Welcome, Introduction, and Goals of the Meeting

Genomic Medicine XI convened leaders in genomic medicine to discuss research directions in genomic medicine implementation. The goals of this meeting were to summarize the current status of genomic medicine implementation research, identify current obstacles to implementation and how to overcome them, and define where clinical implementation of genomic medicine could or should be 5-10 years from now and the strategies for reaching these goals. Additionally, GM XI was intended to inform the NHGRI strategic planning process for 2020, which will define the Institute’s role at the Forefront of Genomics.

Overview of NHGRI’s ‘Genomics 2020’ Strategic Planning Process

On February 12, 2018, NHGRI announced the start of the “Genomics 2020” strategic planning process. This will culminate in the publication of a new strategic plan in October 2020 to commemorate the 30th anniversary of the start of the Human Genome Project. The previous 2011 strategic plan highlighted the importance of genomic medicine and created the foundation for the Genomic Medicine Working Group. Although many of the points made in this plan are still relevant, the field of genomics has changed dramatically over the past 30 years. Genomic research is now funded by nearly all Institutes and Centers of the National Institutes of Health (NIH), along with various organizations in the private sector. NHGRI’s role in the genomic research ecosystem will be at “The Forefront of Genomics®”, with some more mature or specialized areas of genomic research such as cancer or microbial genomics moving outside the primary mission of NHGRI. The Institute will need to prioritize its resources to be the driving force for progress in genomics that empowers other individuals and organizations. The new strategic plan will provide NHGRI with a guide on how to best carry out this role.

NHGRI’s strategic planning elements include workshops, town halls, gatherings at existing meetings, a dedicated web page, social media tools, and the engagement of advisory groups. These elements will ultimately lead to a Finale Meeting in April 2020 and the submission of a manuscript in July 2020.

Session 1: Basics of Implementation Science and its Relation to Genomic Medicine

Much of the benefit of valuable research is lost by the time it reaches the patient; in fact, it can take up to 17 years to turn 14% of original research to the benefit of patient care (Balas and Boren, 2000). Current barriers to implementation, such as unwillingness to change established
practice patterns and lack of payer support, training, follow-up, and infrastructure to embed best practices into clinical workflow, lead researchers to create many healthcare solutions that have the potential to improve healthcare but will never be utilized.

Implementation science is “the study of methods to promote the integration of research findings and evidence into healthcare policy and practice.” Research into both implementation and dissemination is necessary to understand how to best distribute and integrate evidence-based health interventions into clinical practice. NIH currently has a number of trans-NIH program announcements for dissemination and implementation research, focusing on local adaptation of implementation, sustainability of interventions, scaling up of interventions, and de-implementation of ineffective, suboptimal, or potentially harmful care. There are also several implementation science training programs and an Annual Conference on the Science of Dissemination and Implementation in Health co-hosted by NIH and AcademyHealth every December. Implementation challenges vary by each patient care setting or healthcare system’s unique situation, and the burden of integrating a diverse range of challenges (insurance, education systems, specialists, and more) often falls to the patient or caregiver.

Frameworks and models, such as Peter Pronovost’s central venous catheter checklist that led to an 80% reduction in catheter-related bloodstream infections in intensive care unit (ICU) patients, are helpful tools that make implementations more sustainable and generalizable. Each ICU had to adapt the checklist, sometimes substantially, to address its unique needs, suggesting that it was the process of creating the checklist within a common implementation framework rather than the checklist itself that led to widespread improvements. This study emphasized the importance of not only considering outcomes, but also the processes that lead to them.

The NHGRI-funded Implementing Genomics in Practice (IGNITE) program used an implementation model to guide network interactions. IGNITE consists of 6 projects with different genomic interventions with the goal of implementing each intervention in at least one community partner. The program wanted to make sure that the lessons learned from each of these implementations were shared and transferable. To achieve this goal, they used the Consolidated Framework for Implementation Research (CFIR). This framework provides a draft for how to implement genomic medicine, but still needs to be refined. A useful tool for creating institution-specific models is on the Dissemination & Implementation Models website, which allows practitioners to find the best model for their research question or practice problem.

