Network News: Powering Clinical Research

Joseph V. Selby,1 Harlan M. Krumholz,2,3 Richard E. Kuntz,3,4 Francis S. Collins5,6

The Patient-Centered Outcomes Research Institute announces bold plans to build a National Patient-Centered Clinical Research Network that will unite millions of patients through a coordinated collaboration with researchers and health care delivery organizations.

If each patient were an active and informed participant in clinical research as part of their regular health care, a visit to a doctor’s office would have the potential to transform the health of millions of individuals. Indeed, this scenario is within reach: Stakeholders from all sectors are coalescing around the importance of conducting patient-centered research in the real world, health systems are rapidly adopting electronic health records (EHRs), and pilot efforts are demonstrating the feasibility of large-scale research within health care delivery systems (1–3).

This week, the Patient-Centered Outcomes Research Institute (PCORI) announced plans for a National Patient-Centered Clinical Research Network that will unite patient groups, researchers, and health care systems and will ultimately support rapid and cost-effective observational and interventional clinical research studies with active participation from a broad patient population.

THE NEED

The long and successful tradition in the United States of investing in clinical research is in jeopardy. As overall levels of support for biomedical research decline, clinical trials have become increasingly complicated, time-consuming, and expensive. Combined with these pernicious trends is the increasing realization of critical evidence gaps in the practice of medicine. Many of our most pressing questions could be answered by large randomized trials or analyses of clinical data from routine-care settings; enormous amounts of data already reside in EHRs but are not being used in a systematic way.

Successes in clinical research generally require large numbers of diverse participants and the ability to follow their medical experiences over time. But the United States has few preexisting patient cohorts of substantial size and even fewer that encompass diverse populations. Most clinical studies start from scratch and require years to achieve full enrollment (many never do). This “one-off” approach requires repeated construction and deconstruction of the clinical research infrastructure.

Furthermore, as new data reveal increasing levels of disease complexity, conditions we categorize as breast cancer, asthma, or diabetes can now be divided into distinct subtypes with different prognoses and treatment plans. Realizing a future of personalized medicine will require large studies and longitudinal follow-up. If our nation is to continue to support such a research agenda in a time of serious fiscal restraint, we need a new strategy.

THE TIME IS RIGHT

The call for a prospective cohort for the conduct of large-scale U.S. clinical research is not new (4). However, the creation of PCORI and alignment of several developments in science and policy have placed this vision within our grasp.

Committed patients. Thanks in large part to social media and data-sharing initiatives, patients today are more connected and more knowledgeable about biomedical research than ever before. Patient advocacy organizations and online networks have empowered patients to more readily become clinical research participants.

Electronic health record expansion. According to the Office of the National Coordinator for Health Information Technology (ONC), 72% of office-based physicians were using some kind of EHR in 2012, up from 42% in 2008 (5). While major challenges of interoperability and privacy remain, EHR systems have the potential to provide a communication platform across institutions, connecting millions of individuals. ONC efforts to establish EHR meaningful-use criteria should align well with the new Network (6), which can provide a learning environment in which to test the use of these criteria for research in a real-world setting.

Big data and public access. To decipher how patient subgroups respond to selected medical products and interventions, researchers must be able to collect and analyze increasingly large amounts of medical information and transform it into meaningful discoveries. Researchers are generating larger data sets than ever before, from basic science to clinical research; funding agencies, researchers, and the public are pushing for strong public access policies (7) and are eager for a clinical research network that not only encourages data sharing, but relies on it.

Reforming human-subject oversight. There is an ongoing government-wide effort to reform the Common Rule—regulations that govern the protection of human subjects in research—with the goal of increasing protections and decreasing unnecessary hurdles to research. The new Network will support these real-world efforts to align oversight more closely with patient needs. The Network will explore models such as broad consent for research using clinical data and biospecimens and the use of a single institutional review board.

