Precision Medicine Initiative: Participant Engagement and Health Equity

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

July 1-2, 2015
Porter Neuroscience Building
National Institutes of Health
Bethesda, MD

EXECUTIVE SUMMARY

Background
On July 1-2, 2015, the Precision Medicine Initiative (PMI) Working Group of the Advisory Committee to the Director (ACD) of the National Institutes of Health (NIH) held a workshop at the NIH in Bethesda, Maryland, to discuss participant and public engagement, diversity and inclusion, and health disparities considerations for the development of a national research cohort of one million or more Americans. The workshop is part of a series of events and outreach activities that will inform the PMI Working Group report on the design of the cohort and related resources.

The workshop featured panelists and speakers with expertise in participant engagement, recruitment and retention, research with underserved and underrepresented populations, health equity and health disparities, large cohort and long-term longitudinal studies, and patient advocacy. The workshop included Mr. Brian Deese, Senior Advisor to the President of the United States. There was active discussion among meeting participants at the event and on Twitter using #PMINetwork. Workshop registration was open to the public. The workshop was videocast live and a link to the video archive is available via the workshop website.

Workshop Summary
Francis Collins (NIH) opened the workshop, emphasizing that the discussions at this workshop are contributing to the development of the nuts and bolts of the national research cohort proposed under the President's Precision Medicine Initiative. Dr. Collins noted that the cohort needs to be efficient and inclusive by leveraging a variety of existing healthcare organizations, including private healthcare systems and underserved Federally Qualified Health Centers, and considering the inclusion of a wide variety of participants, including children, military and veteran participants, and participants already involved in cohort research studies. He also stated that policy needs for PMI include modernizing institutional review board (IRB) processes, strengthening privacy protections, encouraging data sharing, and establishing consequences for inappropriate re-identification of participants. Finally, Dr. Collins highlighted the goal that participants will be partners in PMI, deeply involved in different aspects of study design, and information sharing.

Following Dr. Collins's remarks, Bray Patrick-Lake (Duke) opened the meeting by encouraging an innovative approach to PMI participant engagement by noting if you "do what you always do, [you] get what you always got." She reminded the audience that the goal of this workshop is to help the ACD PMI working group understand the design features necessary to achieve active community engagement in

the PMI and to the best ways to establish a cohort that can answer research questions relevant to the US's diverse populations.

Session 1: **Envisioning a Cohort that is Participant-driven, Inclusive and Diverse**
Moderator Tony Coles (Yumanity) raised high-level questions about the mechanisms that will enable PMI to establish a diverse cohort and translate discoveries into improvements in healthcare for communities. Dr. Coles and Vernal Branch (patient research advocate), along with the audience, discussed barriers to enrollment, building trust in communities, engaging underserved communities, and engaging healthy and resilient people. Ms. Branch articulated the importance of interacting directly with community members and engaging them in conversations about the value of their contributions to research, including the value to future generations. She emphasized the importance of creative solutions to involve those in underserved and rural communities who may not have electronic health records or easy access to phones and computers.

Key discussion points:
- "Go to where the people are" and the need for "boots-on-the-ground" were repeated messages, encouraging researchers to interact directly with participants at hubs like churches and community centers. Make interactions personal, and tailor messages.
- Knowing the purpose of the research and being involved in research plans fosters participants' ownership and pride in the research.
- Women and mothers can be focal points for inclusion and retention efforts, because they are often responsible for the healthcare of their families.
- It may be important to have strong public education component to the initiative, including educating populations about disease, risk factors, and research.
- Funding review criteria should include recruitment strategies and an investigator's history of success recruiting and retaining diverse groups.
- In order to recruit healthy and resilient people, PMI must make research relevant to them by educating them about future disease risks and the value of their contributions to them as individuals, to their communities, and to others.