The RE-AIM (Reach, Effectiveness/Efficacy, Adoption, Implementation, and Maintenance) framework is another implementation framework that provides specific criteria for measuring public health impact of health interventions. Each RE-AIM dimension provides a different measurable outcome for evaluating effectiveness. Using these measures, RE-AIM can be used to break down, evaluate, and even plan genomic medicine programs by helping identify pragmatic priorities. This focus on real world pragmatic questions enables the utilization of already available data and outcomes and presents an opportunity for intervention within each dimension of the framework. Some other important frameworks are PRISM, PARIHS, the Coordinated Implementation Model, and the Precede-Proceed Model.
Discussion

The IGNITE program showed that there are elements common to genomic medicine implementation efforts that can be used to develop a framework specific to genomic medicine. There is growing evidence that these implementation frameworks and models increase cost effectiveness, which could benefit other NHGRI programs. These frameworks may seem difficult to integrate within the “n=1” environment in which many clinical geneticists work, but common implementation frameworks and models will help clinicians understand the best processes to evaluate singular cases. Fragmentation of healthcare presents another challenge since there is currently no easy way to move a patient’s genomic information with the patient as they are cared for in different systems across their lifetime.

The field of genomic medicine moves quickly, leading to diverse, ‘one-off’ implementation efforts by many health systems that are often driven by economic incentives and local champions in the field. This quick pace results in a wide variety of implementation strategies that may not be guided by standardized frameworks and models and may thus be less useful and generalizable. To enable interoperability across different areas of genomic medicine, solutions should be guided by an accepted implementation framework and engineered to allow for tailoring an implementation plan that is adaptable to an individual site’s unique requirements. These solutions should also gather and retain information that can be used by other sites to facilitate local implementation.

The NIH funding process is not well suited to keep up with the iterative nature of implementation projects and the rapid pace at which funding of implementation studies is needed. The Cancer Moonshot attempted to address this problem by creating implementation centers that would independently identify and conduct new implementation research faster than NIH funding cycles normally allow. Similar centers may be appropriate for genomic medicine implementation. Implementation research is also impeded by skepticism amongst peer reviewers and a lack of investigator-initiated applications; there is thus a need for NIH leadership to build this research community.

Additionally, healthcare systems need to build their own implementation research environment independent of NIH funding. Geisinger, for example, used the results from a large clinical research sequencing program (the MyCode Community Health Initiative) to convince its leadership to support a clinical implementation study that sequenced the ACMG 59 genes in Geisinger employees. The initial data demonstrated the benefits of sequencing to employees and to system leaders. The positive response increased Geisinger leadership’s willingness to conduct future implementation activities.

Misalignment of payment and implementation is also a current challenge. Payers need to know they are paying for treatments and strategies that will directly benefit patients. The Moffitt Cancer Center provided an example of utilizing payer services for more than their intended purpose: microsatellite instability (MSI screening), used clinically to determine eligibility for
immunotherapy, also tests for Lynch syndrome, enabling identification and cascade screening of family members at risk. Consequently, Lynch screening is a valuable implementation science “by-product” of colon cancer patients seeking immunotherapy.

Finally, the use of disruptive innovation such as direct-to-consumer apps to inform and aid genomic medicine information dissemination is currently understudied. NCI’s Health Communications and Informatics Research Branch (HCIRB) currently promotes research in science communications, more of which is needed across the NIH.

Session 2: Resources for Genomic Medicine Implementation

ClinGen and ClinVar work together to improve variant interpretation. ClinVar is an archive of reported relationships between variants and conditions, submitted from a wide variety of sources. It contains records of assertions of pathogenicity for a variant, whether a variant has been observed previously, and, if more than one submitter has reported a variant, whether a consensus annotation has been determined. The aggregated database is publicly available, free, and accepts submissions from registered organizations. As of August 2018, there were over 430,000 unique variants in ClinVar, and the database is working to resolve 18,000 variants with conflicting interpretations. However, since the database is submission-driven, the quality of submissions varies. ClinVar has a star system to help determine the review status of the submission, but users need to look for other measures of quality themselves.

