POLICY

Academic Medical Centers: Ripe for Rapid-Learning Personalized Health Care

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In an attempt to reduce the lengthy process of translating scientific findings into clinical practice, the United States and several European governments are making substantial investments in health information technology, comparative effectiveness research, and increased access to quality health care. New technologies—genomics in particular—are expected to usher in more cost-effective personalized health care. Academic medical centers can play a central role in this transformation through the development of rapid learning environments, evidence generation, implementation research, and education of health professionals and the public.

There is a growing emphasis on health care models focused on prevention and wellness promotion and the application of novel technologies that allow clinicians to more efficiently direct treatment to those most likely to benefit. Personalized health care (PHC) relies on personalized medicine, which makes use of individual patient characteristics that are not routinely assessed in traditional medical practice today, such as genetic and genomic data as well as a patient's values and personal circumstances. PHC has the potential to improve health outcomes while simultaneously lowering costs but has yet to move into the mainstream; hindering this advance are an uncoordinated research environment and a disjointed translational-research infrastructure. Acting as a nexus for discovery, development, and dissemination of tools and clinical health care–delivery models, academic medical centers (AMCs) must play a central role in unleashing the potential of PHC (Table 1).

DRIVING A TRANSFORMATION

Efforts to aggregate person- and family-centered clinical and molecular data and to apply evidenced-based approaches are at the forefront of the U.S. national health care agenda. Moreover, public interest in more effective health care is growing. These trends, coupled with the roughly 15 years needed to translate discoveries to clinical practice, are driving national efforts to transform how clinical data are aggregated and how new approaches are evaluated and applied. A rapid-learning model has been developed to integrate and accelerate this transformation and is beginning to be implemented in health care systems nationally (*1*).

Various participants in translational medicine are already building resources that provide the elements of a rapid-learning, cancer-care system, such as the U.S. National Institutes of Health's (NIH's) informatics initiatives, disease registries, computerized biomedical databases, quality-of-care metrics, and Web-based consumer health information (for example, Medlineplus.gov) (*2*). The Veterans Health Administration has created a computerized health data capture and analysis system, as have integrated health care–delivery organizations such as Kaiser Permanente (*3*). The American Recovery and Reinvestment Act (ARRA) (*4*) and Affordable Care Act of 2010 (*5*) allocated $19.2 billion to the HITECH Act for electronic medical records, meaningful use, and creation of a rapid–learning ecosystem (*1*, *6*, *7*); invested substantially in comparative effectiveness research and the Patient-Centered Outcomes Research Institute (PCORI) (*8*); established the U.S. Food and Drug Administration's (FDA's) Sentinel Network, a nationwide electronic database of adverse-event reports about drugs, biological products, and medical devices that plans to access 100 million records by 2012 (*9*); led to the earmarking by Medicare and Medicaid of nearly $45 billion dollars of future subsidies toward the goal of an electronic health record for every American by the year 2014; and spawned initiatives such as Accountable Care Organizations and Health Innovation Zones. All of these initiatives are intended to move the United States' health care toward a system for learning, comparative effectiveness research, and improved health—and are coupled to a commitment to PHC. However, it has been difficult to transfer such conceptual advances to on-the-ground demonstrations of rapid-learning care on the front line: the clinic.

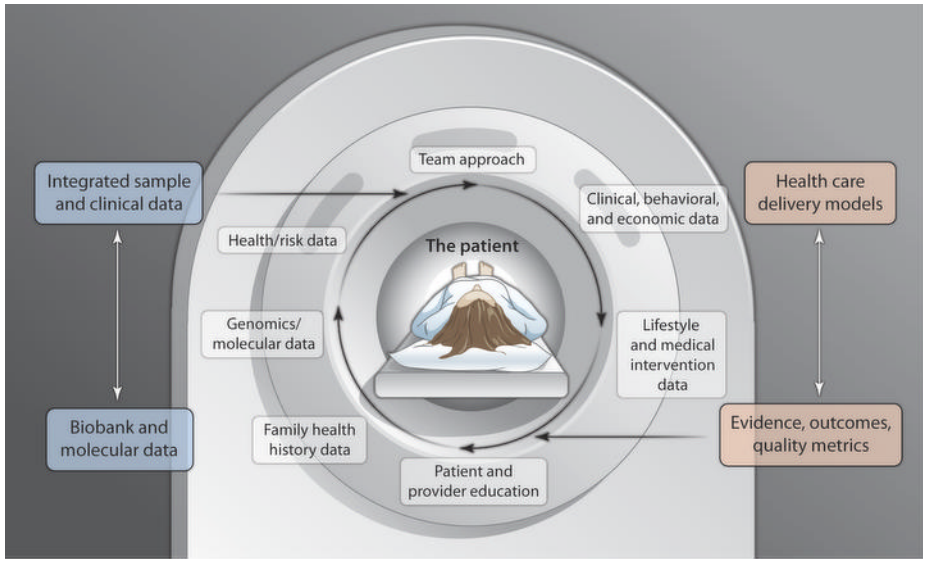

Fig. 1. Fast learner. Depicted is the dynamic, iterative nature of a health care learning system for PHC with its diverse inputs (blue) and outputs (red). A PHC learning system requires biorepositories, genome technologies, interoperable databases, predictive models, patient and provider education, and a team approach. At the center of the activity are patients, for whom the ultimate goal is widely available, high-quality effective medical care delivered at a reasonable price.