Session 2: Public Perspectives about a PMI Cohort
Kathy Hudson (NIH) opened the session by highlighting the importance of participant involvement in research design and governance. Vence Bonham (NIH) presented a summary of the recent [Request for Information (RFI): NIH Precision Medicine Cohort - Strategies to Address Community Engagement and Health Disparities](). The RFI received feedback from 69 domestic and international responders. Key community engagement strategies identified in the RFI responses included: meaningful engagement with participants, developing partnerships early with continuous communication with the community, educating the public and providers about research, maintaining transparent relationships, providing privacy protection, governing with active community partners, and building and maintaining trust between communities and researchers, and addressing engagement barriers. Strategies to address barriers included: considering literacy and language of the research population, developing alternate models for to collect data for participants without electronic medical records (EMRs), and using mobile devices to communicate with and collect data from research participants. A major recommendation in RFI comments was to design the cohort to allow researchers the ability to investigate multiple determinants of health and the ability to study sex, gender, race, and ethnicity differences in health.

Dave Kaufman (NIH) presented results of a Foundation for the NIH (FNIH) survey of 2,601 US adults on their understanding, interest, and willingness to participate in a large-scale research cohort (with many of the features of the proposed PMI cohort). The results were analyzed across several demographic categories (race and ethnicity, education level, socioeconomic status). Overall, survey respondents were supportive of a PMI-like research cohort, with 79% of respondents stating that they think the study should done, and 54% reporting that they would participate in a PMI-like study. There were no significant race/ethnicity differences, although Hispanic individuals and individuals who took the Spanish version of the survey were more likely to participate. Age and education level also influenced willingness to participate, with younger and higher educated groups being more willing to participate in a PMI-like study. Return of health information and information privacy were cited as the most important factors in deciding whether or not to participate, and most respondents believed that researchers and participants should be equal partners in the study, and that participants should be consulted on what questions should be asked in the study and how to disseminate/use study findings.

Key discussion points:
- The successful development of a diverse, large-scale cohort will need:
  o Early and equitable community and individual participant engagement;
  o Transparency and continual communication between cohort researchers and participants;
  o Participant and health care provider education about cohort research; and
  o Additional input on cohort inclusion and disparities research.
- Building trust requires time and commitment, but that trust can be quickly eroded.
- Determining the best ways to engage expectant mothers, children, and adolescents will be helpful for cohort development.
- Health information and research findings should be given back to the participants.
- Results for LGBTQ should be taken into consideration when examining public attitudes about cohort research

Session 3: Inclusion and Engagement Goals Related to Health Equity
This session focused on goals for a diverse cohort, including defining diverse populations and identifying some of the major health disparities that should be addressed. Sarah Gehlert (Washington U in St. Louis) described challenges to reaching members of diverse populations who may lack stable medical care or housing, are not affiliated with organizations or advocacy groups, and encounter poverty-related barriers to participation. Rick Kittles (U Arizona) stated that the cohort can be a great opportunity to study human genetic variation and disease, as there is great genetic diversity within traditionally reported race and ethnicity groups, including African Americans, Hispanic, and Asian Americans. However, most research on risk factors is for people of European descent—who are also often at lower risk. To maximize PMI benefits to all people, the research needs to get beyond Census categories, as this diversity manifests in different responses to drugs and disease risks. James Perrin (AAP) noted that children are the most diverse age group, and they also encounter the greatest health disparities (including disparities in major chronic disease). He argued that enrolling women of childbearing age, children, and adolescents with diverse race and ethnicity and socioeconomic status (SES) will be essential to developing an inclusive and diverse PMI cohort.

Key discussion points:
- The PMI cohort must seek to understand health disparities and proceed cautiously to ensure that it does not increase health inequities.

- Substance abuse and addiction records (and other records that have sensitive and sometimes legal components) are important health issues, but data access for these issues can be challenging because they are often removed from health records for privacy protection.
- Considering the heterogeneity of populations, one million people will be not enough to cover all ages, races, ethnicities, and other subpopulations. Therefore, researchers will need to develop and use creative statistical models and study designs to analyze even small sub-populations.
- Cohort inclusion should be broader than race and ethnicity: SES, geography, LGBTQ, disabilities, education, age, etc. will all be important demographic groups to include in the PMI cohort.