ClinGen is an NHGRI-funded program that complements ClinVar by supporting a number of expert panels that develop consensus expert recommendations for variant interpretations. These expert panels leverage a ClinGen-ACMG interpretation guideline system to assess population, experimental, case/segregation, gene-centric, and computational data for evidence of benignness or pathogenicity. These core ClinGen activities are in addition to several supplemental ClinGen projects aiming at improving the variant interpretation ecosystem. This includes initiatives to encourage patients, clinicians, labs, and researchers to share their genetic and health data. Additionally, an interpretation-discrepancy resolution working group works with clinical testing labs to resolve differences in their ClinVar variant interpretation submissions. This group has strengthened ClinVar by resolving 87% of discordant sequence variant classifications amongst the group of labs involved in the discrepancy resolution workflow. ClinGen also has a patient registry called GenomeConnect that encourages patients to submit and annually update their genetic and health information. This provides a method for tracking outcomes longitudinally and monitoring potential changes in variant knowledge. In ClinVar, researchers can view if GenomeConnect data have been uploaded for a certain variant and can request further information if needed.

Another potential resource is the SPARK Toolbox, created by the IGNITE network as an online information resource library for the field of genomics. It provides tools to help clinicians incorporate genomics into their practices and allows researchers to study the best ways to use genomics in healthcare. It also allows users to create customized implementation guides for their unique environments. The network initially leveraged the expertise of the IGNITE
Pharmacogenetics Working Group to create a user-guided CYP2C19-Clopidogrel implementation guide. The CYP2C19-Clopidogrel guide is a checklist of items and is linked to relevant resources. The interactive experience empowers clinicians and researchers, while allowing the IGNITE network to collect data on the areas of implementation that are prioritized by different healthcare systems. Although some guides might not be scalable, the data collected by the SPARK Toolbox could help identify common implementation practices and challenges specific to genomic medicine.

Discussion

Discussions of the cost of genomic medicine implementation typically focus on payers, but in reality, payers are just a fraction of the economic costs associated with implementation. Therefore, there needs to be a broader view of the real cost of implementation that includes personnel, informatic support, infrastructure, and other attributable costs. Additionally, as the field of precision medicine grows and changes, funding will be needed to support clinicians and healthcare consultants. In order to provide useful guides, experts need to prioritize what questions need to be answered for different stakeholders. IGNITE has published a clinician-level guide to implementation, and ClinVar is currently trying to invite non-genetics providers to a monthly informational call.

The sharing of genomic data is critical to genomic medicine implementation, but patients are understandably concerned that their genomic data be kept secure. Educational opportunities for patients such as those used by the All of Us initiative could help address this issue. Some organizations cite patient consent regulations under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) to avoid sharing genomic data, which can be a barrier to ClinVar receiving data. While the ClinVar submissions do not contain Personal Health Information as defined by HIPAA, and therefore this type of data sharing is not prohibited, there is some sensitivity to the nature of genetic data. To address this, ClinVar does not request entire VCF files and gives guidelines on what kinds of data are appropriate to submit based on a patient’s consent. By determining the allele frequencies at which genomic data become identifiable, experts could create broader guidelines for appropriate sharing, which could help providers understand whether changes in current consent procedures are needed to share genomic data. The HIPAA regulations also contain exemptions for healthcare management programs that are using data to improve the quality of care. Programs such as ClinVar could seek such exemptions.

While clinical data are valuable, functional variant information is also essential for determining clinical actionability. It may be possible to leverage the broader scientific community’s expertise to create a resource of known variant function information. NHGRI has published two Program Announcements to identify novel approaches for relating genetic variation to function and disease (PAR-18-867 and PAR-18-868). Additionally, longitudinal studies are very important. All of Us is working to collect longitudinal data and improve the portability of genomic information.
Session 3: Novel Models of Genomic Medicine Implementation

In the spring of 2017, the Northshore University Health system implemented a Genetic and Wellness Assessment (GWA) tool in Chicago. This implementation intended to provide genomic services across a broad area and responded to increased demand for genomic services. The wellness tool distributed a 30-question optional genomic checklist to all patients before their annual physical via Northshore’s healthcare portal, NSConnect, and a mobile app. The checklist asked questions to identify patients who might benefit from targeted genetic testing and auto-filled answers available from data already in the electronic health record (EHR). Patients’ survey responses were used to generate “Best Practice Alerts” alerting clinicians to a patient that might benefit from genetic testing. The system then provided the clinician with a clear path to follow through with the information. The GWA went live to all sites in November 2017, and 51.2% of patients had responses to the tool that triggered Best Practice Alerts.

