

## **Participant Engagement, Data Privacy, and Novel Ways of Returning Information to Participants**

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### **Introduction and Background**

With the rapid growth and developments in genomics research, data science, and electronic health records, the capacity to integrate an individual's information into their clinical care and realize the goal of precision medicine is on the horizon. To address this opportunity, a large U.S. cohort study has been proposed (“the Cohort”). This Cohort must be participant-centric in concept and design from start to finish; able to collect and share structured data with participants, researchers, and clinicians; and, transparent in purpose, management, and execution. Participants must be incorporated within activities as true partners to reflect their interests, expertise, and responsibilities integral to Cohort success.

This study has the potential to advance participant engagement substantively by designing and implementing innovative methods that support participant preferences and values, which will change over time. The design of systems to engage the public in the Cohort should reflect our multi-cultural richness, our highly mobile population, our disparate access to health care and health care systems, and our myriad combinations of group and individual interests and priorities. Data sharing and privacy mechanisms should reflect current consumer-based fair information practices. Attention to these needs should be evident at every phase of the Cohort's activities. Mechanisms or systems deployed must be adequately resourced or risk damaging the credibility and success of the Cohort. And, to instill and sustain public trust, transparency and inclusiveness must be a guiding principle across Cohort governance, policies, and practices.

Discussions in the working group highlighted several fundamental challenges. These challenges include issues at the intersection of research and clinical care; the need to recruit, engage, and integrate a broad and diverse study population, including existing cohort populations; and, navigation of the complex conglomeration of policies, regulations, and laws pertaining to health research and privacy protection. Each of these represent “45,000 foot” level issues and appropriate consideration for each will entail addressing multiple underlying or collateral topics. Further consideration of these challenges, potential solutions to mediate the barriers they pose, and relevant opportunities to inform or advance systems to resolve them are provided below. To address these issues adequately, cohort design and implementation decisions must be iterative with the consideration of participant and policy implications.

## **Challenges and Proposed Solutions**

### ***Managing the Research/Clinical Intersection***

The discernable distinctions between research and clinical care are amalgamating. However, our understanding of the clinical utility of specific genomic variants now being generated in bulk is nascent, and accepted standards for determining what genomic data are appropriate to inform clinical care or when or how to return this information to individuals, health care providers, or to the medical record are not yet available. This reality deepens the need to clearly define the scope of Cohort goals, activities, and procedures, including the return of research data to participants or their physicians. Participant resources should not only clearly identify how and by whom research and clinical information will be accessed, shared, and used, but any potential implications of the information should be unambiguously conveyed and options for additional resources or support provided.

#### **Proposed solutions to mediate these challenges:**

- Clearly define and communicate the scope and activities for the Cohort. Develop and regularly update clear and concise “toolkits” for participants and clinicians that can be adapted and deployed in multiple settings. At minimum, content should address research procedures, what data will be collected, and, what results may be returned to participants and/or clinicians.
- Provide resources and policies/best practices for when and how the heterogeneous set of providers inside and outside participating institutions will interact with cohort activities.
- Establish an expert body that includes participant members to inform Cohort leadership on specific decisions regarding return of results to participants and providers, including potentially returning full genome sequence data. Variants of unknown significance and ‘n of one’ data should receive particular attention. This group should also inform the broader research community.
- Provide transparent and updated expectations for all parties regarding coverage and payment for any test or procedure conducted in the course of the Cohort.
- Ensure that policies and practices guiding activities at the research/clinical interface are regularly reviewed by an appropriate Cohort governance body, which should include all stakeholder voices.

### ***Engaging ‘New’ Participants and Integrating Existing Cohorts within a Sustainable Cohort***

To achieve the aims of the Cohort and to maintain public trust, participants must be engaged in ways that respect individual autonomy and provide flexibility for personal choices and variability in those choices with time. Also, to avoid participant ‘fatigue’, variable levels of engagement with the Cohort should be possible. This will help to sustain participation in the new cohort and integrate new ‘unaffiliated’ participants as well as participants from existing cohort communities who may have other higher priority interests for their research participation. In addition, Cohort materials and resources should directly address the principles of fair information practices, as well as the potential implications of an individual’s participation for family members. While options for participant preferences must be paramount, the Cohort should clearly acknowledge that combinatorial complexities may limit participant choices.

