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Relevance of Health Literacy to Precision Medicine

Proceedings of a Workshop

Joe Alper, *Rapporteur*

Roundtable on Health Literacy

Board on Population Health and Public Health Practice

Health and Medicine Division

The National Academies of
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Reviewers

This Proceedings of a Workshop has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published Proceedings of a Workshop as sound as possible and to ensure that this Proceedings of a Workshop meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain privileged to protect the integrity of the process. We wish to thank the following individuals for their review of this Proceedings:

CHRISTOPHER M. DEZII, Bristol-Myers Squibb Company
CARLA L. EASTER, National Institutes of Health
RIMA E. RUDD, Harvard University
CARA TENNENBAUM, Food and Drug Administration

Although the reviewers listed above have provided many constructive comments and suggestions, they did not see the final draft of the Proceedings of a Workshop before its release. The review of this Proceedings of a Workshop was overseen by **Hugh Tilson,** University of North Carolina at Chapel Hill. He was responsible for making certain that an independent examination of this Proceedings of a Workshop was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of the Proceedings of a Workshop rests entirely with the rapporteur and the institution.

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In Memoriam

This Proceedings of a Workshop is dedicated to Dr. Margaret Loveland, an accomplished physician and advocate in the field of health literacy, a valued member of the Roundtable on Health Literacy, and an irreplaceable colleague and friend.

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The workshop presentations and reactions to those presentations were both interesting and stimulating, and we would like to thank each of the speakers and panel reactors for their time and effort. Speakers and reactors were, in alphabetical order, Marin P. Allen, Jessica Ancker, Paul S. Appelbaum, Suzanne Bakken, Terry Davis, Jennifer Dillaha, Carla Easter, William Elwood, Lori Erby, Chris Gunter, Kathleen Hickey, Joseph D. McInerney, Benjamin Solomon, Sara Van Driest, Catherine Wicklund, Consuelo Wilkins, and Michael S. Wolf.

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Contents

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

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Box, Figures, and Tables

BOX

FIGURES

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

TABLES

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Acronyms and Abbreviations

AAAS	American Association for the Advancement of Science
CBPR	community-based participatory research
CDRN	clinical data research network
EnTICE[3]	Electronic Tailored Infographics for Community Engagement, Education, and Empowerment
HIPAA	Health Insurance Portability and Accountability Act
ICD	implantable cardioverter–defibrillator
IRB	institutional review board
NHGRI	National Human Genome Research Institute
NIH	National Institutes of Health
NLM	National Library of Medicine
OBSSR	NIH Office of Behavioral and Social Sciences Research
PMI	Precision Medicine Initiative
WICER	Washington Heights/Inwood Informatics Infrastructure for Comparative Effectiveness Research

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1

Introduction[1]

On January 20, 2015, President Obama announced the Precision Medicine Initiative (PMI) in his State of the Union address. The PMI, by developing new approaches for detecting, measuring, and analyzing a wide range of biomedical information including molecular, genomic, cellular, clinical, behavioral, physiological, and environmental parameters, is intended to enable a new era of medicine in which researchers, providers, and patients work together to develop individualized care. The President called for $215 million in fiscal year 2016 to support the initiative, which was to include efforts at several agencies within the federal government. Of this total proposed budget, $130 million was allocated to the National Institutes of Health (NIH) to build a national, large-scale research participant group, or cohort. The PMI Cohort Program is aimed at extending precision medicine to many diseases, including both rare and common diseases such as diabetes, heart disease, Alzheimer's disease, obesity, and mental illnesses such as depression, bipolar disorder, and schizophrenia, by building a national research cohort of 1 million or more U.S. participants.

Many factors have converged to make now the right time to begin a program of this scale and scope, noted Bernard Rosof, chief executive officer at

[1] The planning committee's role was limited to planning the workshop, and the proceedings has been prepared by the workshop rapporteur as a factual summary of what occurred at the workshop. Statements, recommendations, and opinions expressed are those of individual presenters and participants and have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine, and they should not be construed as reflecting any group consensus.

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

the Quality in Healthcare Advisory Group, in his introduction to the workshop Relevance of Health Literacy to Precision Medicine, which was convened by the National Academies of Sciences, Engineering, and Medicine's Roundtable on Health Literacy. Americans are engaging in improving their health and participating in health research more than ever before, electronic health records have been widely adopted, genomic sequencing costs have dropped significantly, data science has become increasingly sophisticated, and health technologies have become mobile. The PMI Cohort Program will be a participant-engaged, data-driven enterprise supporting research at the intersection of human biology, behavior, genetics, environment, data science and computation, and other disciplines to produce new knowledge with the goal of developing more effective ways to prolong health and treat disease. The cohort will broadly reflect the diversity of the U.S. population by including participants from diverse social, racial/ethnic, and ancestral populations living in a variety of geographies, social environments, and economic circumstances and from all age groups and health statuses. Information from the cohort will provide a broad, powerful resource for researchers working on a variety of important health questions. Importantly, the cohort will focus not just on disease, but also on ways to increase an individual's chances of remaining healthy throughout life. The goal of the PMI Cohort Program is to set the foundation for a new way of doing research that will foster open, responsible data sharing with the highest regard to participant privacy and that puts engaged participants at the center of research efforts.

An important challenge to assembling the PMI Cohort will be to reach individuals who are socioeconomically disadvantaged. Individuals who are socioeconomically disadvantaged have lower health literacy; often belong to racial, ethnic, and minority communities; and are often less likely to participate in research studies and biorepositories, said Rosof, and they are also less likely to understand the institutional review board (IRB) process and informed consent, "Health literacy communication strategies and messaging designs are key factors to address these challenges and overcome the barriers to participation in the PMI Cohort," Rosof said.

To explore possible strategies and messaging designs, the Roundtable on Health Literacy formed an ad hoc committee charged with planning and conducting a 1-day public workshop on the intersection of health literacy and precision medicine. According to the statement of task, the workshop was to feature invited presentations and discussions on topics that could include an overview of precision medicine and its potential; the relevance of health literacy to the success of precision medicine efforts; and perspectives and understanding of different groups, such as health care providers, consumers, and insurers. The planning committee was charged with defining the specific topics to be addressed, developing the agenda, selecting and inviting speakers and other participants, and moderating the discussions.

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

The planning committee was also charged with designating a rapporteur to prepare a summary of the presentations and discussions at the workshop in accordance with institutional guidelines.

ORGANIZATION OF THE PROCEEDINGS

The workshop (see Appendix A for the agenda) was organized by an independent planning committee in accordance with the procedures of the National Academies of Sciences, Engineering, and Medicine. The planning committee's members were Suzanne Bakken, Ellen Clayton, W. Gregory Feero, Spero Manson, Ruth Parker, and Catherine Wicklund. This publication summarizes the workshop's presentations and discussions, and it recounts what workshop participants identified as key lessons, practical strategies, and the needs and opportunities for applying the principles of health literacy to the precision medicine. Chapter 2 provides an overview of the communication challenges that have arisen in the genomic era, and Chapter 3 presents a picture of the intersection of health literacy and precision medicine. Chapter 4 discusses the role of health literacy in precision medicine research, Chapter 5 reviews the challenges of communicating risk and uncertainty in the clinical setting, and Chapter 6 addresses the role that health associations and social media can play in communicating with the public. Chapter 7 summarizes an open discussion during which Roundtable on Health Literacy members and workshop participants provided their reflections on the day's presentations and deliberations.

In accordance with the policies of the National Academies of Sciences, Engineering, and Medicine, the workshop did not attempt to establish any conclusions or recommendations about needs and future directions, focusing instead on issues identified by the speakers and workshop participants. Furthermore, the organizing committee's role was limited to planning the workshop. This Proceedings of a Workshop has been prepared by workshop rapporteur Joe Alper as a factual summary of what occurred at the workshop.

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2

Genetic Literacy[1]

Two reasons to promote genetic literacy, or understanding of genes and inherited biological variation, said Joseph McInerney, executive vice president of the American Society of Human Genetics, are to help understand the history and nature of life on earth and to understand the future of health care, including the ethical, legal, and social aspects of health care and the genetic contributions to health care. Understanding the history and nature of life on earth, which McInerney considers to be the fundamentals of basic biology, requires understanding five key concepts, each related in some way to genetics:

- Variation and continuity
- Evolution and the relatedness of all species
- Human evolution and the structure of human populations
- Biodiversity and biogeography
- Regulation of development and differentiation

Genetics is the study of inherited biological variation. Variation is the rule in the living world, not the exception, and this fact is a fundamental concept that McInerney believes all people should understand—if for no other reason than to foster a greater respect for and understanding of variation in their own community. Genetics, he continued, also explains biologi-

[1] This section is based on the presentation by Joseph McInerney, executive vice president of the American Society of Human Genetics, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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cal continuity, not just variation, and the relatedness between cells, between generations, within species across time and space, and across species.

Noting that educators have been thinking about how to teach genetics for more than a half century, McInerney reviewed some of the efforts to understand what should constitute genetic literacy and to develop instructional materials to increase genetic literacy in the nation's students. For example, the Next Generation Science Standards, developed jointly by the states, the National Research Council, the National Science Teachers Association, and the American Association for the Advancement of Science (AAAS), asks students to engage in what McInerney characterized as sophisticated intellectual tasks. One example of such a task would be to make and defend a claim based on evidence that inheritable variations may result from new genetic combinations through meiosis, viable errors during replication, or mutations caused by environmental factors. The Next Generation Standards, he explained, aim to establish some baseline of scientific literacy—in this case, genetic literacy—and do not focus on teaching isolated pieces of information or memorization.

In 2002, McInerney and other members of the education committee of the American Society of Human Genetics, proposed a set of six concept areas for genetic literacy for non-science majors at the undergraduate level (Hott et al., 2002) (see Box 2-1). He remarked that today the committee would have to elaborate on the content of each of these areas differently, given the advances that have occurred in understanding gene expression and epigenetics, for example. In 2009, a colleague of his proposed a completely different approach to content that would start with quantitative and complex traits rather than the single gene traits and Mendelian inheritance that are the usual starting points in genetic curricula (Dougherty, 2009). In that author's view, focusing on Mendelian traits primes many students to think deterministically and with a confused understanding of risk.

With regard to the second reason to understand genetics—to understand the future of health care—McInerney's view is that the United States is moving to a prevention-based health care system that will be informed increasingly by genetic perspectives. This is where genetic literacy and precision medicine intersect. In his opinion, he said, genetics education for the public and health professionals should be aligned—health professionals and the public should be getting the same messages about the genetic contributions to health and disease—and done in partnership. Such a partnership, he added, would shift the standard approach in genetic counseling from nondirective counseling toward more directive counseling with a focus on complex disease. As an example, McInerney said an informal genetic test—a family history—would reveal that he is at significant risk for heart disease, and based on taking a family history, his health care provider should direct

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BOX 2-1
Proposed Genetics Content for Introductory Biology Courses for Non-Science Majors

Content Area I. The Nature of the Genetic Material
Main concept: DNA is the universal information molecule; it allows for genetic variation within and genetic continuity between generations.

Content Area II. Transmission
Main concept: Mendelian patterns of inheritance are directly related to the mechanisms of meiosis.

Content Area III. Gene Expression
Main concept: Phenotypic characteristics result from one or more gene products (proteins) working alone or together in concert with the environment, generally in unpredictable ways.

Content Area IV. Gene Regulation
Main concept: Gene products, in combination with environmental influences, regulate all life processes from conception to death.

Content Area V. Evolution
Main concept: An understanding of genetic variation is essential to an understanding of evolution.

Content Area VI. Genetics and Society
Main concept: The growing ability to analyze and manipulate the genetic material of *Homo sapiens* and other species raises a variety of complex and sometimes controversial issues for individuals and society.

SOURCES: McInerney slides 11 and 12 (Hott et al., 2002).

him to get more exercise, eat right, and take other preemptive actions designed to reduce his risk of developing heart disease.

As an example of the type of genetic competencies health care professionals should have, McInerney listed the categories of knowledge recommended for physician assistants. They should understand basic human genetics terminology and be able to identify patients with or at risk of a genetic condition. They should have interpersonal and communication skills, including the ability to consider various factors that may influence a patient's response to genetic information and to seek coordination and collaboration with an interdisciplinary team of health professionals. With regard to patient care, physician assistants should be able to generate family

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history information, construct an appropriate multigenerational pedigree, and identify and appropriately determine which patients would benefit from a referral for additional genetic services.

McInerney then proposed some central questions to address when developing ways to educate health professional about genetics and precision medicine:

- What content is appropriate, and for whom?
- Which clinical behaviors and attitudes need to be changed, and is that possible?
- How is success defined and measured?

With regard to the first question, McInerney said he struggles to determine how much health professionals need to know to be effective. "Educational content can be accurate, but not necessarily complete in the way that a genetics professional would want to see it or understand it," he said, "and while it is not necessary to turn health care professionals into geneticists, they do need enough information to work effectively in a genetics context in their own clinics."

Concerning the last of these three questions, McInerney noted it is often asked too late in the development of most educational programs. "You should ask this question first, and the evaluator should be at the table with you so they know what your objectives are and they can help you design appropriate evaluations," he said. He added that over many years of working as an educator, he has learned to ask what students need to know, what they should value, and what they should be able to do with knowledge they have gained.

McInerney then made a modest proposal to help integrate genetics into education and mainstream health care. "I think we should be careful about the use of the terms 'genetic disorder' and 'genetic disease,'" he said. "We in the genetics community like to say we believe that genetics is the fundamental science of all health and all disease, but then we talk about genetic disease and genetic disorders. I think we send mixed messages as if there is a category of disease for which there are genetic contributions and a category for which they are not." The definition of genetic counseling that he likes is one from the National Society of Genetic Counseling (Resta et al., 2006, p. 79), which states: "Genetic counseling is the process of helping people understand and adapt to the medical, psychological, and familial implications of genetic contributions to disease."

There are a number of terms that some use interchangeably but that McInerney said have distinctly different meanings. For example, "precision medicine" refers to a medical model that proposes the customization of health care, with medical decisions, practices, and products being tailored

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to the individual patient. "Predictive medicine" entails predicting the probability of disease and instituting preventive measures in order to either prevent the disease altogether or significantly decrease its impact upon the patient, such as by preventing premature mortality or limiting morbidity. "Individualized medicine" represents a way of thinking that incorporates the concepts of genetic variation and notions of the evolutionary nature of disease and adaptive and maladaptive phenotypes in the context of the environment, while "personalized medicine" refers to a way of practicing medicine that is rooted in tests, technologies, and procedures not limited to genetic medicine. McInerney said that physicians get testy at the mention of personalized medicine because they believe they personalize all of their interactions with patients. "We have to be careful about how we couch these concepts for providers and for the public," he said, "for while it might be great to tell the public that the goal is to personalize their health care, clinicians think they are already doing this." He added that he believes it is unimportant for either health care professionals or the public to understand the distinction between genetics and genomics.

McInerney also distinguished between science, which proposes explanations for observations of natural phenomena, and technology, which proposes solutions to problems of human adaption to the environment (Biological Sciences Curriculum Study and Social Science Education Consortium, 1992). The principles of technology, as spelled out by the AAAS (1989), include

- Technology extends our senses, and often relies heavily on inference for interpretation.
- All technologies have unintended consequences.
- All technologies are fallible, and the consequences can be circumscribed or expansive.
- All technologies serve the interests of particular individuals, groups, or agencies.

McInerney said he believes that it is important to include these principles when constructing any program focused on scientific literacy because most people will never encounter the underlying science—in this case genetics—but they will encounter the technological manifestations of that science. In the same way, most people do not encounter the underlying scientific constructs behind the health care regimes they experience, but they do encounter the technology and should understand what the technology is about in a broad sense, he said.

Neuroscientist Sam Harris wrote, "There is an epidemic of scientific ignorance in the United States. This is not surprising, as very few scientific truths are self-evident and many are deeply counterintuitive. It is by no

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means obvious that empty space has structure or that we share a common ancestor with the house-fly and the banana" (Harris, 2010). McInerney's concern is that the counterintuitive nature of scientific knowledge does leave the public susceptible to explanations that are more intuitive, but wrong. He cited creationism and invoking an intelligent designer as an explanation for the way life is organized on the planet as examples.

The most important aspect of science literacy for the public, McInerney said, is the idea that science is a way of understanding and explaining the natural world and how that is different from other types of explanations. Science, he said, relies on evidence and on setting criteria for what counts as good evidence. Science relies on intellectual honesty and strives to be authoritative but not authoritarian. "These are extremely important concepts for understanding what science is and making decisions about what information you will act on," he said.

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3

The Intersection of Health Literacy and Precision Medicine

The workshop's first panel session featured three presentations that provided a further grounding for the rest of the day's discussions. Sara Van Driest, an assistant professor of pediatrics at Vanderbilt University School of Medicine, described what precision medicine is and how it has evolved over time, while William Elwood, the coordinator of the National Institutes of Health (NIH) Basic Behavioral and Social Science Opportunity Network in the NIH Office of Behavioral and Social Sciences Research (OBSSR), did the same for health literacy. Michael Wolf, a professor of medicine and the director of the Health Literacy and Learning Program at Northwestern University's Feinberg School of Medicine, then laid out some of the issues at the intersection of these two disciplines. A discussion, moderated by Ruth Parker, a professor of medicine, pediatrics, and public health at Emory University School of Medicine, and joined by Joseph McInerney, followed the three presentations.

PRECISION MEDICINE AND ITS EVOLUTION[1]

NIH defines precision medicine as an emerging approach for disease treatment and prevention that accounts for individual variability in genes, environment, and lifestyle for each person, Van Driest said. While the words *genes*, *environment*, and *lifestyle* may be the buzzwords found in the press

[1] This section is based on the presentation by Sara Van Driest, assistant professor of pediatrics at Vanderbilt University School of Medicine, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

releases, interviews, and grant applications, she said that she considered the key phrase in that definition to be "individual variability" because it represents the difference between precision medicine and medicine as usual.

Precision medicine is not new, and, in fact, it is already in play for some diseases, Van Driest said. The goal today, she said, is to expand the number of diseases to which precision medicine is applicable, increase the number of physicians who practice precision medicine, and grow the number of patients who can benefit from this approach. While she quoted William Osler as saying, "It is much more important to know what sort of patient has a disease than what sort of disease a patient has," to show that the basic idea of precision medicine is more 100 years old, she credited NIH director Francis Collins for the current emphasis that precision medicine is now receiving. Collins, when interviewed in 2015 about the Precision Medicine Initiative (PMI) and getting his own genes analyzed, said the analysis revealed he had an elevated risk for developing type 2 diabetes, which motivated him to lose weight, exercise more, and eat a healthier diet (Collins, 2015).

In her overview of precision medicine, Van Driest divided the subject into precision therapeutics, diagnostics, and prognostics—a division that she acknowledged was artificial. Concerning precision therapeutics, she said that while physicians treat one patient at a time, they decide on the treatments for those patients they are treating based on data from a population, such as the patients who had enrolled in a clinical trial to test the efficacy of a drug. Precision medicine represents a change in approach that looks to find markers in an individual that predict how that individual will respond to that drug. The question that doctors ask changes, Van Driest said. "Instead of asking which treatment is best for this disease," she said, precision medicine "asks which treatment is best for this patient." Many factors go into answering that question, she said. For example, drug effects can vary from patient to patient, reflecting such factors as the patient's age, sex, and ancestry; interactions with other drugs the patient takes; the environment; the exact diagnosis; and the patient's genetics, in particular as they affect drug absorption and metabolism and the individual's response to a particular drug.

One example of how precision medicine is being practiced today is the prevention of a second heart attack following the implantation of a stent to restore blood flow through a blocked coronary artery. After stent placement, the patients are prescribed an anti-platelet drug, such as clopidogrel, to inhibit clot formation. Every patient is treated with this type of drug because there are good population-based data showing the benefits of taking clopidogrel after receiving a stent (Sabatine et al., 2005). However, Van Driest explained, the benefit that a specific patient receives from clopidogrel depends on whether or not that patient has a specific variant

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

of the gene CYP2C19, which codes for a liver protein that metabolizes a number of drugs, including clopidogrel (Mega et al., 2010; Wallentin et al., 2010). Patients with certain variants of this gene are unable to metabolize clopidogrel and do not realize full clinical benefit from the drug. "Knowing this information about the genotype can help the selection of appropriate medicine because someone who has that high-risk genotype should get a different drug," Van Driest said. Her institution now tests for this specific genetic variant and uses the results to help the clinician and patient decide on the proper course of treatment. She explained that the presence of the high-risk genotype is not a "hard stop" because other factors, such as cost of the alternate drug are also important.

Van Driest said that this type of decision support increases the rate of using alternatives to clopidogrel among people who have the high-risk genotypes (Peterson et al., 2015). While this is an interesting story, she said, the important question is whether people getting the alternative therapies are living longer, healthier lives. "We do not have that answer yet," she said. "When you start subdividing your population by genotypes, it takes many thousands of people to see differences in results, and we have not done this long enough yet to know whether we have a real clinical benefit for patients."

Another example involves the use of precision diagnostics to determine the appropriate therapy for malignant melanoma, an aggressive form of cancer. In the past, Van Driest said, physicians based their treatment decisions on the microscopic features of a patient's specific melanoma. A new approach to classifying melanoma instead characterizes the genetic changes that drive the cells to be malignant. Using this approach, approximately 40 percent of malignant melanomas are found to have specific variants of a gene called BRAF, a discovery that led researchers to develop drugs that inhibit BRAF. For those melanoma patients with the clinically relevant BRAF mutations, BRAF inhibition produces dramatic positive results (Wagle et al., 2011), but as Van Driest explained, that is not the end of this story. Other cancers, such as hairy cell leukemia and certain thyroid cancers, also have these mutations. It also turns out that in most cases at least a few cancer cells evolve a way to circumvent BRAF inhibition, and the cancer returns. "Currently, these BRAF inhibitors are life extending but are not curative," she said. "The goal is to understand more of these molecular mechanisms so we can develop a curative therapy."

Van Driest then turned to a third area of precision medicine—precision prognostics. In the case of Francis Collins, he did not need tailored therapy for type 2 diabetes because he changed his behavior based on his genetic predisposition in order to prevent the disease from developing in the first place. Another well-publicized example of precision prognostics leading to action is the decision of actress Angelina Jolie to have her breasts and

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ovaries removed as a preventive measure after she was tested and found to have a BRCA1 variant.

Unfortunately, identifying genetic variants that can be used to inform precision prognostic is challenging because the genome is full of what Van Driest called "red herrings"—variants that look as if they should cause disease but perhaps do not. For example, she and her colleagues looked at two genes associated with arrhythmia in 2,022 individuals and found 122 rare variants that Van Driest said should cause problems. However, when the data were sent to three expert laboratories that were asked to determine which of the variants would be pathogenic, they agreed on only four of them (Feero, 2016; Van Driest et al., 2016). Then, when Van Driest and her colleagues examined the electronic medical records for these individuals, fewer than 5 percent of the individuals with these supposedly harmful mutations had any signs of arrhythmia in their electrocardiograms, which is the standard diagnostic test for arrhythmia. The conclusion that one of her colleagues drew was, "At a minimum, the language for describing variations' predictive ability should be carefully calibrated to convey, when appropriate, a probabilistic, rather than a deterministic, nature" (Feero, 2016).

Looking to the future, Van Driest said that the precision medicine community needs to start thinking like geographers, who, as she described it, are able to take different types of data, layer them, align them given the borders they know about, and draw useful inferences about the way the world works. Precision medicine is being fueled by the emergence of new types of data that are broader and deeper in their information content, and the field needs to somehow layer those data in a way that allows them to be integrated and provide comprehensive recommendations that while still probabilistic, rather than deterministic, will contribute to longer, healthier lives.