The Northshore GWA tool provides a scalable approach to system-wide genomic medicine integration. It identifies potential at-risk patients and enables proactive screening that may vastly improve primary care. However, it will be necessary to develop methods for educating the medical team and patients, and to improve follow-through on GWA recommendations at each step. Northshore is anticipating researching these challenges, as well as barriers and facilitators to the GWA tool’s implementation, during year two of the program.

The MyCode Community Health Initiative (MyCode CHI) is a precision health clinical research program at Geisinger that aims to return actionable exome sequencing results to patients and their providers while providing an infrastructure for long-term management planning. Geisinger started the MyCode biorepository in 2007 following extensive consultation with patients and other stakeholders. In this consultation it was determined that there was strong interest to have medically actionable results returned; this biorepository allowed Geisinger to develop MyCode CHI. So far, 881 results have been returned to 877 patients. While patients are able to consent to MyCode online, or through a smart device, there is a heavy reliance on in-person consenting. MyCode CHI has developed an infrastructure to support the clinical workflows needed to ensure a robust and responsible return of results disclosure. They are currently measuring process, health, cost, behavioral, and patient-reported outcomes.

Intermountain Healthcare has implemented genomic medicine through its precision oncology workflow. They use a panel of ~170 tumor genes on each patient and the results are interpreted by a molecular tumor board. These interpretations are included on a report, which gives treatment options that are easy to interpret and facilitate ordering of therapeutics. Data from this project showed that patients who had targeted cancer therapy had better overall survival and lower overall weekly oncology related costs than those who had standard chemotherapy. This was also true when they looked at an expanded cohort of oncology patients who were insured by the SelectHealth plan. Due to these data, the SelectHealth plan now covers the cost of genomic testing in oncology patients. These successes have inspired Intermountain to launch other precision medicine initiatives in behavioral health and hereditary
cancer. Hence, a grass roots precision genomics workflow in oncology influenced a health system to consider implementing precision genomics in other clinical programs and services.

Some novel tools have been created for implementation, as well. Limited knowledge about Mendelian disease variants has caused many patients with Mendelian diseases to remain undiagnosed. Vanderbilt created a metric called phenotype risk score (PheRS) to better assess the pathogenicity of Mendelian disease variants. These scores were generated by mapping Human Phenotype Ontology (HPO) terms from the Online Mendelian Inheritance in Man (OMIM) to phecodes from EHR data. The PheRS for a given Mendelian disease is the sum of clinical features observed in a patient weighted by the log inverse prevalence of the feature. A patient with a diagnosed Mendelian disease will have a high PheRS, while a patient with an undiagnosed Mendelian disease will have a low PheRS. Additionally, Vanderbilt used the Exome BeadChip to explore the pathogenicity of 60,000 rare variants. This was done by leveraging OMIM to filter for variants in known Mendelian disease genes and generating a PheRS for each of them. A similar process was used to generate a PheRS for patients recruited through the Undiagnosed Diseases Network (UDN). In theory, a PheRS could be generated for every patient with EHR data. This could help determine which diseases are the most important to diagnose and which are the most likely to be undiagnosed.

Tempus has developed an operating platform for precision medicine that provides precision medicine products by aggregating data to push the field forward. The overall goal of their service is to help treat cancer patients based on the aggregated data of all previous cancer cases. Their platforms integrate clinical, imaging, sequencing, and model data to power clinical and research applications. Tempus has a team of about 150 manual curators that monitor the system’s natural language processing to make sure it has correctly structured data for each patient. After analysis, a report is generated that presents relevant variants, potential drug-matches, and other suggestions to clinicians. This data structuring team could provide valuable insights to other healthcare systems that need data structuring.

Discussion

It is important to engage economically, geographically, socially, and racially diverse patient populations. This may be difficult for certain health systems that do not have access to diverse populations but can be addressed by building collaborations with other health systems.

