Evidence-Based Medicine and the Changing Nature of Healthcare: Meeting Summary (IOM Roundtable on Evidence-Based Medicine)

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2007 IOM ANNUAL MEETING SUMMARY

EVIDENCE-BASED MEDICINE AND THE CHANGING NATURE OF HEALTH CARE

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Elizabeth G. Nabel, and LeighAnne M. Olsen

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The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

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"Knowing is not enough; we must apply.
Willing is not enough; we must do."
—Goethe

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Foreword

Evidence-based medicine (EBM) has been famously characterized by David Sackett as the "conscientious, explicit, and judicious use of current best evidence in making decisions about individual care." The central notion in EBM of the importance of integrating individual clinical expertise with the best available external evidence provides a helpful framework for providers navigating the uncertainty inherent in patient care. The selection of EBM as a topic for the 2007 Annual Meeting of the Institute of Medicine (IOM) signals its potential as a key driver toward greater value and efficiency in medical care. Technological and scientific innovations continue to expand the universe of medical interventions, treatments, and approaches to care, ushering in an era rich with potential for improving the quality of health care but also rife with increased uncertainty about what works best for whom. That uncertainty can—and does—lead to the delivery of services that may be unnecessary, unproven, and sometimes harmful.

This publication, *Evidence-Based Medicine and the Changing Nature of Health Care*, documents the content of the 2007 IOM Annual Meeting. In the years ahead, demographic, epidemiologic, and technologic developments will foist change on health care. Reforms will be necessary to remedy existing shortfalls in access to care as well as to take better advantage of the opportunities provided by innovation, information technology, and broader stakeholder engagement.

At this time in our nation's history, a host of health policy issues dominate the headlines, from the safety of imported drugs to children's healthcare coverage. Amid the cacophony surrounding each debate, the IOM strives to voice objective, independent, evidence-based counsel and

recommendations on critical questions. We know from experience that ascendancy and importance of healthcare access, cost, and quality challenges are no guarantees of action. The IOM's mission is to draw attention to issues and options that lay the groundwork for policy. We work to engage the field, facilitate needed discussion and debate, and develop sound policy recommendations.

The last 2 years have seen a burgeoning interest in convening activities at the IOM: the forums and roundtables that bring together individuals from government, academia, business, and the public at large for collective consideration and action around common problems. The Roundtable on Evidence-Based Medicine draws upon the many perspectives within the healthcare field, informs the debate, and provides an opportunity for dialogue among key stakeholders. The Roundtable's overview publication, *The Learning Healthcare System*, outlines a number of opportunities to transform the development and use of evidence to improve health care. The subsequent workshops and meetings in the Learning Healthcare System series delineate research methods, assess data availability, and describe ways to improve research on the effectiveness of healthcare delivery. The 2007 IOM Annual Meeting drew upon the Roundtable membership for planning and execution and builds upon some of the work of the Roundtable. This publication is the second in the Learning Healthcare System series.

I would like to offer my personal thanks to Roundtable participants, particularly Mark McClellan, Betsy Nabel, and Michael McGinnis, for their contributions as part of the planning committee.

Harvey V. Fineberg, M.D., Ph.D.
President, Institute of Medicine

Preface

The creative and innovative ethic of American medicine is legend and has contributed fundamentally to the breadth, depth, and pace of advances in our capacity for diagnosis and treatment of disease and injury. Indeed, the number of new pharmaceuticals, biologics, medical devices, and healthcare services introduced into American healthcare settings and marketplaces substantially exceeds the capacity to know the circumstances under which a particular intervention is best applied. The consequences of this gap between assessment capacity and available services include increasing uncertainty about what constitutes "best care," a steady expansion in the national and personal cost of medical care, and a substantial growth in concern and distrust among physicians and patients alike. The need is acute for better evidence to guide the decisions of patients and their caregivers on the approaches most appropriate to individual circumstances and preferences.

This need for a more systematic approach to evidence development and application, as well as the prospect of new ways of meeting the need, provides the back-drop for the discussions at the 37th Annual Meeting of the Institute of Medicine (IOM). Entitled *Evidence-Based Medicine and the Changing Nature of Health Care*, this meeting was held on October 8, 2007, and focused on the potential of evidence-based medicine to help deliver the promise of scientific discovery and technological innovation and provide the right care for the right patient at the right time.

The annual meeting was structured to bring together many of the nation's leading authorities on various aspects of the issues—both challenges and opportunities—to present their perspectives and engage in discussion with the IOM membership. Included in the presentations, and documented

in this publication, are summaries of the rapidly changing nature of the science base and tool chest for medical practice; the implications for the costs, quality, and effectiveness of health care; the challenges to individual practitioners; possible means of accelerating the necessary assessment of the appropriateness, effectiveness, and value of medical care; and the policy changes necessary to improve the efficiency and outcomes of the American healthcare system.

Organization of this meeting was facilitated by the experience and commitment of the IOM's Roundtable on Evidence-Based Medicine, in which we are participants. Convened in 2006, the IOM Roundtable is comprised of about two dozen members representing national leadership from the various stakeholder sectors important to progress in health care: patients and the public, providers, service delivery organizations, health researchers, government agencies, employers, insurers, health product manufacturers, and information technology organizations.

The Roundtable's vision is for a learning healthcare system that "draws upon the best evidence to provide the care most appropriate to each patient, emphasizes prevention and health promotion, delivers the most value, adds to learning throughout the delivery of care, and leads to improvements in the nation's health." In effect, the learning healthcare system is one which enlists organizations, providers, and patients in driving the process of discovery as a natural outgrowth of patient care, and ensures innovation, quality, safety, and value in health cares. As a tangible focus for progress towards this vision, the Roundtable has set the goal that by 2020, 90 percent of clinical decisions will be supported by accurate, timely, and up-to-date clinical information, and will reflect the best available evidence. While ambitious, this goal ought to be achievable, given the nation's commitment of more that one out of every six dollars to the delivery of health care.

We are pleased to have had the opportunity to present some of the key perspectives motivating the Roundtable's work over the last 2 years to the distinguished IOM membership, in serving as the planning committee members for the Annual Meeting and as authors of this publication.[1] We would like to also acknowledge our Roundtable colleagues who served as discussion moderators, and, in particular, the individual contributors who donated their valuable time and insights to the scientific program through their presentations and through their efforts to further develop the content into the manuscripts contained in this summary.

A number of IOM staff were instrumental in the preparation and conduct of the meeting, including Afrah Ali, Sandra Amamoo-Kakra, Bryn

[1]The responsibility for the published annual meeting summary rests with the authors and the institution. IOM forums and roundtables do not issue, review, or approve individual documents.

Bird, Allison Brantley, Sarah Bronko, Thelma Cox, Donna Duncan, Patrick Egan, Amy Haas, Geraldine Kennedo, Adam Rose, Autumn Rose, Sara Sairitupa, Judith Shamir, Kristina Shulkin, and Jovett Solomon. The responsibility for assembling the volume from the meeting was carried out by Roundtable staff under the direction of LeighAnne Olsen and included the work of Katharine Bothner, Molly Galvin, and Daniel O'Neill. We would also like to thank Lara Andersen, Michele de la Menardiere, and Bronwyn Schrecker for helping to coordinate the various aspects of review, production, and publication.

As illustrated in this publication, the challenges facing the nation's healthcare system are great, as is its promise. We look forward to expanding the sphere of engagement and action in the field to capture the substantial opportunities identified in this publication and the vision we all share for the health and productivity of Americans.

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Contents

Summary

INTRODUCTION AND OVERVIEW

The rapid pace of scientific discovery and technological innovation over the last several decades is unprecedented and raises the prospect of achieving dramatic improvements in the nation's health and well-being. Yet stakeholders from across the healthcare system, from patients to practitioners to payers, are demanding fundamental improvements to a system that is seen as costly, fragmented, and ineffective. Because of its emphasis on integrating the best available external evidence with clinical experience, evidence-based medicine (EBM) provides a guiding framework for the development of systems and approaches necessary to deliver the promise of 21st century health care—in which knowledge is both applied and generated as a natural outgrowth of the care process, to ensure delivery of the care most appropriate for each individual patient.

The nation relies on the Institute of Medicine (IOM) for independent, science-based advice on matters of biomedical science, medicine, and health. In part, the IOM's strength as an advisory organization lies in its ability to draw upon its membership, which includes distinguished health professionals as well as researchers and leadership from the fields of medicine and health care; and, the IOM annual meeting provides the opportunity for IOM members and other guests to discuss timely topics that are central to the nation's healthcare policies. In recent years, the annual meeting has focused on stem cells, tissue engineering, longevity and health, and pharmaceuticals in the 21st century. With healthcare reform at the top

This publication has been prepared by the authors to document the proceedings of the 2007 IOM Annual Meeting.

of the national domestic agenda, the choice of EBM by the IOM Council as the theme of the 2007 IOM Annual Meeting underscores its centrality and importance to healthcare improvement and offers the opportunity to bring this topic into a broader context as a transforming national priority.

Evidence-Based Medicine and the Institute of Medicine

The IOM has throughout its existence been dedicated to improving the health and health care of Americans. Its seminal contributions to drawing attention to issues and policies important to better quality health care have recently included *To Err Is Human* (2000) and *Crossing the Quality Chasm* (2001). In the face of the growing awareness generated about the nature and implications of the gap between healthcare practice and the evidence base, the IOM Roundtable on Evidence-Based Medicine was established in 2006 to provide a neutral forum for discussions and collective action by healthcare stakeholders to help transform the way evidence on clinical effectiveness is generated and used to improve health and health care.

Underscoring the challenges faced by healthcare decision makers, the Roundtable has defined EBM to mean that "to the greatest extent possible, the decisions that shape the health and health care of Americans—by patients, providers, payers, and policy makers alike—will be grounded on a reliable evidence base, will account appropriately for individual variation in patient needs, and will support the generation of new insights on clinical effectiveness" (IOM's Roundtable on Evidence-Based Medicine, 2006). To support EBM in practice, the Roundtable seeks the development of a learning healthcare system that "draws on the best evidence to provide the care most appropriate to each patient, emphasizes prevention and health promotion, delivers the most value, adds to learning throughout the delivery of care, and leads to improvements in the nation's health" (IOM's Roundtable on Evidence-Based Medicine, 2006).

With the guidance of members and expert panels, the Roundtable has conducted a series of meetings and workshops aimed at fostering progress toward the "learning healthcare system"—a system in which both evidence development and application flow naturally from the care process. In addition to the development of the 2007 IOM Annual Meeting on the topic, the series of workshops exploring the barriers, challenges, and opportunities for this vision include

- The Learning Healthcare System (2006);
- Judging the Evidence: Standards for Determining Clinical Effectiveness (2007);
- Leadership Commitments to Improve Value in Health Care: Finding Common Ground (2007);

- Redesigning the Clinical Effectiveness Research Paradigm: Innovation and Practice-Based Approaches (2007);
- Clinical Data as the Basic Staple of Health Learning: Creating and Protecting a Public Good (2008);
- Engineering a Learning Healthcare System: A Look at the Future (2008);
- Learning What Works: Infrastructure and Clinical Priorities to Learn Which Care Is Best (2008); and
- Making Better Choices: Getting the Value We Deserve from Health Care (2008).

COMMON THEMES: ISSUES, CHALLENGES, AND OPPORTUNITIES

The 2007 IOM Annual Meeting provided the opportunity to juxtapose the potential for health care in the 21st century with current shortfalls and to present to important leaders in the field some emerging resources and key policy opportunities that could help transform health care. Discussions focused on four themes: the forces driving the need for better medical evidence; the challenges with which patients and providers must contend; the need to transform the speed and reliability of new medical evidence; and the legislative and policy changes that would enable an evidence-based healthcare system. During the course of meeting presentations, a number of common themes were identified (Box S-1). Among them were the following:

- *Increasing complexity of health care*. New pharmaceuticals, medical devices, technologies, and predictive data offer much promise for improving health care, but they also introduce high levels of complexity, requiring changes on the parts of both caregivers and their patients.
- *Unjustified discrepancies in care patterns*. The intensity of healthcare services delivered for similar conditions varies significantly across geographic regions, particularly in areas that require discretionary decision making. However, the higher-spending regions often do not deliver better-quality care, hence offering substantial opportunity for reduced spending without sacrificing health outcomes.
- *Importance of better value from health care*. The current healthcare system is not designed to deliver value, and the nation's long-term fiscal challenges are serious and are being driven predominately by excessive medical spending, often on interventions of no clinical benefit. Opportunities exist to eliminate wasteful spending with no

BOX S-1
The Changing Nature of Health Care
Common Themes

- Increasing complexity of health care
- Unjustified discrepancies in care patterns
- Importance of better value from health care
- Uncertainty exposed by the information environment
- Pressing need for evidence development
- Promise of health information technology
- Need for more practice-based research
- Shift to a culture of care that learns
- New model of patient-provider partnership
- Leadership that stems from every quarter

reduction in health care, as well as to improve the overall health outcomes, but agreement is needed both on what constitutes best care and on what constitutes value in health care.

- *Uncertainty exposed by the information environment.* An irony of the information-rich environment is that information important to clinical decision making is often not available, or is provided in forms that are not relevant to the broad spectrum of patients—with differing levels of health, socioeconomic circumstances, and preferences—and the issues encountered in clinical practice. This is due to too little clinical effectiveness research, to poor dissemination of the evidence that is available, and to too few incentives and decision supports for evidence-based care.
- *Pressing need for evidence development.* More and better evidence—including comparative and longitudinal data—is needed to determine the effectiveness and usefulness of new medical interventions, treatments, drugs, devices, and genetic information. There is an untapped potential to reduce healthcare costs and improve quality by developing evidence not only for specific medical interventions, but also for the way health care is delivered.
- *Promise of health information technology.* Electronic medical records (EMRs) and clinical data registries offer tremendous potential both to generate new evidence and to augment randomized clinical trials. Addressing privacy and proprietary issues that limit data access and sharing would help to support a system in which

EMRs, clinical registries, and other types of electronic data could contribute to building a more robust evidence base.

- *Need for more practice-based research*. How might the system better support the notion of a "living textbook of medicine" in which the experience of healthcare diagnosis and treatment is routinely captured in order to better care for those in the future. To develop best evidence for the delivery of medicine that is geared toward the needs of individual patients, investment is needed into infrastructure for the gathering and analysis of healthcare data and information, and standards and protocols to ensure their accuracy and reliability.
- *Shift to a culture of care that learns*. This changing role will require healthcare providers and patients to adopt a culture that supports the generation and application of evidence. Effective culture change must also be accompanied by insurance and reimbursement system reform that encourages development and application of the systems necessary.
- *New model of patient-provider partnership*. With the increasing complexity of care, and the need and demand for more patient involvement, the traditional "physician-as-sole-authority" model will need to adapt to support patients as integral partners in medical decisions.
- *Leadership that stems from every quarter.* Adapting to and taking advantage of the changes in the healthcare environment will take broad leadership. A strategic focus on the development and application of evidence will require the involvement of both the public and private sectors working together, and with policy makers, providers, patients, insurers, and other stakeholders in the steps toward change.

PRESENTATION SUMMARIES

The Changing Nature of Health Care (Chapter 1)

Meeting co-chairs Mark B. McClellan, director of the Engelberg Center for Health Care Reform and Leonard D. Schaeffer Chair in Health Policy Studies and Economic Studies of the Brookings Institution, and Elizabeth G. Nabel, director of the National Heart, Lung, and Blood Institute of the National Institutes of Health, opened the meeting with introductions and overviews of key issues. Comments were also provided as context for each session by the moderators: Denis A. Cortese, chief executive officer of Mayo Clinic; Michael M. E. Johns, chancellor of Emory University; John W.

Rowe, professor, Columbia University; and John K. Iglehart, editor emeritus of *Health Affairs*. A summary of their comments follows. The content of the session presentations also follows, with more detail provided by the authors in Chapters 2 through 7.

Mark B. McClellan and Elizabeth G. Nabel, Meeting Co-Chairs

In his remarks, McClellan focused on two core challenges facing health care in the 21st century: rising and unsustainable costs and the untapped potential presented by biomedical and technological advances. Creating an evidence-based system is essential to achieving both the promise of personalized medicine and the value needed from health care. In the current medical system, practices vary widely, which can affect health outcomes and costs. Treatments effective for some may not actually be beneficial for others, and may even carry significant risks. Needed evaluation of interventions and delivery system issues in real-world practice will require that we look beyond the traditional research focus to new methods and new opportunities presented by emerging data sources, including electronic health records (EHRs) and clinical registries. For sustained change, the system also must be better oriented around value and outcomes. A systems-level approach is needed to align policy and reimbursement to support and reward better quality at lower costs.

Nabel noted that while there is much consensus about the problems with the current healthcare system, agreement and collaborative work are needed to develop solutions. The roles and responsibilities of all stakeholders in the healthcare system are undergoing tremendous transformation; patients, providers, payers, industry, and policy makers alike must work together to contend with these changes and make needed reforms. Providers are operating in an increasingly complex system with an ever-growing amount of medical information and treatment options to consider. The physician-patient relationship is changing as patients have access to more Web-based health information and are more empowered to make decisions about their own health care. Research methodologies will need to be adapted to take better advantage of the increased amount of real-time and real-world data from EHRs and clinical registries. Beyond the evaluation of interventions, methodologies are needed to model and analyze work processes and decision management. This type of research may require restructuring of funding to include research on how to attain changes in work processes and set value in the system.

Both McClellan and Nabel emphasized the many technical and policy challenges that must be overcome to fulfill the vision of the Roundtable. While EBM is increasingly at the forefront of policy making and is driving

various reform initiatives at government agencies, greater collaboration by all stakeholders is essential for progress. An increased role of healthcare product companies and other healthcare industries is particularly important. Public-private partnerships are needed to identify new approaches to the generation and application of evidence in medical practice in order to improve care and reduce costs.

Denis A. Cortese, Chief Executive Officer, Mayo Clinic

Cortese noted that the current system provides no incentives for patients to seek—or for practitioners to provide—high-quality, cost-effective health care. If the value of the healthcare system is measured in outcomes, safety, and service in relation to the cost over time to provide services, the return on our investment is falling far short of its potential.

Current dissatisfaction with health care provides an opportunity to develop a vision, create a strategy, and specify goals for a different kind of healthcare system. The ideal system would reward prevention of the onset of illness, tailor specific treatments for possible cures, control chronic illnesses, and improve patients' quality of life. The system should be affordable for both individuals and the country. The overarching vision, as conceived by the IOM's Roundtable, is one of a learning healthcare system "designed to generate and apply the best evidence for the collaborative choices of each person and provider." The system would support innovation and discovery as a natural outgrowth of care and ensure quality, safety, and value.

Essential to progress toward this shared vision is a better understanding of the forces driving the need for better medical evidence. Chapters 2 and 3 summarize presentations on several of the key issues introduced by Cortese: the tremendous negative economic consequences of the rising, unsustainable costs of health care; implications of the variations in healthcare spending and health outcomes in different regions of the country; the quality and quantity of evidence needed to guide clinical decisions; the increasing diversity of new health products; and the complexity of insights generated by genetic research.

Michael M. E. Johns, Chancellor, Emory University

Chapters 4 and 5 examine how patients and providers might begin to contend with the healthcare system's increasing complexity and the role of information technology (IT) in the process. Johns's introductory comments outlined the challenge presented by the vast amount of healthcare information available to consumers—information of varying quality and complexity. This is daunting even to providers with years of education

and experience, but it is far more challenging to the non-expert. Tools are becoming available that will assist navigation of the information needed to better support healthcare providers, foster improved patient-physician partnerships, and empower patients in the "Information Age." However, attention is also needed on educational efforts to promote a better understanding by patients and providers of what constitutes good evidence for effective care.

As more and better evidence is developed, effective processes and IT systems will be necessary to ensure that healthcare practices actually apply the evidence. Methods for accelerating the dissemination and incorporation of new knowledge into practice should be identified so that it does not take years for providers to catch up on new knowledge and skills. Effective systems must include proper rewards and incentives for providers to implement best practices, as well as mechanisms to pay for information systems and process innovations.

Education is a key component to ensure needed fluency with new systems and capabilities, as well as to increase the appreciation of and demand by the general public for evidence-based care. Practitioners need to work with the public to identify and implement the right healthcare solutions. Needed from healthcare leadership, therefore, is initiative for policies that empower patients and providers to catalyze and implement needed change.

John W. Rowe, Professor, Columbia University

In introducing the presentation summarized in Chapter 6, Rowe emphasized that a key characteristic of the Roundtable's vision of a learning healthcare system is continual evidence development and refinement. Information is acutely needed on the effectiveness of individual drugs, devices, and procedures and systems of care and care delivery and, in particular, how these competing therapies stack up against each other. A major strategy proposed to hasten the development of the needed evidence base is to take advantage of a broader range of methodologies, beyond randomized controlled trials (RCTs). Concerns have been raised that such approaches are not as reliable as RCTs and that time saved employing different research approaches might not be worth the cost in quality and reliability. However, rather than looking at these issues as absolute, Rowe urges researchers and practitioners to identify strategies to enhance the types of data being used to increase the speed and reliability of evidence generated. Chapter 6 includes presenters' views of the opportunities presented by EMRs and clinical data registries for generating real-time evidence. In addition, the potential for developing and delivering increasingly tailored therapies is examined.

John K. Iglehart, Editor Emeritus, Health Affairs

Iglehart sets the stage for the discussion of policy issues and considerations which are included in Chapter 7. Key issues include placing a sharper focus on value in health care, as well as understanding the current political environment that must be navigated to drive change. Iglehart cautions that despite the potential for reform, the overall process of policy making is badly in need of repair. Perversely influenced by a campaign finance system that makes candidates beholden to narrowly focused special interest groups, change will require savvy political strategy, as well as sound policy.

The Need for Better Medical Evidence (Chapter 2)

A close examination of national and regional healthcare spending trends and health outcomes reveals much about where the system is falling short and identifies opportunities for improvement. Presentations at the meeting made the case for more and better medical evidence, which could simultaneously reduce unnecessary healthcare expenditures and improve health outcomes for patients.

Health Care and the Evidence Base

Elliott S. Fisher, professor of medicine and community and family medicine, Center for the Evaluative Clinical Sciences, Dartmouth Medical School, drew upon small-area analyses to underscore the scope of the challenge faced in bringing evidence to bear on current practice and to point out opportunities to improve costs and quality of care. Two categories of treatment are considered: (1) discrete, biologically targeted interventions, which have been the traditional focus of a narrow definition of evidence-based practice; and (2) care delivery strategies that look at how these therapies should be delivered—by whom, where, and with what intensity. For both categories, the evidence base is often limited, and the relative magnitude of uncertainty is often reflected in regional variations in the rate of service use among the Medicare population. Interestingly, these categories have distinct relationships to variations in spending, with higher spending largely due to differences in care delivery: how frequently patients are seen, how much time they spend in the hospital, and the intensity with which they are monitored. When viewed in terms of health outcomes, regardless of organizational level or region, higher spending or intensity of care delivery consistently returns no improvement (and in some cases worse quality or outcomes) (Table S-1). If the organizational structures and practice patterns of the lowest-spending regions of the United States could be adopted across the country, Medicare spending would decline by about 30 percent.

