

Concept Clearance for RFA

Genomic Medicine Pilot Demonstration Projects

NHGRI Advisory Council, February 2012

Purpose

The National Human Genome Research Institute (NHGRI) proposes an RFA to support a consortium of collaborative genomic medicine demonstration projects. The goals of this initiative are to demonstrate the feasibility of, and develop methods for, incorporating an individual patient's genomic findings into their clinical care by: 1) expanding existing genomic medicine efforts, and developing new collaborative projects and methods, in diverse settings and populations; 2) contributing to the evidence base regarding outcomes of incorporating genomic information into clinical care; and 3) defining and disseminating the processes of genomic medicine implementation, diffusion, and sustainability in diverse clinical settings.

Background

Although the potential for genomics to contribute to clinical care has long been anticipated, the pace of incorporating genomic findings into medical practice has been relatively slow. Several medical centers have recently begun programs to use an individual patient's genotypic information in their clinical care (here referred to as "genomic medicine"), encountering many of the same obstacles and developing the same solutions, often quite independently. Ongoing exemplar projects include screening for highly penetrant germline mutations (such as Lynch syndrome and *BRCA1/2*) to identify genetically at-risk individuals; using web-based computerized tools to integrate patient-reported family history information into the electronic medical record (EMR) and provide appropriate clinical decision support (CDS); assaying pharmacogenetically important variants and integrating results into a decision support-enabled EMR for medication selection and dosing; and conducting genomic sequencing to solve diagnostic dilemmas and/or identify potential avenues for treatment. Much of this work, supported largely by institutional rather than NIH funds, is being done in relative isolation and would benefit from more structured collaboration and sharing of approaches.

Skepticism, resistance, and/or inertia from institutions and clinicians present major barriers to implementation of pilot genomic medicine projects, which is often as much a cultural and political exercise within a given institution as a scientific one. Early adopter institutions have typically overcome these barriers by the active engagement, if not personal mandate, of innovative leaders. Involvement of senior institutional leaders has been essential in these settings, with CEOs or other senior executives chairing or serving on committees to select, for example, patients to undergo genome sequencing, or pharmacogenetic tests to be integrated into laboratory and EMR systems.

Expectations for evidence of morbidity/mortality benefits (sometimes to the level of randomized trials for each variant to be implemented) represent another major barrier. While randomized trials are worth pursuing in some instances, painstaking educational and advocacy efforts at early adopter institutions have been effective in communicating the more modest but useful observational evidence of improved outcomes, patient/clinician satisfaction, and cost effectiveness. Highlighting successes, such as reduced hospitalizations following genotype-driven adjustments in warfarin dosing, or dramatic symptomatic improvement or reduced

adverse effects in antidepressant selection, can have major effects on shifting an institution's culture to embrace genotype-guided care.

Needs for Clinical Laboratory Improvement Act (CLIA) certification and/or IRB approval, confusion over appropriate consent and counseling models, difficulty integrating results with existing EMR systems, and burden of interpreting and following up potentially massive numbers of results all represent substantial operational barriers that, once solutions are found, could be transported and adapted to other institutions. Reluctance to adopt a novel patient care strategy, another common barrier, could also be addressed by disseminating successful pilot efforts.

Collaborative projects that connect early adopter sites to interested but less experienced groups could facilitate dissemination and assessment of genomic medicine projects in diverse settings, thus increasing their reach as well as their generalizability. Such projects could help develop best practices for complex tasks such as integrating with laboratory workflows and EMR systems, defining and collecting outcomes of implementation, and delivering complicated genomic information to clinicians and patients. They could also play a key role in collecting evidence of the effects of incorporating this information into clinical care. A consortium of such collaborative projects could become a valuable clearinghouse of successful implementation projects, collecting and disseminating detailed protocols that outline steps needed for patients, clinicians, laboratories, departments, and institutions. Indeed, critical questions to be examined are whether and how approaches developed at highly specialized and resourced tertiary care centers can be adopted in less resource-intensive settings.

Evaluating the impact of such programs and expanding their reach to diverse settings and populations is a high priority in NHGRI's genomic medicine research agenda. Potential limitations of initial approaches, and/or drawbacks of genotype-driven strategies, should also be assessed objectively in multiple settings. Such data will provide a needed evidence base for identifying effective interventions suitable for widespread implementation and reimbursement.