The success of Intermountain’s precision oncology molecular tumor board demonstrated the power of individualized interpretations. Tumor boards have also been successful platforms for educating trainees. Similar expert panels could be created in genomics to assist with interpretations and educate trainees in genomics. Panels such these are usually limited to larger healthcare systems. However, online programs could be leveraged to reach providers in smaller health care communities.

The implementation of genomic medicine in large academic centers has exposed some challenges that will need to be overcome for broader implementation. For instance,
incorporating genomic data into EHR systems is difficult and requires building new reports. Structured data from genomic reports is extremely valuable, but the time and resources for implementation are unavailable in most medical centers. One potential solution to this problem is to use resources from the private sector (such as the curation team from Tempus) to structure patient data. Lastly, failures of implementation models need to be better reported so the broader community can know what to avoid in the future.

Currently, a large amount of genomic medicine evidence is being generated without appropriate follow-up. A genomic medicine data registry, similar to the National Cardiology Data Registry (NCDR), could help with evidence generation and evaluation. This registry could also be attractive to payers. The Genomic Medicine Working Group (GMWG) should reach out to NCDR for advice on how to structure such a registry. Additionally, since research studies are typically funded for 3-5 years, it would be helpful to identify concrete outcomes of implementation research. One of the most useful outcomes is whether patients change their healthcare behavior after interventions; such patient-reported outcomes can provide valuable information that is not always captured by healthcare encounters.

**Debate — “Genomic medicine must become the responsibility of primary care providers”**

**Pro: Carol Horowitz**

Carol Horowitz, a general internist at Mount Sinai, argued that genomic medicine providers typically say that genomic medicine is exceptional and thus requires the support of specialists. However, this same argument was used for HIV and other complex health challenges that are now routinely handled by primary care providers (PCPs). PCPs have extensive experience dealing with (and explaining) complex scientific and ethical issues, which could be a potential strength in genomic medicine. At the same time, it is critical that they work alongside geneticists and genetic counselors in order to receive the necessary support.

**Con: Gail Jarvik**

Gail Jarvik, a geneticist at the University of Washington, argued that it is common for PCPs to pass care on to specialists, and this should be no different for genomic medicine. General practitioners do not have enough training in genomics. For example, medical students at the University of Washington study genomics for only two weeks, far less than the time needed to understand the thousands of genetic diseases, know when to order genomic testing, explain the outcomes and implications, and know when to make necessary management changes. There are even published data showing that non-geneticists are uncomfortable disclosing a VUS to a patient, would make misinterpretations at a high percentage, and do not understand basic genetic concepts such as inheritance. Educating more genetic counselors would be more cost-effective than reeducating all PCPs. Although geneticists do release patients back to their primary care physicians, and may be able to oversee pharmacogenomics, there are too many cases of PCPs incorrectly acting on genomic data to have them not seek specialists for help.
Discussion

While there is agreement that PCPs can handle pharmacogenomics, a consensus is still lacking about their general role in genomic medicine. In reality, over time, genomics care will probably be transferred more and more to primary care physicians. It is possible that genetic counselors will also take on some of this work, although the boundaries are currently unclear. Since it can sometimes take up to 6 months to get an appointment with a medical geneticist, it is necessary to provide adequate support and education to the physicians who are likely to be dealing with this on the front lines. This information will help PCPs and other specialists understand when they may need to hand off their patient to a genomics specialist. Some of this support could come from genetic testing labs, who generate clinical reports. Certain changes to current genomic medicine pipelines could also help provide this support for both geneticists and PCPs. Additionally, “systems engineering” could be utilized to help optimize the role of the geneticist and make reports more easily accessible for primary care physicians.

Lower sequencing costs and increased demand for direct to consumer genomic testing will necessitate the training of primary care physicians in genomics. Fortunately, many younger members of the medical field have shown a strong interest in genomics. A 3-month course for internists modeled after the Genomics Education Programme in England, which provides online resources and self-directed education in genomics for National Health Service staff, could help spread knowledge. The City of Hope Cancer Genetics program, which provides clinicians with a certificate that is recognized by some payers to allow reimbursement for testing, could also be a helpful model. Such clinicians could then serve as genomic medicine consultants to other non-specialists in medical centers and large practices as needed.

