

Key aspects of health system change on the path to personalized medicine

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The tools and knowledge base for personalized medicine practices are being developed as a major transformation is underway in our health care system. Although the foundation supporting the scientific and technological applications that enable individualized approaches in health care continues to be framed, an uncertain health care delivery landscape lies ahead, driven by economic, quality-of-care, and other policy considerations. There are commonalities in the needs and the opportunities for personalized medicine and health care system change, and these 2 facets can mutually inform one another. Here, we examine this interface in the dimensions of innovation and costs, health information technology, evidence development and comparative effectiveness, clinical data standards, consumer tools, and patient safety and public health. Indeed, personalized medicine must offer solutions for broader health priorities if it is to achieve its potential impact. (*Translational Research* 2009;154:272–276)

Abbreviations: CER = comparative effectiveness review; EHR = electronic health record; HIT = health information technology; RCT = randomized controlled trial

Christopher Columbus succeeded in his voyage of discovery to the New World partly because he knew his theory and partly because he knew his weather. The theory, which is science based, was convincing to him. But it was his knowledge of the trade winds that ultimately gave him success.

Personalized medicine promises to deliver new tools of precision, prevention, and effectiveness in health care. This promise is based on the likelihood of useful clinical applications originating from new knowledge in molecular biology, combined with the power of electronic information technology. However promising the theory, the development and deployment of these

tools must occur in today's environment of complexity, challenge, and crisis throughout our health care system. We have our theory, but we also need to know our weather.

The following short overview somewhat reverses the perspective that is typical in considering the prospects for personalized medicine. Instead of looking over the prow of our vessel to survey the opportunities and barriers to a successful journey for personalized medicine, we take the perspective of the environment itself in which personalized medicine must develop. Policy makers and health care professionals alike are seeking change, to the point of "transformation," in the health care system. Strategies for progress like personalized medicine must embrace a role in system-wide change, which includes attention to broader national health and economic needs, if they are to achieve the positive impact they believe possible.

The movement for health system reform and the drive to personalized medicine can mutually inform one another. Indeed, the goal of increasing individualization in care may offer an unusual gift as broader system reform is pursued. The patient-directed objectives of personalized medicine may provide a touchstone that helps keep our health care priorities in proper order as system-wide change occurs. It is appropriate to expect

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that proponents and developers of the tools of personalized medicine should be responsive to the broader system challenge, and should seek out points of intersection between broadscale reform and the development of personalized medicine, and offer solutions.

DISCUSSION

Today, policy leaders routinely describe America's health care system as being in crisis. Long-persistent trends, especially in spending, are widely viewed as unsustainable. Traditional fee-based reimbursement systems are viewed as a rewarding volume of services, with too little capacity to distinguish between differences in quality of care or outcomes for patients. Moreover, advances in medical technology are now widely thought to be major contributors to the rapidly escalating costs of health care and arguments that science and technology provide value are increasingly difficult to sustain.¹ Similarly, whereas present approaches to health care involve vigorous reaction at the onset of disease (typically at a late stage), relatively few resources or efforts are invested in prevention and health maintenance. Quality of care is recognized as uneven, and access to reliable care is negatively impacted by all these factors. With regard to both costs and quality, few effective tools of measurement or control have been at hand.

Increasingly, the cluster of problems in health care is viewed not as a collection of discrete issues but rather as related and self-reinforcing failures that require a system change. Some leading objectives common to many proposed approaches for systemic reform include the following:

- Realignment of incentives to ensure that good quality care and patient health outcomes are central goals throughout the many elements and mechanisms of the health care system.
- Demonstration of value and effectiveness of interventions, with measurement of care quality and outcomes.
- Increased emphasis on disease prevention, health maintenance, and effective management of disease (especially chronic conditions).
- Increased participation, information, and responsibility for consumers in maintaining health.