Need for efficiency. With the unsustainable combination of unprecedented fiscal restraints and a continued escalation of traditional clinical research costs, researchers have both an opportunity and a responsibility to be even more creative and efficient in how we conduct biomedical science. The Network is an opportunity to align the right vision with the right people to get more research productivity from every dollar.

THE NETWORK

Two major PCORI funding announcements (www.pcori.org/funding-opportunities), with total available funds up to $68M over 18 months, describe the Network components: clinical data research networks (CD RNs) and patient-powered research networks (PP RNs). A solicitation will appear soon for a $4M coordinating center ( CC), which will provide project-management support, technical resources, meeting support, and program evaluation (Fig. 1). The Network’s governance structure will ensure that both patients and health systems realize the greatest value from their investments of time and data. A steering committee that comprises Network leaders, patient advocates, federal agency representatives, and PCORI staff will operationalize the entire
enterprise. Network development and function will be guided by a scientific advisory board of research experts that will regularly evaluate the enterprise’s progress and by a special expert group that will provide access to technical expertise in EHRs, advanced laboratory methods, and data management.

Each CDRN will consist of at least two health care delivery organizations that together collect clinical information through EHRs on diverse patient populations of at least 1,000,000 people. To qualify for funding, a CDRN must show that it has the capacity to follow patients longitudinally across care settings and will be expected to support scalable data-access policies that promote broad research use; protect privacy and confidentiality; obtain informed consent; use central institutional review boards; and develop biobanks. Each potential CDRN will propose three pilot cohorts: one for a common disorder, one for a rare disorder, and one for patients with obesity/diabetes.

The PPRNs will be networks of patients, organized around a condition or set of conditions, who are motivated to participate actively in outcomes research. PPRNs will be the test-beds for development of best practices in patient governance, data collection, and use of aggregate data. The idea is to endow these groups with power to improve their care and outcomes, creating an opportunity for them to be partners in research, with jurisdiction and authority. Over time, PCORI will encourage PPRNs and CDRNs to work together to learn how to engage patients in the research process, define the most important patient-centered research questions, and prepare patients for broad participation in research.

In phase 1, PCORI will fund up to 8 CDRNs and 12 to 18 PPRNs. Within the first 18 months, the CDRNs and PPRNs will need to show that they are able to create interoperable databases and partner to initiate and conduct research by capitalizing on each other’s strengths. In 2015, phase 2 support will be available to successful components to stabilize the network infrastructure so others can use it for a wide variety of clinical research studies funded by PCORI, the U.S. National Institutes of Health, the Agency for Healthcare Research and Quality, philanthropy, or industry.

WHAT THE NETWORK WILL MEAN FOR RESEARCH
PCORI’s charge to the Network components is to develop clinical research networks with new synergies and efficiencies that partners

patients with researchers. The Network will allow researchers to design and implement observational studies as well as individual and cluster randomized trials more rapidly and affordably. Following are three examples that could tap into the Network’s power almost immediately.

Atrial fibrillation. This common disorder of heart rhythm affects millions of Americans and predisposes them to stroke and premature death. Four major therapeutic options include traditional anticoagulants, newer anticoagulants, drugs that control abnormal heart rhythm, and invasive procedures and devices (8). Age, gender, underlying illnesses, and genetic factors may influence the effectiveness of different strategies. To understand the natural history of this disease and to identify what therapy works best for whom, we may need studies involving hundreds of thousands of patients—a feat that is impossible with our current clinical trials paradigm focused on singular hypotheses in relatively homogeneous populations. However, a controlled comparative-effectiveness trial of these four interventions could be rapidly designed and implemented within a network collectively caring for tens of millions of patients. Additional highly motivated patients could be recruited from the PPRNs. Such a project would provide an opportunity to tune EHRs for maximal utility and a natural pathway for broad and rapid implementation of the trial results.

mHealth. The Network could provide a vast real-world laboratory for assessing whether mobile health–based interventions that use cell-phone technology and Internet connectivity improve clinical outcomes. Such efforts might center on the assessment of preventive strategies, such as technologies to monitor weight loss or support tobacco cessation, or on chronic disease management, such as glucose monitoring for diabetes, real-time measurement of ambulatory blood pressure, and continuous EKG monitoring for arrhythmias. The network could provide assessments of tools that might improve the quality of clinical research itself. Finally, studies could help illuminate the best conditions for implementation of mHealth into clinical care.