Session 4: Role of Electronic Health Records in Implementation

Genomic Clinical Decision Support (gCDS) systems are a way to distribute information to clinicians. These systems will be needed to bring precision medicine from promise to realization. Challenges to implementing gCDS systems include the management of shared genomic data, the effectiveness of the gCDS systems themselves, and a lack of existing decision support architecture and standard approaches for gCDS systems. These issues were the focus of the Genomic Medicine VII meeting. Effective implementation of gCDS systems will rely on additional IT resource development paired with common frameworks. There are published frameworks for the implementation of gCDS systems which can be applied to issues such as return of results and patient screening. These gCDS systems should be put into a toolbox such as the CDS Knowledge Base (CDS-KB) for dissemination.

Increased data standardization is necessary for implementation, as well. Currently, data are sent from the lab to the clinic in the form of unstructured, largely unstandardized reports. Standardizing the exchange of variants and phenotypes is essential to effective data sharing. This requires the support of Health Level Seven International (HL7), as well as other supporting resources like GA4GH and ClinGen. The HL7 Clinical Genomics working group has been working to develop these standards, but they are facing significant challenges to adoption due to the
depth and breadth of the field and the slow speed of implementation. In May of 2015, NCBI and ClinGen began working together to create an allele registry that provides alleles with centralized identification. This resulted in the Variant Modelling Collaboration (VMC). Still, NCBI needs other organizations to create the policies to understand this variation. This sort of standardization is necessary for phenotypes and diseases, as well.

One of the ways to assemble data into a comparable and consistent format is to create a common data model (CDM). If chosen and adopted correctly, CDMs offer harmonization, define practical data interoperability, and obviate redundant work. Fast Healthcare Interoperability Resources (FHIR) is a flexible large-scale model that provides clinical standards for data exchange between EHRs. It focuses on using small logically discrete units of exchange, which are much easier to use to generate large fixed models, rather than the other way around. Many research projects have adopted FHIR, such as All of Us: Synch for Science, CTSA Next Generation Repository Project, and the NCATS FDA data interoperability initiative. FHIR could be an essential data model for the future of precision medicine.

FHIR is also allowing for better patient engagement. Patient portals are online websites or mobile applications that provide patients with secure storage and access to personal health and medical information. However, many portals are one-sided and have limited use cases, making it difficult to integrate complex genomic health information. SMART on FHIR is a platform that allows app developers to create apps that integrate with healthcare systems that are using FHIR. Through the use of SMART on FHIR, developers can create apps that interact directly with the EHR ecosystem, thus increasing engagement and potential use cases. As FHIR continues to be adopted by healthcare systems, this will allow for greater interoperability and usage.

Discussion

Many healthcare systems are limited by vendor electronic health records that have limited capability to support genomic medicine at the present time. These companies typically won’t integrate CDMs unless there are clear benefits and demand from the user community. Thus, the genomic data science community will have to independently create models that become commonly used in clinical care, which will generate user demand to incentivize EHR companies to adopt them. This can be seen with models like FHIR, where one vendor, Cerner, now uses an underlying FHIR API. However, genomic data are far from being standardized and there needs to be greater participation on the HL7 and FHIR teams.

Panel—What Evidence is Needed for Implementation and When is There Enough?

The panel began with an introduction from healthcare experts with four different perspectives. Keith Stewart from the Mayo Clinic presented a health system CEO perspective. The Mayo Clinic’s Center for Individualized Medicine received initial institutional support and then was encouraged to seek external funds. The Mayo Clinic measures the value of their care as a way to encourage payer reimbursement.
Donald Kearns presented the perspective of the Rady Children’s Institute for Genomic Medicine. Their institute aims to treat the sickest children, with a focus on patients in NICUs and PICUs. Research has been funded by philanthropic efforts. The next step is to use data that show the long-term cost benefits of newborn screening, to get payers to reimburse genetic tests. A newborn sequencing partnership with Medi-Cal has been a big step forward.

Jay Wohlgemuth from Quest Diagnostics presented Quest’s self-insured health plan. It is a progressive health plan that directs employees to care. If there is a proven service that will help employees, then they will cover the cost. This strategy has lowered costs and improved employee satisfaction. Hence, Quest Diagnostics can use their health plan to implement new treatments and disseminate what does and doesn’t work for their employees.