TABLE S-1 Relationship Between Regional Differences in Spending and the Content, Quality, and Outcomes of Care

	Higher-Spending Compared to Lower-Spending Regions[a]
Healthcare resources	• Per capita supply of hospital beds 32% higher (Fisher et al., 2003) • Per capita supply of physicians 31% higher overall: 65% more medical specialists, 75% more general internists, 29% more surgeons, and 26% fewer family practitioners (Fisher et al., 2003)
Content and quality of care	• Adherence to process-based measures of quality lower (quality worse) • Little difference in rates of major elective surgery (Fisher et al., 2003; Wennberg et al., 2002) • More hospital stays, physician visits, specialist referrals, imaging, and minor tests and procedures (Fisher et al., 2003)
Health outcomes	• Mortality up to 5 years slightly higher following acute myocardial infarction, hip fracture, and colorectal cancer diagnosis (Fisher et al., 2003) • No difference in functional status (Fisher et al., 2003)
Physician perceptions of quality	• More likely to report poor communication among physicians (Sirovich et al., 2006) • More likely to report inadequate continuity of patient care (Sirovich et al., 2006) • Greater difficulty obtaining inpatient admissions or high-quality specialist referrals (Sirovich et al., 2006)
Patient-reported quality of care	• Worse access to care and longer waiting times (Fisher et al., 2003) • No difference in patient-reported satisfaction with care (Fisher et al., 2003)
Trends over time	• Although all U.S. regions experienced improvements in acute myocardial infarction survival between 1986 and 2002, regions with greater growth in spending had smaller gains in survival than those with less growth in spending (Skinner et al., 2006)

[a]High- and low-spending regions were defined as the U.S. Hospital Referral Regions in the highest and lowest quintiles of per capita Medicare spending, as in Fisher et al. (2003).
SOURCE: Elliott S. Fisher, 2007.

When there is strong medical evidence, physicians tend to agree on courses of treatment across regions of different spending levels, but they differ widely in areas that require discretionary decision making, such as how often to see a patient with well-controlled hypertension and when to hospitalize a patient with heart failure. For these decisions, neither patient preference nor the malpractice environment is associated with variations in practice; however, the local organizational and policy environment profoundly influences provider decision making. For example, hospitals and physicians operate in a system that rewards the expansion of capacity and

the recruitment of procedure-oriented specialists. Because so many clinical decisions are in the "gray areas," such as how often to see a patient, when to refer to a specialist, or when to admit to a hospital, any expansion of capacity results in a shift in clinical judgment toward greater intensity of treatment.

These findings point to the need for much better evidence about the risks and benefits of discrete biologically targeted interventions, and offer insights to the decisions of clinicians, administrators, and policy makers about approaches to care delivery. Not only do these differences in the way care is delivered explain almost all of the geographical variations in spending; but in many cases, the effectiveness of targeted interventions will also depend on the delivery strategy. Therefore developing the capacity to better evaluate the effectiveness of both categories of treatments offers an immediate opportunity for improving the costs and the quality of care.

Fortunately, the information systems and analytic approaches required to improve the evidence base for both biologically targeted interventions and care delivery are fundamentally the same. For both types of evidence, certain variables such as patients' health outcomes and factors such as age, race, sex, and severity of illness are needed. Improved information systems and electronic health records allow for assessments of both short- and long-term health outcomes and effective patient follow-up. In fact, the capacity to evaluate both care delivery and biologically targeted interventions will be critical, since the lack of information about how the interventions were administered and monitored would sharply limit the ability to interpret studies of biologically targeted interventions. Finally, Fisher extended a challenge to the field of academic medicine and the government agencies that fund its research. Because of the traditional focus on understanding disease biology, the dramatic variations in care delivery among academic medical centers have been largely ignored despite their substantial potential to lower costs and improve care. If all U.S. delivery systems could achieve the same efficiency as some of the top-performing academic medical centers, more resources would be available to expand healthcare coverage and access. Academic medicine has the opportunity to lead the development of a learning healthcare system by taking up this obvious opportunity to improve care quality.

The High Price of a Lack of Evidence

Improving the quality of health care and reducing unnecessary spending is not only a priority for the healthcare system, it has become an important national economic imperative. Peter R. Orszag, director of the Congressional Budget Office, noted that if healthcare costs continue to grow at the same rate as they have over the past four decades, by 2050 Medicare and

Medicaid spending alone would account for 20 percent of the total U.S. economy—an amount roughly equivalent to the entire size of the federal budget in 2007. Although upward-spiraling costs are often misdiagnosed as the consequence primarily of an aging population, lower fertility rates, and longer life expectancy, spending increases actually result mostly from the rising cost per individual beneficiary. In short, the rate at which healthcare costs grow is the central longtime fiscal challenge facing the United States. Simply reducing payment rates of Medicare and Medicaid (and therefore access) may not be consistent with the nature of these public programs. To be sustainable, reforms may therefore need to trigger changes that will have an impact on the overall healthcare system.

Cost increases are being driven by a lack of information on the effectiveness of medical interventions and healthcare delivery and a payment system that accommodates the delivery of low- or negative-value care. Because lower cost sharing increases health costs overall, many have argued for more cost sharing and health savings account approaches. However, while more cost sharing among consumers could help reduce costs, the overall effect would be limited because a significant amount of cost sharing already exists in health plans and because costs are concentrated among the very sick. For example, 25 percent of Medicare beneficiaries account for 85 percent of total costs. Therefore, instituting more cost sharing probably would not be able to reduce costs significantly without impairing health quality.

On the provider side, better evidence and changes in payment incentives could help reduce costs. Evidence on comparative effectiveness is needed for a variety of clinical interventions, but careful consideration of what is meant by comparative effectiveness research and how it would be implemented is necessary. Building out the evidence base across the spectrum of clinical interventions and practice norms by relying exclusively on randomized trials is impractical, but reliance on nonrandomized evidence comes with well-known limitations. Using statistical techniques on panel data sets from EHRs, insurance claims, and other medical data seems to be the only cost-effective and feasible mechanism for significantly expanding the evidence base, but separating correlation and causation is difficult with such an approach. Simply making comparative effectiveness information available is insufficient to impact costs. Releasing information from systematic reviews will have some effects, but they are likely to be modest. Utilization of a broader range of studies—including those using clinical registry or EHR data—will have greater effects, but real gains in improving the quality of health care and reducing costs will come when the results of research are built into incentive payments for healthcare providers.

In sum, there is a pressing need for better medical evidence on what works best for whom. When combined with increased consumer informa-

tion and provider incentives that reward higher-value care, comparative effectiveness research offers an opportunity to reduce healthcare costs and improve health outcomes.

Circumstances Accelerating the Need (Chapter 3)

Scientific and technological advances sometimes offer dramatic opportunities to improve treatments, boost the efficiency of care delivery, and provide more options for patients and providers. However, efforts to adopt and integrate these advances into health care confront complex challenges. Advances in the field of genetics in particular are providing a wealth of information on factors influencing the development of disease. The complexity and costs introduced by these developments and other innovations in medical products also impact the healthcare system as a whole. Providers will be challenged to find ways to evaluate the effectiveness of these new technologies while also ensuring that innovation is continuously supported, captured, and applied to health care.

New Healthcare Product Introduction

Molly J. Coye, founder and chief executive officer, Health Technology Center, discussed the challenge presented by the increased complexity and diversity of new medical devices and interventions to the development of adequate evidence to support healthcare decision making (Figure S-1). The clear benefits of medical technologies have underscored the importance of supporting innovation in healthcare product development, and perhaps most pressing in this respect is the development of new approaches to accelerate the evaluation of new technologies. The complexity introduced by many new technologies has had two major consequences: (1) waste and inefficiency in the processes of evidence generation, due to poorly defined evidence needs with respect to coverage and reimbursement decisions; and (2) delayed action on the potential of transformative technologies that might enable disruptive and positive changes in clinical care and administrative processes. Key challenges for health care are the development of approaches for the early identification of beneficial technologies, as well as for generating the evidence needed to evaluate these emerging technologies.

Recent Food and Drug Administration (FDA) approvals of new products have actually been relatively level. Medium- and low-risk products have been approved each year in far greater numbers than novel products, and off-label extensions of drugs and devices are increasing without any kind of formal evaluation. In addition, providers have been contending with the expansion of IT products, most of which do not require FDA approval. However, Coye argued that emerging technologies, including new

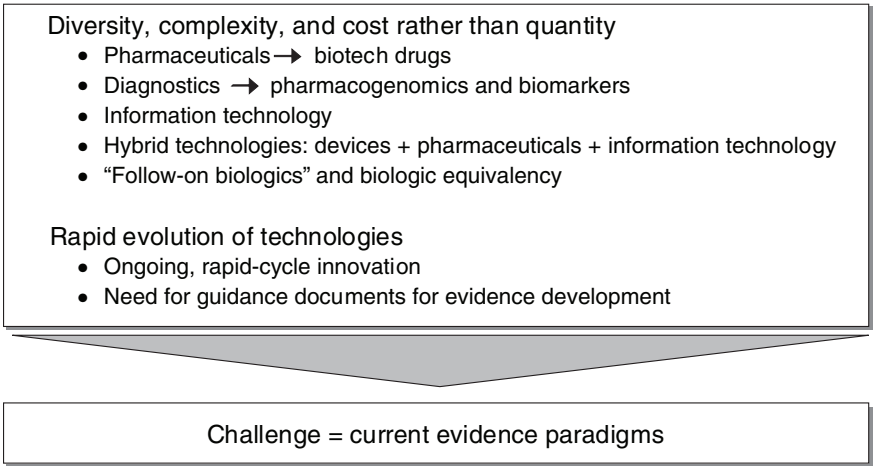

FIGURE S-1 Key challenges to the current evidence paradigm.
SOURCE: Molly J. Coye, 2007.

biologics and hybrid pharmaceutical and device products, present the most pressing burden on current capacities to develop evidence for regulatory and coverage decisions.

For example, the field of biotechnology, including genetic diagnostics and therapies, is growing at twice the rate of chemical pharmaceuticals. Several factors complicate efforts to generate appropriate evidence on the effectiveness of biotech drugs. Often costly and targeting rare or life-threatening diseases, these drugs are in urgent need of assessment, but high patient demand often limits trial participation. Off-label uses for biotech drugs often target unrelated diseases and may quickly become accepted in practice, again limiting opportunities for clinical trials. For "follow-on biologics," the evidence basis for regulatory decisions will likely be fraught with controversy and legal actions until scientific and legal issues relevant to regulatory policy are resolved. Similarly, the number of biomarkers—which combine the knowledge of genetics, proteomics, and bioinformatics—is expanding rapidly in hopes of providing better indicators of normal biological or pathogenic processes or of pharmacological responses to therapeutic interventions. Although they are potentially important for developing diagnostics, appropriate research approaches and regulatory criteria do not yet exist for biomarkers to ensure their appropriate use and relevance to clinical care. Finally, biotech drugs, devices, and information technologies are also converging to produce entirely new classes of technology that

pose substantial challenges to the established evidence paradigm. Devices, information technologies, and hybrid products evolve more rapidly than they can be evaluated in controlled trials, necessitating new evaluation methodologies and approaches.

The complexity of the current regulatory environment is leading to waste and inefficiency because critical research targets have not been identified for technology developers *before* they initiate clinical studies. With the exception of the largest, most sophisticated firms, the understanding of what needs to be demonstrated in order to win coverage, reimbursement, and support from payers and providers varies widely. Coordinated public and private efforts are needed to identify important research targets, including priority populations, side-by-side comparisons of effectiveness with competing technologies, and cost effectiveness.

This regulatory complexity is also obscuring the contributions of certain technologies that have the potential to significantly transform medical care. These transformative technologies—which include telemedicine, remote monitoring of chronic disease, the tele-ICU (remote monitoring of intensive care units), pharmacogenomics, hemofiltration for congestive heart failure, and remote video interpretation—enable a wide range of positive changes in clinical care and administrative processes, reducing net expenditures and improving the value of health care. These technologies provide important opportunities for progress toward national goals of improved quality and efficiency in health care, and—in contrast to biologics and hybrid devices—they present only modest challenges to capacities for evaluation.

Extracting the full value of emerging technologies will advance national goals of quality, efficiency, and improved patient experience and will require new approaches to generating and evaluating evidence. Few transformative technologies are seen as lifesaving treatments, despite the fact that some actually do save lives and lessen the burden of illness. It falls to purchasers, payers, providers, and policy makers to craft new approaches to evaluate and simultaneously foster the development of transformative technologies. Fast Adoption of Significant Technologies is one such effort being pilot tested by the New England Healthcare Institute, in collaboration with the Health Technology Center and the Massachusetts Technology Collaborative. This iterative, coordinated, and proactive approach focuses on accelerating the adoption of classes of technology that lower costs and improve quality and emphasizes rapid design evolution, testing across a variety of care settings and applications, clear definitions of research targets that correspond to value, and a commitment to support the coverage and reimbursement for technologies of demonstrated benefit.

Rapidly Developing Insights into Genetic Variation

In just the past few years, researchers have made striking progress in the study of genomics and genetics (Figure S-2). In 2007 alone, the systematic study of genetic variation across large patient samples revealed more than 75 genetic risk factors for common diseases, tripling the number previously identified. The implications of a vastly expanded amount of new knowledge about human genetics offers great promise for better diagnosis and treatment of disease, but also pose challenges to the healthcare system, according to David M. Altshuler, director of medical and population genetics for the Broad Institute.

Progress in identifying the genetic causes of common diseases holds great promise to catalyze the development of new insights into pathophysiology. However, testing for genetic variations is of uncertain value for the individual patient and the healthcare system. In vivo biological relevance does not necessarily imply clinical utility. The role of inheritance is only one factor in the development of common diseases. In addition, it has become increasingly clear that the inherited contribution itself is divided across many genes. The polygenic nature of common diseases made it difficult to identify any single genetic variant that was reproducibly contributing to

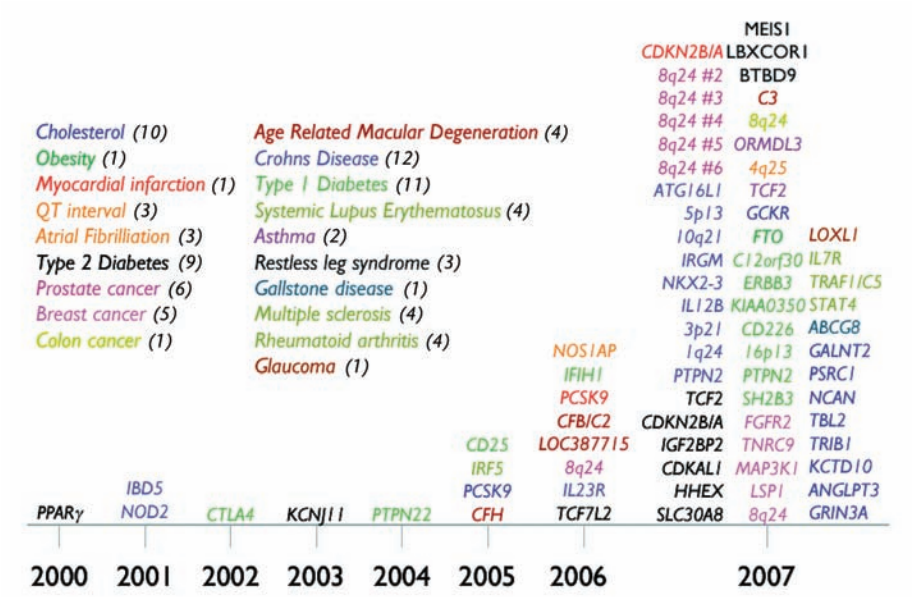

FIGURE S-2 Progress in the identification of gene variants for common diseases. SOURCE: David M. Altshuler, 2007.

risk. Recently, a variety of tools have been developed to enable a simple but comprehensive association study approach for the role of common genetic variants in diseases, and findings have greatly contributed to a better understanding of underlying physiological processes. For example, a common single-letter change in one complement factor influences the risk of developing macular degeneration fivefold or more. Research prior to these genetic studies had not explored the effects of complement factors, and this added biological insight suggests the possibility that targeting the complement pathway might be a key in preventing the disease. Similar discoveries have been made for Crohn's disease and Type II diabetes.

Each of the newly localized genetic variants is common, so they are present in a substantial proportion of the population. Although it is simple to test a patient to determine whether he or she carries a genetic risk factor, whether this is actually useful information to individuals is much less clear. Unlike rare genetic diseases such as Huntington's disease, the risks attributable to these newly found genetic variations are typically very modest. A key challenge is determining whether and how clinical testing for such genetic variations can improve patient care.

To evaluate this question for Type II diabetes, researchers from Massachusetts General Hospital and the Diabetes Prevention Program (DPP) conducted a landmark study of diabetes prevention involving 5,000 people with impaired glucose tolerance. As part of that effort, the DPP examined a study on the gene TCF7L2, which has the largest effect of any single common variant yet described in Type II diabetes. In that study, patients homozygous for the gene variant—between 5 and 10 percent of the participants—had double the risk of contracting Type II diabetes as identical patients who did not have this high-risk genotype. The study results validate that measurement of TCF7L2 conveys predictive information above and beyond the clinical standard. However, an even more interesting finding was that the lifestyle intervention was equally effective in preventing the onset of diabetes in the high-risk genotype group as in the population as a whole. While these results suggest little value in testing for this gene, a diagnostic is available and is being actively marketed for use. Clearly, to develop an evidence-based approach to genetic testing, clinical research is needed to determine how such information might influence individual behavior, health outcomes, and healthcare utilization. Performing such research will be difficult due to a lack of incentives and the rapidly changing nature of genetic information.

While the long-term value of identifying genes and DNA variations that influence diseases could be significant advances in prevention and treatment, the marketing of genetic information is a much more uncertain enterprise that currently lacks evidence for improvement of people's health and well-being.

Contending with the Changes (Chapter 4)

As new technologies and scientific advances continue to revolutionize what is possible in health care, providers and patients at the front lines of care must contend with an increased number of medical options, as well as an overwhelming amount of information to guide their healthcare choices. Adopting new technologies and medical interventions and embedding emerging information into practice will require a cultural shift in the behaviors, beliefs, and practices of individual healthcare providers and delivery organizations. Evaluating the quality and usefulness of medical evidence, putting the evidence into practice, and continuing to adjust and monitor patients' treatment and health outcomes are tasks that both providers and patients will have to perform.

Beyond Expert-Based Practice

William W. Stead, McKesson Foundation Professor of Medicine and Biomedical Informatics and associate vice chancellor for strategy and transformation at Vanderbilt University, postulates that in order to keep pace with new developments and make informed decisions in a timely manner, the healthcare system will shift from expert-based practice, which is built around the extensive knowledge and experience of the physician, to systems-supported practice.

In expert-based practice, the individual expert provides extensive knowledge and technical skill based on his or her education and experience. He or she is expected to remember facts, assimilate data, recognize patterns, judge, and make decisions wisely. Stead suggests the demise of expert-based practice is inevitable given the rapidly increasing gap between human cognitive capacity and the number of facts to consider in a single clinical decision (Figure S-3). However, in systems-supported practice, the focus is on the system's performance. Teams of people, well-defined processes, and IT tools work in concert to produce the desired result consistently. People provide compassion, pattern recognition, and judgment and are supported by well-defined processes that standardize and simplify work flow. IT tools decrease dependence on memory and force action when needed.

While both expert-based and systems-supported practices rely on evidence, the difference is in how they translate evidence into action. Stead described the rigorous, painstaking steps taken by Vanderbilt University Medical Center to develop a systems-based approach to caring for patients on ventilators. Although there is an abundance of evidence surrounding the care of ventilator patients, much of it is not translated into a form that can be used by practitioners. Vanderbilt's team built a set of standard practices

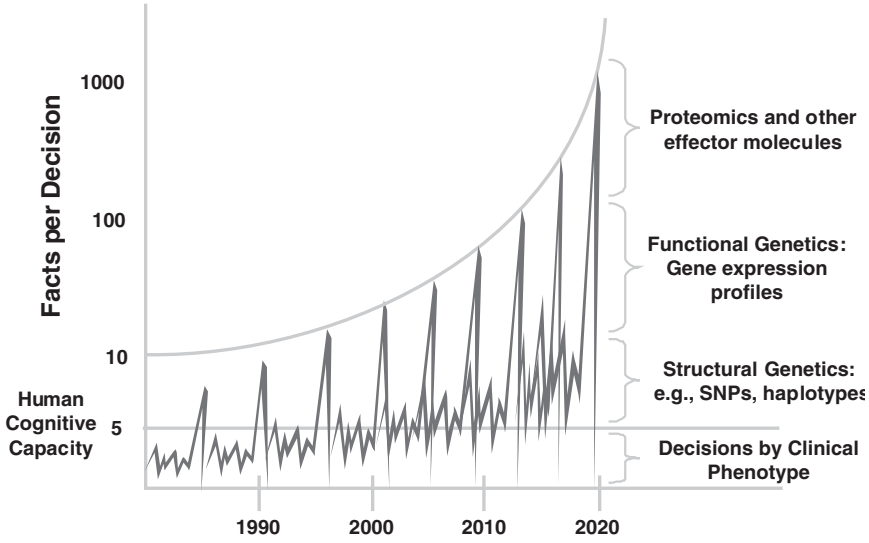

FIGURE S-3 Schematic depicting the increase in number of facts per clinical decision with new sources of biological data.
SOURCE: Daniel R. Masys and William W. Stead, 2007.

with specific process steps for implementing each practice and measures for assessing them.

Moving from an expert-based to a systems-based practice is complicated by the ever-changing nature of health care. The constantly evolving biological systems that healthcare providers work with, combined with the variability of individuals and conditions, make it impossible to standardize treatments. Other industries are able to isolate change in their systems and adjust accordingly, but the rate of discovery in the biological sciences and the introduction of new technologies require rapid experimentation and iterative change. To achieve consistent performance and accommodate a number of clinical problems, the variability in biology and values, and the rate of change in biomedical knowledge, standardization should not focus on specific practices, but on a systems approach to practice. Continuous system development and refinement through iterative cycles of development will yield local standard practices consistent with global knowledge, yet adapted to local resources and capabilities and responsive to changing evidence and system performance. In such a scenario, rather than focusing on managing individual patients as an experiment with an *N* of 1, the expert applies judgment to develop and iteratively refine the system of practice for their organization.

To make these changes, policy makers and payers need to understand the characteristics of health care that make moving beyond expert-based practice challenging. Without this understanding they will continue to ask for and pay for changes that are unlikely to produce the desired result. Healthcare providers need to appreciate the expert's role in the systems approach and understand that the systems approach does not replace or devalue the expert.

The Partnership Imperative in an Evidence-Driven Environment

Underscoring that each individual patient has differing life circumstances, cultural needs, preferences, and socioeconomic status, Marc Boutin of the National Health Council discussed the importance of developing an evidence base that takes into account the unique needs of each patient to deliver and ensure the "right" health care for each person. When used in a strong provider-patient relationship, EBM can help to close the quality chasm in patient care as well as target resources to where they are most effective. However, current efforts to increase the use of evidence in health care have not yet delivered on the promise of EBM. Patients with chronic conditions, for example, require ongoing treatment to maintain their quality of life and enable them to remain productive members of society. Often however, treatments for Medicaid patients with asthma, epilepsy, and depression have been denied based on the "evidence." This may save money for the payer at the time, but it often later results in costly emergency room visits and hospitalizations, in addition to physical or emotional suffering for the patient and financial loss.

If EBM is to be taken up broadly and implemented systematically, its benefits must be better communicated to patients—many of whom assume that the care they are receiving is evidence-based. EBM must also be structured with the realization that what works for 80 percent of patients may actually cause harm to, or be inappropriate for, the other 20 percent. In other words, as public health decision models and epidemiology are incorporated into practice, individual patient data in the hands of an individual health professional should be given *equal* standing to aggregated public health data. More incentives are needed for providers to promote health, wellness, and prevention, and above all, the patient-provider relationship should be protected to ensure that the physician's experience and patient preferences are considered along with the best evidence.

