7 information centers).
39	
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41	1.Hold collaborative meetings with underrepresented groups that are known and ask them to invite to the next meeting(s) all of the individuals they know who maybe helpful or relevant. ("The Farmer in the Dell" approach). Hold these meetings in easily accessed places comfortable for the group- churches, libraries, town halls, schools. Include the prison and jail populations if this is at all feasible.
42	1) Community based research teams - participants are more likely to trust the guidance of a physician or other care providers/members of the community they know rather than that of individuals they've not met before, or who do not seem to have knowledge of local community interests. 2) Collaborate with patient and social advocacy groups 3) Collaborate with religious organizations, community centers, services (e.g., hair salons, barber shops, nail salons), business owners, support groups, social groups, social media 4) Consult with organizations that compile data about prospective populations and their behaviors 5) Have a presence at trade/hobby/special interest events/shows
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Question 2A. Community engagement strategies and partnerships that can facilitate and integrate multiple perspectives at the community and individual level and account for diverse, social, religious, economic, and geographic settings

Obs	Q2A
45	• Employ staff indigenous to the communities where studies will be conducted • Employ Investigators who reflect community and value its culture • Learn the history of the community researchers are entering • Develop and sustain trust which can be facilitated by integrating the following strategies • Engage minority investigators, physicians and other providers e.g., traditional and non-traditional • Engage of Historically Black Colleges and Universities and other Minority Serving Institutions as the primary institution not as a sub-contractor • Engage CBOs as equal partners with a financial incentive • Host town hall meetings and other public pathways for community engagement • Engage faith based partnerships; • Develop partnerships with government, small businesses; non-profits and NGOs;
46	As with PCAHE, SDBB has become an integral part of the San Diego community by implementing similar strategies over the past 60 years. SDBB involves local residents', businesses, churches, and schools in the donation process, community awareness, and health and education activities. One of many events throughout the year is the annual Chargers Drive, a partnership between SDBB and the San Diego Chargers football team. The blood drive and bone marrow registry event includes meeting the Chargers players, entertainment, and the "Wellness Zone," an interactive health and education exhibit for all ages. Last year's "Wellness Zone" included a walk-through exhibit of the human heart and information on how a blood sample can be used for research into the treatment of disease. T hrough this and other events throughout the year, SDBB engages the general public on the benefits of participating in research studies. "A pint of blood will save a life. A tube of blood could save millions of lives." SDBB is a 'trusted' partner in the community that removes barriers and promotes interaction. In collaboration with the BIOCOM Institute and the San Diego Workforce Partnership, SDBB hosts a unique networking and relationship building opportunities for K-12 teachers and life science industry professionals. To integrate multiple perspectives within the San Diego community in SDBB's operations, SBDD's Board of Directors and Advisors include leaders in the community, healthcare, education, biotech and pharmaceutical industry, finance, governance, non-profit and charitable organizations. SBDD also has a robust volunteer base.
47	
48	Partnerships with religious organizations, trade unions, and professional organizations would help to validate the intent of the program and encourage participation.
49	
50	Support for projects that foster academic-community partnerships is essential for identifying key issues that are relevant to historically underrepresented groups. Engaging the support of community stakeholders will facilitate researchers access to the community. Support for focus groups that would allow researchers to better understand the factors that result in non-participation. Research participants should be continuously educated about scientific findings and the importance of participating in research studies. Establishing academic-community sponsored conferences that are held in underrepresented communities is an example of an effective method for disseminating findings.
51	- Local educational outreach (multilingual) regarding risk benefit analysis of participation in U.S. precision medicine cohort by socially, geographically and economically diverse communities.
52	a. Build national and local community action boards who will partner equitably with researchers to engage populations, to identify key research questions and strategies, and build a strong engine to interpret, disseminate and act on research findings. Identify key teams around the US, including the community engagement leaders of the CTSAs and of NIMHD-funded centers and programs, and important stakeholder groups such as Community-Campus Partnerships for Health, to help build these infrastructures. b. Ensure community partners are empowered and have the capacity to make decisions alongside the researchers. Essentially, these partners should help decide the specific focus of the research, and the research strategies. c. Encourage open and honest dialogue, so community leaders are inspired and feel comfortable sharing their best ideas and strategies. d. Facilitate researchers and their teams to become part of the communities they are engaging. This bi-directional exchange is a key to successful engagement e. Ensure that the community partners share in successes, including as co-presenters, co-authors and, certainly, in funding streams. Determine appropriate stipends for partners and participants. f. Develop robust social marketing, social media and grass roots campaigns in partnership with communities and communication experts, to clearly communicate why research in general matters, and why this specific research endeavor is important.
53	
54	Its currently not a priority and no few incentives

Question 2A. Community engagement strategies and partnerships that can facilitate and integrate multiple perspectives at the community and individual level and account for diverse, social, religious, economic, and geographic settings

Obs	Q2A
55	a. Build both national, and local community action boards who will partner equitably with researchers to engage populations, to identify key research questions and strategies, and build a strong engine to interpret, disseminate and act on research findings. b. Identify key teams around the US, including the community engagement leaders of the CTSAs and of NIMHD-funded centers and programs, and important stakeholder groups such as Community-Campus Partnerships for Health, to help build these infrastructures. c. Ensure community partners are empowered to make decisions alongside the researchers. Essentially, these partners should help decide the specific focus of the research, and the research strategies. d. Build capacity of community partners to carry out this important work.Encourage open and honest dialogue, so community leaders are inspired and feel comfortable sharing their best ideas and strategies. e. Facilitate researchers and their teams becoming part of the communities they are engaging. This bi-directional exchange is a key to successful engagement. f. Develop robust social marketing, social media and grass roots campaigns in partnership with communities and communication experts, to clearly communicate why research in general matters, and why this specific research endeavor is important. g. Ensure that the community partners share in successes, including as co-presenters, co-authors and, certainly, in funding streams.
56	--Overwhelmingly participants much rather want personal conversations verus an email or a letter inviting them to participate. Generationally, people would want that facetime/ personal interaction, after all we are asking them to donate out of themselves... --Using the model of community health workers/patient navigators/informed peers who can connect to community members is a sure strategy that works. In surveys within hard-to-reach communities, when asked who people listen to, they still listen to doctors hoever relationships are important to people. What teh ACA did in supporting Communtiy Health Workers is a great service to public health --aligning with the Ten Essential Services of Public Health, one of which is contribution to research. Public health departmentscollaboration in recruitment might be a way to fulfill this service and document that they do.
57	
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60	Transparency of operation and education on the purposes of PMI, its expected outcomes, their significance in advancing health and promoting health equity, must be major components of the effort. Broad use of social marketing as well as face-to-face town meetings can both build trust and provide education. Those providing continuous reporting on PMI and providing the education must reflect the diversity of the population whose participation is essential to the success of the enterprise. Organizations such as the National Urban League, National Council of LaRaza, and National Congress of American Indians, can be asked to nominate representatives to serve on the community component of PMI's governance.
61	If we want to involve a specific group, we have to directly reach that group. In order to collect representatives from all the social, religious, economic and geographical setting, it is essential to get touch with the people from the underrepresented settings. Informative meetings should be held in the gathering places they usually frequent, in order to propose them to participate. Such meetings should explain them the importance of this Initiative and the relevance for public health, and especially the benefits that might come to themselves as a community (by the identification of a possible health discrimination and if possible its correction) but also as individuals (by keeping their personal health under control and by achieving facilities in access to healthcare in case they are too poor to have a complete health insurance). Also, informative material and proposal of participation should be provided to everyone at certain specific moments of the life: when starting to serve a term of imprisonment, or when finishing serving a term of imprisonment, when starting or finishing a program of rehabilitation, when enrolling at the university, when graduating at the university, when retiring (this is especially important to achieve the fundamental task to enroll elder people)…
62	Make the project easy for community partners to implement. Requiring too many steps or multiple face-to-face meetings is unrealistic. In other words, simplify the design of the research protocol so that maximum participation is possible.
63	Lung Cancer Alliance has demonstrated that effective community strategies can be implemented if partnerships are established prior to program design.
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Question 2A. Community engagement strategies and partnerships that can facilitate and integrate multiple perspectives at the community and individual level and account for diverse, social, religious, economic, and geographic settings

Obs	Q2A
66	Individuals and communities must be met where they are and where they live. Frictionless experiences - part of church, temple, schools, are pathways to being easy and embedded, again lead by the community themselves. The community will need tools to help determine and implement the preferences of the community, as well as the individuals within it, with regard to the research, data sharing and privacy standards with which they wish to govern the process.
67	This effort would benefit from both a national advisory board, and also local/subgroup advisory boards of community gatekeepers and successful researchers. There are experts in community-based participatory research who have successfully engaged multiple communities, who should be key collaborators. This takes time and resources – more than what has been put forth for typical genetic studies. There is not one partnership that will work in every setting. Local approaches have been most successful, combined with an approach that offers ownership of the study and its aims. For example: “Our participation in the African American/Rural/Native American Precision Medicine Initiative is important because we need to identify the individual factors that can influence health and effectiveness of treatment in people like us. We can be in the lead group on this effort.” True partnerships require knowledgeable investigators who are familiar with the potential mechanisms of health disparities and how to assess them. You know you are doing the right thing when participants from underrepresented groups are becoming part of an informal recruitment and outreach network.
68	NIH should convene a consortium of academic medical centers to address issues of sex and race in precision medicine. Many academic medical centers (AMCs) are undertaking their own precision medicine initiatives and have successfully recruited underrepresented participants from communities, often in collaboration with community-level partnerships, such as AMC partnerships with local community health centers and other community-based organizations. As these centers move forward with precision medicine initiatives, a mutually beneficial relationship should be developed between AMCs and NIH, with NIH demonstrating leadership through recent changes to its research policies targeting improved collection, analysis and reporting of data stratified by sex and race/ethnicity, which will result in the integration of sex and race/ethnicity differences in all aspects of precision medicine.
69	

Question 3A. The barriers to participation in the precision medicine cohort and strategies to address those barriers

Obs	Q3A
1	Identifying locations within local communities that are the most productive in recruiting participants. Maintaining continuation of participants (i.e., avoid drop out and lost to follow-up)
2	
3	The most likely barriers to participation in the precision medicine cohort, particularly among minority populations, will be lack of understanding of the program, lack of understanding of how it might benefit them or their families, and sometimes outright suspicion of any such efforts in the community. Before we established our program, research was feared in our community, and seen as something that was ‘done to them’ by people who took information and specimens and then disappeared. No feedback is a serious disincentive. We strongly suggest that finding locations where ongoing programs especially community-based participatory research (CBPR) are established so that issues of trust and education can be more easily overcome. It will be necessary to educate people in simple terms that knowledge of the specific (genetic) background of individuals can lead to widely understood concepts, such as use of medications, risk for cancer and of chronic diseases such as diabetes, and how these familiar health challenges can be overcome through better knowledge using specific illustrations coming from communities of color or minority communities
4	Barriers to participation in the precision medicine cohort are similar to those encountered by patients with health care issues. Access and insurance (or lack thereof), are among the major barriers. Marshfield Clinic has established a clinical outreach system that includes 55+ regional clinics and tele health programs to address access issues encountered by indigent patients. MCHS regional clinics are dispersed throughout central and northern Wisconsin providing a reasonable driving distance for individuals located in the geographically isolated (rural) areas. MCRF research extends well beyond the walls of the main campus into the regional clinics and tele health applications are used for recruitment and research data capture. In addition, a charity care program that offers reduced price services, including free care, is offered to qualified individuals in medical need. Population migration can be a barrier to precision medicine outcome assessment. The MCHS medical and dental population has relatively low migration in and out of the MCHS service area (less than 3 percent). Tracking systems and longitudinal medical and dental care history supported in Marshfield’s electronic health record is captured for each patient, thus allowing researchers to follow cohort participants over time. PMRP and PLCO participants have been followed 12 and 17 years respectively. The Marshfield Epidemiology Surveillance Area actively follows approximately 125,000 patients since 1991 using the Clinic’s EHR.
5	Previous studies have examined potential barriers to participation in genomic research and have found underrepresented minorities are hesitant to participate in research for reasons such as lack of trust, lack of familiarity of scientific concepts, and lack of transparency of the research process. To overcome these barriers, the AAMC recommends NIH researchers utilize the foundational principles of community-engaged research when designing a research program. The principles can provide guidance on how to appropriately and bi-directionally engage with communities so barriers such as lack of trust and lack of transparency are mitigated. The AAMC also suggests the NIH work with community-based organizations to develop effective communication and educational programs about Precision Medicine Initiative research studies, their goals, results and relevance for communities’ priority local health needs and concerns. Non-for-profit hospitals as well as public health agencies are required to conduct community health needs assessments, the results of which can help PMI researchers understand the local health needs of community residents and thus tailor their message – and their science – to address those needs.
6	Patients presenting to emergency departments often have symptoms that lead to laboratory testing and blood sample collection. Research has demonstrated that acceptance of research participation in the emergency department setting is high-up to 90% at some sites. Research also shows that underrepresented minorities are equally or more likely to participate in research as other potential participants in this setting. This presents an excellent opportunity collect samples for genomic, metabolomic, proteomic, and other systems biology analyses. Frequently emergency departments are connected to electronic health records, allowing complete annotation of biological samples with underlying disease. In fact, research involving collection of biological specimens for biomarker discovery, evaluation and validation is central to many institutions’ emergency care research infrastructures. Emergency medicine researchers are leaders in methods for obtaining highly accurate data from medical records. In addition to the patients themselves, family members are often present when a patient presents to the emergency department. This creates the opportunity for direct familial links to be annotated and enrolled together. There are a number of examples where this fact has been leveraged for accessing an otherwise challenging population to recruit into studies.

Question 3A. The barriers to participation in the precision medicine cohort and strategies to address those barriers

Obs	Q3A
7	The biggest barriers to participation to traditional cohorts are perception of risk in medical research, low perception of benefit and opportunity costs associated with participation. The ideal solution to addressing the perception of risk and benefits would involve a holistic reform of the consent process. As someone that has signed hundreds of consent forms for research, I can tell you that they are all designed to protect researchers more than patients. Consent forms are about as comprehensible as the iTunes end-user license agreement. Consent forms need a single page, bullet-point summary at the start that state all potential risks and benefits clearly in terms the average patient can understand. Opportunity costs need to be addressed by using mobile technology and electronic medical records to minimize these costs and eliminate these costs where possible.
8	3. The interconnected, warp speed world in which we live has moved beyond brand slogans of “we bring good things to life” or “think different” to brands that can act as global citizens exerting leadership to create a future that makes life better. One’s health, the health of mankind, and the health of the planet can provide enlightened organizations with a differentiated pathway to lead and rise above. “Precision Medicine” presents as compelling expression of a pathway for consumers to take control of their health and for visionary institutions interested in health to lead and influence life. The NIH is such a visionary.
9	Our community advisors have also helped us to appreciate potential barriers to participating in biomedical research. Our CABs have assisted us in developing research recruitment materials that reflect local concerns and questions about research. Recognizing that trust in the integrity of science is critical to our biobank’s mission, we have sought to engage our CABs as partners in the research process. Another strategy we have employed is to connect community partners across individual advisory boards. By bringing together our CABs, we have the opportunity to learn from one another and consider perspectives that might not have been voiced in a particular region or research setting. In collaboration with the Mayo Clinic Center for Clinical and Translation Science Office for Community Engagement in Research, we engage with a wider array of stakeholders in the research process, ensuring that discussions about our biobank do not take place in isolation. Alliances among CABs can provide opportunities to understand potential barriers to research participation that might not have been initially obvious. With the increasing availability of web-based video conferencing applications, it may be possible to establish a virtual CAB network that incorporates perspectives across a national network of community advisors.
10	Here are some barriers we see to participation in PMI cohort: • Reliance on EHRs and other data provided by doctors at participating institutions. Those in underrepresented groups are also those more likely to receive care from a variety of physicians and types of medical practices (e.g. telemedicine, a patchwork of free clinics, mobile medicine vans). Not all of those health care providers use or have access to the same EHR system. When a patient moves between and among various providers, her record is not updated in a systematic way. PMI will be most successful if members of the cohort are followed up for five, ten, twenty, or even fifty years. To do that, PMI should find novel ways to integrate EHR data stored across multiple platforms and track patients across multiple EHR platforms. • Privacy concerns of potential participants. Participants may be concerned that current regulations do not protect them from forms of genetic discrimination and stigmatization. • Lack of clarity about how PMI will provide benefit and to whom, and what is the role of each individual participant in contributing to that benefit. Absent knowledge of the kinds of research questions that will be asked and/or the kinds of researchers who will have access to the database, it is difficult for potential participants to discern the benefits of research.
11	One strategy to address privacy concerns would be for the government (i.e. the Supreme Court) to issue clear legal definitions of health data ownership. Below is a suggested framework: 1. First Degree Ownership or Citizen Ownership of Health Data First degree ownership typically resides in the individual from who's body the health data is derived. Currently, most data will have the first degree ownership designation of de-identified vs private citizen. In time, patient engagement involving micro-consent will likely become the norm. In some instances, current entities will claim first degree ownership over the human data they manage as "second degree", legal guardians described below. It will be helpful for patients to understand whether the entity they are working with recognizes them as first degree owners or claims first degree ownership of health data. Ideally, patients in the precision medicine cohort would have first degree ownership - and a patient friendly materials transfer agreement (reflective of their rights). 2. Second degree ownership - Legal Guardians of Citizen Health Data Second degree ownership is the entity that is legally responsible for damages and/or fines due to potential harms associated with security/privacy breaches of an individual(s) health data above. Legal guardians manage their second degree ownership of via forms requiring citizen signature/consent. 3. Third degree ownership - Creators of derived works pertaining to health data. Third degree ownership consists of the legal rights and responsibilities from derived works (i.e. ownership over genomics annotation, not raw patient data itself).
12	

Question 3A. The barriers to participation in the precision medicine cohort and strategies to address those barriers

Obs	Q3A
13	
14	• Limited knowledge of PM is a deterrent to participation. Recommended strategies should include informational meetings with high quality video explaining the President's initiative and inclusion of footage from his State of the Union address. Material should define precision medicine, usage of personal health data and ownership of this information, define the benefits to the participants and greater community, protections for participants, and plans to disseminate individual (MyChart) and aggregate (newsletters/websites) findings. • For low-income participants with limited access to health care, being informed of the results from their data and biospecimen contributions could be the only means by which they know of their individual risk factors for disease or chronic conditions. Will participants in the PMI cohort be provided with medical care as part of their compensation? If their cohort participation will provide them with medical care, long term commitment to the PM cohort conditions would be strengthened. • Will the researchers be anonymous to the participants? Contributing data to an institution is less motivating than to researchers with whom one can identify. Not knowing who the researchers are and what studies will be done with the data reduces the self-determination of potential participants.
15	A major issue in longitudinal cohorts is often retention of subjects. Integrated healthcare systems with robust EHR systems already have longitudinal data and samples on patients in their care throughout lifetime of enrollment, both retrospectively and prospectively. Annual turnover rates in HMORN health systems average around 13%. HMORN research centers have extensive experience recruiting populations typically underrepresented in research and many sites have partnered with safety net and other organizations serving underrepresented populations. Other approaches being used at HMORN sites to improve involvement in research for traditionally underrepresented groups include translation and customization of recruitment materials, bilingual recruitment staff, implementation of Community Advisory Boards for relationship building within the community, and establishment of "centers of excellence" within the site. In addition, because our patients receive care in our systems and generally trust our systems, recruitment efforts among HMORN research centers are generally more successful. The HMORN Virtual Data Warehouse (VDW) (federated standardized data files) also includes claims data that allows the capture of longitudinal data from clinical activity taking place outside of the specific provider group. For entities that have a system-owned health plan, a subset of patients that leave a given system may also retain insurance coverage through the system; thus allowing capture of data on external care received through claims and improving the amount of data available on individuals from these underrepresented populations in a precision medicine cohort.
16	Demographic shifts in populations are invariably are accompanied by genetic and lifestyle changes that, in turn, affect health in a positive or negative way. The implications of this proposed million-cohort study to the "precision physician" construct is significant. The young Asian community is an excellent target population which has already shown participatory-friendly behavior over the past decade and a half.
17	
18	Individual privacy concerns over misuse of cohort data will be a significant barrier to participation. People have mixed views; however, individuals generally favor the use of personal health data for societally beneficial research, but have grave concerns about harmful use by payers, employers, and others in the healthcare system. The rights of participants need to be well defined. Solutions should be both written and digital, anonymized, and de-identified, but allow participants to see how data is used for society in research and by health practitioners. High level ways to address concerns are: Clear and simplified process to opt out at any point in time; Clearly scoped project mission that defines how data will be used and by whom; User-friendly tools and secure participant portal that allows participants to view collected data and its usage. Affordable mobile device availability is more pervasive than ever, but access to health and wellness information and technology is complicated and sometimes prohibitive. Success depends on ease-of-use metrics, device and app proficiency, choice of multiple device platforms, and protected, compliant sharing options. Mentoring or tech education will ensure participants are using mHealth devices (wearables, digital blood pressure monitors, or connected weight scales) accurately to ensure high-quality data collection. Platform choices need to include iOS, Android, PC, Mac, etc to ensure that enterprise solutions are compatible with both existing and new devices and applications. Gathered, analyzed, and validated data should be sharable with the appropriate degree of transparency and concurrency with EHR standards and methodologies.