HEALTH LITERACY AND ITS EVOLUTION[2]

In 2000, Elwood said, health literacy was defined as the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions (Ratzan and Parker, 2000). By 2014 that definition had expanded somewhat to become the degree to which individuals can obtain, process, understand, and communicate about health-related information needed

[2] This section is based on the presentation by William Elwood, the coordinator of the NIH Basic Behavioral and Social Science Opportunity Network in the NIH OBSSR, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

to make informed health decisions (Berkman et al., 2010). The important feature to notice, Elwood said, is that health literacy is not simply about medical decisions. It involves myriad other issues such as knowing how to take a medication, how to be fit, how to monitor one's health on a smart phone, and how to use proper ventilation when cooking to avoid exposure to particulate matter and being able to discuss with a health care provider how the environmental effects of living near a freeway can effect personal health.

Since 2004, OBSSR has led three special program announcements on understanding and promoting health literacy. NIH has funded and administered more than 500 investigator-initiated grants aimed in this area, Elwood said. These programs, he added, have generated more than 9,600 health literacy publications indexed in PubMed. The health literacy literature operationalizes and places this topic in clinical, personal, and health-specific settings to demonstrate that while health literacy may be rooted in an individual's capacity to obtain, process and understand health related information, such capacity is constantly in flux given a person's milieu, the groups to which a person belongs, the type of setting, and the wellness and disease issues that person faces at any given moment. "A person's health literacy is dynamic," Elwood said.

When one reviews the health literacy literature, Elwood said, several themes emerge, including

- Disease-specific contexts such as Alzheimer's disease, diabetes and its sequelae, cancer or HIV treatment adherence;
- The setting, context, and situation in which health information is exchanged, such as in medical clinics, emergency rooms, pharmacies, and schools;
- Literacy in target population groups, such as African American health literacy or Native American health literacy; and
- Wellness issues, such as food portion control, sufficient weekly physical activity, age- and time-appropriate vaccinations, and timely cancer screenings.

The literature also emphasizes communication between individuals and through mediated means such as family discussions, shared decision-making processes, and negotiation processes to obtain informed consent or research participant consent.

Health literacy is starting to benefit from the development of research models, including the cultural and linguistic tailoring of interventions, social-network analyses, and wait-listed, randomized controlled trials. The field is also seeing the development and testing of new and existing tools to measure health literacy, to test whether health information is sufficiently

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clear so that typical patients are likely to understand that information, and to assess the reliability and validity of tests across different patient populations, different types of health care providers, and different types of health care organizations.

Another theme in the literature is the hypothesis-generating research being conducted in the health literacy field. One example Elwood cited was of a qualitative study involving general practitioners, patients, and pharmacists that aimed to test different approaches for improving adherence to prescription medications among people with chronic conditions. Another study tested different types of conversations to determine which are most effective at identifying the life-sustaining treatments that Chinese-American elders envision before they become unable to speak for themselves (Fung et al., 2010).

Based on his review of the health literacy literature and the outcomes of the projects NIH has funded, Elwood concluded that health literacy is a dynamic state of being that depends on individual circumstances, experiences, mental and physical status, and even on the biophysical processes going on in the body. Communication is a substantive component of anyone's health literacy, for communication is how people convey their needs, transmit information, and seek recognition that the meaning they have corresponds to that held by others. Health literacy research, Elwood said in closing, studies communication, thought, and other socio-behavioral processes that facilitate knowledge, abilities, and skills to obtain and maintain optimal health and well-being.

THE PRECISION MEDICINE INITIATIVE AND WHY HEALTH LITERACY MATTERS[3]

There are multiple ways in which precision medicine and health literacy intersect, Wolf said. One relates to how the benefits of precision medicine will be realized in the clinical setting in the future. At this intersection, the challenge will be to transmit information that results from the study of genomics between the health care provider and the patient in a way that engages the patient and enables the patient to take action. The second intersection, which Wolf, Suzanne Bakken, and Ruth Parker discussed in a commentary (Parker et al., 2016) and which was the focus of Wolf's presentation, concerns the role health literacy will play in ensuring that the

[3] This section is based on the presentation by Michael Wolf, a professor of medicine and the director of the Health Literacy and Learning Program at Northwestern University's Feinberg School of Medicine, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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PMI can successfully recruit 1 million Americans who will be fully informed about the research in which they will engage.

Referring to the appropriation of $215 million to the PMI for fiscal year 2016 as a "significant event," Wolf said that paying attention to health literacy throughout the life of this project will be important in order to avoid generating data that cannot be used. He said that while he is enthusiastic about the effect that health literacy can have on the PMI, he is realistic enough to recognize that there are challenges the field will face as it tries to impart what it has learned with the aim of providing value to the PMI and maintaining participation rates throughout the duration of the project. The PMI, explained Wolf, is asking the 1 million participants to agree to a long-term relationship, to undergo a research medical exam and prescription assessment, to have their blood drawn, to complete health surveys, to use and share environmental exposure and lifestyle information using mobile technology, and to share information in their electronic health record. "When you put these all together, this is a lot to ask of the participants," Wolf said.

In his view, the health literacy challenges start with building trust in the project and the researchers involved in the PMI and helping potential participants understand the PMI's purpose and its near- and longer-term value. The next challenge will be to ensure participants are giving truly informed consent—that they know precisely what they are signing up for when they agree to participate in the PMI. How successfully these first two challenges are addressed will dictate the quality of the data that the project will get from the participants because many of those data will come from patient-reported outcomes and will thus depend on the ability to retain participants in the study. Wolf's concern is that if trust and understanding have not been established and if participants are not fully aware of why they are participating and what is required of them, there will not only be attrition but uneven attrition across the different subpopulations that the PMI wants to enroll and follow.

The final health literacy challenge will be to continually inform participants about what the PMI is learning and to convey to them the value of being part of this national effort. "Can we convey the PMI's purpose, importance, and value for community and for the individual participant?" Wolf asked. While some may participate for altruistic reasons—in particular, to contribute to the formation of knowledge—Wolf said that this can be a difficult concept to grasp. "I think we will find many people are looking for immediate or more contextualized value for being in the study." He also noted that this challenge is something the research and health literacy communities have been working on for three or four decades. One piece of addressing this challenge, he said, is to help the providers and clinicians involved in this study convey that value to their patients.

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As Wolf mentioned with regard to the participation challenge, the health literacy field is not starting from scratch. Three decades of health literacy research has shown repeatedly that many people, especially those with limited health literacy, misunderstand health information on prevention, disease etiology, treatment, and research consent (Ownby et al., 2015). In his opinion, Wolf said, genetics may be among the most complicated subject areas for the general public to understand—an opinion that research appears to support (Erby et al., 2008). Wolf also pointed to research from Michael Paasche-Orlow (Paasche-Orlow et al., 2003; Sugarman and Paasche-Orlow, 2006) showing that the readability and understandability of consent forms was low, and he described a 2013 follow-up on which he and Paasche-Orlow collaborated showing that the situation has not changed much in the intervening decade since those first studies were published. The advent of the Health Insurance Portability and Accountability Act, or HIPAA, has only made consent more complicated, he added. "We continue to not recognize that it is a hard and abstract challenge for people to grasp the value and need to participate, and those with low health literacy are even less likely to participate," he said.

In fact, Wolf said, research has shown repeatedly that for many reasons, the level of health literacy cannot be separated easily from demographic and socioeconomic factors (Kressin et al., 2000) and that most psychometric tests in wide use today have not been appropriately validated for use among audiences with lower levels of literacy (Wolf et al., 2005). Research has also shown that retention in cohort studies is challenging and that participants with limited health literacy are at greatest risk for attrition (Rabbitt et al., 2004). Wolf also noted that individuals with limited health literacy have lower rates of health and mobile technology use, including the use of portals to access electronic health records (Bailey et al., 2015; Smith et al., 2015). All of these issues intersect with the goals of the PMI, Wolf said.

With regard to psychometric tests, Wolf noted that the research field has begun to recognize that how someone responds to a health questionnaire depends on that person's health literacy. "What that means is that how someone with low health literacy understands and responds to a question may be vastly different than how a person with adequate health literacy skills responds to the same question," Wolf said. "While this should not come as a complete surprise, it does mean that the results may be invalid."

Addressing these challenges, Wolf said, requires exercising some common sense and taking time to think about these challenges before diving right into the research process. "If we are going to make such a large investment in funds to have this incredible cohort, and to move this unprecedented project forward, we just want to make sure it gets down right," he said. Doing it right, as he put it, requires first operationalizing the mean-

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ing of a "patient-powered" study, a phrase that appears often on the PMI website but whose meaning Wolf said he has no clear understanding of. Next, it is important to test the clarity and effectiveness of any recruitment messages before unveiling them to the public. "If we cannot articulate and explain the value of being involved in this study, then we can expect to see the problems I just mentioned," he said.

It will be important, he added, to recognize the need for a sizable investment in "shoe leather strategies" to ensure that communities in medically vulnerable and underserved areas in the country, where low health literacy is likely to predominate and where participation rates are historically low, are not underrepresented in the PMI Cohort. The problem, however, is there are not many success stories in the literature regarding recruitment from these vulnerable and underrepresented communities.

To be successful, Wolf said, the PMI will have to validate any instruments in the health survey to make sure that all concepts can be well understood across all levels of health literacy. It will also have to consider multifaceted approaches to retaining people in the study over the long term and to properly train and perhaps even retrain participants in the use of mobile technology (Chan et al., 2014). As a final comment, Wolf said he wondered if assessing health literacy should be a component of the PMI. "If we know this is going to be a factor that could lead to disparity, then we need to measure it to make sure that there are no differences," he said.

DISCUSSION

Ruth Parker started the discussion by summarizing the important messages she had heard from the workshop's first four speakers. Joseph McInerney spoke about how genetics content relates to an ability to understand life, and Van Driest stressed that precision medicine requires probabilistic rather than deterministic thinking. Given what a big challenge numeracy is in the United States, Parker said she was concerned that many Americans will find probabilistic thinking, which carries the connotation of statistics and risk and probability, to be a significant challenge. Elwood, she continued, spoke of the public good that comes from health literacy research and of the commitment of funders to continue enabling the research that will improve the communication of health information to taxpayers. Concluding, Parker said that Wolf had challenged the health literacy community to get involved in the PMI and had noted the problems that would likely arise should health literacy not be an important consideration in the PMI. She said that she agreed with Wolf that measuring health literacy should be included in the PMI but added that she was worried that the "train has already left the station."

She then asked the panelists for their ideas on how best to convey

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to the public the benefits it stands to gain from participating in the PMI. McInerney said he would emphasize the dual benefits to the community and individual. "There are contributions that one can make by participating in this research that may benefit the individual involved," he said, "but we hope the prospect of benefiting the larger community is much greater." He also said that he wants potential participants to understand the potential of the PMI to produce new knowledge that will integrate information about biological variation with what is known about human physiology to generate new insights about health and disease, with an emphasis on health that equals the emphasis on disease. In addition, he said it is important to explain uncertainty to potential participants.

Van Driest said she would like to see the PMI community engage with meteorologists to help with developing explanations for uncertainty, prediction, and probability and would like for the research community to think about how to explain the idea of a confidence interval in a way that potential participants can grasp. Elwood said he would like to see an effort aimed at encouraging potential participants to ask questions and speak up when they do not understand a concept presented to them, while at the same time empowering researchers and practitioners to encourage the public to ask more questions. Wolf provided a similar response. "I want to find ways to empower the public to ask questions, to get engaged, to not accept confusion," he said. Toward that end, he said he believes there is a need to find avenues to insert the public into the research process to a greater extent than has been tried before with other large-scale projects so that the public does not just have a voice but actually helps in some regards to determine the PMI's direction by providing real-time feedback that is assessed over time, not just in a cross-sectional manner.

Linda Harris from the U.S. Department of Health and Human Services asked when the PMI was going to start. Van Driest replied that the initial 1-year effort to develop pilot studies, communication tools, and recruitment strategies began in late February 2016.

Cindy Brach from the Agency for Healthcare Research and Quality said that she thought the term "precision" presents a challenge because it implies an illusion of certainty, which runs counter to Van Driest's emphasis on probabilistic rather than deterministic information. Brach then asked the panel to comment on the importance of genetic information relative to other types of information that could be connected to health, such as environmental impacts. Van Driest said the PMI is focusing on genetics because it is the area of science currently providing the most new data to drive research. "We are starting to routinely collect genetic or genomic information as part of clinical trials and to be able to flesh out the effects of different genotypes within study populations," she said. The research goal of the PMI, she added, is to use genetic information as a model for how to

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collect, analyze, and apply data about other factors, such as environmental impacts, so as to make medicine more precise. Van Driest also questioned whether 1 million people would be a big enough population to sort out all of the contributions to health and disease from all of the factors that could be involved.

The long history of genetic counseling also argues for a focus on genetics, said McInerney, who added that there is a significant literature from the genetic counseling community on how to communicate uncertainty and probability. "We should look to that literature, and we have some genetic counselors in the room who can help us understand that," he said. Referring to Brach's comment about emphasizing genetics versus environmental factors, McInerney said he hopes that PMI does not reinforce the age-old notion of genes versus environment. "If there is an underlying message from the Precision Medicine Initiative, perhaps it can be that it is always genes *and* environment," he said.

Elwood commented on the importance of looking beyond specific racial and ethnic target populations because of the genetic mixing that has occurred in the United States. As an example, he noted that while Tay-Sachs syndrome occurs predominantly in descendants of Ashkenazi Jews, the Jewish diaspora has led to genetic intermixing in the United States between Jews and non-Jews. "There could be a fifth-generation descendant of Ashkenazi Jewish people who does not identify as Jewish at all, and yet it is through precision medicine that that person might get picked up as vulnerable to Tay-Sachs," Elwood said. "This is an example of gene–environment interaction in terms of the social environment and identity and part of what makes us uniquely American." Precision medicine, he added, can provide insightful data because ethnic and racial identity is such a fluid construct in the United States.

With the payoff from the PMI coming in the future, Terry Davis from the Louisiana State University Health Sciences Center asked what messages the public should be getting today about this initiative. McInerney replied that the message should be that there may be some benefit to the individual, but that the greater hope is that the PMI will provide a great deal of information that will benefit everyone. In his opinion, he said, that is the central message inherent in all biomedical research, whether it is a specific clinical trial for a new colon cancer therapy or the PMI. Van Driest said she thought that an important message would be one explaining that the promise of precision medicine is really about potential, not a guarantee. As an example of what she is worried might happen, she referred to comments she hears about the Human Genome Project not producing great advances for the public—which is not true, she said, but which is the public's perception. She also said she thought it important to spread the message to clinicians and patients that genomic information is already being used to

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understand individual response to some commonly prescribed medications. "Communicating those kinds of successes will help motivate recruitment and retention," she said. Another important message to convey, she added, is that the PMI will help provide a better understanding about how individual variation is important to human health. "It is important to send the message that if I only study people that look, act, and behave like me, I am not going to learn anything important," Van Driest said.

Wilma Alvarado-Little from Alvarado-Little Consulting asked if there was any consideration being given to the importance of knowing one's family history, which can be a challenge for first-generation immigrants and refugees in particular. Van Driest said that there is some good work ongoing on how to take, document, and share family histories. One aspect of this is to empower patients when they are uncertain about family medical history to call a relative right then who might have that information. As far as how that was being woven into the PMI, Van Driest said she was not sure, and neither was McInerney. McInerney did note, though, that the American Society of Human Genetics is working to educate health care professionals about better approaches to taking a family history and is also working with the insurance industry to promote the idea that primary care providers should be reimbursed for the time needed to take a good family history. "We know that most primary care providers are not going to take a three-generation family history the way a trained geneticist would," he said. His organization is also working to educate primary care physicians about certain red flags that come up in family histories, such as the early onset of disease and the presence of multi-focal disease, both of which can indicate a significant genetic contribution. He also said that there are projects under way to help individuals collect their family histories before they go to the doctor and that electronic health records need to incorporate family histories in a more consistent manner.

In the last comment in the discussion session, Ernestine Willis from the Medical College of Wisconsin expressed her concern that the PMI might not truly be community-based, patient-powered, participatory research. She also said she hoped that the failures of the National Children's Study would emphasize to those leading the PMI how critical it is for the research community to be fully committed to returning data to the community and sharing the knowledge gained through the public's participation in the project.

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4

Health Literacy in Precision Medicine Research

The workshop's second panel session comprised three presentations on different ways in which health literacy plays a role in precision medicine research. Suzanne Bakken, the Alumni Professor of Nursing and a professor of biomedical informatics at Columbia University, spoke about the recruitment of research subjects and issues of privacy and consent. Consuelo Wilkins, the executive director of the Meharry-Vanderbilt Alliance, discussed engagement and retention. Paul Appelbaum, the Elizabeth K. Dollard Professor of Psychiatry, Medicine, and Law and the director of the division of law, ethics, and psychiatry at Columbia University, addressed the reporting of results. Marin Allen, the deputy associate director for communication and public liaison and the director of the Public Information Office at the National Institutes of Health (NIH), and Benjamin Solomon, the chief of the division of medical genomics at Inova Translational Medicine Institute, then provided their reactions to the three presentations. Their comments were followed by an open discussion moderated by Laurie Myers, the director of global health literacy at Merck & Co., Inc.

HEALTH LITERACY, INFORMED CONSENT, AND COMMUNICATING WITH RESEARCH PARTICIPANTS[1]

The Washington Heights/Inwood Informatics Infrastructure for Comparative Effectiveness Research (WICER) project is aimed at developing the

[1] This section is based on the presentation by Suzanne Bakken, the Alumni Professor of Nursing and a professor of biomedical informatics at Columbia University, and the statements have not ben endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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informatics infrastructure for comparative effectiveness research, and, as Bakken explained, it can provide a foundation for the Precision Medicine Initiative (PMI). WICER was inspired by the Framingham Heart Study and shares a focus on cardiovascular disease with that study, but it was conducted in a largely Latino immigrant community in the northernmost section of Manhattan with significant health disparities. A unique feature of this study, Bakken said, was the availability of data from a variety of sources, including Columbia University Medical Center, the Visiting Nurse Service of New York, a skilled nursing facility in the area, and a community-wide survey. The initial goals for the project, Bakken said, were to develop the information infrastructure to pull these data elements together in a way that produces a true understanding of the community's health, to make those data available via a browsing tool that helps researchers understand the needs of the community, and to use the resulting knowledge to improve the health of the community. Bakken extended those goals to develop approaches for giving the data and information gleaned from it back to the individuals who had generated the data and to the community at large. Two studies conducted under the WICER umbrella, one dealing with consent and the other with ways of sharing a participant's tailored research results, are of particular relevance to precision medicine, Bakken said.

Discussing the first of these, she said that the extensive literature on consent shows that members of racial and ethnic minorities are less likely to consent to participate in research for a variety of reasons. WICER's cohort of 2,271 people was 97 percent Latino, primarily Dominican; was 72 percent female; and had a mean age of 49.6 years. One-third of the cohort had less than an eighth-grade education, and another third had less than a high school education. About 80 percent of the cohort members were immigrants, and most had insurance through Medicare or Medicaid. "When you look at those kinds of socioeconomic factors and expected health literacy level," Bakken said, "we know these are individuals who typically have been underrepresented in research in general, let alone research that would include collection of genomic information."

Bilingual community health workers were used to collect the data, and snowball sampling—a non-probability sampling technique in which existing study participants recruit future subjects from among their acquaintances—was used to take advantage of the social networks of the study subjects and of the community health workers. Bakken said that this was an expensive, but critical way to collect data from those not typically represented in research, and that 90 percent of the data were collected in Spanish. The three dependent variables in this study were a willingness to have survey data linked with electronic health record data, a willingness to provide bio-

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specimens for long-term storage and use, and a willingness to be contacted for research by investigators outside of the WICER team.

More than 96.3 percent of the WICER cohort consented to link their survey data with their electronic health record data, and 87.5 percent said yes to being contacted by someone outside of the research team. The lowest level of consent, 53.2 percent, was for long-term storage of biospecimens, which Bakken said was better than expected based on formative work that she and her colleagues had conducted in the community. "We were pleased that by working on building trust with the community, involving the community health workers, using snowball sampling, and other steps we were able to get that level of biospecimen participation," she said.

With regard to specific correlates of consent, Bakken said that having Medicare or Medicaid increased the odds of consent to biospecimen collection but decreased the odds of agreeing to data linkage. Males were less likely to consent to being contacted again for participation in future research. The only variable that was significant to all three types of consent was health literacy, which turned out to be the most important variable when controlling for all the other variables.

Turning to the second study on information sharing with WICER participants, Bakken said that the approach in that one was to apply some of what she and her colleagues had learned in their work on participatory design of infographics (Arcia et al., 2015, 2016) to genomics and other types of results reporting. She and her colleagues formed 22 focus groups, most of them conducted in Spanish, involving 102 research participants who were shown multiple designs of infographics (see Figure 4-1). One finding was that when working with these populations, giving data in the absence of context is meaningless. "If the visualization did not convey context, the group would create the story that went with the data," Bakken said. She and her colleagues are currently conducting comprehension testing, which Bakken said should allow the team to create consumer-facing and provider-facing applications.

One of the most complex designs for discussing blood pressure (see Figure 4-2) ended up being the preferred design, Bakken said, and feedback from the group revealed that instead of simply being told whether their blood pressure was high or not, the people preferred to receive additional context such as information about the risks associated with hypertension. In presenting the risks, her team used both common language and professional language. "We wanted to make it easy to understand, but we felt it was important that they be able to communicate with their clinicians who might use some of the professional language," said Bakken, who also showed an infographic that communicated results and actions to take to improve those results (see Figure 4-3).

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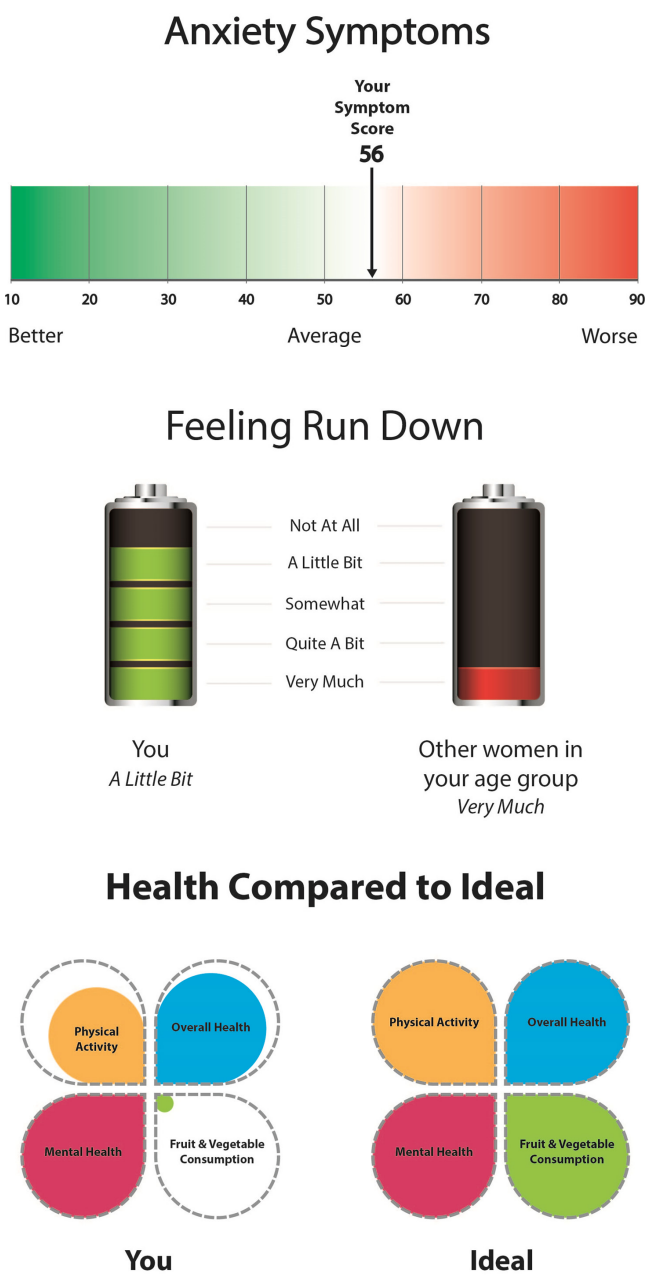

FIGURE 4-1 Some test infographics.
SOURCES: Bakken slides 13, 14, and 15.