Such is the broader environment within which the paradigm of personalized medicine and the development of its tools must take place. Although a consistent definition has been elusive, personalized medicine is usually described in terms of its expected benefits for patients from care, guided by evidence, that distinguishes them from other patients. The term is often used to describe scenarios in which the enhanced precision and effective-

ness are made possible by factors particular to the individual or to a disease. In turn, such individualization is believed to enable care that will be *preventive*, *preemptive*, *predictive*, and *participatory* in a manner and to a degree not previously achievable.

- Improved disease prevention is made possible through the early recognition of disease risks based on constitutive biologic factors that reveal future potential for disease manifestation.
- Preemption and management of disease in early stages is enabled by the identification of molecular or other indicators (biomarkers) prior to the manifestation of signs or symptoms.
- Prediction of a specific patient's clinical response to various medical interventions is aided through the probabilistic associations of benefits and risks of the interventions with molecular level characteristics of the patient.
- Increased participation by the patient in health care decision making, compliance with care strategies, and healthy behavior choices are all supported by the individualization of information and through technologies that monitor, treat, and inform the patient outside the clinical setting.

The parallels between the features of the personalized medicine paradigm and the broader goals of system reform are tantalizing, including the potential for these expected capabilities of personalized medicine to reduce waste, increase efficiency, and improve cost effectiveness. However, these characteristics are end points and ideals. They do not describe pathways for development of the tools of personalized medicine, and for the most part such tools are not used widely enough at this time to have an effect on systemic change. They represent a promising strategy that is yet to be played out. For example, the complexity of data required to support personalized approaches to health care will require a substantial overhaul in the clinical research infrastructure to meet evidence requirements to justify their applications and costs.²

The point here may be obvious, but it is useful to make it explicit: The health care system and the economic universe of which it is a part have underlying imperatives, which now increasingly present themselves as urgent challenges (eg, "sustainability"). The development of a new paradigm for care delivery cannot expect to achieve success if it does not place itself within the context of these broader needs and challenges.

At the same time, these broader challenges largely supercede the particulars of care delivery itself. They are imperatives that cannot be ignored, yet their objectives are not identical with the goals of the health care enterprise—improved patient outcomes and health

status. A new paradigm for care, if it is well founded, may have a unique gift of perspective and guidance to offer. It may help inform broader system reform and indeed help guide it toward true “transformation.” But it is up to the proponents of the new paradigm and the developers of its tools to make these connections.

In this spirit, we offer a few suggested aspects where the expressed goals of health system reform intersect closely with the needs of the personalized medicine paradigm.

Innovation and costs. Concern over costs and spending is the strongest driver in the quest for health care system reform. Personalized medicine is a model that envisions improvement in patient care and outcomes built especially on innovation through science and technology. In many quarters, the emphasis on technology may put personalized medicine under automatic suspicion as a cost driver.

At the same time, technological innovation in personalized medicine is especially focused on new capacity to detect disease and steer interventions in ways that increase effectiveness. These benefits include identification of increased personal susceptibility to disease, detection of disease in much earlier stages than previously feasible through diagnostic tools made possible by scientific discovery, and guidance for treatment with greatly increased likelihood of effectiveness, based on factors particular to the individual or the disease.

The knowledge base of individual biologic differences that is now being assembled will support innovation in key medical product areas for regenerative medicine and preventive health strategies that can lessen long-term disability costs. These applications are particularly important in the face of increasing demographic and economic consequences of health care for an aging population.

Proponents of personalized medicine point to the potential for reduced spending through the avoidance of disease or late-stage treatment as well as reduction in trial-and-error treatment approaches. Skeptics would be justified in asking for the numbers. Preventive diagnostics might produce new costs without yielding substantial health or spending benefits. The cost effectiveness of preemptive disease discovery and of diagnostic-guided therapies might vary with the cost of the diagnostic or other factors.

Innovators correctly point to reimbursement schemes that currently offer little latitude for adjusting payment to achieve new kinds of results, especially for diagnostics. But the standoff between differing viewpoints on the cost and care roles of technology will continue until reliable predictive techniques and rapid confirmatory capacities are developed for ascertaining costs and value over varying time frames.