Question 3A. The barriers to participation in the precision medicine cohort and strategies to address those barriers

Obs	Q3A
19	Retention is often an issue in longitudinal cohorts. Integrated healthcare systems with robust electronic health record (EHR) systems already have longitudinal data and samples on the patients in their care. Individuals often stay within integrated healthcare systems for longer periods of time, allowing for collection of data from prenatal throughout lifetime of enrollment. Some integrated systems, such as Geisinger, also care for a very stable population, including data on multiple generations of a family. Utilizing integrated healthcare systems maximizes the longitudinal data available through both legacy and prospective data collection.
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21	A. There will be variation among communities in terms of existence of electronic medical records, and access to various models of mobile phone technology. Consider alternate models for patient-entered data, such as paper-based, telephone, mobile phone, and online patient-entered data. B. Consider a plain-language public education campaign for people who do not understand the value proposition and benefits of genetic testing, how their information will be used, and any protocols for allowing them to control and/or track how their information will be used. There are substantial knowledge deficits here that will need to be addressed. Consider partnering with genetic counselors for this educational work as they are experienced in discussing testing with patients and participants. C. Public education about GINA is very important, including exactly where to call or provide the website if someone feels that they are the victim of genetic discrimination. Also, since GINA does not cover certain types of insurance, such as life, disability, and long-term care, we recommend that this program use very transparent language concerning the exact purpose of and protections offered by GINA. D. Members of the public may feel that the mobile phone tracking and other techniques for gathering phenotypic data or data about environmental exposures is intrusive. Public education is needed about how genetic data can only be interpreted in the context of this phenotypic data.
22	Deaf individuals need to have information in American Sign Language, their primary language, not written English - for legal and understanding reasons. Language People has a patent on the technology for translation of English into ASL for consent and informed agreement procedures.
23	The importance of including diverse populations at high risk for health disparities in biorepositories and our finding that higher health literacy increased the odds of consent in all three instances suggests that special attention is needed to improve the readability of consent documents related to Precision Medicine and the associated processes for obtaining consent. Immigrant status only influenced data linkage, which required no further contact from the study team so required little effort on behalf of the participants. One potential reason for the influence of government insurance, which was used as a proxy for socioeconomic status, on biospecimen storage and use may be the fact that participants were explicitly compensated for provision of biospecimens although they were not compensated for long-term storage and use.
24	A strong alliance between community members and researchers will be needed to address barriers of participation in communities that may distrust research & medical care providers. Use of health liaisons that are from the community of interest (e.g. promotores in Latino communities) and partnering with existing local organizations that serve under-represented communities can help increase trust between under-represented communities and researchers. This may include partnership with religious organizations, Boys and Girls Clubs, and Tribal Councils. The emphasis should be on local organizations that have personal relationships with the communities they serve rather than national organizations. Using clearly worded consent forms in multiple languages written at a 5th-8th grade reading level with simple text layout will also reduce barriers to ensuring that literacy does not pose a barrier to informed decision-making about participation. Additional investments would need to be made to spur innovations that address barriers to participation in large cohort studies. For example, the use of mobile approaches to facilitate participation may have different opportunity costs in lower vs. higher income groups. Understanding these impacts and developing meaningful strategies will be very important. There are also likely to be significant barriers posed by interpretation of regulatory requirements in some institutions. For example, more conservative IRBs may be more restrictive in the types of recruitment approaches that they will allow. Although IRBs must have autonomy, consideration should be given to providing additional support and guidance to IRBs as they review precision medici
25	historical mistrust lack of access inadequate healthcare provider training unintended outcomes lack of awareness of clinical trials
26	

Question 3A. The barriers to participation in the precision medicine cohort and strategies to address those barriers

Obs	Q3A
27	1. Mistrust of medical and health care professionals and establishments a. Thoroughly research past abuses of power inflicted upon minority communities b. Identify strategies such as using key informants within communities to relay the benefits of research TO THAT COMMUNITY. c. Establishment of support for communities before request for information is made. 2. Lack of knowledge of benefits and process d. Have a trusted community member or minority researcher develop materials to explain positive benefits and potential risks of participation. Utilize eCLAS Standards to ensure materials are appropriate for the intended audience
28	The March of Dimes foresees at least three major barriers to public participation in the PMI: lack of information, lack of accurate information, and misconceptions about the project. Individuals obviously cannot sign up to participate in the PMI if they are unaware of it. As noted above, a broad range of partners will be necessary in order to recruit an appropriately diverse cohort. However, the information potential participants receive must be accurate and appropriate. The scientific enterprise has witnessed many examples of worthy projects that failed to fulfill their promise because inaccurate or incomplete information was disseminated. The PMI and its partners will need to have a robust communications strategy that includes monitoring of many platforms to identify rumors or misinformation and correct them as quickly and aggressively as possible. Finally, the public may have certain assumptions or misconceptions about this project that must be dispelled before they will consider participating. Foremost among these will be concerns about privacy, and how their personal data will be collected, stored, used, and made available to others. The PMI must have a detailed public plan explaining how these issues will be addressed in order to give the public an appropriate level of comfort with participation.
29	There has to be protections such as the ones state in the Nagoya Protocol for human genome data and products from that data whether diagnostics, therapeutic or in synthetic biology for people of the Americas. Especially American Indians who have tribal sovereignty and international political/legal status because there is likely an abundance of novel variants at high frequency and much mechanistic information to be gleaned from their genomes. They are the poorest of the poor in every North and South American country and they have no great representation in law, governance, business or medicine that their voice and interests will be heard. Simply put, we do not trust "altruistic" endeavors based on resources from the Americas...because historically we have been left out on our land. The US has so far failed to adequately consult with tribal groups on this issue. To create incentive , you most go past individual rights to privacy an consent contained in GINA and protect communal rights.
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32	1- Cultural, behavioural and historical as well as current factors 2- Disease incidence and/or duration of survival/ rate (African-American) 3- Fear, unfounded rumours and underestimated or overlooked general misconceptions 4 Potential stigmatization of the target group/cohort 5- Unintended adverse consequences 6- Individual response to therapy and outcomes 7- Personal, social and geographical determinants 8- Economic and environmental factors 7 lack of integrated disease surveillance and response approach
33	A lack of trust in research can be overcome by engaging participants in a common purpose other than solely through a message of personal health promotion. We were able to mobilize minorities with high rates of diabetes, hypertension and obesity through a shared goal to help a younger generation in need during a critical window of development from ages 4-9 when they are learning to read.
34	N/A
35	I think you can make the case that the *entire* cohort could be from the deep south, where there is a great representation of African-Americans (with the most diversity of genetics, and with great diversity in environmentally-related outcomes). The statistics for the area south of Tennessee for smoking, cancer, and other environmentally-relevant health issues are also stunning. This would be a statement to the American people that we are going to boost up the area of our country that is in most need of help, and at the same time learn lessons that will help all Americans. I think you could add Florida and Texas in order to ensure Latino involvement. Why not have this cohort be HIGHLY enriched for those whose health needs the most attention?

Question 3A. The barriers to participation in the precision medicine cohort and strategies to address those barriers

Obs	Q3A
36	Our current attempts to enroll patients for Whole Genome Sequencings (WGS) have met the most resistance due to the lack of protections afforded by GINA. An update in this act would greatly alleviate concerns regarding the long-term consequences of WGS. Lack of education regarding sequencings that addresses fears about things like cloning, information about carrier statuses, associated risk rates, and types of medical issues that currently are not genetically understood will be necessary. National and local education efforts should begin well before recruitment. Genetic counselors and other health care professionals who are not affiliated with the research or recruitment should be available to discuss the risks of this type of testing. The provisions and exclusions of GINA should be addressed from the beginning and throughout all education and community efforts.
37	Based on Booz Allen's clinical research experience, there are several participation barriers: privacy, fear, cost, and understanding. 1) Privacy: Recent findings demonstrate that research subjects can be identified by combining study data with public data. The PMI should address privacy concerns with straightforward and positive messaging coupled with technology to safeguard participants' data. The PMI should focus on ensuring security, maintaining limited access to information, requesting permission, and reiterating respect of the right to choose the type of information to share and at regular intervals. 2) Fear: Many people will opt out of participating in the study due to fear of discrimination, fear that the research will identify new underlying medical conditions, fear that participation will impact their employment and lifestyle. We recommend establishing cultural congruence between research support staff and participants; develop physician, patient, and family programs to educate and inform the patient as well as the physician. 3) Cost: It may be cost prohibitive for many people to participate in a study due to time commitment, location of the study, and other factors. Both cash and non-cash incentives should be employed to mitigate this barrier. Non-cash incentives could include child care, free meals, and centrally located meetings. 4) Misunderstanding: Many participants may not understand the goals of the study and what the findings might mean. It will be important to develop tailored study communication and outreach tools that are culturally and linguistically appropriate that explain the goals of the study in simple language.
38	Trust is a key factor in willingness to participate in research. Profound differences have been found between people of color and Whites in their response to trust questions related to research including how privacy would be protected, how the government would use data, and invasiveness of research. For Asian populations, we have found in our recruitment that an increase of face-to-face visits and using culturally competent staff was necessary to ultimately gain trust. Religious beliefs, health related fears/beliefs, and time demands are also factors that can act as barriers to research participation, for majority and minority populations. Contingency management is effective and may be a useful framework to consider. In addition to monetary incentives for participation, additional assistance in other areas may also increase participation. For example, offering transportation assistance and child care may enable participation. Promoting the benefits of participation can also combat this barrier. Our experience, which is supported by the research, has shown that attrition is reduced if participants are "sold" on the study. For this to be done, staff must also champion the study. To gain respondent cooperation, staff at every level must believe in the purpose of the cohort and sell the importance of the respondent's participation. Additionally, traditional family and gender roles impact participation. For example, in some cultures, the male head of household might speak for the entire family while other cultures have a more matriarchal approach to decision making. Understanding the cultural influences is key to recruitment.
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41	Solicit participation at clinics in community hospitals, Public Health centers, and free or very low cost programs and on clinic days with both written information AND person-to-person recruitment. Also, form alliances with the schools through the PTA's and technical and community colleges. Explain carefully orally and in writing what the research covers and how it has benefited others using case illustrations.
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Question 3A. The barriers to participation in the precision medicine cohort and strategies to address those barriers

Obs	Q3A
45	Barriers • Community distrust for the research institution • Community lack of knowledge of research processes and practices • Community interest or need for research topic particularly if there is no benefit for community • Lack of understanding of technical • Researchers ignorance of the community's culture and history • Education on the need for a precision medicine cohort • Lack of high level Investigators who reflect the population being studied • Lack of information • Transparency of the research process • Shared findings/results of research in lay language • Lack of engagement in the process • Inaccessibility of research site • Unavailability..lack of transportation, childcare, Strategies to Address Barriers • Engage community from onset-planning, decision-making, etc. • Indicate benefit to community • Provide transportation • Address technical language in lay terms (community engagement can facilitate this) • Researchers must learn the history of the community they are entering • Create Community Health Advisory Networks (CHANs) in each community • Disseminate health education materials and health promotion activities; • Opportunities for testimonials • Ensure transparency with the Community • Provide opportunities for annual community-wide participatory outreach activities • Collaborate with other community groups on health fairs; community forums; • Build partnerships with local print, radio and television media outlets • Conduct presentations on research findings/results • Provide appropriate trainings/education on research • Provide bi-directional learning opportunities with community and investigators
46	There are many barriers to participation, and these barriers may differ from community to community and between groups (ethnic, sex, age and SES) within a single community. Blood centers have effectively addressed two universal barriers, site distance and time. Although JHS was a partnership between several colleges and national institutions (NHLBI and NCMHD), there was a single health exam and biospecimen collection site, the University of Mississippi Medical Center. The JHS did not require multiple exam centers since the study was focused on participants residing in Jackson. San Diego is the eighth-most populous city in the U.S. (3.2 million) and the county is larger than the combined area of Rhode Island and Delaware. Travel time from the eastern boarder of the county to University of California –San Diego Medical Center is approximately 90 minutes. The diversity (ethnicity and SES) within the county dramatically differs between the local communities in San Diego County. Conducting a cohort study similar to JHS or larger in San Diego County would benefit from multiple sites. In addition to SDBB's main site, the blood center has 5 additional sites scattered throughout the County. Additionally, SDBB's state-of-the-art bloodmobiles travel to local communities in the County collecting donations from 9 to 4 sites daily. A donation center or mobile unit is usually within 15 minutes or less from the donor. Proximity eliminates travel time and provides the donor/participant flexibility.
47	
48	!. Concern about the misuse of this information to the detriment of the participant. Current efforts to subvert GINA are discouraging. 2. Inclusion of the military in the protections of GINA would help military families participate. Currently it it still legal for the military to discriminate based on genetic information. 3. Americans are cautious about sharing any medical information for fear of being dropped by insurance, or fired by employers. Even with legal protections in place, they do not trust that these cannot be subverted by employers and insurance companies.
49	The precision medicine initiative proposes to use electronic health records to link cohort participants' medical information, biological specimens and behavioral and environmental data. There are barriers to the inclusion of substance use disorder (SUD) treatment information in EHRs due to federal confidentiality protections (42 CFR Part 2). These protections require that patient consent be obtained before sharing SUD treatment information, which makes these data harder to obtain than other health care data. We are concerned that, due to the complexity of this initiative and the need to move quickly, these data will be left out, as they were when the American Recovery and Reinvestment Act funds supported the development of health information exchanges (HIEs). Unfortunately, most HIEs have been unable to retrofit these systems to manage SUD treatment data as required to comply with 42 CFR Part 2. Such an omission would undermine the larger initiative by creating an incomplete and skewed data set, and would disproportionately affect vulnerable, underserved patients and exacerbate disparities. Excluding persons with addiction from the cohort will prevent research into one of our nation's most significant public health problems, a primary disease with profound secondary impacts on the course of other diseases, health care outcomes, and overall health care costs. As such, funding solicitations should explicitly require applicants to describe how they will navigate the confidentiality requirements of 42 CFR Part 2 in establishing the cohort to ensure that patients with a current, past or future SUD diagnosis are not excluded from this important initiative.

Question 3A. The barriers to participation in the precision medicine cohort and strategies to address those barriers

Obs	Q3A
50	Aside from common structural barriers (lack of transportation, work conflicts), there are many issues of trust that surround participating in clinical research studies. It is important that community stakeholders are identified to help with facilitating trust in the community. Language barriers are also critical and there needs to be established support for staff who can communicate with research participants. Health literacy barriers are also present, which may require participant education.
51	- Perception and/or lack of data security on personal information and its sharing between the public and private sectors.
52	a. Ensure materials area available at low literacy, in multiple languages, and in multiple mediums. Do not require literacy for participation. b. Avoid the fate and reputation of much research, considered by communities to be “drive-by research” that leaves no impact on the communities where researchers recruit. Guarantee that all participants will have access to the precision medicine database, just as researchers do. Commit that all findings will be shared, specifically with every research participant, through regular updated communication in plain language (and multiple languages), and more broadly with the communities they come from. c. Offer stipends that recognize the time these efforts require. d. Build strategies and messages with community partners from the target groups and with communications experts. Make sure images of the study reflect the diversity of participants we should enroll. e. Make this fun! It should be viewed as a party that can’t be missed, and even better, as a team that they need to join, as they want it to win, and without each unique person, it cannot win. Send thank you, birthday and study anniversary cards. f. Go to patients. Make it easy. Have church Sundays, street fairs, and other events to engage populations. Have evening and weekend recruitment hours. g. Use lotteries to incentivize. h. Engage leaders of leading biobanks (such as the BioMe Biobank at Mount Sinai, Director Dr. Erwin Bottinger) who have recruited diverse populations, with great success, into biobank studies.
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54	viewed as difficult participants
55	The Center for Health Equity and Community-Engaged Research at Mount Sinai has a library of successful engagement strategies to recruit patients to diverse studies, including diabetes prevention, genomics, cardiovascular disease, cancer, and maternal and child health. We would be happy to share strategies. We regularly recruit patients historically underrepresented in research including through food pantries, churches, schools, social clubs, barbershops, and local organizations.
56	--Limited understanding in the general public about genetics and what it means. Success in securing participation ought to start with education --Mistrust for medical science in general is big --The internet and TV shows make inaccurate facts believable to the public. There is a socital trend to not question what is presented to them, so when you introduce this kind of study, the public might immediately imagine things like 'cloning' etc. --People who are not connected to community leaders or an organization would not be included. Those 'isolated' individuals are disadvantaged with this type of study using community helath workers who can go out ad find tehse individuals migth be a way to address this barrier --Making data exclusive to where electronic health records are vailable will result in misisng a large part of rural populations --Going back many times for re-consent would deter particpation and cause lack of trust
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58	•Barrier: language/health literacy; strategy: language software, and patient engagement software for marketing purposes •The number one complaint from healthcare/study participants is parking and getting to and from appointments. Public transportation or ride services could be included as a cohort benefit. •A “range” of compensation for participation in studies could be offered (i.e. a small stipend similar to those used for Jury duty). •Home visits: Leverage home health and hospice providers to potentially extend their services i.Collaborate and recruit larger firms (Emedisys, Gentiva, Interim, et al) that have better technology and wider reach. ii.This strategy would be particularly relevant for hospice cancer patients, and the next wave of Precision Medicine targets, which will likely include neurodegenerative diseases and depression. •Marketing to the general public regarding the need for data to populate the cohort will be a significant barrier. Strategies: effective communication of expected benefits from participation (i.e. health insurance, clinical trial participation, more robust health care)
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Question 3A. The barriers to participation in the precision medicine cohort and strategies to address those barriers

Obs	Q3A
60	Trust is the most significant barrier to participation. Our Center for Public Health and Community Genomics has carried out a number of projects in which communities of color received education in genomics and helped shape genetics policies. The project "Communities of Color and Genetics Policy" elicited participation by using the partnership approach, with significant community engagement in all aspects and at all levels. Rather than having PMI perceived as "them" doing it to "us", it must be carried out as a collaborative effort. Using a public health approach will help. This means highlighting public goals: population-based disease prevention and promotion of health equity; rather than emphasizing drug development and expensive technologies.
61	To stress the assurance of complete protection of data and privacy is the only way to overcome people’s suspicion in sharing their own data, which is the main barrier to the participation. Also, different levels of data sharing might be proposed in order to enroll people who cannot in any case renounce the exclusivity of some personal data. In this way, one might for example agree to share his genome, his motoric and dietary habits and other things but not, say, data about the proximity with other people or the mood in his own voice when telephoning. Or vice versa. To allow excluding some kinds of data from the sharing might be a great incentive for a lot of people. Another very big barrier is the requirement to adopt smartphones or smartwatches or other similar devices in order to provide data. This is a tremendous barrier for people of the lowest classes, since in the poor conditions they live in, to wear any device is unimaginable. This would mean a complete exclusion of the poorest and an enormous lost for the research. Also, this kind of electronic devices are also a strong cultural barrier: people belonging to certain cultural groups, or more in general the elder people, might be prevented from participating by the requirement of these devices. An alternative program to collect lifestyle and environmental data should be provided (for example interviews and questionnaires) in order to include these wide and historically underrepresented classes.
62	Time is a barrier for everyone, whether they are under-represented or not. Keep it short - people are more likely to participate if they don't have to wait for hours or spend 30 minutes listening to someone talk about the project.
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66	There are significant barriers to everyone participating because this is taking place in the very broken healthcare system. These are heightened by the fact that marginalized communities will be even farther from the goals of the biomedical research enterprise in its current state. The relevance of these projects, their lack of proximal solutions to real suffering, and the usual lack of integration into people's lives all must be overcome. I believe the strategy of giving this to the community to drive is the first and foremost one. I would trust the community to know what it needs to get the job done, and then give them adequate resources. Often projects like this give the largest funding to traditional established entities, and leave little for communities, thus dooming them to failure.
67	The biggest potential barriers to this type of research are investigators who wish to diversify the “face” of the cohort without genuine interest in addressing health disparities, without true understanding of the possible mechanisms through which health disparities occur, or commitment to community partnerships and the effort that it takes to achieve genuine, flourishing partnerships. Barriers to participation are created by rushing into recruitment without collaborating with key people from the community and other successful researchers. Barriers are created by making underrepresented groups feel like they are being “plugged in” to an existing study, not because there is genuine interest in their community and family, but because someone told the researchers they need to fill a quota. Other major barriers are created by setting aside “outreach teams” for underrepresented groups and then starving them of the resources they need to do their jobs. The steps to overcoming barriers to recruitment are different in each setting. These steps can be identified for each ethnic/racial/linguistic/socioeconomic/gender/regional setting via community advisory collaborations and leveraging already-successful efforts across the country. Then, we need to demonstrate the commitment to not skip any steps and to honestly evaluate the success of each step.

Question 3A. The barriers to participation in the precision medicine cohort and strategies to address those barriers

Obs	Q3A
68	Trust is an important barrier to overcome when engaging historically marginalized and stigmatized groups who have been mistreated by the health care system. In order to build trust and effectively engage patients, direct patient involvement is essential and patient engagement must be integrated in each step of the precision medicine process. Safety and privacy safeguards must be in place and patients, particularly those from underrepresented groups, must be aware of privacy, information security, data sharing, and any other potential issues that could arise. Transparency and privacy are primary conditions of patient participation. Public campaigns around safety and privacy should be included in the process. Patient trust is a significant source of tension in precision medicine due to related historical events involving genetic testing among marginalized groups. Community outreach needs to be done by members of the marginalized communities in order for trust-building to occur and for successful precision medicine initiative and cohort recruitment to happen.
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Question 4A. Ways to avoid potential stigmatization of subpopulations, and to manage unintended adverse consequences of the precision medicine cohort

Obs	Q4A
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3	There are a number of potential ways to mitigate stigmatization of populations particularly those with health disparities. The first will be to address the disease issues that are important to this community and to point out how this will help to improve the prevention, diagnosis and treatment. A second important point is the recruitment of participants by people from the community who are trained to be able to explain the importance of the study and who can connect directly through language and culture with the participants. A third important method of limiting stigmatization will be choosing locations where the lead institution in precision medicine has a well-established program in the community that is being targeted. Finally, assuring feed- back of information from the program to the community is the only guarantee of sustainability and avoidance of misunderstandings or inappropriate messages. The presence of institutional programs that are recognized as beneficial to the community are likely the most powerful litigators of refusal, stigmatization, suspicion and other barriers.
4	Developing strategies that avoid stigmatization of subpopulations will be extremely important when recruiting individuals for genetic studies. Individuals will not participate in these studies if they believe that they will be singled out. One way to deal with this challenge is to extend information and participation to all community members without censor. In addition, standardizing processes so that participants are treated in a similar manner and receive information using similar methods is important across all recruited populations. We plan to build on our inclusive experience with the PMRP cohort by continuing to mirror clinical practice and involving all subpopulations regardless of socio economic status. MCHS treats all patients in a similar manner and seamlessly integrates treatment services. For example, Marshfield does not turn away low-income or non-insured individuals. MCHS works together with FHC to provide low cost/no cost insurance options to qualified individuals without stigmatization. Marshfield's EHR is configured to be non-discriminant. Care providers are unaware of a person's economic status unless they specifically ask. Clinical data is captured and displayed in a similar fashion for all patients.
5	Underlying assumptions of genetic predisposition to disease may perpetuate social inequalities, and stifle the community engagement process. The literature has shown findings from research studies fuel the perception that disparate health outcomes experienced by communities of color are linked to shared genomes rather than shared environment, social status, or income levels. The AAMC recommends the NIH develop culturally sensitive communication strategies when reporting the findings from the Precision Medicine Initiative. By utilizing race and ethnicity as a proxy in recruitment, analysis, and communication of findings, the NIH runs of the risk of implying genetic differences by race, when categories of social experience or ancestry may more accurately characterize differences in health.
6	
7	There is a genuine risk of "genomic privacy leaks" for non-participants in the cohort. For example, if a father signs up and his three children sign up, the four genomes combined contain enough information to infer (on average) about 90% of the mother's genome, even if she is not consented, is unable to consent or refuses to consent to participation in the study. While the vast majority of Americans will not care, legal challenges from a handful of non-consented "indirect participants," could potentially cripple the entire effort. The best way to avoid the doomsday scenario is to address the possibility in advance and to define policies (or even laws) that prevent the abuse of "synthetic genomes" for non-consented participants.
8	4. We will collaborate with the NIH and its partner organizations to create strategies, messaging architecture, activation implementations, content, and relationships designed to build the reputation, standing, and consumer profile of the "Precision Medicine" campaign, and drive the adoption of the underlying technologies that fuel its growth and cohort adoption. These efforts will be focused on creating a narrative and activations that blend the positive impact of your offerings on society and consumer interest with compelling storylines, respected third party validators, strategic business and creative partners, and popular culture messengers. Examples might include launch strategies, pro-social programs, specialized content, public-private partnerships, and events of varying sizes that raise the profile of both the NIH itself and the "Precision Medicine" initiative as the innovation platform and vision for our collective health and well-being.
9	No response provided.

