National Advisory Council for Human Genome Research

May 15, 2023

Concept Clearance for RFA

Network of Genomic-Enabled Learning Health Systems (gLHS)

Purpose:
NHGRI proposes two RFAs to support a network of genomic-enabled learning health systems (gLHS) to identify and improve approaches for clinical integration of genomic information in a virtuous cycle of implementation, assessment, refinement, and re-implementation. Specifically, this initiative would: 1) support a coordinating center (CC) and 4-6 established or emerging gLHS clinical sites to share their genomic medicine implementation practices and identify those most suitable for cross-network implementation; 2) use these practices to conduct 2-4 pilot implementation projects network-wide and evaluate their impact; and 3) develop and refine successful gLHS implementation strategies as resources that can be broadly shared and adopted, including in resource-limited settings.

Background:
A learning health system (LHS), also called a "rapid-learning health system," is one in which internal data and experience are systematically integrated with external evidence and the resulting knowledge is put into practice. In an effective LHS, generalizable knowledge can potentially be captured from every patient encounter and delivered to clinicians to modify their practice, ideally allowing them to "learn from what they do and do what they learn." The LHS concept has gained significant momentum in health systems in recent years due in part to advances in electronic health records (EHRs) and information technology, as well as increased emphasis on rapid translation of new knowledge into improved care. The goal of an LHS is to enable health systems to rapidly fill evidence gaps and refine them as needed to improve the quality of care delivered. Data are collected and analyzed to assess the impact of adoption and identify areas for improvement, and those insights are then used to inform and optimize clinical practice in a virtuous cycle of continuous quality improvement.

Genomic information can be integrated at any step in this process to produce genomic-enabled learning health systems (gLHS). gLHS can facilitate rapid incorporation and evaluation of *genomic*-informed care, particularly if multiple interoperable gLHS collaborate to generate evidence of their effectiveness. Such systems have begun to adopt the full cycle of implementation, evaluation, refinement, and re-implementation of genomic medicine in true gLHS fashion, while others may be considered "gLHS-capable" but not having fully adopted all steps of the gLHS virtuous cycle. A few examples of genomic medicine interventions that have been successfully implemented on a system-wide (though site-specific) basis include genomic identification of actionable genetic conditions, EHR integration of genomic information for genetics-care delivery, EHR-identification of monogenic disorders, genome sequencing in critically ill infants, and targeted pharmacogenetic testing. Site-specific approaches such as these could be extended across individual gLHS as collaborative implementation projects to enhance interoperability and produce implementation tools and resources for wider dissemination.

Leveraging individual health systems' data and best practices in collaborative efforts to identify and implement effective genomic interventions requires adoption of common data standards and systems. Fostering interoperability of integrated genomic data across health systems to facilitate genomic medicine implementation was a key recommendation of the 2015 National Academies Genomic-Enabled Learning Health Care Roundtable report.

Significant strides in improving genomic data exchange and interoperability have since been made, as exemplified by the successful deployment of the "Genetic Cancer Risk Detector (GARDE)" program in three large health systems utilizing two different commercial EHRs. Expansion of these early successes through wider adoption of standardized genomic data elements, access procedures, and consent provisions provides an opportunity to expand upon and enable integration of genomic data into health information exchanges (HIE) that share individual-level EHR information among providers, across clinical facilities, and with patients to coordinate and improve clinical care. Expansion to under-resourced settings must also be a priority of the program to address current barriers to accessing genomic testing and expert consultation and increase the availability of such approaches to all.

The potential for gLHS to move genomic discoveries rapidly into clinical care through systemic implementation was highlighted in the NHGRI 2020 Strategic Vision, particularly the possibility of extending gLHS studies across multiple health systems to reveal common challenges and solutions. To explore successful implementation models and possibilities for collaboration among them, NHGRI convened Genomic Medicine XIV – Genomic Learning Healthcare Systems in August 2022. Establishing a network to promote sharing and collaboration across gLHS was a key recommendation of that meeting.