The Promise of Information Technology (Chapter 5)

Although the widespread use of the Internet brings information to the fingertips of healthcare providers and patients, providers often have just a

few minutes to choose which data are most relevant, evaluate the quality of the information, and find ways to incorporate it into clinical practice. Also, while more information is empowering consumers to become full partners in their healthcare decisions, they must find a way to keep track of this information and decide how it will be useful to them.

Information Technology Tools to Support Best Practices of Healthcare Providers

Robert Hayward, associate professor of the Departments of Medicine and Public Health Sciences and director of the Centre for Health Evidence (CHE) at the University of Alberta, noted that in the messy informational environment of front-line care, the availability of evidence alone will not lead to improved health. IT will become an increasingly important vehicle for linking evidence to improved outcomes by providing information that is supported with convenience and capacities for discrimination and integration. Examples of IT that serve these needs of clinicians are described.

Key characteristics of a convenient decision support environment are outlined by the "Rule of Fives": it must be "responsive," with evidence sources immediately accessible and available for searching within five seconds; "proximate" to practitioners on the front lines and ready to be searched within no more than five mouse clicks; "guessable"—taking no more than five minutes for sufficient orientation; "comprehensive"—serving at least five distinct information needs (e.g., communication, collaboration, evidence access, decision support, documentation, news); and "rewarding" in that users experience five practice-changing rewards per week of system use. In addition to external evidence, convenience also requires access to "internal evidence" derived from organizational data repositories and relevant to specific organizational patient populations and settings.

Evidence discrimination requires functions to support recognizing, gathering, and reflecting upon internal and personal evidence. For example, the Nemours Foundation, which provides pediatric care in multiple states, is supplying information environments specialized to individual practitioners, such as emergency room physicians, surgeons, or nurses. These environments provide at least five evidence services: evidence selection, evidence synthesis, evidence in context, evidence management, and evidence literacy training. Collaborative evidence management tools led to the emergence of "communities of inquiry" in clinician groups and changes in the organization that over time increased capacity for use of the best external evidence.

Finally CHE has developed integration systems that monitor evidence behaviors in practice. The systems analyze patterns of information use in practice to provide feedback on the quality of the information environment,

use of internal and external evidence, level of information seeking and reflection, and support for organizational change.

Collectively these tools provide an information culture that rewards explicit approaches to uncertainty and the use of just-in-time knowledge by making it easier for decision makers to find, collaborate around, and use information.

Information Technology Tools that Inform and Empower Patients

The past two decades have seen an explosion of data and information relevant to medical care, which is projected to grow by a factor of thousands in the coming years. Yet the information will not be useful unless it is accessible to the right people at the right time (Figure S-4). Peter M. Neupert of Microsoft's Health Solutions Group suggests that consumers are taking a more active role in navigating the health system out of necessity, and that these engaged consumers will increasingly become disruptive agents of change in the health ecosystem—demanding better and more integrated information as well as tools to support their healthcare decisions. The availability, portability, sharing, and use of health information will be key to achieving this transformation.

This shift in responsibility is inevitable because the consumer cares more about health outcomes than other stakeholders in the system. With

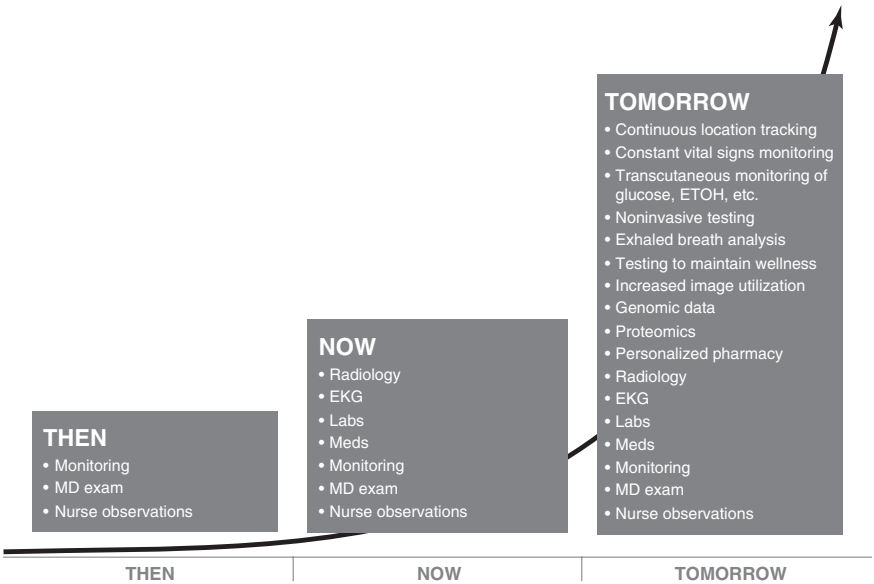

FIGURE S-4 Data advances in medicine.
SOURCE: Peter M. Neupert, 2007.

consumers driving change, competition for healthcare dollars of individuals will likely result in a system oriented around quality, transparency, and accountability. In short, EBM will no longer be purely a clinical term as consumers increasingly recognize the importance of evidence to guide decisions about health care. To facilitate this change, public and private sectors should work to support consumers with best evidence and information management tools, as well as to reverse the fragmentation of the healthcare system and health data.

Microsoft recognized that a truly consumer-focused healthcare information system would also need a private and secure data storage and sharing platform enabling the exchange of data between thousands of health applications and devices. Along these lines, the company released in beta HealthVault™, a free Web-based platform designed to put people in control of their health data. It helps them collect, store, and share health information with family members and participating healthcare providers, and it provides people with a choice of third-party applications, services, and devices to help them manage things such as fitness, diet, and health. HealthVault also provides a privacy- and security-enhanced foundation on which a broad ecosystem of players—from medical providers and health and wellness device manufactures to health associations—can build innovative new health and wellness management solutions to help put people in control of their and their family's health.

Collectively these tools are an important step toward achieving the vision of a patient-centered healthcare system.

Transforming the Speed and Reliability of New Evidence (Chapter 6)

Keeping pace with scientific advances and medical innovations will require an evidence base that adapts and builds over time to provide information that is timely and up-to-date. A reliance on clinical trials is impractical due to limitations such as cost, amount of time to complete studies, and inability to generalize results to broader populations. Moreover, RCTs cannot answer many important questions about medical interventions and care delivery. EMRs and clinical registries offer the opportunity to capture important data and information at the point of care and speed the generation of evidence to inform clinical practice. New tools such as biomarkers, modeling, adaptive trial designs, and patient enrichment approaches are helping to accelerate the development and evaluation of tailored therapies.

EMRs and the Prospect of Real-Time Evidence Development

George Halvorson, CEO of Kaiser Permanente, discussed the potential of EMRs, if well designed and adequately compiled and supported, to revolutionize medical research. Advantages include instant access to a wealth of

data; provision of comprehensive and longitudinal data that can span decades; access to massive data sets from millions of patients rather than the narrower populations of traditional studies; and greater flexibility in data utilization. These data could be used to support highly structured clinical trials, track progress and care results in the post-market environment well into the future, and analyze population health data in new ways.

Electronic data will allow researchers to search for unforeseen correlations in ways that were previously impossible. For instance, files could be searched to determine if there is a relationship between specific patient populations and various diseases and comorbidities. Caregivers can gain up-to-the-minute information on which treatments are working for which patients with just-in-time learning and searches within EHRs. In the future, providers could even examine genetic correlations.

Some examples of important research facilitated by EMRs at Kaiser Permanente include the recognition of adverse effects of Vioxx in certain patients and the identification of adverse reactions in patients a number of years after treatment with heart stents. Medical records provide great potential in terms of follow-up studies and longitudinal data. As more organizations utilize EHRs for research, they should be careful to design records with research goals in mind. For example, careful consideration is needed to ensure that EHRs facilitate outcome analyses, support clinical trials, have data approaches that incorporate genetic information, and contain data sets that can be sorted by relevant demographics such as race, ethnicity, gender, or economic status.

Five medical conditions drive more than half of healthcare costs in the United States (mood disorders [depressive and manic depressive disorders], diabetes, heart disease, hypertension, and asthma) (Druss et al., 2001) and present the opportunity to dramatically improve care, as well as reduce costs. Payment models, delivery structure, data reporting, community priorities, and education should all be aligned toward the generation and application of evidence on how these five diseases are best treated. Building the right electronic data sets, which enable these types of analyses, will transform medical research into a direct tool of medical reform.

Research Methods to Speed the Development of Better Evidence—The Registries Example

Eric D. Peterson, professor of medicine at the Duke Clinical Research Institute, outlined how clinical registries provide infrastructure and resources that help to address current shortfalls in the cycle of evidence development and adoption. Clinical trials tend to involve younger, healthy patients, treated in ideal conditions, and to measure short-term treatment efficacy. Yet the full measure of an intervention's safety and effectiveness

can be determined only when it reaches the real-world market of patients and caregivers. Registry data are collected at the point of care and offer the opportunity not only to augment existing evidence development but to accelerate evidence adoption in practice.

Clinical registries are clinician-organized networks for collecting detailed patient information for a given population, often defined by a particular disease or treatment. Ideally, registries would accurately capture detailed clinical information at key points and events in a patient's life. These data would also be linkable with other data sources and enable the user to construct a long-term record of a patient's care and health outcomes. In addition, the registry could be accessible to health services and discovery researchers, as well as to clinicians.

The majority of these features exist or are being planned by the major cardiovascular provider-led registries, such as the Society of Thoracic Surgeons' National Cardiac Database, the American College of Cardiology's National Cardiac Data Registries, and the American Heart Association's programs. The size and scope of these programs are substantial, and although participation is voluntary, a growing number of external forces are providing strong incentives for their engagement. For example, a large healthcare insurer encourages registry involvement as a condition for obtaining "Premium Provider Status," and some states are requiring participation as part of state-based programs. In addition, more registries are being launched or planned for carotid stenting and acute coronary syndromes, congenital heart disease, and cardiovascular imaging.

As registries enter the electronic age, progress in several areas—such as standardization of data elements; clarification of patient privacy rules; development of new data harvesting tools; connection of longitudinal databases; and growing collaboration among professional societies, insurers, and government regulators—is allowing for more integrated and cross-purpose clinical registries.

The data and infrastructure provided by clinical registries can aid evidence generation in several ways—for example, providing data for national epidemiological and health services research. The Surveillance, Epidemiology, and End Results Program of the National Cancer Institute provides information on cancer incidence and survival in the United States, and cardiovascular registries have been used to determine national variability in disease treatment, disparities in care among patient subgroups, and trends in treatments over time.

Data can also be used to provide larger patient samples for genomic research, such as genome-wide association studies that attempt to link a given genetic variation to a disease state, offering incredible potential to better predict patients' susceptibility to the disease and their response to treatments. Clinical registries offer opportunities to have detailed pheno-

typic and longitudinal outcomes for a very large cohort of patients. These longitudinal data are also useful for post-market surveillance studies that track long-term outcomes of therapies used in diverse patient populations and under different clinical conditions and settings.

Registries could improve efficiency in the design and conduct of RCTs, and practical clinical trials might eventually be embedded within clinical registries. In situations where randomized treatment comparisons are not possible, observational comparative effectiveness studies using registries provide another source for evidence development.

Finally, as a tool for quality assessment and improvement, registries can also ensure that evidence is fully and appropriately translated into clinical practice. Historically, registries have been useful in uncovering issues of overuse, underuse, and misuse of proven therapies in clinical practice. This information can provide specific guidance on what is not working and how to fix it and, ultimately, help practitioners deliver better care.

Even with all of their advantages for evidence generation and application, participation is often voluntary and resources for clinical registries are shrinking in light of demands from government and insurers for alternative performance assessment data. Physicians also worry that clinical information might be used against them in a malpractice lawsuit. Clinicians need to make a strong case that registries are best run and most valuable when they remain in the hands of clinicians.

Product Innovation—The Tailored Therapies Example

Steven M. Paul, president of Lilly Research Laboratories, discussed how the dual challenges of rising costs and realizing the potential of biomedical research have been reflected in the recent experience of biopharmaceutical companies. Stakeholders are demanding more information on the effectiveness of therapies, as well as more predictable and demonstrable health outcomes. Despite these heightened expectations, there is an efficacy and safety gap for today's drugs. Paul noted that only about 50 percent of patients respond to any given therapy, and many of these do not respond in the same way. This increased focus on outcomes has put a burden on biopharmaceutical research development in terms of both longer development timelines and overall costs.

To contend with this changing environment, biopharmaceutical companies are exploring the concept of tailored drug therapies: the right drug, for the right patient, at the right dose and the right time. For years, medicines have been tailored using biomarkers such as blood pressure, LDL (low-density lipoprotein) cholesterol levels, and hemoglobin A_{1c}, but new tools for discovery and development are accelerating movement toward personalized medicine. Tools such as imaging modalities are increasingly

becoming more sophisticated in certain areas of drug therapies. However, the root causes and factors contributing to the progression of disease are often very complex and the routine development of more personalized drugs is a distant prospect.

Tailored therapies represent a paradigm shift for drug development away from traditional approaches such as phased clinical trials to what is termed "value-based" drug development, which identifies the subpopulations of patients that would most benefit. This allows drug companies to stratify clinical development by identifying which agents should move to phase II or phase III clinical trials, and also assists in terms of marketing drugs. This shift may provide an important advantage given the current regulatory and market pressures on drug development. According to Paul, drug patents are shorter than they were previously—ranging from about 10 to 12 years today, as opposed to a previous life span of 17 to 20 years, making it difficult for drug companies to get new drugs to the market before patents expire. With increased pricing pressures along with regulatory requirements, there is a paucity of new medicines from big pharmaceutical and biotech companies.

The ability to stratify drug development using biomarkers and the tailoring approach offers potential for reducing costs and approval times. Many companies also have tied their drug development efforts to an accompanying biomarker strategy to accelerate the identification of safety and efficacy issues. However, such stratification poses financial challenges for pharmaceutical companies. Based on the investment necessary for developing a drug, if only a small subset of patients benefit, companies might have a difficult time generating returns. However, this is often offset by a higher value proposition, longer days/duration of therapy, and better reimbursement. The big challenge for drug companies in the coming decades will be to develop drugs that can be tailored to patients, while balancing the formidable risks and costs of drug development.

Policy Changes to Improve the Value We Need from Health Care (Chapter 7)

Many of the most important advances needed to bring more evidence into the healthcare system will face political hurdles. Proposals such as establishing universal EHRs, determining how to measure the quality of care services, and revamping the payment system will require political and legislative muscle and continuing oversight. Therefore, making a strong case to policy makers and the public for the importance of supporting the development and application of evidence in health care is crucial for facilitating positive change. Two presentations advanced some key considerations and opportunities for progress.

Regulatory and Healthcare Financing Reforms

Donna E. Shalala, president of the University of Miami and former U.S. Secretary of Health and Human Services, raised several important points for healthcare leaders to consider as they incorporate EBM in healthcare reforms. First, there is a suspicion among healthcare professionals that EBM is primarily about cost-cutting. Attention is needed to how these efforts are framed, and a primary lesson from the 1990s underscores the fact that the power of words must be recognized. Second, the political system powerfully affects the quality and delivery of health care. Often, large, single-payer systems of care are viewed as the key to improve evidence-driven transformation of care. However even within single-payer or large-purchaser systems such as the Department of Veterans Affairs and Medicare, and even where the evidence base is strong, implementing change has been challenging. Therefore, the expectation that Medicare or Medicaid can lead efforts to reform healthcare delivery through introducing more evidence should be questioned. Despite a strong evidence base for many proposals, each step toward implementing change affects a constituency and the members of Congress supported by those constituencies.

In looking at successful public health efforts to apply evidence to healthcare policy, such as the efforts of the U.S. Department of Health and Human Services to increase childhood immunizations in the 1990s, three conditions are important for change: a very specific goal, consensus on the problem, and a public-private partnership on how to provide the solution. However, unlike the politically uncontroversial initiative for childhood immunization, clear answers on how to bring about change do not exist for many current problems in health care. Although all healthcare professionals want the best care for their patients, the structure of the healthcare system, payment methods, and expectations of patients for an evidence-based system can lead to many complications.

Complicating these issues is the fragmentation of the healthcare system and research institutions. Centralization of these efforts has been suggested by some but healthcare leaders and the public need to consider whether a central research agency will be able to withstand political fallout for unpopular evidence. The experience of the Agency for Healthcare Research and Quality's predecessor, the Agency for Healthcare Policy and Research, suggests that establishing a base of support for research is important, but political protection is also necessary for those who conduct and translate potentially unpopular research findings.

Healthcare leaders must also consider whether there is enough political will and pressure to make big changes in health care. To make grand social policy changes, there must be consensus on both the problem and the solution, as there was when Social Security was enacted and in the development

of Medicare and Medicaid. Although there is interest by presidential candidates to move toward an evidence-based system of health care, making this a reality will require healthcare professionals to make a strong case as shrewdly as possible.

Defining and Introducing Value in Health Care

Michael E. Porter, Bishop William Lawrence University Professor at the Harvard Business School, argued that for any meaningful reform to occur, the healthcare system must organize care and delivery around the value it provides patients, as measured by patient health outcomes per dollar spent. Much of the confusion around improving health care comes from different definitions of value for the various actors in the system (e.g., healthcare providers, insurers, device manufacturers, patients) working at cross-purposes toward undefined goals. Organizing reform efforts around improving value will unite the interests of all parties and is fundamental to achieving many other goals, such as equity in health care and cost containment.

Outcomes and costs should be measured separately and compared to determine value. This is especially important in health care because one of the most powerful ways to contain costs is to improve outcomes, such as through early detection or less invasive treatment. Treating cost containment itself as a goal, instead of a patient value, has been a major stumbling block to improving the value of health care.

Value in health care is largely unmeasured in the United States. Measuring value depends on properly measuring health outcomes and then comparing the total costs in achieving them. Currently, there is much confusion about measuring processes instead of outcomes. Measuring structural factors such as adherence to best practices, protocols, or guidelines is an imperfect indicator of health outcomes, although studies have shown that deviation from them can lead to poor outcomes. Guidelines are often incomplete and fail to adapt care to individual patient circumstances. In addition, process guidelines can slow innovation because they often need to be refined as new evidence becomes available. Similarly, focusing solely on health indicators as outcomes provides an incomplete picture. Indicators such as hemoglobin A_{1c} levels used as a marker of blood sugar control in diabetes care should be closely correlated with acute episodes and complications. They are predictors of results, not results themselves.

Patient value is found in the integrated care of a patient's medical condition rather than care from a single specialist or discrete intervention. Care for a medical condition such as breast cancer, diabetes, asthma, or congestive heart failure usually requires multiple specialists. Value for the patient is created by the combined efforts to care for that medical condition and any other comorbidities patients may have. Therefore, the value of

health care is often revealed only over an extended period of time, through measuring long-term outcomes such as sustainability of recovery, the need for more interventions, or the occurrence of treatment-induced illnesses. Yet because health care is often fragmented by facility or specialty, outcomes and processes tend to be mismeasured. Providers tend to measure only their own interventions or services, even if this is not what determines overall value. Gathering long-term longitudinal data on outcomes is challenging, and even more so because of current organizational processes and practices. These same obstacles also hinder accurate measurements of costs.

For every medical condition, multiple outcomes collectively define patient value. Measuring the entire hierarchy of outcomes will be essential to improving value. Doing so will enable progress to be made at different rates and different levels of care. As survival rates get very high, for example, research could be focused on the speed of treatment or reducing discomfort. Advancements in medical science have led to the development of therapies to address a great majority of medical conditions in some way—including organ transplantation, new cancer therapies, and joint replacement. Today, there is the opportunity not only to develop new therapies but to improve and reduce the cost of existing therapies.

To determine value, the full costs of care must be measured. Like outcomes, costs should be measured for medical conditions over the cycle of care. Providers and health plans need to work together to measure the cumulative costs by activity for each individual patient over time. Health plans will play an important role in measuring costs, and the focus of reimbursement for health care should shift to bundled models for medical conditions. Health plans, providers, employers, and government policy can all contribute to making measurement of value in health care a reality. If all of the parties in health care could truly measure and embrace value as the central goal, opportunities for improvements in healthcare delivery would be almost limitless.

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1

The Changing Nature of Health Care

INTRODUCTION

The 20th century witnessed many truly revolutionary advances in health care. Research into the causes of infectious diseases and the development of vaccines and pharmaceuticals quelled once-devastating illnesses such as polio and smallpox. The first successful organ transplant occurred in 1954, and now, thousands of transplants each year—more than 28,000 in 2007—are prolonging the lives of recipients (UNOS, 2008). Over the past decade alone, better understanding of the mechanisms that cause disease has improved the ability to prevent, diagnose, and treat common afflictions such as diabetes and heart disease. The innovation underlying such progress continues to advance and accelerate change, while many new technologies and medical interventions provide new options for care and treatment. Between 1991 and 2003, for example, the number of medical device patents per year doubled (AdvaMed, 2004), and the biotechnology patents tripled over roughly the same time (BIO, 2006). Increasingly, discoveries in the biological sciences are being applied toward the development of medicines and treatments targeted to refined subsets of patients to better address genetic or life circumstances.

Recent advances in research, however, are not producing commensurate improvements in the quality of the health care received. In a 2005 survey about perceptions of health care, 60 percent of Americans said they did not believe that the United States had the best healthcare system in the world, and 41 percent said they knew of a time when they or a family member had received the wrong care (Research!America, 2005). These perceptions are

borne out by recent reports and analyses and were highlighted in several IOM Annual Meeting presentations summarized in this publication. For example, despite spending more on health care than other industrialized nations, the United States lags significantly in basic measures of quality such as overall life expectancy at birth and infant mortality (Anderson, 1997; Mathers et al., 2001; OECD health data, 2006). Additional reports characterize a healthcare system that is highly fragmented and prone to errors (IOM, 2000, 2001). Unnecessary spending, duplication of efforts, and widespread disparities in spending and health outcomes across geographic areas are also common features of health care (IOM, 2007b). Underlying many of these shortfalls is a system struggling to contend with the changing nature of health care—from shifting patient demographics and disease burden to the increased complexity of therapy and treatment options and factors to consider as part of clinical decision making.

Systems of care, historically devoted to the prevention and treatment of infectious diseases and discrete episodes of acute care, are now increasingly occupied with the management of chronic health conditions such as heart disease, diabetes, and asthma. In fact, half of those reporting a chronic illness suffer from more than one (Wu and Green, 2000). Chronic illnesses make up the leading cause of illness, disability, and death in the United States, and also account for 78 percent of U.S. health expenditures (AHRQ, 1998). In contrast to acute care, chronic care processes often require sustained coordination across multiple specialists and facilities, a characteristic that is currently testing the limits of an often-fragmented healthcare system.