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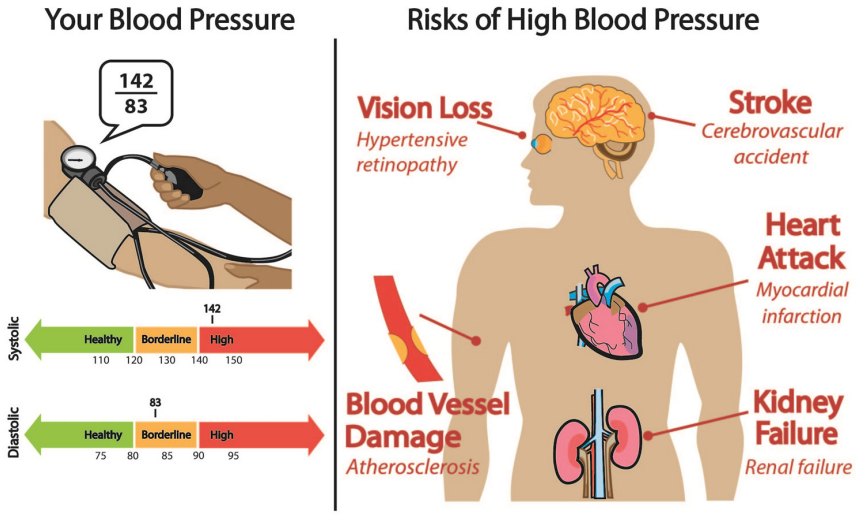

FIGURE 4-2 Preferred design for conveying information about blood pressure.
SOURCE: Bakken slide 16.

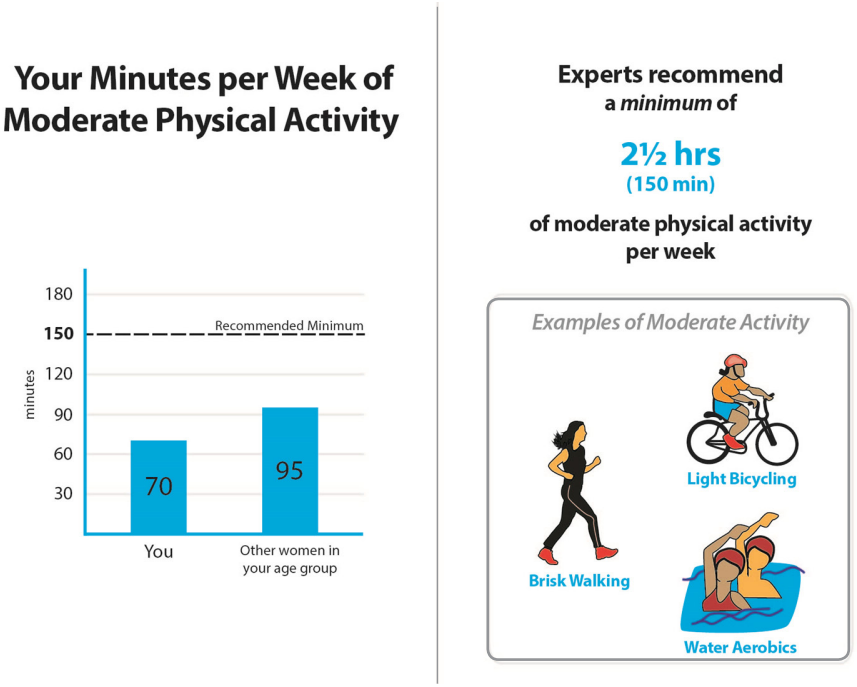

FIGURE 4-3 An infographic to display results and actions to change those results.
SOURCE: Bakken slide 17.

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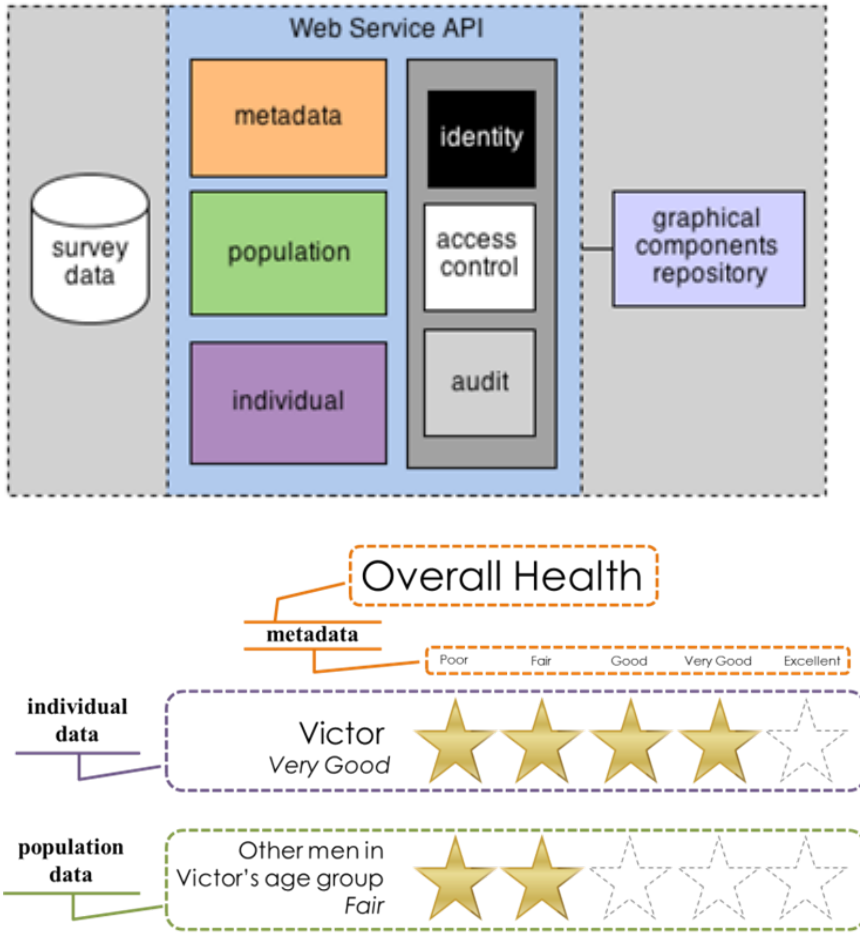

FIGURE 4-4 The EnTICE[3] Framework and sample infographic.
NOTE: API = application programming interface.
SOURCES: Bakken slide 18 (Arcia et al., 2015).

To create these tailored infographics, Bakken's team developed the EnTICE[3] (Electronic Tailored Infographics for Community Engagement, Education, and Empowerment) framework (Arcia et al., 2015) (see Figure 4-4). She and her colleagues have now presented these graphics at six town hall meetings, all of them conducted in Spanish, and have returned the survey data collected in their study to the participants. Participants at the town hall meetings had the opportunity to ask questions and were engaged in discussions of WICER in terms of the PMI Cohort. They were also given the opportunity to provide a biospecimen. As Bakken said she expected,

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when the discussions highlighted the importance of the PMI to people who come from the Dominican Republic, those attending the town hall meetings were quite enthusiastic to participate.

In closing, Bakken said that there are multiple aspects of health literacy that affect precision medicine in general and in assembling cohorts in particular. "I think it is vital that we combine health literacy with the principles of engagement with research participants," she said. Advances in informatics can provide a foundation for tailored approaches, but it will be critical to test messages before introducing them to various target populations. "We cannot just decide what might work," she said. She also said that her team will soon make the EnTICE[3] framework and their infographic designs available as an open-source software package and that she is eager to see how well they can be used or adapted for use in other communities.

ENGAGEMENT AND RETENTION[2]

Engagement is bidirectional and has to have an element of co-learning to be successful, Wilkins said; it is not the same thing as outreach, which is unidirectional. There are many different approaches to engagement (Cunningham et al., 2015) (see Figure 4-5), and the best strategy to pursue depends on the type of input and information needed. Some strategies, she explained, are appropriate when the goal is to get participants involved for a limited time, such as in a one-time survey, online polling, semi-structured interviews, or focus groups. Others, where the participants are treated more like equals and require some comfort level to "sit at the table," are required for a program as large, comprehensive, and long-term as the PMI. This second group of strategies involves community stakeholders in advisory and governance roles, as members of the research team, and in some cases as co-principal investigators.

This multi-tiered strategy has been operationalized in a single project organized by the Mid-South Clinical Data Research Network (CDRN) that involved more than 5,000 people at different levels of engagement; the project was part of a larger effort to recruit three cohorts totaling more than 20,000 individuals for studying obesity, coronary heart disease, and sickle cell disease. Wilkins said that when she proposed engagement at this scale, many had their doubts that it would succeed. In fact, it did succeed and the result, she said, is a system and network that is more likely to engage and involve people over the long term. She added that this engagement

[2] This section is based on the presentation by Consuelo Wilkins, executive director of the Meharry–Vanderbilt Alliance, and an associate professor of medicine Vanderbilt University School of Medicine and Meharry Medical College, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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FIGURE 4-5 The continuum of community engagement in research.
SOURCES: Wilkins slide 2 (Cunningham et al., 2015).

strategy is likely to be important for retention as well. "If you have not thought about retention when you are designing the program, there is very little chance that you will meet your retention goals at the end," she said.

One key lesson about engaging stakeholders that emerged from this project is to get them involved early and to engage multiple stakeholders (Wilkins et al., 2013). "You cannot just have one person at the table who is not part of the research team and call that engagement," Wilkins said. It is also important, she said, to be deliberate in the way that stakeholders are engaged, to take the time to educate stakeholders, to give stakeholders the time to become informed before asking for their input and advice, and to provide feedback to them. It is also important to clearly define roles and expectations, to make the experience bidirectional, and provide opportunities for co-learning, as she had already mentioned.

As Wilkins and her colleagues at Vanderbilt began preparing for what was to become the PMI Cohort Program Pilot, they thought it might be important to understand what their patients and community thought or knew about precision medicine and its importance, and to do so they distributed a survey through the Vanderbilt patient portal. Wilkins explained that the demographics of those who responded to the survey were not representative of the Vanderbilt population, but rather of those who most often used the patient portal. Nonetheless, the survey results provided useful information about how little even this well-educated subset of Vanderbilt's community knew about precision medicine or pharmacogenomics (see Figure 4-6). They also showed that for all races and ethnici-

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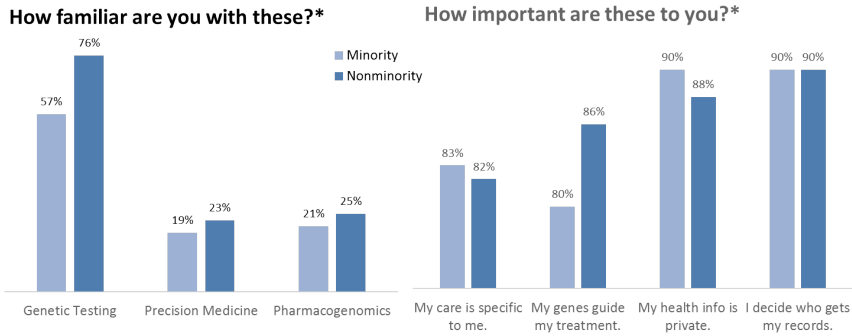

FIGURE 4-6 Survey results on the familiarity and importance of precision medicine. NOTE: * Scores based on 5-point Likert scale. Participants who chose "Moderately" and "Extremely" were included in the above scores for each category. SOURCE: Wilkins slide 6.

ties the concepts underlying precision medicine were important, as were privacy concerns.

The survey also posed questions about health literacy, numeracy, and willingness to participate in biomedical research. Caucasians and African Americans had similar levels of health literacy, though there was a bigger difference between these groups when it came to numeracy. Wilkins said she was surprised by the low level of numeracy among this group of well-educated individuals. The survey results also showed that race and levels of health literacy and numeracy all predicted willingness to participate in research, though the numeracy level was the biggest predictor. From these results, Wilkins concluded that it will be important in an era of precision medicine to develop effective methods for communicating risk, probability, and other concepts that depend on numbers rather than just words.

Wilkins then reviewed the engagement plan she will be leading as part of the PMI Cohort Program Pilot (see Figure 4-7). Over the course of 1 year, this initiative will prototype the PMI Cohort Program website, consent form, data tools for collecting basic information, and the participant portal, and it will also pilot several strategies for recruitment and retention as well as advanced data collection tools. To test methods for achieving the broad engagement needed to assemble the PMI Cohort, she and her colleagues will be using a community engagement studio model they developed that allows people to come to the table and provide input on research at any stage or phase of research. She and her colleagues will be doing user testing on a number of different models (Heller et al., 2014; Paskett et al., 2008; Yancey et al., 2006), Wilkins said, and they will then launch them as pilots to get broader review.

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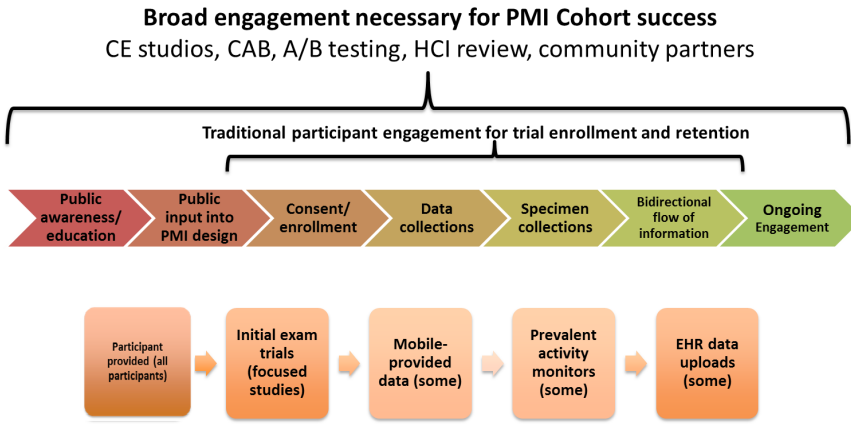

FIGURE 4-7 Vanderbilt's PMI Direct Volunteers Pilot Preparatory/Prototyping Initiative.
NOTE: CAB = community advisory board; HCI = human computer interaction; PMI = Precision Medicine Initiative.
SOURCE: Wilkins slide 8.

In the first week after the PMI Cohort Program was announced, Wilkins said, she and her colleagues had already identified 17 priority populations they will need to engage in the PMI Cohort Pilot Program. The presumption, she said, is there will be people who are knowledgeable about precision medicine—some of whom have family histories of genetic conditions and others who are just interested—and who will immediately want to participate. There will be other groups of people, however, who have no knowledge of precision medicine, who have never participated in research, or who are concerned, distrusting, and weary of the process in general. "We will have to have boots-on-the-ground approaches to engaging them," said Wilkins, who added that of those 17 priority populations, several are composed of racial and ethnic minorities and one consists of people with limited health literacy. She emphasized that members of each of these 17 priority populations will be seated at the table and will provide input on the content and strategies and participate in user testing.

From the early work they have done on prototyping the portal and on methods of delivering data back to the participants, it is clear that those who have lower health literacy are not able to understand all of the great deal of information they are presented with. Wilkins said it will be critically important to find a way to return value to all of the participants if the goal is to retain them in this research over the long term. "What is valuable to someone with a genetic condition in their family is not going to be relevant

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to most people, especially those who have limited health literacy," Wilkins said. "Thinking about how to address those differences and provide something of value to those with low health literacy so they remain engaged in the work will be important."

Wilkins concluded her remarks by noting that engaging populations of interest will require tailoring various approaches to meet the needs of those specific groups. "When we are thinking about this large group of 1 million people, we need many strategies for engaging individuals," she said. With regard to retention, she said the key will be to build relationships and trust, and for some of these populations, especially those that have been marginalized and disenfranchised from the research community, building relationships and trust will take time and additional resources.

MAKING DECISIONS ABOUT REPORTING RESULTS[3]

One issue with returning the results of gene sequencing to individuals who participate in the PMI Cohort—and eventually to all patients—is that a whole-genome sequence has the potential to yield secondary findings about a participant's genetic makeup that may have profound implications, Appelbaum said. Studies of participants' preferences, he noted, have found consistent interest in knowing about these secondary findings, particularly if they are clinically actionable. In addition, a growing number of federal agencies and expert panels have recommended that at least some secondary findings from genome sequencing be made available to participants. The logic of returning these results to participants is that those data may include information that is medically actionable or, if not medically actionable, is personally actionable, perhaps in how someone structures his or her life or finances. The carrier status of a recessive condition could have reproductive implications, and pharmacogenomic information could have implications for current or future drug responses. Given these possibilities, Appelbaum said, the challenge is to engage with patients in a way that helps them make meaningful decisions about the information they want or do not want to receive.

Several years ago, Appelbaum and his colleagues surveyed genetics researchers who had presented their research at the American Society of Human Genetics meeting or who had grants focused on genome sequencing (Klitzman et al., 2013). As part of the survey, they asked 234 genomic investigators what information they thought should be shared with partici-

[3] This section is based on the presentation by Paul Appelbaum, the Elizabeth K. Dollard Professor of Psychiatry, Medicine, and Law and the director of the division of law, ethics, and psychiatry at Columbia University, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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pants during the informed consent process before the participants made a decision about the return of secondary findings. The researchers also asked what benefits (see Table 4-1) and risks (see Table 4-2) should be disclosed. The survey found, Appelbaum said, that more than half of the researchers, and in many cases more than three-quarters of the researchers, endorsed returning all of this information to research participants.

Appelbaum and his colleagues then asked the researchers what else should be disclosed, and many researchers endorsed returning information that might have implications for the participants' relatives or that might affect family relationships. Nearly all the researchers mentioned the potential importance of participants sharing information with family members, and some two-thirds of the researchers thought it was important to talk with the participants about how secondary findings with implications for relatives would be handled if the participants became incompetent or died. Other topics the researchers thought should be addressed with participants included the possibility that subsequent studies on banked biospecimens could return secondary findings later in life, data security procedures, and

TABLE 4-1 Benefits That Should Be Disclosed from Secondary Findings of Genome Sequencing

	Researchers (n = 241)		Participants (n = 20)	
Benefits	%	Count	%	Count
A treatable disorder might be identified	94.5	225	95	19
Prophylactic measures may be available to prevent some disorders	84	200	95	19
Modern reproductive techniques (e.g., preimplantation genetic diagnosis) may allow carriers to have children with minimal risk of specific disorder	63.4	151	85	17
Knowing pharmacogenetic status can increase the likelihood of efficacy of some medications and reduce the change of adverse reactions	67.6	161	90	18
Knowing one's propensity for developing particular condition can help with life planning	57.6	137		
Knowing whether they carry a disease mutation can relieve anxiety for some people			85	17

SOURCES: Appelbaum slide 5 (Klitzman et al., 2013).

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TABLE 4-2 Risks That Should Be Disclosed from Secondary Findings of Genome Sequencing

	Researchers (n = 241)		Participants (n = 20)	
Risks	%	Count	%	Count
The risk of false-positive findings	94.5	225		
The risk of false-negative findings	85.7	204		
The findings may be wrong			90	18
Possible negative psychological responses	82.8	197	90	18
The danger of falsely concluding from a negative result that they are not susceptible to a result, e.g., because of limitations of the testing and existing knowledge	78.6	187	90	18
Possible confusion resulting from the ambiguity of the results	76.1	181	80	16
The possibility that the interpretation of the findings might be different in the future as more knowledge is acquired	85.7	204	90	18
The risk of stigma/discrimination (e.g., in insurance) if information about their test results becomes known	71.8	171	90	18
Possible need for further testing, counseling and follow-up, and the unavailability of fund from the study to pay for it	84.9	202	85	17
Risks to data security and confidentiality	53.4	127	85	17

SOURCES: Appelbaum slide 6 (Klitzman et al., 2013).

the penalties for researchers failing to protect or possibly use a participant's genomic information. Other issues that researchers suggested should be flagged for participants were possible paternity-related findings or findings of incest and also whether the participant's choices could be overridden in certain circumstances, particularly when those secondary findings turn out to be actionable. More than three-quarters of the researchers believed that participants should give consent at the time of initial participation for potential contact at some future date and also should consent to placing secondary findings into the participant's electronic health record.

Taken together, these information choices represent a great deal of information that must be conveyed to participants, particularly in the context of getting consent to participate in a study in the first place. When asked about how much time they would be able to spend on this topic, the researchers said they believed they could allocate only 15 to 30 minutes

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for this portion of the consent process, which Appelbaum said creates a dilemma. "Cramming all of that information into 15 to 30 minutes is either not possible, or the information may be given so quickly that the likelihood that someone would understand would be about nil," he said.

The solution to this dilemma is to develop new approaches to getting consent, Appelbaum said, and based on the survey responses, interviews, and a literature review, he and his colleagues identified four potential models to consider (Appelbaum et al., 2014). The first was the traditional model of getting consent upfront: participants are given all of the information at once while consenting to participation in the underlying research, they sign a consent form, and the process is over. The advantages of this model are that it resembles the traditional consent process familiar to the research community, the participant receives all of the information about potential secondary findings prior to deciding whether to participate, and the participant can choose which the types of secondary findings to receive or whether to opt out of receiving these findings. The potential disadvantages of this model are that it adds time and information to an already lengthy and complex process and the participants' preferences may change after the initial consent.

The second model uses a staged consent process, in which there is a brief mention at the time of initial consent of the potential for secondary findings and the potential for recontact, and there is a second, more detailed consent process if reportable results are found. The advantages of this model are that it reduces the time spent discussing secondary findings during the initial consent for the large number of people who are not going to have secondary findings, and it allows more detailed and specific information to be provided later to those who do. This model also allows the participant to make decisions about secondary findings closer to the time that they can receive those findings—thus allowing them to take their current circumstances into account when making the decision—and it also allows them to maintain choice about which types of secondary findings to receive or whether to opt out altogether. The potential disadvantages include the costly and burdensome need to follow up with participants and the potential that recontacting a participant may reveal unwanted information about a secondary finding and negatively affect the participant. "Think about how well you would sleep after a discussion in which you were told there may be information you may or may not want to know," Appelbaum said. Finally, the participant's decision to enroll in the underlying research project would be made without full information about the potential return of secondary findings.

The third model, mentioned by some of the researchers, was the mandatory return, one-size-fits-all model. In this model, which is based on the original American College of Medical Genetics and Genomics recom-

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mendations on secondary findings in clinical genomic testing (Green et al., 2013), participants consent to the return of specific categories of secondary findings at the time and as a condition of enrollment. The advantage of this approach is that it simplifies consent at enrollment—the participant receives information only about selected secondary findings and does not have to choose which findings to receive. This model also clearly defines the researchers' obligations to return predetermined secondary findings, and the participant maintains a degree of choice about whether to participate in the study. The potential disadvantages include restricting the participant's choices—they cannot choose which findings to receive and cannot refuse to accept the designated findings—and this lack of participant choice could become a disincentive to enrolling in genomic research. In addition, efforts to recontact participants could be costly and burdensome for researchers.