Question 4A. Ways to avoid potential stigmatization of subpopulations, and to manage unintended adverse consequences of the precision medicine cohort

Obs	Q4A
10	As research on genetics advances, we ought to be very careful about how genes are named. For example, the "warrior gene" or the "feel-good gene" have popped up in the media, and have become associated with a particular phenotype (such as skin color). Scientific racism can perpetuate stigmatization (e.g. the idea that persons with black skin have the "warrior gene" and so are innately more inclined to violence and aggressive behavior). Moreover, genetic discrimination on the basis of propensity for psychiatric illness or substance abuse may occur. Epigenetic data is not current protected by GINA, for example, but may lead to re-identification of those who are substance abusers or may have been at one point in time. PMI ought to anticipate ways of studying genetics, and particularly epigenetics, that may not be covered by current regulations. (See, e.g., Philibert, Terry, Erwin, et. al. "Methylation array data can simultaneously identify individuals and convey protected health information: an unrecognized ethical concern" Clinical Epigenetics 2014, 6:28.) Privacy safeguards could help avoid stigmatization by concealing identity. But crucially, governance of the database must also make transparent the approval process to gain access to the data in PMI. Transparent governance, ideally through some sort of participatory democratic process, is key to gaining trust of potential participants, and safeguarding them against stigmatization.
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13	EngageUC is a NIH/NCATS-funded study to identify best practices for biorepository governance and consent. The study involves all 5 of the University of California (UC) medical center campuses. EngageUC works with researchers, regulators, and community members on governance and is using a randomized trial to provide evidence on best practices for consent. With respect to unintended adverse consequences, EngageUC community engagement activities with lay Californians generated 3 evidence-based recommendations that may be of relevance for a US Precision Medicine cohort. Participants emphasized the need for both strong oversight of biorepositories and associated research, as well as significant sanctions for researchers and institutions for the mishandling of samples and data. Participants anticipated that the return of unwanted or ambiguous results would have significant consequences for donors; they strongly recommended that donors be able to choose whether or not to receive research results from their own samples. Finally, acknowledging that some research could be objectionable to donors and contribute to public distrust and diminished participation, participants recommended a strong and meaningful role of lay individuals on biobank governance advisory boards. In addition – although this recommendation received somewhat less enthusiastic support than the others described above – many recommended that the interpretation of research results be done by a trusted healthcare provider. In sum, lay Californians felt that with informed representation and input, community stakeholders could protect donors' interests without requiring that the donors be involved in the granular management of their own samples and data.
14	• Open communication channels which identify lead researchers by name, oversight body (OHRP/IRBs), steps for reporting and notifying participants of adverse events, and how data is being used. • IRB agreements and communications should be readable at levels appropriate for the target populations. Explanations of the possibility of unintended adverse consequences should be written to protect the potential participant. • When possible, recognize the participants as "Science Heroes" or Citizen Scientists • Show respect in all interactions with participants
15	The ability to maintain an active and ongoing dialogue with members can avoid miscommunication and misunderstanding that might lead to potential stigmatization of subpopulations or other adverse consequences. The patient populations in the HMORN tend to be relatively stable, with some sites averaging 20 years of membership on average. This long term relationship with the healthcare system allows for the opportunity to re-contact participants and engage in ongoing conversations using multiple mechanisms beyond clinical visits to interact with individuals. The HMORN also has internal networks that focus on disorders with risk for stigmatization and potential for adverse outcomes. The Mental Health Research Network (MHRN), has Scientific Interest Groups devoted to child and adolescent mental health, and diversity and health equity. The purpose of this group is to develop relevant guidelines and philosophies for avoiding issues such as stigmatization and adverse events. The Cancer Research Network (CRN) and other HMORN researchers are exploring genetic markers related to improved treatment outcomes or increased risk for disease. While one goal is to find biological markers rather than to identify racial or ethnic populations that may be more at risk for adverse outcome, it will be critically important to have input from community members of any subpopulation that may be more predisposed to certain outcomes in order to manage any unintended adverse consequences. These internal networks such as the MHRN and SIGs, like the PER SIG and Genomics SIG, provide infrastructure to successfully manage unintended consequences of a precision medicine cohort.
16	

Question 4A. Ways to avoid potential stigmatization of subpopulations, and to manage unintended adverse consequences of the precision medicine cohort

Obs	Q4A
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19	Continual and purposeful engagement of community members in research is crucial to avoid potential stigmatization of subpopulations in a precision medicine cohort. Individuals from these communities should be partners with the researchers in order to help manage the unintended consequences. Recently there has been heightened attention, again, to the topic of stigma—some of this work is characterized as the 'science of changing social norms.' Clearly there is potential, given a new target for 'labeling', for patients to be identified and 'targeted'. There has been some work in this space specifically focused on characterizing and reducing stigma associated with diagnoses such as HIV and cancer that may help to inform how to reduce and avoid stigma. Erving Goffman (1963) reminded us that the original use of the term 'stigma' was Greek and intended to denote bodily signs of moral status. Today, stigma appears to be related to the reduction of an individual to a single characteristic that defines the whole person as tainted by a characteristic. It will be important to focus on sociological research related to precision medicine. Precision medicine, by its very nature, is an individualized approach to the care of individuals based on a constellation of genomic and phenomic characteristics. Additional communications research will be necessary to develop messaging strategies that focus on this quality of precision medicine. Language, used properly and properly explained, will focus less on the disease process (stigmatizing signs) and more on the capacity of medicine to individually address treatment.
20	The best way to avoid potential stigmatization of subpopulations and manage unintended adverse consequences of the PMI is to involve the communities in the decision making process and allow them to have oversight regarding the dissemination and use of data. There is no current paradigm to implement this within the current data sharing policies of the federal government. It would take a bold, novel initiative on the part of NIH to develop and maintain such a plan regarding the PMI.
21	A. A mechanism to avoid stigmatization and unintended adverse consequences is to ensure that participants have access to high-quality genetic counseling. Participants who are well-educated about their genetic test results are more likely to avoid adverse consequences based on misunderstanding the data. Genetic counseling, by definition, is the process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease. Certified genetic counselors are also specifically trained to address misunderstandings and feelings of stigmatization. They are also trained in issues relating to cultural sensitivity and how to address the needs of patients with diverse backgrounds. B. The chance of stigmatization can be lowered by involving a diverse review board. C. It is critical that participants who have their genetic data returned to them can access appropriate treatment and/or preventive care based on that information. Barriers to this include: 1) lack of universal access to health insurance, and; 2) lack of multi-disciplinary care that can offer the necessary preventive strategies in a streamlined and efficient manner. Very few multi-disciplinary care teams exist that are organized around specific genes. Creating incentives to develop these programs will ensure that PMI participants can fully benefit from the data they receive. Otherwise participants will need to schedule multiple appointments with multiple specialists, possibly at multiple healthcare centers/clinics.
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24	Using strong principles of community-based participatory research both from the beginning of cohort development and in the context of specific studies using the resource will provide an excellent foundation for reducing and managing unintended adverse consequences. There should be strong access principles that provide guidance to investigators about the kinds of research that would and would not be appropriate. The access review process and publication review process should also include community representatives who will likely be better situated than scientists to anticipate potential consequences at the community level. Training for members of the access committee on issues regarding the role of research in social justice, equity, and stigmatization would also be important. Requiring scientist participation in training about health disparities and historic injustices in research could also help create a scientific community that is more sensitive to these issues. The CITI platform has relevant modules that could be utilized or adapted for this purpose. There is often an assumption that vulnerable populations access care in the same manner and frequency as mainstream populations, which in many cases is incorrect. Disenfranchisement of groups from mainstream health care leads to episodic and urgent care where the engagement of patients around precision medicine is likely to be ill timed and inappropriate. A culturally competent approach should be used to reach these populations outside the delivery system to ensure broad and diverse participation in the PMI, using an approach that may focus less overtly on health care.

Question 4A. Ways to avoid potential stigmatization of subpopulations, and to manage unintended adverse consequences of the precision medicine cohort

Obs	Q4A
25	Create narrative that makes it acceptable to work through specific health challenges. Creative marketing and messaging is necessary.
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27	1. Clearly communicate the request and BENEFIT TO THE COMMUNITY. For minority populations that have been victims of medical malpractice, abuse, exploitation, racism, etc. from the medical community, highlighting the positive effect clinical research on minorities can have on the ENTIRE population may not be a good strategy. It is reminiscent of past experimentation on racial minorities for the benefit of society as a whole, which was wrong (i.e. USPHS Syphilis Study, Johns Hopkins procedures on African Americans). Researchers should instead focus on possible benefits to individual communities (African Americans, Latinos, Native Americans, etc.). 2. CLEARLY outline plan for continued follow-up after data is collected BEFORE starting research. Participants should be confident that they are not being used and that they will be informed of the results. 3. Institute a process for ongoing feedback during the research process and ways to address concerns. This process should be articulated before any research begins.
28	
29	Allow American Indians to maintain control, storage and management of their own data. Provide a mechanism through IHS, the BIA or a new department to fund education, training and infrastructure so that tribes can control their own image and cultural dissemination in regard to genomic data.
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32	- Building community resilience risk communication programmes - Social grouping, community and community leaders information communication - Community forums, faith-based and trade communities partnership in Precision medicine information and education, - Fraternity organisations, voluntary and philanthropic organisations outreach and awareness, - Ethnic groups, neighbourhood associations engagement - US Government health and pharmaceutical policy and regulatory reforms to precision medicine - Global health policy and regulatory reforms to precision medicine
33	
34	N/A
35	I think you can make the case that the *entire* cohort could be from the deep south, where there is a great representation of African-Americans (with the most diversity of genetics, and with great diversity in environmentally-related outcomes). The statistics for the area south of Tennessee for smoking, cancer, and other environmentally-relevant health issues are also stunning. This would be a statement to the American people that we are going to boost up the area of our country that is in most need of help, and at the same time learn lessons that will help all Americans. I think you could add Florida and Texas in order to ensure Latino involvement. Why not have this cohort be HIGHLY enriched for those whose health needs the most attention?
36	Again, please consider adding more protection to GINA. Consider removing any threats or perceived threats of data being used for policing purposes. Nation-wide educational efforts well before enrollment will be required; education should be directed at all residents not just those interested in participating. The general public will be made aware of the findings of this research, and the best way to prevent discrimination is through thorough education. Population-specific disease prevalence should be anticipated and expected. Subpopulation community outreach should also focus on preparations for these types of events at the outset, and the community should guide the possible responses. The public reporting of such findings on a large scale may isolate subpopulations even further and cause mental and physical health decline. Educational, psychological, and medical needs for both individuals and communities should be identified. Infrastructure should be in place prior to identifying these findings to allow for a swift initiation of support prior to the public release of these findings. Additional resources may include population-based screenings, town hall meetings, free access to medical resources for counseling and/or treatment options, and other community interventions that may alleviate anxiety. Allowance for personalized education should be included in the planning. The inevitable release of these findings should include education to the majority with a mind to not sensationalize findings (if at all possible).

Question 4A. Ways to avoid potential stigmatization of subpopulations, and to manage unintended adverse consequences of the precision medicine cohort

Obs	Q4A
37	The PMI cohort is involved in defining subpopulations for mental illness, cancer, or other disease research areas. There is a recognized risk the participants will face different levels of stigma associated with participation in health research, and trials associated with these conditions. Booz Allen has worked with communities that could encounter stigmatization like the Wounded Warriors and Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury programs. Working with these programs in the community and workforce, we have developed physician, patient, and family programs and materials to educate and inform about what can be expected. Mitigation Strategies include: 1) Research studies must promote the benefits to individuals, families, and communities to help encourage health research activities. Educational outreach on background in the diseases will reduce stigmatization. 2) Research has shown that participants are more willing to participate when non-profits are involved. Working with non-profit disease organizations, using their educational material with PMI material, and showcasing insurers and employer examples and policies that support for PMI will lower stigmatization risks. 3) Gain the trust and support of key community leaders (e.g. religious leaders, providers of hospice care, local business owners). Educational interventions should focus on information about the benefits that will be shared by the community, and particularly, the impact on family members. Similar to NCI initiatives, establish Community Advisory Boards (NCI uses them) and identify "peer supporters" who are participants that have the disease and can share their stories to address stigmatization issues head
38	Transparency and confidentiality are key to avoiding stigmatization and unintended adverse consequences. In addition, the reputation of the study is important to retention and future participation. Ensuring that the use of the data and samples collected are guided by written protocol that is strictly followed and communicating this to participants in a way that is easily understandable will assist with this goal. Consent papers should clearly outline all the measures being taken to protect identity and be presented in plain language. The IRB process adds a layer of protection for study participants and this should also be explained. Based on focus groups conducted by Battelle, we found that once participants enroll in a study, they have shown their commitment to the purpose of the study. Participants want to be assured, though, that those they are sharing their information with are being good stewards. Participants desire feedback on how they have contributed to the aims of the study. Providing regular, nontechnical progress reports to participants will increase their understanding of the aims of the study and strengthen their commitment. While media involvement is important for a large study as this, it is important to protect participant identity. This may mean not identifying communities selected for the study or if the sample is selected from particular providers not divulging those selected for the study. Finally, sensitivity training of staff further ensures that subjects are protected from unintended consequences in how they are treated as study participants.
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41	Have available resources that can address issues that are identified; ex.- Pro Bono or low cost clinics to treat PTSD, community services to address various issues as you do not want to have people be in a vacuum for information or opportunities to have issues addressed.
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45	• Learn the community and its population before entering (community engagement) • Community is an equal partner beginning at the inception of the research • Create community advisory boards that including lay experts and professionals • Ongoing open and honest communication • Provide bi-directional learning opportunities with community and investigators prior to the study • Ensure transparency throughout the research process with specific actions to address violation or breach thereof • Community representation on manuscripts, publication and ancillary study committees with specific actions to address violation or breach policies

Question 4A. Ways to avoid potential stigmatization of subpopulations, and to manage unintended adverse consequences of the precision medicine cohort

Obs	Q4A
46	A national ‘cohort’ study of a million or more participants representative of the general population will uncover genetic, behavioral, and environmental factors that contribute to disease/disorders more common in some subpopulations. Reported research outcomes could possibly have unintended adverse consequences. Native Americans have the highest alcohol-related death rates in the U.S. among all ethnic groups. The how and why alcoholism is more prevalent in Native American communities remains unknown. Oversampling the Native American population in a PMI ‘cohort’ study may reveal genetic variations and health determinant factors that contribute to alcoholism. This information would be invaluable in developing prevention programs and effective treatment protocols. At the same time, a generalization of the research results could lead to stigmatization of this subpopulation. To avoid potential discrimination and exclusion as a result of reported research findings, education and careful messaging of sensitive research outcomes is key.
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48	1. characterization of some genetic diseases as connected with a particular ethnicity should be avoided. "Jewish diseases" or sickle cell as a "Negro disease" serve to discourage participation. This kind of "profiling" should be avoided since these diseases do occur outside of these focal groups, and doctors sometimes (wrongly) rule them out too quickly when the person does not appear to be Jewish etc. 2. ALL people should be encouraged to participate, not only those who know they have a genetic disease in the family. The approach of the Susan Love Foundation's ARMY OF WOMEN is a very positive one that enrolls all women. A similar approach, helping people to see the power of reporting together, would be helpful. 3. Requirements for citizenship status would need to be omitted, as the fear of reprisals against aliens discourages people from coming to hospitals and participating in programs like this one. 3. a Single National database of electronic health records, with mandatory reporting, would be the only way to compiled such a cohort. Enrollment of HOSPITALS rather than INDIVIDUALS would achieve a great deal more enrollment of traditionally underserved populations.
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50	Exclusion criteria should be evaluated for potential biases towards certain groups. It is often the case that historically marginalized groups are excluded from research studies because they do not "neatly" fit in to the study criteria. NIH reviewers need to be sensitive to studies that include individuals with multiple competing factors. Larger cohorts should be recruited in order to parse out potential confounds. Methods and tools used in the research study (e.g., cognitive measures, psychiatric screeners) should be evaluated for potential biases as well.
51	- Safeguards to ensure balanced reporting of adverse consequences with consideration for social, religious, economic, and geographic factors.
52	a. Develop all consent forms, return of results, and communications with members of the target populations. For example, in our NHGRI, IGNITE network-funded GUARDD study, Black community leaders developed materials with us to explain that one in 7 people of African Ancestry have a variant that greatly increases their risk for kidney failure. They helped us explain the risk and the potential benefits of testing that we were aware of and developed simple genetic education materials. They also identified and helped us communicate potential benefits we would never have thought of. This included a possible reduction of a tendency of white physicians to think black patients on dialysis were simply non-adherent with their medications, as they would understand there is more to illness than bad behavior. We recruit 100 patients per month in Harlem and the South Bronx using this strategy. b. Ensure the target populations review, improve and approve study materials. c. Employ opinion leaders and celebrities who resonate with diverse populations to champion the initiative, who say they joined, and ask their networks to do the same. d. Proactively ask for problems, using easy to access feedback opportunities, so that early challenges faced by recruiters and participants can be identified and addressed. Be transparent with challenges, seeking input to solve them. Pilot extensively with community feedback to identify challenges before rolling out programs.
53	
54	hire staff from the community & proper supervision

Question 4A. Ways to avoid potential stigmatization of subpopulations, and to manage unintended adverse consequences of the precision medicine cohort

Obs	Q4A
55	a. Develop all consent forms, return of results, and communications with members of the target populations. For example, in our NHGRI, IGNITE network-funded GUARDD study, Black community leaders developed materials with us to explain that one in 7 people of African Ancestry have a variant that greatly increases their risk for kidney failure. They helped us explain the risk and the potential benefits of testing that we were aware of and developed simple genetic education materials. They also identified and helped us communicate potential benefits we would never have thought of. This included a possible reduction of a tendency of white physicians to think black patients on dialysis were simply non-adherent with their medications, as they would understand there is more to illness than bad behavior. We recruit 100 patients per month in Harlem and the South Bronx using this strategy. b. Ensure the target populations review, improve and approve study materials. c. Employ opinion leaders and celebrities who resonate with diverse populations to champion the initiative, who say they joined, and ask their networks to do the same.. d. Proactively ask for problems, using easy to access feedback opportunities, so that early challenges faced by recruiters and participants can be identified and addressed. e. Be transparent with challenges, seeking input to solve them. f. Pilot extensively with community feedback to identify challenges before rolling out programs.
56	--Stigmatization comes from misinterpretation of information that is put out. D not disseminate information that is not checked and approved by the communities. --On the other hand, precision medicine cannot censor information, it has to relate the scientific discovery to an individual profile e.g.ethnicity. Finding this balance is challenging to prevent stigma --Ultimately consumers of the information are the practitioners. How to prevent profiles from influencing insurance? There needs to be accompanying new policies --People do not separate research entities from the government. In their mind, their data will be shared with the government for sure
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60	Again, by having trusted representatives of subpopulations play significant role in PMI's governance, they will be alert to recognize potential stigmatization and suggest ways to avoid it. These individuals can serve as liaisons bringing community concerns to be addressed by PMI governance, and spreading the word about PMI's positive potential to their constituents.
61	
62	Utilize the resources at hand and work first on community leaders, to engage the cohort population. Address language barriers , making sure that researchers have a native speaker in the group to better facilitate open dialogue. Learn about the cultural expectations of the subpopulation to avoid inadvertently offending anyone.
63	Lung Cancer Alliance recognizes that the issue of stigma is an ongoing problem across all populations affected by lung cancer. This unfair stigma must be addressed with the understanding that no one deserves to die from the disease.
64	
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66	Subpopulations should determine what their collective and individuals sensitivities are and manage those. The Platform for Engaging Everyone Responsibly (PEER) allows communities and subpopulations to set preferences specific to community sensitivities - for example, a community could decide that their data will not be used for ancestry, or predisposition to alcohol but could be used for diabetes or cancer studies. In addition to individual preferences, PEER allows community policies and standards, state and local laws, federal laws and so forth to also help determine the governance of the information and results.
67	Meaningful involvement of community members from a very early stage in development of aims, procedures, analyses, and communication of results. On an individual basis, the informed consent process should be a very interactive one, where capacity to consent is assessed in part by the ability of participants to explain the study, its aims, risks, and benefits, in their own words. Examples of unintended adverse consequences should be discussed with community representatives early on in the process of developing methods for this study. Proper measurement of the environmental and social factors (non-biological) that influence health, and the proper use of these measure in analyses, is critical.

