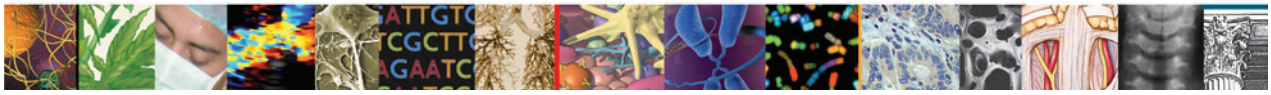

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Perspective

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A HALF-CENTURY OF PROGRESS IN HEALTH: THE NATIONAL ACADEMY OF MEDICINE AT 50

Advancing the Learning Health System

J. Michael McGinnis, M.D., M.P.P., Harvey V. Fineberg, M.D., Ph.D., and Victor J. Dzau, M.D.

Discovery leads to progress when its lessons are absorbed and applied. Society is in the early stages of a transformation of learning in health, health care, and biomedical science. Accelerating developments that began in the 20th century have set the stage for a revolution in knowledge generation and application for progress in health. Evidence development that has been episodic, deliberate, and insulated is becoming more continuous, query-based, and relational — and the health system is both contributing and benefiting.

The National Academy of Medicine (NAM) is working to facilitate this change. Recognizing that technological and methodologic advances could improve on the pace, generalizability, and costs of innovation in health and medicine, the NAM (previously the Institute of Medicine [IOM]) has envisioned and helped steward the evolution of a continuously learning health system (LHS).[1] In 2006, the IOM offered the first working definition of an LHS as a system "in which science, informatics, incentives, and culture are aligned for continuous improvement, innovation, and equity — with best practices and discovery seamlessly embedded in the delivery process, individuals and families as active participants in all elements, and new knowledge generated as an integral by-product of the delivery experience."[2]

Underpinning this vision is an appreciation that health is shaped by multiple forces: genetic predispositions, social circumstances, physical environments, behavioral choices, and medical care.[3] Engagement by myriad stakeholders — from medical care, public health, social, cultural, and research arenas — is therefore required to assess, understand, and improve individual and population health. Similarly, knowledge to guide those actions must derive from, and be useful to, all participants, especially the people whose health and well-being are the anchoring aim.

Until recently, it has not been possible to unify such disparate elements to achieve continuous learning in health care. Learning through structured observation and documentation is central to the scientific method, but the multifactorial nature of many health threats presents a formidable challenge to anyone seeking reliable insights. On the data front alone, widespread adoption of even basic vital statistics records is largely a 20th-century development. Things began to change with the construction of larger-scale, multifactor databases, exemplified by the 1948 launch of the Framingham Heart Study, which introduced continuous

learning from a real-world population over an extended period.

The LHS elements described in the IOM's 2006 definition — science, informatics, incentives, and culture — have changed significantly over time.[2] In terms of evidence development, multi-institutional research networks have been added to rapidly growing clinical trial investments. The digital revolution has introduced the capacity to capture, store, retrieve, evaluate, and respond in real time to observations of human experiences. Unchecked growth in health care costs has created demands for accelerated assessment of outcomes and value, especially in light of the rapid development of more and higher-cost treatments and diagnostics. Attention and tools have emerged to enlist patients and families as more active and informed participants in the care and learning processes (see timeline).

Science. Opportunities for near- and longer-term assessment continue to expand. Large-scale studies — including those adding biologic specimens and data and material repositories, such as the UK Biobank created in 2006 — promise more comprehensive insights on health risks and prognosis. Larger-scale health systems, such as Kaiser, Geisinger, Group Health, HCA Healthcare, and Intermountain, established continuous-assessment capacities for their own populations, while also developing collaborative agreements for clinical research, such as the HMO Research Network, established in 1994. Increasingly, condition-oriented patient registries and continuous-care-improvement networks, such as the Patient-Centered Outcomes Research Institute's PCORnet and the Improve Care Now initiative for pediatric bowel disease, have been established.

The potential for learning from ever-larger clinical databases and longitudinal studies was given a transformative boost by the sequencing of the human genome in 2003, and the National Institutes of Health (NIH) launch of the All of Us initiative is an example of the learning opportunity. The development's full applicability is still unfolding, but the possibility of more complete and individually specific information on interactions among genes, environment, behavioral patterns, social circumstances, and medical care has fueled the promise of precision medicine, precision public health, and precision health.