Health information technology. Near-universal support for adoption of electronic health records (EHR) is a striking feature of health system reform plans. For at least 5 years, this support has been bipartisan in nature and has generally been echoed by medical professional organizations, even while the numbers of providers adopting EHR systems has lagged.

Personalized medicine, while often characterized primarily as the application of advances in genomics and other areas of molecular biology, depends equally on advances in electronic health information exchange, storage, processing, and analysis. These 2 fields in concert provide the knowledge content and data processing capabilities that seem capable of supporting a leap in individualization and precision in care, as well as providing new technological tools (eg, decision support) to the provider and patient alike.

The aspects of health information technology (HIT) that make it promising for personalized medicine may be the same ones that would be convincing for physicians and other providers as they contemplate EHR adoption. Personalized medicine looks to HIT to provide substantial new support and results in clinical care. The identification of such value-giving applications could provide worthwhile guidance in the development and subsidization of HIT.

An example is newborn screening testing services provided by public health programs to detect inherited disorders, particularly those requiring critical intervention. Now long-established throughout all 50 states and probably the most far-reaching medical use of genetic testing today, newborn screening is nonetheless hampered in its effectiveness by inadequate communications. Problems range from simple inadequacy of information exchange technologies to nonuniformity in coding and terminologies. Urgent follow-up from screening, notably the detection of patients with phenylketonuria, may be satisfactory, but other factors like hearing tests are frequently misplaced, longer term benefits that could be derived for patients as a result of infant genetic screening are typically lost over time. These problems could be addressed effectively and inexpensively through HIT approaches, but clinically oriented applications like this are not necessarily apparent to HIT developers. Input from those who measure the value of HIT in terms of clinical results for patients could be of high value for system reform and personalized medicine alike.

Evidence standards and comparative effectiveness research. In recent years, health care reform leaders have placed new emphasis on the importance of a strong evidence base for treatment decisions, as well as the desirability of measuring the comparative effectiveness of alternative interventions.³ Both areas have high

importance for successful development of personalized medicine; in turn, the needs of personalized medicine should be informative for those who wish to advance these tools.

Largely as a result of scientific tradition and the evolution of product review by regulatory health agencies, a general scheme of standards for medical evidence has emerged, in which the randomized controlled clinical trial (RCT) occupies a dominant role. This schema arose over a long period of time in which the accumulation of data was limited and slow. With the advent of HIT and health information exchange, the potential for rapid and voluminous accumulation and analysis of data is at hand. Increased roles for observational research and modeling should become possible in developing evidence, and a reconsideration of the standards for evidence in guiding treatment may be appropriate.

For personalized medicine, a broadening of evidence standards would be crucial. High costs and long time frames associated with RCTs might be reduced, and with them the costs of research and development. However, the adoption of new standards of evidence will require proof that alternatives to the RCT and other traditional approaches can yield comparable assurance and protection for providers and patients.

The potential for a comparative effectiveness review (CER) poses a different challenge and opportunity for personalized medicine. If a CER includes the opportunity to demonstrate improved effectiveness within subpopulations, then it may serve as an ally for personalized medicine in stimulating the development of products that are narrowly targeted to patients with specific genetic or other characteristics. Alternatively, to the extent that CER might be confined to the comparison of existing therapies, it might yield the unintended result of narrowing the universe of accepted treatments and constricting incentives for innovation. Proponents of personalized medicine can help policy makers avoid choices that would impede potentially valuable and cost-effective developments.

Clinical research data standards. Closely associated with the potential benefits of HIT and health information exchange is the need for the standardization of data and messaging. Important progress has been made in developing consensus-based pathways for standards development. An area requiring special attention is clinical research data, including clinical genomics data.