The fourth model, which Appelbaum said was one he and his colleagues had not thought of until it was suggested by some of the survey respondents, is the outsourcing model, in which participants are referred to third parties for both consent and the return of secondary findings. Arguably, Appelbaum said, this model works better in a research setting than in a clinical setting, but it takes the responsibility of explaining and conveying clinical findings out of the hands of researchers and presumably puts it in the hands of clinical experts. The advantages of this model to the researchers are clear in that it allows them to avoid the entire issue and only leaves them with the obligation of returning each participant's raw data. The potential disadvantages of this model are that the participants may not become aware of medically significant data within the raw data and that services for genomic interpretation and counseling are not widely available today. In addition, this approach could exacerbate health disparities because further interpretive services may be costly and thus limited to wealthy participants.

With the four models in hand, Appelbaum and his colleagues went back to the original pool of researchers to ask for their views about the models given two situations, one in which there were no resource constraints, and the other with real-world resource constraints (Appelbaum et al., 2015). The researchers were also asked to rate the characteristics of the various models. The results, Appelbaum said, were somewhat surprising (see Table 4-3). In the no-constraints situation, the researchers were split between traditional consent and staged consent, with little support for the outsourced model, even though that would be the least burdensome for researchers, and almost no support for the mandatory return model.

In the real-world situation, almost half of the researchers chose the traditional consent model, while far fewer favored the staged consent model because of the time and effort needed to recontact participants each time

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TABLE 4-3 Researchers' Favored Models of Consent

No Resource Constraints	Real-World Constraint
Traditional consent (32.3%)	Traditional consent (47.8%)
Staged consent (32.3%)	Outsourced consent (18.7%)
Outsourced consent (13.1%)	Staged consent (13.1%)
Mandatory return (8.6%)	Mandatory return (6.6%)

SOURCE: Appelbaum slide 18.

results became available. Outsourcing had somewhat higher levels of support, but again, few researchers liked the mandatory return model.

When the models' attributes were rated, traditional consent was rated first in every category except in terms of the burden it places on researchers. "This was a big surprise to us," Appelbaum said, "but it may be that people like doing what they have always been doing and are comfortable with." From these results, Appelbaum concluded that there was no consensus concerning which consent model was optimal and also that there is a great deal of concern about the resources needed to stage consent.

Appelbaum concluded his presentation by noting that many whole-genome sequencing studies will generate some number of secondary findings of clinical or personal significance and that there is a rough consensus among researchers that at least some of these secondary findings should be offered to research participants. The complexity of obtaining informed consent will push the field away from the traditional model, he predicted, but which model becomes dominant—perhaps a hybrid of two or more of these models or one yet to be developed—will depend on a mix of practical concerns and normative considerations.

REACTIONS TO THE PRESENTATIONS[4]

Marin Allen first commented that variation and continuity are important concepts for health literacy, just as they are for genetic literacy, which

[4] This section is based on the comments by Marin Allen, deputy associate director for communication and public liaison and director of the Public Information Office at NIH, and Benjamin Solomon, chief of the division of medical genomics at Inova Translational Medicine Institute, and the statements are not endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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Joseph McInerney had stressed in his presentation. She then pointed to Bakken's idea that, in an important change to the business-as-usual approach, health literacy needs to be considered at the earliest stages of the recruitment process, not measured later once the research has begun. The notion of comparing an individual's results to those of neighbors was an interesting idea, she said, but she wondered if also adding a comparison to "perfect circumstances" to the graphics Bakken presented might be worth testing. She also commended Bakken for her team's strong emphasis on cultural respect in its approach to her studies and for how thorough the team was when thinking about subpopulations.

With regard to Wilkins's presentation, Allen said the notion of bi-directionality is also one of continuous feedback and that two-way communication between the researcher and participant should be continuous rather than in stages. Allen thought that Wilkins's recognition of what often happens when there is a single representative of the community on advisory boards is important in the health literacy environment. In that setting, individuals can be intimidated, and furthermore, they do not really represent the community and instead represent their own needs or aspirations. She also said that she thought the patient portal as a proxy for the interested community member was an important concept that offered the potential to understand that particular population.

Turning to Appelbaum's presentation, she said she thought that the emphasis in the four models he presented was what she called "CYR, or cover your researcher," in that they all are legally and ethically defendable but do not address the topics that researchers are frightened of telling people. She said that yet another model is necessary, one that incorporates health literacy and frames these difficult conversations to make them more useful for more people more of the time.

To put his comments into context, Benjamin Solomon first described the precision medicine work his organization has been doing for the past 5 years. He and his colleagues have done whole-genome sequencing on nearly 10,000 people in 3,000 families and have been monitoring the health of these individuals. From that perspective, he said, his view is that the research community at large has generated both a great deal of excitement around genomics and precision medicine and a great deal of hype. While it was exciting to see President Obama standing next to the double helix at a State of the Union address, he said, he worries that patients and research participants expect a great deal from taking part in the PMI without realizing how early it is with regard to what can be learned from genomics and the tremendous variability in the human genome.

One important point that Solomon said he took from the three presentations was the need for flexibility and the ability to change models as the field learns. This will be a challenge, he acknowledged, for fields that are

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used to traditional research models with checks and balances and logistics. Just as Appelbaum described the need for a different model of consent, Solomon said the research community needs to have different models for how it conducts its studies as the precision medicine field grows with the new knowledge and experiences that will come from carrying out these research projects.

Another message that Solomon said all three presentations alluded to was that it is going to be tremendously expensive in terms of time and personnel to get participants enrolled, engaged, consented, and informed. One point that he said he wishes the public understood was that the people they will interact with in this project are just a small percentage of the total personnel involved and that there are many people working behind the scenes on data analysis, data security, and other critical aspects of this type of endeavor.

Finally Solomon brought up what he said he suspected might be a controversial topic—the idea that this effort should extend to children and not just adults. "If we are doing precision medicine and want to learn what affects a person's health and well-being, it is challenging if we start in the adult realm," Solomon said. "I know doing this type of research in pediatrics raises bioethical concerns, but I worry we are going to lose the opportunity to learn from children and to learn how disease and health really progress if we do not start early in the lifespan."

Laurie Myers remarked on how hard these concepts are to communicate to patients, but she said that she is optimistic after hearing the three presentations that it will be possible. In Bakken's presentation, she said, she heard that it is possible to engage in a culturally respectful manner participant groups that have been historically underrepresented. Wilkins pointed to the importance of two-way engagement as being more than just an afterthought and of involving participants in many ways throughout a research project. From Appelbaum's presentation, Myers said, she got the message that the field still needs to figure out the best way to get informed consent from research participants—to help them understand the important points and not just overwhelm them with information. Allen reiterated the notion of continuous feedback and cultural respect, and Solomon highlighted the difficulty of communicating to patients what precision medicine can do for them when the field is still very much in its infancy.

DISCUSSION

Cindy Brach began the discussion with an idea for a different model of consent that is derived from the new division-of-labor, team-based models being implemented in primary care practices. In this model, participants might first watch a video at their own pace and then have a chance to ask

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questions to the person charged with obtaining informed consent from participants. Brach reiterated the importance of developing and testing communication tools at the beginning of the research process and noted how impressed she was with the graphics that Bakken's team had developed using this approach. Brach also noted the point that McInerney had made about learning lessons from the genetic counseling field. She added that she found the staged model of consent troubling on ethical grounds.

Appelbaum said he believes that this project could embrace the idea of subject educators or even participant educators in an aggressive manner and, by doing so, provide an example of a new approach to consent that could extend into the clinical realm as well as the research realm. In his opinion, he said, the problem with doctors and researchers trying to obtain consent from a patient or participant is that these experts no longer know what the non-expert does not know. He said he believes that some combination of technology with dedicated educators and participants who are trained to teach rather than obtain consent could provide a better approach to consent. He noted that a colleague of his at Columbia is leading an effort to develop 3- to 5-minute videos covering discrete topics related to genomic research, including secondary findings.

Bernard Rosof asked Bakken to list some lessons she had learned that might allow other communities to accomplish what she and her colleagues have done in the Upper West Side of Manhattan. The most important lesson, Bakken said, is to get the community participating from the beginning, which in the case of her work meant going into the community and developing an understanding of what the community members thought was most important in terms of the information they wanted to receive back from the research. Community participation continued throughout the process of her team prototyping infographic designs. Another lesson, she said, was the need to iterate to make sure that the designs would work in specific cultural contexts. She said that cultural context proved to be more important than health literacy level in the community she was studying and that more information made the infographics more meaningful, which in turn led to increased understanding.

Betsy Humphreys from the National Library of Medicine (NLM) said she hoped that the type of research discussed at the workshop would provide feedback to improve the genetic reference and gene information tools that NLM develops in collaboration with other NIH institutes. In fact, she said, she is optimistic that the PMI Cohort will be a good base for research on issues of health literacy, consent, and communicating genomic information to populations of different socioeconomic, educational, cultural, and ethnic backgrounds. With regard to returning information to study participants or to the public, Humphreys said that there will be a group of participants whose primary motivation will be getting back every piece

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of information generated, and as a result the consent process will have to include alerting participants that they may receive information that will not be well explained.

Humphreys also wondered if anyone had thought about recruiting families into the PMI Cohort and the possibility that as the study proceeds, those enrolled as children will rebel against being in the study when they become teenagers. Myers added that teenagers are becoming aware of genomics and genetic testing thanks to the popular media, and she cited an episode of the reality show The Kardashians that she watched with her 16-year-old daughter in which the grandmother had breast cancer, the family was being tested for BRCA mutations, and one of the sisters resisted because she did not want to know if she had one of the deleterious mutations.

Wilkins said that parent–child dyads are a priority population and that representatives of that population are involved in discussions about what it means to be involved in the PMI Cohort. "This is a different discussion if the child is an adolescent versus a toddler," she said. She also agreed that the PMI provides a unique opportunity to study health literacy and communication, given the PMI's emphasis on giving results back to the participants. "How do we do that in a meaningful way, especially with so many different subpopulations, expectations, literacy levels, and educational attainment?" she asked. In her study, she said, a team member from Vanderbilt's Effective Health Communications Core helps put in place mechanisms not only to design effective methods for recruiting participants but also to help understand how member of the different populations will respond to information and what will be needed to retain them in the study over the long term. "I would say we are preparing for the very broad range of information that people will want to get back," Wilkins said. "We want to have a system in place that allows us to respond to the needs, values, and preferences of everybody who is involved."

Jennifer Dillaha from the Arkansas Department of Health commented that she sees a quality consent process as a systems property, not a property based on individual behaviors or on the characteristics of the people in the system. In thinking of relationships with the community as a systems property, the challenge becomes establishing the PMI so that it sustains the quality of relationships and communication regardless of whether certain visionary individuals stay with the initiative. "How do we make this a property of the work we are doing and not one that depends on certain individuals doing what they think is the right thing?" Dillaha asked.

Wilkins agreed strongly that there has to be a process in place for sustainability, particularly for the public awareness, education, and genomic literacy pieces. The approach that her team is taking is to identify local and national community organizations, rather than individuals, as partners. Her

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hope is that if the project goes beyond the pilot phase, a national coordinating center will work to maintain these partnerships over the long term. One idea is to have PMI ambassadors around the country representing both geographic and demographic communities; these ambassadors could come from advocacy organizations that are already established in the different communities, Wilkins said. She expressed her surprise at how much people in various organizations already know about the PMI, though she said President Obama's public support for the PMI is likely the reason for the increased public awareness. "I think that does open some doors that can create some sustainability," she said.

Wilma Alvarado-Little noted that one of the infographics Bakken showed (see Figure 4-1) included mental health status, and she wondered how mental health–related findings might be returned to participants, given that mental health is not a subject for discussion in some cultures. Bakken responded that the importance of including mental health items came from community-based organizations and community members on the design team who felt that stress, in particular, was not adequately represented. As a result, questions related to different types of stress were added to the survey, though the only stress that was significant turned out to be financial stress. However, the team included a safety plan that would trigger an intervention for anything alarming related to mental health or to blood pressure.

Earnestine Willis, who heads a community-based participatory research (CBPR) project, commented on the importance of recognizing available assets in the community when conducting this type of complex research program, and she asked Wilkins if her team had some mechanism in place to ensure that the PMI Cohort pilot has a shared vision with the involved communities. In particular, she was concerned that the PMI does not clearly embrace the complementary role that participants need to share with researchers. Wilkins responded that the PMI is not a CBPR project and that, based on her experience, training, and prior involvement in community-engaged research, she believes the PMI's framework does not lend itself to CBPR. "There are many pieces that are predetermined," she said. "It is disease agnostic from the beginning. It is a cohort that is being established with no health condition identified a priori, and it is a group of people who will serve as a database for future research. As such, I think it would be challenging to make it into a CBPR," Wilkins said. In fact, she said, from her perspective as a community-engaged researcher, the PMI Cohort may be more engaged than any prior project conducted by the genetics and genomics community, but she would not call it partnered.

Wilkins then explained that her institution, in partnership with the University of Miami, was about to launch a center of excellence for precision medicine and population health that will focus on African Americans and Latinos. The planning process for this center included community members

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from both Nashville and Miami who provided input into the design of the center and its health priorities, as well as on their concerns about privacy and trust. "I am not sure I would call that a CBPR either because it is about infrastructure, but I think it is more engaged and responsive to the needs of the community," Wilkins said.

To Michael Villaire from the Institute for Healthcare Advancement one troubling aspect of precision medicine is that it will ultimately place a burden on individuals to contextualize challenging information and use it to make difficult decisions. Given that situation, he wondered if the consent process might have an option of asking participants if they were interested in having another, trusted person present when they receive information to help them make sense of it and make appropriate decisions. Appelbaum said that there will be options for people to share the information they receive and the ways in which they receive that information and that good clinicians and researchers have always been open to bringing somebody with them to help interpret and work through information. He then added that there is work in progress testing the utility of an online consent process with hyperlinks that would enable a participant to get more information on specific topics, if desired, with a simple mouse click. A video library could be used in the same way, he added. He said that his colleagues are starting a study in which they will ask people whether they are more comfortable receiving information online or face-to-face and then look at the outcomes in terms of information assimilation. "There is a great deal of opportunity for individualizing the consent process," he said.

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5

Communicating Risk and Uncertainty in the Clinical Setting

The workshop's third panel session featured two presentations addressing the challenges of incorporating health literate methods in communicating risk and uncertainty with patients. Lori Erby, the associate program director for the Johns Hopkins University/National Human Genome Research Institute (NHGRI) and Genetic Counseling Training Program and an adjunct assistant professor in the Department of Health, Behavior, and Society at the Johns Hopkins Bloomberg School of Public Health, talked about effective communication in the clinical setting, and Jessica Ancker, an associate professor of health care policy and research at Weill Cornell Medical College, discussed the challenges of communicating risk to low-health-literacy populations. Terry Davis, a professor of medicine and pediatrics at the Louisiana State University Health Sciences Center, and Cathy Wicklund, the director of the Graduate School in Genetic Counseling and an associate professor in the Department of Obstetrics and Gynecology at Northwestern University, then gave their reactions to the two presentations, and Laurie Francis, the senior director of clinic operations and quality at the Oregon Primary Care Association, moderated an open discussion among the workshop participants.

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CLINICAL COMMUNICATION TO INCREASE PATIENT UNDERSTANDING[1]

Verbal communication presents a challenge for individuals with limited health literacy, and conveying information related to multifactorial disease is particularly challenging, Erby said, adding that she first became interested in health literacy while completing her training as a genetic counselor. "When you think about the laundry list of elements that might go into a person's precision medicine calculation, that will be a very complex communication context," she said. Fortunately, she added, evidence already exists that supports specific communication interventions that could be important in a health literacy environment. At the same time, she questioned whether there should be a push for precision communication alongside precision medicine. "Is a one-size-fits-all list of techniques what we really want, or should we take the opportunity now to be doing more than that?" she asked.

Erby referred to Howard Koh's model of organizational health literacy which relies on a universal precautions approach (Koh et al., 2013). She said that she would focus on the productive interactions component of that model which takes place between the health care team and the patient and family. She then discussed the challenge of communicating information verbally. Focus group studies of patients who had lower levels of education or who had difficulty managing their care found consistently that these people felt they could not understand what was being presented to them and that even if someone spoke directly to them, they felt the information was not accessible and that nobody was listening to them (Baker et al., 1996; Bennett et al., 2006). Even when interventions were put in place, such as teaching people orally in a class, these individuals had low levels of health knowledge (Baker et al., 1996; Schillinger et al., 2004; Williams et al., 1998).

Erby and her colleagues (2008) have found that individuals with lower levels of literacy do learn less from verbal exchanges. In one particular study, individuals listened to and watched a video of one of two genetic counseling sessions. One session was a standard prenatal genetic counseling session, and the other was a cancer genetic counseling session. In both settings, people with lower levels of health literacy had lower levels of knowledge at the end of the session. However, even those individuals with

[1] This section is based on the presentation by Lori Erby, the associate program director for the Johns Hopkins University/National Human Genome Research Institute and Genetic Counseling Training Program and an adjunct assistant professor in the Department of Health, Behavior, and Society at the Johns Hopkins Bloomberg School of Public Health, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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higher levels of health literacy scored no higher than 50 or 60 percent on a relatively easy test of their knowledge at the end of the exercise, Erby said.

Given these results, Erby and Johns Hopkins colleague Debra Roter began thinking about how they would look at the communication exchange in a way that would provide some insight about what might be difficult to grasp for a person who has limited health literacy skills. They decided to look at the elements of a verbal exchange that might be parallel to factors that others had studied in print materials, such as the use of jargon or generally complex language (Doak et al., 1996). The elements that she and Roter examined included jargon, complex language uses such as complex sentences and multisyllabic word use, and dialog pacing and interactivity, which involve presenting information in chunks and in a way that engages the listener (Roter et al., 2007) (see Figure 5-1). They also operationalized how to look at concept density, how information can be contextualized in a personalized versus generalized manner, and whether there are elements of the content itself that make comprehension difficult.

Using this framework, Erby and her colleagues are now looking at comprehension of genomic information in a group of individuals who have mild cognitive impairment and who may be at risk of developing Alzheimer's disease. She explained that the communication used in this study has been

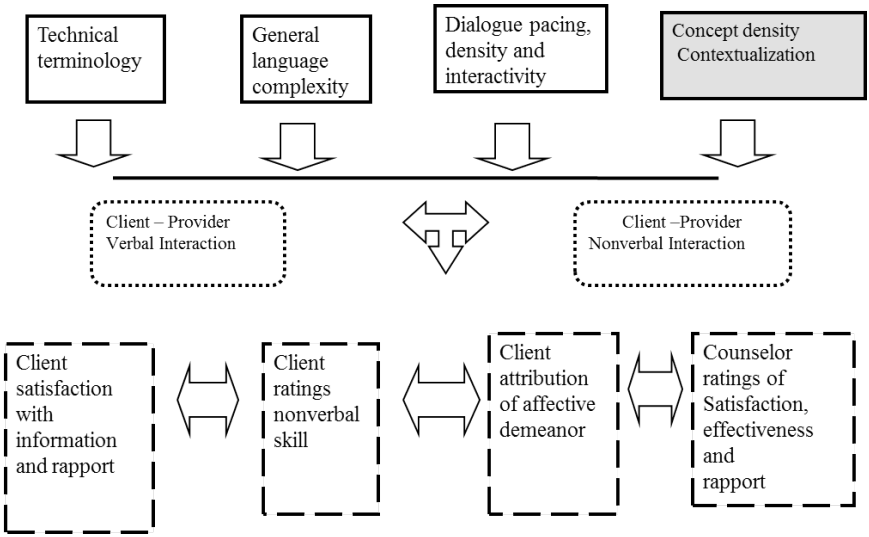

FIGURE 5-1 Framework for understanding oral literacy.
SOURCES: Erby slide 8 (Roter et al., 2007).

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thought through in terms of the concepts that will be disclosed in the clinical visit at which results will be disclosed. Moreover, the clinicians in this study, largely genetic counselors, are highly trained at working with this group of patients. Nonetheless, there has still been substantial variability and jargon use in the taped sessions. For example, one session included the use of the terms allele, MCI, prevalent, cognitive, revert, vascular, dementia, oxygenated, comorbidities, buccal, heterogeneous, hippocampus, and phenotyping.

In a study in which volunteers were asked to watch a randomized selection of 96 simulated genetic counseling sessions involving an average of 30 different genetic counselors and to imagine themselves as the client in each session, Erby and her collaborators found that the level of understanding of these "analogue patients" was strongly affected by things that increased the complexity of the language, whether the use of jargon or the use of generally complex language (Roter et al., 2007, 2009). The analogue patients had much higher satisfaction scores when the genetic counselor was more interactive. When the researchers measured the analogue patients' knowledge after watching these taped session, they found that less literate analogue patients learned more when the sessions were interactive and the information was personalized, and they learned less when the sessions contained high language complexity. What Erby found most interesting was that the analogue patients who scored higher on the health literacy measure scored lower on knowledge when assigned to the interactive sessions. "This was completely counterintuitive to us," said Erby, who added that it points to the need for precision communication tools. "We need to think about the characteristics of the people we are communicating with because they matter in terms of their different ways of learning," she said.

Another study Erby mentioned, conducted by other investigators, looked at the differences in how health care providers and family members spoke when discussing informed consent (McCarthy et al., 2012). Perhaps not surprisingly, she said, the physicians in the study spoke with greater language complexity and with more words per turn than the patient's family members.

As Erby had noted earlier, multifactorial disease is a particularly challenging context in which to communicate information is all areas of medicine, not just in the context of genetics. Not only is the information complex, but provider knowledge and comfort and patient understanding and values play essential roles in determining communication effectiveness. Erby said that much is known about how patients understand genetic information and about the difficulties they have in grasping genetic concepts. "We also know that how people apply genetic and other information to their decision making and the actions they take is going to be tied to their personal values," Erby said. "If where we want to go with precision medicine is to

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not just inform people of their risks but help them act upon those risks, we need to be thinking in our communication about what the information we give them fits within their own system of values."

She added that the provider piece is important, too, particularly because physicians who are not classically trained as geneticists and who are not completely comfortable talking about genetics and genomics will, in an era of precision medicine, be increasingly called on to deliver such information. While acknowledging the importance of the work that Joseph McInerney discussed earlier about efforts to help educate health professions about genomics and make it easier for them to have fruitful discussions with their patients, Erby said that the discomfort non-geneticists feel with this subject matter is going to affect the communication process negatively.

There is evidence to support particular communication interventions—specifically, the universal precautions that the Agency for Healthcare Research and Quality has promulgated, said Erby. These include

- Listen carefully and try not to interrupt patients when they are talking; pay attention and be responsive.
- Use plain, nonmedical language.
- Use the patient's words.
- Slow down; speak clearly and at a moderate pace.
- Limit and repeat content; prioritize what needs to be discussed, limit information to three to five key points, and repeat those points.
- Be specific and concrete.
- Show simple graphics and use demonstrations.
- Invite patient participation; encourage patients to ask questions and be involved.
- Apply teach-back.

What does not exist to any extent, however, is research relating actual variation in communication practice to actual patient outcome, Erby said. Having that information will be essential, she said, for developing communication practices for these more complex scenarios in which people are trying to understand multiple risks and integrate those with their own lifestyles. She suggested that the Precision Medicine Initiative (PMI) Cohort, with its million individuals, presents an opportunity to study different communication contexts and how they can be improved. She noted in closing that none of the competencies expected of genetic counselors explicitly mentions health literacy even though those competencies involve counseling and education specifically and, more generally, facilitating informed decision making that matches clients' needs.