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RAPID-LEARNING PHC

Personalization of health care is made possible by matching increasingly detailed patient data (such as demographics, clinical parameters, behavioral indicators, personal values and needs, biomarker assessment, and genetic and genomic parameters) with the best-available evidence for enhanced outcomes. An emerging and promising approach to accelerating the incorporation of evidence-based medicine into practice is the rapid-learning model, which integrates data routinely generated through patient care and clinical research and feeds these data into a growing set of coordinated databases (Fig. 1).

Using information and data capture technologies as well as clinical decision support tools resident in the AMCs, the system "learns" by routinely and iteratively (i) capturing data systematically; (ii) analyzing collected data both retrospectively and prospectively; (iii) implementing findings into subsequent clinical care; (iv) evaluating resulting clinical outcomes; and (v) generating additional hypotheses for future investigation (*1*). Thus, information purposefully obtained in real time in the course of routine clinical practice drives the process of discovery and ensures that a focus on continuous innovation, quality improvement, safety, and value is intrinsic to the health care system. This model may be particularly appropriate for efforts to incorporate personalized medicine into clinical care. However, the existing patient databases designed for clinical care are not always adequate for translational and clinical research: Data quality is frequently poor, missing data are ubiquitous, and linkages across data types (for example, financial, appointment, demographic, procedures, medications, vital signs, etc.) are not always captured or accurate. Full implementation of the rapid-learning model requires that AMCs undergo a data-management and -collection redesign so that the information realizes its fullest potential.

Common discovery resources. Well-annotated human tissue samples linked to clinical and outcomes data are invaluable sources for discovery research and for the validation of biomarkers of disease and of response to therapy, which are the underpinnings of molecular diagnostics for PHC. However, such collections can be difficult to find and access, can be of variable quality, and can be too expensive to justify their generation for a single development program (*10*). AMCs' core competencies provide access to human subjects, biological specimens, and annotated clinical data; therefore, as part of mainstream patient care, AMCs must lead efforts to develop, integrate, and adopt standards for governance and stewardship of these resources. Such standardization will allow consistent delivery of diagnostic information across institutions and provide efficient data sharing for research, thereby lowering the barriers to discovery and development of new PHC tools. A recent Institute of Medicine workshop explored the need for public-private partnerships to facilitate access by investigators to high-quality biospecimens linked to high-quality clinical and phenotypic data both from AMC- and industry-driven clinical trials (*11*).

Table 1. Opportunities for AMCs to advance PHC.

Activity	Challenges to implementing PHC	Resources and capabilities of AMCs	Opportunities for AMCs
Rapid-learning health care	Nonuniform data capture Integration of research methods into health system workflow	Information technology Electronic data capture Clinical-decision support Health-services research	PHC learning laboratories Data governance policies Comparative effectiveness research Knowledge dissemination
Development of common discovery resources	Limited awareness of availability of biological samples Limited ability to combine data sets Paucity of standardized biobanks	Access to research subjects, biological samples, and annotated clinical data Organizational structure capable of centralizing biobanking activities	Development of data standards for clinical sample characterization and annotation Centralization of biobanking Data and sample sharing across labs and institutions Value-creating partnerships with industry and payers
Establishing evidence for initial PHC adoption	Historical lack of funding for clinical evidence development Uncertainty around levels of evidence necessary to achieve adoption, coverage, and regulatory clearance	Synergistic co-location of research and clinical care Established relationships with payers and industry	Value-creating partnerships with industry and payers to gather evidence of utility Development of data standards for PHC usage, outcomes, and costs
Enabling of clinical effectiveness research and population studies	Limited coordination of PHC implementation and data collection among providers and payers	Along with payers, AMCs have access to treatment-history and health-outcomes data	Development of data standards for electronic health records (EHR) to foster cross-institutional data mining Multicenter outcomes research using deidentified clinical data
Overcoming barriers to implementation of new models of care	Perverse microeconomic incentives of providers—focus on "sick care"	Culture that promotes innovation Flexibility in developing care models	"Learning laboratories" for new models of care, quality metrics, and accounting
Modernizing health professional and public education	Limited genomic literacy among providers and public	Scholarship and education is a core mission	Train next generation of MDs in genomics and PHC

ESTABLISHING EVIDENCE FOR INITIAL ADOPTION

The implementation of many PHC tools has been delayed by the limited availability of data that demonstrate clinical utility and value. Recently, for example, the Centers for Medicare and Medicaid Services (CMS) found insufficient the evidence that demonstrated that pharmacogenomics-guided warfarin dosing improves health outcomes for Medicare beneficiaries and thus denied coverage for *CYP2C9* and *VKORC1* genetic testing outside of prospective, randomized-controlled clinical trials. Development of evidence in support of PHC has been challenged by traditional approaches. Funding for translational research has been inadequate to support randomized, prospective clinical studies of new biomarkers, and the diagnostics industry has lacked the resources and the financial motivation to support such studies. In addition, the historical approach of a randomized trial for every novel clinical question is likely to be too cumbersome, costly, and slow because biomarker discoveries outpace our ability to study individual biomarkers fully in a clinical trials model. For these reasons, clinical trials may not be the main source of evidence generation; rather, use of the rapid-learning model across a network of AMCs and industry partners might harness a national capability to drive the efficiency and acceleration of PHC adoption and implementation.