Session 4: Challenges in Recruiting and Retaining Disadvantaged and Underrepresented Populations and Best Practices for Overcoming Them

Esteban Burchard (UCSF) opened this session by stating that 40% of the US population is of non-European descent, but 96% of studies are done with people of European descent. This panel focused on challenges to recruitment and retention of diverse and disadvantaged populations and potential solutions for the PMI cohort. Lucile Adams-Campbell (Georgetown) asserted that eligibility criteria are often too restrictive, and the PMI cohort should not exclude people with existing health issues related to social and environmental factors (including obesity). She also noted that face-to-face interactions outside of medical settings are integral to community education and engagement strategies, and the study goals and methods must be relevant to the study populations. Carol Horowitz (Icahn School of Medicine, Mt. Sinai) described her experience engaging with African American communities in New York City and discussed the importance of designing studies with inclusion in mind, engaging people in the community, and building trust directly and indirectly through community intermediaries. She noted that, in her experience, people take pride in their participation and need to be treated as essential members of the team. They also want to see the research results, including genetic information. Finally, warned against "cherry picking" easy to recruit populations. Kiang Liu (Northwestern) emphasized the importance of conveying the purpose of the study through public lectures, outreach in churches, via voter registration lists, and elsewhere.

Key points from the discussion:
- Research succeeds where the recruitment team reflects the community. Training members of the community as part of research teams presents workforce development opportunities.
- Maintaining long-term longitudinal cohort involvement requires continual engagement and continual return of information. Newsletters about the study, an up-to-date website, birthday cards, and other regular communications are important to participants. Community governance boards can help identify useful methods to return study information.
- Determining what information to return and how to return it should be done up-front and with community input.
- It is imperative to have ways to refer people to needed medical care for conditions or risk factors identified in the study. Some participants will not have an established doctor or healthcare provider relationship.
- Participants should be compensated for their contributions, not simply incentivized—incentives that are not aligned with the values of the study population diminish the intrinsic value of the contribution to research for participants.
- Information returned to participants, even if it is not individualized, is one of the most effective motivators to participate in research.
- NIH should include recruitment strategies in peer review, and researchers should be honest and seek help if they are falling behind on recruitment during the award.

Session 5: Establishing Collaborative and Inclusive Governance in a Large Study
Susan Sheridan (PCORI) stated that participant involvement helps drive translation and implementation of research findings by enabling research that is relevant and trusted. Communication must be continual and bi-directional, and input must be sought when plans are still mutable (prior to institutional review board review). Potential governance models include participant representatives on committees or separate all-participant committees. Al Richmond (CCPH) pointed out that while institutional review boards protect individuals in research, there is a historic gap for the protection of communities. Community-based processes can contextualize research, enhance ethical design/conduct/impact of research, increase literacy, capacity and ownership in the process, and provide oversight for aspects of the research that are not considered by federal regulations. Challenges for community review processes include: infrastructure, funding, and respect/recognition for the process and its participants. Consuelo Wilkins (Vanderbilt U) raised the importance of establishing governance structures that are able to both seek broad input from large groups of stakeholders and receive rapid feedback on fast turnaround decisions. For successful participant involvement in governance, involve people early, demonstrate value, compensate, offer training, prepare people, elicit feedback, define roles, and be deliberate about who and how many people to engage.

Key points from the discussion:
- There are many ways to define community. Communities are not homogeneous, and each individual is a member of many communities.
- Numerous suggestions were made for how the PMI cohort can ensure protection of vulnerable communities and individuals while making PMI data widely available for broad research use. Suggestions included: involving community members in determining how research will be reviewed, asking what might stand in the way of participating in PMI, and giving options for restricting sharing of some data.
- Spero Manson (UC Denver) used the term "personalized research," referring to participant engagement in governance and also to personal choices in data use and sharing.

Session 6: What Would a Direct-from-Participant (DFP) Cohort Model Look Like?
The panelists shared their experiences developing successful research efforts in different communities. Susan Love (Dr. Susan Love Research Foundation) discussed the success of creating an "Army of Women" email list to recruit a diverse range of women into vetted clinical trials. She stressed that social media is an effective recruitment tool and that recruiting through women is particularly effective because they manage the health of their families. Megan O'Boyle (Phelan-McDermid Syndrome Data Network) described her organization's International Registry, which aims to consolidate information about patients in a single database; the registry houses data from 65% of patients with Phelan-McDermid Syndrome, and involves participants in in governance decisions. Sally Okun (PatientsLikeMe) expressed that patients can and should be drivers of research and that patient-generated health data is both credible and valuable. Sharon Terry (Genetic Alliance) discussed how important it is for participants to have control over their data and be able to interact with it. She also highlighted the potential of PMI to break down cultural barriers to research, including changing our language to stay away from "us and them" and making it about "we," as well as minimizing exclusion criteria to allow more people to participate in research studies.