Key system components are also under increased pressure. For example, as noted in Session 2 of the meeting, the traditional "physician-as-expert" model of care relies on a physician's extensive knowledge, experience, and memory to guide care. However, clinical encounters often require providers to manage a significant number of variables and factors for any one medical decision (IOM, 2007a). The number of journal articles, technology assessments, and practice guidelines that any provider must read to stay current is now well beyond human capacity and the rapid evolution of care practices and availability of many therapeutic alternatives compound this already overwhelming body of information available to guide clinical decision making. Despite the quantity of information available, there are also substantial shortfalls with respect to the quality of information available to guide decision making. Evidence is often not available or not presented in a form useful to practitioners at the point of care delivery. Often, when evidence is available, it has little relevance to the questions and patients faced by healthcare professionals in clinical practice. For example, clinical trials of intervention efficacy are of limited generalizability—often excluding older populations or patients with multiple comorbidities, lim-

ited to assessing short-term outcomes, or conducted under circumstances that minimize factors that might decrease an intervention's effectiveness in practice. Also, as emphasized in several presentations, very little evidence exists on the comparative effectiveness of one course of treatment versus another. While 5 percent of the overall healthcare expenditure is devoted to research, the majority of that is spent on basic research or product development (Research!America, 2006). It is estimated that, currently, less than 0.1 percent of the nation's $2 trillion health expenditures is invested in assessing the comparative effectiveness of available interventions (AcademyHealth, 2005; Moses et al., 2005).

In today's complex clinical environment, contending with the challenges and realizing the yet untapped potential of technological and biomedical research innovations will require a sharper focus on the evidence as a way to drive improvements in the effectiveness and efficiency of the healthcare system. To orient our existing expertise and emerging resources towards improved development and application of evidence in health care, a broad view of the changing nature of health care and implications for capacity and necessary cultural change is needed. The challenges to creating an evidence-driven healthcare system are great, but so, too, is the potential reward: affordable health care, based on evidence of what works that improves health outcomes for individual patients. Leadership is needed from the healthcare professions to reach consensus on the problems and solutions and to facilitate the necessary change. This was the focus of the 2007 Institute of Medicine (IOM) Annual Meeting.

EVIDENCE-BASED MEDICINE AND THE IOM

Since its establishment in 1970 by the National Academy of Sciences, the IOM has been committed to advancing the quality of health care in the United States and has undertaken many important studies on the topic. Perhaps the most widely known are a series of reports by the Committee on the Quality of Health Care in America. The first of these reports, *To Err Is Human,* estimated that as many as 98,000 patients die in any given year from medical errors that occur in hospitals and established ensuring patient safety a critical first step in improving quality of health care. A year later, a follow-on report, *Crossing the Quality Chasm*, focused on the delivery system as a whole and issued a call to action to improve system performance in the six dimensions of quality—to ensure safe, effective, patient-centered, timely, efficient, and equitable care.

Expanding the evidence base to support quality medical care for each patient poses an ongoing challenge to healthcare improvement, and to contend with this issue, in 2006, the IOM convened the Roundtable on Evidence-Based Medicine. Over the last 2 years, the Roundtable has ex-

plored, through its series of meetings and workshops on the learning healthcare system, the key opportunities and challenges to establishing evidence as the linchpin of the healthcare enterprise. Collectively, the Roundtable seeks the development of a healthcare system that is designed to generate and apply the best evidence for the collaborative healthcare choices of each patient and provider; to drive the process of discovery as a natural outgrowth of patient care; and to ensure innovation, quality, safety, and value in health care. Roundtable activities focus on accelerating the development of a learning healthcare system; expanding the capacity to generate evidence on medical care that is the most effective and produces the greatest value; and improving public understanding of the nature, importance, and dynamic character of medical evidence.

The IOM convenes annual meetings dedicated to the examination of topical and critical issues in health care and health policy. With healthcare system reform at the top of the nation's domestic agenda, the IOM Council's selection of evidence-based medicine (EBM) as the subject for its 2007 annual meeting underscores its centrality and importance to fundamental improvements in the nation's health and health care. The meeting was structured to provide an overview of some of the key issues and challenges as well as to present some of the primary opportunities for progress that have emerged from the work of the Roundtable.

The chapters in this publication provide important perspectives on the changing nature of health care: from the forces driving the need for better medical evidence and the many new challenges confronting patients and providers to opportunities to transform the speed and reliability of new medical evidence and enable an evidence-based healthcare system. To provide context for these discussions, comments were provided by the meeting co-chairs Mark B. McClellan and Elizabeth G. Nabel and by session moderators Denis A. Cortese, Michael M. E. Johns, John W. Rowe, and John K. Iglehart. A summary of these perspectives follows.

Challenges and Opportunities

Mark B. McClellan, M.D., Ph.D., Brookings Institution

Two core challenges are facing health care and health policy in the 21st century. Healthcare costs are rising and not sustainable, and a tremendous, largely untapped potential exists for much better health through better, more targeted treatments. In principle, better evidence will result in higher confidence about what works for every patient in the healthcare system. This is a precondition to achieving what health care should be about in the 21st century—care that is based on solid evidence about what will work in particular patients.

With the advent of electronic medical records (EMRs), clinical data registries, and other new forms of electronic data, care is becoming rich with information that can reveal patterns of disease mechanisms and markers of risks and benefits. These data also hold promise for instilling a greater confidence in health care than currently exists for a system that offers widely varying medical practices, with possible consequences for outcomes and definite consequences for costs. In addition, even treatments effective for some may not be beneficial for others and may carry significant risks. With the cost of health care rising along with its benefits, creating an evidence-based system will be critical to achieving the promise of personalized medicine in which treatments are more effectively targeted to those that benefit, an achievement well worth its cost.

Although there has been progress toward this goal, attaining such a system remains a distant prospect. Better disease models and evidence relevant to the treatment of individual patients is lacking, despite publications and news stories that seem to suggest otherwise. Also, much of the current data are not from traditional randomized controlled trials (RCTs), creating a dilemma about the relevance of EBM in clinical practice. Some practitioners believe that if evidence is developed using traditional RCTs, it may not be reflective of the complexities of populations and the delivery settings in real-world practice. For example, even if different practice methods appear to have a similar effect in an overall population, this may not be the case for different subgroups or different types of patients within that population.

The key elements that should inform strategies for change are contained within these pages. As Michael E. Porter notes in Chapter 7, while simple steps such as price controls or restrictions on access to control costs might seem useful on the surface, they have failed in the past. Instead, a new vision is needed, marked by effective evidence and targeted treatments that account for the diverse characteristics—findings, histories, validated biomarkers, and preferences—of the various patient groups in this country. With the complement of secure EMRs, access to these patient and population characteristics will bring relevant evidence to healthcare decision making. This will, in turn, lead to better results and higher value.

Clearly, there will be challenges along the way to gather the evidence necessary for the backbone of this type of healthcare system: data must be consistent; low-cost alternatives to RCTs must be agreed upon; electronic systems should be integrated; and sophisticated longitudinal databases, such as provider-led clinical registries, should be supported.

In addition to studying the discrete interventions of particular drugs or particular modalities in treatments, the performance of healthcare systems themselves should be addressed. The variations in care discussed by Elliott S. Fisher in Chapter 2 must be aligned. Also, costs will increase and value

will be compromised if patients receive care from a number of different providers who do not collaborate effectively. To study these delivery system issues in real-world practices, traditional approaches such as RCTs will not be effective.

Policy challenges must also be addressed. As George C. Halvorson acknowledges in Chapter 6, small shifts in the system will not create fundamental change. Value and outcomes cannot be achieved by micromanaging practices, but rather by providing support for better care at a lower cost. Rewarding better quality and lower costs will give healthcare professionals the opportunity to deliver quality care and still make ends meet. By the first rule of economics, "You get what you pay for," the healthcare support system must be changed to pay for the care we want. This includes changing reimbursements to focus on higher value.

Making these changes will provide an opportunity for patients to become more involved, and not simply through cost sharing. Many opportunities exist for people with chronic diseases to improve their own health, since most care is actually self-care. In our traditional insurance system, these individuals do not always have the opportunity to make choices that can save money. However, recent reforms have begun to allow chronically ill patients in this country to control the services they receive. For example, the tiered benefits in Medicare allow beneficiaries to save money by switching to generic drugs—one of the main reasons that Part D in Medicare is less expensive than projected. There are a number of programs being implemented around this concept of shared savings, in which healthcare professionals working together reap savings when they document better outcomes at a lower cost. However those savings are accomplished—through system redesign, information technology (IT), or remote monitoring systems—they are a step toward a bundled reimbursement approach that focuses on the effective outcomes in our healthcare system while promoting better care for everyone in it.

Clearly, the technical and policy challenges of fulfilling the vision of EBM are great. In spite of these challenges, the promise of EBM has put it at the forefront of policy making. The Food and Drug Administration is working to implement major new reforms, including plans for a public-private partnership to support a post-marketing surveillance system to gather data on drug risks and benefits. Also, Congress is considering proposals for a major initiative to support the generation of comparative effectiveness information about healthcare interventions. In addition to work by the federal government, the practice of EBM will require numerous public- and private-sector strategies and collaborations. Needed are new approaches to the evaluation and adoption of medical best practices, new methods for drawing appropriate conclusions from vastly expanded data resources, and new approaches for using evidence to improve care and

reduce health costs. The process will not be easy, but unlike previous times, there are now widespread calls from healthcare leaders for the reforms needed to develop a system that delivers efficient and effective care. The IOM has the opportunity to catalyze that change.

Elizabeth G. Nabel, M.D., National Heart, Lung, and Blood Institute

Healthcare reform will be one of the top domestic issues of the political agenda in the next presidential election, making our focus on EBM and the changing nature of health care very timely. The roles and responsibilities of all healthcare stakeholders are undergoing transformative change and—whether we approach reform as providers, payers, researchers, health product developers, or consumers—there is much to learn from all who are involved in these collaborative discussions about how to contend with the rapid changes in the healthcare system.

Healthcare providers, whether involved in delivering or reimbursing care, face a unique set of challenges as care is increasingly informed by and organized around rapidly evolving evidence. Developing better approaches to reimbursement and other mechanisms that support the delivery of quality care are at the forefront for all providers, and many pilot projects are already under way. A key consideration, as illustrated throughout this report, is the strong influence of local cultures on practice patterns. They can prevent the infiltration of evidence-based decision making, but they can also lead to great innovation to support the application and development of evidence. The papers by William W. Stead and George C. Halvorson in Chapters 4 and 6 discuss lessons learned from their efforts to harness electronic health record (EHR) systems for improved application of evidence in practice and improved capacity for research and discovery, respectively. However, these local solutions may need restructuring to succeed at a national level. There has been considerable advocacy for sharing best practices nationwide, but it may be necessary to set goals and work backwards to align the systems.

For consumers, access to care is a priority but an additional, emerging challenge will be to ensure that incentives for research and care are properly aligned to support care focused on individual patient needs, circumstances, and preferences. The very nature of patient-physician relationships is also undergoing a rapid change as healthcare data are increasingly captured and made available in various forms through IT. Patients will be presented with more health information from a variety of sources and, increasingly, they will be pivotal in making decisions about their own health care. As we are reminded by Peter M. Neupert in Chapter 5, most of health care is self-care and much of the care delivered throughout this country is family-based. Family health managers and the availability of secure personal health

records will be critical to informing and providing increasingly individualized patient care.

EBM will also impact researchers. Methodologies to generate evidence are evolving and need to be continually defined and adapted. EHRs will provide the opportunity to quickly gather large amounts of data from real-world practice and produce evidence in real time, but how these data can be used appropriately and effectively will be a major challenge for researchers and practitioners. Clearly, developing evidence that draws from and informs real-world care practices is a science, and improved methods for modeling and analyzing work processes and decision management are needed. This may require restructuring of the way we fund research.

Federal agencies, such as the National Institutes of Health, the Food and Drug Administration, the Centers for Medicare and Medicaid Services, the Agency for Healthcare Research and Quality, the Department of Defense, the Veterans Health Administration, the Centers for Disease Control and Prevention, and others, will be essential components of this dialogue and can demonstrate leadership by partnering across agencies, as well as with others in the private sector. Healthcare product developers in particular will be absolutely critical to the success of EBM, and collaborations that take advantage of this sector's talent and expertise can be facilitated and encouraged through public-private partnerships. There is no doubt that the work to transform our healthcare system will be challenging. Many healthcare leaders have been working on improving the system for decades; but we all need to get on with finding a solution now.

The Need for Better Medical Evidence

Denis A. Cortese, M.D., Mayo Clinic

In the United States the cost of health insurance is rising faster than wages at a rate that is not sustainable, but the quality of care—measured in outcomes, safety, and service—is much lower than it should be. Especially in comparison to other countries, the value of medical care in the United States is low but even among individual states of the United States the variability in the value of health care delivered is dramatic. Only 10 percent of the states provide high-value care on average, and the value of care in the United States on a whole is well below what should be expected. Given the current approach to health care, however, these shortfalls are not surprising. Across the healthcare system, competition and rewards are not based on value, and there are scant incentives for patients to seek—or for professionals to provide—high-quality, cost-effective health care.

In reality there is no true healthcare system. There never has been a conscientious attempt to design and maintain a system that would create

value. We now have an opportunity to take the steps to develop a vision, create a strategy, and specify goals for a true system of health care in the United States. Yet what should a healthcare system do? Some important elements would include enabling the assessment of an individual's risk for developing an illness; rewarding the prevention of the onset of illness; making accurate, precise, and timely diagnoses; tailoring specific treatments to individual needs; and controlling chronic illness. In sum, a healthcare system should improve the quality of life and aim to keep people as well as possible, while ensuring that healthcare expenditures are affordable for both individuals and the nation. In essence, a reformed healthcare system should provide individuals with high-value health and health care.

The overarching vision of a learning healthcare system conceived by the IOM's Roundtable on Evidence-Based Medicine begins to describe the healthcare system needed to truly support value and improve health. Such a system would be "designed to generate and apply the best evidence for the collaborative choices of each person and provider; to drive the process of discovery as a natural outgrowth of patient care; and to ensure innovation, quality, safety, and value in health care." Essential to informing this vision is an understanding of some of the key forces driving the need for better evidence. As outlined in Chapters 2 and 3, these forces include rising and unsustainable costs, wide variations in the quality and cost of health care delivered across the United States, and the complexity of care introduced by the emerging insights from genetic research and the diversity of new health products.

Contending with the Changes

Michael M. E. Johns, M.D., Emory University

Many of the issues discussed throughout this publication are important for moving forward with needed healthcare system reform, but my focus is on key considerations for providers and, to some degree, patients. Most pressing in this respect is an improved understanding of what constitutes good evidence of effective care and outcomes. For a profession that adopted the scientific method about a century ago, there is alarmingly little evidence for the effectiveness of much of what is taught and practiced today.

To get to an evidence-based, value-driven health system we have to align all of our professional educational programs to teach new systems and capabilities. Introduction to key concepts in EBM should begin, at the very least, at the college level. In addition, the dissemination and incorporation of new knowledge into practice must be accelerated so that it does not require a decade or more for the average provider to adopt new knowledge and skills. As more and better evidence is developed, effective processes

and IT systems are needed to ensure that healthcare practice utilizes best evidence. These systems should also have feedback loops to continuously improve on the evidence. Systems must be interoperable and scalable and must also incorporate the patient into the decision-making and care provision processes. To be effective, systems must include the proper rewards, incentives, and financing for providers, as well as the means to pay for required processes and IT systems and innovations.

The general public will need education and support to be able to use the copious medical information becoming available, as well as to gain an appreciation for information that is backed by solid evidence. Practitioners need to work with the public to help ensure that we find the right healthcare solutions for individual patients. The complexity of clinical evidence is daunting even for experienced, trained professionals who diagnose and treat disease; but it is far more challenging to the non-expert. Reducing this complexity is key to empowering patients—not only as better informed consumers of health care, but also as active partners in improving health outcomes. In addition, the right kinds of professional support should be made available to patients, whether through health coaches or other sorts of new professionals who can support and educate patients on the best evidence-based processes for health care and healing.

It is clear that we are still at a rudimentary level of conceptualization and implementation of an evidence-based, value-driven healthcare system and that we still have a long way to go. Finding ways in which patients and providers can be *proactive* in catalyzing and implementing the needed changes is essential.

The Promise of New Evidence

John W. Rowe, M.D., Mailman School of Public Health, Columbia University

A learning healthcare system is defined as one in which the usual and customary activities associated with the production, distribution, utilization, and financing of healthcare services result in the simultaneous development and capture of data that are essential to the monitoring and evaluation of health care delivered. A wide variety of information is contained in these data including, but not necessarily limited to, patient characteristics (e.g., genetics, race, ethnicity, socioeconomic status, behaviors, clinical conditions, functional status), environment, biologically targeted interventions, providers, outcomes, and costs; and opportunities are emerging to take better advantage of these data to guide care. Through efficient organization and analysis, and provision of findings at the point of care, these data are a rich resource for informed decision making.

Two general categories of decisions require an expanded evidence base. The first category includes the use of drugs, devices, and procedures. The second category concerns the management of care itself, including the organization of care, IT, types and effectiveness of providers, and clinical pathways. Both categories require not only effectiveness information but also comparative effectiveness information, including cost or value. As emphasized in Chapter 2, attention is needed on the evaluation of drugs, devices, and procedures, as well as on systems of care and the healthcare professionals that are involved in the provision of the care.

One of the major strategies proposed to hasten development of the required evidence base includes migration away from traditional reliance on RCTs and inclusion of a variety of other approaches and data sources. These include cluster analyses, registries with or without "coverage with evidence development" financing, and other innovative approaches. While such efforts may indeed supplement RCTs and accelerate the development of the needed evidence, there are concerns among many that such approaches do not have the reliability of the "gold standard" RCT, and that the time saved may not be worth the price paid in quality and reliability of the evidence. Is the question really black and white, or are there strategies to enhance the types of data being used to build the evidence while at the same time hedging against the pitfalls of lower quality and less reliability? The papers featured in Chapter 6 offer insights on the opportunities presented by EHRs and clinical registries, as well as some of the challenges of using these data to inform the development of effective healthcare interventions.

Policies to Improve Value from Health Care

John K. Iglehart, Health Affairs

Public policy has a major role in shaping and driving the development of an improved healthcare system. The following chapters illustrate the potential of EBM to transform health care, and important policy considerations are detailed in Chapter 7. However, it is vital to keep in mind the substantial challenges inherent to the processes of policy making. In short, these processes are badly in need of repair because they have been corrupted by the corrosive impact of election campaign finance monies. Today, many members of Congress are in a permanent state of running their campaigns for reelection. It is not unusual for campaigns to raise millions from the very private interests that seek a return on their investments in the form of public policies that serve their own narrow interests, rather than the public's interest. Presidential politics has become a billion-dollar enterprise, and one has to wonder what kind of impact that sort

of money has on public policy. Is the public being served or sacrificed through this process?

COMMON THEMES FROM THE 2007 IOM ANNUAL MEETING

As suggested by the opening comments, the 2007 IOM Annual Meeting highlighted both the shortfalls of the current system, as well as the tremendous potential for an evidence-driven and value-based health care. The meeting was structured to provide an overview of the key challenges and opportunities for progress and improvement. Session 1 (Chapters 2 and 3) reviewed the need for better medical evidence, characterizing not only the waste and inefficiency endemic to health care and the unsustainable trajectory of healthcare expenditures, but also the challenges presented by medical technologies of increased diversity and complexity and an increasingly sophisticated understanding of genetic contributions to disease. Challenges faced by patients and providers in using evidence to better guide healthcare decisions were reviewed in Session 2 (Chapters 4 and 5). Also considered in these chapters were ways that advances in IT affect opportunities for improved access to health information and decision support. IT will also help transform how evidence is developed. The potential of EHRs, clinical data registries, and new research methods to speed the generation of evidence, as well as drive innovation and the development of tailored therapies were discussed in Session 3 (Chapter 6). The last session of the day was devoted to discussing how policy changes might facilitate better stakeholder alignment on how health care is structured and incentivized to deliver high-value health care.

During the course of the meeting, a number of common themes were identified (Box 1-1).

- *Increasing complexity of health care.* New pharmaceuticals, medical devices, technologies, and predictive data offer much promise for improving health care, but they also introduce high levels of complexity, requiring changes on the parts of both caregivers and their patients.
- *Unjustified discrepancies in care patterns.* The intensity of healthcare services delivered for similar conditions varies significantly across geographic regions, particularly in areas that require discretionary decision making. However, the higher-spending regions often do not deliver better-quality care, hence offering substantial opportunity for reduced spending without sacrificing health outcomes.
- *Importance of better value from health care.* The current healthcare system is not designed to deliver value, and the nation's long-term

BOX 1-1
The Changing Nature of Health Care
Common Themes

- Increasing complexity of health care
- Unjustified discrepancies in care patterns
- Importance of better value from health care
- Uncertainty exposed by the information environment
- Pressing need for evidence development
- Promise of health information technology
- Need for more practice-based research
- Shift to a culture of care that learns
- New model of patient-provider partnership
- Leadership that stems from every quarter

fiscal challenges are serious and are being driven predominately by excessive medical spending, often on interventions of no clinical benefit. Opportunities exist to eliminate wasteful spending with no reduction in health care, as well as to improve the overall health outcomes, but agreement is needed both on what constitutes best care and on what constitutes value in health care.

- *Uncertainty exposed by the information environment.* An irony of the information-rich environment is that information important to clinical decision making is often not available, or is provided in forms that are not relevant to the broad spectrum of patients—with differing levels of health, socioeconomic circumstances, and preferences—and the issues encountered in clinical practice. This is due to too little clinical effectiveness research, to poor dissemination of the evidence that is available, and to too few incentives and decision supports for evidence-based care.
- *Pressing need for evidence development.* More and better evidence—including comparative and longitudinal data—is needed to determine the effectiveness and usefulness of new medical interventions, treatments, drugs, devices, and genetic information. There is an untapped potential to reduce healthcare costs and improve quality by developing evidence not only for specific medical interventions, but also for the way health care is delivered.
- *Promise of health information technology.* EMRs and clinical data registries offer tremendous potential both to generate new evidence and to augment RCTs. Addressing privacy and proprietary issues

that limit data access and sharing would help to support a system in which EMRs, clinical registries, and other types of electronic data could contribute to building a more robust evidence base.

- *Need for more practice-based research*. How might the system better support the notion of a "living textbook of medicine" in which physicians routinely collect and record data on the treatment and outcomes of their patients in order to better care for those in the future?
- *Shift to a culture of care that learns*. To develop best evidence for the delivery of medicine that is geared toward the needs of individual patients, investment is needed into infrastructure for the gathering and analysis of healthcare data and information, as well as standards and protocols to ensure their accuracy and reliability. This changing role will require healthcare providers and patients to adopt a culture that supports the generation and application of evidence. Effective culture change must also be accompanied by insurance and reimbursement system reform that encourages development and application of the systems necessary.
- *New model of patient-provider partnership*. With the increasing complexity of care, and the need and demand for more patient involvement, the traditional "physician-as-expert" model will need to adapt to support patients as integral partners in medical decisions.
- *Leadership that stems from every quarter.* Adapting to and taking advantage of the changes in the healthcare environment will take broad leadership. A strategic focus on the development and application of evidence will require the involvement of both the public and private sectors working together, and of policy makers, providers, patients, insurers, and other stakeholders in the steps toward change.

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2

The Need for Better Medical Evidence

INTRODUCTION

Many Americans assume that the health care they receive is based on strong medical evidence of intervention and treatment effectiveness. However, as suggested by regional analyses, recommended care is often not delivered and insufficient evidence often leads to wide practice variations with little to no health benefit to patients (Fisher et al., 2003b; McGlynn et al., 2003). In addition to negatively impacting health outcomes, practice inconsistencies have dramatic effects on the overall costs of health care—costs which represent the most pressing fiscal challenge to the nation. Papers in this chapter examine the drivers of practice variations and healthcare costs and suggest the potential for an improved evidence base to improve the efficiency and effectiveness of healthcare services.