Informatics. Organized information empowers learning. The digital revolution has progressed in parallel and intertwined with advances in science and evidence development. Since the 1959 invention of the microchip, the 1983 establishment of the Internet, and the 1990 creation of the World Wide Web, efforts to develop automated health monitoring and health record storage devices have grown enormously. Many of the advances most useful for the LHS relate to developments in database management and assessment that constitute the basic infrastructure of the learning system, and companies such as Google, Apple, and others are bringing that capacity to the individual level. These include analytics involved in artificial intelligence and machine learning that could vastly increase the scale, speed, and sophistication of LHS operations.

One example of digital technology's potential for advancing the LHS was the REDUCE MRSA study. Designed and implemented through a partnership that grew out of the NAM Leadership Consortium, this cluster-randomized trial demonstrated that a universal decolonization strategy led to a 44% reduction in all-cause central-line–associated bloodstream infections in intensive care settings. The ability to draw, in real time, on data from 74,000 patients in 43 hospitals yielded results in 18 months that, the authors noted, would have taken 64 years for a single hospital.[4]

This and similar examples illustrate how, in addition to directly facilitating, improving, and documenting patient care, digital technology could transform research and evidence-development capacity. The combination of digitally encoded, real-time monitoring devices, electronic medical records, and computational power developed over the past four decades will accelerate, with dramatic potential for improving both patient care and knowledge generation.

Incentives. Incentives matter. The pace of LHS evolution is shaped by the incentives at play: economic incentives for a more efficient, effective, and equitable system; professional incentives to accelerate real-time learning and adjustment; and demand incentives from the public for a higher-performing health system. In the

Selected Advances toward a Learning Health System (LHS).

AHRQ denotes Agency for Healthcare Research and Quality, CMS Centers for Medicare and Medicaid Services, FDA Food and Drug Administration, HEW Department of Health, Education, and Welfare, HHS Department of Health and Human Services, IOM Institute of Medicine, NAM National Academy of Medicine, NIH National Institutes of Health, and RWJF Robert Wood Johnson Foundation.

1940s

1948: Framingham Heart Study begins (NIH), generating evidence from routine care

1950s

Advances in digital computational capacity (GE, IBM, and other companies) enable information storage, retrieval, and processing

1960s

Development of bioinformatics, including digital monitoring and electronic medical records, permits automated data capture, storage, and processing

1970s

Deming, Senge, and others promote continuous quality management and improvement

1980s

1980: *Healthy People* and *Objectives for the Nation* (HEW/HHS) set benchmarks for optimizing health system impact

1984: U.S. Preventive Services Task Force (HHS) provides template and process for ongoing assessment of changing evidence

1990s

1993: Dartmouth Atlas Project begins (Dartmouth, RWJF), exploring blended impact of evidence, incentives, and culture on outcomes

1994: HMO Research Network collaborative is created (Kaiser) to accelerate learning from real-world data

1996: Google begins, transforming and democratizing personal access to health and medical knowledge

2000s

2001: *Crossing the Quality Chasm* (IOM/NAM) explores culture and standards for continuous improvement and care quality

2002: "The Case for More Active Policy Attention to Health Promotion" (Health Affairs) examines influence on health from domains outside health care

2003: *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care* (IOM/NAM) describes deep impact on health from structural bias and cultural factors

Human genome sequenced (Human Genome Project), providing a template for understanding biologic mediation of effects of other domains

2004: Office of the National Coordinator for Health Information Technology (ONC) established (HHS) to advance digital infrastructure for learning

2006: Learning Health System initiative (IOM/NAM) defines LHS concept, focus, and elements

UK Biobank created (UK Medical Research Council, Wellcome Trust) for long-term assessment of effects of gene–environment interactions

2007: Apple introduces the iPhone, with the potential to bring personalized knowledge and computing to the individual

2008: Sentinel Initiative (FDA) begins continuous postintroduction assessment of medical product safety

2009: Health Information Technology for Economic and Clinical Health (HITECH) Act provides a mandate and funding for building digital health infrastructure