Key discussion points:
- Survey fatigue is a frequent problem for large research initiatives, which can make it difficult to find the right balance of soliciting information and re-contacting participants for participation in different studies.
- Prioritization of research questions is a complex undertaking, and should involve participant input, including shaping research questions relevant to their personal disease experience and priorities.
- Allow for and respect individual preferences for privacy and data sharing.
- Reaching out to the underrepresented requires creativity, for example, Genetic Alliance has worked with Walmart employees to collect medical histories and PCORnet has partnered with CVS.

Session 7: Participant Perspectives on Data Sharing and Data Use

The panelists discussed successful models of data sharing that address participant privacy. Laura Bierut (Washington U – St. Louis) spoke of the challenges presented by complex and sometimes conflicting consent options, leading her to prioritize broad consent and broad sharing even if it means excluding some potential participants who are unwilling to give broad consent. She also discussed the barriers to data sharing related to substance abuse and mental health. Matt Might (U Utah/NGLY1.org) expressed his belief that participants should have access to their own data and should control how their data are shared. He also noted that IRBs are often overprotective and may restrict data sharing more than participants would want. Robert Ring (Autism Speaks) described his organization's commitment to disrupting norms to enable sharing and broad data access for research, while acknowledging the challenges that arise as a result. Nancy Roach (Fight Colorectal Cancer) emphasized the importance of educating communities with low health literacy about information and data sharing in research.

Key discussion points:
- Data sharing is often overly restricted because of commercial or academic interests, not because of patient privacy concerns.
- It is important to respect participants' preferences about how much data they would like to share and to set clear ground rules for data access before data collection begins.
- Excluding vulnerable populations (such as people with mental illness) to protect their privacy can do more harm overall. However, some communities, such as Native American tribes, do have serious concerns about data-sharing that must be addressed.
- Families of affected individuals are a good initial source of unaffected individuals for PMI recruitment.
- Data-sharing should be a prerequisite for researchers to participate in PMI.
- Data repositories must be interoperable and have some uniformity; PMI creates an opportunity in this realm. NIH should ensure that technology and interventions developed with participant data are accessible to communities involved in research and are not prohibitively expensive.

Special Session: White House Vision for the Precision Medicine Initiative

Brian Deese (Senior Advisor to the President) conveyed that the Precision Medicine Initiative is a priority for the country and a personal passion for the President. The PMI goals are ambitious and will require creativity and collaboration. Deese echoed Francis Collins' message from the previous day that the time is right for PMI: technology is pushing the frontier of what is possible and there is abundant support and enthusiasm from the public to make the Initiative possible. Deese called for several goals for the PMI: 1)

create opportunities to participate for everyone that wants to, and have a cohort that reflects the diversity of the US population and can serve to understand and address health disparities; 2) robust engagement of all stakeholders; 3) the right policy toolkit to enable research; 4) include more creative partnerships that would expand the tools of research; and 5) keep privacy and security at the core of this initiative while enabling broad data access and sharing. He also called for getting the right research protections in place, developing tools to support partnerships, streamlining regulations concerning genomic technologies, and garnering support from Congress.

Session 8: Interagency Proposed Privacy and Trust Framework for the PMI Cohort
Tania Simoncelli (OSTP) and Christina Heide (OCR) presented the key principles for the Interagency Proposed Privacy and Trust Framework for the PMI cohort to build trust between participants and researchers and protect participant privacy. The development process for these principles included expert roundtables, a review of the bioethics literature, and analysis of existing frameworks. The framework includes seven broad categories of principles: governance, transparency, respecting participant preferences, reciprocity, data sharing, access and use, data quality and integrity, and security. The principles are grounded in 10 fundamental assumptions about the PMI cohort: the PMI cohort should present a new model for research, engage participants as partners, have participants represented in governance, include diverse data sources, create a public resource for broad access to data, facilitate access to participants' own health data, be diverse/inclusive, have a robust data security framework, transcend traditional consent to build and maintain public trust, and have some degree of centralized governance.