The majority of U.S. healthcare expenditures today are related to the care and treatment of chronic conditions such as heart disease, diabetes, and asthma, which affect almost half of the U.S. population. Evidence for effective strategies for care delivery in these areas is limited, resulting in care that is fragmented, uncoordinated, and characterized by unnecessary duplication of services. In Elliott S. Fisher's paper, small-area analyses reveal that differences in care delivery explain almost all of the geographic variations in spending across the United States, and that higher-spending regions of the country perform worse in measures of technical quality than regions that spend less money. When there is strong medical evidence, physicians tend to agree on courses of treatment across regions of different spending levels. Building an evidence base for areas in which physicians currently

use their own discretion, such as the comparative effectiveness of various treatment options, or decisions about how often to see a patient with well-controlled hypertension and when to order certain medical tests, could greatly improve the quality of care and reduce costs. In fact, if all regions adopted the practice patterns of the most conservatively spending regions of the country, health outcomes could be significantly improved and U.S. healthcare spending could decline by as much as 30 percent.

Peter R. Orszag's presentation illustrates the serious consequences that excessive healthcare spending poses to the nation's economic well-being. If spending growth trends continue as they have over the past four decades, by 2050 Medicare and Medicaid spending will account for 20 percent of the total U.S. economy. Although often ascribed to effects of an aging population, lower fertility rates, and longer life expectancies, this long-term fiscal challenge is driven almost entirely by excessive healthcare costs—or costs per beneficiary. Slowing overall healthcare cost growth without limiting access will require changes that impact the overall healthcare system and providing better evidence to inform decision making will be an important first step. Comparative effectiveness research that draws upon the emerging electronic health record and clinical registry data resources may be the only cost-effective and feasible mechanism for bringing about the evidence-base expansion needed. Real gains in improving the quality of health care and reducing costs will come when the evidence of medical effectiveness is tied to incentive payments for healthcare providers. A combination of increased cost sharing on the consumer side combined with changes in the incentive system for providers informed by best evidence offers an important opportunity to substantially reduce healthcare costs and improve quality.

HEALTH CARE AND THE EVIDENCE BASE

Elliott S. Fisher, Dartmouth Medical School

The U.S. healthcare system faces serious challenges and the Institute of Medicine (IOM) has played a critical role in calling for fundamental transformation of the delivery system to achieve the vision of a patient-centered, high-quality, equitable, and effective delivery system (IOM, 2001, 2006). There is also a growing recognition that our current delivery system is failing to deliver on the promise of improved health offered by advances in biomedical knowledge, and the future pace of change may widen this gap substantially.

The IOM Roundtable on Evidence-Based Medicine was established "to help transform the way evidence on clinical effectiveness is generated and used to improve health and health care" (IOM, 2007a). The key notions are to provide better evidence about the risks and benefits of interventions and

to support better application of that knowledge to clinical practice. Several recent reports highlight the growing consensus on the need for expanded support for comparative effectiveness research that provides better information about the risks and benefits of specific treatments (IOM, 2007b).

This paper draws on the traditions of small-area analysis to underscore the scope of the challenge faced in bringing evidence to bear on current practice and to point to the opportunity for improving both the costs and the quality of care by ensuring a broad definition of the need for evidence.

Categories of Care: Biologically Targeted Interventions Versus Care Management Strategies

As we consider the relationship between evidence and clinical practice, it is worth considering two broad categories of interventions: discrete, biologically targeted interventions and care delivery strategies.

Biologically targeted interventions are focused on a specific anatomic problem or disease process. Examples include the decision about whether to adopt a specific screening test for cancer or whether to treat a patient with prostate cancer with surgery or radiation therapy. Such interventions can be well specified not only in terms of the underlying anatomic or physiologic problem to be addressed, but also in terms of the expected intermediate and long-term outcomes and how these vary across clinical subgroups. Many of the dramatic improvements in health outcomes achieved over the past decades are a result of the advances in biomedical knowledge and the development of such biologically targeted interventions. These are the traditional focus of technology assessment, clinical guidelines, and a narrow definition of "evidence-based practice."

A second category of "decisions," which I refer to as care delivery strategies, is rarely considered explicitly in the day-to-day practice of clinical medicine. This category refers not to *what* care is provided (what drug, what device, what surgical procedure) or to *whom* (which patients should be offered the intervention), but to *how* a specific biologically targeted therapy is delivered: *who* should provide the care (patients themselves, advanced practice nurses, primary care physicians, or specialists); *where* care should be delivered (home, outpatient facility, or hospital); and *how intensively* patients should be monitored and reevaluated. Questions about care delivery also encompass system- and policy-level issues, such as how care should be organized, what kinds of resources should be deployed, how care should be paid for and financed, and how to improve the quality of care.

There are three reasons to distinguish these two categories of decisions. First, the effectiveness of many (if not most) discrete biologically targeted interventions can depend critically on how care is provided: risk-adjusted

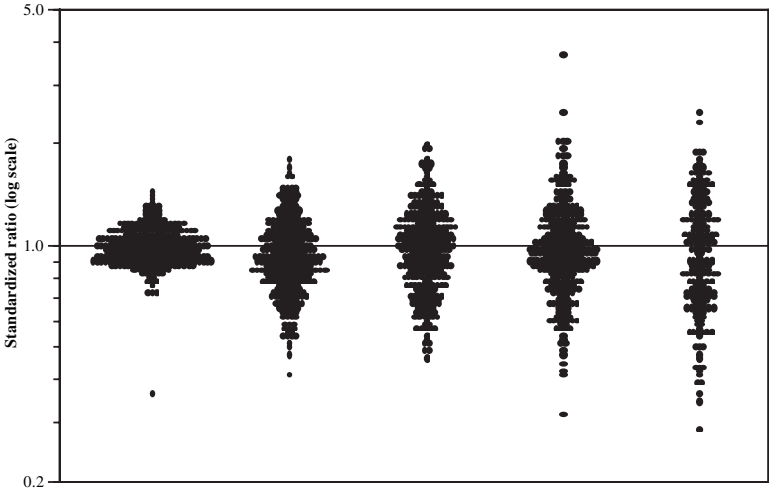
surgical mortality rates, for example, vary severalfold across hospitals (Birkmeyer et al., 2002; O'Connor et al., 1991). Second, as discussed below, regional and provider-specific differences in costs are largely due to differences in the intensity of care delivery: addressing the rapidly rising costs of care will require much better evidence about how to organize and deliver care effectively and efficiently. Finally, I argue that the infrastructure required to provide better evidence on discrete, biologically targeted interventions is fundamentally the same as the infrastructure required to improve care delivery. As we build our capacity to improve evidence, we should be careful to address the need for better evidence along both dimensions.

Current Practice and the Evidence Base: Biologically Targeted Interventions

The recent IOM workshop on evidence-based medicine highlighted the many limitations of the current evidence base, focusing primarily on the challenges surrounding biologically targeted therapies (IOM, 2007a). Highlights include the lack of any evidence on the efficacy or effectiveness of many interventions, the difficulty of extrapolating from trials carried out on selected populations to those with multiple chronic conditions, and the growing recognition that the benefits of interventions vary according to the underlying risk of the population: trials that show benefit for the average patient may not reveal that many lower-risk patients may be harmed by receiving the procedure while those at greater risk receive substantial benefits. The growing recognition of the importance of comparative effectiveness research can be attributed to the increasing attention focused on these issues.

The relative magnitude of the uncertainty surrounding the use of selected, discrete, biologically targeted therapies can be illustrated by the regional variations in rates of these services among the Medicare population (Figure 2-1). We have found it useful to distinguish effective care (treatments where the evidence of benefit is strong and no trade-offs among benefits and harms are involved) from preference-sensitive care (treatments where patients' values about the different outcomes may vary[1]) (Wennberg et al., 2002). An example of the former would be hospitalizations for hip fracture: the diagnosis is straightforward and the therapy (inpatient surgical repair of the fracture) is required. Variations in utilization rates are due entirely to underlying variations in the incidence of the disease. Examples

[1]The importance of ensuring that care is aligned with patients' well-informed preferences applies not only to discrete, biologically targeted interventions, but also to care delivery strategies.



	Hip fracture discharges	PSA	Cardiac catheterization	PCI	Radical prostatectomy
Coefficient of variation	12.7	25.2	28.0	34.0	38.5
Interquartile ratio	1.19	1.40	1.44	1.43	1.71
Extremal ratio	3.95	4.33	4.20	11.50	8.69

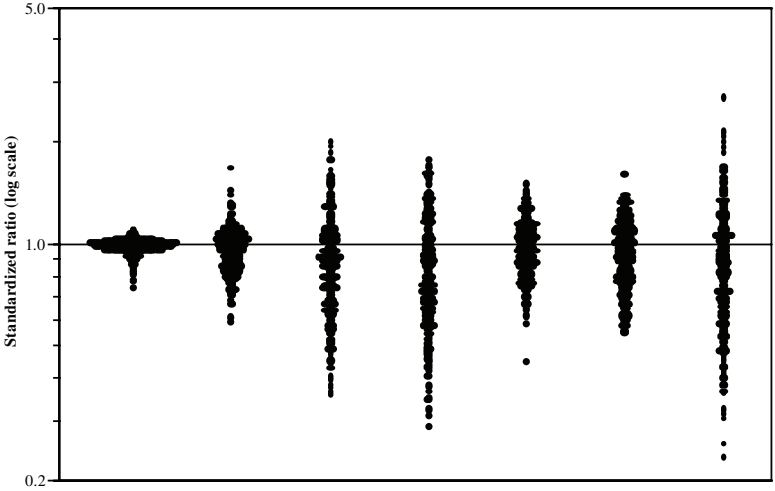
FIGURE 2-1 Variation in utilization rates of specific, biologically targeted interventions.
NOTE: Each dot represents the ratio of the rate of the specified intervention in one of the 306 U.S. Hospital Referral Regions to the U.S. average for that intervention (log scale). All rates are calculated on an annual basis for fee-for-service Medicare enrollees age 65 and over. PSA refers to prostate-specific antigen testing at least once during the year. PCI refers to percutaneous coronary interventions. Data are from the Dartmouth Atlas of Health Care.

of the latter would include screening for prostate cancer (where patient attitudes toward the risks of treatment must be weighed against the still unproven benefits of screening) or percutaneous coronary interventions for stable angina (where the modest benefit in terms of angina relief must be weighed against the lifelong need for anti-platelet therapy among other risks). When we look at common biologically targeted interventions—both diagnostic and therapeutic—we see dramatic variability across the United States. Addressing these variations will require not only better information about risks and benefits (comparative effectiveness research), but also ensuring that treatment decisions reflect the well-informed judgments of patients rather than the opinions of providers (O'Connor et al., 2007; Wennberg et al., 2007).

Current Practice and the Evidence Base: Care Delivery Strategies

There are also marked differences across regions in the way care is delivered (Figure 2-2). Although virtually all Medicare beneficiaries have access to care (defined as at least one physician visit during the year) and there is thus little regional variation in the age-, sex-, or race-adjusted rate of at least one physician visit, we see marked variability in the use of other care delivery strategies. Because variation in use of these services is associated with the local capacity of the delivery system (how many physicians, how many hospital beds), we have long referred to these services as "supply-sensitive."

One of the fundamental reasons for distinguishing care delivery strategies from the use of biologically targeted interventions is their distinct



	At least one visit	Primary care visits	Medical specialist visits	10 or more MDs (L6M)	Medical discharges	Inpatient days	ICU days (L6M)
Coefficient of variation	5.1	14.2	33.6	35.9	18.7	20.5	41.7
Interquartile ratio	1.05	1.21	1.56	1.64	1.30	1.36	1.75
Extremal ratio	1.48	2.80	5.61	6.12	3.37	2.88	11.65

FIGURE 2-2 Variation in utilization rates of care delivery strategies.
NOTE: Each dot represents the ratio of the rate of the specified service or strategy in one of the 306 U.S. Hospital Referral Regions to the U.S. average for that service (log scale). Visits, medical discharges, and inpatient days are calculated on an annual basis for fee-for-service Medicare enrollees age 65 and over. Data for the proportion of enrollees seeing 10 or more physicians and for intensive care unit (ICU) days are for Medicare enrollees with chronic illness who are in their last 6 months of life (L6M). Data are from the Dartmouth Atlas of Health Care.

relationship to variations in spending. Figure 2-3 displays the relationship between spending and the utilization rates of specific types of services across U.S. regions. Each dot represents the ratio of the utilization rates of the specific service in regions that fall in the highest quintile to the utilization rate in the lowest-spending quintile of regional per capita Medicare spending. To control for potential differences in the underlying health status of populations across regions, these analyses are based on long-term follow-up of patients initially hospitalized with hip fracture, colon cancer, or acute myocardial infarction (Fisher et al., 2003a). Higher spending is not associated with greater use of biologically targeted interventions: whether these are treatments that all patients should receive (effective care) or in-

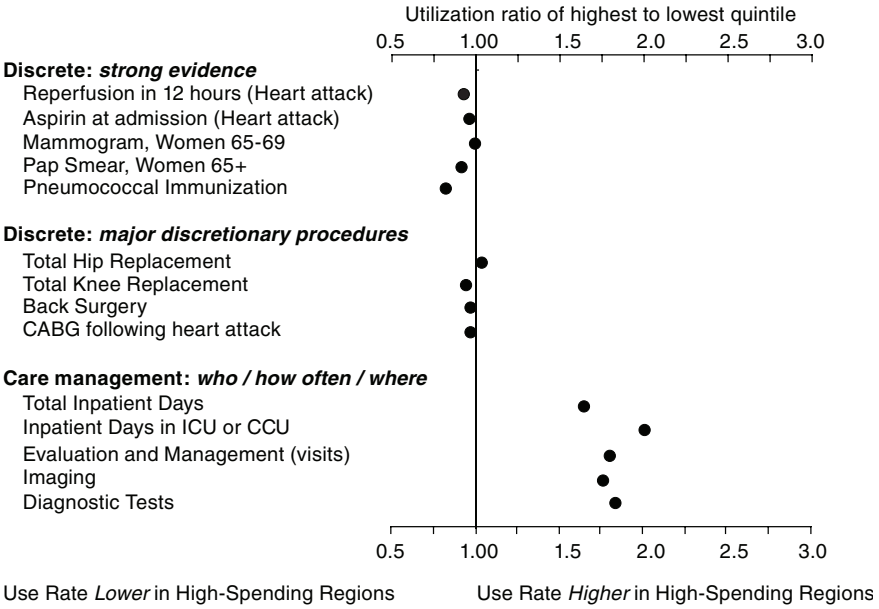


FIGURE 2-3 Ratio of utilization rates for selected specific services among cohorts of Medicare beneficiaries in high- versus low-spending regions.
NOTE: High- and low-spending regions were defined as the U.S. Hospital Referral Regions in the highest and lowest quintiles of per capita Medicare spending. Data for mammograms, Pap smears, and pneumococcal immunizations were ascertained from a representative sample of the Medicare population. Data for all other utilization rates reflect either acute care for patients with heart attacks (reperfusion and aspirin administration) or the weighted average of utilization rate ratios during one year follow-up after initial hospitalization for acute myocardial infarction, hip fracture, or colorectal cancer. All data are from Fisher and colleagues (Baicker et al., 2007).

terventions where patients' judgments about how they value the risks and benefits should determine the treatment choice (preference-sensitive care). Higher spending, however, is largely due to differences in care delivery: how frequently patients are seen (evaluation and management services), how much time they spend in the hospital, and the intensity with which they are monitored (diagnostic tests and imaging).

Spending, the Intensity of Care Delivery, and Health Outcomes

The critical question underlying the variations in practice and spending is their relationship to health outcomes. Over the past 10 years, a number of studies have explored the relationship between higher spending and the quality and outcomes of care (Table 2-1).

Patients' Experiences and Outcomes

Whether the study was carried out at the state level (Baicker and Chandra, 2004), across hospital referral regions (Fisher et al., 2003a), or across the major academic medical centers within the United States (Fisher et al., 2004), a consistent pattern is found: the quality of care as reflected in process measures of care is worse when spending—and the intensity of care delivery—is greater. Among patients hospitalized with hip fractures, colon cancer, and acute myocardial infarction who were followed for up to five years, mortality rates in higher-spending regions and hospitals were no better or slightly worse than in lower-spending delivery systems (Fisher et al., 2003a). In regions where spending growth was greatest, survival following myocardial infarction improved more slowly than in regions where spending growth was slower (Skinner et al., 2006). Finally, Medicare beneficiaries' overall satisfaction with care was no better in higher-spending regions and their perceptions of the accessibility of care were somewhat worse (Fisher et al., 2003a).

Physician Attributes, Practice Settings, and Perceptions of Care

On a per capita basis, the highest-spending quintile of hospital referral regions have 65 percent more medical specialists per capita, 75 percent more general internists, and 25 percent fewer family practitioners than the lowest-spending quintile. A substantially higher proportion of physicians are foreign medical graduates, fewer are board certified, and they are much more likely to practice in small groups than physicians in lower-spending regions (Sirovich et al., 2006). When surveyed, physicians in higher-spending regions are more likely to report that the continuity of care with their patients is inadequate to support high-quality care and that the quality

TABLE 2-1 Relationship Between Regional Differences in Spending and the Content, Quality, and Outcomes of Care

	Higher-Spending Regions Compared to Lower-Spending Ones[a]
Healthcare resources	• Per capita supply of hospital beds 32% higher (Fisher et al., 2003a) • Per capita supply of physicians 31% higher overall: 65% more medical specialists, 75% more general internists, 29% more surgeons, and 26% fewer family practitioners (Fisher et al., 2003a)
Content and quality of care	• Adherence to process-based measures of quality lower (quality worse) • Little difference in rates of major elective surgery (Fisher et al., 2003a; Wennberg et al., 2002) • More hospital stays, physician visits, specialist referrals, imaging, and minor tests and procedures (Fisher et al., 2003a)
Health outcomes	• Mortality up to 5 years slightly higher following acute myocardial infarction, hip fracture, and colorectal cancer diagnosis (Fisher et al., 2003a) • No difference in functional status (Fisher et al., 2003a)
Physician perceptions of quality	• More likely to report poor communication among physicians (Sirovich et al., 2006) • More likely to report inadequate continuity of patient care (Sirovich et al., 2006) • Greater difficulty obtaining inpatient admissions or high-quality specialist referrals (Sirovich et al., 2006)
Patient-reported quality of care	• Worse access to care and greater waiting times (Fisher et al., 2003a) • No difference in patient-reported satisfaction with care (Fisher et al., 2003a)
Trends over time	• Although all U.S. regions experienced improvements in acute myocardial infarction survival between 1986 and 2002, regions with greater growth in spending had smaller gains in survival than those with lower growth in spending (Skinner et al., 2006)

[a]High- and low-spending regions were defined as the U.S. Hospital Referral Regions in the highest and lowest quintiles of per capita Medicare spending as in Fisher et al. (2003a).

of communication is insufficient to support high-quality care. In spite of the substantially greater per capita supply of both beds and specialists, physicians in higher-spending regions are more likely to perceive scarcity: they are more likely to report that it is difficult to get a patient into the hospital and that it is hard to obtain adequate medical specialist referrals.

These findings are consistent with the hypothesis that the lower-spending regions represent a reasonable benchmark of efficiency. In fact, if all U.S. regions could safely adopt the organizational structures and practice patterns of the lowest-spending regions of the United States, Medicare spending would decline by about 30 percent (Fisher et al., 2003a; Wennberg et al., 2002). While it may not be realistic to reduce spending by that

amount, the magnitude of the differences in practice and the fact that the differences in spending are largely due to differences in care delivery point to an important opportunity: improving efficiency will require attention not only to the comparative effectiveness of biologically targeted interventions, but also to addressing the underlying causes of the differences in care delivery across regions and systems.

Underlying Causes of the Differences in Care Delivery: Evidence and Theory

The Evidence

A number of studies have explored the underlying causes of the regional differences in spending and the intensity of care delivery. Patients' preferences for care vary slightly across regions, but not enough to explain the magnitude of spending differences seen. For example, Medicare beneficiaries in high-spending regions are no more likely to prefer aggressive end-of-life care than those in low-spending regions (Barnato et al., 2007; Pritchard et al., 1998). Differences in the malpractice environment are associated with differences in both practice and spending, but explain less than 10 percent of state-level differences in spending and have a comparably small impact on differences in the growth in spending across states (Baicker et al., 2007; Kessler and McClellan, 1996). The role of capacity is clearly important, but the hospital bed supply and physician supply combined explain less than 50 percent of the difference in spending across regions (Fisher et al., 2004).

The most recent studies have focused on the use of clinical vignettes to explore how physicians' judgments vary across regions of differing spending levels. These studies have found that physicians in higher-spending regions were no more likely to intervene in cases where evidence was strong (such as chest pain with an abnormal stress test), but were much more likely to recommend discretionary treatments (such as more frequent visits, referral to a specialist, or use of imaging services) than those in low-spending regions (Sirovich et al., 2005).

A Likely Diagnosis: Capacity, Payment, and Clinical Culture

These findings suggest a likely explanation for the dramatic differences in spending across regions and the paradoxical finding that higher spending seems to lead to worse quality and worse outcomes. Current clinical evidence is an important, but limited, influence on clinical decision making. Most physicians practice within a local organizational context and policy environment that profoundly influences their decision making,

especially in discretionary clinical settings. Hospitals and physicians each face incentives that will in general reward expansion of capacity (especially for highly reimbursed services) and recruitment of additional procedure-oriented specialists. When there are more physicians relative to the size of the population they serve, physicians will see their patients more frequently. When there are more specialists or hospital beds available, primary care physicians and others will learn to rely upon those specialists and use those beds. (It is more efficient from the primary care physician's perspective to refer a difficult problem to a specialist or to admit a patient to the hospital than to try to manage the patient in the context of an office visit for which payments have become relatively constrained.)

The consequence is that what—given the state of current evidence—are "reasonable" individual clinical and policy decisions lead in aggregate to higher utilization rates, greater costs, and inadvertently, worse quality and worse outcomes. The key element of this theory is that because so many clinical decisions are in the "gray areas" (how often to see a patient, when to refer to a specialist, when to admit to the hospital), any expansion of capacity will result in a subtle shift in clinical judgment toward greater intensity.

Implications for Evidence Development

These findings and their likely explanation point to the need for much better evidence. We need evidence about the risks and benefits of discrete, biologically targeted interventions and how these risks and benefits vary across different subgroups of the population, especially those often excluded from current randomized trials (IOM, 2007b), but we also need much better evidence about care delivery. No matter how good our clinical evidence about specific interventions becomes, many—if not most—clinical decisions will still require judgment. Also, because there will always be gray areas, we will need evidence that can guide clinicians, administrators, and policy makers when they are making decisions about care delivery.

Although the need for evidence may appear overwhelming, an important opportunity lies in recognizing that the information systems and analytic approaches required to improve the evidence base for biologically targeted interventions and for improving care delivery are fundamentally the same (Table 2-2). In the ideal world of improved information systems and electronic records that might allow relatively routine assessment of both short- and long-term health outcomes and effective follow-up of patients, the capacity to evaluate both care delivery and biologically targeted interventions would be critical, at least in part because lack of information about the local context (delivery system attributes) would sharply limit our ability to properly interpret studies of biologically targeted interventions.