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THE CHALLENGE OF LOW HEALTH LITERACY WHEN COMMUNICATING RISK IN THE CONTEXT OF PRECISION MEDICINE[2]

The promise of personalized medicine is that it will generate personalized therapies, but it will also generate hard-to-understand personalized risk and benefit information, Ancker said. She added that if the goal of the PMI is to broadly reflect the diversity of the U.S. population, then it is important to recognize that the PMI Cohort will include a significant number of people with low literacy (Kutner et al., 2006) and an even larger number of people with low numeracy (Ancker and Kaufman, 2007; Galesic and Garcia-Retamero, 2011). Low health literacy and numeracy are associated with other markers of disadvantaged status, she added, including poverty, lower educational attainment, belonging to a minority race or ethnicity, and a lack of insurance, and these in turn are often associated with various medical issues.

When thinking about risk, it is important to recognize that much of the information about risk will be quantitative information, Ancker said. As a result, the numeracy component of literacy will present a particular challenge that the PMI will need to address. People with low numeracy will, for example, have a hard time drawing meaning from the statement, "You have a 5 percent cancer risk." It is known that people with low numeracy are likely to have an inflated perception of what that number means; it could feel more like a certainty to someone with low numeracy than to someone with high numeracy (Peters et al., 2012; Reyna et al., 2009). Research has also shown that when that framing is flipped from "You have a 5 percent chance of getting cancer" to "You have a 95 percent chance of not getting cancer," people with low numeracy are more likely to be influenced by the change in frame than people with higher numeracy (McNeil et al., 1982; Peters et al., 2011).

Ancker remarked that when Appelbaum pointed out that about 5 percent of the people in the PMI Cohort would have a secondary genetic finding, he also automatically translated that, saying that 19 of 20 will not. "I thought that was interesting because even for this highly numerate room, you switched the framing back and forth so that people could hear it both ways." She also noted that he switched the format of the message, going from a percentage to a frequency format, and she explained that people with low numeracy are more influenced by this kind of formatting difference. They are less likely, she said, to recognize that 5 percent is the same thing as 5 out of 100, and there is even evidence that they are more likely

[2] This section is based on the presentation by Jessica Ancker, an associate professor of health care policy and research at Weill Cornell Medical College, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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to perceive 5 out of 100 as a higher risk than 5 percent because it is more concrete and easier to visualize (Peters et al., 2011).

As an aside, Ancker said that statistics have been used as a rhetorical device historically to promote racist interpretations and racist policies (Parrott et al., 2005), and that a book called *The Bell Curve* has polluted the use of the term "bell curve" by arguing that African Americans were less intelligent than whites. As a result, Ancker said she tries to avoid using that term when teaching introductory biostatistics and introducing the concept of the normal distribution (Finucane et al., 2000). "All of this is to say that numbers are not necessarily perceived as objective pieces of truth as much as we hope as a scientific matter that they would be," Ancker said.

The good news, she said, is that addressing these issues is not just about the patient. Certainly, Ancker said, the patient brings skills and knowledge to the table, but the person providing the information also brings a certain degree of communication skill—or lack of skill. In addition, the resources used to augment and assist in the communication process can also play a positive or negative role in communicating risk, depending on whether or not those information resources are designed in a way that bridges the gap between readers of different levels of skill (Ancker and Kaufman, 2007; Paasche-Orlow and Wolf, 2007; Rudd, 2010). The larger context of a person's social networks, as well as social media and traditional media, can also play a positive or negative role in access to, interpretation of, and application of health risk information, as can the health care delivery system.

Indeed, Ancker said, it is relevant for health care systems to consider whether they are devoting the necessary resources to making patient education materials that are appropriate for low-literacy audiences and to training their medical providers to communicate effectively. "Those decisions are being made at a larger level," she said, "and that larger level is itself embedded in the entire society, which decides things such as whether people have access to health insurance." The bottom line, she added, is that whether people have the ability to apply risk information to problems in their own lives in an effective way is a product of all of these factors, not just an individual's skills.

From the perspective of the PMI and health care delivery, this observation means that there are a number of places to intervene beyond the patient, such as at the provider level or the information resource level. One project that Ancker has been involved with, in collaboration with the National Library of Medicine (NLM), developed a system-level intervention that improved access to information at the Institute for Family Health, a federally qualified health center network in New York City (Ancker et al., 2011). This project involved deploying an electronic patient portal so that patients could access their medical records. Initially, the health network had

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an opt-in policy and an English-only portal, which led to significant racial disparities in using the system, which Ancker and her colleagues' analysis identified. After the initial analysis, the health network switched to an opt-out policy—everyone now has a patient portal account unless specifically declining—and deployed a Spanish portal and created a mobile app. The result was that racial disparities disappeared almost entirely, Ancker said. "This is an example of a system-level effort to ensure access to information, and we are seeing the payoff in terms of who is using this information," she noted.

In a related project, the same health network worked with NLM and Epic, the electronic health record vendor, to embed hyperlinks to low-literacy educational materials in the clients' electronic health records. Ancker's analysis has found that these links are being used more often by the demographic groups that historically have had higher rates of low literacy. "We are seeing these links being used disproportionately by the people we think need it most, which is exciting," she said.

Information-level interventions can also move things in the right direction, she said, particularly when it comes to using different approaches to talking about risk. "We can use numbers, words, and various visualizations, including the type Suzanne Bakken described," Ancker said. "The take-home message is that the choice of which to use has a great deal to do with what you are trying to tell people." For example, if the purpose is to persuade someone to take action, it might be useful to present information in a way that magnifies the difference in risk before and after taking action. However, a different presentation might be useful if the purpose is simply to compare the before and after risk without seeking to influence the viewer's judgment (see Figure 5-2). While one of these approaches is obviously more persuasive, it may not be ethical to persuade people one way or another if they are comparing two different treatments with two different benefits. Information can also be presented in a way that is intended to motivate a behavior, Ancker said, such as graphics designed to encourage smokers to quit developed by the American Cancer Society.

After displaying several other graphics that presented risk in different formats that had the goal of helping people draw meaning from numbers, Ancker noted that the choice of information format may also depend on the intended audience's literacy and numeracy. For example, low-numeracy readers are more likely to believe that 1 in 2,000 is a smaller risk than 1 in 5,000 or that 140 out of 1000 is bigger than 14 out of 100. Survival curves (see Figure 5-3) are another way of presenting information that works better for experts, while icon arrays (see Figure 5-4) work better with patients than experts. She cautioned, though, that while innovation can be good, it is important to test new approaches because the results they produce may be counterproductive (Zikmund-Fisher et al., 2011).

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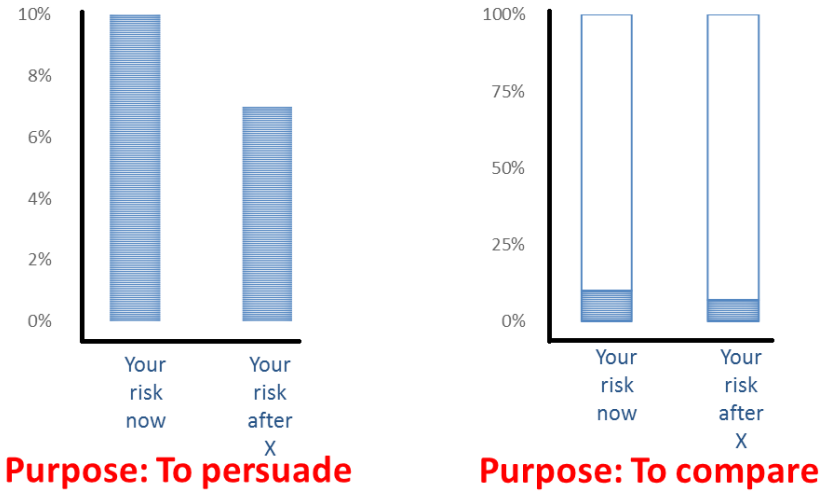

FIGURE 5-2 The choice of information format depends on the communication purpose.
SOURCE: Ancker slide 13.

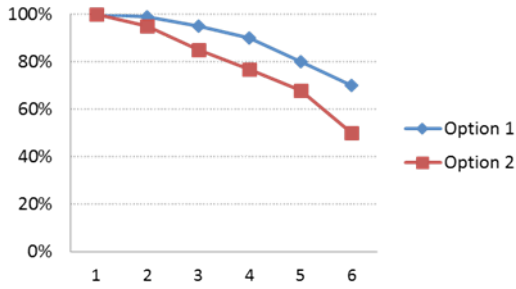

FIGURE 5-3 Survival curves require expertise or training to interpret correctly.
SOURCE: Ancker slide 16.

"Medicine is not one size fits all," Ancker said, "so should we be surprised that information is not one size fits all?" Her hope, she added, is that the next big step from the PMI is the precision communication initiative. "That is what we should be heading toward," she said in closing.

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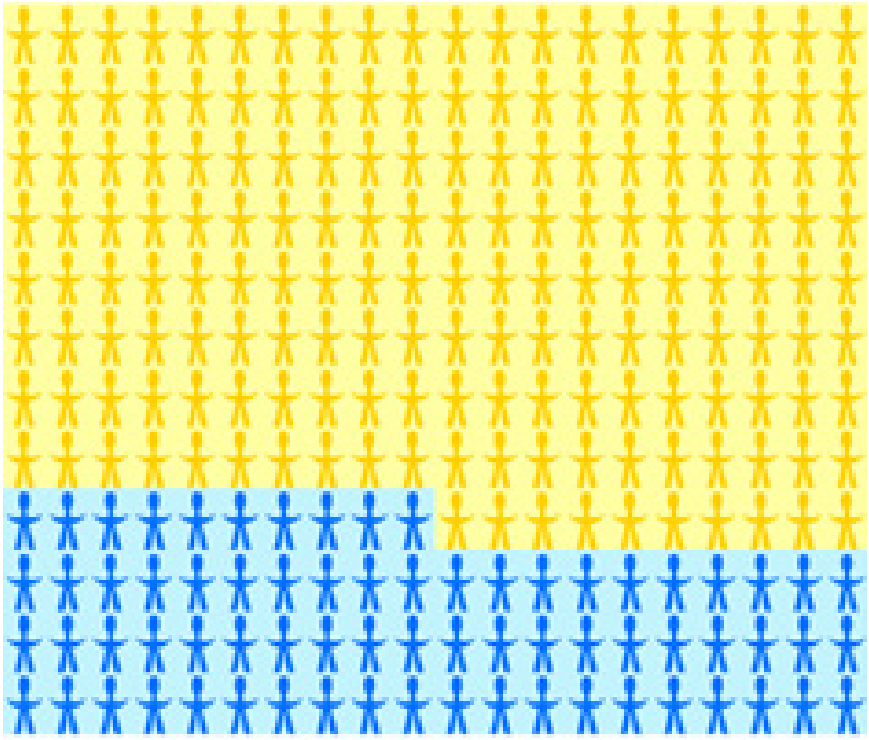

FIGURE 5-4 Icon arrays are better accepted by patients than by experts.
SOURCE: Ancker slide 16.

REACTIONS TO THE PRESENTATIONS[3]

Davis's first reaction was that neither presentation mentioned the importance of having a normal conversation in a normal tone of voice when it comes to building relationships and trust. She also noted that great clinicians follow the doctrine of "ask before tell," that is, that one should ask a little about patients to find out where they are in their lives and what they want to know before presenting findings and risk. Davis said that the message to slow down when presenting complex information to patients

[3] This section is based on comments by Terry Davis, professor of medicine and pediatrics at the Louisiana State University Health Sciences Center, and Cathy Wicklund, director of the Graduate School in Genetic Counseling and associate professor in the Department of Obstetrics and Gynecology at Northwestern University, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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is important, as was the information about jargon. "We are swimming in jargon," Davis said. "We do not even know when we use it unless somebody calls us on it, and usually the patient will not do that." The need to personalize messages and the means of communicating them was another important lesson from the presentations, she said, as was the need to help primary care providers develop the skills to understand and communicate this new type of information—which they may not be comfortable with—to their patients. So, too, was the need to test graphics to make sure they are conveying the intended message. As Davis noted, a picture is worth a thousand words, but which thousand is what is important.

She also said that she thought Ancker's emphasis on framing risk was important, and she added that verbal cues, facial expressions, tone of voice, and body language can also act as framing cues that affect how a patient perceives risk. So, too, can a person's life experience. As an example, she cited a hypothetical woman who learns that she has a BRCA mutation that increases her risk of developing breast cancer. If everyone that woman knows who has had breast cancer has died, that will frame her belief about what her risk is going forward. Davis also said she appreciated Ancker's comments on the need to help patients apply the information they receive to their specific situation.

With regard to making a person's information available through a portal, Davis cautioned that receiving information without having a learned intermediary to put it in context can cause fear and anxiety. As an example, she recounted the story of a colleague who had a spot on her lung, went online to her portal, read the radiologist's report, and became very scared. "She needed a learned intermediary, a physician she trusted, to help her make sense of what the radiologist said," Davis said. In the same way, while having apps and graphics is good, patients will still need trusted relationships with people to help them put information in context.

Cathy Wicklund said she thought that precision communication was the key concept that came out of the two presentations. She cautioned, however, that the idea that information and risk estimates are important to people could be a product of the assumptions that researchers and clinicians, herself included, make based on their cultural views that information is important. She says that she sees this in her first year genetic counseling students who are so excited about all of the genetic information they have and believe their patients should be just as excited to hear it all. This gets to the importance of first listening to the patient and finding out what they want and then crafting a message that fulfills those wants.

Wicklund also noted the importance of understanding risk perception. "We have to be cognizant of all the things that account for people's perception of what their risk is and how they make decisions," she said. What makes for an informed decision and what that means is an interesting

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question, said Wicklund, and a good decision for a particular individual might be one that has less regret or conflict or that boosts a particular individual's confidence concerning what lies ahead. Deciphering what a given patient needs will require more than standardized approaches and scripts, Wicklund said; it will take a conscious effort on the part of clinicians and providers to develop the skills necessary to apply precision communication. It will also require health care systems to give clinicians the time to listen to their patients and use those learned skills.

As a final comment, Wicklund cautioned that the PMI needs to be careful about respecting autonomy, and she said that it should move away from a paternalistic view of "This is what the participants need to know." However, it is also important to recognize that not everybody values autonomy in the same way and that, depending on the culture a person comes from, he or she may not want choices. This will be an important point to remember, she said, as the PMI works to assemble a diverse cohort.

Laurie Francis then commented that she appreciated the emphasis the two panelists gave to bidirectional communication and to the concept of variability in the style of communication in which both providers and patients engage. She said that she was also struck with the need for the health literacy community to examine how to explain the intersection between genetics, lifestyle, environment, and behavior. "It feels as though we concentrate on how to explain genetics to people, but it does not feel we spend time inviting conversations around lifestyle and understanding a person's environment and experiences," she said, asking the panelists for their thoughts on how clinicians can learn to listen better and invite participation in a way that builds trust and engages patients.

Erby said that she agreed completely that building a foundation for a relationship with the patient is critical and that focusing just on explaining genetics is not going to make everything else fall into place. "Risk is hard for people to capture," she said, but she added that there is evidence that partnering with patients, making them feel that the conversation is starting from a place that is important to them and accounts for where they are in their lives, can be an important anchor point for a discussion about risk. Ancker referred to the extensive work that has been done on patient portals and other consumer-facing technologies which shows that one predictor of success is the ability to get support when needed. Having access to support is a demonstration, she said, that the system cares about the individual. One predictor of success for a patient portal, Ancker said, is whether patients know that they can use it to communicate directly with their providers to engage in bidirectional conversations that strengthen the patient–provider relationship. Erby added that she and her colleagues believe that well-designed technology should be able to improve communication and strengthen the patient–provider relationship but that there

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needs to be a conscious effort to ensure that the technology does in fact accomplish that task.

Wicklund remarked that focusing on long-term outcomes—rather than on the short-term outcome of what needs to be conveyed in a specific patient–provider encounter—might enable the health care team to build the relationships and trust that will provide insights into a patient's life that point to ways to improve the patient's ability to retain information and act on it. Too often, Wicklund said, clinicians focus on the short-term outcome of covering everything on a check list. Davis agreed that too often clinicians are giving diagnoses in a vacuum of not knowing much about a patient's lifestyle and concerns. As an example, she said that when a clinician tells a patient he or she has diabetes, the one-sided conversation is usually about changing the patient's lifestyle and checking blood sugar levels. In the meantime, the patient is worrying about dealing with the insurance company and paying for insulin supplies. Wicklund also reiterated Ancker's comment that doctors like numbers better than patients do, and so a patient may not understand the benefit of maintaining a certain blood sugar level.

In addition to the importance of understanding where a patient is coming from before deciding what to say to that patient, Ancker said it is also incumbent on the clinician to state explicitly what he or she is trying to achieve. "What I find is that clinicians are often fuzzy about whether they are trying to provide information or whether they are trying to persuade," Ancker said. She explained that, in her experience, clinicians often say they want to provide information when what they really mean is they want a patient to take a specific action. While the medical profession considers it ethical to try to persuade people to take actions that will benefit their health, there are cases—such as choosing a particular medical treatment—where it may not be ethical. "If we do not acknowledge that we have goals as well, I think we may fail ethically," she said.

Wicklund said she agreed completely with Ancker on that point and suggested that the conversation should include setting an agenda and pointing out gaps between what the clinician and patient want and to not be apologetic about doing so. She also said that genetic counselors have changed their approach so as to be nondirective as often as possible, though there will be times when persuasion and giving advice and recommendation is appropriate, in which case it is important to be transparent about that being the goal.

DISCUSSION

Among the conversations that clinicians have trouble with, Ruth Parker said, are those about value, affordability, and cost, and she questioned if the field of genetic counseling has learned any lessons about affordability and

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how to operationalize conversations about affordability in the context of the market-driven, multi-billion-dollar health care enterprise. Erby replied that because insurance has not historically reimbursed completely the costs for expensive genetic tests, genetic counselors have been addressing affordability for a long time, and it is an uncomfortable discussion. "As professionals, we do not want the thing that drives the patient's decision when they are feeling vulnerable [to be] the cost," she said. While there has been little research on this challenge, Erby said, she has learned from talking to her colleagues about how they have approached this subject, and how she has approached it is to be upfront with patients and tell them that this is an uncomfortable subject and that affordability can be a factor in the choices they make. Then, once that is on the table, she tries to work with patients to plan alternative approaches that they may be able to afford.

Wicklund said that this is a topic she and her colleagues have discussed in the context of the PMI. "It is one thing to enroll people in this cohort, but if we are going to give results back to them, we also have to think critically about access to subsequent services," she said. "If people cannot have access to follow-up services with appropriate screening or appropriate health care, then we are creating even more disparity." She said she believes that there is an ethical obligation to follow through with those enrolled in the PMI Cohort and become involved in their care, their access to services, and them getting the support they need in the community. Concerning how to have these conversations, Wicklund said she struggles with the right way to approach them. She said that she and her colleagues often debate whether to offer some course of action to a patient knowing the patient cannot afford it. "I do not think we have good models, theories, or research to demonstrate what would be the best way to go," Wicklund said.

Ancker added that, from her perspective, the United States has made an arbitrary distinction between what is covered by health insurance and what is not. Other societies, she said, have drawn that line in other places. She noted that cost is only external from the clinician's point of view, while it is completely internal from the perspective of the patient. "As a patient, it is part of your experience of health, medicine, and illness," she said. "Cost is one of the components of decision making because of the way we have set up our system." Wicklund said she thought that was an important point.

Communicating risk and uncertainty has long been a problem in health care, Bernard Rosof said, and this is particularly true now that health care has become more team-based care. Rosof asked the panelists if they had any thoughts on what the health care team needs to learn about communicating risk and uncertainty. Ancker said that researchers are actually the people who need to learn, and what they need to learn is how to productively employ all of the information that precision medicine will generate. Researchers, she said, need to work with patients and providers to learn

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how to get information into practice and then use that information to teach the health care team members. Rosof then commented that how to communicate risk and uncertainty is not something that is currently taught in medical school, but perhaps it should be. Francis added that thinking about genetic risk in the context of lives of people who may be at risk of homelessness or hunger could serve as a good reminder to the community about relative importance.

Davis wondered if part of the problem is that clinicians and researchers are more certain about things than is warranted. "We have a hard time saying 'I do not know, and I do not know what is going to happen,'" she said. Erby said that there are times when it may not serve the patient well for the clinician to convey his or her uncertainty. "We need to be clever about how we train our clinicians to make those assessments," she said. As an example from her own clinical experience, she said that if something had a risk of 1 in 300, she would inform the patient of the risk and explain that she was not certain how it would play out in that patient's life, and she would help the patient deal with the uncertainty; on the other hand, if the risk was 1 in 10,000, she would not tell the patient about the risk.

Ancker said that this comes back to identifying goals. The goal may be to raise someone's awareness of being in a danger zone, which is why she thought Bakken's stoplight graphic was an effective choice of conveying blood pressure information. However, she said, there may be other situations where understanding the magnitude of the difference in risk between two actions may be important, and in that situation it may make sense to discuss the actual numbers and put them in context through a discussion with the patient.

Stacey Rosen from the Hofstra Northwell School of Medicine at Hofstra University made two points. First, she reminded the workshop that students learn in medical school that the first vital sign is the one that matters. Keeping this idea in mind, she said, would allow both patient and clinician to frame how much information and also the type of information each patient gets. Her second point was that cost-related issues are going to be important in how these discussions are framed. "I think bringing cost into these decisions is going to become part of how we have to train clinicians because it has become part of the decision-making process," Rosen said. Parker added that one of the building blocks for a health-literate health care organization is being able to communicate clearly what is covered by a patient's insurance, which is another way to look at affordability. Both Rosen and Davis commented that most clinicians have no idea what various procedures cost or what a patient's insurance will cover.

Steven Rush from UnitedHealth Group asked how precision medicine is going to deal with the portion of the communication process that stops when a patient gets bad news. As an example, he cited the well-known

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phenomenon that happens when a patient receives a diagnosis of cancer: the next thing he or she hears is nothing. A day or two later, reality sets in, and the patient then has many questions for the provider. Erby replied that she was glad Rush raised that point because it gets to the notion of conveying the right information to the right person in the right way at the right time. Timing is critical, she said, and the clinician needs to think in advance about where the patient will be at the moment he or she gets the information and what will be most helpful then and going forward. She noted the tendency is for clinicians to want to convey all of the information they have at once, while research shows that most people can only take in two or three new ideas at a time.

Rush then asked where psychological readiness fits in the algorithm being built for precision medicine. Rosof responded that there is a model for dealing with this that involves the health care team helping the patient move from crisis care to health-literate care. When the patient leaves a physician after receiving certain diagnoses, there should be a team that then sits with the patient for a time to address any concerns and questions the patient might have. Christopher Dezii from Bristol-Myers Squibb added he was struck by the gaps that exist in communicating risk and uncertainty.

Wilma Alvarado-Little commented that much of what she has heard is embodied in the first course that students take when pursing a master of social work degree—meet patients where they are and then take them to where you hope it will be helpful to them. She asked if the panelists could provide any guidance on how to work with a visually impaired patient who cannot pick up on non-verbal cues or see informative graphics or else with a hearing-impaired patient. Ancker responded that from an informatics point of view, one notable exception to the meaningful use provision that patients should have access to their medical records concerns people with either visual or auditory limitations. Wicklund said that part of the training for clinicians has to be to not rely on one mode of communication and to understand that words are a very small percent of what is actually conveyed in communication. This will be a deliberative process, she said, and she added that the PMI explicitly wants to enroll individuals with cognitive impairments and other disabilities, so information will have to be made accessible for all individuals by using a battery of approaches. Betsy Humphreys from NLM added that technology, particularly technology developed for telemedicine and telehealth, may be able to help in this regard. For example, she said, she knows a psychiatrist and mental health counselor who knows American Sign Language and uses telemedicine to provide services to a much broader group of patients than would be possible if it was necessary to meet them in person.