The value of leveraging these ongoing implementation projects by bringing them together and expanding them to diverse sites was recognized by NHGRI's Disease-Oriented Genomic Medicine Working Group and recommended at its two recent Genomic Medicine meetings. These recommendations were endorsed by the National Advisory Council on Human Genome Research and its Genomic Medicine Working Group in May and September, 2011.

This initiative will support the establishment and operation of a consortium of collaborative, multi-site projects in genomic medicine to expand, evaluate, and disseminate genomic medicine efforts in diverse settings and populations.

Research Scope and Objectives

These RFAs would support 3-5 multi-site pilot demonstration projects and one Coordinating Center to adapt ongoing successful genomic medicine projects, or initiate new ones, to expand the implementation of genomic medicine. Each collaborative project would involve one lead site with one or more successful implementation projects, and 3-5 partner sites with limited or no expertise in implementation of genomic medicine. Inclusion of diverse settings such as community hospitals, primary care practices, specialty groups, and military or Veterans' Administration hospitals, and under-served populations such as disadvantaged or non-European ancestry groups would be particularly encouraged.

Optimal demonstration projects would be expected to include: 1) evidence of (or a plan for obtaining) institutional endorsement, practitioner involvement, and patient participation; 2) an identified group of clinicians willing to learn about, receive, and act upon genotyping results on their patients; 3) a CLIA-certified genotyping environment and efficient workflow for collecting, assaying, and reporting results; 4) a process for integrating genotype results into patients' EMRs and providing clinical decision support in settings with such capabilities, and alternative non-computerized processes for those without sophisticated EMRs; 5) defined outcomes of implementation such as patient and clinician satisfaction and uptake of recommended interventions, cost, or morbidity and approaches for collecting and assessing them; and 6) a plan for sustaining, and possibly expanding, successful implementation projects once NIH funding support ends. Leveraging available institutional support and other resources, such as NIH Clinical Translational Science Awards, and identifying a clear path to sustainability of the implementation project, such as securing third-party reimbursement, would be strongly encouraged. Projects designed to contribute objective evidence most likely to influence uptake and reimbursement of genomic medicine interventions would also be encouraged.

Shortly after award, the 3-5 multi-site collaborative projects, with their lead and partner sites, would meet as a consortium to share research plans; identify commonalities in approaches, barriers, and solutions; and develop common resources such as educational, reporting, and evaluative tools. The Coordinating Center would collect and disseminate detailed protocols that outline steps needed for successful implementation at the level of patients, clinicians, laboratories, departments, and institutions. It would also organize broader, open meetings of the genomic medicine community, similar to NHGRI's recent and planned genomic medicine meetings and likely in conjunction with twice-to-thrice yearly meetings of the consortium, to further expand the reach and implementation of genomic medicine. Interaction and coordination with related NHGRI projects such as the Return of Results Consortium (RFAs HG-11-003 and HG-11-004), Clinical Exploratory Sequencing Centers (RFA HG-10-017), Electronic Medical Records and Genomics Network (RFAs HG-10-009, HG-10-010, and HG-11-022), and NIGMS's Pharmacogenomics Research Network, will also be led by the Coordinating Center.

Given the expected commonalities in infrastructural and institutional needs across collaborative demonstration projects, the potential to expand specific projects beyond the initial lead-partner sites to lead and partner sites in other projects in the consortium will be actively explored and encouraged. Creating a cadre of institutions implementing and evaluating the use of genomic results in clinical care, and collecting and disseminating successful approaches, is expected to lead to more rapid development and adoption of effective genomic medicine programs.

Mechanism of Support

This RFA would use the NIH U01 (Cooperative Agreement) award mechanism. Anticipated duration of the program is four years, with the first year costs being lower to allow for protocol adaptation, infrastructure development (educational materials, laboratory workflows, EMR integration, etc.) and subsequent ramp-up at partner institutions.

Funds Available

NHGRI would commit approximately \$3 million in FY2013, and \$4.4M per year in the subsequent two years, to support 3-5 pilot demonstration projects each comprising one lead and 3-5 partner sites, plus a consortium coordinating center. Support would be sought from other NIH Institutes, and consideration would be given to elevating priority for projects where co-funding is proposed.