Concept Clearance for RFA (U01)

Family History Implementation in the Challenging Setting of Routine Clinical Care

National Advisory Council for Human Genome Research, September 2012

Purpose

The National Human Genome Research Institute (NHGRI) proposes 2 related RFAs to develop and evaluate methods for the collection and utilization of accurate Family History (FHx) data in the time-pressured setting of practicing clinicians. The goal of this initiative is to translate current approaches, typically developed in research settings, to successful use in routine clinical settings. Specific objectives are to: develop streamlined methods for entry and interpretation of FHx data in electronic health records (EHRs); develop and evaluate risk algorithms using these streamlined methods; and increase the efficiency and inter-operability of FHx data collection and use, in preparation for incorporation of genomic technologies in clinical care.

Background

Collection of FHx data has long been part of the standard medical history, but it is often truncated or eliminated due to the severe time constraints of modern clinical settings. Recent data from the Electronic Medical Records and Genomics (eMERGE) Network, for example, showed that only 2 of 5 major clinical systems captured any FHx information at all in their electronic medical records (EMRs)[1] and in those two over 70% of the records were incomplete or missing. Yet the value of this information is undeniable; a positive FHx is a well-established risk factor for a host of both rare and common conditions that, in aggregate, account for the majority of health care costs, morbidity, and mortality in the U.S. population. FHx is also central to personalized approaches to health care informed by genomic data; an FHx of diseases such as coronary heart disease for example, represents the single strongest measure we have to date of genomically-mediated risk of common diseases.

Despite clear evidence of the importance of FHx to assessing disease risk, practical and efficient means of collecting FHx data in time-pressured clinical settings are lacking. Such approaches might include a streamlined set of screening questions, rather like the "CAGE" questionnaire for alcoholism, which could be used in all patients and followed up in a subset as appropriate. Strategies for integrating patient-entered data, including FHx tools such as My Family Health Portrait, into EHRs are also needed. Additionally, research on how and when FHx should be utilized to optimize health outcomes, and on what conditions FHx collection is most likely to improve health outcomes, is desirable. Such gaps in the research base were highlighted in the 2009 NIH State of the Science (SoS) Consensus Development Conference Family History and Improving Health (http://consensus.nih.gov/2009/familyhistory.htm).

[1] Note: Electronic medical records (EMRs) are a digital version of patient charts used within a single practice, while electronic health records (EHRs) are designed to be shared across all providers involved in a patient's care. Personal health records (PHRs) contain the same types of information as the EHR but are designed for patient access and are controlled by the patients.

The clinical validity and utility of FHx data have been demonstrated for several conditions since the 2009 SoS conference, but better methods are needed to collect, interpret, and utilize FHx in busy clinical settings. Increased adoption of EHRs and PHRs permits development of integrated electronic tools for standardized FHx collection that will also facilitate assessment of health outcomes and attendant health care costs. Such electronic tools also provide powerful opportunities to develop and study risk algorithms incorporating multiple data types, including personal medical history, behaviors, FHx, and eventually genotyping or sequencing results, to more effectively individualize health care decision-making. In addition, the privacy issues for family members raised by FHx collection should be examined in clinical settings.

These RFAs seek to address the gaps identified by the 2009 SoS conference through the improvement of methods to collect and utilize FHx data, along with evaluation of these streamlined methods for risk classification and potential impact on patients and family members. Such improved methods will position NHGRI and its investigators to use data from clinical settings to participate in assessing the added value of genomic variant data to risk prediction, beyond that provided by FHx and other clinical and risk factor information. This will become increasingly possible as dense genotyping and sequencing data become incorporated in clinical care. In addition, wider availability of FHx data obtained from relatives who also have sequence data available, enriched by phenotypic information from EHRs or PHRs, may provide valuable clinical insights on the potential phenotypic consequences of rare sequence variants.

Research Scope and Objectives

These RFAs would support 4-6 Study Investigators and a Coordinating Center to develop and validate efficient and effective electronic approaches for clinicians to collect, interpret, and utilize FHx as a measure of genomically-mediated risk of disease.

Applicants would be expected to propose streamlined methods for electronically collecting and interpreting accurate FHx that expand the uptake and use of this information in routine clinical settings (such as primary care practices). Methods for gathering FHx data that can be shared with other clinicians as needed for patient care would also be of much interest, along with evaluation of the acceptability and added value of proposed FHx approaches to clinicians. All applicants would be expected to propose and apply streamlined, clinically-targeted FHx data collection and interpretation methods in clinical practice, to develop risk algorithms based on streamlined methods, and compare those risk algorithms to algorithms derived from more extensive FHx approaches and, where needed, to standard clinical practice. This will permit evaluation of the added value of streamlined to standard FHx and clinical data in modification of risk classification or prevention and screening recommendations. Studies might examine how to incorporate FHx with other information (including genomic, clinical, and environmental data) in routine clinical care, or how to enter FHx into the EHR (such as by the patient, relative, or clinical assistant) for easy retrieval and interpretation. Studies could also include research into the economics and efficiency of the FHx collection process as well as the development of complementary PHR FHx interfaces for data entry and access by patients. Research into familial implications of streamlined FHx data collection in clinical settings might involve investigating patient perceptions of sharing FHx data within the family. Clinical research could

also be conducted utilizing the FHx data collected, for example, associating a particular genomic variant with a constellation of related phenotypes in the FHx data or additional risk associated with a FHx of multiple complex diseases.

Applicants would be encouraged to focus on complex conditions with a strong FHx component such as, but not limited to, asthma, birth defects, cancer, cardiovascular disease, diabetes, and neuropsychiatric conditions. Inclusion of diverse populations (such as minority and health disparity populations) and clinical settings (such as academic and community medical centers, specialty practices, and emergency settings) would also be encouraged.

Applicants would be expected to describe for what sorts of research use and/or data sharing participants (including patients, relatives, and clinicians) have given or would be asked to give informed consent, including how the privacy issues raised by FHx collection will be addressed. Development and dissemination of user-friendly and open-access methods for electronic FHx collection and use would also be encouraged. All methods for electronic FHx collection would be required to meet current standards for both EHR intra- and inter-operability, and encouraged to harmonize with related data collection standards such as PROMIS, PhenX, and eMERGE. High programmatic priority would be given to studies that address diverse populations and clinical settings, diverse approaches to entering FHx data into the EHR (such as by the patient, relative, or clinical assistant), multiple diseases or traits, conditions of relevance to collaborating NIH Institutes, and larger sample sizes sufficient to demonstrate clinical relevance.

Shortly after award, investigators would meet to share proposed study designs, EHR and PHR descriptions, FHx collection and interpretation strategies, and quality control approaches and to identify potential joint analyses and collaborative research. They would meet again 3 times a year to review progress and joint analyses, refine collection methods, identify common goals and best practices, and discuss lessons learned. A separate RFA would be issued for a Coordinating Center to provide support for scientific, analytic, and administrative coordination. 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), and the Electronic Medical Records and Genomics Network (RFAs HG-10-009, HG-10-010, and HG-11-022) would also be led by the Coordinating Center. Making FHx collection and interpretation methods available for use in other currently funded NIH programs would also be encouraged.

Mechanism of Support

This initiative would use the NIH U01 (Cooperative Agreement) award mechanism. Four to six U01 Study Investigator awards would be made along with a Coordinating Center.

Funds Available

NHGRI will commit roughly $4M per year for four years ($16M total) to support these awards. The four-year duration is needed to allow for longitudinal follow-up of patients to assess impact on clinical care. Several other ICs have expressed interest in participating in this initiative and priority may be given to conditions that are of relevance to contributing ICs.