Examples of novel partnerships with AMCs that develop evidence and drive clinical effectiveness research are beginning to emerge. For example, Kaiser Permanente of California partnered with Genomic Health and the University of Southern California's Keck Medical School to study the clinical utility of a prognostic test for breast cancer recurrence among Kaiser Permanente patients (*12*). Strategic public-private partnerships of this type will be even more powerful when common standards are developed that support data interoperability, quality assurance, and governance across health systems. The NIH's Clinical and Translational Science Awards (CTSA) program seeks to fund 60 centers of translational research as a consortium and should provide the foundation of infrastructure and standards required to begin to share data across AMCs, as has been done by the HMO Research Network (*13*). The CTSA institutions present an opportunity to leverage the emerging data architectures that span bench research and community health. With open access to data, scholars and policy-makers could determine the factors that affect clinical uptake and the resulting economic and health impact of new technologies that promote PHC.

IMPLEMENTING NEW MODELS OF CARE

Although all parties ultimately stand to gain from the implementation of PHC, economic incentives currently present substantial barriers to realizing its implementation (*14*). For example, PHC models, if successful, would shift patients from high-margin inpatient procedures to low-margin (or, at present, uncovered) outpatient screenings and interventions. For PHC to be realized, AMCs must demonstrate leadership in care delivery by exploring new economic models. To support such models, CMS offers select payment demonstration programs that attempt to align payment with health promotion and improved health outcomes and away from service volume (*15*). Unfortunately, these demonstration programs are traditionally created by Congressional mandate and dependent on Office of Management and Budget approval before they can be implemented. Thus, increased experimentation and collaboration between CMS and AMCs to create new business models for PHC should be advocated to both Congress and the Executive branch. Failing Federal support, another potential solution is for AMCs to work directly with private payers locally to create their own demonstration projects, designating a portion of the delivery system as research and development units to test new models of care and new technologies within those models. These sites would use the rapid-learning model to explore the impact of PHC on health outcomes and costs of treatment, while payers would cover the development of evidence (*16*). For those models that prove successful in improving care quality or access, AMCs could work with payers to build sustainable reimbursement models that provide the appropriate financial incentives. Through iterative demonstrations and experimentation, a new model could be identified as an alternative to this expensive status quo.

EDUCATION: PROFESSIONALS AND THE PUBLIC

As PHC evolves, AMCs will need to develop a workforce able to implement it. Although consumers are enthusiastic about genomics and are hopeful about its impact, they also have a low knowledge base about genetic and genomic testing and risk communication. Education of health professionals and the public must be a priority if we are to advance PHC. The risks of misuse or inappropriate expectations for genomic testing are high (*17*). Given the rapid advances in this field, it will be challenging to keep health professionals informed about the benefits, risks, limitations, and appropriate clinical applications of new tools as they become available. Risk prediction and modeling as well as risk communication are not part of traditional training of providers. AMCs should be proactive in developing these skills and the knowledge base and clinical decision–support systems for providers while at the same time incorporating the concept of PHC into traditional educational models and medical school curricula.

The advent of direct-to-consumer genomic testing has only served to intensify the educational needs of the lay public, health care providers, and policy-makers. Several surveys have documented the below-average physician knowledge of genetics (*18*). The importance of education in the application of pharmacogenetics has been described (*19*), but at present there are no broad initiatives to orchestrate genetics and genomics education of medical professionals, trainees, and the public at large. Basic genomic literacy is critical for patients, physicians, and communities if these groups are to engage in the translational research and clinical studies that are required to bring about a change in health care paradigms (*20*). In addition, providers should be well versed in the role of social determinants of health and the importance of crafting care plans that take into account a patient's personal circumstances.

AMCS AS LEADERS IN PHC

Individually, each stakeholder in health care delivery stands to gain from a comprehensive strategy to implement PHC. AMCs can be instrumental in integrating, facilitating, and catalyzing the needs of health care providers, academia, industry, government regulatory agencies, and the private and public payers. However, AMCs will need to adopt a culture of transparency and willingness to share as democratization of information dissemination becomes the norm. Bringing about the health care transformation enabled by PHC requires the assembly of diverse stakeholders who are all focused on the application and translation of genomics and related modalities with the goal of improving the health of

individuals and driving efficiency in health care delivery. The interdisciplinary nature of the AMC can be leveraged to position these institutions at the epicenter of research, education, and clinical care. A crafting of a network of AMCs that focus on addressing the specific challenges described above would be a major step forward in developing and enabling the continuum of strategies required for PHC to realize its full potential to improve health and health care.

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