Communicating Precision Medicine Research: Multidisciplinary Teams and Diverse Communities

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Education in genetics · Genetic communication · Multidisciplinary team · Precision medicine · Risk communication

Abstract
Introduction: Precision medicine research investigates the differences in individuals’ genetics, environment, and lifestyle to tailor health prevention and treatment options as part of an emerging model of health care delivery. Advancing precision medicine research will require effective communication across a wide range of scientific and health care disciplines and with research participants who represent diverse segments of the population. Methods: A multidisciplinary group convened over the course of a year and developed precision medicine research case examples to facilitate precision medicine research discussions with communities. Results: A shared definition of precision medicine research as well as six case examples of precision medicine research involving genetic risk, pharmacogenetics, epigenetics, the microbiome, mobile health, and electronic health records were developed. Discussion/Conclusion: The precision medicine research definition and case examples can be used as planning tools to establish a shared understanding of the scope of precision medicine research across multidisciplinary teams and with the diverse communities in which precision medicine research will take place. This shared understanding is vital for successful and equitable progress in precision medicine.

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Introduction

Precision medicine is an emerging model for health care delivery that considers differences in individuals’ genomics, environment, and lifestyle to offer tailored interventions for prevention and treatment. The term carries forward much that was previously referred to as personalized medicine [1]. While the emphasis is on finding the right care for the individual patient, precision medicine introduces an ambitious expansion of the scope and volume of information to be included in tailoring strategies for patient care, including not only genomics – the primary focus in calls for personalized medicine – but also exposure data, behavioral information, and social determinants of health [2]. Research required to test and validate precision medicine in clinical practice thus must include a multitude of data types. In turn, it is necessary that investigators from multiple disciplines work in concert to accurately interpret and translate these data for clinical application [2, 3]. Participant diversity in race, ethnicity, gender, and socioeconomic status is also paramount but thus far lacking [4, 5].

The value of multidisciplinary research has been recognized by leading research agencies, including the National Institutes of Health (NIH) [6]. Scientific innovation requires collective creativity [7], and funding announcements frequently require multidisciplinary teams [8]. Multidisciplinary collaboration has been integral to the success of several research consortia addressing aspects of precision medicine research, including Centers of Excellence in Ethical, Legal, and Social Implications Research [9], the Pharmacogenomics Research Network (PGRN) [10–13], the Electronic Medical Records and Genomics Research (eMERGE) Network [14, 15], and the Clinical Sequencing Evidence-Generating Research (CSER) Consortium [16].

Communication across multidisciplinary collaborations can be challenging, particularly due to a lack of conceptual clarity and consistency in the definition of terms used across different disciplines, often for the same or similar concepts [17, 18]. This challenge is amplified when research teams seek to work in partnership with communities. In this setting, scientific experts must not only develop plain-language explanations for technical concepts but also engage community partners to help them understand salient cultural, material, social, and historical factors that are relevant to the research. Scherr et al. [19] acknowledge that critical communication moments will arise in the course of precision medicine research efforts to integrate its results into health care. Noting that “communication failures may significantly disrupt critical advancement,” the authors point to the importance of effective communication across multidisciplinary teams and the need to develop a common language for teams conducting precision medicine work [19]. Specific challenges communicating about precision medicine research and eventually precision health care with community members include explaining the possible benefits of participation in precision medicine efforts, potential privacy implications, and the potential for receiving unexpected and unwanted information [20].

The authors of this manuscript are researchers from two multidisciplinary teams engaged with several American Indian and Alaska Native (AIAN) communities and research review processes for precision medicine research projects across the USA. In this context, it has become apparent that researchers must provide concrete examples and definitions of precision medicine research to accurately elicit tribal leadership’s, tribal health care providers’, and community members’ questions and concerns about precision medicine and precision medicine research in AIAN communities [21, 22].

The definition of precision medicine, and the research required to enable it, leaves much room for interpretation. For example, concepts such as “genetic change” must be explained and clarified as its meaning can include such diverse phenomena as inherited risk, somatic mutations, epigenetic influences, and alterations in the microbiome that may be set in motion by social and environmental exposures. Furthermore, the meaning of the “environment” needs to be clarified and extended beyond “lifestyle” [23] and concerns such as historical trauma, structural inequities (e.g., related to access to education or employment), and changes in diet and other behaviors occurring with urbanization and acculturation must be considered [24–27].