In the anticipated environment of health information exchange, data from many sources may become available for aggregation and analysis. This includes the prospects for use of data from clinical health care delivery, with HIT tools providing information and guidance to providers, and subsequent outcomes becoming available via feedback to researchers—a “bench-to-bedside

and bedside-to-bench” circuit supporting the so-called “rapid learning health care system.”⁴

To be useful, such a data exchange would need to be standardized both with regard to terminology and with regard to the adequacy of detail in the data being captured. A virtual medical data trove on a national scale might be possible, but it would only be useful in research if sufficient detail was provided. At the same time, clinicians should not be so burdened by data capture standards as to reject the project. Personalized medicine, seeking to deliver more effective results for more narrowly defined populations, would be well served by such a wealth of data.

Patient safety and public health. In recent years, there has been intense pressure on federal agencies to develop policies, infrastructure, and strategies to overcome many dimensions of harms that exist in health care today.^{5,6} Enhanced detection capacity for medical product adverse events has been developed using genomic platforms and detailed databases that are now widespread throughout the pharmaceutical development pipeline to improve the understanding of risk and subpopulations predisposed to potential adverse events. Early manifestations of the potential for individualization of risk assessment include the use of pharmacogenomic tests for polymorphisms accountable for aberrant drug metabolism and drug–drug interactions that have led to regulatory changes affecting labeling and prescribing conditions for certain medications.

Recent public health experiences with contaminated food products by microbes and illicit chemical contaminants have led to major renovations in public health infrastructure for surveillance of the nation’s food supply. Genomic and proteomic technology platforms are now widely used for detecting potentially harmful agents and understanding the pathogenic effects of xenobiotics and pathogens. Building on the infrastructure and knowledge gained from these applications, new opportunities will likely emerge to integrate individualized therapeutics and prevention strategies into modern medical practice.

Consumer tools. Health care reform puts a heavy emphasis on new participatory roles for consumers. Developers of personalized medicine tools will generate products that are likely to support that goal. Even in cases where tools are originally developed with providers in mind, it is likely that successful products may spill into the consumer space, especially with regard to information products.

For example, decision-support tools aimed at aiding in the interpretation of genetic information are designed for professionals but prove useful for consumers as well. An early example is risk assessment tools using family health history information. The Surgeon General’s “My Family Health Portrait” web tool (<https://family>

history.hhs.gov), which was recently updated to demonstrate standardized information, is an example of a platform enabling development of consumer-oriented risk-assessment tools.

The first indications of commercial consumer marketplace for the application of genomic technologies have come in the form of services offered to the public with a probabilistic assessment of health risks. Although controversial from the standpoint of the lack of clear actionable health information, these services have shown innovative applications of infrastructure and scientific capacity built out from publicly available genome wide association databases. The growing strength of consumer empowerment coupled with greater availability and sophistication of information technology in health care are creating a powerful force for change outside from outside the formal health care delivery system that will focus on individualized needs and interests. The alignment of these forces represents future opportunities for personalized medicine.

CONCLUSION

In today's environment of reform, the changing health system and the paradigm of personalized medicine can mutually inform one another. Proponents of personalized medicine have long believed that this model has much to offer toward the goals of system reform. Equally, however, the objectives and elements of system reform should provide useful guidance in the development of the tools of personalized medicine.

Included above are a few areas, guided by the priorities of health system reform, where proponents of personalized medicine should be attentive to national priorities, and where the paradigm of personalized medicine can help inform planning and policy decisions. Other areas that might be important intersections for system change and personalized medicine might include quality measurement, data sharing, use of modeling, and clinical decision support.

The integration of personalized approaches into health care practice to date has largely been organic and episodic in nature with technology enhancements customized for niche applications. Technology and science unfold at an unprecedented rate, but clear goals and strategies for evidence development and translation into practice guidelines have been lacking. Undoubtedly, reforms in patient access and the arrival of new health care financing models can bring opportunities to integrate personalized medicine in health care. Under these pressures, increased attention to new strategies in prevention, tools to guide effective use of technologies and services, and better measures of objective health outcomes are strategic tools that can help achieve the broader purposes of reform. Innovative applications of the science and technology that support individualized approaches to medical decision making can be a spark for future health solutions that will help address the challenges encountered in the restructuring of America's health care enterprise.

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