#### **Proposed solutions to mediate these challenges:**

##### ***Recruitment***

- Identify strategies to reach beyond traditional recruitment infrastructures with specific attention to reaching those without ready access to health care.

- Consult with participants from existing cohorts to identify challenges or concerns for engaging in the proposed new Cohort.
- Provide simple and transparent information about the Cohort, including:
  - Basic study risks and benefits;
  - Additional resources with more detailed information to supplement basic materials; and,
  - Clear definition of the ‘minimally viable data set’ for the Cohort, including transparent communication about any consequent minimum levels of engagement for Cohort activities.
- Adopt innovative approaches to informed consent and privacy documents (or platforms) that:
  - Allow participants to choose (and change) data use and sharing preference;
  - Describe how participants can access their own information;
  - Describe what information others might access or use; and,
  - Describe the process for others accessing information.

*Maintaining participant involvement:*

- Consult with others who are developing, or have developed, tools for participant or consumer communications that can be adapted to the Cohort needs (*e.g.*, social media strategies).
- Provide mechanisms for remote and convenient participation (*i.e.*, day or night).
- Encourage the development of multi-platform accessibility (*e.g.*, APIs for disposable phones).
- Promote the integration of “low transaction cost” technologies for data collection.
- Explore options to gamify data collection technologies to encourage “task” completion.

*Return of results:*

- Offer individual-level data that could be informative or useful to participants’ health care or health-related decisions (*e.g.*, pharmacogenomic variants), including relevant information for them or their provider to learn more about any possible implications.
- Provide automated feedback relevant to participants, such as trend data, aggregate comparisons to subsets within the cohort, or participant portals or dashboards through which to follow the access and use of their data, and any aggregate findings generated.
- Establish systems to communicate with participants and providers about specific results as information about clinical utility or actionability is updated.

*Governance:*

- Establish an overarching participant advisory group within the Cohort governance system to inform key decision points for Cohort design and implementation to promote consistent implementation and support across the cohort.

***Policies, Regulations, and Laws***

Current research oversight processes would present substantial challenges for the management of a distributed cohort study of the magnitude necessary to advance precision medicine. Collaborative, centralized, and streamlined systems will be required to establish robust oversight systems that reflect the realities of the large study design and the number of parties (individuals and institutions) involved. Without resourceful and practical approaches to meet the range of ethical, fiduciary, and legal

responsibilities participating organizations hold, it will be extremely difficult to achieve optimal diversity among study sites and, therefore, among the study population.

With regard to protecting privacy, the network of applicable policies, regulations, and laws usually begin with the premise that data must be sequestered to avoid inappropriate use. For the Cohort, where broad data sharing will be essential, research and health data management requirements will vary greatly based on institutional policies and state and federal requirements applicable to participating sites. Compliance systems, therefore, must assert the premise for data sharing, emphasize data security, and be adaptable to accommodate multiple types of research organizations, data collection sites (including remote collection modalities), and the intrinsic mobility of the anticipated study population.

Additionally, the translational nature of the science that the Cohort is intended to advance, and its goal to improve the delivery of precision medicine, will involve FDA oversight. This is challenging because the specific requirements will not only be different for different aspects of the study, but they are likely to shift as the science and the technologies utilized evolve (*e.g.*, as technologies move from 'research use only' to FDA approved or cleared devices).