The layers of complexity and scope of precision medicine research must be communicated clearly to support collaboration with AIAN communities [21, 22]. Transparency is particularly important to enable large precision medicine research efforts to move forward equitably in underrepresented populations [28]. Some AIAN groups have shown interest in participation in genetic research, with the understanding that research is to be conducted with transparent research practices, under the oversight of AIAN leadership, and must directly benefit the health of AIAN communities [21, 22, 29–33]. Research using biospecimens is an especially sensitive aspect of research, requiring individual and community protections [34–36]. Trustworthy practice also requires
that researchers include the community in discussion throughout the entire research process and not wait to communicate with the community until the end of the research project [12, 28, 37–40]. While researchers should provide a clear definition of precision medicine research scope for all communities with which they work, AIAN tribal communities are sovereign nations with the authority to require that researchers do so [41–44]. This paper describes the process this multidisciplinary team used to address these needs and presents the products that resulted from this process, including a definition of precision medicine research and case examples to illustrate its scope among the research team.

Materials and Methods

This work is based on a collaboration between two research consortia: (1) the Northwest-Alaska Pharmacogenomics Network (NWA-PGRN), a collaboration of researchers from Oregon Health & Science University, Southcentral Foundation, the University of Montana, and the University of Washington and tribal communities in Alaska and Montana partnered to address pharmacogeneric and precision medicine research with AIAN populations [10–13, 45]; and (2) the University of Oklahoma’s Center for the Ethics of Indigenous Genomic Research (CEIGR), a university and community partnership Center of Excellence in Ethical, Legal, and Social Implications Research that formed to support AIAN communities to determine how to best approach genomic research [46, 47]. The NWA-PGRN and CEIGR investigators have expertise in anthropology, bioethics, epigenetics, genetics, pharmacology, and public health and collaborate with six AIAN communities across the USA on genomic research projects addressing community-identified health priorities related to genomic and precision medicine research. To prepare for community discussions about what constitutes precision medicine research, as well as its potential benefits and concerns, these teams convened a working group to develop precision medicine research case examples.

Case Example Development Process

Through regular teleconferences, working group members suggested examples to illustrate a range of precision medicine research applications. During this process, the group reached consensus about the scope of precision medicine research and defined next steps to develop case examples.

Health topics of highest priority to the tribal communities partnering with the NWA-PGRN and CEIGR were discussed. The working group divided into pairs based on interest and expertise to develop current, plausible examples on specific topics of interest to the AIAN communities they partner with, including diabetes/obesity, asthma, vitamin D insufficiency, colon cancer, medication management, and mental health. As discussion advanced, however, it was recognized that different components of precision medicine research could cut across multiple disease foci. The group decided to reorient the process to develop examples based on different precision medicine approaches and research strategies that could address health outcomes of interest to AIAN communities. The precision medicine approaches highlighted were genetic risk assessment, pharmacogenetics, epigenetics, microbiome, mobile health (mHealth), and electronic health record (EHR) research. Based on experience working with AIAN communities, the group identified five areas of content to be addressed for each example: (1) description of topic area, (2) example of research application, (3) involvement required of AIAN community members, (4) possible benefits of the research, and (5) possible drawbacks of the research [21, 22, 29, 30, 32, 48, 49].

A subcommittee (WB, JAB, SBT, EB) standardized the case examples to ensure similar length and a tenth-grade reading level for accessibility to individuals with a wide range of backgrounds. The revised examples were then brought back to the larger team for review and final revision. Once the larger team reached consensus on the definition and case examples, the precision medicine definition, case examples, and this draft manuscript were reviewed by the SCF community-level research review committee, including tribal leadership, for AIAN community acceptability and revised based on recommendations provided prior to journal submission [42].

Results

The need for a unified precision medicine definition quickly became apparent as working group members used different sets of ideas and language to describe precision medicine research. For example, views differed within the group about whether genomics is a necessary component of all precision medicine. In addition, the group debated the definition and significance of social environment as a component in precision medicine research. These points are particularly relevant to inclusion of the case example concerning EHR-based research and to the inclusion of social and behavioral environments in epigenetic and microbiome research. To align the group to a common understanding of the boundaries of precision medicine research, the group developed a working document to define precision medicine research, which was refined during the process of developing the case examples.

