

VIEWPOINT

Embedding Cardiovascular Research Into Practice

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Cardiovascular medicine currently lacks high-quality evidence needed to inform many important decisions that patients, physicians, and other health care practitioners and health systems must make regarding the prevention and treatment of cardiovascular disease.¹ At the same time, clinical research costs are escalating while government and industry funding is increasingly constrained. Bridging this gap between the need for evidence and the resources available to generate it will require harnessing creative solutions that leverage changes already under way in health care delivery.² In this Viewpoint, we discuss key limitations of the current research system and describe an evolving national infrastructure with the potential to increase health research substantially.

The Old Paradigm

Due in part to the **poor quality of data collection and variability of practice in routine patient care, clinical research has evolved as a specialized activity conducted in parallel to clinical practice.** This in turn has given rise to specialized research clinics, but even research done in clinical care settings was thought to require separate operational and research data systems, with the latter served by a separate cadre of personnel.

However, issues related to ethical research conduct also contributed to this bicameral arrangement. In addition to articulating key ethical concepts, the 1979 Belmont Report helped crystallize the idea of research as an activity distinct from clinical practice and governed by different responsibilities. But while the report represented a watershed event in clinical research, much has changed in the decades since its publication.

Separate ethical frameworks and parallel data systems for research and practice have **substantially increased research costs and timelines and spurred migration of clinical trials to countries with comparatively low labor costs.**³ The mutual isolation of research and practice also raises concerns about whether studies performed in a separate research context can truly inform clinical practice. Further, inconsistency in regulatory oversight of knowledge-generating activities is increasingly apparent at the borderline of quality improvement and research: even though they often address identical topics, quality improvement programs often settle for suboptimal designs and methods to avoid being classified as research. These unintended but perverse incentives ultimately harm patients by slowing the discovery and dissemination of best practices.

The New Landscape

The Institute of Medicine's concept of a "learning health system"⁴ envisions virtuous cycles in which consumption of evidence (evidence-based practice) is complemented by generation of evidence (practice-based evi-

dence) so that each health care encounter contributes incrementally to informing practice. **Adopting better, more accessible longitudinal electronic health data presents new possibilities for understanding care delivery and outcomes.**

In addition, a recent report⁵ provided a novel framework for ethical oversight of learning activities, one centered on the degree of risk to research participants rather than on arbitrary classifications of research activities. This construct recognizes that many quality improvement activities conducted under oversight that apply to clinical operations share numerous characteristics with clinical research that requires expensive oversight. Taken together, these advances—a commitment to knowledge development as part of practice, better and more accessible data, and an ethical framework based on risk rather than outmoded divisions between quality improvement and research—may allow many unanswered questions to be addressed and will increase patients' and clinicians' confidence in the choice of preventive measures, diagnostic tests, and therapies.

Converting continuous learning into actionable, informative protocols that are acceptable to health care systems poses many challenges. In addition to critical issues of ethics oversight and patient consent in learning health systems, administrators and clinicians are under pressure to meet efficiency standards, leaving little time to pursue the creation of new knowledge in practice. Additionally, current electronic health records (EHRs) are not optimized for research uses, and each system has its idiosyncratic definitions and coding standards for clinical data.

Seeking to address these issues, the National Institutes of Health (NIH) initiated the Health Care Systems Research Collaboratory⁶ to foster innovative approaches to integrating research with care delivery. Integrated health systems with EHRs were encouraged to propose pragmatic clinical trials. The first round of 7 projects selected for funding share 3 salient features: **all are multicenter studies, their interventions are incorporated into routine care rather than added to it, and each uses EHRs to identify eligible patients** and collect relevant data. For example, the University of Iowa launched the Nighttime Dosing of Anti-Hypertensive Medications: Blood Pressure Medication Timing Study (BPMedTime), a pragmatic clinical trial; another study coordinated by the University of California, Irvine—the cluster randomized trial Active Bathing to Eliminate Infection (ABATE)—will investigate whether chlorhexidine bathing and Methicillin-resistant *Staphylococcus aureus* decolonization can reduce infections and readmissions in over 200 non-critical care units in more than 50 hospitals belonging to the Hospital Corporation of America. In its first year, the Collaboratory has made sig-

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nificant progress in achieving consensus on ethics oversight, curating and sharing data across systems, and implementing protocols to minimize disruption of busy practices.

Opportunities in Cardiovascular Disease

These recent developments offer significant opportunities for cardiovascular specialists seeking to stem the leading cause of death and disability. However, education and the innovative leveraging of existing capabilities will be critical to these efforts.

First, **specialty education programs should incorporate the conceptual basis for learning health system methodology.** Physicians and other clinicians should understand that robust EHRs not only enable more communication with patients and other health care practitioners, but also facilitate aggregate analysis to inform optimal approaches to care.

Second, education should **explore improvements to ethical oversight of learning activities.** The NIH is supporting a substantial effort to elucidate the views of the public, patients, and clinicians regarding learning activities that include not only "traditional" research but also surveys, quality improvement, and comparative effectiveness studies. Matching levels of oversight to participants' degree of risk could ameliorate administrative burdens and delays and focus effort on protocols where intensive oversight is beneficial.

Third, **cardiovascular specialists are well poised to contribute to a sophisticated fabric** for learning activities. Existing registries offer granular, high-quality, comprehensive data and can be leveraged as primary data collection instruments, thereby substantially reduc-

ing research costs. However, for long-term diseases such as heart failure, atrial fibrillation, hypertension, and hyperlipidemia, it will be important to integrate registry data with data from EHRs and the growing array of patient-reported outcome measures. Initial experiences in Sweden (TASTE)⁷ and the United States (SAFE-PCI)⁸ demonstrate that randomized trials can be conducted within ongoing registries for a fraction of the cost of traditional trials. The Collaboratory trial described earlier (BPMedTime) will pilot electronic capture of key outcome data from EHRs to address the surprisingly unanswered question of whether daily blood pressure medicines should be taken at night or in the morning.

As electronic data sources mature and methods for aggregating and analyzing them improve, public health and personalized medicine can increasingly exploit a common data infrastructure. The Collaboratory experience shows that it is possible to implement rigorous, efficient, and economical trials that combine observational and interventional methods, including randomization, to yield information directly relevant to patient care.

Technological solutions are within reach, but progress depends on strong partnerships with clinicians and delivery systems, and on well-designed oversight systems that enable researchers and operations experts while protecting patients and the public and including them in decision making. Rapid development of this new model in cardiovascular medicine can have significant benefits for public health, but fully informed patients and clinicians who understand the central role of the learning health system will be crucial to these efforts.

ARTICLE INFORMATION

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