Question 4A. Ways to avoid potential stigmatization of subpopulations, and to manage unintended adverse consequences of the precision medicine cohort

Obs	Q4A
68	To avoid unintended adverse consequences of developing precision medicine initiatives (PMI) and cohorts that do not include adequate numbers of women, more than half the world's population, investigators should be required to have deep expertise in the realm of women's health and in the study of sex and gender differences. For example, women who have never smoked are three times more likely than nonsmoking men to get lung cancer. Although the number of women participating in lung cancer clinical trials has risen women—particularly those from racial and ethnic minorities—are still less likely to enroll in these trials than men. Even when studies include women, researchers often fail to analyze data by sex or include hormone status or other sex- and gender-specific factors. We believe that the ambitious goals of the PMI cannot be achieved if you fail to include sex and gender differences and women as well as experts from these fields. Funding for PMI should be contingent upon a mandatory requirement that investigators provide access to sex-stratified analyses derived from research that is conducted and supported under the PMI as well as all federally-funded projects. NIH and other research agencies already require the inclusion of adequate numbers of women and of underrepresented groups in clinical trials, as well as the reporting of such inclusion.
69	

Question 5A. Safeguards that should be implemented to reassure communities of the net positive potential of the precision medicine cohort to understand health and disease and improve the health of all segments of the US population

Obs	Q5A
1	Community input into the research methods before implementation, community input into on-going review of processes, as well as review of data collected, and critique and input into reports and manuscripts prior to publication.
2	Allow participants to self-organize within the PMI research cohorts based on groups they designate, and then enable those groups to determine which projects they participate it or how they participate. Researchers talk about a federated data model, but a logical extension of that would be a federated participation model. If done correctly, this could lead to an increase over time in participation by communities that otherwise might have, or traditionally have had reason to have, concerns about participating. Participants should be told about every use of their data and should have the opportunity to opt-out, for any reason, of any use of their data.
3	The best safeguard to reassure communities of the positive potential of the precision medicine program is ongoing relationship, ability to communicate honestly and directly with the population, investment in the health and well-being of that population by the Institute conducting the precision medicine program, and return of information to the community. The community needs a degree of ownership. Thus the major component of reassurance of the positive benefits of this will be constant communication (including listening), education and dialogue involving people who are respected and trusted by the community. Once again NIH will have much higher likelihood of success with this program if locations for the program are chosen based on existing and ongoing community-based programs by the institutions that are conducting the precision medicine study.
4	Recommended safeguards that reassure communities of the net positive potential of precision medicine would include ongoing communication of research findings, engagement of community members for oversight on data use and regular communications explaining the benefits, discoveries and issues confronting genomic medicine. Safeguards will require emphasizing to the public that participant identities are protected; data is secure and appropriately managed. In addition, showing benefit to participants by incorporating actionable information into the EHR for clinical care.
5	The AAMC commends NIH for developing a more comprehensive and effective policy for sharing genomic information more widely. As noted in a November 20, 2013 comment letter in response to “NIH Genomic Data Sharing Policy” AAMC recommends a final policy which should restate the NIH’s commitment to community engagement in the research process and complementary efforts to promote health equity in the application of genomic research. Research participants should be reassured that the results and findings from the studies will be relevant and applied appropriately to their communities perhaps by framing PMI research as one response to community health needs assessment-identified priority health needs. Additionally, we urge the NIH to ensure that the research findings are communicated back to the community in the most efficient and effective way. Providing an in-depth informed consent is crucial to ensuring protections for research participants. The AAMC encourages NIH to utilize innovative practices for consent, such as the dynamic consent model, which allows individuals to indicate an initial interest in participating in a research project and have the opportunity to provide consent on an ongoing basis. This particular consent model promotes autonomy and active participation which provides reassurance to individuals from underrepresented groups about participating in the precision medicine cohort. Providing research participants with new opportunities by which they elect to participate in research studies and give informed consent to share information and samples, increases the level of transparency of the research process and adds a level of reassurance to the research participant.
6	
7	Policies or laws to protect unconsented indirect participants whose genomes may be largely inferrable from other participants will be important. Laws against genetic discrimination in employment or insurance will ultimately become necessary, either through this cohort or through the eventual widespread availability of sequencing.
8	5. To promote the positive potential and future growth of the effort while competing in our “here today, gone tomorrow” marketplace, the NIH needs to build a well-defined brand for “Precision Medicine” in effect, a marketing campaign that must: [1] convey a compelling and evocative brand story and; [2] maximize the number of contacts its key audiences have with the “Precision Medicine” program. To do so requires clearly identifying what the NIH wants the “Precision Medicine” brand to represent, and then, working very closely with the organization and its key partners on delivering this promise at every cohort contact point in ways that integrate the offering into the very fabric of people’s lives and showcase what the NIH is doing. And, most importantly, how it will save lives, enables progress, and makes life better.

Question 5A. Safeguards that should be implemented to reassure communities of the net positive potential of the precision medicine cohort to understand health and disease and improve the health of all segments of the US population

Obs	Q5A
9	Leveraging local community engagement activities can help broaden the scope of awareness of the Precision Medicine Cohort. Existing community engagement activities at academic medical centers, such as those supported by the National Center for Advancing Translational Sciences, currently reach a wide-range of stakeholders, including community healthcare providers, patient advocates, and others. These engagement activities can help in raising awareness of the potential value of the Precision Medicine Cohort. Consistently reassessing research participants' views of emerging research trends and new genomic technologies through community engagement, surveys, and other means is essential to maintaining public trust. This information can inform decisions about the use of stored biological materials and guide the pursuit of new research collaborations. We encourage NIH leadership and others to take advantage of existing community engagement structures and work closely with academic partners with strong ties to their local communities.
10	Outreach programs to disseminate news about PMI (including safeguards) could reassure communities. PMI should underscore that research on the cohort is aimed at understanding health and disease rather than anthropological, sociological, and/or historical research. Different conceptions of what "health" is affect to what extent certain research counts as understanding health. Will the advisory committee be operating under a wider or narrower definition of what counts as research on understanding "health?" According to the committee, what kinds of research projects do not contribute to our understanding of health and disease, and so would be denied access to data provided by cohort members? Transparency about what kinds of research will occur using the data retrieved from members of the cohort will reassure them of net positive potential for health. Specific examples help. Specific examples of what kind of research will NOT be allowed access to the PMI database also helps to clarify the goals of the project. This type of information may bear on the decision-making process for participants about whether or not to enroll. A transparent and participatory form of governance of PMI could meet these suggestions. Public discussion involving potential research participants of what ought to be the goals of federally funded database and who ought to be allowed access to the database and for what purposes would reassure those participants of the positive potential of PMI.
11	Patient Empowerment I'm concerned that credentialing will be used to prevent patients and patient advocacy groups from having access to their own data. I'd rather see technology deployed that determines the risk of re-identification for each query, with patients able to establish a threshold for those accessing the data.
12	
13	EngageUC is a NIH/NCATS-funded study to identify best practices for biorepository governance and consent. The study involves all 5 of the University of California (UC) medical center campuses. EngageUC works with researchers, regulators, and community members on governance and is using a randomized trial to provide evidence on best practices for consent. Diverse lay Californians that participated in intensive deliberative and educational engagements as part of EngageUC recommended several safeguards to engender the public's interest, trust, and confidence in large-scale medical/genomic research. First, participants strongly supported the creation of public education campaigns about the role of medical research, biorepositories, and the role of research volunteers in medical discovery. Citing campaigns such as those for organ donation, participants felt that it would help the public better understand and appreciate these efforts. Second, participants broadly supported the creation of stakeholder advisory groups that would meaningfully be involved in the oversight of the governance of biobanks; such groups would include lay individuals that represented the diversity of stakeholders and affected communities. Participants identified such stakeholder-informed governance as the most appropriate and appealing form of protections for donors and potential donors, as compared to consent forms that enlisted donors in the granular management of their own tissues and data. Third, some participants felt the return of research results to donors was an especially appealing aspect of research participation, but others disagreed. Nearly all, however, felt that donors should have the choice as to whether to receive results or not.
14	• Support community-led models to facilitate ethical conduct of precision medicine such as Community Review Processes (CRPs) and Community Advisory Boards (CABs). Investment in existing community infrastructures will reflect both individual and community benefit from precision medicine. IRBs and DSMBs focus on individual protections, while CRPs and CABs protect community infrastructure and culture. Safeguard policies need to be established to facilitate reciprocal communication between precision medicine administrators and researchers, participants, and the medical community to determine how confidentiality is maintained, ownership of data, rules of data use. • Educational materials describing precision medicine and progress updates should be developed for various audiences, languages, and education levels and disseminated using ongoing multi-pronged approaches.

Question 5A. Safeguards that should be implemented to reassure communities of the net positive potential of the precision medicine cohort to understand health and disease and improve the health of all segments of the US population

Obs	Q5A
15	The involvement of patients and other community stakeholders as partners in research is an important safeguard to ensure precision medicine research will benefit and improve the health of all segments of the US population. The HMORN PER SIG researchers and their HMORN sites are actively working to engage appropriate stakeholder populations in the development of research questions and protocols to ensure potential for precision medicine research to benefit those populations and to answer questions and improve outcomes important to those communities. There is growing realization that research shops ideally need to engage with community members on at least two levels to effectively understand the needs, experiences, and fears of patients: the broad perspectives provided by community advisory panels composed of members with a range of demographic and diseases characteristics, and the deep insights of members who partner with individual research teams that are studying very specific health conditions or diseases. The former contributes to the evolution of a patient centered research agenda, improving both community member and researcher capacities to identify areas of misunderstanding, and to the passive dissemination of these efforts more broadly in the community. The latter encourages even more intimate and arguably much more effective relationships among community members and researchers that contribute to improved understanding by both parties of the nature of research, the patient experience, and how to use those deeper understandings to ensure that their research together leads to better patient outcomes.
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18	Oversight: The cohort project itself and the data collected should be subject to several layers of oversight; at least one layer of oversight should be from an external, independent entity, such as an advisory board that includes diverse representation from academia, industry, medical sector, and the general public. Transparency: This project must operate with the highest level of transparency possible, including frequent project updates to key stakeholders. Up-to-date metrics of patients enrolled, data collected, approved/rejected projects, etc should be provided in an accessible format. There must be clearly documented policies and procedures for handling research misconduct. Control of Data Use: Cohort participants must be granted exquisite control of their data. Beyond a master consent to participate, patients should have the ability to electronically opt-in to any studies seeking to use their data. Patients should be able to opt out of any study using their data at any time. Incidental Findings: Occasionally, research may reveal new factors (genetic, lifestyle, etc) that are associated with risk for a specific disease. There must be a clear process for presenting this risk to participants prior to release of publications to journals or other outlets. Co-localized compute with data storage: The cohort data should reside in a cloud-computing environment that contains significant computing resources co-located with data storage. This would stop proliferation of patient data across hundreds of disparate research sites, which would greatly improve data management and security.
19	
20	The current genome data sharing policy does not include any accountability by NIH or the Federal government for any potential breaches of data use agreements by investigators. The institutions employing the offending investigators are the entities that hold them accountable. In addition, any sanctions would be implemented after the fact, after the damage is done. Therefore, any risks to the unintended or unapproved use of data are borne completely by the participants and communities, which likely have little resources to protect themselves. This needs to be addressed in order to reassure the communities that they won't suffer potential stigmatization or adverse consequences from the PMI.
21	A. Transparency around how participant data is being used, in a way that also takes into account participant feedback on a continual basis, will help assure patients that their data is being used in a way that benefits them. People need to understand how their data is being used, and that they support those efforts. This sort of “dynamic informed consent” will also allow researchers to recontact participants to re-consent them when new ideas, hypothesis, or technologies arise. B. Individuals who are found to have actionable variants from their testing, such as a mutation in BRCA1 or BRCA2, will likely have relatives who can benefit from testing for the identified actionable variant. This process is called “cascading through a family.” Communicating that the testing can benefit entire families, and not just individuals, should help to reassure communities of positive impact of the PMI. Genetic counselors are trained to explain the process for familial cascading with patients and study participants, so partnering with them will help achieve this goal.
22	

Question 5A. Safeguards that should be implemented to reassure communities of the net positive potential of the precision medicine cohort to understand health and disease and improve the health of all segments of the US population

Obs	Q5A
23	Communication appropriate for the community of interest is essential. Given the importance of face-to-face communication in the Latino community, we have just completed six Town Halls with our WICER participants presenting their WICER participation in the context of Precision Medicine. During the Town Hall, we presented their individual WICER survey data as infographics designed for those with low health literacy and presented group data regarding the percentage of WICER participants who had consented to data linkage, contact for future research contact, and biospecimens. We shared information about Precision Medicine starting with Obama's state of the union speech and described next steps for them should they wish to participate more broadly in precision medicine initiatives including being re-consented for deposit in dbGAP.
24	The best strategy is to demonstrate value in tangible ways how communities will benefit from scientific discoveries made with their consented sample/data. This involves return of appropriate information and results to participants as they desire. Safeguards and appropriate funding needs to be available to return results in a conscientious and responsible way (e.g. provision of genetic counseling by licensed genetic counselors as part of results return). Given the limited availability of genetic counselors, research will be needed to determine other ways in which results can be responsibly returned. Returning results to participants in a responsible way comes at a cost and will require additional effort and financial support. It is critical to extend legal protections related to genetic discrimination. There must be an expansion of GINA (Genetic Information Nondiscrimination Act) so that it goes beyond prohibiting discrimination in health insurance and employment, and also includes life, disability and long-term care insurance. Without this expanded coverage, underrepresented communities may fear further increased discrimination, contributing to the vicious cycle of health disparities. Key to the success of the PMI will be building a network of diverse communities that participate as full partner-- a community-based equivalent of the practice-based research networks. There should be an emphasis on community engagement and long-term commitment to this network, where researchers and community members are bona fide partners in: shared decision making, developing appropriate research priorities, cultural competence, and building the evidence base that informs personalized care in community-based settings while maintain
25	Encourage journal reviewers to revisit clinical trial eligibility criteria to ensure patients of color are being recruited and retained consistently in clinical trials. Tie journal publication to substantive and relevant inclusion of patients of color.
26	
27	1. Clearly communicate the request and BENEFIT TO THE COMMUNITY. For minority populations that have been victims of medical malpractice, abuse, exploitation, racism, etc. from the medical community, highlighting the positive effect clinical research on minorities can have on the ENTIRE population may not be a good strategy. It is reminiscent of past experimentation on racial minorities for the benefit of society as a whole, which was wrong (i.e. USPHS Syphilis Study, Johns Hopkins procedures on African Americans). Researchers should instead focus on possible benefits to individual communities (African Americans, Latinos, Native Americans, etc.).
28	As noted above, the PMI must have a detailed plan for protecting the privacy of individuals' personal information and for ensuring that all research using it is appropriate and important. The public should have access to clear, simple, detailed information about how data will be used for studies, and how those studies are deemed important enough to merit the use of their data. Finally, the public should have access to ongoing, regularly updated information about the PMI studies under way, their progress and lessons learned scientifically, as well as culturally.
29	Make international agreements that protect uncontacted people as in the Amazon so that countries like Australia, China and India cannot use their access of public databases to patent or commercialize American Indian and Amerindian DNA products or products derived from mechanistic revelations or as part of synthetic systems.
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31	
32	- Engagement between authority and community - Occurrence with contemplation questions (why this time, specific families, ethic group, community, district) -Social community mobilisation support team in local languages, distribution of posters and IEC materials) -Integrated collaboration with the health facilities and across disciplines as well as sectors. -Social and traditional culture - Infrastructure and facilities improvement such as digital health coupled with resources development in precision medicine - Understand the public perceptions, social and economic measures n precision medicine impact

Question 5A. Safeguards that should be implemented to reassure communities of the net positive potential of the precision medicine cohort to understand health and disease and improve the health of all segments of the US population

Obs	Q5A
33	
34	N/A
35	I think you can make the case that the *entire* cohort could be from the deep south, where there is a great representation of African-Americans (with the most diversity of genetics, and with great diversity in environmentally-related outcomes). The statistics for the area south of Tennessee for smoking, cancer, and other environmentally-relevant health issues are also stunning. This would be a statement to the American people that we are going to boost up the area of our country that is in most need of help, and at the same time learn lessons that will help all Americans. I think you could add Florida and Texas in order to ensure Latino involvement. Why not have this cohort be HIGHLY enriched for those whose health needs the most attention?
36	Nationwide education efforts explaining the current limitations of healthcare and the potential for improvement of individual and community outcomes as a result of precision medicine with an honest discussion of the current anticipated limitations should begin well before the formal design and recruitment. The design should include and address public perception following general education efforts. Education will be key to building the community's trust. Disclosure of plans to support communities who may have devastating findings should be communicated at the outset in an effort to maintain full transparency. A fundamental need that should be addressed at the outset will be re-educating the existing health care workforce. These health care professionals will need to be able to both educate and care for a new set of patients who have a wide range of genetic conditions and predispositions that previously have been unknown. The impact of this movement on the current health care system should not be underestimated. If returning individual results, everyone should be educated fully on the meaning of secondary findings, even if not returning these types of results. Scenarios and hypothetical return-of-results should be presented to provoke thoughtful deliberation about their true desire for this information and the emotional impact of this type of information. Personalized education is going to be especially important for women who are or might become pregnant. Lastly, education regarding the importance of family history and risky behaviors should be emphasized nationwide from the outset and throughout this initiative.
37	Booz Allen understands the need for appropriate and continuous communication with the PMI cohort to address barriers and net negative views of clinical research and demonstrate the impact of their contributions to the greater health initiative. Communication methods to facilitate education (marketing at community events, churches, social media) should be employed to showcase the net positives of the PMI cohort including: a) Drive new era of translational R&D and patient treatment, where a tailored approach to healthcare and disease treatment will be used to optimize health and longevity; b) Directly receive benefits of research to rapidly improve health outcomes for direct family members, including offspring and siblings who are high risks for diseases. As knowledge on PMI is shared with the community, PMI members can become community messengers for the new findings; c) Empower current groups facing health disparities that their contribution to this research is the best way to quickly overcome the decades of research deficits. Sharing recent developments and efforts to overcome disparities within these communities is key to show the potential benefits from their contributions. Safeguards need to be established and communicated in lay terms: 1) Ethical and IRB policies are in places protecting groups from being "experimented upon;" 2) Communicate that individual's data will be safeguarded under federal information protection laws (e.g. HIPAA or Federal Information Security Management Act). The PMI should make clear the security controls that safeguard all data, and how data is de-identified before analysis to protect individuals from identification.
38	We recommend a two-pronged approach to community engagement which will result in a positive reception in diverse communities. First, a broad based media campaign can support this goal of promoting understanding of the positive potential of the precision medicine cohort which is why we suggest that NIH develop the national, targeted, coordinated community awareness campaign supported by high level government officials, community leaders, and celebrities and integrate that into a variety of media. Diverse representation in any marketing effort including all written material about the study, online presence and media awareness efforts. This includes racial and ethnic diversity as well as diversity in age, family status and sexual orientation. In this way, potential participants will be able to see themselves in the marketing. Second, as well as highly visible public supporters, it is important to have local/grassroots support. Having respected people in the community, be that a mayor, clergy, teacher, etc., is reassuring to local communities that the study has been vetted by someone respected and is good for the community.
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Question 5A. Safeguards that should be implemented to reassure communities of the net positive potential of the precision medicine cohort to understand health and disease and improve the health of all segments of the US population

Obs	Q5A
41	
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45	• • Creation of a community ethics advisory board with specific actions to address violation or breach research ethics • Develop, implement, and enforce policies that acknowledge “the notion that the domain of ‘knowledge production’ is not the sole right of academic researchers”. • Develop community IRBs and REBs that are specifically designed to protect communities from at risk practices with specific actions to address violation or breach of either • Develop, implement and enforce safeguards to protect all data collected with specific actions to address violation or breach research ethics IRBs and REBs may be unintentionally placing communities at risk by continuing to use procedures inappropriate or unsuitable for CBPR. IRB/REB procedures require a new framework more suitable for CBPR. IRB/REB procedures require a new framework more suitable for CBPR, Flicker S1, Travers R, Guta A, McDonald S, Meagher AJ Urban Health. Ethical dilemmas in community-based participatory research: recommendations for institutional review boards. 2007 Jul; 84(4):478-93
46	An independent oversight structure is needed to ensure transparency and accountability of those organizations that are conducting PMI ‘cohort’ studies at a community level. The oversight structure should be tiered: national, regional, and community. For example: a community-based oversight council would be composed of community leaders in Southern California (San Diego County, Orange County, Los Angeles, etc.); a regional West Coast oversight council would be composed of a members from each of the community councils in California, Oregon, Washington, Hawaii and Alaska; and, the national oversight council would be composed of representatives from each of the regional oversight councils. The tiered approach provides rapid responsiveness on a local level and a consistent flow of communication from a national level to the community and vice versa. Oversight councils would ensure the studies are executed with transparency, full disclosure of risks and benefits, and the informed consent of participants. Oversight councils will also ensure the health benefits derived from the PMI are translated back to the participants and their local communities.
47	
48	1. Legal assurances are required -- strengthening GINA, extending it to the military, and extending it to all people regardless of immigration status. The health of any one American depends on to a great extent on the health of the person sitting next to them on the bus -- whether or not that person is a visitor, legal or illegal immigrant, or citizen. Healthcare and health reporting should not depend on such things. 2. When issues are uncovered, there should be assurances that them medical system will FOLLOW UP on medical problems, meaning we need health care for all. It is unethical to determine that someone has cancer and not provide a path to treatment. If people participate in this database, there should be at least some assistance in access to care. 3. Personal freedom and choice should be guarded whenever possible. That is, two people with recessive CF genes might still marry, might still choose to have children, AND be offered appropriate guidance and assistance from the medical system.
49	
50	Participants and community members should be allowed access to the latest research findings (even if preliminary). Community members should be informed of all stages of the research and why all stage is necessary for the larger research goal. They should be encouraged to voice concerns about the research process, have questions answered in a timely fashion, and it should be explicit to how their participation is improving health and disease among segments of the US population.
51	Storage of personal data in de-identified form; adequate data security/protection; dissemination for specific well-defined purpose (understand health and disease and improve the health of all segments of the US population)
52	
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54	communities need to see a positive impact from participation.