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6

Communicating with the Public

The final session of the workshop examined two aspects of conveying information to the public about precision medicine. Kathleen Hickey, a cardiac nurse practitioner and an associate professor of nursing at Columbia University Medical Center, discussed precision medicine from the perspective of the nursing profession, and Chris Gunter, the director of communication operations at the Children's Health Care of Atlanta's Marcus Autism Center, addressed precision medicine in social media. Jennifer Dillaha, the medical director for immunizations and the medical advisor for health literacy and communication at the Arkansas Department of Health, and Carla Easter, the chief of the Education and Community Involvement Branch of the National Human Genome Research Institute (NHGRI), then provided their reactions to the two presentations, and Catina O'Leary, the president and chief executive officer of Health Literacy Missouri, moderated an open discussion following the reactors' comments.

A NURSING PERSPECTIVE ON HEALTH LITERACY AND PRECISION MEDICINE[1]

Kathleen Hickey has been a nurse practitioner in a cardiac clinic that sees patients and families with a variety of inherited cardia arrhythmias,

[1] This section is based on the presentation by Kathleen Hickey, an associate professor of nursing at Columbia University Medical Center, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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and in that role she has had to communicate very clearly and concisely what those conditions mean to the affected individuals and their families. She said that she had entered the field in an era prior to the sequencing of the human genome, yet even then she and her clinician colleagues knew that arrhythmias ran in families and that there were genes yet to be discovered that were playing a role in the sudden cardiac deaths they were seeing in these families. At the same time, a new technology was developed—the implantable cardioverter–defibrillator (ICD)—that could save lives, and she recounted how she had to adapt to the literacy of the patients and families at risk when she spoke with them about this new technology.

Some patients, she said, would want to see the actual device, to touch it. Others wanted to talk to a patient who already had one implanted to find out what it felt like to have the device inside the body and what a shock felt like. Some of the younger female patients would want to speak to other young women who might be planning a pregnancy. Patients wanted to know if they could exercise and if the device would affect their lives. "I had to adapt my speaking to the literacy of the patients and also pare information into soundbites they could understand," Hickey said.

Then came the Human Genome Project and the discovery of many monogenic disorders that can cause arrhythmias and for which there are now genetic panels of tests to screen patients and identify those at risk for such conditions as long QT syndrome or Brugada syndrome. "This is very powerful information because unfortunately the first arrhythmia can be the last arrhythmia," Hickey said. Now, in this era of precision medicine, she not only had to communicate about the therapies that existed but also about genetic testing and the meaning of the results from those tests for both patient and other family members who might be silently at risk.

Her first step to meeting that challenge was to develop her own literacy by attending the Summer Genetics Institute, a 2-month laboratory- and classroom-based course offered by the National Institute of Nursing Research. This experience, Hickey said, allowed her to learn the language and then be able to read and understand the growing literature concerning genetic testing and communicate that information to patients and families in clear and concise language. This training also allowed her to interact more effectively with other members of the health care team.

As she started evolving as a professional and working with these patients and families, she began to realize that there had been little research done on how having an ICD implanted affects an individual's quality of life and perceptions of life and what the long-term implications were of having a positive or negative genetic test result. One study that she and her colleagues conducted (Hickey et al., 2014a) found that patients were able to integrate a diagnosis over time into their lives and that a positive genetic test did not have a profound impact on quality of life. In another study,

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Hickey and her collaborators examined what cardiac and genetic testing meant to their Dominican patients, who are often of lower health literacy (Hickey et al., 2014b). Through a series of qualitative interviews, she and her colleagues found these individuals were afraid of dying suddenly, regardless of whether or not they had the life-saving ICD device implanted inside them, and, if the device was implanted, they were afraid of getting shocked because they did not always completely understand that the ICD shock was what was terminating their arrhythmia and saving their lives. There was also guilt about passing on a mutation to their offspring, which is one of the real-world concerns clinicians need to address. Hickey noted that this work continues.

Hickey said she has been fortunate over the years to sit on many advisory boards and panels, often as the only nurse or nurse practitioner. One such panel, convened by the American Heart Association, found that there is a critical need for genetics and genomics competencies among cardiovascular and stroke clinicians (Musunuru et al., 2015). This panel developed a set of key content areas whose subject matter all cardiovascular and stroke clinicians should learn in order to avoid a big disparity between clinicians who understand this new language and those who do not. The panel then created a scientific statement with essential genetic/genomic content and developed a half-day boot camp for practitioners that the panel offered for the first time at the November 2015 annual meeting of the American Heart Association.

The boot camp was open to practitioners and non-practitioners alike, and anyone who wanted to attend was directed to a series of 16 preparatory videos to watch before the boot camp. The boot camp was designed to be an interactive experience, with breakout groups that would include nurses, statistical biologists, basic scientists, and clinicians looking at a series of challenging cases and discussing them. The dialog, Hickey said, focused on pedigree analysis, risk assessment, next-generation sequencing, pharmacogenetics, and the interpretation of common gene variants as well as some rare variants. As a facilitator in one of the breakout groups, Hickey said, she found a huge difference among practitioners in terms of subject matter literacy. She concluded from this experience that more of these types of activities will be needed going forward and that the field has to develop ways of educating the next generation of practitioners so that they can communicate clearly with the public.

Hickey has also worked with the American Academy of Nursing on recommendations for how advanced practice nurses can contribute to precision medicine (Williams et al., 2016). As their colleagues in other fields had done, the advanced practice nurses concluded that there is a need for genomic health literacy resources that are appropriate for people from diverse socioeconomic and cultural backgrounds. “We need to advocate

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for these and test them in various populations, and we need to also make sure that the consents we are using for genetic information align with a person's preferences," Hickey said. She noted that as technology changes, patients' information needs and the consent process may also change, and, as a result, developing appropriate materials and consent processes today will not be a one-time activity but instead will require ongoing research and development work.

Genetically trained professionals, Hickey said, are instrumental in taking comprehensive four-generation family pedigrees, ordering diagnostic testing, recognizing "red flags" and phenotypes of various genetic conditions, providing counseling and education, and supporting patients and families. From her experience working with genetic counselors as part of a health care team, Hickey has learned how important it is to put genomics into a context that is meaningful to the patient and to do so long before delivering the results of any tests. Patients need to know, starting from the first contact with the genetics professional, why they are there and why it is important that they provide a comprehensive family history, and practitioners need to understand the individual's goals for seeking a genetic evaluation and recognize that sometimes this information may not be clear to the individual patient or family.

Health organizations have been playing an important role in educating both health professionals and patients about genomics, Hickey said. As examples, she mentioned the American Heart Association and the International Society of Nurses in Genetics, members of the latter were working with and caring for patients and families and communicating with the public regarding a variety of inherited disorders long before the Human Genome Project. The Hypertrophic Cardiomyopathy Association, StopAfib.org, and the Sudden Arrhythmia Death Syndromes Foundation are focused on inherited arrhythmia disorders, and Hickey said that what has impressed her about these organizations is that the founders themselves are affected by genetic conditions and have come together to change policy, to engage families, and to educate the public. These organizations have also worked to get automatic defibrillators installed in public places and schools and are getting schools to test children before they take part in sports.

Hickey also mentioned the work of the American Nurses Credentialing Center, which developed a new genomics competency for nurses. This competency, which was released in 2015, calls for nurses to have a portfolio they can submit that demonstrates their proficiency in genomics. She said that this type of credentialing activity will become increasingly important as precision medicine makes inroads into clinical practice. "This will be another way to support genetics counselors, geneticists, and other practitioners," Hickey said, "and, quite frankly, there are not enough trained people to go around as we embark on the Precision Medicine Initiative."

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Working with the American Heart Association and StopAfib.org, Hickey and her research and clinical cardiology collaborators created a portal called AFIB Town (see Figure 6-1). This portal is designed for patients with atrial fibrillation, one of the most common cardiac arrhythmias, to get information, create their own profiles, and develop wellness goals, but it has also been used by providers who need information. Hickey's said that her goal is to expand AFIB Town to include genomic information in the future and to make it possible for a clinician to access a patient's information, including life history, medications, and symptoms, prior to meeting with the patient. Her hope, she said, is that similar types of portals could be developed as places where a clinician would create a precision or personalized care roadmap that would enable two-way communication between the clinician and the patient.

Hickey concluded her remarks by saying that health-literate communication in the era of personalized medicine is evolving and that it will take

FIGURE 6-1 AFIB Town, a patient portal designed to provide information on atrial fibrillation.
SOURCE: Hickey slide 10.

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a number of different types of professionals having various competencies and taking advantage of a range of advances in technology to produce the best outcomes for all individuals. She commented on how useful it might be someday to download information about a person's physical activity from a wearable fitness monitor to an electronic health record and then add genomic information in a way that protects the privacy and advances the care of the patient.

PRECISION MEDICINE AND SOCIAL MEDIA[2]

In February 2016, the White House issued a fact sheet announcing key actions to accelerate the Precision Medicine Initiative (PMI). This fact sheet, Gunter said, listed 40 different affiliated projects with by different organizations nationwide. At least one-quarter of these organizations have stated explicitly that they will use social media and another 10 or so implied that they will use social media. The importance of this, she noted, is that for social media-driven efforts to be successful, they have to encourage two-way communication.

As an example of the power of a two-way social media approach, Gunter cited a paper in the journal *Nature* (MacArthur et al., 2014) that started as a discussion on Twitter she was having with a colleague, about a report that had appeared in the journal *Science Translational Medicine* in 2011 (Bell et al., 2011). The earlier paper had stated that 27 percent of the mutations that were identified when doing genome sequencing of children in neonatal intensive care and pediatric intensive care units and that had been cited in the literature as being deleterious mutations were actually common polymorphisms or had been annotated incorrectly. "As a geneticist, it was not acceptable to me that 27 percent of the time we are giving parents the wrong information," Gunter said. She and her colleague were discussing their concerns about these findings via Twitter, and they decided to work with NHGRI to convene a workshop at which geneticists would develop guidelines and standards for investigating the causality of gene variants in human disease. Gunter said that, to her, an equally important part of the effort to develop standards was to get the word out about this paper and to stimulate discussion, so the group published in a multidisciplinary journal and used social media to publicize the paper, including Twitter and various blogs at NHGRI, the Simons Foundation for Autism Research, and a genome community called Genomes Unzipped, and they also worked with their own institutions to generate web articles. "This is the kind of action I

[2] This section is based on the presentation by Chris Gunter, director of communication operations at the Children's Health Care of Atlanta's Marcus Autism Center, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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encourage researchers to do," Gunter said. "You have to get your research out there to reach the people who need to see it."

What social media is good at achieving with respect to communicating advances to the public, Gunter said, is eliminating what she called the "middlemen" of both the media and institutional press offices. Most scientists interact with the public via their academic papers, clinical interactions, university courses, or working with university press officers and then getting upset when that person gets crucial details wrong. Gunter recommends using the whole range of new media: websites, blogs, Twitter and Facebook, videos and podcasts, and even public lectures, all of which represent new avenues for engaging the public. In a successful example, a colleague of hers used the internet news website Reddit to announce the creation of an online deletion registry for individuals with a rare 3q29 chromosome deletion and their families. Within 1 day of posting this announcement, two clinicians had already responded that they would tell their families about this registry. Gunter's colleague reported that this was crucial in allowing her to contact a large number of families with this deletion.

Gunter's organization uses its Facebook page to announce research studies and to let the autism community know about articles about autism and also to encourage discussion. She acknowledged that many researchers are hesitant to use Facebook in their professional lives, but she said she encourages them to get over that reluctance and accept Facebook as a means of increasing their connection with the public and getting their research into broader circulation on their terms. She said she is a proponent of Twitter for the same reason and explained that Twitter can be thought of as a site for "microblogging" and that it works best when updated frequently with varied content and when the tweets show some personality.

Prior to the advent of social media, mass communications researchers proposed a theory that the mass media disseminated important messages through a two-step process in which opinion leaders served as the conduit to individuals (Katz and Lazarsfeld, 1955). More than four decades later, Gunter said, researchers at Microsoft showed that the same holds true today, with information on Twitter going through a number of opinion leaders who then disseminate the message out to their friends and followers (Wu et al., 2011). Gunter said that she encourages scientists and clinicians to get on Twitter and be those key opinion leaders. For example, the 2014 International Meeting for Autism Research set up a room in which researchers and clinicians could field questions submitted via Twitter and tweet answers using the same hashtag. Over the course of an hour, this activity generated more than 4.3 million impressions, which represents the number of times those tweets went across the Twitter stream to everyone following that hashtag. "If only 10 percent of those people were actually online, and if 10 percent of those online were reading the tweets as they

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came across, then potentially 43,000 people saw us saying that autism is not correlated with vaccines," said Gunter, who called that a good science communication day.

Gunter then explained that autism is not only a spectrum of disorders, but that it is diagnosed by having traits on the spectrum of three different areas: social communication deficits, repetitive behavior, and restricted interests. She noted that at her institution, one of the nation's largest centers for the care of autism, a diagnosis of autism in individuals referred to the clinic is confirmed only 60 to 70 percent of the time because her institution uses gold standard instruments that most referring clinicians do not use when making their provisional diagnosis. Due to the wide range of differences among autistic individuals, what precision medicine will be to the autism community specifically, and in mental health in general, is still up for discussion, Gunter said, and she encouraged the roundtable to continue thinking about health literacy in the context of behavioral and mental health.

"If there is any field that needs to have impeccable science communication, it is autism research," Gunter said, referring to the belief held by some lay people that scientists want to do genetic research to eradicate autistic people. She acknowledged that while neither she nor any researchers she knows have that as the goal, the fact is that it doesn't matter what researchers' actual goals are in this extreme example; the autism community will never participate in or support research if its members believe this to be true. This situation, she said, points out the problem with the deficit model of science communication, which holds that people have a deficit of knowledge and if the scientific community can just remedy that deficit, then people will take predictable actions based on new knowledge. "That does not always happen because people's heads are not empty, and they do not always make rational decisions with new information," Gunter said.

Gunter referred to a recent study in which parents of children with autism and scientists were asked how the media has affected the public's attitude toward individuals with autism (Fischbach et al., 2016). Ninety percent of parents and 88 percent of scientists thought the media did a good job of improving public attitudes toward individuals with autism and reducing the stigma associated with autism. However, while some 80 percent of the scientists said they would be interested in serving as a resource, only one-third of them actually were doing so. "That makes me very frustrated," Gunter said. "We have to talk about our work and the challenges that are involved."

To illustrate some of the challenges that clinicians face in using social media to disseminate information, Gunter discussed the Simons Foundation for Autism Research VIP Connect Project, which in 2015 created autism resources specific to different genetic variants linked to autism. The project

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has created infographics (see Figure 6-2) and webpages for each of the genetic variants and provided links to public communities and private Facebook groups as well as to research opportunities that arise. While all of this is great in theory, Gunter said, in practice the only people posting so far on the public Facebook page are people from the Simons Foundation, which

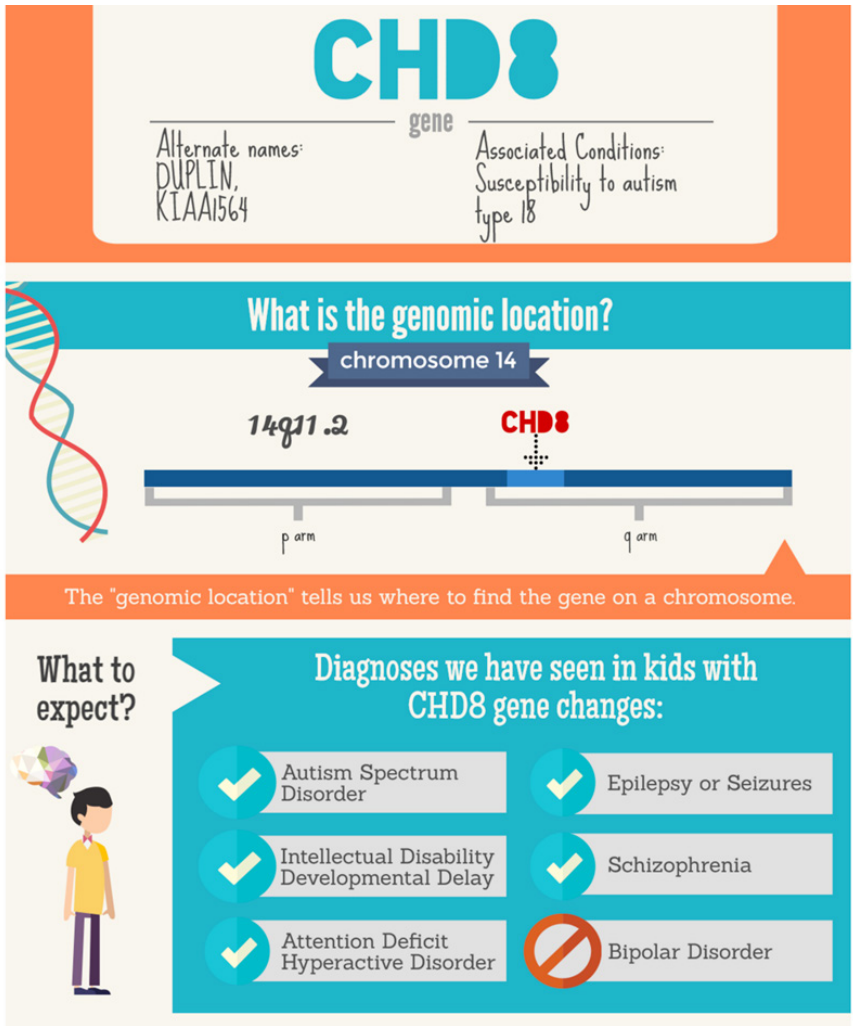

FIGURE 6-2 A webpage with links to resources related to a specific gene variant associated with autism.
SOURCE: Gunter slide 18.

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suggests that the Foundation still has work to do to get the community to engage with these resources. This is a common problem with building new outreach sites, Gunter said.

Another effort, which serves as an example of why thoughtful messaging and engagement are important in precision medicine, involves a collaboration between the autism advocacy organization Autism Speaks and Google whose goal is to sequence the genomes of more than 10,000 families affected by autism. Gunter said that similar projects aimed at sequencing the genomes of people with cancer to find genetic subtypes that link to specific diagnostics and treatments have been met with enthusiasm. The autism community, however, does not respond the same way, however, and the response to the project has been muted. The project has been hampered, too, by its name, MSSNG, which seems to imply that people with autism are missing something—an impression that prompted the creation of the hashtag #notmssng on social media. Gunter quoted the autism self-advocate John Elder Robison, who said, "In the context of a research initiative, this is at best insensitive and at worst seriously offensive." Communication about any project will also affect what institutions planning to collect DNA for sequencing, such as Gunter's own genetics group, decide about whether to be affiliated with this project.

In her closing remarks, Gunter explained that different members of the autism community prefers different terms to describe autism (Kenny et al., 2015). It is incumbent on the research and clinical communities to ask people which term they prefer and not let this be a barrier to communicating with the members of a given community. Gunter also noted that just using social media is not enough to achieve good bidirectional communication. "You need to have a thoughtful plan for engagement to go with it," she said. "You need to listen to what the community wants and even what they want to be called." In the behavioral and mental health areas in particular, she added, it is important to recognize that "normal" or "typical" is not always the goal, and failure to recognize that fact will make it difficult to realize the promise of precision medicine.

REACTIONS TO THE PRESENTATIONS[3]

Dillaha responded to the two presentations by noting that they both highlighted the need for clear and concise communication with the public.

[3] This section is based on the comments by Jennifer Dillaha, the medical director for immunizations and medical advisor for health literacy and communication at the Arkansas Department of Health, and Carla Easter, the chief of the Education and Community Involvement Branch of the National Human Genome Research Institute, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine.

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Hickey's presentation, she said, spoke to the need for health care workers to adapt their communications to meet the needs of the patient and raised the possibility that members of the health care or PMI team could serve as interpreters for difficult concepts and jargon. Hickey highlighted the importance of asking explicitly what new information means to the patient, to which Dillaha added that the same question needs to be asked explicitly for clinicians. In both cases, Dillaha said, it is important to support developing competencies in training and to provide health-literate resources and tools for health care professionals and the public. The challenge, she said, is to enable the health system and researchers to interface effectively with the public and provide the public with the skills and capacity to interface with the health system and research enterprise. These are two sides of the coin of health literacy, Dillaha said, and both sides needs to be addressed.

She continued by saying that if the health literacy community has learned anything over the past decade, it is that people in health care systems often have the wrong idea about how much the general public understands. In other words, people in the health care often overestimate how well the people they serve understand the information given to them. "This means that the people involved in the PMI need to care deeply about whether people understand what they are trying to do and to take appropriate action to confirm understanding," Dillaha said. If that does not happen, the risk is that it will be impossible to establish the fundamental foundation of trust and understanding that Michael Wolf discussed in his presentation. Without trust, the public will react negatively, she said, and the results will be on display across social media.

Carla Easter remarked that though it has been a decade since the Human Genome Project was completed and the move into precision medicine has already begun, there is still a need to develop competencies in genomics among practitioners. She supported Hickey's idea to work with professional organizations to develop those competencies, which the Human Genome Project did not do effectively, and to think hard about what the public wants to know about the ethical aspects of precision medicine. In particular, Easter stressed the importance of engaging communities and easing their concerns that precision medicine is the new eugenics or a means of singling out individuals as being different from the community. "We tend not to think much about this as scientists," she said, "but for some communities this is very much in the forefront."

Easter said she strongly supported the idea of using social media not only as a means of communicating information and building support for the PMI, but also as a means of recruitment to the PMI Cohort. She said she thought social media would be a great way to reach adolescents and even younger Americans in order to help them both understand the initiative and engage in conversation about it. As an avid Twitter user, she said,

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

she has witnessed many social movements getting their start on Twitter, including the Black Lives Matter movement. "If you want to reach diverse communities," she said, "you need to think about the platforms they are on and how we can think about using social media as a way to reach out to those communities."

While most of the thinking about precision medicine has focused on actionable disorders, Easter noted that Gunter's presentation raised important questions about how precision medicine fits with behavioral and mental health issues and the possibility that it could lead to marginalizing individuals with certain disorders. Easter also questioned if there are things the PMI could learn from other large initiatives, such as the ongoing BRAIN initiative, about using social media and other avenues to connect with multiple audiences and communities.

DISCUSSION

Catina O'Leary started the discussion by pointing out that there is difference between writing a research paper and sending out thoughtful tweets and perhaps responding to tweets in a thoughtful, productive manner. She then asked Gunter if there are ways for the research and clinical communities to learn the skills for using these new media productively and to be comfortable when communicating out from under the institutional protective umbrella associated with more traditional forms of communication through journals and via press officers. For those who do not use Twitter, Gunter said, the first step is to sign up, follow a number of people, and then observe how they engage the Twitterverse. She noted that there are many scientists on Twitter, Francis Collins being one of them, she and Easter being two others. She also advised exercising common sense. "Do not say anything on Twitter that you would not say publicly," she said. Gunter also said that many universities have policies regarding the use of social media as well as communication officers that will help with such use. The final point she made was that it is critical to remember who the audience is, and she noted that there are many geneticists and genomics researchers who communicate among themselves using Twitter with little interest in reaching the public, which she said she thought was fine. She also said it is important to realize that there are many members of the general public who are interested in how scientists do their job, and she cited a colleague who tweets interesting findings about individual cases in ways that do not reveal patient identity or violate patient privacy.

Linda Harris, who said she was thinking about the impact of precision medicine, asked how the health literacy and genomics communities can help parents, caregivers, and partners talk to their loved ones about the conditions they have. Hickey replied that communities and organiza-

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

tions are becoming more aware of this issue and the importance of the caregiver as an information conduit. One approach may be to schedule separate appointments for parents or caregivers at which they could have their questions answered. These conversations, Hickey said, will have to be individualized. Harris said she thought that perhaps social media could help by creating a platform for exchanging information when it is needed. Dillaha cautioned that the goal is to exchange factual information, and social media is not always a source of factual information.