Proposed Scope and Objectives:
NHGRI proposes to establish a coordinating center (CC) and 4-6 gLHS clinical sites (CS) to form a gLHS Network for sharing and developing current best practices for implementing, evaluating, refining, and re-implementing genomic medicine interventions. During the first year, the CC and CS will work together to identify and select among a list of potential best practices for Network-wide implementation projects. In collaboration with NHGRI, the Network will select 2-4 pilot implementation projects that have the best evidence to improve outcomes, warrant broader implementation, and are amenable to efficient system-wide alterations such as EHR prompts or order set changes. The Network will implement and evaluate these practices in years 2-4. Key goals will be to assess and improve integration of genomic information into EHRs and create methods to enhance interoperability across systems. Year 5 will be devoted to assessing the impact of integration and implementation, using lessons learned to refine tools and resources for wider dissemination. The CS will be responsible for identifying and sharing within (and eventually beyond) the Network their best practices for genomic medicine implementation. The CC will coordinate sharing and implementation efforts across the sites through in-person meetings, conference calls, working groups, etc. It will also compile and organize selected best practices and methods (for example, for EHR integration, results reporting, decision support, provider education, community engagement) for broader distribution to a wide range of healthcare settings.

Expectations of CC and CS: CC and CS applicants will be expected to demonstrate a track record of using gLHS approaches in their health system, including in underserved and diverse communities and settings. They will be expected to identify and include in their sites champions from resource-limited settings who will provide their unique expertise and perspectives to broaden the applicability of Network products and potentially increase the likelihood that they will be adopted across a wide range of settings. CC and CS applicants should also have expertise in community and stakeholder engagement, implementation science, change management, and health services research. The Network will be expected to include engagement with communities and other relevant stakeholders to help prioritize tools and resources to be developed and to prioritize interventions addressing health issues of importance to them. CC applicants should also demonstrate experience in coordinating efforts among a wide range of investigators and clinical groups. CS applicants should have experience integrating (or capability to integrate) genomic information into their EHRs, evidence of their ability to extend their approaches to low-resource settings and diverse

U.S. populations, demonstrated readiness for change, capacity for their EHR to interact with other systems to enhance interoperability, ability to implement pilot implementation projects in a gLHS model, readiness to work with peers in a network setting, and willingness to share and improve upon their existing gLHS approaches. They should also commit to implementing agreed-upon approaches Network-wide to conduct 2-4 pilot genomic medicine implementation projects as described below.

Pilot implementation projects: Network-wide genomic medicine interventions will be selected and designed to demonstrate and enhance the ability to exchange genomic results, recommendations, and workflows across CS. Pilot projects with significant evidence supporting the value of or need for broader implementation will be selected from existing programs at the CC and CS or from similar systems. Other criteria for selecting projects will be defined by the Network but could include ease of implementation, efficiency, and cost; generalizability across systems including low-resource settings; and impact on health inequities. Implementation projects should also assess ability for a patient's genomic information to follow them across multiple providers. Improved interoperability and communication of genomic findings between clinicians and laboratories will be another key goal for the implementation projects, ideally through electronic exchange of structured data that can be readily integrated into EHRs and laboratory systems.

Evaluation and best practices: Assessment metrics for selected projects should include outcomes of value to patients, communities, health systems, payers, clinicians, and other stakeholders. Evaluation and review of findings from the implementation projects will also be used to refine approaches and develop gLHS implementation resources that can be used by other health systems. These resources should include facile approaches for integrating genomic results in the EHR, real-time monitoring of or dashboarding the status of implementation, and tracking the outcomes of interventions.

Broadening participation in gLHS: As use of genomics increases in clinical medicine, products of the Network can enable health systems to implement gLHS approaches, helping to ensure genomic information is effectively evaluated and used to improve care. To help minimize disparities in care, gLHS products should be feasible across a range of health systems, including low-resource settings and genetically diverse populations. Implement-ation resources produced by the Network will be designed to help other providers adopt gLHS approaches and potentially facilitate their participation in this and similar networks.

Relationship to Ongoing Activities:
This RFA will be NHGRI's and NIH's first initiative focused on exploring and developing gLHS. While other NIH ICs currently fund a number of programs broadly referencing LHS approaches, only a handful incorporate genomic information, and none supports consortium approaches for developing best practices. Other NHGRI efforts focus on implementation and evidence generation without the iterative virtuous cycle that makes LHS so effective in rapid generation and translation of new knowledge to improve medical care.

Mechanism of Support:
U01 cooperative agreement
Two RFAs will support: 1) a single award to a CC; 2) 4-6 CS. NHGRI staff will seek participation and co-funding from Institutes and Centers with related interests.

Funds Anticipated:
$5.3M per year for a total of 5 years. Funds will be sought from other ICs and used to increase the number of sites or pilot projects.