Key discussion points:
- PMI cohort governance should be adaptable, centralized, inclusive, transparent, and maintain substantive participant representation.
- The PMI cohort should include transparent communication with participants (including about mistakes, breaches, or changes in plans) and giving participants access to research information (including individual results).
- Participant preferences for greater or lesser ongoing interactions, data sharing, and access to information should be respected.
- Data access should be tiered, and data should be protected from unauthorized use(s) and compelled disclosure (potentially through Certificates of Confidentiality). There should be serious and enforceable consequences for re-identification and data misuse.
- The PMI cohort must uphold data quality and build a strong security infrastructure.
- Although success in achieving "privacy and trust" will be difficult to measure, there should be concrete metrics of success measured over time to evaluate how the PMI cohort is performing in these capacities.

Session 9: Keys to Building and Sustaining Participant Engagement in the PMI Cohort
The panelists discussed successes and challenges in sustained research engagement with participants in large-scale cohort studies. Sohini Chowdhury (Michael J. Fox Foundation for Parkinson's Research) discussed the importance of longitudinal participation, involving people with risk factors for a disease but no manifestation of the disease, and ensuring that people feel like they are an integral part of the project. The Foundation accomplishes this by returning data, encouraging those who are not eligible for studies to help with recruitment, and by disseminating information on research advances and how data has been used. Kelly Edwards (U Washington) emphasized that researchers need to be driven by the

purpose of giving back to participants and communities. She argued that developing relationships with communities is important because people will remember the way you make them feel and will be more forgiving of missteps. Sue Friedman (FORCE) discussed the importance of engaging participants at all levels of a project, including governance and research-topic generation. She warned of survey fatigue and asking too much of participants. Holly Peay (DuchenneConnect Registry) noted that you have to understand and respond to the motivations of different groups to participate in research, whether it is altruism, return of data, or access to clinical trials.

Key discussion points:
- Some successful strategies for reducing participation burnout include targeting questions to specific groups, and letting people respond or participate on their own schedule.
- Educational components motivate people to continue. Providing more research information results in more actively engaged participants. It is important to tell people how their data will be used and how it has contributed to research advances, and let participants interact with their information—access it, share it on social media, etc., if they wish to do so. Giving people access to a website to see how data are used, how often it is downloaded, and what publications result, also encourages participant engagement in the research study.
- The PMI cohort should get feedback from participants (e.g., engagement surveys, two-way communication) to improve their experiences in research and follow up when people withdraw to see what can improve participant experiences.
- Peer-to-peer engagement is a good way to retain participants.
- Creating an inclusive culture where participants can articulate what research questions they want to see fosters engagement.
- Allocating sufficient resources to engagement is the key to its success.

Session 10: Case Study - Given a Set of Assumptions What Would It Take to Integrate Existing Cohorts into PMI?
The panelists in this session described their experiences with large cohort studies and large databases. Catherine Schaefer (Kaiser Permanente) described the Kaiser Permanente Research Program on Genes, Environment and Health (RPGEH), an online research resource that brings together multiple data sources (surveys, biospecimen data, genetics, EMR, and environmental exposure data from GIS) from 210,000 participants. Maureen Smith (NUgene Biobank) described the Northwestern University Biobank, which generally recruits healthy participants, and presents unique challenges compared to recruiting pre-established disease groups. The NUgene Biobank has a community advisory board and would like to enhance active engagement by shifting to a more interactive partnership with participants. She also noted the importance of providing participants with reliable information and educational materials at an appropriate level. Donna Antoine-LaVigne (Jackson Heart Study Community Outreach Center) described the Jackson Heart Study, which is in its 15th year and has 5,301 African American participants. Jackson Heart has structured ways to engage community members, like including participants on the steering committee and subcommittees. They also have five community health advisory groups and local undergraduate and graduate education programs. They have an 80% retention rate, which Dr. Antoine-LaVigne attributes to continual engagement and longstanding, personal relationships. They have a list of physicians to refer participants to if needed. Challenges she noted include the underutilization of research data and slow translation of research results into the clinic.