Finally, Bob Nussbaum from Invitae presented the perspective of a genomic testing company. Invitae is a sequencing company that believes that one of the largest barriers to genomic medicine implementation is the high cost. By decreasing the cost of testing, Invitae hopes to eliminate this challenge and make genetic testing more accessible.

Discussion

There is no current consensus about how much evidence is needed for genomic medicine implementation. However, an increase in education and engagement with providers could help to reach this consensus. For example, inviting primary care providers to try out pharmacogenomics testing and incentivizing providers to become involved with generating evidence in genomics may increase clinician trust.

In many cases, the necessary evidence exists though it may be imperfect; better utilization of the evidence being generated will keep genomic medicine from being held hostage by perceptions of “not enough evidence.” It remains difficult to convince providers to integrate genomic medicine into their routine practice. One potential solution is to present genomic medicine as an innovation that will set medical systems apart from their competitors. Another significant challenge to implementation is repeated testing. Instead of convincing providers to order tests each time they have an indication, it might be more effective to comprehensively genotype or sequence individuals once in their lifetime, and then make this information available to future providers. At the same time, with the constant influx of new genomic information, it is necessary to weed out what truly works and what doesn’t. Therapies that have been clinically validated may be prioritized even if they have not yet been proven to have clinical utility.

Another barrier for broad genomic medicine implementation has been a lack of data on the outcomes of implementations. Although discussions about genomic medicine traditionally focus on payers, it is employers who are actually paying for the majority of their employees’ services through health plans. Medically sophisticated employers who have started to provide genomic medicine for their employees could be leveraged to gather data on outcomes. The GMWG could help genomic medicine implementation by providing a basic genetics formulary.
that explains what employers should and should not provide to their employees. A more complicated formulary could be developed for progressive employers interested in providing special “above and beyond” services. GMWG could work with employer consortia to reach consensus on what employers need the most, and then to ensure the formularies are implemented in a way that evidence is captured and publishable. Hence, a model could be created where traditional research networks create resources for implementation and employers implement and create data on the outcomes.

In the future, the healthcare system will need to account for technological developments that will increase consumer access to genomic testing and the influx of data that will come with it. Currently, the healthcare system does not have the infrastructure to use these data productively. Thus, providers will need to be better educated on how to interpret genomic data. Also, all stakeholders in the healthcare system will need to be engaged to decide what modifications to the healthcare system need to be made to cope with the large amount and availability of genomic data. Genomics England has already successfully engaged multiple stakeholders. Efforts in the United States could learn from this initiative.

**NHGRI’s Strategic Planning Process—Focus on Genomic Medicine**

NHGRI’s strategic plan in 2020 will focus on integrating genomics into medical practice. This will require standards and systems that can help implement genomic medicine into everyday practice, as well as increased training and education. During this process, NHGRI will be determining what it can reasonably own as a leader at the forefront of genomics. Suggestions for NHGRI’s strategic plan with regards to genomic medicine included an increased focus on variant standardization, medicine-based evidence, and engagement with both community health centers and patients. Attendees also suggested that NHGRI increase research on implementation sustainability and phenomic variation, and that the Institute continue its efforts in sequencing of newborns and children. More specific recommendations are available in the [strategic planning summary](#).

**Summary and Next Steps (see Executive Summary for more specifics)**

Evidence for genomic medicine implementation will continue to be critical to drive the field, and an increase in implementation research is needed from both NIH and external sources. However, in many cases, the evidence already exists for implementation and therefore other barriers need to be addressed. One major challenge to genomic medicine implementation is the lack of generalizability of frameworks, models, and data standards. Finally, better education and support of PCPs, healthcare experts, specialists, employers, and patients is required to help bring genomic medicine into everyday clinical practice.

Responding to recommendations from this meeting, the Genomic Medicine Working Group plans to reach out to the National Cardiovascular Data Registry for insight on creating a similar genomic medicine data registry. The GMWG will also work with employers such as Quest...
Diagnostics to organize a meeting with employer consortia and explore developing an employer formulary. Finally, the GMWG may create a white paper based on this meeting.