#### Proposed solutions to mediate these challenges:

- Identify opportunities to streamline research oversight that maximizes participant protections and respects different state and local laws and cultures.
- Develop policies to address liability considerations for participating institutions and providers.
- Develop harmonized requirements for privacy protection under HIPAA and the Common Rule that participating organizations and investigators can follow to meet their cumulative obligations.
- Establish clear standards for data provenance and rules for access based upon transparent and traceable practices that support direct participant data sharing and data sharing choices.
- Incentivize the development of an electronic research record for the Cohort to be interoperable with commonly used electronic health record systems and able to provide various partitions for different information categories with appropriate access protocols.
- Design and continually update clear data security standards and transparent data management principles in accord with the latest state of the art technologies.
- Ensure any mobile technologies deployed within the Cohort are engineered to collect and transmit data with no potential for copies to the device or service providers.
- Create flexible pathways through which to conduct FDA regulatory oversight requirements, developing clear and up-to-date guidance and definitions to support sponsor and institutional compliance and sustain scientific innovation.

#### **Opportunities Offered through the Cohort:**

As noted above, to gain and sustain public trust, the Cohort must be designed and implemented transparently and with participants engaged as full partners. Many of the proposed solutions to meet the challenges to the Cohort study directly represent opportunities, in that there is the potential to enhance practices through qualitative and quantitative analyses of the engagement activities deployed. Indeed, it is important to consider not only the biomedical research enabled through such a large and diverse cohort, but also the ethical and social questions about research participation and the delivery of precision medicine care that will be possible to address on a scale not possible before. Examples of such opportunities are listed below.

### *Engage participants in advancing health research and innovative care systems*

- Study what types of information or options for additional research participation participants are interested in receiving from the study, how they prefer to receive it, and how they use it.
- Study how participant preferences change with time, what life or health events affect those changes, and what support or resources will be needed as precision medicine advances.
- Pilot standards and methods for the return of variants of unknown significance and ‘n of one’ data, including explicit consideration of the benefits and challenges of various models.
- Explore if and how cohort data ‘mining’ might be acceptable to participants in order to provide predictive analytics or identify other information of interest, *e.g.*, relevant clinical trials.
- Collaborate with specific communities to explore the elements of precision medicine that are meaningful for their members, how to communicate with them about those priority issues, and what incentives or benefits make research participation a valuable investment for their time.
- Study the tensions and opportunities possible through engaging families in Cohort research.

### *Develop, deploy, assess new mechanisms to inform and protect participants (patients)*

- Convene local leaders in research oversight and relevant federal agencies to identify and develop processes to streamline the oversight, while not eroding participant protection.
- Research participant preferences, needs, and acceptable trade-offs on a large scale to understand considerations regarding research and data sharing in real time scenarios.
- Develop novel ways to communicate, inform, and educate the public about research and health issues broadly, which will build capacity for an engaged and informed public. Increased public comfort with the science underlying precision medicine will be important to prepare individuals to be partners in health care decisions down the road.

### *Advance learning health care processes*

- Identify weak phenotypes able to drive therapeutic development for rare diseases and understanding of the spectrum of disease and its underlying pathways.
- Conduct studies to learn how physicians engage and interact with precision medicine information and what support and resources or infrastructure are needed to promote quality care of patients.
- Build infrastructure for clinical decision support tools to provide real time education to practitioners to inform patient care as precision medicine extends across clinical settings, increasing access to the technology.
- Develop comprehensive participant information portals for individual information to provide clear, navigable feedback to participants and enhance patient-provider discussions and shared decision-making.
- Apply new technologies, communications strategies, and social media applications developed through the Cohort to other research infrastructures and health care practices.
- Establish pathways for evidence development to inform equitable coverage and reimbursement decisions and promote broad access to precision medicine tools.

## **Summary**

Recent and on-going innovations in genomics research, data science, and electronic health records herald the potential for precision medicine to transform clinical care. The proposed large U.S. Cohort,

while presenting myriad scientific possibilities, offers similar opportunities to transform traditional participant engagement practices and include participants as partners in the research from data collection to data use. While the research-clinical intersection, recruitment and engagement of participants, and the complex sphere of policies, regulations, and laws pertaining to health research and protections pose challenges to the creation and success of a cohort of this magnitude, we are confident that the potential solutions proposed in this white paper provide a platform for deliberate and constructive steps forward. As the possibilities for the Cohort are defined and specific details about the study's scope and design begin to emerge, it will be possible to reduce the solutions proposed here to concrete options and actions.

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