During the standardization process, the subcommittee collated the various definitions of precision medicine research from the topic-specific examples and developed an overarching, standalone precision medicine research definition (S1 File). The precision medicine research definition begins with a brief overview of precision medicine research followed by high-level examples of precision medicine research (Box 1). Next is a description of how precision medicine research might be accomplished using a variety of data sources from large data sets, followed by a description of the potential benefits and risks of doing precision medicine research for both individuals and
communities. Last, the definition provides a description of the All of Us research program as an example of a precision medicine research project with active recruitment and a description of how researchers would gain access to All of Us program data collected for precision medicine research.

In addition to the precision medicine research definition, this process generated six precision medicine research case examples as detailed below, addressing genetic risk assessment, pharmacogenetics, epigenetics, microbiome, mHealth, and EHR research (S2 File). Each example includes five standardized sections, using a frequently-asked-questions format, answering questions often asked by AIAN community members [21, 22, 29, 30, 32, 33, 48, 49]. The first section provides lay definitions followed by a description of plausible research conduct for research with the community, what a participant might need to do to participate in that type of research, and the possible benefits and drawbacks to the research.

**Genetic Risk Assessment**

Genetic risk is anticipated to play an important role in precision medicine and is therefore an important component of precision medicine research. Research in this area evaluates inherited susceptibilities to health risks. For example, rare gene variants in the BRCA1 and BRCA2 genes confer a high lifetime risk of developing breast and ovarian cancer. Other rare gene variants are associated with high risk for other conditions that disproportionally affect AIAN communities, including colorectal cancer and coronary heart disease. Although these gene variants are likely to be present in only a small proportion of the population, their identification can enable tailored prevention and early detection efforts. Other gene variants result in moderately increased risks for common conditions of interest to AIAN communities, such as asthma and diabetes, and could inform public health research through the evaluation of interactions between genetic risk and environmental exposures [50]. For example, a genetic risk for asthma may not be expressed in a clean air environment, but the same risk may be amplified by exposure to cigarette smoke or other environmental stressors.

**Pharmacogenetics**

Pharmacogenetics research investigates how genetic testing can be used to increase therapeutic efficacy and improve drug safety based on an individual’s genetic profile. Pharmacogenetics may provide the most concrete example of how precision medicine can be implemented into everyday health care delivery, with pharmacogenetic testing associated with improvement in drug response in many therapeutic areas including psychiatry, cardiovascular disease, pain management, and cancer [51–54]. Yet, even with the potential to improve patient outcomes, underserved populations – including AIAN communities – continue to be underrepresented in pharmacogenetics research [45]. Community members in NWA-PGRN studies are familiar with pharmacogenetics due to past and ongoing research conducted with their communities, and some have shared first-hand experience with the potential side effects of prescription and over-the-counter drugs [37, 55, 56], which may be addressed by this research.

**Epigenetics**

Epigenetic research studies how structural modifications that do not change the sequence of DNA can alter gene expression, resulting in changes in health risk. DNA methylation and histone modification are two of the more commonly studied forms of epigenetic modification. For example, environmental and behavioral factors including diet, lifestyle, social experiences, and exposure to pollutants are all thought to contribute to epigenetic changes. These changes persist as cells divide and can thus be passed on to future generations, where they may contribute to long-term risk for chronic conditions such as diabetes. The effects of historical trauma, changes in diet associated with urbanization or lack of access to subsistence foods, and persistent health disparities are relevant health priorities of AIAN communities that epigenetics may be able to address [57–59].

**Microbiome**

Human microbiome research studies microbes, including bacteria, fungi, parasites, and viruses that have residence on and within the healthy body. With respect to precision medicine research, microbiome information may produce biomarkers for diagnosing disease, refining current probiotics and prebiotics, discovering new pharmaceuticals, identifying opportunistic pathogens, and predicting antibiotic resistance [60]. Precision editing of the microbiome may mitigate microbial-connected illnesses as well as an array of multifactorial conditions of concern to AIAN communities, including obesity, diabetes, cardiovascular disease, and cancer [61]. For example, the microbiome is implicated in inflammatory diseases of the gastrointestinal tract, such as colitis, and it has been demonstrated that the severity of inflammation can be reduced by treatments that change the way microbes grow [62]. Therapeutic approaches informed by microb-
ome research might include the use of medications or other interventions that influence changes in the microbiome.