Key points from the discussion:

- Preferences and practices for returning individual results (including genetic results) are evolving. The panelists said their studies are currently grappling with how to return results, how to deal with potential follow-up needs, interactive consent possibilities, and how to engage individual participants and the community in these decisions.
- Existing cohort participants may be able to be recruited into the PMI cohort, because many current cohort participants have consented to broad use of their data and/or given permission to be re-contacted.
- Participants vary in their desire for engagement—some simply want to participate and contribute once without ongoing interaction.
- Establishing a PMI cohort governance structure that respects the current governance of existing cohorts that agree to become part of the PMI cohort could be complicated. Creative solutions will be necessary to establish these partnerships.

Conclusion and Next Steps

Bray Patrick-Lake concluded the workshop by thanking the speakers, panelists, and attendees for their active participation and candid contributions to the discussion. The ACD PMI Working Group report will incorporate themes and suggestions from this workshop, and will be completed in September. Ms. Patrick-Lake encouraged participants to continue the conversation via the NIH Feedback Blog, to tune in to the final ACD PMI workshop on Mobile and Personal Technologies in Precision Medicine on July 27-28, 2015, in Santa Clara, California, and to provide feedback on the Interagency Privacy and Trust Framework. Finally, she encouraged people to take what they had learned during this workshop and apply it.

Recurring Points Made at the Workshop

There is great enthusiasm for the Initiative: People are enthusiastic about the potential of the PMI cohort for precision medicine progress and many people are excited to participate. People may be more willing to share data than researchers or institutions might expect (though individual preferences vary and should be respected).

The PMI should include participants as full partners: Governance should include participants, and participant preferences should be given equal weight for decisions about research priorities, data sharing, and return of results. Shifting the way researchers and participants interact will involve changing the language used by researchers -- shifting from "us/them" to "we," "team," etc.

Health disparities research: the PMI cohort should be designed to address health disparities and the ability to investigate the multiple determinants of health. It is important to find ways to engage individuals who do not have EMRs, move frequently, have limited access to mobile devices, or who live in rural areas without easy communication. Providing transportation, childcare, etc. may be important for reducing barriers to participation.

Define inclusion goals broadly: Communities are internally diverse, and individuals are members of many communities. An inclusive cohort should recruit the widest variety of individuals by race, ethnicity, sexual orientation and gender, age, health status, SES, educational level, and geography. Populations defined as "vulnerable" should be included in research, given that "protecting" vulnerable populations by excluding them from research may in fact harm them.

Continual engagement and communication: There is no "one size fits all" for participating individuals or communities, so flexibility is critical for participant engagement. Boots-on-the-ground community engagement is essential, especially to target underserved/underrepresented populations. It is important to foster a sense of community and pride among cohort participants. Meaningful relationships, transparency and trust are essential and promoted by recruiting individuals through trusted institutions such as churches, community centers, and barbershops. Public trust in the PMI cohort requires adequate infrastructure and resources to support sustained engagement for the duration of the PMI cohort.

Making participation meaningful: Researchers should engage with participants and communities to convey the purpose of the research and how their data will be used so that participants can appreciate the value of the research. Participants should be compensated for their contributions, not simply incentivized, as incentives that are not well-aligned with the values of the community diminish the intrinsic value of participants' contribution to research. Returning study information (aggregate and/or individual, as appropriate) is one of the most effective motivators for participation. Participants want timely and continual return of results throughout the research process. Translation of findings to affect health outcomes, communication about how research contributed to new applications and making resulting health applications accessible are essential.

Address policy gaps related to data access and privacy: Federal and state agencies should continue to work together to ensure that policies addressing data sharing and data access provide robust protection of participants while enabling widespread data sharing. Building and sustaining public trust will be supported by developing transparent policies to respect participant preferences, protecting participant privacy, enabling data security, and enforcing penalties for misuse of PMI cohort data.