Wilma Alvarado-Little asked the panelists for any guidance they could share on how to have a conversation with an individual who is the first person in a family to have a genomics-based diagnosis. "How can that individual be prepared to share information with other family members?" she asked. It is important, Hickey said, to recognize when a patient is in such shock that he or she shuts down. At that time, perhaps the session should be more about counseling than passing along information, and the clinician should realize that it may take multiple meetings to get across all of the information an individual and family member may need. Gunter recommended having genetic counselors involved in those conversations, particularly to help deal with the issue of family members feeling at fault. She also noted that sometimes there are more unknowns than knowns associated with a given finding. In autism, for example, there are now some 100 genes implicated to some degree with autism, but there is no answer to questions about how those genes are linked and what the implications are of having one of those linked genes.

Michael Villaire asked Easter if anyone was thinking about how to address the type of urban legend that can arise out of topics that are complex, difficult to understand, and perhaps scary to some people. He could imagine, he said, that people could worry about what researchers are doing with their biospecimens and genes and from there start thinking about genetically modified organisms and genetic manipulation. Easter replied that NHGRI has a panel of individuals from around the country and from different ethnic and socioeconomic backgrounds that it has worked with to find out what members of their communities worry about and what they think about these types of issues. These conversations led over the course of 1 year to the creation of infographics that would address those types of questions. "It was very time-consuming but very important to build trust with this group so that they could provide us with true insight into their concerns and not feel as though their concerns would be unmet or that their concerns were not valuable," Easter said. NHGRI's approach, she said, has been to make this a grassroots effort and to find as many individuals as possible to talk with in order to allay those fears early. "I think they are now more willing to be part of the Precision Medicine Initiative because they feel as though they have a healthier idea about what it is and have a

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

better way of getting the information into their communities with our support," she said.

Hickey said that her group took exactly the same approach in Manhattan's Washington Heights community when the PMI was launched to get feedback from the community right from the start. Gunter added that although it may seem easier to spread misinformation, that notion should not keep this community from putting the right information out to the public.

Bernard Rosof had a similar question to Villaire's in that he wanted to know how to effectively counteract misinformation. Gunter said that one approach is to "hijack" a hashtag on Twitter that is being used to spread disinformation and put factual information out to that linked audience. She cautioned, though, that it is important to recognize that there are often emotions connected with that misinformation and that one should not join a conversation on social media with the attitude that people are wrong and just do not understand the science. Be calm and let the data speak for themselves, she said, and, as an example of that philosophy, she referred to a new evidence-based guide to parenting (Haelle and Willingham, 2016) that does not take the tone of "If you do not follow this, you are wrong." Rather, it lays out the studies and the data and lets the readers decide what the best approach is. The same authors have also written a guide to talking with one's friends about vaccines that advocates the same approach of laying out the data. At her institution there are faculty who have family members with autism, yet they choose to vaccinate their own children and serve as an example without exercising judgment.

Easter said that NHGRI worked with the Smithsonian National Museum of Natural History to create an exhibition on genomics that reached more than 3 million people in Washington, DC, and more as it has traveled around the country to places such as Milwaukee, Wisconsin; Peoria, Illinois; and Wichita, Kansas, where genomics is not something that typically shows up at the local science center. It is important to realize, Easter said, that this is a long-term endeavor and that it takes time and effort to make sure factual information overcomes misinformation. Rosof agreed and said that to overcome the fear of vaccination, the autism center at his institution had to go into the community, visiting churches and community centers and disseminating health-literate information. Using social media was not enough to get factual information into all areas of the community, he said. He said that he and his collaborators are starting a project that will look at those practitioners who achieve high rates of immunization with their patients in parts of the country where immunization rates are extremely low. His hypothesis is that communication ability and health literacy are playing a key role in achieving high rates of immunization. Gunter

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

said it is likely that the research will find that some of these practices simply will not take patients who will not vaccinate their children.

Terry Davis recounted her surprise when the head of the pharmacology department at her institution wrote an article for a local tabloid publication commenting on new research in addiction treatment. Gunter responded that she was an editor of a blog called Double X Science, which had the goal of writing about hard science topics at the level of the stories in magazines such as *Glamour* and *Elle*, and one of the blog entries she wrote explained the implications of the Supreme Court's decision on BRCA1 testing. Writing for these types of publications and social media outlets requires balancing accuracy and completeness while still getting across a great deal of information, she said. Hickey said that Telemundo is a good venue for getting accurate information to the Spanish-speaking population.

Ruth Parker said that she recommends that anyone funded by or connected to the PMI should enroll in the cohort as a means of fostering communication among the research community and the public. She also said that she wonders if there are ways, such as creating a website where participants could post questions and get answers, to make two-way communication a structural piece of the PMI so that the PMI would get constant feedback on what the participants and the public really want to know, not just what the research community thinks they want to know. Hickey replied that engaging the public and advocacy groups in a more active manner, as Parker suggested, is essential. "The PMI cannot be us telling them," she said. Advocacy groups, she added, can be valuable partners because they get engaged and stay engaged. Easter suggested that while getting input from a million people as a group is laudable, it may be more informative to get input from smaller groups that would provide more focused questions that are specific to their communities. "I think finding these small groups of people and then getting information from them is well worth the effort," Easter said. Gunter said that allocating funds for such efforts will be crucial for enabling researchers to go into communities to have those direct contacts.

Gunter said she thought that Parker's idea of enrolling everybody who plays a part in the PMI in the cohort was interesting given that geneticists at the 2015 meeting of the European Society of Human Genetics debated whether geneticists should get their genomes sequenced. The majority, she said, thought that they should not. The geneticists gave all sorts of reasons, many of them reasonable, including that doing so would take away resources from those who really need to have their genomes sequenced. Thus, she cautioned there may be resistance to Parker's idea.

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7

Reflections on the Day

Linda Harris opened the workshop's final discussion session and said that one thing she would like to hear more about when explaining precision medicine to the public is details about using genomic information to inform lifestyle, physical activity, and diet—and not only in terms of actions to take, but also with regard to dosage. She was referring to the possibility that given a certain genetic background, too much exercise may have unintended consequences. Suzanne Bakken commented that she would continue to mull over the difference between accurate and complete, something that she had not considered before. She said she would also think more about the history of tailored health communication and how that differs from what today is being called precision communication. Ruth Parker remarked that she sees a great deal of promise in marrying health literacy to precision medicine.

Cindy Brach said she began the day thinking that risk communication is hard and that after the day's discussion, she is even more worried about meeting the challenge of communicating risk because doing so is not objective but rather normative. She said that she worries that the information people receive from genomic sequencing could lead to an increase in unnecessary health care as people learn they are at risk for some condition and feel the need to do something about it without understanding the context or size of that risk. "I think the discussion has raised a number of health literacy questions about responsible discovery," she said. "When is it appropriate to expose people to all of this genetic information, and how can we help people use it to improve their lives, as opposed to increasing their risk of unnecessary procedures?"

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

Michael Villaire said that he is excited that precision medicine is the next step in the evolution of medical care, but he is concerned about the density of information that precision medicine will generate, given that people already have a difficult time understanding treatment options and choosing among them. While he is heartened about the awareness that health literacy will be important, he said he worries that when it gets down to level of the face-to-face clinical encounter, the infusion of health literacy will not be enough to explain this information in a way that benefits patients. He also expressed concerned that people will misuse the information they receive to suit their particular situation, and as an example he referred back to the lifestyle changes that Francis Collins made after learning he was at risk of developing type 2 diabetes. Someone learning that he or she is at low risk of developing type 2 diabetes may, for example, respond to that information by adopting a diet that is unhealthy for other reasons. Health literacy, he predicted, will play an important role in minimizing that risk.

Earnestine Willis referred to Michael Wolf's remarks on the intersection of the Precision Medicine Initative (PMI) and health literacy and reiterated the importance and challenge of building trust and understanding among populations and subpopulations that have been historically disadvantaged and underserved by the health care system. The importance of Easter's emphasis on getting boots on the ground now cannot be overstated, Willis said, nor can the issue of affordability and the cost to health care providers of providing health-literate information. "Precision medicine is going to change how we practice," Willis said.

Marin Allen commented that she sees a nexus around the topic of risk communication and the associated challenges, and she said she hoped the roundtable would think more about this subject. She also commended the link between bi-directionality and skills that was brought up over the course of the day and of the need to engage practitioners to improve their communication skills.

Andrew Pleasant from the Canyon Ranch Institute said that he was an early participant in the Cornell Genomics Initiative, which added an ethical, legal, and social issue dimension to the Human Genome Project. This led to the realization that it is important to consider who is not at the table when having discussions about genomics and precision medicine, and in the case of this workshop, Pleasant pointed out, the public did not have a representative present, nor did the mass media or the religious community. Pleasant also said that the field of public communication of science and technology predates that of health literacy, and he mentioned two books—*Between Understanding and Trust*, which came out in 2000 and concerns the public communication of science and technology, and *Health Literacy: A Prescription to End Confusion*, which the Institute of Medicine released in 2004—as an illustration of the different approaches these two fields take.

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

"Health literacy is mired in a deficit model," Pleasant said. "We heard that today. We heard a little about the engagement or participation model, less about the contextual model, and nothing about what the public communication field would call the lay expertise model that values the expertise the public brings to the process." He said he wondered if precision medicine, by valuing different sources of expertise, will change health literacy more than health literacy influences precision medicine. He also said that to be successful, health literacy will need to be better at identifying which approaches work for which people.

Stacey Rosen said that in her opinion, precision medicine promises to be disruptive on many levels even at this early stage of data collection. She said she is encouraged, though, by the early inclusion of ethics, cost containment, and health literacy in the PMI because these important considerations are often not discussed until after scientific discovery is made. Laurie Francis echoed Rosen's excitement about how health literacy is being discussed early and the fact that it is bringing to the table the idea that the patient is the expert in communication, not the research community. The day's discussions, she said, repeatedly stressed the importance of making the PMI patient-centered and of understanding the context of people's lives when communicating with them. Catina O'Leary added that the emphasis on community, diversity, and developing multiple frameworks was also encouraging, although she reiterated Pleasant's comments about missing input from the public at the workshop.

O'Leary then said that she was a little dismayed about the idea that 1 million people may not be a big enough cohort to realize the full potential of the PMI. As an operations person, she said, she is confident that it will be possible to recruit, engage, motivate, and retain a cohort of this size, but also that it will be hard to do so, particularly when it comes to the last 10 percent of the cohort. This last 10 percent is important to retain, O'Leary said, because its members are different from those in the first 90 percent. It will also be challenging to layer health literacy on top of this effort, and figuring out how the health literacy community can support the PMI. One comment that worried her, she said, was that the train may have already left the station even though the PMI is but 1 week old. Finally, she highlighted the need to consider how mental health and substance abuse will complicate health-literate communications.

James Duhig from AbbVie Inc. said he thought that the suggestion of examining how the meteorology community explains risk and probability was a good one, and he noted how venues such as reality television can make complex information relatable and actionable to the general public. He had a question, though, about how the roundtable can convene stakeholders to share best communication practices with others. He suggested that that the health literacy field could share best practices by demonstrat-

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ing them on smaller groups within the context of the PMI, and he questioned whether the roundtable could focus efforts relating to collaboration on communication practices that could lead to the optimization of the overall PMI effort.

Christopher Dezii said he appreciated how the challenge of creating and sustaining the PMI Cohort kept coming back to developing and maintaining strong, effective avenues of communication. Steven Rush voiced the same appreciation, and he then asked how what the PMI hopes to achieve is different from shared decision making and to what extent shared decision making was taking place today. He also wondered what motivates people to engage in shared decision making. One topic that he said he would like to hear more about was the readiness to accept information and use it to make changes, and he said he thought the roundtable could bring together stakeholders to discuss how health care can be redesigned to help people process information better. Addressing these issues, he said, could produce a business case to support health literacy. Kim Parson from Humana also commented on the importance of communication but added that communication has to become conversation. "It is going to be important to put as much emphasis on how we have those conversations with patients and families and learn what their expectations are for sharing and understanding the findings being shared with them as we are putting on the communication process," Parson said.

Wilma Alvarado-Little agreed that there needs to be an emphasis on encouraging discussion, not just communication, and she said that that will require partnerships, particularly with communities where there is a level of mistrust because of past misdeeds by the research community. She voiced concern over the possible costs associated with following up on genomic information and over the potential impact on various populations, and she noted the challenges of conducting conversations in languages other than English and with patients from cultural and spiritual backgrounds that may react in different ways to this type of information. She applauded the work being done in Spanish while noting that there are other large communities in the United States that use languages other than English or Spanish.

Terri Ann Parnell from Health Literacy Partners agreed with Alvarado-Little's emphasis on addressing language needs and with Pleasant's idea that the PMI could provide opportunities to advance and change the field of health literacy. In her opinion, she said, the PMI challenges the health literacy community to be more agile in its thinking and to consider working with new types of partners outside of the health care enterprise that have done a better job engaging, empowering, and educating their constituents. Parnell also said she was concerned about the information overload that the PMI may place on patients, adding that it will be important to keep that concern in the forefront as the field moves forward.

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

Lori Hall from Eli Lilly and Company said she was struck by the disruptive nature of the PMI, which she said can be both good and bad. The PMI will deeply affect public trust and the nature of patients' relationships with both clinicians and the health care industry as a whole, she said, and it will require unprecedented collaboration among all stakeholders to make sure that the relationships that result are good ones. Hall added that one stakeholder not heard from at the workshop was the pharmaceutical industry, and she said that she wondered what role her industry can play in furthering the goals of the PMI. She suggested that the pharmaceutical industry might be able to help with recruitment, given that finding participants in clinical trials is a challenge the industry deals with regularly. She also said she wondered if one approach to recruitment and retention might be to honor participants as clinical research heroes. "I think there is something to say for helping participants feel they are not just a cog in a wheel or a commodity in a process, and instead that they are the expert on themselves and they will help in ways that exceed expectations," Hall said.

Terry Davis said that she had four take-away messages from the workshop. One was the important role that health literacy will play in recruiting and retaining vulnerable populations. A second message was the importance of building relationships and trust in the community. A third was the need to hire and train people to act as navigators and coaches to help individuals be full participants in this effort. The final message was that it is possible with the right approach to create informative graphics that more easily communicate risk to the public.

Betsy Humphries agreed with the comments that precision medicine could have as big an impact on health literacy as health literacy will have on precision medicine. One message that she found interesting, she said, was that any deterministic view of health and health care is a mirage—that the science of genetics and the interaction of genetics with environment and lifestyle creates probabilities for outcomes. Many people, however, do not want to hear that message, she said. They want definitive answers when they see their health care providers. Addressing this disconnect will be a challenge, she said, but one she believes will drive the health literacy community to learn more about how to communicate effectively and honestly with the public.

Another voice missing from the day's conversations was that of patient advocates, said Laurie Myers, who pointed out that there was not a single speaker or moderator who did not have an advanced degree. She said that it will important to consider from a patient's perspective what genetic information will mean to that patient's family and how children and adolescents will have different opinions than adults or a health care providers about what information they want to know. Other concerns that participants are likely to have will include whether they can have a caregiver present

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during the conversation and how they will pay for follow-up visits once they receive the free information from the PMI. Privacy is a very important issue to patients, as are the fears that there will be discrimination, that their health insurance premiums will increase, or that they will be fired based on the results from genomic sequencing. Given all of the publicity about credit card breaches, it should not be surprising that privacy is on the minds of the public, Myers said.

Myers noted that patients are also likely to want to know what will happen if they change their minds about participating in the future or about what kind of information they want to know. They may even want to know if they or anyone else will benefit financially should something be discovered from their biological samples and where and how those samples are stored. Myers highlighted the challenge of helping patients understand the meaning of their data, given how little is actually known today about the link between specific mutations and health outcomes. Participants may also want to know what would happen if the PMI ceases to be funded after the next election cycle.

Jennifer Dillaha said she was worried about the impact of the huge data load from the PMI on primary care clinics that are already struggling with electronic health records and health literacy. "Is this going to completely overwhelm the primary care system in my state so that it cannot provide the necessary patient support?" asked Dillaha, who works in Arkansas. "What needs to be in place so that all of the people who receive this information or participate in the PMI can be appropriately supported in a health-literate way where they receive their health care day in and day out?" Answering these questions, she said, will require focusing on the patient, not the data or the disease. Her concern, she said, is that if that is not the focus and if these data cannot be used in a way that improves the quality of care, the PMI has the potential to do many things badly. Having said that, based on the day's presentations and discussions, she said she has good reasons to hope that the end result will be positive.

Bernard Rosof, providing the final comments of the day, reiterated the importance of understanding the audience for whatever information there is to be passed between participants and providers. That will be a challenge, he said, because of the scope of the PMI and the multifaceted audiences that will exist within the PMI Cohort. Rosof then raised the issue of how the PMI is going to measure how successfully it is communicating with participants, which will first require determining what the PMI wants the learner to know, to value, and do with the information received. Rosof suggested that one reason progress has been slow in meeting the goals spelled out in the Institute of Medicine report *Crossing the Quality Chasm* was that the community attempting to change the system did not understand its audience terribly well and did not know how to measure success.

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Appendix A

Workshop Agenda

Roundtable on Health Literacy

Relevance of Health Literacy to Precision Medicine: A Workshop
March 2, 2016

Open Session

8:30-8:40 a.m.	Welcome and Workshop Overview *Bernard Rosof, M.D., Chair, Roundtable on Health Literacy*
8:40-9:00 a.m.	Communication from the Genomic Era to Precision Medicine *Joseph D. McInerney, M.A., M.S.* *Executive Vice President* *American Society of Human Genetics*
9:00-10:30 a.m.	The Intersection of Health Literacy and Precision Medicine
9:00-9:05	Introduction of speakers *Ruth Parker, M.D. (moderator)* *Professor of Medicine, Pediatrics, and Public Health* *Emory University School of Medicine*
9:05-9:20	What is precision medicine and how has it evolved over time? *Sara Van Driest, M.D., Ph.D.* *Assistant Professor of Pediatrics* *Vanderbilt University School of Medicine*

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

9:20-9:35	What is health literacy and how has it evolved over time? *William Elwood, Ph.D.* *Office of Behavioral and Social Sciences Research* *National Institutes of Health*
9:35-9:50	Issues at the intersection of precision medicine and health literacy? *Michael S. Wolf, Ph.D., M.A., M.P.H.* *Professor, Medicine and Learning Sciences* *Feinberg School of Medicine* *Northwestern University*
9:50-10:30	Discussion (to include McInerney)
10:30-10:45 a.m.	BREAK
10:45 a.m.-12:30 p.m.	Health Literacy in Precision Medicine Research
10:45-10:50	Introduction of speakers *Laurie Myers, M.B.A. (moderator)* *Global Health Literacy Director* *Merck & Co., Inc.*
10:50-11:05	Recruitment and messages (include privacy and informed consent) *Suzanne Bakken, R.N., Ph.D.* *Alumni Professor of Nursing and* *Professor of Biomedical Informatics* *Columbia University*
11:05-11:20	Engagement and retention *Consuelo Wilkins, M.D., MSCI* *Executive Director* *Meharry–Vanderbilt Alliance*
11:20-11:35	Results reporting *Paul S. Appelbaum, M.D.* *Elizabeth K. Dollard Professor of Psychiatry, Medicine, and Law* *Director, Division of Law, Ethics, and Psychiatry* *Columbia University*

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11:35-11:45	Reactions *Health Literacy Reactor:* *Marin P. Allen, Ph.D.* *National Institutes of Health* *Precision Medicine Reactor:* *Benjamin Solomon* *Inova Translational Medicine Institute*
11:45-12:30	Discussion
12:30-1:30 p.m.	LUNCH
1:30-3:00 p.m.	Communicating Risk and Uncertainty in the Clinical Setting
1:30-1:35	Introduction of speakers *Laurie Francis, M.P.H. (moderator)* *Senior Director of Clinic Operations and Quality* *Oregon Primary Care Association*
1:35-1:50	Communicating for understanding *Lori Erby, Ph.D.* *Associate Program Director* *Johns Hopkins University/* *National Human Genome Research Institute* *Genetic Counseling Training Program*
1:50-2:05	Communicating risk to low health literacy populations *Jessica Ancker, Ph.D.* *Associate Professor of Healthcare Policy and Research* *Weill Cornell Medical College*
2:05-2:15	Reactions *Health Literacy Reactor:* *Terry Davis, Ph.D.* *Louisiana State University Health Sciences Center* *Precision Medicine Reactor:* *Cathy Wicklund, M.S.* *Feinberg School of Medicine* *Northwestern University*

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2:15-3:00	Discussion
3:00-3:15 p.m.	BREAK
3:15-4:45 p.m.	Communicating with the Public
3:15-3:20	Introduction of speakers *Catina O'Leary, Ph.D., LMSW (moderator)* *President and CEO* *Health Literacy Missouri*
3:20-3:35	The role of health associations *Kathleen Hickey, Ed.D., FNP, ANP, FAHA, FAAN* *Associate Professor of Nursing* *Columbia University Medical Center*
3:35-3:50	Precision medicine in social media *Chris Gunter, Ph.D.* *Director of Communication Operations* *Children's Healthcare of Atlanta's* *Marcus Autism Center*
3:50-4:00	Reactions *Health Literacy Reactor:* *Jennifer Dillaha, M.D.* *Arkansas Department of Health* *Precision Medicine Reactor:* *Carla Easter, Ph.D.* *National Human Genome Research Institute* *National Institutes of Health*
4:00-4:45	Discussion
4:45-5:30 p.m.	Reflections on the Day
5:30 p.m.	ADJOURN

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Appendix B

Biographical Sketches of Workshop Speakers, Moderators, and Reactors

Marin P. Allen, Ph.D., is the deputy associate director for communications and public liaison and the director of the Public Information Office in the Office of Communications and Public Liaison (OCPL) in the office of the director of the National Institutes of Health (NIH). OCPL is responsible for all phases of internal and external strategic communication. The Public Information Office is a focal point for health and science writing, health literacy, clear communication, plain language, cultural competency, and language access initiatives. It is also responsible for NIH programs and resources for the public including regular publications in print and on the Web: *The NIH Record*, *NIH: News in Health*, and *Research Matters!* The Public Information Office also manages the NIH visitors center and the NIH Nobel Laureate Hall, special events, and grantee public information office relations. Prior to 2004, Dr. Allen was the communications director and public liaison officer for the National Institute on Deafness and Other Communication Disorders (NIDCD) at NIH. She led the NIDCD's first communications, legislation, and policy office programs. Dr. Allen has 30 years of communications, public health education, outreach, and media relations experience. Before joining NIH, she directed public relations for Gallaudet University (GU) from 1988 to 1990. From 1981 to 1990, she was on the faculty, and during her service there she became a tenured full professor in and the chair of the Department of Television, Film, and Photography in the School of Communication at GU. Prior to working at Gallaudet, Dr. Allen was a media specialist with the White House Conference on Aging. At the beginning of her career, she was a faculty member in communications at the University of Maryland, College Park. Dr. Allen

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

has two Emmy awards for programs she produced that aired for 5 years on the Discovery Channel and PBS. She was elected for two terms to the board of governors of the National Academy of Television Arts and Sciences DC chapter and as an emeritus member of the Board of the Council on International Non-Theatrical Events (CINE). She is a two-time CINE award winner. She has been involved in trans-agency efforts in health literacy, cultural competency, behavioral research communication, women's health, and health communication. Dr. Allen is the NIH representative to the U.S. Department of Health and Human Services working group on health literacy and has been a repeated contributor to Healthy People efforts for 2000, 2010, and 2020 in communications, health information technology, and health literacy. During her academy experience, Dr. Allen has taught in all areas of public communication and health policy.