Mobile Health

mHealth technologies track individual, patient-specific data to aid in bridging the gap between clinical research and lived experiences. For example, mobile devices are capable of supporting snapshot assessments of social and environmental indicators. In addition, sensor technologies in mobile phones and wearable fitness tracking devices provide opportunities for direct, passive assessment of personal health indicators [63]. mHealth applications have the capability to monitor critical parameters such as blood glucose, blood pressure, and heart rhythm [64]. Through GIS technology, this patient-specific information can be tied to geographic location, thereby opening opportunities for fine-grained analysis to evaluate and contextualize health behavior. Precision medicine research approaches with mHealth, such as All of Us, have explicit plans to collect data through mobile technology. mHealth research lends itself to personalized disease management, the tracking of which creates a large repository of data points that will aid in the development of precision medicine. At the same time, these data collection technologies raise important privacy concerns as the level of personal detail in the data can permit ready reidentification.

EHR Data

The real-time collection of patient health information and clinical care in the EHR is integral to moving precision medicine research forward, as are adaptations in the EHR to accommodate genomic data [65]. Health researchers and health care systems conduct aspects of precision medicine research when they use EHR data to identify population-level patterns that indicate opportunities to improve patient care [66, 67]. This vast repository of data is currently used to develop predictor algorithms for preventive health, risk for surgery complications and death, Alzheimer’s disease, suicide attempt, and antibiotic resistance [68–71]. Machine learning techniques can supplement precision medicine research with information derived from other electronic data sources, such as biorepositories [72]. Primary and secondary care EHR data can potentially guide the use of precision medicine in health care delivery; in turn, data produced in these visits and recorded in the EHR will help investigators to refine the application of genetic risk, pharmacogenetics, epigenetics, microbiome, and mHealth in precision medicine research.

Discussion/Conclusion

This multidisciplinary team developed case examples to foster discussion on whether and how precision medicine research aligns with tribal health priorities and community perspectives regarding privacy, return of results, and data stewardship. A shared definition of precision medicine research brought the group to a common understanding of what precision medicine research entails and helped to guide the development of the case examples. These concrete examples of precision medicine research can be used to promote discussion of potential health care or policy proposals that might emerge from precision medicine research studies, as well as the implications of precision medicine research for privacy, return of results, and data stewardship to communities and research participants. For example, the precision medicine research definition, as well as the pharmacogenetics and genetic risk examples, were used to develop newsletter and newspaper articles to raise awareness of precision medicine research with AIAN communities [73]. The precision medicine research definition and the case examples were recently used to facilitate discussion in dialog and deliberative forums to gather perspectives of how precision medicine research may align with tribal health priorities, return of precision medicine research results to tribal communities, and data stewardship of precision medicine research data [33, 74]. Post-deliberation survey data from the cross-site deliberation, which brought leaders from across several tribes together, found that the majority of deliberants (7 of 10) found the information presented was “clear and easy to understand” [74].

In addition to providing draft language on the scope of precision medicine research that research teams can consider when working with communities, the case examples offer an opportunity to introduce potential benefits and harms. Each example points to specific ways in which precision medicine approaches might improve health care. They also offer insights into the kind of burdens participants in precision medicine research might experience and the potential risks to individuals and communities, including privacy concerns related to the nature and scope of data collected in precision medicine research.

An interesting area of clarification for the group was around the topic of secondary data analysis and the inclusion of the EHR as an aspect of precision medicine research. Researchers routinely use the EHR as a data source for primary research as well as for secondary data analysis. The EHR is a significant potential source of data for
precision medicine research [75]. However, many research participants want more information about the research in which their information is used, including de-identified information [36]; and the secondary use of data for research purposes has been noted as a concern by AIAN leaders [30] and by Indigenous people throughout the world [44]. Additionally, other populations have asked for transparency regarding use of EHR for research purposes [76]. Moreover, how EHR data are used [77], the inclusion of the community in the analysis and interpretation of the data [78], and who the EHR data can be shared with [79] are of known concern to many AIAN communities. This example emphasizes the need for multidisciplinary teams to develop a shared vernacular and intent regarding precision medicine research and to consult with communities throughout the research process, including secondary data analysis.