Question 5A. Safeguards that should be implemented to reassure communities of the net positive potential of the precision medicine cohort to understand health and disease and improve the health of all segments of the US population

Obs	Q5A
55	See above
56	--When you start enrolling people, the consent process almost has to be a day long seminar --Collection of data works best if conducted by community members themselves --Have to construct a very thorough argument on why the study is beneficial to the participant beyond 'it is good for science' --Some examples of ecology versus individuals is refugee populations who have been thru war experiences (historical trauma)
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61	Suspicion about sharing personal data is the main barrier to participate in the cohort: assurance of the exclusively scientific, clinical, and sociological aims of the data collection should be stressed and expressed in a completely clear form. Also, a complete privacy and anonymity protection should be guaranteed, clearly stating it as an obligation towards the participant. Also, the potential recruit, should be clearly assured about the complete public disclosure of the whole research procedures and achievements. All of this should be extremely clearly stated at any step, from the very first touch with the potential volunteer, up to the final enrolment in a complete and official form. On the other side, the positive relevance of the Initiative for the research and for the society must be stressed: this Initiative is a unique opportunity to light up the determinants of many diseases, and to work on to prevent and to cure them and to repair social disparities. It should be explained that to participate in the cohort means to participate in a health and social improvement.
62	Make a clear mission statement in very simple terms that anyone could understand. Set a timeline and determine benchmarks to make sure that goals are being met. Use examples and tell stories. People relate to other people who are like themselves.
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66	The communities values should be respected, and the community should determine safeguards - these will vary and are contextual.
67	I am not sure that there will be a net positive as it is phrased here, even if it the study successful at recruitment and design to address health disparities. This is because the findings of this work may determine that structures that maintain disparities in social status, wealth, opportunity, and education may be fundamental sources of health disparities and that individual solutions on the prevention or treatment side may never move the needle enough. In my opinion this needs to be an aspect of the conversation with communities. Engaging the community in a respectful and collaborative discussion about the study, proof of willingness to add new questions/aims/measures/procedures and engage researchers with these community-generated research ideas, are among the safeguards that should be employed.
68	Data stratified by sex and race/ethnicity are often not available to researchers and clinicians. The availability of data for analysis by third parties and for public review could greatly accelerate our understanding of sex and racial/ethnic differences and similarities, and why they matter in precision medicine and to health care writ large. By examining differences by sex and race/ethnicity, we can improve transparency to reassure communities of the impact precision medicine initiatives have on specific subgroups as well as the entire population.
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Question 1B. Priority health disparities research questions that can be uniquely addressed within the proposed precision medicine cohort

Obs	Q1B
1	What are the political and economic factors that influence/cause health disparities? What policy level changes are needed to address the political and economic factors that influence/cause health disparities? What strategies are necessary to bring about policy level changes to decrease health disparities? Which strategies are most effective in bringing about policy level changes that decrease health disparities.
2	If some or all of the precision medicine cohort is enrolled via a rigorous sampling strategy that is based on specific sampling of populations/groups of interest--i.e., the groups between which there are or might be disparities--then any disparities research question could be addressed within that appropriately-sampled group.
3	• Contribution of ancestry to susceptibility to common diseases • Contribution of common mutations unique to minorities contributing to susceptibility to common diseases • Contribution of ancestry to drug effectiveness and drug reactions. • Contribution of common mutations unique to minorities contributing to drug effectiveness and drug reactions. • Rare mutations contributing to diseases in minority populations • Contribution of genetic variability and behavioral health • Genetic variability and gene expression levels
4	Distinguish the interplay between genetics and the environment that cause stressors by socio economic status.
5	AAMC defines health disparities as "measureable, systematic, and avoidable differences in health between groups, stemming from differences in levels of social advantage/disadvantage." In light of that definition, a focus on genetics is insufficient for a comprehensive health equity research agenda. We commend NIH for its inclusion of risk factor and socioeconomic data in addition to genetic information in the PMI dataset. The AAMC recommends the NIH adopt a multi-level, systems approach when analyzing PMI data in order to fully understand the root causes of inequities and the interactions between those causes. Further, PMI data could be aligned with other data sets including public health data, community health needs assessment data, and electronic health record data to create an even fuller picture of the systems that give rise to and perpetuate health inequities. This data integration will create a powerful tool accessible to existing initiatives such as PCORI's PCORnet and NIH's Big Data to Knowledge (BD2K). The accumulation of biospecimen, environmental, and behavioral data generates a body of data that allows for multi-level analysis. The AAMC urges the NIH to encourage and create opportunities for cross-site research collaboration that utilizes the full body of data that the PMI collects.
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7	Given the correlation between health disparities and groups that are historically underrepresented, efforts to address engagement with underrepresented groups will be broadly effective toward reducing health disparities in the long run as well. Oversampling underrepresented groups and groups with health disparities will help to overcome historical deficits in research and to achieve the necessary statistical power to make definitive inferences about gene-disease-environment relationships for these groups.
8	1. Using the approaches outlines above, together with a mobile app, participants can not only identify and participate contributing to one of th elargest science projects in history, but can engage in learning about obtaining and engaging with their own health data, and therefore with their own health and health improvement. This is the REAL OPPORTUNITY - while engaging 1 million to contribute their DNA, tens to hundreds of millions can be engaged in a discussion about health, health data, their own engagement with health and contributing to science.
9	No response provided.
10	PMI should engage with community members and potential participants to determine which research questions they are interested in addressing and what matters most to various segments of the population. Efforts should be made to engage underserved and underrepresented populations especially, as is common in public health research.
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14	• Identification of health disparities questions should be carried out collaboratively to validate the scientific and practical aspects of precision medicine approaches. For example, scientific questions can assess device effectiveness but may not assess participant quality of life while using the device. • Carefully designed health disparities questions should target specific populations such as 'Are the new US Preventive Services Task Force guidelines appropriate for frican American men?'

Question 1B. Priority health disparities research questions that can be uniquely addressed within the proposed precision medicine cohort

Obs	Q1B
15	Genetic predisposition to disease and response to treatment, communication of complex genetic information to individuals and populations, and the integration of genomics into EHRs and clinical practice to personalize and improve health of all individuals are important research questions in precision medicine currently under investigation in member HMORN sites. These approaches have the potential to identify genomic variation that could account for some health disparities across social, racial and ethnic groups.
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19	What are the cost factors associated with dissemination of precision medicine? Will traditional notions of health services research including disparate access and utilization demonstrate that vulnerable populations are not exposed to precision medicine? Can lessons learned about disruptive innovation improve access to lessons learned in precision medicine more quickly? Are there populations that are more likely to experience greater benefit from precision medicine approaches? If so, how do we identify those populations and insure rapid access? Are there certain conditions that are expected to improve with precision medicine? If so, what are those conditions and who are the populations most likely to be impacted by advancements? What can we learn about the environment-gene interaction that will in act allow a more precise treatment strategy for individuals? What is the minimum technology and therefore cost necessary to develop precision medicine approaches for those who have found high quality care out-of-reach in the past? What new health literacy approaches will be necessary to ensure that patients and families understand precision medicine? Will these vary within subpopulations? How much information do patients want?
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21	A. The PMI represents a unique opportunity to identify disease-associated variants in individuals with non-European ancestry and to deposit these variants in ClinGen so they are available for use in both research and clinical genetic test interpretation. B. Genetic studies have been done primarily on individuals of European descent. Most of the assumptions, such as hotspot regions in the genome or filtering protocols in analysis pipelines such as minor-allele frequencies, are based on the experience from that European population. If the PMI is successful in recruiting communities' representative of other ethnic backgrounds, the assumptions will need to be revisited to ensure that they are accurate with greater diversity in the data.
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24	Increasing access to, and utilization of, appropriate preventive medical services and medications is an important area of health disparities research that this cohort can help address. Certain under-represented populations are at increased risk for subtypes of cancer, diabetes, heart disease, and cognitive impairment, among other diseases. For example, there are significant disparities in kidney disease, and recent studies have identified genes associated with increased susceptibility that could be used to develop and study approaches to early intervention. There are also disparities in the use and efficacy of existing primary and secondary preventive services which could be addressed. Also, when multiple treatment approaches or medications are available, determining the approach or medication with the highest uptake, adherence, and effectiveness in each subpopulation should be a top priority. Evaluating the impact of genetic factors on different drug classes, and in particular older generics, would also be very valuable related to diseases in which disparities are persistent. Studies could be designed to address the paucity of data about pharmacogenetic variation in underserved populations since the PM cohort would be large enough to permit stratification and analyze genetic variability in key g
25	What will be the role of African American men's health within the context of equity and policy? How do we engage the men and build a culture of health with respect to their health and well-being? What role will health and equity in all policies play with respect to African American men and health disparities?
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27	1. The biological manifestation of racism (infant mortality, cardiovascular disease, cancer) in minority populations regardless of socioeconomic status. 2. Lupus 3. Sickle Cell Anemia 4. Aggressive Breast Cancer 5. The role of place on adverse health outcomes, specifically chronic disease 6. The role of long-term historical trauma on health outcomes, specifically illnesses like Type II Diabetes, cardiovascular disease, and mental disorders on African American and Native American populations

Question 1B. Priority health disparities research questions that can be uniquely addressed within the proposed precision medicine cohort

Obs	Q1B
28	The March of Dimes urges the PMI to prioritize the examination of disparities in perinatal health and birth outcomes as an early focus of its work. Significant disparities exist in every category of birth outcomes, including prematurity, low birth weight, and birth defects and rare disorders as well as maternal conditions such as hypertension and gestational diabetes. Studying the interplay between genetics and the environment in a large, diverse cohort could yield extremely important, actionable insights within a very short timeframe. The March of Dimes is currently studying some of these issues of genetics and the environment through our network of Prematurity Research Centers based at major academic institutions. Adding the power of the PMI cohort would leverage this existing investment and accelerate the pace of treatments and cures dramatically.
29	Because conditions like obesity and diabetes are shared between many people of former European colonies, their trajectory toward those conditions are not genetic because they don't share ancestry. Their commonality is social hierarchies remaining from European colonizations. To be fair, genome research must put more than the 5% allocated toward ELSI research in Indigenous communities to address conditions with huge social determinants contributions. In Indigenous populations, conditions with multiple inputs are a waste of money to study with genomics...focus instead on pharmacogenomics and other "Discrete"questions in genomics. Precision medicine is in envisioned to help outliers and those individuals with familial or private alleles...this has to be adjusted for indigenous groups (and countries like Mexico) where there are very long runs of homozygosity in the entire populations, otherwise you will miss these vital tails of distribution to the ideal and priority of the individual.
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32	- Economic, environmental and geographical determinants/ factors on obesity related cardiometabolic risk and diseases, mechanisms and individual response to therapy and outcomes - Inequalities and stigmatization of African-American subpopulation and Indian-Americans - 1- Cultural and historical as well as current factors that predispose African-American subpopulations to higher disease incidence and/or shorter survival to cardiometabolic diseases(HTN, CVD, Cancer and Diabetes) - African-American genomic architecture variability and lifestyle interactions as they affect the incidence of progression of obesity, CMD incidence, prevalence and wellness
33	The US is facing an obesity and dementia epidemic. Daily physical activity can help prevent and alleviate obesity and a host of chronic conditions affecting the body and the brain. However, just one in five adults meet US physical activity guidelines. Although evidence from randomized controlled trials demonstrates the effectiveness of increasing physical activity, middle aged and older adults have difficulty initiating and adhering to exercise programs. This problem appears to be magnified by socioeconomic disadvantage, attributable in part to neighborhood factors that may restrict opportunities for regular physical activity. In addition, following retirement, opportunities for daily physical activity and engagement become more restricted. This pattern of reduced activity at a time when aging adults need it most for health promotion necessitates novel approaches to increasing physical activity in daily life. The design and ready availability of large-scale activity promotion strategies that can modestly delay the onset and course of cognitive and physical functional aging and risk for dementia, frailty, and disability by 6 months to 1 year have tremendous potential to reduce burden at the level of the individual, the family, and society. However, we have yet to identify large-scale community int
34	N/A
35	I think you can make the case that the *entire* cohort could be from the deep south, where there is a great representation of African-Americans (with the most diversity of genetics, and with great diversity in environmentally-related outcomes). The statistics for the area south of Tennessee for smoking, cancer, and other environmentally-relevant health issues are also stunning. This would be a statement to the American people that we are going to boost up the area of our country that is in most need of help, and at the same time learn lessons that will help all Americans. I think you could add Florida and Texas in order to ensure Latino involvement. Why not have this cohort be HIGHLY enriched for those whose health needs the most attention?
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Question 1B. Priority health disparities research questions that can be uniquely addressed within the proposed precision medicine cohort

Obs	Q1B
37	Through Booz Allen team's experience leading research studies and conducting health disparities research, we provide several recommendations for addressing health disparities within the PMI cohort. 1) Engagement of underrepresented populations: The PMI cohort provides an opportunity to identify and test strategies to overcome study participation barriers such as mistrust and fear of breach of privacy among health disparity populations, particularly with genetic studies. 2) Environmental factors and health: A primary determinant of health outcomes is where an individual lives, works, and is educated. The PMI cohort provides an opportunity to examine the neighborhood factors that contribute to health disparities. Factors such as the number of parks/recreation centers, fast food outlets, grocery stores with healthy options, building conditions, all contribute to disparate health outcomes and areas with limited resources often experience greater rates of health outcomes such as hypertension, diabetes asthma, and childhood obesity. 3) Examination of Literacy and Health: Mobile Health is an approach for reducing disparities among individuals that may have lower levels of literacy. Using touchscreen computers and mobile devices may increase participation and interest in research among groups that may no
38	Health and wellbeing are affected by many factors that co-exist, interact and compound one another. Similarly, populations that are disparately affected by one condition, may not be the same populations disparately affected by another. Precision medicine has the opportunity to significantly impact the health and wellbeing of those at risk for negative health outcomes. Data collected within the precision medicine cohort could be utilized to answer the overarching question, "How can population-based data be utilized empirically to ensure all individuals have the ability to achieve positive health outcomes?" Research questions within this may include: • How does intergenerational transmission of chronic poverty impact medical outcomes related to cardiovascular disease, diabetes and cancer? • How do physical environment, social-economic environment, and co-morbidities impact an individual's ability to achieve successful clinical outcomes? E.g., Rates of violence within a patient's community, travel distance to primary care, and diagnosis of more than one chronic condition. • How do physical and social-economic environments impact the ability to effectively treat mental illness among historically disparate populations (e.g., African American, Native American, Rural, LGBT)? • What correlating factors r
39	Our current understanding of health disparities is likely hampered by our lack of understanding about the genetic, sociocultural and environmental factors contributing to chronic and infectious disease in diverse populations. In order to address this, for example, other initiatives, such as the Wellcome Trust and Human Heredity and Health in Africa are beginning to gather the data and formulate the methods needed to understand the complex interplay that creates health disparities among ethnic groups for diseases such as type 2 diabetes, hypertension and obesity worldwide. To prioritize health disparity research questions in the Precision Medicine Initiative, we need to expand genomic research efforts to increasingly diverse populations. There is building evidence that doctors can make more accurate diagnosis when using patient's genetic ancestry to make comparisons (instead of inferred or assumed ancestry) for diseases like chronic kidney disease, pulmonary disease and certain cancers. In addition, simply recruiting diversity within genomic medicine infrastructures is expected to inform health disparities research questions; for example, in people with Native South American ancestry, a particular variant of a protein that transports cholesterol into cells is common and is strongly associated with
40	Recently our group has been conducting research on ethnic differences between African Americans and Caucasians in their definition of what it is to be a "smoker." We have found significant differences in these two groups in who they would consider a smoker and who would not be, using a newly developed measure that addresses variations in the definition of smoking. Given that broad questions ("Are you a smoker?") are subject to different interpretations, we suggest that the cohort be given our measure of the definition of smoking, in hopes of determining individual differences in what is considered to be smoking and how definitions of smoking change as an individual continues or stops use of tobacco. These data could prove to be helpful in developing more reliable and valid self-report measures of tobacco use.
41	What predisposes individuals to develop the consequences of ACE and PTSD and what are the genetic and social determinants of resiliency? What, of the information that can be gleaned, are individuals most eager to learn about?(Provide the options) Which genetic factors are relevant to helping decide whether therapy or medication or a combination of both will be most effective for different psychological conditions.
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Question 1B. Priority health disparities research questions that can be uniquely addressed within the proposed precision medicine cohort

Obs	Q1B
46	The JHS focused on identifying CVD risk factors in African Americans. JHS was designed to address a specific health disparity, the higher CVD mortality rate in African Americans over other ethnic groups. Prioritization of health disparities will result in a PMI composed of a collection of JHS-like studies versus the development of a rich data resource that has the potential to address a broad spectrum of known and as yet unrecognized health disparities. The PMI 'cohort' should be inclusive regardless of racial or ethnic group; religion; SES; gender; age; mental health; cognitive, sensory, or physical disability; sexual orientation or gender identity; geographic location; or other characteristics historically linked to discrimination or exclusion. ARIC study and JHS participants were selected randomly via a drivers license registry and Accudata America commercial listing, respectively. The registries provided name, address, zip code, and if available phone number, age group, and family components. Blood centers are essentially an existing, unstudied, longitudinal, ongoing cohort of diverse, healthy participants accompanied by decades of donor's electronic health/wellness records and access to biospecimens. One of the strategies all blood centers use for donor recruitment, across ethnicities and st
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48	1. How widespread are recessive traits in the general population? 2. How widespread are traits that might incline an individual toward disease, or facilitate the spread of that disease within this person? 3. Given one of those traits, are there things that can be done to lessen the risk of these things actually occurring? (e.g., the genetic trait increases the risk, but balancing the chemical problem or changing diet or lifestyle could bring that risk back down to a manageable level).
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50	Questions about *How* to prevent, intervene, and identify risk factors associated with with conditions such as diabetes, obesity, heart failure, HIV/AIDS, and stroke that disproportionately affect underrepresented communities is critical. However, in addition to these questions, it is important to examine how attitudes about health, health literacy, social support networks, SES, community factors, and cultural-related variables influence prevention and intervention efforts.
51	- Influence of gender, race and ethnicity on diabetes, cancer, heart and neurological diseases and musculoskeletal conditions (osteoporosis, osteoarthritis)
52	a. Study the multiple determinants of health and their interactions (personal, social, economic, environmental factors) on disease risk, disease mechanism, and individual response to therapy. b. Use novel social media strategies to crowdsource new ideas for research, and local events with facilitators to identify new questions and community ideas for research, benchmarking off of participatory budgeting exercises. c. Engage multiple communities in these exercises, including patient disease groups, geographic, racial and ethnic groups, LGBT populations, clinicians, entrepreneurs, and policy makers, to identify their key questions.
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55	a. Study the multiple determinants of health and their interactions (personal, social, economic, environmental factors) on disease risk, disease mechanism, and individual response to therapy. b. Use novel social media strategies to crowdsource new ideas for research, and local events with facilitators to identify new questions and community ideas for research, benchmarking off of participatory budgeting exercises. c. Engage multiple communities in these exercises, including patient disease groups, geographic, racial and ethnic groups, LGBT populations, clinicians, entrepreneurs, and policy makers, to identify their key questions.
56	--We recognize this is a very challenging project but the promise of it is worth making it a reality! --People exposed to agents in farms are motivated to learn about effect of generational exposures on their children e.g. PBB study ongoing at Michigan State University --Trauma effects. War refugees are increasing in numbers. Historical trauma might possibly change DNA and susceptibility to disease over time. Historically, Michigan has a large population of refugees (Somalia, Vietnam, Arab countries). These populations can be looked at as a generation who has had an environmental experience collectively and not necessarilty as individuals. Trust within these comunities is a big issue. --Disparity in pre-disposition to cancer remains a priority research question to address and answer for its implications for screening and care --Returning veterans is a special population to focus on
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Question 1B. Priority health disparities research questions that can be uniquely addressed within the proposed precision medicine cohort

Obs	Q1B
59	How do environment, geographic, historical, economic, and psychosocial factors interact with not only genetic factors but other environmental and psychosocial factors over time? How does this interaction influence or translate into information that could help guide the development of specific effective precision medicine scenarios? What are the genetic and environmental factors across the lifespan that influence the development of disparities in risk and progression of hypertension, chronic kidney disease, and other chronic diseases?
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61	To compare people's health inclinations regarding certain diseases, independently from their genome, could highlight social environments and behaviors that might be considered as discriminating. The complete analysis of the genome proposed to the cohort volunteers, studied in relation to their health inclinations, might be extremely helpful to distinguish what might be attributed to genes and what is independent (or partially independent) from them. Also, such a cohort offers a unique opportunity for a comparative study on the epigenomes, which might be the key element in order to understand health disparities and possibly to link them to a determinant.
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63	Statistics have shown a disproportionate number of African American men and veterans have been diagnosed with lung cancer. Yet, investigating these anomalies has not been a public health priority. Lung Cancer Alliance suggests that targeting research in these areas could lead to new understanding of lung cancer risks and causes that could be applied to all types of lung cancer.
64	* modifiable risk factors for cognitive aging, alzheimer's disease, and cerebrovascular disease. There are huge disparities across racial/ethnic minority populations and there is suggestive evidence that these can be prevented. * lifecourse development of disease and opportunities to intervene.
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66	Diabetes Obesity Asthma Effects of the built environment Environmental effects on quality of life and health Prematurity The effect of food deserts
67	This cohort, if successful, will uniquely be able to address questions about the nature and relative contributions and interactions of environmental and genetic factors as causal mechanisms for disparities in health. Specifically, cognitive aging should be a priority outcome of the Precision Medicine Initiative. The population of the US is aging, and cognitive impairment, most of which is caused by wither cerebrovascular or Alzheimer's pathology, will have a significant and devastating impact on society. There are major research gaps in what we know about disparities in cognitive aging. Efforts such as ADNI, ACTIVE, and recent Alzheimer's prevention trials, while well-funded and well-intentioned, are not able to address disparities because of unsuccessful recruitment of ethnic minorities. In the example of the ACTIVE trial, while a large proportion of African Americans were included, they were not at all representative of the population of healthy older Black Americans, but were very well educated and from limited geographic regions. Furthermore, measures that are needed to characterize some of the social, environmental, and biological mechanisms of disparities in the outcomes in this study were not included.
68	Research questions that examine both sex and race/ethnicity and the intersection of the two are essential to address health disparities and achieve the highest standard of health care for all. Therefore, PMI must include sex and race/ethnicity differences as key elements when developing research questions. In addition, research questions should include questions related to epigenetics as a key area of study relative to the influence of health determinants and should be integrated in all aspects of the PMI research. Genetics offers new opportunities to develop more precise treatments and care for priority populations. However, genomic information should not be overused for assessing disease risk and care and addressing health disparities. Other influences should be examined in research questions posed including lack of access to care, biases in medical settings, socioeconomic factors, lifestyle choices, and other environmental factors must be considered. An overreliance on genetics, instead of focusing on systemic factors, will not address root causes of health disparities, and may make these disparities worse. For example, one study of tobacco-related health disparities found that although genetics increased opportunities to tailor drug treatments, looking at other health disparities related to t
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Question 2B.Opportunities to study the relative influence of health determinants (e.g. personal, social, economic, environmental factors) on disease risk, disease mechanism, and individual response to therapy

Obs	Q2B
1	NIH research on health disparities should examine the relationship between election campaign contributions, particularly from wealthy elite and corporations, to candidates for office in the U.S. Congress, both House of Representatives and the Senate and the later positions and votes by those elected on bills considered, and particularly budget allocation for funding health disparities research and intervention programs to address the etiology, and implementation and dissemination. Similarly, research should be conducted on the relationship between lobbying by special interest groups, including corporations, on positions and votes taken by those elected on the bills considered in Congress, particularly budget allocation for funding health disparities research and intervention programs to address the etiology, as well as implementation and dissemination. In order for NIH to conduct such research on health disparities social and political scientists need to be included on interdisciplinary research teams, and the research should draw upon social and political science theories and research methods.
2	There are a whole range of theoretical opportunities, but whether they would fit will depend on the specifics of the PM cohort and research participants.
3	Our experience has come from a community-based randomized cohort of minority participants in which we have measured and are following the burden of high priority diseases. In the process we gather data on personal, social economic and environmental factors that may determine their risk for certain diseases and perform clinical examinations, including imaging. Accompanying these data we now have a robust archive of biological specimens (RNA, DNA, serum, plasma, urine) in order to try to assess the interaction of the personal, social, economic and environmental factors with background genetics. Because we are interested in the social determinants of health this perspective has allowed us to create a population where we can indeed look at the social environmental factors of health in the context of the genetic background of our population. We are now beginning to work with a similar cohort in another city to pool participants and data to enlarge our chances for significant observations. Thus a well-constructed personalized medicine program can use this kind of model by accumulating greater numbers across similar community based programs across the country.
4	To conduct studies that assess the relative influence of health determinants, you need participants that fall into each of the health determinant categories. Obtaining cohorts that are representative of the population (versus representing the ability to pay for health care services) is essential to reduce bias when learning about the effects of social, economic and environmental factors on disease risk. Marshfield embraces the concept of delivering health care and dental services based on an individual's need rather than an individual's ability to pay for those services and could contribute to larger studies evaluating health determinants on disease risk. Social, economic and environmental factors are important factors that should be considered as covariates in analyses assessing disease risk, disease mechanisms and response to therapy. These indicators are often difficult to obtain without asking participants directly about their health habits, exposures and activity. The PMRP cohort has collected this information using standardized dietary (Food Frequency Questionnaire (FFQ), and Dietary Health Questionnaire (DHQ)), environmental (PhenX Toolkit), occupation and geocoding data captured along with over 30+ years (average for the PMRP cohort) of medical and dental data captured in Marshfield Clinic Information Systems (MCIS) in-house developed comprehensive EHR. Standardizing this data is extremely important if sharing across sites. Finally, MCHS has the ability to standardize patient care practices across the system and then implement treatment interventions at one or a few sites for comparison. This feature enables us to control for health system variables when evaluating individual response to therapy.
5	Through the study of multi-level interactions, PMI researchers can investigate the potential causes and protective factors of health inequity which can be identified across the many data streams collected by the PMI, permitting analysis of effect modification between such variables. These findings will greatly advance research that seeks to identify the extent to which lifestyle, environmental, and genetic variability cause population disparities in disease incidence, prevalence, and outcomes. For example, even if one's genetic disposition might increase risk of disease, practical interventions targeting an individual's behavior and environment can potentially lower that risk of disease.
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7	The biggest opportunity in a next-generation precision medicine cohort will be the ability to collect so much data for an individual that the individual's own natural history can serve as a reliable measure of the effect of environment or the efficacy of an individual therapy. For example, if an individual shows a statistically significant increase in miles walked in the months after a treatment, it should be possible to tease apart the effects of the treatment from other potentially confounding factors. Ultimately, precision medicine has to address the individual. To support this end, a true precision medicine cohort needs to have statistical resolution down at the level of the individual as well. With unprecedented access to data sources on individuals, it should finally be possible to achieve that resolution.