TABLE 2-2 Relationship Between the Information and Approaches Required to Improve the Evidence Base Around Biologically Targeted Interventions and Care Delivery

	Discrete, Biologically Targeted Interventions	Approaches to Care Delivery
Example of research question	How effective are endovascular carotid artery stents in the prevention of stroke?	How should primary care offices be organized to provide care to patients with heart failure?
Outcomes of interest	Survival, functional status, quality of life, total costs	Survival, functional status, quality of life, total costs
Comparison of interest	Carotid stent vs. medical therapy	Offices meeting criteria for "medical home" vs. other primary care offices
Important patient-level factors required for either adjustment or stratification	Age, sex, race, severity of illness, comorbidities, socioeconomic status	Age, sex, race, severity of illness, comorbidities, socioeconomic status
Contextual factors required for adjustment or stratification	Attributes of care delivery system	Attributes of care delivery system
Applicable methods	Randomized trials and/or population-based observational studies	Randomized trials and/or population-based observational studies
Key notion	Compare biologically targeted interventions, while accounting for patient and contextual factors	Compare care delivery strategies, while accounting for patient and contextual factors

Moving Forward: A Challenge to Academic Medicine

The critical importance of healthcare spending to the future financial health of the U.S. government and the economy in general has received growing attention (Orszag and Ellis, 2007). Our capacity to provide affordable healthcare coverage to the U.S. population and our ability to pay for the new biologically targeted interventions that are under development will clearly depend not only on the costs of the interventions but also on the costs of delivering those interventions. Academic medicine—and the federal agencies that provide research support—have largely focused on improving our understanding of disease biology, while ignoring the need to understand and address the dramatic variations in care delivery among academic medical centers (Wennberg et al., 1987).

Table 2-3 points to the magnitude of the opportunity—and the challenge—for academic medicine. The upper portion of the table focuses on the degree to which each of these five members of the *U.S. News and World Report's* "Honor Roll" of academic medical centers is able to deliver proven clinical interventions to eligible patients during an acute inpatient stay. The lower portion of the table highlights the differences in spending and overall intensity of care. The specific data focus on care provided in the last six months of life, but these patterns of practice are highly predictive of how these institutions treat other seriously ill patients. All five provide

TABLE 2-3 Performance of Selected Major Academic Medical Centers on Measures of Adherence to Biologically Targeted Treatments and the Intensity of Care Delivery

	UCLA Medical Center	Johns Hopkins Hospital	Massachusetts General Hospital	Cleveland Clinic Foundation	Mayo Clinic (St. Mary's Hospital)
Provision of discrete, biologically targeted evidence-based interventions					
Composite quality score on measures of inpatient technical quality	81.5	84.3	85.9	89.2	90.4
Spending and care delivery for patients with serious chronic illness during last 6 months of life					
Medicare spending	50,522	43,363	40,181	28,077	26,330
Physician visits	52.1	29.8	42.2	32.2	23.9
Hospital days	19.2	17.1	17.7	14.6	12.9
Intensive care days	11.4	4.3	2.8	3.5	3.9
% admitted to hospice	26.1	31.5	19.6	34.2	25.5
% seeing 10 or more physicians	57.7	44.3	54.6	46.8	43.0

NOTES: Hospitals were selected for inclusion because they were ranked as the top five academic medical centers on the *U.S. News and World Report's* 2007 "Honor Roll." Utilization data are for 1999-2003. Composite quality score was calculated from CMS data for 2005, which are from the Dartmouth Atlas of Health Care.

high-quality inpatient care. The differences in care delivery, however, are substantial: patients at the University of California, Los Angeles, have twice as many visits, spend about 50 percent more time in the hospital, and cost about twice as much as those treated at the Mayo Clinic in Rochester, Minnesota, or the Cleveland Clinic.

If all U.S. delivery systems could achieve the apparent efficiency of a Mayo or a Cleveland Clinic, the resources available to expand coverage to the uninsured or to provide interventions of proven benefit to those who are not be able to afford them would be substantial. Failure to address this challenge would call into question not only the scientific integrity of the enterprise (Are we really committed to asking important questions?), but also our moral authority as healthcare providers (How can we continue to ignore obvious opportunities to improve quality and the future affordability of care?).

Academic medicine has the opportunity to lead the development of a learning healthcare system. Such an effort should include a focus not only on the science of disease biology and improving the evidence to support the use of biologically targeted interventions, but also on the sciences of clinical practice and the evidence to support improvements in care delivery (Wennberg et al., 2007).

THE HIGH PRICE OF THE LACK OF EVIDENCE

Peter R. Orszag, Congressional Budget Office

The nation's long-term fiscal challenge has largely been misdiagnosed in popular descriptions. It typically is described as being driven mostly by the aging of baby boomers, with lower fertility rates and longer life expectancy causing most of the long-term budget problem. In fact, most of that long-term problem is driven by excess healthcare cost growth—that is, the rate at which healthcare costs grow compared to income per capita. In other words, it is the rising cost per beneficiary, rather than the number of beneficiaries, that explains the bulk of the nation's long-term fiscal problem.

You can see this phenomenon arising even over the next decade: Figure 2-4 shows the Congressional Budget Office's (CBO's) projections for spending on Social Security, Medicare, and Medicaid through 2017. As the figure shows, Social Security rises by about 0.5 percentage points of gross domestic product (GDP), from 4.2 percent of GDP to 4.8 percent over that period. Medicare and the federal share of Medicaid rises from 4.6 percent of GDP to 5.9 percent of GDP—an increase of 1.3 percentage points of GDP, or roughly twice as much as Social Security even over the next decade.

If you look over longer periods of time, the basic point is accentuated.

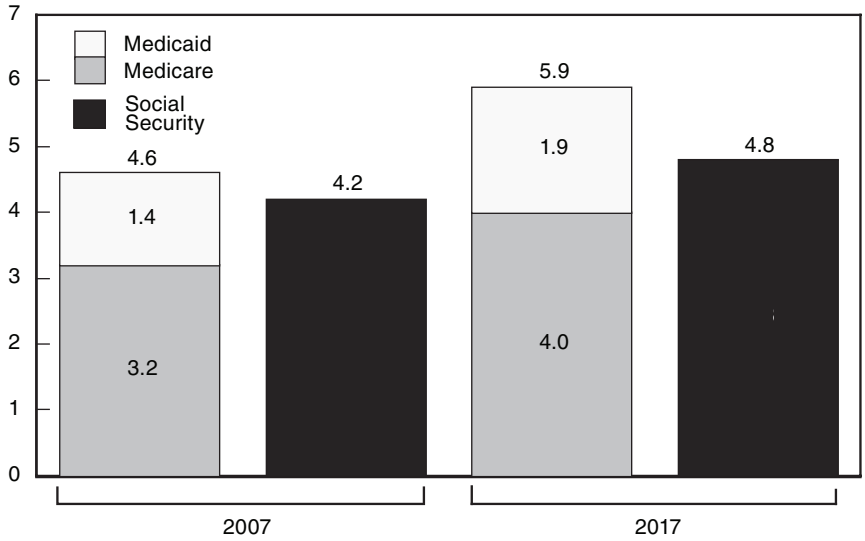


FIGURE 2-4 Spending on Medicare and Medicaid and on Social Security as a percentage of GDP, 2007 and 2017.

Figure 2-5 shows a simple extrapolation in which Medicare and Medicaid costs continue to grow at the same rate over the next four decades as they did over the past four. (Even with no change in federal policy, there are reasons to believe that this simple extrapolation may overstate future cost growth in Medicare and Medicaid. CBO has recently released a long-term health outlook that presents a more sophisticated approach to projecting Medicare and Medicaid costs under current law, but a straight historical extrapolation is shown here for simplicity.) Under that scenario, Medicare and Medicaid would rise from 4.6 percent of the economy today to 20 percent of the economy by 2050; 20 percent of GDP is the entire size of the federal government today.

The most interesting part of Figure 2-5 is the bottom line, which isolates the pure effect of demographics on those two programs. The only reason that the bottom line is rising is that the population is getting older and there are more beneficiaries on the two public programs. The increase between today and 2050 in that bottom dotted line shows that aging does indeed affect the federal government's fiscal position. Yet that increase is much smaller than the difference in 2050 between the bottom line and the top line. In other words, the rate at which healthcare costs grow—whether they continue to grow at 2.5 percentage points per year faster than per capita income, or 1 percentage point, or 0.5 percentage point, is to a

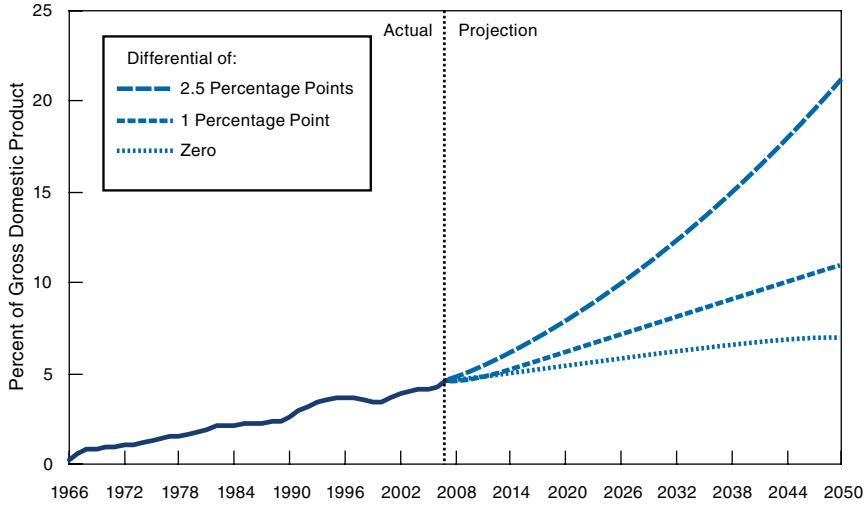


FIGURE 2-5 Total federal spending for Medicare and Medicaid under assumptions about the health cost growth differential.
SOURCE: Congressional Budget Office, 2007.

first approximation the central long-time fiscal challenge facing the United States.

It is common to say that the sooner we act the better off we are, and just to calibrate that, Figure 2-6 shows that if we slowed healthcare costs growth from 2.5 percentage points to 1 percentage point starting in 2015—which would be extremely difficult if not impossible to do, but is helpful as an illustration—the result in 2050 would be a reduction of 10 percent GDP in Medicare and Medicaid expenditures for the federal government relative to no slowing in the cost growth rate. That 10 percent of GDP difference is half of what the federal government spends today.

All of this may seem pretty challenging and is further complicated by the fact that it is implausible that we will slow Medicare and Medicaid growth in a sustainable way unless overall healthcare spending also slows. The reason is that if all you did was, say, to reduce payment rates under Medicare and Medicaid, and then try to perpetuate that over time without a slowing of overall healthcare cost growth, the result would likely be substantial access problems that would be inconsistent with the underlying premise and public understanding of these programs. One therefore needs to think about changes to Medicare and Medicaid in terms of the impact they can have on the overall healthcare system.

From that perspective, there appears to be a very substantial opportunity embedded in this long-term fiscal challenge facing the United States:

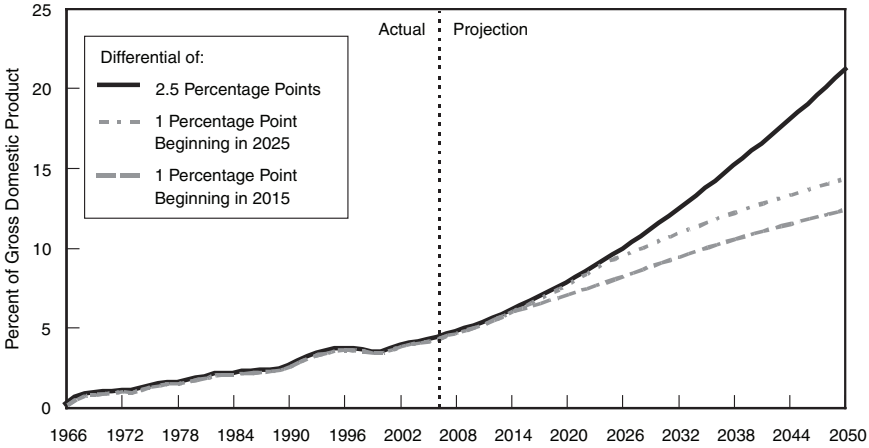


FIGURE 2-6 Effects of slowing the growth of spending for Medicare and Medicaid.
SOURCE: Congressional Budget Office, 2007.

the possibility of taking costs out of the system without harming health. Perhaps the most compelling evidence underscoring this opportunity is the significant variations across different parts of the United States that do not translate into differences in health quality or health outcomes (Figure 2-7).

The question then becomes, why is this happening? To me, it appears to be a combination of two things. One is the lack of information specifically about what works and what does not. The second thing is a payment system, on both the provider and the consumer sides, that accommodates the delivery of low-value or negative-value care.

On the consumer side, despite media portrayals to the contrary, the share of healthcare expenditures paid out of pocket—which is basically the relevant factor for evaluating the degree to which consumers are faced with cost sharing—has plummeted over the past few decades, from about 33 percent in 1975 to 15 percent today (Figure 2-8). All available evidence suggests that lower cost sharing increases healthcare spending overall, and collectively we all pay a higher burden, although the evidence is somewhat mixed on the precise magnitude of the effect by which lower cost sharing raises overall spending.

This observation leads some analysts to argue that the way forward is more cost sharing and a health savings account approach, and this can indeed help to reduce costs. However, two things need to be kept in mind in evaluating this approach. The first is that a significant amount of cost

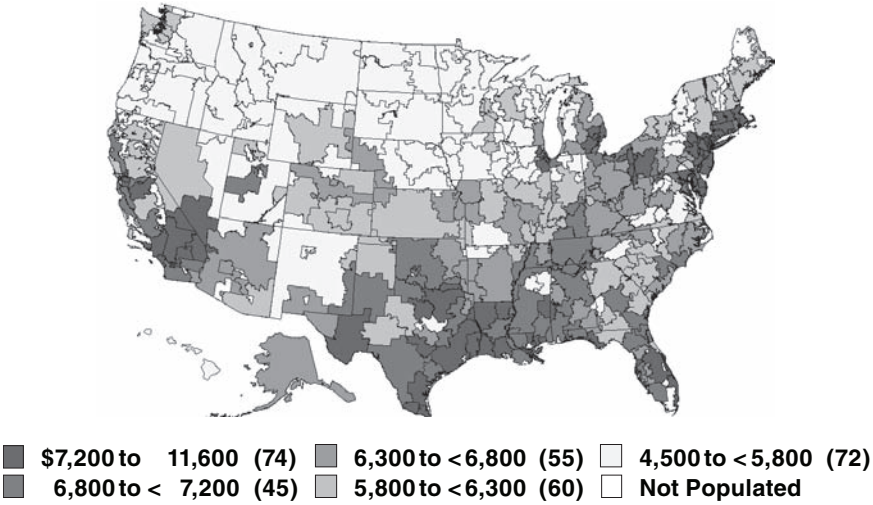


FIGURE 2-7 Medicare spending per capita in the United States, by hospital referral region, 2003.
NOTE: The numbers in parentheses indicate the number of regions in each group.
SOURCE: The Dartmouth Atlas Project, 2003.

sharing is involved in existing plans. Moving to universal health savings accounts would thus not entail as great an increase in cost sharing, and therefore as much a reduction in spending, as you might think. Second, there is an inherent limit to what we should expect from increased consumer cost sharing because healthcare costs are so concentrated among the very sick. For example, the top 25 percent most expensive Medicare beneficiaries account for 85 percent of total costs, and the basic fact that healthcare costs are very concentrated among a small share of the population is replicated in Medicaid and in the private healthcare system. To the extent that we in the United States want to provide insurance, and insurance is supposed to provide coverage against catastrophic costs, the fact that those catastrophic costs are accounting for such a large share of overall costs imposes an inherent limit to the traction that one can obtain from increased consumer cost sharing. In sum, increased cost sharing on the consumer side can help to reduce costs, but it seems very unlikely to capture the full potential to reduce costs without impairing health quality.

This leads us to the provider side. On the provider side, the accumulation of additional information and changes in incentives could improve efficiency in the delivery of health care. There is growing interest in comparative effectiveness research, and the original House version of the State

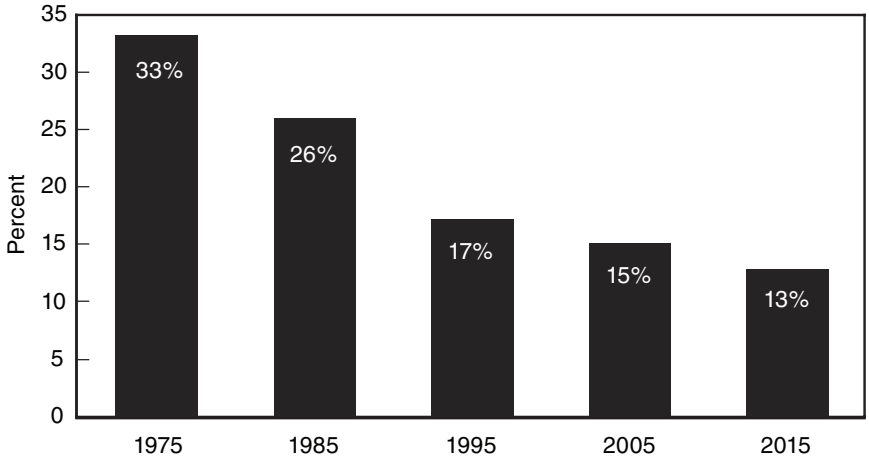


FIGURE 2-8 Share of personal healthcare expenditures paid out of pocket.

Children's Health Insurance Program legislation had some additional funding for comparative effectiveness research. Other policy makers seem interested in expanding comparative effectiveness research. We need, though, to ask some hard questions about what we mean by comparative effectiveness research and how it would be implemented.

The key issues are what kind of research is undertaken and the standard of evidence used. As Mark McClellan has noted, comparative effectiveness research will very likely have to rely on nonrandomized evidence. The reason is that it seems implausible that we could build out the evidence base across a whole variety of different clinical interventions and practice norms using only randomized control trials, especially if we want to study subpopulations. On the other hand, economists have long been aware of the limitations of panel data econometrics, where one attempts to control for every possible factor that could influence the results—typically, that attempt is far from perfectly successful. There is thus a tension between using statistical techniques on panel data sets (of electronic health records, insurance claims, and other medical data), which seems to be the only cost-effective and feasible mechanism for significantly expanding the evidence base, and the inherent difficulty of separating correlation and causation in such an approach.

In terms of the budgetary effects of comparative effectiveness research, a lot depends on both what is done and how it is implemented. If the effort only involves releasing the results of literature surveys, the effects would likely be relatively modest. If new research using registries or analysis of

electronic health records is involved, there may be somewhat larger effects. The real traction, though, will come from building the results of that research into financial incentives for providers. In other words, if we move from a "fee-for-service" system to a "fee-for-value" one, where higher-value care is awarded stronger financial incentives and low-value or negative-value health care is penalized by smaller incentives, or perhaps even penalties, the effects would be maximized. The design of such a system is very complicated and difficult to implement, but this is where the greatest long-term budgetary savings could come.

In conclusion, it is plausible to me that the combination of some increased cost sharing on the consumer side and a substantially expanded comparative effectiveness effort, combined with changes in the incentive system for providers, offers the nation the most auspicious approach to capturing the apparent opportunity to reduce healthcare costs at minimal or no adverse consequences for health outcomes. The focus of this publication is thus central to addressing the nation's long-term fiscal challenge.

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3

Circumstances Accelerating the Need

INTRODUCTION

The current pace of development in science and technology is unprecedented. In health care, these innovations have produced a variety of new therapies to treat everything from heart disease to joint injury; and product development is increasingly informed by advances in areas such as genetics that are providing a wealth of new information on how genes influence disease. These developments have the potential to dramatically improve care and treatment options for many patients, but they also introduce a level of complexity and cost in medical interventions that will impact the healthcare system. Healthcare providers are increasingly pressed to find new, reliable and rapid ways to evaluate the effectiveness of new medical technologies.

To illustrate the challenges posed by emerging technologies to the current established evidence paradigm, Molly J. Coye explores the substantial diversity and complexity of new medical products. Biopharmaceuticals, information technology (IT), and hybrid devices are often not suited to the evaluation approaches geared towards more traditional technologies such as pharmaceuticals, devices, and imaging modalities. In addition transformative technologies, which are often information-based and have the potential to improve healthcare processes and delivery, are often not recognized or supported—resulting in waste and inefficiency, as well as missed opportunities to significantly transform medical care. Acutely needed are new approaches to the generation of evidence regarding the benefits, cost-effectiveness, and appropriate application of new technologies.

The need for more and better evidence is echoed in David M. Altshuler's paper on the implications for healthcare providers of the increasing amount of new knowledge about human genetics. Past studies of genetic contributions to diseases focused on rare Mendelian diseases in which identified genes were highly predictive of disease development. However, in recent years, hundreds of genes have been identified as "risk factors" for more common diseases such as diabetes and heart disease. These findings offer important insights into pathophysiology but are currently of limited clinical utility. In addition, very little is known about how people interpret and use information about genetic risks. While there is enormous potential for personalized medicine, there are also great risks for unintended consequences. As genetic tests are developed and made available for clinical use, better evidence is needed on how their application impacts the healthcare system.

NEW HEALTHCARE PRODUCT INTRODUCTION

Molly J. Coye, HealthTech

Over the past three decades, the central preoccupation of health technology policy has been to cope with the rising tide of new pharmaceutical and imaging products introduced each year (McGivney and Hendee, 1990; Willems and Banta, 1982). The impact of these new technologies on cost and total expenditures has been an important and continuing challenge to national goals of cost containment and to the efficient use of health resources (Eisenberg and Zarin, 2002). In the last decade, a new understanding of the role and value of medical technology has evolved. Influential studies by Cutler, McClellan, and others have defined the benefits of medical technologies (Cutler and McClellan, 2001) and urged consideration of how best to encourage innovation. Somewhat surprisingly, however, the actual number of new products presented for regulatory approval has not increased significantly over the past decade (Figures 3-1 and 3-2).

The principal challenge for health technology policy is not the quantity of new products presented for assessment. Instead, the complexity and diversity of emerging technologies, including new biologics and hybrid pharmaceutical and device products, is increasingly straining the ability of developers and researchers to generate evidence adequate for regulatory and coverage decisions. National efforts to improve and accelerate the evaluation of new technologies by federal agencies may well be overwhelmed without restructuring and investments in technology assessment proposed recently by Wilensky, Reinhart, and others (Reinhardt, 2001; Wilensky, 2006). The first part of this review considers patterns among emerging tech-

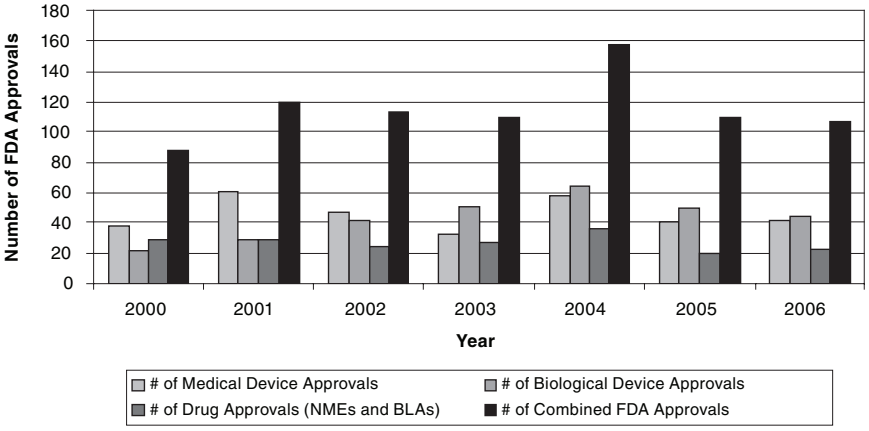

FIGURE 3-1 Number of FDA approvals per year, 2000-2006.
SOURCE: U.S. Food and Drug Administration, Center for Biologics and Research. Data derived from Owens, 2006.