Pharmacogenomics. The Network could facilitate large-scale trials to examine conflicting pharmacogenomic data. For example, some research has associated specific CYP2C19 genotypes with decreased responsiveness to clopidogrel (Plavix), a powerful

Fig. 1. Patient powered. Shown is the proposed organization of the National Patient-Centered Clinical Research Network. Supported by a Coordinating Center, CDRNs and PPRNs will create a sustainable network of health care centers with interoperable EHRs and active patient participation, all overseen by the PCORI staff, board of governors, and their advisors.
anti-platelet drug used in patients at risk for myocardial infarction or ischemic stroke (9). On the basis of those findings, the U.S. Food and Drug Administration added a black box warning to the drug (10). However, subsequent research has raised questions about the clinical importance of this genetic information. Within the Network, researchers could swiftly conduct a large randomized trial aimed at understanding the role of CYP2C19 genotyping in clopidogrel response.

WHAT THE NETWORK WILL MEAN FOR PATIENTS

Besides size and scalability, what distinguishes this effort is that patients are at its center. Indeed, patients within the Network will have access to cutting-edge research studies. But perhaps the greatest power of the Network will be the prominent voice it gives to patients. PPRNs and CDRNs will create pathways for motivated patients to act as respected partners who can influence decisions about research studies that could ultimately change the course of their own care.

WHAT THE NETWORK WILL MEAN FOR HEALTH SYSTEMS AND CLINICIANS

The network will place health care delivery organizations—and the caregivers they employ—in a highly active role in the conduct of clinical research. The Network will provide sufficient financial support for on-site research staff. And there will be other benefits: CDRNs will have the opportunity to quickly take advantage of research outcomes, market their role as health pioneers, have a voice in Network governance, and offer their providers an enriching professional experience through participation in meaningful cutting-edge research. In addition, Network research should provide vital information about health care delivery models that can be used to improve operations.

CHALLENGES AND RISKS

PCORI’s creation of the Network is a bold step that will push the boundaries of U.S. ingenuity. But all bold initiatives have risks and challenges. One concern is that EHRs may never reach the level of accuracy or completeness needed for valid research. This underscores the importance of ONC’s efforts to define “meaningful use” of EHRs to support data quality and completeness. Another is that patients might opt out because of privacy concerns or fears that stem from past incidents of unethical research. Business managers of health services organizations might perceive the research agenda as conflicting with their primary role—health care delivery. All of these potential challenges can be addressed, but that will require the utmost care in project design and oversight.

Success in transforming the clinical research enterprise hinges on the development of research teams, patient-engagement platforms, software, tools, and technologies that do not yet exist. However, these challenges should not deter a scientific and consumer community as strong as ours. Both for their own health and that of future generations, U.S. researchers and patients need a national research network. The climate is right for immediate action.

REFERENCES AND NOTES


Acknowledgments: The authors thank S. Devaney for assistance in preparation of the manuscript.

10.1126/scitranslmed.3006298

Network News: Powering Clinical Research
Joseph V. Selby, Harlan M. Krumholz, Richard E. Kuntz and Francis S. Collins

First published 23 April 2013
DOI: 10.1126/scitranslmed.3006298

ARTICLE TOOLS  http://stm.sciencemag.org/content/5/182/182fs13
REFERENCES  This article cites 3 articles, 1 of which you can access for free
http://stm.sciencemag.org/content/5/182/182fs13#BIBL
PERMISSIONS  http://www.sciencemag.org/help/reprints-and-permissions

Use of this article is subject to the Terms of Service