Question 2B.Opportunities to study the relative influence of health determinants (e.g. personal, social, economic, environmental factors) on disease risk, disease mechanism, and individual response to therapy

Obs	Q2B
8	Using a mobile app platform to connect all participates to this effort, ongoing research can be conducted by continuing to engage the interested population, including asking them to share more information in the interest of scinece WHILE offering something of value back to the individual which helps engage them in the empowerment of managing their own health. Our group experience and programs have engaged more people in the world on specific causes than any other efforts in modern history. We understand how to engage massive populations, how to get those populations to contribute and how to continue to keep them engaged in an ongoing interaction and conversation - all necessary to achieve the stated goals herein.
9	No response provided.
10	Opportunities to do so are great if there are easy, simple ways to obtain and update data on health determinants like those mentioned. A major barrier is that much of that data is participant-submitted (e.g. data on diet, exercise). Simply overlapping environmental or sociological data onto subsets of the PMI cohort will not achieve the "precision" that the research cohort is expected to achieve. Data on the average income, diet, lifestyle, etc. of a 20-something Caucasian male living in Washington, DC may not be a good indicator of the lifestyle of a particular participant – though it is certainly much easier to attain. The more precise the data obtained, the clearer the picture that will emerge. The PMI working group might discuss whether it is appropriate to compensate research participants to supply precise, consistent, and reliable data using various mHealth technologies.
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14	• We have some good experience with recognizing these determinants, but need to do a better job creating multi-pronged and coordinated approaches to address the health determinants which contribute to health disparities. HOPE Works, an obesity intervention initiated at our institution, was implemented within the context of social and economic determinants of health (education, poverty, employment issues). Micro-enterprise and community-led strategic planning alleviated the economic burden influencing health status.
15	HMORN healthcare systems already contain longitudinal data across a broad range of health determinants on patients within their EHRs and other data repositories and have developed research to add to new scientific knowledge regarding illness progression. Many HMORN systems care for patients in rural areas and/or areas where other population disparities exist. In areas of stable populations, HMORN systems also care for, and already have established data, on multiple generations of families. Prior research in HMORN sites consistently shows that members trust their healthcare system, and are willing to participate in research conducted by these systems. Many HMORN sites also routinely collect environmental and behavioral data, such as depression, physical activity, and some family history. Additionally, the HMORN contains interdisciplinary researchers embedded within their healthcare organizations, who utilize a range of research methodologies. Therefore, HMORN sites have in place the academic resources to interrogate, evaluate, augment, existing data to improve health. For example, the entire process of identification, development, collection and integration of new patient reported outcomes data into the EHR may be completed with a high degree of efficiency because HMORN embedded researchers have access to and work closely with health systems administrators, information technology specialists and patients to move this work forward. This model of embedded research allows for more rapid evaluation and implementation of research findings and evidence-based expansion of the content of existing large EHR databases in order to expand the type of data they contain and the types of research questions that can be addressed.
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19	Studies such as those referenced in the question will be important to conduct in settings with health care, research, and community engagement across the systems of health care. These will allow the integrated approach recently suggested in the Adolescent Brain Cognition and Development RFA, combining imaging, genomic studies, and environmental and social studies. The combination of epidemiological studies intended to characterize health problems and identify causal mechanisms for diseases—social, environmental, biological-- various heritability studies, and clinical studies will insure that a more complete picture emerges and provides clarity about appropriate interventions.

Question 2B.Opportunities to study the relative influence of health determinants (e.g. personal, social, economic, environmental factors) on disease risk, disease mechanism, and individual response to therapy

Obs	Q2B
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24	One potentially powerful social determinant of health outcomes is racism or discrimination. Mechanistic studies of the impact of racism on physiology and gene expression are needed. Also, predictive modeling will be a strong approach to studying the relative influence of different factors on health in this study cohort. The rich characterization of many factors, including genetic, environmental, and social factors, on a large, diverse population can inform predictive models of disease risk and models that predict the benefits (and potential harms) of certain interventions or medications in specific subpopulations. These models can in turn inform the development of clinical trials, guidelines, and policies aimed at reducing health disparities. Predictive modeling of adherence and response to cancer therapy, diabetes medication adherence, and side-effects of common medications may be important focus areas. The development of exposure metrics that would allow for the characterization of environmental exposures over time would also be extremely valuable. There are a number of data resources available through various state and federal initiatives, often in collaboration with local power companies. Developing these data repositories into research tools would be extremely valuable.
25	We need to ensure that we specifically value, target, and engage African American men and boys.
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27	1. Focus on poverty within minority populations as it relates to feelings of autonomy and self-efficacy a. Determine any links between level of self-efficacy and health behaviors like smoking, poor eating habits, lack of exercise, etc. 2. Examine social determinants through a lens of access, affordability, and ability to enact positive change
28	Once again, the March of Dimes urges the PMI to study the relative influence of health determinants, including social determinants, on perinatal health and birth outcomes. To provide just one illustrative example, rates of preterm birth rose dramatically in the U.S. population over the past 30 years, and have only recently begun to decline by modest but important increments. Clearly, the U.S. population did not experience any generalized evolution in genetics or physiology that would account for these changes. This increase in preterm birth rates, which affected millions of infants and families, must have been caused by changes in the interaction between certain genetic factors and environmental exposures involving major segments of the population. Those factors and their interplay with genetics remain mysteries of disease risk and mechanism that the considerable power of PMI cohort could help solve, leading in turn to more targeted therapies.
29	Because conditions like obesity and diabetes are shared between many people of former European colonies, their trajectory toward those conditions are not genetic because they don't share ancestry. Their commonality is social hierarchies remaining from European colonizations. To be fair, genome research must put more than the 5% allocated toward ELSI research in Indigenous communities to address conditions with huge social determinants contributions. In Indigenous populations, conditions with multiple inputs are a waste of money to study with genomics...focus instead on pharmacogenomics and other "Discrete"questions in genomics. Precision medicine is in envisioned to help outliers and those individuals with familial or private alleles...this has to be adjusted for indigenous groups (and countries like Mexico) where there are very long runs of homozygosity in the entire populations, otherwise you will miss these vital tails of distribution to the ideal and priority of the individual.
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32	- unravel genetic and genomic architexture of our diverse population to medications - Understand the population-based pharmacogenomics - Elucidate on individual or diseases drug(s) related toxicogenomics and proteomics - Building community resilience risk and diseases communication programmes - Reliable evidence based policies
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34	N/A

Question 2B.Opportunities to study the relative influence of health determinants (e.g. personal, social, economic, environmental factors) on disease risk, disease mechanism, and individual response to therapy

Obs	Q2B
35	I think you can make the case that the *entire* cohort could be from the deep south, where there is a great representation of African-Americans (with the most diversity of genetics, and with great diversity in environmentally-related outcomes). The statistics for the area south of Tennessee for smoking, cancer, and other environmentally-relevant health issues are also stunning. This would be a statement to the American people that we are going to boost up the area of our country that is in most need of help, and at the same time learn lessons that will help all Americans. I think you could add Florida and Texas in order to ensure Latino involvement. Why not have this cohort be HIGHLY enriched for those whose health needs the most attention?
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37	To enable researchers with opportunities to conduct analysis across health determinants, a future PMI research platform must provide discoverability and access to the varied data associated with social, economic, environmental factors, disease, therapy, and disease outcomes. Booz Allen has experience in developing production level data and analytic warehouses and recognizes the value of combining the data with genomic, imaging, and other analysis data (e.g. genomic clustering) to conduct multivariate and novel network statistical analyses. The analysis results could better identify the combination/level of health determinants associated with disease risk and therapy outcomes by incorporating health disparities data from national databases (e.g. Environmental Protection Agency's Air Quality System Data Mart, and the National Cancer Institutes' National Cancer Database, Census Data, American Community Survey). E.g., the cancer research community, led by NCI initiatives, have shown association of race/ethnicity, socioeconomic status, and breast cancer subtypes in the National Cancer Database (Sineshaw, Breast Cancer Res Treat 2014). The PMI cohort study will bring about new sub-type analysis and strengthen or disprove genetic-phenotypic associations of disease prevalence based on limited data sets. PMI can further refine generalized findings on subpopulations by analyzing and identifying the confounding factors among the health determinants and genetic data. For example, the Genetics of Asthma in Latino Americans (GALA) identified variation in the genetic ancestries among the Hispanic, groups and ethnic-specific genetic factors tied to observed differences in physiologic response to albuterol: albuterol treatment was
38	Emphasis on the complex interactions between different health determinants allows us to understand their influence on population-level as well as individual health outcomes. Prospective study design is best for establishing relationships between health outcome of interest and exposure variables, due to difficulties in developing accurate retrospective exposure history profiles. In large prospective cohort studies investigators collect information over time, enabling investigators to assess whether and when subjects are impacted by disease and how this may be associated with their prior observed exposure(s). There is opportunity in this study for investigators to establish a temporal relationship between health determinants and an outcome, or follow the natural development of a condition over time. With detailed individual data, investigators can compute and compare incidence rates for different exposure groups; eventually using the data to answer questions about the associations between "risk factors" and disease outcomes. The temporal dimension, whereby exposure occurs before outcome, gives some indication of causality. At the population level, public health interventions can be assessed using this cohort. The effectiveness of precision medicine therapeutic interventions can also be assessed within subpopulations who have common disease and genetic profiles. It is recommended that community level data from other public use data sets be utilized. For example, Battelle is completing data collection for the Healthy Communities Study which includes characterization of community interventions to address childhood obesity. This and other existing data may be useful tools to minimize costs of some community data collecti
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Question 2B.Opportunities to study the relative influence of health determinants (e.g. personal, social, economic, environmental factors) on disease risk, disease mechanism, and individual response to therapy

Obs	Q2B
46	Blood centers, like SDBB, are essentially an existing, unstudied, longitudinal, ongoing cohort of diverse, healthy participants accompanied by decades of donor’s electronic health/wellness records and access to biospecimens. Although not comprehensive, health determinant information is collected or can be derived from the standard donor registration and mini-physical examination process. For example, health risk behaviors, exposures and travel are self-reported and the donor’s address can be crossed references with geographic information system tools to determine SES and potential environmental exposures. During the blood donation and recovery period, there is ample opportunity for the PMI ‘cohort’ study to collect a comprehensive set of health determinant information (not already collected using mHealth devices) through electronic surveys, education, and in person interviews. Since ‘healthy’ donors eventually become unhealthy, a collection of longitudinal health determinant data from ‘healthy’ PMI participants paired with the donor’s health/wellness records and -omics data profile will be a valuable resource in identifying disease risks and mechanisms, as well as predicting intervention response.
47	
48	The first step here is to RECORD those differences, not to JUDGE them. For example, the Harvard Nurses' Study has been recording those different choices for years without judgment. Current efforts to legislate changes in lifestyle choices are badly conceived (e.g. penalties in healthcare costs for people who are overweight). This kind of judgment or legislation or penalty will only confuse the data collection, stigmatize people, and discourage people from participating in a program that clearly thinks ill of them before they even begin.
49	
50	Examining factors such as social support, peer networks, attitudes, and psychological characteristics such as optimism, resiliency and coping are important health determinants.
51	- Build digital tissue bank containing de-identified molecular (proteomics, metabolomics etc.) and tissue imaging information on U.S. precision cohort (from patient medical records and lab tests, insurance claims) to determine influence of health determinants (e.g. personal, social, economic, environmental factors – collected through genomic analysis, wearable sensors, medical records) on disease risk, disease mechanism, and individual response to therapy
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53	
54	there's a need to collect data on social and structural factors that impact access, adherence, and outcomes
55	
56	--We could gather data on many environment and social determinants of health without getting to individual data. Geography, migratory factors e.g. victims of Hurricane Katrina displaced in Atlanta and Houston witll be different than natives of the areas --With enough money, could access existing databanks
57	We applaud the overall goals of the Precision Medicine Initiative. However, these goals cannot be achieved unless children are part of this important research effort. Extensive research now points to the conclusion that health disparities must be understood from a life course health development perspective which details the dynamic processes whereby diverse social and environmental exposures interact with biological forces from preconception onward to shape health development trajectories.1 A growing body of research shows that early adverse childhood experiences are associated with enduring changes in the nervous, endocrine and immune systems and with future adult chronic disease and longevity.2,3 The complex associations between early social and economic disadvantage and future health states and health status disparities need to be better understood and this would best be achieved with cohort data that includes children. 1. Halfon N, Larson K, Lu M, Tullis E, Russ S. Lifecourse health development: Past, present and future. Matern Child Health J. 2014;18(2):344-365. doi:10.1007/s10995-013-1346-2. 2. Danese A, McEwen BS. Adverse childhood experiences, allostasis, allostatic load, and age-related disease. Physiol Behav. 2012;106(1):29-39. doi:10.1016/j.physbeh.2011.08.019. 3. Gilbert LK, Breiding MJ, Merrick MT, et al. Childhood adversity and adult chronic disease: An update from ten states and the District of Columbia, 2010. Am J Prev Med. 2015;48(3):345-349. doi:10.1016/j.amepre.2014.09.006

Question 2B.Opportunities to study the relative influence of health determinants (e.g. personal, social, economic, environmental factors) on disease risk, disease mechanism, and individual response to therapy

Obs	Q2B
58	•Efficient research, which can blend clinical data with environmental data will need a robust technology infrastructure. Big Data Appliances, combined with "Open Source" software analysis programs can be engineered to combine and normalize these data types today. Once "normalized", these combined data sets can be explored by a wide range of traditional and evolving business intelligence tools. •Because financial data is not normally captured in clinical trials, additional consent would be required. Technologies capable of blending financial data with sophisticated genomics data will be necessary. •Currently, several leading academic institutions (i.e. MD Anderson, U-Penn, UPMC, Mayo) utilize existing technologies that identify groups using extremely finite criteria around demographics, genetics, primary and secondary diseases.
59	Multiple dimensions of health disparities should be considered and measured. Not only just the individual-level factors (e.g., SES, diet quality, behavior, clinical risk factors, therapeutic interventions, compliance), but also community-level factors (e.g., neighborhood economic level, neighborhood segregation, walkability, built environment) and genetic factors (e.g., hemoglobinopathies, APOL1).
60	
61	Comparing the genome of people with similar clinical condition might help to provide an assessment of what might be attributed to genes and what to extra genetic conditions. In this analysis we suggest to focus on groups living in difficult social situations, like the working class, the unemployed, the sons of immigrants, the uninsured, the people belonging to races and to religions or to cultures not fully accepted, women in sexist workplaces, people living in the suburbs, homeless, people at the edge of society, rehabilitated or rehabilitating after criminal episodes. Comparing the genomes of these kinds of people to the genomes of other people living in easier and more stable and prosperous situations, might be a unique opportunity to understand the causes of a disease that are independent from genetics, and that are just due to social inequalities translated into health disparities. To focus these social inequalities causing health disparities is something to pursue. In particular, we suggest focusing on the epigenome as a possible intermediate of the environment: epigenetic differences might be the key factor to understand health disparities due to social inequalities.
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63	
64	* Critical to include careful, valid, and robust measures of social factors across the lifecourse - including socioeconomic, psychosocial, and environmental conditions. * Important to use modern causal inference tools to decompose effects and understand mediation and relevant lifecourse models.
65	To date, precision medicine has largely referred only to pharmacogenomics and using genetics to predict responses to drugs. This cohort provides the opportunity to go beyond that. A key area that has been overlooked is variability in response to certain lifestyle factors, e.g. exercise. Exercise, though known to be a generally positive and useful preventive medical treatment, is highly variable in the physiologic efficacy between individuals - even when adherence is the same. This cohort could provide a novel opportunity to understand inter-individual variability in responses to exercise for a variety of physiologic and clinical outcomes.
66	
67	My primary comment here is that relative influence can only be determined if the measurement of environmental factors and potential mechanisms is thorough, valid, and relevant among underrepresented groups.
68	The field of epigenetics is a critically important to precision medicine. Epigenetic influences that are gendered are particularly important and often overlooked. For example, the mechanism(s) of the impact of violence on the risk for chronic disease in both women and their offspring is poorly understood. Women may also be disproportionately affected by environmental pollutants in which the mechanisms and impact on genetics is poorly understood. For precision medicine to be successful at addressing health disparities, all members of society, including women and racial and ethnic minorities, must be included at every step of the process from adequate numbers represented in clinical trial research to genetic testing of European, Asian, and African descents. Research cohorts should be required to oversample for racial and ethnic minority groups and female participants to ensure adequate understanding of and genetic markers.
69	

Question 3B.Opportunities to obtain new scientific knowledge regarding individual variability in genes, environment, and lifestyle and their interactions as they affect the incidence of progression of illness where there are significant population disparities in disease incidence, prevalence, and outcomes

Obs	Q3B
1	
2	Same response as in #2: it depends on who is enrolled & how they are enrolled and followed.
3	What is the extent of variability in the effects of gene expression in different environmental situations, e.g. urban versus rural lifestyle, exposure to toxins, etc.? How does lifestyle impact gene expression in different ethnic groups What is the extent of variability in gene expression in different occupational exposures? How do genetics affect the onset and progression of chronic conditions? Why do some people with diabetes develop particular complications? For example, why do only some people with non-alcoholic liver disease progress to non-alcoholic steatohepatitis and cirrhosis? The same can be asked of those who abuse alcohol and tobacco. Do genetics determine whether a diabetes patients will develop renal failure?
4	The use of technology to assist in gathering and analyzing data over the past years has increased exponentially. Much of the data required to obtain new scientific knowledge either already exists in EHRs, is available via publically available data sets or requires collection from study participants. There are several opportunities which require the advancement of methods before this can occur: 1) developing more efficient data mining and analysis techniques for genetic and EHR data; 2) developing tele health technology to capture standardized patient data; 3) developing methods to link to publically available data sources to obtain environmental information; and 4) developing data sharing models/standards that allow sharing of data across institutions, thus accelerating the discovery process by making data more readily available.
5	To encourage innovation in patient care, the AAMC recommends the PMI work to fully evaluate how genes and gene-environment interactions contribute to health. We commend the NIH PMI for “intentionally oversampling underrepresented populations” which will allow researchers to analyze genetic material associated with characteristics such as race, environment, or other lifestyle data of individuals who may or may not have a disease. Additionally, epigenetic studies will allow researchers to evaluate environmental influences on the activation of certain disease-causing genes. Since one of the concepts of precision medicine is “the application of prevention and treatment strategies that take individual variability into account”, exome sequencing is another recommended method for obtaining new scientific knowledge. AAMC member-institutions are at the forefront of studying the clinical applications of exome sequencing. For example, the UNC Chapel Hill School of Medicine, NC Genes program is one of five Clinical Sequencing Exploratory Research projects that will study ways for healthcare professionals to use genome sequencing information in a clinical setting. The UNC research team has also implemented whole exome sequencing (WES) in medically underserved groups and is working to identify barriers to recruitment and retention of patients in the study as well as how WES can be expanded to other medical institutions.
6	
7	The biggest opportunity in terms of raw efficiency for associating genes with function will be an aggressively oversampling of the rare disease community. Rare genetic diseases by their nature exaggerate the effect (or the absence) of a particular gene. The number of individuals necessary to achieve statistical significance about a gene-disease drops dramatically in the case of rare disease, to the point where 20,000 rare disease genomes may ultimately yield more insight about genes than 200,000 "healthy" genomes.
8	No response provided
9	No response provided.
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14	• Integrate real-time data collection of biospecimens, social and physical environment, and lifestyles should be considered. Specific to social environment, factors should include patient/provider communication, social support, patient activation measures, provider decisions to share information and patient decision-making practices. Sam Cykert, MD UNC-Chapel Hill has made in advances in this area for both breast and lung cancer disparities.