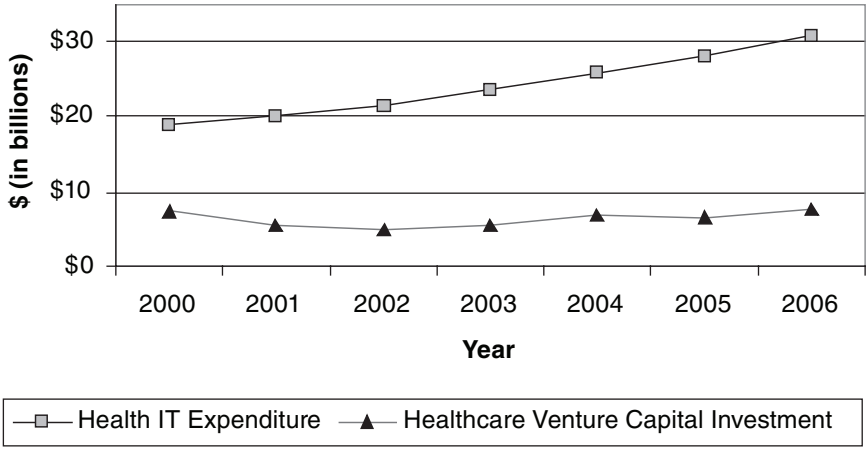

FIGURE 3-2 Health IT expenditure versus healthcare venture capital investment, 2000-2006.
SOURCE: National Science Foundation, Division of Science Resources Statistics. Data from http://www.altassets.com/casefor/sectors/2005/nz6545.php, and PwC/NVCA MoneyTree™ Report, Thomson Financial, http://dorenfest.com/doc/pressrelease_Feb2004.pdf.

nologies that will complicate efforts to develop evidence for policy decisions about their benefits, cost effectiveness, and appropriate application.

In the second part of this review, we consider two consequences of complexity that are less well understood. The first is the waste and inefficiency that prevails because we have not defined critical research targets for the developers of technology *before* they initiate clinical studies. For all but the largest and most sophisticated of firms, the understanding of what needs to be demonstrated in order to win coverage, reimbursement, and even support from payers and providers varies widely. Developers need coordinated public and private efforts that will provide early identification of important research targets, including priority populations, side-by-side comparisons of effectiveness with competing technologies, cost effectiveness, and other aspects; and purchasers and providers, in turn, need the improved information for policy decisions and clinical guidance.

The second consequence of complexity is the public and private failure to recognize and act on the potential of certain technologies to significantly transform medical care. The new concept of transformative technologies is proposed to distinguish technologies that enable a wide range of disruptive and positive changes in clinical care and administrative processes, reducing net expenditures and improving the value of health care. They constitute important opportunities for progress toward national goals of improved quality and efficiency in health care, and—in contrast to biologics and hybrid devices—they present only modest challenges to our capacities for evaluation. As Newhouse has pointed out, health care may be the most inefficient of all sectors in its ability to extract value from resources consumed (Newhouse, 2002). To meet Newhouse's challenge—to extract the full value of emerging technologies—it will be necessary to understand the barriers to evidence generation, evaluation, and policy formulation particular to transformative technologies.

Despite a widespread impression that the pace of new technology introduction is escalating (Kessler et al., 2004), the most common measure of it—Food and Drug Administration (FDA) approvals of new products—finds the pace steady and relatively even (FDA, 2006) (Figure 3-1). This "steady state" is reflected in the equally modest trends in total venture investments in health products and services (Figure 3-2). On the other hand, the FDA approves medium- and low-risk products each year in far greater numbers than approvals for novel products, and off-label extensions of drugs and devices proliferate without systematic evaluation (Gelijns et al., 2005). In the last half-decade, providers have also been contending with the rapid expansion of IT products, many of which do not require FDA approval. Unfortunately, there are no data available on the number of new IT products introduced, but expenditures in this area have increased steadily over the past 5 years. In 2004, the Hospital Financial Management Association

survey report estimated that IT spending would grow by nearly 9 percent per year to reach $30.5 billion in 2006, a pattern that appears to have held (Figure 3-2).

Substantial progress is under way in two broad areas that cut across the overlapping domains of emerging pharmaceuticals, biotechnology, devices, and IT. First, policy makers now agree that comparative effectiveness research is urgently needed to support coverage and reimbursement decisions (IOM, 2007b). Second, requirements for formal post-market surveillance have been developed as Coverage with Evidence Development (Tunis and Pearson, 2006; Tunis et al., 2007).

Diversity, Complexity, and Cost

The challenges for evidence generation and technology evaluation lie in the diversity, complexity, and cost of emerging technologies, rather than the pace of new product introduction. Requirements for evidence generation and evaluation processes in effect today were largely designed to assess pharmaceuticals, devices, and imaging modalities. As biotech drugs, devices, and IT expand and converge, however, the difficulties these classes of technologies will pose for the established evidence paradigm become clearer (Keenan et al., 2006). These include the shorter development period for devices and IT, often one to three years rather than ten years or more for chemical or biotech drugs, and the additional sciences necessary to evaluate devices and IT, adding engineering and software to biology and chemistry. The cost of biotech drugs is generally much greater than that of pharmaceuticals because they are often targeted to rare or life-threatening diseases and inspire urgent patient demand, making assessment more urgent but also making it difficult to induce patients to participate in randomized trials.

Pharmaceutical and Biotechnology Drugs

The decline in the introduction of new pharmaceutical drugs over the past decade is well recognized (Burns, 2005). More important for our consideration here, the processes for research and regulatory approval are relatively well understood. In comparison with biotechnology drugs, hybrid devices, and nanotechnology, the pipeline for traditional pharmaceutical products offers relatively few novel problems. The field of biotechnology drugs ("biotech drugs"), including genetic diagnostics and therapies, is growing at twice the rate of traditional (chemical) pharmaceuticals (Pauly, 2006), and the cost of the treatments as well as their efficacy has made evidence generation increasingly urgent. Recent approvals have permitted market entry of biotech drugs that cost as much as $300,000 per year for the life of the patient (Myozyme) or $100,000 per treatment episode

(Acthar). In 2007, the Biotechnology Industry Organization (BIO) reported that more than 400 biotech drug products and vaccines were currently in clinical trials (BIO, 2007).

Biologically targeted drugs often carry very high prices because they target rare, severe, or fatal diseases with high physician and patient demand, and because there is no established pathway to generics (the FDA concept of bioequivalence for generics has yet to be developed for biotech drugs; see discussion of "follow-on biologics," below). This raises the stakes for evidence development, regulatory review, and patent protection significantly because the off-label uses of biotech drugs often target quite unrelated diseases (Calfee and Dupre, 2006) and may quickly become accepted in practice with limited opportunity for clinical trials. Avastin, as a case in point, was originally approved for treatment of colon cancer. It was subsequently found to be effective in treatment of acute macular degeneration (AMD), and physicians began to use it off-label for this purpose. The company then developed a new formulation of Avastin, named Lucentis, approved and marketed for AMD at a much higher price. More recently, physicians have extended the use of Avastin to breast and lung cancer, and the company reportedly plans to develop new formulations for each of these diseases as well. As with most other biotech drugs, once physicians believed that Avastin was effective for off-label uses, it became very difficult to enroll patients in randomized trials. All of these factors complicate efforts to generate appropriate evidence on the clinical and cost effectiveness of biotech drugs.

Biomarkers are measured as indicators of normal biological or pathogenic processes, or of pharmacological response to therapeutic interventions (IOM, 2007a). Nucleic acid testing is the most rapidly growing segment of the in vitro diagnostic laboratory business. Spending for DNA testing exceeded $1 billion in 2001 and is estimated to be growing at 30-35 percent a year (Goldsmith, 2004). Combining knowledge of the human genome with developments in genomics, proteomics, and bioinformatics, research on biomarkers represents an important beachhead for personalized medicine. The number and complexity of biomarkers is expanding rapidly, and a coalition of pharmaceutical companies, the FDA, and other regulatory bodies has been established to study the role of biomarkers in predicting patient susceptibility to adverse drug events.

In March 2007, the Institute of Medicine (IOM) issued a report, *Cancer Biomarkers: The Promises and Challenges of Improving Detection and Treatment*, recommending a coordinated federal process to identify and evaluate biomarkers. While the IOM strongly endorsed the importance of biomarkers as a means of improving clinical effectiveness and protecting patients from the adverse consequences of unnecessary or inappropriate treatment, the report also described the many important uncertainties sur-

rounding the development of new test systems and new methodologies for their assessment. The report also called for new processes for modeling the effects of, evaluating, coding and pricing biomarkers, and for new approaches to pricing and to conditional coverage that would require more data collection (IOM, 2007a). The intense interest from developers, regulators, and scientists in biomarkers reflects not only their clinical importance, but also the difficulty of designing appropriate research approaches and regulatory criteria (Burns, 2005). Most physicians are unfamiliar with gene expression profiles, of course, and will need more than the statistics on diagnostic accuracy used for regulatory decision making to interpret test results for their patients.

Follow-on biologics are biotech products that are developed as similar versions of already approved protein products (also known as follow-on protein products, biogenerics, or biosimilars). Approval of biosimilars has proceeded in Europe, but developers in the United States strenuously oppose these products because follow-on products may be able to enter the market early—well before the patent period for the original biologic has expired—without risk of patent infringement. While Congress, the Department of Health and Human Services and the FDA consider the complex scientific and legal issues involved in developing a regulatory framework for follow-on biologics, it is likely that the evidentiary basis for regulatory decisions will be fraught with controversy and legal actions.

Devices

The evidence requirements for most types of medical devices, as for pharmaceuticals, are reasonably well established. The links between initial concepts, early investments, clinical results, regulatory approval, and reimbursement and dissemination are much clearer than for biologics and many hybrid technologies that combine devices with drugs, biologics, and IT. Venture investors play an important role in financing the development of evidence to support emerging devices, and their smaller companies have been described by Burns as the "farm teams" feeding larger companies such as Medtronic and Stryker (Burns, 2005; Coye, 2006; Iglehart, 2005). As larger device companies acquire smaller firms, greater investment in evidence generation becomes possible.

Device manufacturers are also following the path cleared by pharmaceutical firms in launching direct-to-consumer advertising—most recently for Stryker's "Jack Nicklaus Hips" and "Triathlon Knees" designed for women. As for pharmaceuticals and biologics, moreover, the overriding need is for assessments of the comparative effectiveness of devices, including cost effectiveness, and for broader and more accountable post-market

surveillance programs. Post-market surveillance will also address the rapid extension of products to populations not covered in initial approvals.

In a few cases the science underlying the development of medical technologies appears to outstrip or even obviate the need for clinical evidence. Proton beam therapy has been approved, and favorable reimbursement assigned, in the absence of clinical data for effectiveness, based instead on the physics of the equipment and expected clinical benefit. For the first time, the FDA-based approval of a therapy on the physical properties of the product. Proton therapy facilities can cost up to $200 million to construct and equip and have a "footprint" equivalent to two football fields. Proton beam therapy has been reimbursed at a premium over other forms of radiation therapy since 2001.

A growing proportion of devices are implants, including cardiac, orthopedic, and neurologic, and many of these are hybrids of pharmaceuticals, biologics, and IT (chips). Each implant has novel characteristics specific to the placement of the implant, the durability of the materials and mechanical processes, the reliability of electrical and chemical processes, and the clinical effects of the implants. Ample evidence of the complexities of these can be seen in the Coverage with Evidence Development model developed by the Centers for Medicare and Medicaid Services (CMS) for coverage of implantable cardiac defibrillators (Tunis and Pearson, 2006), or in concerns about the durability of neural stimulation devices implanted in the brain to treat benign essential tremor (approved by the FDA in 1997) and Parkinson's (2002).

Information and Communication Technologies

After many years of slow development and market penetration, investments in information and communication technologies and provider adoption are finally accelerating. Federal leadership has played a unique role in driving adoption since the 2004 presidential executive order that declared a national goal of a paperless health system within a decade (Bush, 2004). Consumer demand for access to personal health information has even fueled novel direct-to-consumer advertising of personal health records by health plans and technology vendors such as Microsoft. Spending on IT, including business processing and IT services is forecast to reach 23 percent of hospital budgets by 2011 (Modern Healthcare, no date).

At the same time, relatively few studies have evaluated the effects of investments in information and communication technologies on healthcare quality, patient experience, and resource utilization. Because information and communication technologies are largely unregulated, there is little reason for the developers of these technologies to conduct formal studies. What research is conducted tends to consist of small, uncontrolled time

series—evidence useful for marketing but inadequate for policy decisions. Even in the case of telemedicine (a highly effective series of innovations and set of technologies that support provider-to-provider systems of remote consultation and medical management), most studies have been small and, although favorable as a whole, have not driven significant adoption over the past two decades. This research has also been inadequate to the task of influencing public policy; despite strong evidence that telemedicine could play a critical role in solving national problems of access to care and the scarcity of health professionals, including beneficial effects on quality, patient and provider experiences and cost, it was not until 2000 that federal and state policies began to invest in the necessary infrastructure, provide reimbursement, and lift barriers to the deployment of telemedicine (Gutierrez, 2001).

IT is not a product in the same sense that a pill or a device is a product. Instead, it enables processes. By collecting, storing, retrieving, and displaying data, IT enables a wide range of important clinical and support or administrative processes. In many cases, therefore, the development of evidence regarding the impact of IT on clinical care, cost, patient and provider satisfaction, and other endpoints must measure not just whether a particular IT application is employed, but how the process has been adopted and adapted. Extraneous issues such as physician or nurse resistance, the degree of fragmentation of community providers, or the existence of other systems such as hospitalists, may influence results as much as the characteristics of the technology itself. Although these challenges are daunting, the need for evidence development is urgent because of the potential for systemic improvements in quality and cost (Middleton, 2005).

Wireless technologies are an excellent example of the challenges inherent in evaluation of IT that are designed for clinical or for administrative purposes, but result in improvements for both. Over the next half-decade, for example, wireless technologies will increasingly support critical clinical care processes and administrative tasks. Radio-frequency identification (RFID) was initially marketed for tracking equipment in hospitals and is now being extended to clinical targets such as medication management, the tracking of surgical sponges, and, in combination with computerized white-board systems, patient flow through emergency departments. In research designed to improve operating room productivity, RFID has also reduced the time required for surgeries and increased the proportion of staff time available for direct patient care in surgery and recovery. Other wireless communication devices enable improved response times and enhanced coordination of care. Most promisingly, new developments suggest that RFID in combination with electronic medical records can provide real-time assessments of compliance with clinical protocols and generate prompts to guide clinical practice. RFID is even useful in monitoring elderly patients

with cognitive disorders and will be marketed to caregivers for home use as well as to institutions.

Yet published, peer-reviewed evaluations of the impact of RFID-enabled systems are almost nonexistent. The companies that develop and sell RFID systems—and many emerging technologies—are generally small, with limited resources, and the slow penetration of these systems means that revenue expectations do not justify investment in larger studies. As Garber has pointed out, the expense of high-quality clinical trials is an "insuperable barrier" for many of these small companies, deterring them from entering the market despite superior products and creating a growing domination by large firms (Garber, 2006). Because more comprehensive studies are not available, furthermore, it is difficult to convince health plans and providers that the results will justify the costs and the challenges of managing disruptive change. From a health policy perspective this is a regrettable and self-reinforcing pattern of lost opportunities to improve the safety, quality, and timeliness of care, as well as patient satisfaction and efficiency.

As RFID applications are developed for clinical processes such as medication compliance, biosensor monitoring, and behavioral tracking, the complexity of assessments in a field of rapidly evolving and multiple functionalities will challenge policy makers. This is exacerbated by the continued reengineering and improvement of products, particularly of IT and devices, while clinical trials are proceeding. When a product does not "hold still," evidence regarding the effect of an earlier version of the product is of limited utility.

Transformative Technologies

RFID is only one of a growing number of products that enable, and depend for their effect upon, the redesign of important clinical and support processes. Some developers of emerging technologies, such as those that combine IT and devices for the monitoring and coaching of chronic disease patients, assert that their products should not be described as "technologies" at all, but rather as "services," because they require the ongoing participation of vendor-deployed or customer staff in reorganized care processes in order to achieve optimal impact.

It is easy to understand how such technology-enabled services differ from traditional pharmaceuticals or devices that are expected to perform in a defined manner, independent of ongoing provider care processes. This also explains why the results of such technology-enabled services often vary quite dramatically, even when the technology itself is consistently installed across a number of provider sites. The variation results from differences in the capabilities of the organizations using the technologies to restructure

their care processes and implement the necessary changes, which may include new roles for professionals and other workers, remotely operated systems, decision support, changes in care settings, and many other aspects of care.

Telemedicine, RFID, remote monitoring of chronic disease, the tele-ICU (remote monitoring of acute care), pharmacogenomics, hemofiltration for congestive heart failure, and remote video interpretation are just a few of the emerging transformative technologies that, if fostered, promise to advance the quality and efficiency of health care in America. While these technologies disrupt care processes and business models, they are not "disruptive" as Christensen has used this term (Christensen, 2006)[1] because they may be more expensive than the work processes or products they replace—while reducing net expenditures on health care—and are higher performing, because they frequently improve patient experience and clinical outcomes as well as economic performance.

Remote in-home monitoring of patients with chronic disease has yielded remarkable improvements in measures of self-management, in patient satisfaction, and in decreases in emergency services and hospitalizations. In studies of these devices used for uninsured, high-risk people with diabetes, for asthma in high-risk pediatric patients, and for adults with chronic diseases including hypertension, heart failure, chronic obstructive pulmonary disease, and diabetes, emergency room visits and hospitalization rates have dropped by one-third to one-half. In a recent report, Partners HealthCare found cost reductions of 25 percent. The New England Healthcare Institute estimates that utilization of remote monitoring by just 25 percent of appropriate patients with congestive heart failure would result in national savings of $500 million, and the Veterans Health Administration has deployed remote monitoring for more than 25,000 patients with multiple chronic diseases, and is continuing to expand the program (Pare et al., 2007).

Remote monitoring of chronic disease patients fundamentally enables providers to redesign care processes in order to comply more closely with evidence-based medicine. Like the "e-ICU" (tele-ICU) system for remote

[1]Christensen uses "disruptive" for technologies that are newer, less expensive, and lower performing than established products. The disruptive technology slowly encroaches upon and eventually replaces the established vendor through product enhancements. In contrast, transformative technologies are new, result in lower net health expenditures per episode or patient-year (although the new technology itself may be more expensive than established products), and are higher performing, that is, produce similar or superior quality (including the possibility of greater convenience or satisfaction for patients) while reducing net expenditures. A similar revision of the concept of disruptive technology was introduced in *Nanotechnology Now* in an ongoing discussion of the concept on Internet magazines and blogs: "Any new technology that is significantly cheaper than current, and/or is much higher performing, and/or has greater functionality, and/or is more convenient to use." See http://www.nanotech-now.com/disruptive-technology.htm.

management of intensive care units (ICUs), RFID tracking of care, and many other transformative technologies, its successful use depends greatly on organizational capacities for change management, clinician support, and reimbursement systems that can protect the providers and provider organizations against financial losses.

For pharmaceuticals, biotechnology, and devices, the FDA and CMS have markedly improved the clarity of evidence requirements and thresholds for approval and coverage. In the case of most transformative technologies, however, there is no concomitant delineation of research targets and criteria for public and private coverage and reimbursement. Many companies developing transformative technologies are small, and the limited resources they can devote to trials of their products are frequently wasted on studies that provide convincing evidence of quality and cost improvements but fail to address key issues of concern to employers, health plans, hospitals, or physicians. There is a critical need, therefore, for new processes that will link purchasers, payers, clinicians, and the developers of technology in efforts to define research targets and to pursue an iterative agenda of evidence generation, product and process improvement, and coverage and reimbursement.

In defining research targets, such a collaborative process will also stimulate even greater innovation to improve the performance of technologies against those targets, spurring the proliferation of products within each category and the rate at which each individual technology evolves. Of course, technologies within a single category often vary enough to make studies of one product only suggestive of the effect that others in the same category might have. Green has an interesting perspective on this, based on evolutionary theory: "Evolution passes, at times, through innovative cycles of progress—when diversification of design leads to perfections of form—with the concomitant production of many unsuccessful models." In the evolution of device designs for total knee replacements that began in the 1960s, for example, "some of these implants are, by modern standards, bizarre-looking." Yet, "not surprisingly, all total knee replacement implants now resemble the normal knee and consequently are difficult to distinguish from each other" (Green, 2001).

This has useful implications for research and regulatory policy, particularly with regard to the evaluation of transformative technologies. Our current processes of research, regulatory approval, and coverage and reimbursement decisions are highly linear. With an evolutionary approach to evidence generation and assessment, this would be supplemented in certain cases by iterative, coordinated, and proactive efforts to evaluate and foster technologies that will advance national goals of quality, efficiency, and improved patient experience.

An early demonstration of this approach has been piloted as the Fast

Adoption of Significant Technologies (FAST) by the New England Healthcare Institute, in collaboration with the Health Technology Center and the Massachusetts Technology Collaborative (New England Healthcare Institute, 2007). FAST was established to create and test methods by which healthcare payers and providers can actively accelerate the adoption of advanced technologies that lower costs and improve quality. Stakeholders, including federal and private policy makers, purchasers, payers, and users, have been convened to investigate the potential of classes of emerging technologies to enable major improvements in the quality and efficiency of health care. Because technologies and services typically evolve rapidly in early stages, the initiative focuses on classes of technology rather than single products, seeking technologies that address a substantial patient population; significantly improve patient outcomes; reduce the overall costs of care; manifest low market penetration for high-value uses; and are constrained by barriers to broader dissemination that can be addressed by the stakeholder group.

In the first two rounds of screening for candidate technologies, more than 30 technologies were reviewed; five have been selected for further analysis to determine whether the evidence regarding clinical benefit and cost reduction is sufficient to cause the stakeholders to engage in efforts to reduce barriers to its adoption. In the case of one such technology, the tele-ICU, stakeholder advocacy has resulted in a statewide initiative to implement e-ICU networks across Massachusetts. In another, the New England Healthcare Institute has joined with the Partners HealthCare Telemedicine Department and public and private payers in a demonstration of home-based remote patient management to provide additional quality and cost outcomes data and illustrate how to effectively structure reimbursement to providers who offer the service. As progressively more rigorous tests of these evolving technologies demonstrate their contributions to net savings, as well as quality enhancements, the strategies to support coverage and reimbursement can become more focused and intensive.

Stakeholders should expect multiple products to emerge in each category of transformative technologies and individual products to evolve rapidly as research suggests opportunities for redesign. As in earlier proposals for post-market surveillance, research will have to be iterative in order to test the potential of emerging technologies across a variety of care settings and applications. Active involvement by stakeholders, their clear definition of targets that correspond to value, and their commitment to support the coverage and reimbursement for technologies that reach target thresholds will create a market for those technologies and stimulate further investment in research and development.