There are limitations to the precision medicine definition and precision medicine case examples described here. The precision medicine definition and case examples were developed as a starting point for the research team to come to a common understanding of what constitutes precision medicine research. These documents were not intended to be shared with the public as written but instead were designed to outline the elements that should be addressed when working with communities on precision medicine research projects. The tenth-grade reading level may need to be adjusted prior to dissemination for public audiences. In a similar vein, the definition and case examples may be useful when training students and staff new to precision medicine research teams, and in these instances, more technical language might need to be incorporated. Last, a communication expert was not part of the multidisciplinary team. Future areas of research on this topic should include individuals with expertise in science or health communication who may be able to fully consider more applicable readability formulas or other communication tools that could add value to a revision of the precision medicine research definition and/or case examples.

Clear communication of the scope of precision medicine research and eventually precision medicine in health care delivery is necessary to engage health care stakeholders (e.g., providers, patients, policymakers) [22, 80]. Multidisciplinary input is required to develop training material for researchers and health care delivery staff to communicate with the public about precision medicine [81]. Procedures for communicating genetic test results, including genetic risk and for fostering behavior change to address such results have been identified as an area of needed development [82]. Interdisciplinary training programs and university clinical programs could use the shared definition and case examples to facilitate classroom discussion on communicating individual- and community-level risks and benefits of precision medicine research. The precision medicine research definition document could be used as a reference document for staff in the informed consent process for precision medicine research or clinical care. The materials put forth by this multidisciplinary working group provide starting points with a shared language that can be used to develop training materials for community members and leaders, as well as students, trainees, and fellows, providers, and other professionals involved with the advancement of precision medicine. Furthermore, the materials can assist in communication of precision medicine research efforts and results involving diverse research and lay communities.

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Statement of Ethics

The information reported in this manuscript did not involve human subject research and is exempt from Institutional Review Board review. However, a draft of this manuscript was reviewed and approved on April 14, 2020, by Southcentral Foundation (tribal community partner) Research Review committees and Board of Directors in Anchorage, Alaska, prior to journal submission. For further inquiries, please contact the corresponding author.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Conceptualization: Wylie Burke and Vanessa Y. Hiratsuka. Case examples curation: Julie A. Beans, Susan B. Trinidad, Erika Blacksher, and Wylie Burke. Funding acquisition: Wylie Burke, Vanessa Y. Hiratsuka, Bert B. Boyer, Erica L. Woodahl, and Paul Spicer. Methodology: Wylie Burke, Julie A. Beans, Susan B. Trinidad, and Erika Blacksher. Project administration: Julie A. Beans and Wylie Burke. Supervision: Wylie Burke and Vanessa Y. Hiratsuka. Developed case examples: Julie A. Beans, Vanessa Y. Hiratsuka, Susan B. Trinidad, Erika Blacksher, Wylie Burke, Cecil M. Lewis Jr, Erica Woodahl, Bert B. Boyer, Paul Spicer, Patrick M. Gaffney, and Nanibaa’ A. Garrison. Writing – original draft: Julie A. Beans, Vanessa Y. Hiratsuka, Susan B. Trinidad, Erika Blacksher, Wylie Burke, Cecil M. Lewis Jr, Erica Woodahl, Bert B. Boyer, and Paul Spicer. Writing – review and editing: Julie A. Beans, Vanessa Y. Hiratsuka, Susan B. Trinidad, Erika Blacksher, Wylie Burke, Cecil M. Lewis Jr, Erica L. Woodahl, Bert B. Boyer, Paul Spicer, Patrick M. Gaffney, and Nanibaa’ A. Garrison.

Data Availability Statement

The precision medicine definition and case examples developed as part of this process are included in this article and its online supplemental files (see www.karger.com/doi/10.1159/000525684 for all online suppl. material). For further inquiries, contact the corresponding author.

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