Question 3B.Opportunities to obtain new scientific knowledge regarding individual variability in genes, environment, and lifestyle and their interactions as they affect the incidence of progression of illness where there are significant population disparities in disease incidence, prevalence, and outcomes

Obs	Q3B
15	As a national network of embedded research organizations, the 18 US-based healthcare systems in the HMORN provide care over time for over 15 million members (1 in every 22 Americans). Through research and clinical practice, these systems have integrated tools such as EHRs, patient portals, and telephone survey cores that allow for efficient collection of patient reported data. This data is linked to clinical encounters and other data. Some HMORN healthcare systems also have biobanks of genetic information linked to clinical and patient reported data. Many HMORN sites also have access to biorepositories of tissues and other biological samples (e.g. tumor blocks, serum, urine, etc.) that are also linked to clinical and patient reported data sources. The ability to collect patient reported outcomes related to lifestyle, environmental exposures, and other determinants and link this information to clinical care as well as to genetic information will be critical to discovering new knowledge regarding genetic variability in disease progression and population disparity. However, the quality of large databases is only as good at the data they contain. Many of the interdisciplinary researchers working within HMORN health systems utilize mixed-methods approaches to evaluate the data being collected in order to ensure that these data provide an accurate picture of the concepts they were designed to represent, and ultimately that the results of studies using these data are interpreted appropriately.
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18	This cohort will present numerous opportunities to gain new knowledge about the interactions between genes and environmental factors that underlie disease. For most genetic association studies (e.g. GWAS studies), we generally have very little environmental or other lifestyle choices to complement the genetic data. Thus, there is limited understanding of the G x E interactions and how they drive disease development or even how these interactions may affect disease course or treatment effectiveness. A similar scenario exists for lifestyle data (fitness, daily tobacco use, etc.), which is generally collected as very coarse-grained information-- not collected in standard format-- and is patient reported (i.e. subject to bias and inaccuracies). Therefore, personal wearable (health and fitness sensors) and environmental sensors should be featured prominently in the efforts of this initiative to elucidate the bases of human disease. These devices present unique opportunities to collect objective and quantitative data. For example, air quality sensors could be used to assess environmental differences that may be important to the development of diseases such as asthma. The sensor data could be combined with economic or other societal data to shed light on disparities in disease rates. Efforts should be made to engage device makers (e.g. Fitbit) to provide free or lower-cost alternatives for personal wearables that would ensure the most equivocal representation of this type of data from all populations included in the cohort.
19	Integrated healthcare systems with electronic health record (EHR) systems already contain longitudinal data on patients to be able to add new scientific knowledge regarding illness progression. Many of these systems care for patients in rural areas and/or areas where other population disparities exist. In areas of stable populations, these healthcare systems often care for, and already have established data, on multiple generations of families. Data also consistently show that members trust the healthcare system, and are willing to participate in research conducted by these systems. This opens opportunities for significant longitudinal collection of lifestyle information, environmental information, behavioral information, and other data related to health determinants as well as disease progression and medical treatment. Some of this data is already being collected in these healthcare systems. Geisinger collects information on physical activity in children, has geocoded the addresses of a majority of their membership, consistently screens for depression and family history during primary care visits, and has collected environmental and other data on biobank participants with the standardized PhenX questionnaire.
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Question 3B.Opportunities to obtain new scientific knowledge regarding individual variability in genes, environment, and lifestyle and their interactions as they affect the incidence of progression of illness where there are significant population disparities in disease incidence, prevalence, and outcomes

Obs	Q3B
24	Collecting meaningful and comprehensive information on environment and lifestyle can help us disentangle important causes of diseases. We should aim to have solid information on behavioral factors (e.g. from surveys as well as biomarkers, such as self-reported tobacco use data, serum cotinine levels, and identification of relevant genetic variants), and detailed data on environmental exposures (shorter-term via biomarkers and longer term from environmental data repositories), as well as genetic information. The Kaiser Permanente Research Bank (KPRB) is currently being developed as a collaboration across all 7 KP regions, which provides extensive geodiversity and member diversity (> 50% of our members are non-white). Because of its diversity and the rich clinical data resources provided by our electronic health record, the KPRB could serve as an extremely important resource in PM efforts targeting health disparities. Over the next few years, the KPRB will recruit an additional 280K participants to complete its collection of a 500K member biobank that includes general, pregnancy and cancer cohorts. Participants provide a blood sample, complete surveys, and provide broad consent for use. These specimens, with linked data from KP's diverse and loyal members, will yield tremendous scientific insights on genetic, behavioral, and community level influences. KP's Geographic Information System (GIS) database also captures data for both physical environmental exposures (air, water, pesticides) and social/built environment (censu
25	We need to ensure that we specifically value, target, and engage African American men and boys across the life course.
26	
27	
28	Yet again, the March of Dimes would propose that perinatal health and birth outcomes provide a rich and significant field of inquiry regarding individual variability and its impact on disparities in disease incidence, prevalence and outcomes. In recent decades, scientists have come to recognize that each perinatal condition like preterm birth or low birth weight is not a monolithic disorder with a single etiology; rather, each is a syndrome representing the common outcome of a host of conditions and pathways. Individual variation indisputably plays a critical role in explaining why two mothers, by all appearances similar in every key aspect and experience, can have widely varying pregnancies and birth outcomes. The March of Dimes would emphasize again that studying perinatal health and birth outcomes could yield early, actionable insights that would improve maternal and child health within years, not decades.
29	Such studies exist in American Indian communities but can be enhanced by increasing the amount of spotlight on border tribes that straddle the US/Mexican border where they share the same genetics but health outcomes are much better in Mexico. However this has to be done with much attention to tribal sovereignty and ownership of samples, DNA and RNA isolations and Data. It is highly unethical and a 'cheat' to obtain the information you want from US citizens from latin america. This highly undercuts American Indian sovereignty.
30	Social media contain a lot of useful data from different populations. Mining and combining these data with other data sources, such as the PMI cohort and EHR data, can answer useful research questions.
31	
32	- unravel genetic and genomic architexture of our diverse population to medications - Understand the population-based pharmacogenomics - Elucidate on individual or diseases drug(s) related toxicogenomics - Health quality and outcomes prediction - Better understanding of interaction between diseases, functions and causality molecules - Better understanding of causal networks - Reliable evidence-based policies
33	
34	N/A
35	I think you can make the case that the *entire* cohort could be from the deep south, where there is a great representation of African-Americans (with the most diversity of genetics, and with great diversity in environmentally-related outcomes). The statistics for the area south of Tennessee for smoking, cancer, and other environmentally-relevant health issues are also stunning. This would be a statement to the American people that we are going to boost up the area of our country that is in most need of help, and at the same time learn lessons that will help all Americans. I think you could add Florida and Texas in order to ensure Latino involvement. Why not have this cohort be HIGHLY enriched for those whose health needs the most attention?
36	

Question 3B.Opportunities to obtain new scientific knowledge regarding individual variability in genes, environment, and lifestyle and their interactions as they affect the incidence of progression of illness where there are significant population disparities in disease incidence, prevalence, and outcomes

Obs	Q3B
37	Booz Allen staff's experience in working with health disparities data (e.g. Jackson Heart Study data, CDC studies) and playing an active role in genomics data handling for the VA Million Veterans Program provides perspective on obtaining new scientific knowledge. This knowledge could lie in the following areas: 1) validate previous research outcomes through increased sample size, individual genes, lifestyle, and economic information (Garraway, Cell, 2013); 2) build upon limited genome-based research with the advent of WGS or different GWAS using participant's stored biospecimens (Simonds, Journal of NCI, 2013); and 3) with advanced data analysis tools, we can study the relationship among different diseases with different genes using network analysis, combining historical information that may not be limited to one disease type (Fanner, Eur Resp Jour, 2014). The PMI diverse cohort enables investigations into a) molecular/genetic heterogeneity present in clinically homogeneous patient populations, and b) how acknowledged risk factor for a certain disease in the general public may not have expected contribution to a disease in a subgroup population. Booz Allen is engineering its research capability to construct a computerized adaptive diagnostics system to potentially provide the following diagnostics that evolve with population-dependent genetic variability: 1) Use One-, Two-, Three-, and Four-Parameter Logistic Model to match up individuals' disease progression and genomic information (i.e., genes, genetic errors, mutati
38	Tailoring of medical treatment to the individual characteristics of each patient requires classifying individuals into subpopulations that differ in their susceptibility to a particular disease, in the biology and/or prognosis of those diseases they may develop, or in their response to a specific treatment. (Ref: Wikipedia for Precision Medicine). Availability of molecular profiling tests (example: DNA) is critical to provide precision medicine. Genetic and physiological make up, in addition to a person's personal experiences and interactions with the environment plays a significant role in health disparities such as varying incidence and severity of disease. Some biological effects are modified by environmental exposures and the overall admixture of the population. Linking different data sources would provide almost all exogenous and endogenous exposures including exposures from diet, lifestyle, and internal biology which are critical to disease etiology which is popularly captured as "Genetics loads the gun, but environment pulls the trigger". With the linked data, one can understand the differences and similarities between individuals using epidemiological and statistical methodologies. On the treatment side, the information gained could help in developing customized medical products or devices, preventing harmful drug interactions, increasing efficiency in prescription medicine, and reducing costs associated with healthcare.
39	A diverse population offers tremendous opportunities to study the interplay between genes and environmental risk factors given that exposure to various lifestyle and environmental risk factors vary substantially between populations with different ethnic backgrounds. These factors include for instance, diet, supplement use, medication use, hormone use, physical activity (both occupational and leisure), smoking, alcohol use, or occupational exposures to name a few. Overall including a diverse population will increase the range of exposure to various environmental risk factors and, hence, the ability to identify associations and gene-environment interactions. Furthermore, changes in lifestyle and environmental risk factors may lead to substantial larger disease burden in specific population, suggesting that potentially the genetic background makes a specific population more susceptible to the lifestyle and environmental risk factors than other populations. Examples are the high burden of obesity and type 2 diabetes in Native American populations exposed to a Westernized lifestyle or the dramatic increase in colorectal cancer rates in Asian populations that co-occurred with a Westernized lifestyle. Studying these populations provide unique opportunities to potentially identify gene-environment interactions. However, up to this point sample sizes have been limited.
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41	Correlations of genetic factors to conditions of vulnerability to substance abuse, obesity, sociopathy, as well as components of resiliency- handling loss and adversity without physical and/or psychological impairments
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Question 3B.Opportunities to obtain new scientific knowledge regarding individual variability in genes, environment, and lifestyle and their interactions as they affect the incidence of progression of illness where there are significant population disparities in disease incidence, prevalence, and outcomes

Obs	Q3B
46	Leveraging the blood centers' infrastructure and donor base for a national 'cohort' study will provide significant research knowledge and a positive impact in our communities. Blood centers, like SDBB, are currently partnering with research institutions and industry to obtain –omics data (genomics, proteomics or metabolomics) for research and clinical studies. San Diego is an innovation hub composed of biotech, pharma, mHealth, and high-tech companies and academic and medical research institutions. SDBB's partnerships provide an unrivalled opportunity to obtain "new" scientific knowledge with current technologies, as well as those in the pipeline.
47	
48	In order to gain the most from this effort, we need very broad participation of a large number of people over a long period of time. The best way to achieve that is through electronic health records and mandatory reporting over the entire country. Only in that way can we track people as they move around the country, as their health changes over time, and as they progress through life. Voluntary reporting is only good if people make a concerted effort to continue their participation. The medically underserved are unlikely to make that effort without appropriate incentives.
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51	- Collection and analyze metagenomic data (Example intestinal track) over progression of illness/treatment against data from digital pathology (molecular and tissue imaging data), medical records, mobile devices and wearable sensors.
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53	
54	understanding does not naturally lead to improved health. Interventions that address health conditions should document impediments and successes in addressing these impediments.
55	
56	--There have been studies published that showed different treatments work for different populations. Need to look at the valdiity of these --Using existsing data resources and lessons learned e.g. ACS's collection of over 300,000 records during a 7-year span for the same purpose unveiled numerous challenges. It is important to connect with these precedent efforts
57	We believe that if children are not included in such a significant study it will be a significant missed opportunity for both children and for the medical community at large, particularly following the closure of the National Children's Study. Overwhelming evidence suggests that gene-environment interactions very early in development have profound effects on the emergence of adult diseases such as diabetes, cardiovascular disease, cancer, and psychiatric illness. Both the individual genetic code that predisposes to these diseases and the epigenetic mechanisms that control gene expression will likely be available to the clinician and family prenatally or in the first months or years of life. Many adult conditions have their antecedents in childhood, and the inclusion of children in a cohort study of the size and scope proposed in the Initiative provides the potential to improve the understanding of these antecedents and how they develop in adulthood, leading to more effective treatments for an array of illnesses. We encourage the Working Group to include a broad age range of participants in the cohort so that data may be collected across the lifespan, from infancy through old age. Further, we urge that pediatricians and child health experts be systematically incorporated into the planning and implementation phases of the Initiative so that children and adolescents have a strong voice at the research table.
58	
59	More efforts should be devoted to understanding the extent to which the life-course intersects with variability in genes, environment and lifestyle as they affect progression of disease. This approach would enable knowledge to be developed that addresses how to avoid chronic disease as adult if certain psychosocial and environmental conditions exist or could be changed in the in utero environment (e.g., obesity, diabetes, and hypertension during pregnancy) and during childhood.
60	

Question 3B.Opportunities to obtain new scientific knowledge regarding individual variability in genes, environment, and lifestyle and their interactions as they affect the incidence of progression of illness where there are significant population disparities in disease incidence, prevalence, and outcomes

Obs	Q3B
61	To analyze the different environmental and social conditions corresponding to different health conditions might be a unique opportunity to determine whether social disparities correspond to health disparities. In particular, we suggest to consider the health disparities related to social discriminations like episodes of racism or sexism or homophobia or bullying, considering different levels: from slight favoritism in the workplace to situations of constant fear and real risk to be attacked or killed. We suggest comparing the health differences among groups that might be damaged by any form of social discrimination. This would allow an achievement of precise data about the correlation between difficult social situations and diseases predisposition, providing a unique opportunity to understand health processes.
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64	Careful accounting for social confounders of genetic patterns.
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67	The PMI should consider leveraging birth cohorts of diverse people and representative studies of people in childhood/adolescence as major sources of the cohort so that causal mechanisms of disparities can be better determined. Examples of larger scale studies are the Kaiser Permanente Northern California cohort, Project Talent, Add Health, and PSID. There are many smaller scale studies of infants, children, and families, whose participants have now aged and are at higher risk for disease, who could be recontacted for participation.
68	The 1993 NIH Revitalization Act made inclusion of women and racial and ethnic minorities in health research a national priority. Yet, despite progress, women and minorities have not achieved equity in biomedical and health outcomes investigations. The science that informs medicine—including the prevention, diagnosis, and treatment of disease—routinely fails to consider the crucial impact of sex and gender. Females are often excluded from animal and human studies or the sex of the animals is not stated in the published results. Researchers frequently do not enroll adequate numbers of women or minorities in clinical trials or, when they do, fail to analyze or report data separately by sex and sex-race/ethnicity. This hampers our ability to identify important differences that could benefit the health of all. The evidence on sex differences in major causes of disease and disability in women is mounting, as are the gaps in research. Therefore, new scientific knowledge acquired from PMI must address these gaps by examining the impact of sex, race and ethnicity on disease incidence, prevalence, and outcomes. Funding for scaling up efforts to identify genomic drivers in cancer must be contingent upon the researchers' inclusion of both female and male cells to gain a better understanding of individual variability and the affect of progression of illness. Inclusion of female cells should allow for the effect sizes in the literature and would ensure adequate power to find significant sex effect if indeed present.
69	

Question 4B. Novel methods to gather data on geographic, environmental, and social determinants of health

Obs	Q4B
1	NIH research on health disparities should examine the relationship between election campaign contributions, particularly from wealthy elite and corporations, to candidates for office in the U.S. Congress, both House of Representatives and the Senate and the later positions and votes by those elected on bills considered, and particularly budget allocation for funding health disparities research and intervention programs to address the etiology, and implementation and dissemination. Similarly, research should be conducted on the relationship between lobbying by special interest groups, including corporations, on positions and votes taken by those elected on the bills considered in Congress, particularly budget allocation for funding health disparities research and intervention programs to address the etiology, as well as implementation and dissemination. In order for NIH to conduct such research on health disparities social and political scientists need to be included on interdisciplinary research teams, and the research should draw upon social and political science theories and research methods.
2	Leverage existing data, especially publicly available data, as much as possible as the primary source of exposure information.
3	Connection of participants to social media sources Measurement of sensor data such as accelerometer, pulse, ecg, BP and other data measure by sensors or similar means and genetic variability and onset of diseases. Collection of environmental particulate matter or specific chemicals in sentinel sites across the US coupled with GPS data, disease onset and gene variability Have online enrollment with simple modalities and feedback. Feedback will include information from real time analysis of the extensive database Merging of cohort data with other ‘big data’ to determine many outcomes. Examples are shopping data from food stores, use of recreational facilities etc. Measurement of ranges of biomarkers using ‘omics to determine their relationship to genomic data. Collection of imaging data to determine structural and functional changes associated with genomic sequences.
4	MCRF has had successful data gathering implementations using tele health applications and devices. These applications (if designed appropriately) make it easy and convenient for individuals to participate in data collection activities. The use of SMART phones is an excellent example of where technology has removed the barriers for data collection and makes it easier for research study participants to respond to questions in a timely and convenient manner. For example, MCRF has created several tele health mobile device applications that enable researchers to collect data for flu tracking, farm mapping, and managing a teenage population of diabetic patients.
5	Both the Institute of Medicine and the Office of the National Coordinator have proposed the inclusion of social, behavioral, and psychological data in hospital electronic health records (EHRs). Included in the proposed panel are questions about sexual orientation, education, employment status, food and housing security as well as other lifestyle and environment questions. The AAMC recommends the NIH work with health systems in preparation of these data’s availability to align this new information with PMI data in order to gain information on geographic, environmental, and social determinants of health. Health services research efforts can support the understanding of how to validly collect these data. The AAMC encourages NIH to leverage health information technology in order to gather different types of data about participants. However, the uptake of certain technologies may vary in different populations. PMI’s intention to provide assessment data to participants using mobile devices or wearable sensors requires NIH to understand how subgroups accesses and obtain medical information. In a previous comment letter response to FDA’s report on “Ensuring Access to Adequate Information on Medical Products for All, With a Special Focus on Underrepresented Subpopulations,” the AAMC provided recommendations to identify communication pathways that will be effective to reach populations who many not benefit from infrastructure and technologies that facilitate communication through electronic means and social media.
6	As mentioned above, emergency departments are geographically based resources. Identification of geographic patterns and exposures can be linked to patients presenting to individual emergency departments.
7	Mobile phones can already track geographic data with high precision. Mobile phones don't record all environmental factors directly, but many environmental factors are predictable through robust machine learning models from readily available data. For example, access to a user's twitter feed is sufficiently powerful to predict whether or not the user is a smoker with high accuracy. Access to a user's amazon purchasing history or Google search history (if granted) is perhaps the richest possible source of information on a user from which many other factors (including environmental ones) can be inferred. For a given user, facebook's social graph is a rich source of information about social relations. Combined with a twitter feed or a facebook feed or a Google search history, it constitutes a kind of digital phenome.
8	4. Use of participants cell phone and a novel app can address this opportunity in an easy, convenient and inexpensive way to stay in communication with a large population of sample contributors and a larger population interested in science, health egagement and interacting with their own health data.

Question 4B. Novel methods to gather data on geographic, environmental, and social determinants of health

Obs	Q4B
9	No response provided.
10	mHealth technologies and many of the hundreds of thousands of apps now available for tracking health and lifestyle data present exciting opportunities to gather data on geographic, environmental, and social determinants of health. We must keep in mind, though, that those devices are subject to user error, inconsistent usage, and technological failure, which will skew data. They also raise ethical issues. For example, cameras worn on one's body reliably track food intake, but also divulge information about those in proximity to the person wearing the camera. The PMI working group might discuss whether it is appropriate to compensate participants for their precise, consistent, and reliable contributions to the database of geographic, environmental, and lifestyle data.
11	Simple Mobile Maps of the genome (and/or body) for deploying micro-consent Data literacy will be key to the success of the project. Simple, visuals of the body and/or genome could help facilitate patient engagement. Entities could use their facilities mapping infrastructure to build mobile maps of the genome such that individuals in the cohort could exercise micro-consent for their genetic data and self-organize around variants. It's important patients have a sense of mastery and control over their genetic data. Biological Domains instead of EHRs The exponential data model for this cohort would be patients picking a trusted registrar for their personal health domain and then patients, self-organizing around their data. In that model, patient data would migrate to where it created the most value for them and their communities. A single, unique, domain per patient with micro-consent scales much cleaner than fragmented, redundant copies of a persons data across entities that have little/no accountability to return anything to the patient.
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14	• Utilize and combine Robert Wood Johnson's County Health Rankings Report with patient reported outcomes (PRO) collected via mobile devices, interactive voice response (IVR), and home visits. Use GIS and PRO to map access to fresh fruits and vegetables, convenience stores, and walking trails.
15	The HMORN uses various geocoding algorithms to link external public use data on population characteristics, environmental attributes, and social system determinants of health to their EHR and membership data. Many HMORN sites also have part or all of their member population geocoded, allowing for additional research into environmental and other determinants of health. Some HMORN sites have also already collected comprehensive environmental exposure information on members using a standardized tool (PhenX) enabling comparison between sites. The HMORN also has an active genomics special interest group (SIG) of over 40 researchers actively utilizing these data resources to study geographic, environmental, and social determinants of heath.
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23	Mobile technologies, environmental sensors, and social media have the potential to gather such data. Application of data science methods is necessary to take full advantage of such data.