Jessica Ancker, M.P.H., Ph.D., received an A.B. degree magna cum laude in history and science from Harvard University, and initially pursued a career in journalism and medical writing and editing. She then earned a master of public health degree from the Department of Biostatistics at Columbia University's Mailman School of Public Health in 2004. She went on to complete a Ph.D. at the Columbia University College of Physicians and Surgeons in 2009 as a National Library of Medicine/Robert Wood Johnson Foundation Predoctoral Fellow in the Department of Biomedical Informatics. Dr. Ancker joined Weill Cornell Medical College in 2009, and since 2011 she has also held a faculty position in the Weill Cornell Graduate School of Medical Sciences. Dr. Ancker uses both qualitative and quantitative methods in her research. She is a recognized expert in the field of health numeracy and patient decision making. In addition, she conducts health information technology evaluation research, which has been published in leading journals in informatics as well as in general medical journals. She currently holds a K01 grant from the Agency for Healthcare Research and Quality for a 5-year series of studies on patient use of health information technology.

Dr. Ancker is also a committed educator. She co-developed and leads the department's certificate programs in health information technology and health analytics, and she teaches in its master's program in health informatics. She has received awards for teaching excellence from both Weill Cornell Medical College and the American Medical Writers Association.

Paul S. Appelbaum, M.D., is the Elizabeth K. Dollard Professor of Psychiatry, Medicine, and Law, and the director of the Division of Psychiatry, Law, and Ethics in the Department of Psychiatry at the College of Physicians and Surgeons of Columbia University; a research psychiatrist at the New York State Psychiatric Institute; and an affiliated faculty member at Columbia

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Law School. He directs Columbia's Center for Research on Ethical, Legal, and Social Implications of Psychiatric, Neurologic, and Behavioral Genetics and heads the Clinical Research Ethics Core for Columbia's Clinical and Translational Science Award program. He is the author of many articles and books on law and ethics in clinical practice and research, including four that were awarded the Manfred S. Guttmacher Award from the American Psychiatric Association and the American Academy of Psychiatry and the Law. Dr. Appelbaum is past president of both the American Psychiatric Association (APA) and the American Academy of Psychiatry and the Law. He has twice served as chair of the APA Council on Psychiatry and Law and of the APA Committee on Judicial Action, and he now chairs the APA's *Diagnostic and Statistical Manual of Mental Disorders* Steering Committee. He was a member of the MacArthur Foundation Research Networks on Mental Health and the Law and on Mandatory Outpatient Treatment and is a network scholar for the Network on Neuroscience & Law. Dr. Appelbaum has received the APA's Isaac Ray Award for "outstanding contributions to forensic psychiatry and the psychiatric aspects of jurisprudence," was the Fritz Redlich Fellow at the Center for Advanced Study in the Behavioral Sciences, and has been elected to the National Academy of Medicine.

Dr. Appelbaum is a graduate of Columbia College, received his M.D. from Harvard Medical School, and completed his residency in psychiatry at the Massachusetts Mental Health Center/Harvard Medical School in Boston.

Suzanne Bakken, R.N., Ph.D., is the Alumni Professor of Nursing and a professor of biomedical informatics at Columbia University. Following doctoral study in nursing at the University of California, San Francisco, she completed a National Library of Medicine postdoctoral fellowship in medical informatics at Stanford University. The goal of Dr. Bakken's program of research is to promote health and reduce health disparities in underserved populations through the application of innovative informatics methods. A major focus of her current grant portfolio is the visualization of health care data for community members, patients, clinicians, and community-based organizations. Dr. Bakken currently directs the Center for Evidence-Based Practice in the Underserved and the Reducing Health Disparities Through Informatics pre-doctoral and postdoctoral training program, both funded by the National Institute of Nursing Research. She also served as principal investigator of the Agency for Healthcare Research and Quality–funded Washington Heights Inwood Informatics Infrastructure for Comparative Effectiveness Research (WICER) and its follow-up study, WICER 4 U, which is focused on promoting the use of WICER infrastructure through stakeholder engagement. She has also received funding from the National Cancer Institute, the National Library of Medicine, and the

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Health Resources and Services Administration. Dr. Bakken has published more than 200 peer-reviewed papers. In 2010 she received the Pathfinder Award from the Friends of the National Institute of Nursing Research. She is an elected fellow of the New York Academy of Medicine, American Academy of Nursing, and American College of Medical Informatics and is a member of the National Academy of Medicine.

Terry Davis, Ph.D., a pioneer in the field of health literacy, is a professor of medicine and pediatrics at Louisiana State University Health Sciences Center in Shreveport. For the past 25 years she has led an interdisciplinary team investigating the impact of patient literacy on health and health care. Seminal achievements include development of the Rapid Estimate of Adult Literacy in Medicine and creation of user-friendly patient education and provider training materials that are being used nationally. Dr. Davis has more than 120 publications related to health literacy and health communication. She has served on health literacy advisory boards for both the American Medical Association and the American College of Physicians (ACP). She was an independent agent on the Institute of Medicine's Committee on Health Literacy and a developer of the American Medical Association's Train-the-Trainer Health Literacy Curriculum. Currently she is a member of the Healthy People 2020 Health Literacy/Health Communication Section and serves as a health literacy advisor to the U.S. Food and Drug Administration. Dr. Davis chaired Louisiana's statewide Health Literacy Task Force, the first legislatively mandated health literacy group in the nation. She received the Louisiana Public Health Association's Founders Award for Significant Achievement in Public Health Research. As a frequent speaker at national conferences, she has integrated her research findings into practical lessons for providers and policy makers. Dr. Davis is the health literacy principal investigator (PI) on a National Institutes of Health grant for the Louisiana Clinical and Translational Science Center, an unprecedented collaborative effort among eight academic institutions in Louisiana. She is PI on a 5-year National Cancer Institute health literacy intervention to increase regular breast and colorectal cancer (CRC) screening among patients in federally qualified health centers. Building on this work she was recently awarded an American Cancer Society grant to evaluate follow-up strategies to improve regular CRC screening in rural clinics in the state. Dr. Davis is also working with Drs. Mike Wolf and Ruth Parker on Agency for Healthcare Research and Quality–funded studies to improve patient understanding and actual use of prescription medication labels in English and Spanish. Along with a team from the University of North Carolina and the University of California, San Francisco, she has been funded by the ACP to develop and test practical self-management guides and videos for patients with diabetes, chronic obstructive pulmonary disease, coronary

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

artery disease, obesity, and rheumatoid arthritis. The American College of Physicians Foundation has distributed more than 5 million copies of these guides.

Jennifer Dillaha, M.D., is the medical advisor for health literacy and communication at the Arkansas Department of Health. Under her leadership low health literacy has been recognized as an important public health problem in Arkansas, and the health department has made improving health literacy a cross-cutting priority in its strategic plan. In November 2013, Dr. Dillaha became the medical director for immunizations in addition to her role in health literacy. Prior to her current roles, Dr. Dillaha served as the special advisor for strategic initiatives in the Office of the Director from June 2010 to April 2013 and as the director of the Center for Health Advancement from August 2005 to June 2010. Dr. Dillaha is currently the chair of the Partnership for Health Literacy in Arkansas, which is the Health Literacy Section of the Arkansas Public Health Association. She is a physician with specialty training in internal medicine and subspecialty training in infectious diseases and in geriatric medicine. She has faculty appointments as an assistant professor in the University of Arkansas for Medical Sciences College of Public Health, College of Medicine, and Regional Programs.

Carla Easter, Ph.D., is chief of the Education and Community Involvement Branch at the National Human Genome Research Institute (NHGRI). She played a major role in the development of the NHGRI/Smithsonian exhibition Genome: Unlocking Life's Code and its accompanying website, and she serves as a liaison to the K–12 and university community as a speaker on genomic science and career preparation and pathways. Dr. Easter also has served as an adjunct faculty member at the University of the District of Columbia Department of Biology, Chemistry and Physics. From 2003 to 2006, Dr. Easter was director of outreach for Washington University School of Medicine's Genome Sequencing Center. Before assuming her role as outreach director, Dr. Easter was a research associate in the Department of Education at Washington University (2001–2003) where she explored the notions of science among secondary students. She served as pre-college coordinator for the National Aeronautics and Space Administration Summer High School Apprenticeship Research Plus Program and project associate for the Quality Education for Minorities Network. From 1997 to 2000, Dr. Easter conducted postdoctoral research at Washington University School of Medicine on the virulence factors associated with *Streptococcus pyogenes*. Dr. Easter earned her bachelor's degree in microbiology from the University of California, Los Angeles, and her doctoral in biology with an emphasis on molecular genetics from the University of California, San Diego.

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

William Elwood, Ph.D., joined the Office of Behavioral and Social Sciences Research (OBSSR) at the National Institutes of Health (NIH) in August 2009 as the coordinator for the new NIH Basic Behavioral and Social Science Opportunity Network. He also will coordinate and promote other OBSSR-led initiatives that advance research in the basic behavioral and social sciences. Prior to joining OBSSR, Dr. Elwood worked at the Center for Scientific Review, where he was scientific review officer for the Community-Level Health Promotion study section for 5 years. During that time, Dr. Elwood served on and chaired a variety of trans-NIH committees including the Community-Based Participatory Research Scientific Interest Group, the NIH Diversity Council, and the Staff Training in Extramural Programs Committee. Dr. Elwood received his Ph.D. in human communication from Purdue University. His scientific books and articles have concentrated on the attitudes and beliefs of hard-to-reach populations and the influences that cultural and personal values and community settings have on mental health, health-related behaviors, and participation in civic life. His research was supported by NIH, the Ounce of Prevention Fund, Substance Abuse and Mental Health Services Administration, and World Health Organization/Pan American Health Organization. Prior to joining NIH, Dr. Elwood conducted community-based research throughout the United States and Mexico on substance abuse prevention, drug use epidemiology, substance abuse treatment, evaluations of welfare reform programs and public housing initiatives, and efficacy studies of interventions aimed at sexually transmitted diseases and HIV. During that time, Dr. Elwood also established the Houston Community Drug Epidemiology Workgroup to provide more comprehensive descriptions of established and emerging substance abuse problems in the nation's fourth-largest city. He also served as associate American editor of *AIDS Care: Psychological and Socio-medical Aspects of AIDS/HIV*.

Lori Erby, ScM, Ph.D., CGC, is the associate program director for the Johns Hopkins University/National Human Genome Research Institute (NHGRI) Genetic Counseling Training Program and an adjunct assistant professor in the Department of Health, Behavior and Society at the Johns Hopkins Bloomberg School of Public Health. Prior to her employment with the NHGRI, she was trained as a genetic counselor and then obtained her Ph.D. in health, behavior, and society at the Bloomberg School. She has been practicing as a genetic counselor for almost 15 years and has been continuously involved in research and training efforts aimed at improving communication practices as genetic and genomic technologies evolve. Using a combination of qualitative and quantitative research methods, her work examines the links between variation in communication and outcomes for patients, with a particular interest in understanding mechanisms to improve

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communication for populations with limited literacy skills. Her previous work with the Genetic Counseling Video Project explored characteristics of the clinical interaction that pose challenges for patients with limited literacy skills, and she is currently extending that work through a project related to communicating Alzheimer's disease risks to adults with mild cognitive impairment.

Laurie Francis, R.N., M.P.H., is the senior director of clinic operations and quality at the Oregon Primary Care Association. She has been working in health care for the past 20 years to improve health and well-being in individuals and communities. After working in critical care and beginning a number of prevention-type programs, she realized that the social and economic issues were interfering significantly with the opportunity to achieve high levels of health and well-being at the individual and community level. More than 13 years ago, Ms. Francis founded a community health center (medical, dental, behavioral health, and education, including GED, adult literacy, family literacy, early childhood education) where she has learned much about patient health, staff well-being, organizational vigor, and leadership's role in helping or hindering these areas. She has delivered numerous talks concerning patient-centeredness, staff engagement, organizational alignment, health literacy, and measurement systems that drive improvement. Ms. Francis has published in the areas of health literacy, outcomes, and self-efficacy. Prior to joining the Oregon Primary Care Association, she directed the Montana Primary Care Association, an organization that supports access to care for all in Montana. Currently, she is part of a group convened by the Institute for Alternative Futures to consider social determinants of health and working actively to incorporate promising practices of these determinants in patient-centered health home planning. Her educational background includes a bachelor's degree in human biology (Stanford University), a degree in nursing (Montana State University), and a masters' degree in public health (University of Washington).

Chris Gunter, Ph.D., serves as the director for communications operations at the Children's Healthcare of Atlanta's Marcus Autism Center, and as an associate professor in the department of pediatrics at the Emory University School of Medicine.

Dr. Gunter earned her Ph.D. in human genetics at Emory University in 1998, studying fragile X syndrome and the mechanisms of dynamic mutation. She then moved to Case Western Reserve University and completed both postdoctoral work on X chromosome inactivation and an editorial fellowship at the journal *Human Molecular Genetics*. From 2002 to 2008, Dr. Gunter served as a senior editor for the journal *Nature*, handling the areas of genetics, genomics, and gene therapy. She then joined the Hudson-

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Alpha Institute for Biotechnology as the director of research affairs, where her responsibilities included creating an academic environment, providing scientific content for multiple audiences, and establishing a new international conference series in immunogenomics. Currently, she is a frequent lecturer on the editorial process for publishing in scientific journals, the changing landscape of publication, and the importance of outreach and engagement using all media. At the Marcus Autism Center, Dr. Gunter coordinates genetics activities and science communication, working with researchers and the public to publish and translate scientific findings.

Kathleen T. Hickey, Ed.D., F.N.P., A.N.P., FAHA, FAAN, is an assistant professor of nursing at the Columbia University School of Nursing. She also holds a joint appointment in the Division of Cardiology (electrophysiology) as both a family and adult nurse practitioner. Her interdisciplinary research is focused on cardiogenetics, the clinical care and management of those with atrial and ventricular arrhythmia, and the prevention of sudden cardiac death. Her recent grant awards include an R03 from the National Institute of Nursing Research focusing on arrhythmia telehealth monitoring, a Clinical Translational Service Award–funded pilot award focusing on cardiogenetics, and a Columbia University Glenda Garvey Teaching Academy award on remote electronic learning. She was the first recipient of Columbia University School of Nursing's Outstanding Young Investigator Award in 2007. This summer, Dr. Hickey attended the National Institute of Nursing Research Summer Genetic Institute to gain a deeper understanding of the application of genetics as it relates to her focus in area of cardiac electrophysiology. Her teaching in the classroom and clinical setting have focused on such topics as advanced cardiac physical assessment, basic concepts of arrhythmia management, and the care and management of those with internal cardioverter defibrillators and pacemakers. She has published in numerous peer-reviewed journals.

Joseph D. McInerney, M.A., M.S., has been executive vice president of the American Society of Human Genetics (ASHG) since March 2013. He received his training in genetic counseling at the State University of New York–Stony Brook in the mid 1970s and spent the next 22 years working on genetics education for pre-college and college students and on other programs at the Biological Sciences Curriculum Study (BSCS), in Colorado. He was director of BSCS for the last 14 years of his tenure there. From 2000 to 2010, McInerney was director of the Baltimore-based National Coalition for Health Professional Education in Genetics, where he led the development of educational programs for a broad range of health professionals on a wide variety of topics in genetic medicine. He has published more than 100 papers, reviews, and book chapters in the scientific and science

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Relevance of Health Literacy to Precision Medicine: Proceedings of a Workshop

education literature. He is an elected fellow of the American Association for the Advancement of Science (1996) and the recipient of the Award for Excellence in Human Genetics Education from ASHG (2005), the Natalie Weissberger Paul Award for National Achievement from the National Society of Genetic Counselors (2005), and the Art of Advocacy Award from Genetic Alliance (2009).

Laurie Myers, M.B.A., has led health literacy strategy for Merck since 2011, and her role has recently expanded to include both U.S. and global responsibility. She focuses on the integration of health literacy externally and across divisions at Merck. Key projects include patient labeling, packaging, clinical trials, and patient education. She has regularly engaged with payers, integrated health systems, and large medical groups to discuss health literacy. Ms. Myers actively participates on several external projects, including acting as co-chair of the Harvard Multi-Regional Clinical Trials Center Return of Results Group, serving on the European Medicines Agency lay summaries working group, and working with the Walgreens/Northwestern/Alliance of Chicago partnership, measuring the impact of the Universal Medication Schedule on patient adherence and health. She is passionate about creating health literacy champions outside of the field and hence speaks at conferences focused in other areas, including adherence, patient engagement and advocacy, market research, Drug Information Association, and lay summaries, in both the United States and Europe. Ms. Myers joined Merck in 1999 and has worked in several therapeutic areas in market research, marketing communications, and pharmacy and distribution. She received her M.B.A. in health care management from the Wharton School at the University of Pennsylvania and graduated magna cum laude with her B.A. in psychology from Yale University.

Catina O'Leary, Ph.D., serves as president and chief executive officer of Health Literacy Missouri (HLM). Under her direction, HLM's service network has expanded to include some of the largest employers in Missouri, including pharmaceutical companies, hospital systems, business coalitions, and community-based organizations. Chosen by the *St. Louis Business Journal* for professional excellence and dedication to the community, Dr. O'Leary is a member of the 2013 class of "40 Under 40" leaders. She was recently selected to join FOCUS St. Louis' 39th Leadership St. Louis class. Before her appointment as chief executive officer of HLM, Dr. O'Leary was a faculty member at Washington University School of Medicine in the Department of Psychiatry and the Program on Occupational Therapy. At Washington University, her community-engaged research centered on methods to engage underserved populations in health and social service programs. She focused specifically on women's health.

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Dr. O'Leary is the past president and continues to serve on the board of The Bridge, a drop-in shelter that offers daily meals and basic social services to homeless and at-risk St. Louisans. She also serves as vice president for Magdalene Saint Louis, a nonprofit organization that helps women who have survived abuse, prostitution, trafficking, and addiction by providing a community where they can recover and rebuild their lives. Dr. O'Leary earned her B.A. in psychology from the University of Mississippi and her M.S.W. and Ph.D. in social work from the George Warren Brown School of Social Work at Washington University.

Ruth Parker, M.D., is a professor of medicine and public health at the Emory University School of Medicine. She developed one of the first measurement tools to quantify patients' abilities to read and understand health information—the Test of Functional Health Literacy in Adults (TOFLA). She also co-wrote the definition of health literacy used by Healthy People, the National Institutes of Health, and the Institute of Medicine (IOM) report *Health Literacy: A Prescription to End Confusion*, and she is the developer of a model of health literacy that is achieving growing recognition in the United States and internationally. Dr. Parker worked to define medication labels as an issue at the intersection of health literacy and patient safety, and she co-wrote the seminal white paper on the topic, which was presented to the IOM at a workshop on standardizing medication labels. This led to pivotal work by the U.S. Pharmacopeia (USP), where Dr. Parker worked on an expert panel to create standards for improved medication labels. This standard has now been published by USP. Dr. Parker also works with the U.S. Food and Drug Administration as a scientific expert special government employee regarding medication labels and with the Nonprescription Drug Advisory Committee as an expert in consumer understanding of medication labels. Dr. Parker is also a strong advocate for health literacy and its importance to health. She has worked tirelessly with professional societies, federal and state agencies, and congressional staff to inform them about health literacy issues and to encourage them to recognize health literacy as a priority issue.

Benjamin Solomon, M.D., an accomplished scientist and medical geneticist, is dual board certified in pediatrics and clinical genetics through the National Human Genome Research Institute. At Inova Translational Medicine Institute, Dr. Solomon leads the Medical Genomics Division—a group of clinicians and researchers that focuses on providing genetic and genomic medical care, discovering new explanations for genetic disorders, and studying the best ways to integrate cutting-edge genomic resources into clinical practice. Previously Dr. Solomon held positions at the National Institutes of Health researching the genetic and genomic causes of both rare

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and common conditions, especially certain types of congenital anomalies. The author of more than 90 peer-reviewed articles and book chapters, Dr. Solomon serves as an editor on a number of medical journals, has edited several medical textbooks, and is actively involved in genetic/genomic training and education.

Sara Van Driest, M.D., Ph.D., is an assistant professor of pediatrics at the Vanderbilt University School of Medicine. Dr. Van Driest's research program focuses on the development of tools to use large data sources such as electronic medical records and DNA sequences to predict and improve children's response to medication (personalized pediatrics).

Catherine Wicklund, M.S., is the director of the Graduate Program in Genetic Counseling at Northwestern University and an associate professor in the Department of Obstetrics and Gynecology. She has more than 20 years of experience in clinical genetic counseling and has provided prenatal and pediatric genetic services. She served on the board of directors of the National Society of Genetic Counselors (NSGC) first as Region V representative, then as secretary, and was president in 2008. Currently she is a member of the Illinois Department of Public Health's Genetic and Metabolic Diseases Advisory Committee, the Advisory Committee on Hereditable Disorders in Newborns and Children, the American Society of Human Genetics representative on the Scientific Program Committee of the 2016 International Congress of Human Genetics, and the NSGC representative on the Institute of Medicine Roundtable on Translating Genomic Based Research for Health. Ms. Wicklund's research interests include issues regarding whole-genome/exome sequencing and personalized medicine, psychosocial and counseling issues, and professional issues including workforce and access to and delivery of genetic services. She is a co-investigator on the Electronic Medical Records and Genomics Network, which aims to bring personalized medicine into broader clinical use. She received her master of science degree in genetic counseling from the University of Texas Graduate School of Biomedical Sciences and is a diplomat of the American Board of Genetic Counseling.

Consuelo H. Wilkins, M.D., MSCI, is the executive director of the Meharry–Vanderbilt Alliance, a strategic partnership between Meharry Medical College and the Vanderbilt University Medical Center. Her primary responsibilities include developing and supporting collaborative initiatives in biomedical research, community engagement, and interprofessional learning. She holds faculty appointments as an associate professor of medicine at the Vanderbilt University School of Medicine and Meharry Medical College. Dr. Wilkins is widely recognized for her work in stakeholder

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engagement. She is principal investigator of a Patient-Centered Outcomes Research Institute award, Improving Patient Engagement and Understanding its Impact on Research through Community Review Boards. As the co-director of the Meharry–Vanderbilt Community Engaged Research Core in the Vanderbilt Institute for Clinical and Translational Science, she brings together academic researchers and community members to improve community health and health care through community-engaged research. Her prior research focused on understanding the complex intersection among cognitive impairment, frailty, and depression. Prior to joining the Vanderbilt faculty in 2012, Dr. Wilkins was an associate professor in the Department of Medicine, Geriatrics Division, with secondary appointments in psychiatry and surgery (public health sciences) at Washington University School of Medicine, St. Louis. She served as the founding director of the Center for Community Health and Partnerships in the Institute for Public Health; the co-director of the Center for Community Engaged Research in the Clinical and Translational Science Awards; and the director of Our Community, Our Health, a collaborative program with Saint Louis University to disseminate culturally relevant health information and facilitate community–academic partnerships to address health disparities.

Michael Wolf, Ph.D., M.A., M.P.H., is a professor of medicine, an associate division chief (internal medicine and geriatrics), and the director of the Health Literacy and Learning Program (HeLP) within the Feinberg School of Medicine, Northwestern University. He also holds appointments in cognitive sciences, communication studies, medical social sciences, psychiatry and behavioral sciences, and surgery. As a health services researcher and cognitive-behavioral scientist, Dr. Wolf has extensively studied cognitive, psychosocial, and health system determinants of health, specifically in the area of health literacy and health communications research. His work has primarily focused on understanding health care complexity. Dr. Wolf has led several large-scale, pragmatic trials to evaluate multifaceted interventions to promote patient engagement in health, targeting chronic disease self-management, medication safety, and adherence.

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