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Genomic Medicine XI: Research Directions in Genomic Medicine Implementation
September 5-6, La Jolla, CA
Executive Summary

NHGRI's eleventh Genomic Medicine meeting convened leaders in genomic medicine, healthcare systems, and informatics to identify and address major challenges in genomic medicine implementation. Specifically, the meeting aimed to: 1) Summarize the current status of genomic medicine implementation research; 2) Identify obstacles to genomic medicine implementation and how to overcome them; and 3) Define where clinical implementation of genomic medicine could or should be 5-10 years from now, and how to get there. Attendees at Genomic Medicine XI also provided input on NHGRI's 2020 strategic planning process for 2020, which will define the Institute's role at the Forefront of Genomics. More details about the strategic planning process are available in the [strategic planning summary](#).

Lessons Learned:

Implementation frameworks, tools, and methods:

- Implementation checklists, such as the one used by Pronovost et al. to reduce central line infections, are most effective when they are customized for each unique site
- Implementation centers for genomic medicine are designed to rapidly incorporate new knowledge to improve implementation more quickly than NIH funding cycles allow
- Skepticism in the peer review system about implementation science coupled with a lack of investigator-initiated applications limit implementation research funding
- Partnerships between health systems improve the inclusion of economically, socially, and racially diverse populations
- Changes in patient healthcare behavior and healthcare utilization after interventions may be good outcome measures of intervention effectiveness
- Primary care providers (PCPs) need to be involved in genomic medicine because geneticists tend to refer back to them after making diagnoses, and the number of geneticists and genetic counselors is insufficient to provide genomic medicine services
- PCPs may be capable of providing some aspects of genomic medicine, such as pharmacogenomics, but need support from genomic specialists and testing labs, particularly for rare, monogenic conditions
- ClinGen's Allele Registry is a potential resource for data standards
- Phenotype risk scores (PheRS) can be leveraged to identify probable Mendelian diseases by surveying EHRs for distinctive phenotypes
- FHIR is evolving to be the standard for genomic medicine in EHR.
- The SMART on FHIR platform can be used to develop apps to engage patients
- In many cases, a wealth of evidence already exists for genomic medicine that justifies implementation

- Tumor boards and similar expert panels have been shown to improve practice standards and could be applied to improve genomic interpretations and educate trainees

Economics:

- An increase in patient demand and growing evidence about the benefits of genomics may help convince healthcare systems to support implementation
- Reimbursement is a driver of implementation but can also be leveraged to identify additional opportunities for intervention, such as reimbursement for microsatellite instability testing prior to immunotherapy leading to incidental identification and cascade testing of Lynch syndrome families
- Employers are an important stakeholder group in genomic medicine as they are responsible for much of the healthcare expenditure and may have a lower threshold for evidence than payers
- Due to the growing amount of sequence data, more investment in people and informatics infrastructure is needed to apply the information to patient care

Recommendations:

Implementation:

- Develop an implementation framework specifically for genomic medicine that combines the most relevant elements of existing frameworks, such as CFIR and RE-AIM
- Develop “de-implementation” guides for variants reclassified from pathogenic to benign, and genes for which evidence of association with disease is weak such as the majority of genes implicated in long QT syndromes, so that testing that is contraindicated is rapidly abandoned
- Include labor and informatics costs in analyses of the cost of implementation
- Expand and disseminate genomic data sharing guidelines to help providers understand what levels of consent are needed
- Model on private sector resources, such as the data structuring teams provided by Tempus, to standardize the structure of genomics data for clinical reports
- Increase communication between scientists/clinicians and informaticians through groups like ClinGen, GA4GH, and the HL7 Clinical Genomics Working Group to create specialized data standards that fulfill systems’ and clinicians’ needs
- Establish a precedent for comprehensively genotyping individuals once in their lifetime and having that information follow them rather than repeating genomic tests

Resources and tools:

- Seek safe harbors (for healthcare management programs that are using data to improve the quality of care) for data sharing in programs such as ClinVar
- Since expert panels for variant interpretation are not scalable, explore leveraging AI to create more efficient systems
- Create a genomic medicine data registry, similar to the National Cardiology Data Registry (NCDR), to help attract payers and generate and evaluate evidence

- Collaborate with employer consortia to create a basic genetics formulary that explains what employers should and should not provide to their employees, based on best evidence and outcomes, with extension to conditions with less evidence for more progressive employers wishing to contribute to knowledge generation
- Work with employers to ensure such formularies are implemented in a way that evidence is captured and publishable
- Avoid being “held hostage” by perceptions of insufficient evidence; instead, improve utilization of the evidence being generated, even if imperfect, while identifying its weaknesses and gaps to iteratively improve the process
- Create a resource similar to the Clinical Pharmacogenomics Implementation Consortium for non-PGx genes, inclusive of non-Mendelian conditions and polygenic risk scores
- Improve interoperability of frameworks by creating infrastructure that would provide a customizable pathway to implementation, based on the specific situation
- Develop artificial intelligence models, like neural networks, to help guide genetic testing for geneticists, laboratories, and primary care providers
- Use systems engineering to develop attractive data portals for clinicians and patients, to reduce reliance on specialists and improve understanding among all stakeholders
- Increase the use of gCDS toolboxes such as the [CDS Knowledge Base \(CDS-KB\)](#) to increase dissemination and allow for broader adoption

Research:

- Collate research findings that demonstrate employer benefits from genomic medicine adoption to increase employer acceptance and implementation
- Establish an implementation research community both inside and outside NIH networks
- Increase research on genomic medicine dissemination and communication methods to help determine the impact of distributing genomic information, including the use of apps and direct-to-consumer testing
- Study disruptive innovations such as direct-to-consumer apps to inform the public and aid dissemination of genomic medicine information
- Improve reporting of failures of implementation models so the broader community can know what to avoid in the future
- Develop standardized outcomes of implementation (such as whether patients change their healthcare behavior after interventions) to facilitate implementation research

Education:

- Create limited genomic medicine training courses for primary care providers similar to the [Genomics Education Programme](#) in England
- Develop similar programs to certify non-genetics clinicians as “genomic consultants” who could be distributed across medical centers and large practices, such as the [City of Hope Cancer Genetics certification](#).
- Support guideline development groups to establish genomic medicine guidelines