Question 4B. Novel methods to gather data on geographic, environmental, and social determinants of health

Obs	Q4B
24	Partnerships with commercial sources of "Big Data" may help enrich the precision medicine cohort, but this should be done with the permission of participants to access their social media data. Significant effort should be expended to ensure that participants understand what sharing their data means, as there are significant privacy issues associated with sharing. The government should also develop much more secure strategies to protect this data from incursion. Unfortunately, the recent hacking of federal data systems will greatly undermine confidence in the ability to protect this data. Although disease-based advocacy groups may favor sharing of personal information regardless, other communities will likely have more reservations. Improvements in text-mining and natural language processing software may also help to facilitate the use and analysis of unstructured data fields, such as the information found in clinical notes and other text fields of electronic medical records. As novel methods are developed, safeguards should be in place and emphasized to protect participants against potential social harm and further disparities.
25	We need to ensure that we specifically value, target, and engage African American men and boys across the life course.
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27	1. Self-reporting of indicators from participants through mobile devices a. Use social media (Facebook, Twitter, Instagram), and easy-to-use mobile sites to collect data from participants, including older adults.
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29	Such studies exist in American Indian communities but can be enhanced by increasing the amount of spotlight on border tribes that straddle the US/Mexican border where they share the same genetics but health outcomes are much better in Mexico. However this has to be done with much attention to tribal sovereignty and ownership of samples, DNA and RNA isolations and Data. With more attention to false and contrived scarcity created by the difference between individual and communal economies (capitalist vs Indigenous).
30	The use of mobile technologies, particularly mobile apps, can help researchers gather these data. For example, this technology can facilitate data collection on whether members from underrepresented groups residing within certain neighborhoods are more likely to be exposed to detrimental environmental factors, have certain lifestyles and so on that negatively affect their health status.
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32	- Integrated digital approaches (RS/GIS on socio-epidemiologic determinants) - 2nd and 3rd generation surveillance approaches to risk and diseases - Surveillance response systems in precision medicine
33	We use wearable accelerometers and GPS to measure frequency of low-intensity, physical activity in daily life that remains largely undetected by self-report and by a focus on traditional exercise (e.g, swimming, golfing, biking, gardening) that may be less achievable in sociodemographically at-risk older adults living in Baltimore and other urban cities due to unsafe sidewalks and neighborhoods. Our accelerometer data in at-risk older adults suggest that even modest increases in daily walking activity by 200 steps per day are related to better cognitive and brain health. We see the value of extending these methods to the study of real-world, low-intensity physical activity interventions set in the community as a target for future behavioral interventions to safely promote activity and decrease risks for diabetes, dementia, heart disease and other chronic diseases.
34	N/A
35	I think you can make the case that the *entire* cohort could be from the deep south, where there is a great representation of African-Americans (with the most diversity of genetics, and with great diversity in environmentally-related outcomes). The statistics for the area south of Tennessee for smoking, cancer, and other environmentally-relevant health issues are also stunning. This would be a statement to the American people that we are going to boost up the area of our country that is in most need of help, and at the same time learn lessons that will help all Americans. I think you could add Florida and Texas in order to ensure Latino involvement. Why not have this cohort be HIGHLY enriched for those whose health needs the most attention?
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Question 4B. Novel methods to gather data on geographic, environmental, and social determinants of health

Obs	Q4B
37	Booz Allen provides solutions that highlight novel cohort data collection using social media (Epidemico) and advanced technologies (INTREPID). Epidemico tracks vaccine sentiment in real-time to quickly assess reactions to public perception via its capabilities to incorporate news and social media (50k+) data feeds in 15 languages. This could be adapted to a) assess pilot engagement methods in health disparity groups, b) track community sentiment from PMI, c) collect additional social data responses to PMI data collection questions. INTREPID (INstant TRacking- Epidemic Patient ID) is a biometric-enabled clinical trial data capture device used for accurate participant identification and enable rapid and secure data collection, including geo-location and possible environmental sensor data. These examples showcase tools to extract data from social and environment/geographic sources, with analytical ability to identify red flags during recruitment or data encounters with PMI (sentiment analysis, geographic location confirmation, etc.). Other novel methods for enhancing environmental data include 1) the use of industrial or occupational hygienists, extensively used by NCI to calculate long-term carcinogen exposure in factories/work environments; 2) accessing cohort members' residence data through CDC's Environmental Health Analyst GIS system. Minimal loss of PMI participants due to follow-up is key. The following resource could be used for tracking transient participants: HUD low-income housing applications, Sta
38	New technologies have provided novel approaches for gathering data related to social, geographic, or environmental determinants of health. Social media (SM) provides a window into how the subject receives and disseminates health information. An app designed for the study could record information in the subject's feed. These feeds could be analyzed with natural language processing to identify any health or risk behaviors. In some SM services identification of "friends" networks is also possible providing at least a first order approximation of the subject's social network, another key but often hidden factor in health/risk behaviors. Geographic data can also be collected through mobile cell phones. GPS data can shed light on participants' daily activity while sensors can gather data on environmental contaminants or health data. Many data sets reflecting environmental health determinants are publicly available and can be organized to create multidimensional views of the subject's surroundings. Data from commercial sources allows for automated estimation of possible health factors such as local availability of health care, nearby groceries, and crime. Other sources such as federal agency websites or databases can add health dimensions such as environmental hazards and disease trends. These quantitative and visual data can be complemented by qualitative data gathered through focus groups, interviews, or surveys. Locally-relevant health information may not always be available; therefore, qualitative data gather
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46	In addition to novel, cost-effective infrastructures for recruiting and managing 'cohort' participants, mobile technologies and crowd-source research platforms would be extremely useful and cost-effective in health determinant data collection. The Health eHeart Study, a collaborative project between UCSF, American Heart Association, and technology partners, uses the internet, mobile apps, sensors and links to EHRs to collect data to study risk factors, prevention and treatment of heart disease. The California Teachers Study (CTS) investigates the higher rates of breast and other cancers among female teachers. This prospective, collaborative cohort study between several California universities and research institutions with the California State Teachers Retirement Systems follows over 133,000 current and retired public school teachers or administrators. In addition to questionnaires collecting detailed information on health, diet, environmental exposure, social behavior, stress, and sleep patterns, the study also collects biospecimens for research purposes. CTS implemented a Data Management System (DMS, a Salesforce.com Customer Resource Management (CRM) system –like platform) to access data in real-time and communicate with the study's participants. Similar to the San Diego Blood Bank (SDBB) donor program and its mySDBB mobile platform, CTS's DMS facilitates every step of the process from scheduling appointments to biospecimen collection and storage. These approaches adopted by Health eHeart Study, Califor

Question 4B. Novel methods to gather data on geographic, environmental, and social determinants of health

Obs	Q4B
47	It is well conceptualized and supported by the literature that health and health potentials need to be understood more broadly in the social context than in the mere medical context. The HOUSES research program originally started with support from an NIH grant-funded project in 2006 to develop and validate a suitable measure for socioeconomic status for clinical research and practice concerning inequities in health. Successful completion of the original project has enabled researchers and clinicians to apply the HOUSES index to identify unrecognized inequities in many health outcomes and health care access among both adults and children and to formulate innovative strategies to address the concerns. Some examples of important milestones accomplished are 1) identification of unrecognized inequities in health in the Olmsted County population, 2) detection of uneven distribution of pertussis during the outbreaks, and 3) detection of an association between building features and serious infection. As the demands for using the HOUSES index beyond Olmsted County from researchers and clinicians increase, we are planning to expand the program to 10 new adjacent Southeast Minnesota counties (initially), followed by expansion to all regions (19 additional counties in MN) served by the Mayo Clinic Health System. We envision ultimately expanding it to the state or national levels. Despite the significance of socioeconomic measure in health research, it is frequently unavailable in common data sources for clinical resea
48	Considering new mutations, for example, the key things to note are where the parents were living and working the year BEFORE this child was born, and what health issues if any they were experiencing. We will only be able to track this through the recordings of the medical system in combination with interview questions (where do you work?). Individuals are not likely to remember the level of detail needed to determine such factors.
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51	- Digital pathology (molecular and tissue imaging data), mobile devices, wearable sensors, human-machine collaborative environments (example IBM Technologies including WatsonPaths and Watson EMR Assistant).
52	a. Study the multiple determinants of health and their interactions (personal, social, economic, environmental factors) on disease risk, disease mechanism, and individual response to therapy. b. Use novel social media strategies to crowdsource new ideas for research, and local events with facilitators to identify new questions and community ideas for research, benchmarking off of participatory budgeting exercises. c. Engage multiple communities in these exercises, including patient disease groups, geographic, racial and ethnic groups, LGBT populations, clinicians, entrepreneurs, and policy makers, to identify their key questions.
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54	utilizing natural experiments to assess impacts on health
55	a. Learn lessons from the Patient Powered Research Networks on incorporation of patient-reported outcomes and sharing data with all participants. b. Use mobile technology to collect data, such as accelerometers, drones for air sampling, peak flow meters connected to smartphones (i.e. Cohero Health) c. Partner with leading tech companies (google, apple,…) to enable uses of their smartphones to collect and upload data, and do so across multiple platforms, as low income, diverse populations use different platforms. Work with populations to offset costs of increasing their use of data to become members of the cohort. Reward use of technology with instant feedback on how others in their region and nationally are responding.
56	--Working with corporate partners. Employers might be willing to let staff take a day off to participate --Collaborating with centers where there is potential to have diverse participants --Engaging pathologists to do the genetic testing so diagnosis and treatment can be more accurate and referral to genetic counseling and testing can be made for the entire family --Using 'hot spots' (cancer clusters) and tapping into biobanks from those same areas
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Question 4B. Novel methods to gather data on geographic, environmental, and social determinants of health

Obs	Q4B
58	•Income level is one of the biggest determinants of health. “Care navigators” can have the unique ability to improve outcomes for patient populations. They should be specifically trained in genetics in order to adequately translate the importance of participation in the PMI and the various care directives that will result from participation. •Any technology that gathers disparate data sets should be open source and interoperable because it will enable a wider range of potential people to participate using myriad device types built on the same standard. Integrating these data would be simplified and less expensive. •We encourage the PMI to explore the linkage between pollution data, water quality, travel, and use of public transportation with genetics data and disease. Initially this could be captured via traditional paper methods but over time the data should be captured automatically with fit bits, scales, and publically available data mapped to one’s location at the time using GPS. All of this data should flow into a data reservoir and be explored using cohort explorers and other appropriate open source tools.
59	Focus on mapping the intersection of chronic disease and psychosocial factors in the residential landscape. This detail would enable more questions to be addressed regarding how environmental factors interact with social and psychosocial factors to influence disease development and progression. Consider offering free mobile devices to cohort participants to enable them to record representative time-activity patterns and images over specified periods of follow-up that could be integrated with interview data collected during the same time period to enable the recording and construction of more reliable and valid measures/models of time-dependent exposures to geographic, environmental, and social determinants of health.
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61	The cohort might be ideally divided according to several criteria in order to isolate people living in a particular social situation from the others. For example, we might consider people from the working class in comparison with people from the middle and the upper classes. People educated in public schools in comparison with people educated in private schools. People with and without health insurance. People living in the suburbs. Unemployed. People belonging to a particular religious group, or to a particular ethnicity. All these conditions might be considered as indicators of different situations of social unrest or discrimination. Comparing (from a clinical point of view) people who live in these chosen conditions, with people who do not, might be a way to notice whether any disease or predisposition to disease is statistically more spread in any particular social group. This might be a track to highlight a social determinant for the diseases at issue. To proceed by isolating more specific social situations in that group, would then provide increasingly realistic hypotheses about the identification of the social determinant(s). As an ultimate check, comparing the epigenomes of the people undergoing that social situation with people who do not, might be extremely interesting in order to achieve a complete understanding of the process.
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64	Leverage existing data sets and foster data linkages.
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66	Sensor data with privacy settings determined by the people and the community
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68	Current ways of defining phenotypes are incomplete. Novel methods to gather data must examine more sensitive ways that allow us to redefine risk and disease. It is necessary for us to consider newer methods of collecting more sensitive physiologic data. In addition, we must be open to the fact that our current classification of disease may be incorrect, especially when it comes to sex differences in disease. For example, is diffuse atherosclerotic disease, seen more commonly in women, the same disease as obstructive coronary artery disease? Primary care physicians are on the front line of care in the United States and could serve as an excellent source for gathering data on the geographic, environmental, and social determinants of health impacting their patients’ daily lives. To ensure women benefit from precision health and important data on women’s health needs are collected, it will be essential to train OB/GYNs, nurse midwives and family planning providers in precision medicine (Yang, Ginsburg & Simmons, 2012.) Data collected directly from populations who are not in a health care setting will also be critical to collecting the types of data that will move the field of precision medicine forward.
69	Provide for the periodic collection of urine and/or saliva specimens to test for the presence of illicit or unprescribed drugs, to determine the extent, correlates, causes and consequences of such drug misuse. Self-reported use has been shown to be unacceptably susceptible to underreporting.

Question 5B. Novel ways to assess the historical as well as current factors that predispose the individuals in certain population groups to higher disease incidence or shorter survival

Obs	Q5B
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3	Use of ancestry markers to group people in various ways and then look at gene variability in the ancestry groups Development of selected pedigrees to determine familial association with rare diseases and genomic mutations.
4	Partnering with organizations that provide health care assistance to socioeconomically disadvantaged populations or subgroups is one way to gather social determinants of health data. For example FHC and MCHS have a longstanding history and shared goal of providing health care services to geographically dispersed rural populations. Most individuals in such cohorts will be low-income or otherwise socially disadvantaged during their FHC contact period. The FHC captures a variety of data points that could be used to assess health. MCHS captures longitudinal residence on its patients. This could be linked to publically available data sources (e.g. census) for environmental assessments. Such data combined with Marshfield's longitudinal EHR data could contribute to analyses to assess disease incidence and risk.
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7	Across all individuals (but especially among individuals with rare diseases), comparing the predicted frequency of alleles based on a background level of mutation and the observed frequency is a powerful predictor of the pathogenicity of a variant. Historically, population databases have not been large enough to deploy a technique like this across the entire genome, but a million participants is starting to approach the necessary size to achieve the requisite statistical power. The recent revolutions in deep learning and compressed sensing provide opportunities to extract correlations for sub-populations that might have historically been too small in which to achieve statistical significance. Recently developed probabilistic programming languages (such as Church) will enable researchers to build hypothetical models of gene-health relationships that previously would have been too painstaking or intractable to construct and test.
8	No response provided.
9	No response provided.
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14	• The accumulated stressors of oppressive forces such as racism, sexism, and heterosexism, together with economic marginalization divert health trajectories as noted above. Forming research designs together with communities affected by historical and current risk factors for higher disease incidence or shorter survival will allow for the inclusion of population specific strength-based adaptive strategies. How are affected communities and individuals dealing with these risk factors now? Researchers first can learn from internal resilience strategies developed by affected populations before attempting to design interventions to address these factors. • Encourage Family Health History education efforts at family reunions and other large family events. Promote the Precision Medicine cohort and provide families access to family-level prevention plans (recommended screenings and prevention strategies based on family health history and research) modeled after cancer survivorship plans. Integrate military records and environmental exposure maps (radiation, chlorine gas, pollutants, brownfields, proximity of childhood homes to bus stations, railway stations, railways, ferries, and freeways) to assess historical exposures
15	Longitudinal data sets have the potential to compare historical and current approaches to care that can impact outcomes. While the historical datasets may be less complete due to the more limited use of electronic health records, entities that have been involved in health services research have rich datasets that can supplement clinical records. The VDW of the HMORN was established in 2003 and includes historical datasets predating its creation. Some individual sites have electronic data back nearly 20 years. While not created for the purposes of the precision medicine initiative, the availability of these data combine with biospecimens from research participants allows the possibility of historical analysis using rigorous retrospective research methods.
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Question 5B. Novel ways to assess the historical as well as current factors that predispose the individuals in certain population groups to higher disease incidence or shorter survival

Obs	Q5B
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24	Longitudinal health records, such as KP's electronic health record, provide status on factors of interest as they change over time (e.g., tobacco/alcohol use, physical activity, health conditions, residential address). Maps, satellite imagery, land use analyses and other sources that were originally not assembled for research purposes also provide important sources of historical data. Such data coupled with pollutant modeling, poverty level information, and occupational coding/history could help inform predictive models of disease risk. This information, linked to a good family history of disease, genetics, and biomarker assays can be useful in advancing our knowledge of the natural history and prognosis of a disease in individuals of susceptible populations. Further investigation should be done on biomarkers that can reflect the history of disease from the earliest manifestations to terminal stages; these biomarkers should be extracted from high quality biospecimens consented by participants with known environmental exposures/risk factors.
25	We need to ensure that we specifically value, target, and engage African American men and boys across the life course.
26	
27	1. Include questions related to historical trauma and lessons learned from elders and previous generations regarding health decisions and behaviors. a. Resources include: A conceptual model of historical trauma: Implications for public health practice and research M Sotero, Journal of Health Disparities Research and Practice 1 (1), 93-108; Curtin, Philip D. "The slavery hypothesis for hypertension among African Americans: the historical evidence." American Journal of Public Health 82, no. 12 (1992): 1681-1686. ; Osher, T., L. Garay, B. Jenninigs, D. Jimerson, S. Markus, and K. Martinez. "Closing the Gap: Cultural Perspectives on Family-Driven Care." Technical Assistance Partnership for Child and Family Mental Health p. 15 (TA Partnership) (2011).
28	The March of Dimes is currently funding a handful of studies that examine social determinants of health, such as stress and racial discrimination, and their impact on preterm birth risk. We would be pleased to share with PMI experts the factors that went into developing and structuring these studies, as well as lessons we are currently learning as they get under way.
29	Such studies exist in American Indian communities but can be enhanced by increasing the amount of spotlight on border tribes that straddle the US/Mexican border where they share the same genetics but health outcomes are much better in Mexico. However this has to be done with much attention to tribal sovereignty and ownership of samples, DNA and RNA isolations and Data. With more attention to False and Contrived scarcity created by the difference between individual and communal economies and property rights (capitalist vs Indigenous). This is the major driver for a longevity estimate of 57 years for American Indians in South Dakota. State laws and business practices as well as Federal incursions or failure to meet treaty obligations neuter tribes from any meaningful economic or social progress.
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32	- Population architecture and admixture using GWAS - genetics, genomics, archaeological and anthropology relationship and associations - Genomic trait association studies in diverse ethic groups
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34	N/A

Question 5B. Novel ways to assess the historical as well as current factors that predispose the individuals in certain population groups to higher disease incidence or shorter survival

Obs	Q5B
35	I think you can make the case that the *entire* cohort could be from the deep south, where there is a great representation of African-Americans (with the most diversity of genetics, and with great diversity in environmentally-related outcomes). The statistics for the area south of Tennessee for smoking, cancer, and other environmentally-relevant health issues are also stunning. This would be a statement to the American people that we are going to boost up the area of our country that is in most need of help, and at the same time learn lessons that will help all Americans. I think you could add Florida and Texas in order to ensure Latino involvement. Why not have this cohort be HIGHLY enriched for those whose health needs the most attention?
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37	A variety of data sources and methods can be used to supplement published observational studies and scientific literature to assess disease risk factors. For example, novel data sources that can provide information on disease risk include wearable technologies, and mobile devices. Novel approaches that can be applied to assess different disease risk factors include: mapping social networks and mining digital and online data sources. Booz Allen staff's experience and technology development in genetic-phenotypic solutions (for Million Veteran's and other non-profit areas) open up more opportunities of novel assessment on factors predisposing certain individuals to higher disease incidence or shorter survival to examine the following 2 items. 1) Assess whether certain genomic information (i.e., genes, genetic errors, mutations, and sequence) are informative and conducive to a certain disease through Generalized (Non)Linear Mixed Models that model individuals' disease progression as random effects and genomic information as fixed effects. Such approach would open up novel ways to a) Validate a causal relation between genomic information and disease incidence in a certain population; b) Evaluate latent dimensions of ge
38	There may be opportunities to enroll large fractions of the population within specific communities targeted by design – allowing for multiple in-depth studies of population-health within the cohort. Here we define population health as the collective health outcomes of the population within the community, how these outcomes are changing over time, and how these outcomes are the product of multiple determinants of health, including medical care, genetics, behaviors, social factors, and environmental factors. While some determinants are at the individual level, others are common among members of a community. By taking a population health approach, NIH may identify communities across the nation with high disease burden and health disparities. Assessing the effectiveness of personalized medicine within these challenged populations may advance our understanding of how these therapies may work. Other positive aspects of engaging large fractions of communities in research studies include higher rates of participation and retention; engaging the public health and healthcare communities into the study; and lower operational costs due to high concentration of study participants within selected communities. Battelle conducted
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41	Try to have family groups participate; grandparent, parent and child
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46	The 'normal' blood donation process includes gathering health, travel and medication information, consenting, provision of information back to the donor, and collecting biospecimens. The same processes are performed in longitudinal cohort studies. Layering the collection of health data and biospecimens onto an existing blood donation program is more convenient for the participant/donor, is an efficient use of the collection site's time, insures consistency, and provides a cost-savings to the PMI. The data collected at baseline (initial blood donation) and follow-up (subsequent donations) are consistent. Each blood collection process begins with completings a donor registration form that includes donor demographics, disease history, infection exposure, medications taken, travel abroad, and other self-reported information followed by a 'mini-physical', including pulse check, blood pressure, temperature, a hemoglobin measurement and review of medical history. Additional data specific to the PMI Cohort study can be integrated in the registration and mini-physical. The standard whole blood donation process (registration through recovery) takes approximately 1 hour. During blood donation and recovery there is ample oppo

Question 5B. Novel ways to assess the historical as well as current factors that predispose the individuals in certain population groups to higher disease incidence or shorter survival

Obs	Q5B
47	As the HOUSES research program is based on measuring one's address information and its associated real property data, it captures changes of socioeconomic background over time from past to current, which enables life-course approach in research. Apart from the advantages from geocoded data for the HOUSES index enabling geospatial analysis and real property data for the HOUSES index allowing assessment of the impact of building features on health risk (eg, accidental falls), the HOUSES program enables life-course approach. We thought this is a potential resource promoting precision medicine as socioeconomic background greatly accounts for individual variability in addition to genetic variability. Particularly, given the missing heritability of genes or SNPs, the focus needs to be shifted toward gene-environment interaction.
48	If we were able to provide basic healthcare to everyone, including migratory workers, we could ask and record questions about family health history, work history, and other details that would improve our ability to track the environmental exposures that might have influenced their health.
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51	Combination of digital pathology, big data analytics, patient specific predictive modeling and human-machine collaborative environments (example IBM Technologies including WatsonPaths and Watson EMR Assistant)
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56	--Some data relevant to social determinants of health can come from environment assessment tools e.g. visual ways to look at features of a community (ecological)
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59	More attention could be paid to collect information from historical records/archives that would enable analysis of how the great migration of southern Blacks to the northern, western and eastern portions of the US during the 1900s either contributed to or helped to mitigate disease onset and thus influenced early markers for health disparities by race and geography.
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61	First of all, it is essential to be sure to recruit enough people from the groups at issue in order to have significant data. For this, it is essential to pay special attention in informing them about the initiative and to encourage their participation. When a group among the participants is identified as historically predisposed to higher disease incidence, dedicated interviews or questionnaires should be presented to them. This is mainly to check they have correct information and reasonable respect of the main sanitary and hygienical rules. If they do not result sharing any especially unhealthy behavior or misinformation, thanks to the cohort we have the opportunity to sequence their genome and to check whether they share any genetic predisposition. Otherwise, looking at the epigenome might be an interesting idea. Considering their epigenomes in the light of their environment and of their behaviors, and on the other side of their special disease predisposition, might help to identify behavioral or environmental factors endangering their health. In case, the Initiative is an opportunity to inform these people about their risky positions and behaviors, discussing together about the possibility to change them to sa
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64	* Natural and quasi experiments, including policy based instrumental variables, regression discontinuity approaches, etc. * Integrated with a thorough understanding of plausible biological mechanisms. * Integrate observational and experimental evidence to better understand social factors and identify causal effects
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Question 5B. Novel ways to assess the historical as well as current factors that predispose the individuals in certain population groups to higher disease incidence or shorter survival

Obs	Q5B
67	Natural experiments, such as policy changes across time and region would be excellent ways to study historical factors that may predispose individuals to disease or poor disease outcomes. Changes in compulsory school laws, integration of schools, changes in housing, and other exogenous events can be evaluated for impacts on health and interactions with genes on health. There are also a host of studies in which people were randomized to certain early life conditions, like Tennessee STAR and the Moving to Opportunity study, where the cohort should be followed and included in the PMI.
68	Understanding the family history across generations will be important in understanding risk of disease. In addition to disease, this family history should include factors such as a history of violence, smoking, SES, and more. When family history of this specificity is not available, the development of proxies, such as location of family—history of slavery, and more, could be important.
69	