2010s

2010: *The Healthcare Imperative: Lowering Costs and Improving Outcomes* (IOM/NAM) outlines the sources, magnitude, and impact of misaligned financial incentives

Affordable Care Act passed, with provisions for aligning system performance and learning

2013: Culture of Health Program launched (RWJF) for sustained emphasis on social determinants of health status and outcomes

Best Care at Lower Cost: The Path to Continuously Learning Health Care in America (IOM/NAM) promotes continuous learning to eliminate health sector performance gaps

JASON health data report and 2014 HHS Task Force response (ONC, AHRQ) call for medical–social national-scale LHS

2014: Fast Healthcare Interoperability Resources (FHIR), a health data exchange between applications and among standards, developed

2015: The Medicare Access and CHIP Reauthorization Act (MACRA) and *Vital Signs: Core Metrics for Health and Health Care Progress* (IOM/NAM) advance payment, measures, and accountability focused on value and learning

Nationwide Interoperability Roadmap (ONC) sets a goal of interoperable individual, clinical, community, and research data by 2024

2016: Public Health 3.0 initiative launched (HHS) to integrate public health across sectors

Alternative Payment and Accountable Health Communities Models (CMS) provide health financing incentives for medical–social service bridges

21st Century Cures Act mandates personal data access, transparency, apps, and decision tools

2017: *Learning Health Systems*, an open-access journal, established as a resource for cross-domain communication on advances

2018: CHRONIC Care Act creates Medicare and Medicaid incentives to integrate behavioral and social services

All of Us initiative launched (NIH) for continuous data generation on multiple health factors and outcomes

2020s

2020: Evidence Accelerator launched (FDA) for collaboration on accelerating real-world evidence on Covid-19

Coronavirus Aid, Relief, and Economic Security (CARES) Act and Operation Warp Speed (HHS) support collaborative large-scale science and focus on finance and equity failures

United States, economic incentives have too often been pulling in the wrong direction. Continued reliance on a fee-for-service model means that payments are oriented to individual service units rather than to outcomes. The result is a $4 trillion health care system (in 2020), with at least a third of those expenditures estimated to have no effect on health status.

As health costs, including out-of-pocket expenses, continue to rise, there is a growing need for a better understanding of health returns on investment. Health care organizations, payers, employers, and government have reason to invest in infrastructure that would generate actionable information in real time. Recognition of the power of social circumstances to drive health status and costs of care increases demand for more integrative payment strategies that are more prepared for, and responsive to, lessons learned from the delivery of health and health care services. The 2010 Affordable Care Act contained a strategic framework for increasing accountability, value, and equity in health system financing, and though implementation has been slow to take advantage of the relevant provisions, there is growing sensitivity to the importance of a system that learns and responds more quickly.

Culture. Culture conveys learning. In a true LHS, clinicians and health systems, public health and social services, businesses and community organizations, and individuals and families are not only seamlessly linked but are also active contributors to and beneficiaries of the learning culture. Because trust is a core requirement for broad participation, asymmetries in the cultural dynamics among various groups must be reconciled. Inclusiveness is core, and an LHS for all must therefore be positioned to recognize, mitigate, and manage health effects of social status, racism, and other forms of discrimination.

An audio interview with Dr. McGinnis is available at NEJM.org

Twenty years ago, the IOM published two seminal reports, *To Err Is Human* and *Crossing the Quality Chasm*, calling for health care that is patient-centered, safe, effective, equitable, efficient, and timely. Those reports launched a national movement for health care safety and quality. This journey, which has transformed the national mindset, has no end point. New diagnostics and therapeutics bring new challenges, and forces outside the clinic doors continue to affect both health and the effectiveness of health care. Though the journey is continuous, we can identify critical markers of progress. In an LHS, stakeholders are committed to safety, effectiveness, efficiency, and equity for every person and to ensuring that performance is measured, transparent, adaptive, and secure.[5]

These responsibilities speak to the importance of intensified attention to basic operational requirements of health care to enable the LHS: equitable access, personal focus, interoperable systems, collaborative data analysis and use, linked and integrated resources, targeted and meaningful accountability, culturally infused learning, publicly and privately networked activities, and local and global communication. Each of these aspects warrants robust strategic mapping, with attention to their interrelationships.

The Covid-19 pandemic has made the importance and urgency of the LHS painfully evident. U.S. shortfalls in delivering an effective, coherent, and equitable response for Americans have had tragic and quantifiable consequences in the unnecessary loss of lives. With available technology and knowledge, an LHS with interoperable public and private communication and collaborative patterns and feedback loops could have substantially accelerated identification, treatment, containment, advice, testing, monitoring, and adjustment.

A comprehensive LHS spans disease prevention, cure, and management. It builds on advances from genomics to social determinants and takes advantage of discoveries at all levels of biomedicine and public health. It uses ever-expanding data systems and capacities for analysis and interpretation. It functions at both population and individual levels. It works collaboratively across institutions and constituencies. It constantly scans and uncovers opportunities for real-time improvement in the experience, cost, and outcomes of care.

Over the years, the NAM has collaborated with professional societies, patient and citizen groups, health care organizations, public health leaders, payers, employers, product manufacturers, information technology companies, and government agencies to foster various elements, linkages, and capacities for continuous learning and action. LHS leadership now comes from many organizations, associations, companies, and publications, both nationally and globally. The NAM remains committed to helping advance the vision, progress, and benefits of the LHS, and we believe the next 50 years will see substantial progress toward a health system that is increasingly effective, efficient, and equitable for all.

The series editors are Victor J. Dzau, M.D., Harvey V. Fineberg, M.D., Ph.D., Kenneth I. Shine, M.D., Samuel O. Thier, M.D., Debra Malina, Ph.D., and Stephen Morrissey, Ph.D.

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Is Learning Worth the Trouble? — Improving Health Care System Participation in Embedded Research

Richard Platt, M.D., Gregory E. Simon, M.D., and Adrian F. Hernandez, M.D.

Despite frequent calls for creating a learning health system and increasing the use of real-world evidence, the pace of medical research is inadequate, and clinical trial capacity in the United States is insufficient to address important questions. Embedded pragmatic clinical trials (ePCTs)[1] could generate real-world evidence without the limitations associated with observational studies or the time, expense, and lack of generalizability that are barriers to conducting conventional randomized clinical trials. Such trials are integrated into standard care, involve existing clinicians instead of dedicated research staff, and use routinely collected clinical data.

Our experience working in the coordinating center of the National Institutes of Health (NIH) Health Care Systems Research Collaboratory has demonstrated the feasibility of conducting innovative multicenter ePCTs for various conditions. The Collaboratory's studies typically target conditions that affect large numbers of patients and assess interventions that have the potential to improve quality-of-care measures and demonstrate benefit over a short period (1 to 3 years). Most studies evaluate a service or treatment added to usual care, such as universal decolonization to prevent nosocomial infection or strategies for increasing the uptake of colorectal cancer–detection tests. Many use cluster randomization, with individual clinics or hospitals assigned to each study group. At best, the strategy under evaluation is delivered as part of usual care. Although these features aren't required by the NIH, they make participation in ePCTs more attractive and more feasible for health systems because such studies offer actionable information and the barriers to participation are relatively low. When findings are directly related to quality or safety, health system leaders and clinicians are more motivated to accept the constraints imposed by research.

There remains, however, a substantial unmet need for trials addressing societal, public health, or community needs that aren't directly related to immediate health system priorities. Such trials generally compare various drugs, devices, or other therapies; involve randomization at the patient level; and require informed consent. The Covid-19 pandemic has highlighted the need for rapid, efficient trials. Whereas the U.K. RECOVERY trial quickly demonstrated the benefit of dexamethasone for hospitalized patients with Covid-19 receiving respiratory support,[2] the United States is still implementing platforms for conducting embedded multicenter Covid-19 treatment studies.[3] Beyond Covid-19, there is a need for trials such as the NIH-sponsored PREVENTABLE trial, which is examining whether statins can prevent dementia in elderly people.[4] The importance of expanding clinical trial capacity is highlighted by the fact that the Patient-Centered Outcomes Research Institute (PCORI) chose to fund retrospective, observational studies of second-line therapy for type 2 diabetes because it considered the resources required to conduct such a trial to limit its feasibility.[5] Although the findings of these kinds of studies will eventually be important for clinicians and delivery systems, the incentive to participate is low because such studies provide no immediate benefit in terms of cost, quality metrics, or patients' care experiences.