Transformative technologies have often been "orphan technologies," because they are disruptive, developed by small companies with limited re-

sources for research and marketing, and ignored by purchasers. In the case of orphan pharmaceuticals, the public realized that technology evaluations designed to protect them from harm did not reliably advance valuable technologies through testing and deployment, largely because of weak business incentives for investment in research and development. Few transformative technologies rise to the level of urgency felt by individual patients who believe that they are prevented from accessing lifesaving treatments, despite the fact that some transformative technologies actually do save lives (tele-ICU reductions in mortality rates) and lessen the burden of illness (remote monitoring of chronic disease reductions in hospitalization and improvements in functionality and satisfaction).

It falls to purchasers, payers, providers, and policy makers, then, to craft new approaches to evaluate and simultaneously foster the development of transformative technologies. The critical role that technologies will play in enabling the delivery of evidence-based medicine was anticipated by the IOM in *Crossing the Quality Chasm*: "Carefully designed, evidence-based care processes, supported by automated clinical information and decision support systems, offer the greatest promise of achieving the best outcomes from care for chronic conditions" (IOM, 2001).

In the decade ahead, the most notable contributions to improvements in healthcare quality and efficiency will be these—innovations in IT or combinations of IT with portable or implanted devices such as sensors or drug dispensing systems. Pharmacogenomics or biomarkers will be the leading exception to this phenomenon, and presage the emergence of biotechnology as the dominant source of enhanced value in health care in the next decade. In both cases, the challenge remains: to generate the evidence needed for critical evaluations of emerging technologies, without failing to identify and foster technologies that may be significant sources of benefit.

RAPIDLY DEVELOPING INSIGHTS INTO GENETIC VARIATION

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The underlying biological processes responsible for individual risk of disease remain poorly understood. It was recognized early in the 20th century that inheritance contributes substantially to the risk of diseases in the population. In the 1980s tools and methods made it possible to identify genes for rare disorders caused by mutation of a single gene. These studies taught us that an unbiased genetic approach most often identifies causal processes that were unexpected based on other methods of investigation. Understanding the genetic basis of common diseases remained intractable, however, until recent approaches from genomics and genetics made possible the systematic study of genetic variation across large patient samples. In

2007 alone, more than 75 genetic risk factors for common diseases were found, tripling the number known going into that year.

Progress in identifying the genetic causes of common diseases holds great promise for catalyzing a new understanding of pathophysiology: the information is unbiased with regard to prior hypotheses, is based on human rather than model systems, and reflects a causal rather than a reactive process (genotypes are assigned during the randomization event of meiosis and are unchanged by lifestyle and disease). In contrast, genetic testing for such variants is of uncertain value for the individual patient and the healthcare system, because in vivo biological relevance does not necessarily imply clinical utility.

The role of genetics in common diseases is going to be quite different from the traditional experience with Mendelian diseases such as Huntington's disease. In the case of single-gene disorders, the mainstay of genetic medicine for many years, prediction is powerful. Mendelian diseases were selected for study precisely because mutation of a single gene was necessary and sufficient to cause the disease. They were studied not for their genetic similarity to common diseases (it has long been clear that most diseases are polygenic and environmentally mediated), but because they were of great importance to the rare families that carried them and were amenable to research.

Thousands of Mendelian discoveries were made before general progress in common diseases, leading physicians and the public to attribute great explanatory power to genetic information. Moreover, there is a sense in the population that genetic causes of disease are hard to modify with lifestyle or treatment. This, too, is circular reasoning: the diseases were targeted for study precisely because they are Mendelian—that is, that modifying genes, environment, and behavior has at most modest ability to alter the outcome. These two factors have led to widespread overestimation of both the power of genetic prediction and its intractability to therapy.

The Role of Genetics in Common Diseases

In contrast, common diseases are not solely determined by genes, but are modifiable by other factors. Moreover, it has long been clear that the inherited contribution to disease is itself divided across multiple genes. Initially, researchers used the same methods so successfully applied to Mendelian diseases, hoping that only a few genes would explain a sizable percentage of the risk for diseases such as diabetes, schizophrenia, and heart attack. The failure of this method indicated that there must be many individual genetic contributors that together explain the fraction of risk attributable to genotype. With many genes each contributing, it was clear

that the genetic causes of common diseases would never be predictive in the manner of Mendelian diseases.

The polygenic nature of common diseases made it difficult to identify any single genetic variant that was reproducibly contributing to risk. Initially, investigators tried to stack the deck in their favor, focusing on studies of candidate genes—those previously hypothesized to play a role in pathophysiology. While there were many claims of success, few proved reproducible. This was due to some combination of underpowered studies, overly loose statistical standards for claiming a positive result, and (as it has turned out) the presence of few true genetic risk factors in previously identified candidate genes.

Based on the failure of these earlier approaches, a variety of tools were developed to enable a simple but comprehensive association study approach for the role of common genetic variants in common disease. The approach was built on the human genome project and efforts to characterize and catalog human genetic variation. Using these methods, it is possible to compare the genetic makeup of patients with a particular disease to that of people who lack the disease. Samples can be drawn from populations or from families, and researchers can try to determine particular genetic variants that track with the disease. These approaches were first proposed in the mid-1990s, but a decade passed before they could be tested in their generality.

In the last 2 years, as these tools have come online, more than 75 bona fide genetic contributors to common disease were reported in the literature. These were spread across more than 20 common diseases, including Type I and Type II diabetes; cholesterol levels; heart attack; rheumatoid arthritis; lupus; age-related macular degeneration; prostate, breast, and colorectal cancer; and many others. In multiple diseases, 5, 10, or even more individual genetic variations have been found. Despite the fact that only the most common genetic variants have been tested, many new clues have been identified in terms of genetic risk factors for common diseases.

In some cases, the discoveries have instantly yielded biological clues. For example, age-related macular degeneration is a typical, common disease among perhaps 5 percent of the population. Previous approaches of human genetics research had not yielded any results for specific genes or mutations that were robust and reproducible. However, in the last few years, at least four or five common genetic variants that been identified that have twofold or greater effects on population risk.

Everybody carries some combination of these genetic variations. In the aggregate, more than half of the risk for age-related macular degeneration is inherited. These genetic variations explain a difference in risk among individuals of more than a hundredfold (Figure 3-3).

The importance of these findings is deeper than simply a predictive test: four out of the five genetic risk factors found are in fact complement

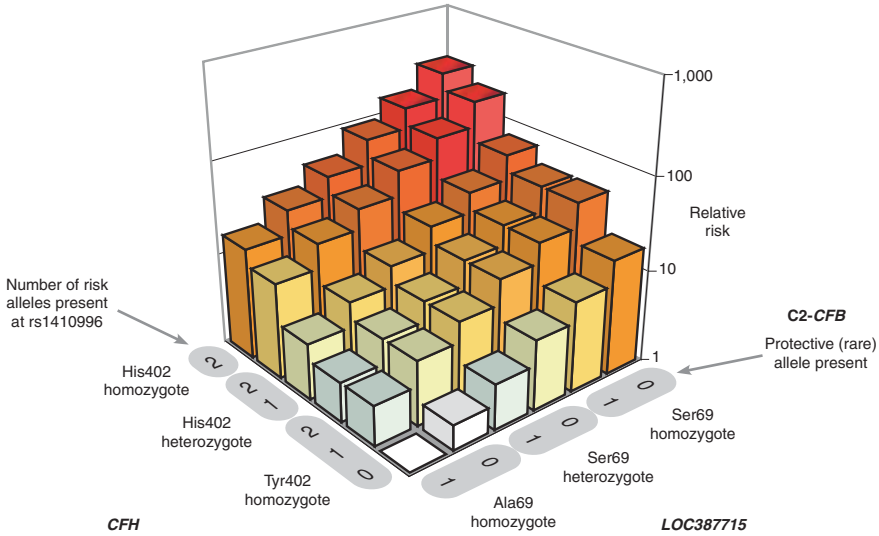

FIGURE 3-3 Age-related macular degeneration and common variants in complement factors.
SOURCE: Maller et al., 2006.

factors, providing a new insight into the pathophysiology of the disease. Many thousands of papers have been published on age-related macular degeneration and on complement factors. Yet prior to these unbiased genetic studies, none of those papers had proposed that complement factors were the underlying biological cause of age-related macular degeneration. Common single-letter changes in one complement factor influence risk by fivefold or more. This biological insight suggests that targeting the complement pathway might be valuable in arresting the underlying pathophysiology and even preventing the disease in the first place.

Similarly in Crohn's disease, more than a dozen genetic risk factors have been identified. Two themes have emerged: defects in innate immunity and in autophagy. Autophagy is a well-studied process, but its relevance to inflammatory bowel disease was not appreciated. With unbiased, genome-wide scans highlighting the role of autophagy, investigators immediately had a target pathway with in vivo human relevance. Colleagues at Massachusetts General Hospital, the Broad Institute, and Dana Farber Cancer Institute were already working on autophagy drug development for myeloma when this discovery was made in Crohn's disease. The new link provided by genetics allowed investigators to very rapidly bring their forces together in a way that otherwise might never have occurred.

Genetic research surrounding another common disease, Type II diabetes, suggests a primary role for beta-cell dysfunction. Both the Mendelian and the common forms of Type II diabetes are characterized by defects in insulin secretion, but to date not in insulin resistance. While this in no way argues against the role of insulin resistance, it has highlighted for many investigators the central role of beta-cell function in the pathophysiology of Type II diabetes.

Determining the Value of Genetic Information

Each of the newly localized genetic variants is common, so they are present in a substantial proportion of patients. Moreover, it is simple to test a patient to determine whether or not he or she carries these genetic risk factors. Whether this information is useful is much less clear. First, the risk attributable to the newly found genetic variations is typically very modest. For the most part, the individual risk factors found have effects of between 10 and 50 percent increase in risk per copy. Because there are multiple genetic variances, the aggregate risk is greater than any individual one, but nonetheless it is a far cry from the hundredfold or thousandfold risks of Mendelian mutations.

A key challenge will be to determine whether and how clinical testing for such genetic variations can be used to improve patients care. For Type II diabetes, we set out to evaluate this question with colleagues in the Diabetes Prevention Program (DPP) and Massachusetts General Hospital. The DPP is a landmark study of diabetes prevention, involving 5,000 people with impaired glucose tolerance. This randomized trial showed that intensive lifestyle change, or treatment with metformin, could substantially reduce the rate at which patients developed Type II diabetes over the course of the trial.

The study examined in the DPP a gene called TCF7L2, originally identified by deCODE Genetics, which has the largest effect of any single common variant yet described in Type II diabetes. In the DPP we found that patients with the high-risk homozygous genotype—about 5 to 10 percent of participants—had about double the risk of contracting Type II diabetes than otherwise identical patients who did not have the high-risk genotype.

Because the DPP was both a multiethnic sampling of the U.S. population and prospective, this result validates that measurement of the TCF7L2 genotype does convey predictive information above and beyond standard clinical measures. However, an even more interesting finding was that the lifestyle intervention was as effective in the high-risk genotype group as in the population as a whole (Figure 3-4).

These results offer a hopeful message—that genes are not destiny and that a patient should not give up on lifestyle changes because he or she

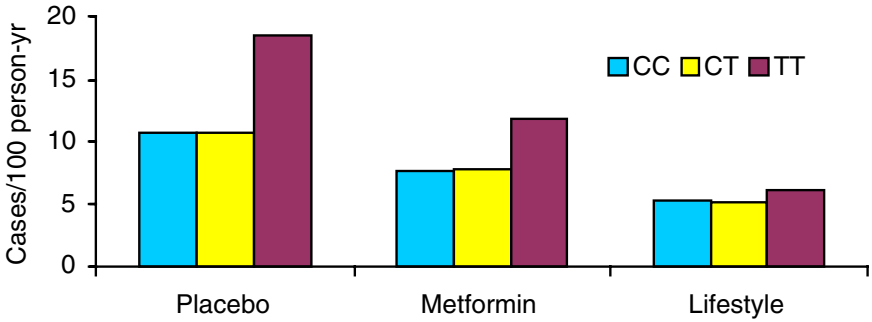

FIGURE 3-4 TCF7L2 and risk of T2D in Diabetes Prevention Program.
SOURCE: Data derived from Florez et al., 2006.

thinks the genes will defeat them. In addition, the value in testing for this gene becomes questionable, since the vast majority of patients with Type II diabetes do not have the high-risk genotype and they would benefit from the lifestyle intervention as well. This past summer, however, the discoverers of TCF7L2 began advertising it to physicians as a tool for patients. They argued—based in part on the DPP study—that patients who got the TCF7L2 test were at greater risk genetically for developing Type II diabetes and would change their lifestyle once they learned of this risk. They further assumed that those who tested negative for TCF7L2 would not change their behavior; thus, only good would come of it.

Of course, these assumptions apply to some people. If told they are at higher risk, they will work harder to prevent the disease. If they are told they are not at higher risk, they will understand that they are not fully protected and will maintain their lifestyle as well. Yet others are likely to respond in an unpredictable manner. For example, some people may overinterpret a positive result, believing that genes are destiny, and perhaps feel discouraged from working hard to prevent the disease. Others who have a negative test may overestimate how protected they are. There is simply no way to know how people will react without more research.

Clearly, if evidence-based use of genetic tests is desired, clinical research is needed in particular, to determine how exposure to such information impacts individual behavior, health outcomes, and healthcare utilization. The most rigorous design would be clinical trials in which study participants are randomized to receive genetic information or standard care and outcomes are then compared.

Performing such trials is going to be extremely difficult, particularly because of the lack of incentives and the rapidly changing nature of the tests. Traditionally, clinical trials are driven by incentives such as being able

to sell a drug. It is not clear that the financial rewards for selling genetic tests could support expensive clinical trials. Moreover, genetic information is changing rapidly, and any given clinical trial of genetic information will likely be out of date (superceded by a more informative version of the test) before it is complete. These are difficult challenges, and it is hard to think of solutions that do not carry their own risk of slowing down progress and the availability of information that the public may want.

In conclusion, there has been rapid progress in identifying genes and DNA variations that influence common human diseases. The long-term value of this research will, I believe, be in its unique ability to take an unbiased look at causes of common diseases in humans. The biological understanding gained will be a basis for progress, and my hope is that it will lead to improved prevention and therapy.

In the meantime, however, the typing and hyping of genetic information and so-called personalized medicine have already begun. In my view, this is a much more uncertain enterprise, and if we are not careful we may never know its real value, because it will become a routine part of health care before we know whether it actually helps to improve people's lives.

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4

Contending with the Changes

INTRODUCTION

As new and more complex medical interventions are developed and scientific knowledge about disease origins and progression continues to expand, the healthcare system will need to adopt approaches that ensure evidence generated is relevant to real-world patient populations and is incorporated effectively into clinical practice. Essential to these approaches will be new roles and responsibilities for the patients and providers at the front lines of care. Anticipated shifts in the behaviors, beliefs, and practices of these stakeholders are described in this chapter.

Because of the overwhelming amount of new evidence and information that healthcare providers must incorporate into their practices, William W. Stead suggests that the healthcare system will shift from expert-based practice, which is built around the extensive knowledge and experience of the physician, to a systems-supported practice centered on teams supported by well-defined processes and information technology (IT) tools. While both approaches rely on evidence for decision making, the difference is in how evidence is translated into action. Stead describes how this approach has been used at Vanderbilt University Medical Center (VUMC) to improve care of patients on ventilators and discusses the major barriers inherent to health care that might limit broader implementation of this approach, and possible solutions.

In his paper, Marc Boutin highlights the diversity of patients, each with differing life circumstances, cultural needs, preferences, and socioeconomic status. Broader acceptance of evidence-based medicine (EBM) will require

an evidence base that appropriately accounts for these differences, and better communication to patients on the importance of best evidence in healthcare decision making. Strengthening the patient-provider relationship is also essential to ensuring the use of EBM results in the best medical outcomes and closes the quality chasm across geographic regions, treatment settings, and patients' socioeconomic levels.

BEYOND EXPERT-BASED PRACTICE

William W. Stead, M.D., and John M. Starmer, M.D.[1]

Introduction

Most healthcare providers believe their practice is evidence-based. Their education includes the scientific basis of health and disease. They have been trained to use scientific literature to compare alternative approaches to diagnosis and treatment. They do their best to stay up-to-date through reading and conferences. Yet despite their attention to evidence, studies repeatedly show marked variability in what healthcare providers actually do in a given situation. When challenged about why they do not practice consistently, healthcare providers point out that health care is both art and science. Explicit evidence is available for only a portion of what they do.

Instead of focusing on the use or non-use of evidence, we contrast expert-based practice to a systems approach to practice. Both approaches use evidence. The difference between the approaches is the way in which the evidence is translated into practice. We provide a framework of steps for developing, using, and iteratively improving a systems approach to practice. We provide examples using VUMC's approach to ventilator management. We conclude with implications of our experience with a systems approach to practice for healthcare workforce and infrastructure policy.

[1]This paper presents ideas developed through VUMC's efforts at the intersection of quality improvement, evidence-based medicine, and informatics. C. Wright Pinson has provided executive oversight for quality, and Nancy Lorenzi has facilitated the informatics components of quality. Larry Goldberg and Marilyn Dubree provided executive leadership for the ventilator management initiative. Lee Parmley and the Critical Care Committee provided medical direction for ventilator management. Devin Carr prototyped change in nursing practice for ventilator management. John Bingham and the Center for Clinical Improvement supported process mapping and performance audits. John Doulis and the Informatics Center developed information technology tools.

Expert-Based Practice

In expert-based practice, the focus is on the individual's performance. The individual expert provides extensive knowledge and technical skill based on education and experience. The individual expert is expected to remember facts, assimilate data, recognize patterns, judge, and make decisions wisely. The individual expert's opinion is valued. Disagreement among experts is expected. The result is no better than the performance of the individual expert. The individual expert is responsible for recognizing and learning from his or her mistakes.

System-Supported Practice

In system-supported practice, the focus is on the system's performance. Teams of people, well-defined processes, and information technology tools work in concert to produce the desired result consistently. People provide compassion, pattern recognition, and judgment. Well-defined processes standardize and simplify work flow. IT tools decrease dependence on memory and force action when needed. Agreement among individuals is required. The desired result is expected every time. Each failure feeds back to support just-in-time correction or iterative adaptive design. The system of behaviors, processes, and tools makes it easy for the individual to do the right thing every time.

Figure 4-1 depicts our systems approach to practice. The left-hand circle represents cycles of iterative system development and refinement. We focus our efforts by working on one population at a time. By population, we mean every instance of the circumstance that we want to manage to a consistent outcome, such as patients on a ventilator. A patient is likely in multiple populations at once. The first system development step is selection and definition of a high-priority population to target. A population might be high priority because of risk for morbidity or mortality, such as patients with central lines who have a high incidence of nosocomial bloodstream infection. Another population might be a priority because of opportunity to reduce cost by streamlining throughput, eliminating unnecessary procedures, or using more cost-effective drugs. We try to make the definition of the population explicit. This definition consists of the environmental, clinical, or procedural characteristics that collectively frame the circumstance we want to manage consistently. We restrict the definition to characteristics that are present in our information systems or can reasonably be obtained through supplemental manual audit. Once we agree on such a definition, we can identify each member or instance of the population across our enterprise.

The second system development step involves gathering the evidence

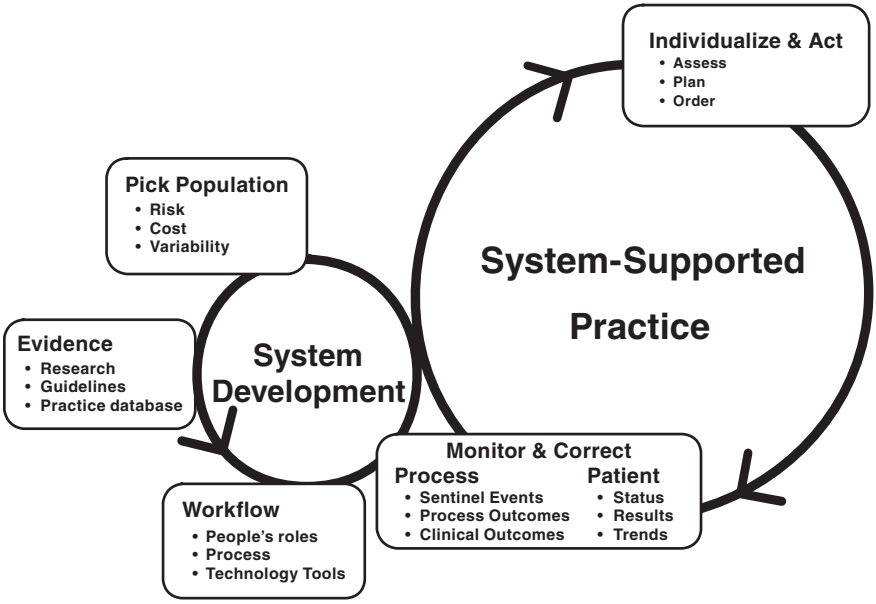

FIGURE 4-1 The systems approach to practice joins system development to system-supported practice. The left-hand circle represents the four steps in each iterative cycle of system development. The right-hand circle represents the two steps in each cycle of system-supported practice.

related to that population into a common fact base. We look for three types of evidence. We search the literature for clinical trials related to the target population. We obtain consensus practice guidelines related to the population from the literature and from sources such as the University Hospital Consortium (UHC) and quality improvement organizations. We obtain the pathways, protocols, and order sets from our practice groups that relate to the target population. We reduce this information into a table with a row for each explicit practice related to the target population and a column showing the recommendations for each practice for each of the above sources. This table highlights variance in available evidence. We then charge a core team of subject matter experts to develop a "straw person bundle" for use across the enterprise. The bundle is a set of standardized practices with specific process steps and measures of performance for each practice. The core team also drafts one or more overarching idealized processes that would result in consistent execution of the bundle. The core team is not a representative consensus-forming body. Instead, it is as small as possible while bringing critical information to the table across medicine, nursing,

ancillaries, etc. These individuals work as a team, viewing each member as a partner in the solution, rather than as representative of an area. We complete the common fact base by documenting the performance of our units or practice groups against the "straw person" set of standardized practices through either electronic or manual spot audit.

The third system development step makes the jump from the shared fact base to cross-enterprise agreement. This agreement includes a set of standard practices; metrics to assess performance on each practice; explicit definitions for both practices and metrics; simplified standard work flows to implement the practices; IT tools; staffing and education; and implementation time line. When the needed agreement cuts across disciplines and care settings, we take time out for a day of cross-enterprise design. We bring together executives that will have to approve change in policy or resource allocations, medical and nursing leadership of each affected practice group or unit, representatives of affected ancillaries and subject matter experts from clinical areas, quality improvement process, informatics, and finance. After sharing the fact base, we identify points of disagreement and use breakouts to work alternative solution designs. We constrain the design by restricting suggestions to ideas that can be implemented across the enterprise in 6 weeks to 3 months. Longer-term suggestions are noted and parked for future consideration.

The fourth system development step involves monitoring performance at the population level and iteratively refining the system of practice as needed. Sentinel events are monitored as early indications of unexpected problems during the rollout of changes. Metrics provide an early indicator of where we are and are not achieving reproducible performance on the set of standard practices, and we adapt education, tools, or process as needed.

The rapid cycle iterative nature of the system development steps cannot be overemphasized. For example, an initial population definition focuses an initial search for evidence. Our review of the evidence may suggest modification of the population definition followed by a revised search for evidence. Similarly, the bundle of practices developed from the evidence guides the initial audit of our performance. Our review of the audit may feed back suggestions for refinement in the bundle.

The right-hand circle of Figure 4-1 depicts the related iterative cycles of system-supported practice in the care of an individual patient. System-supported practice is not cookbook medicine. At the start of each cycle, the clinical team assesses the patient, develops or refines the plan of evaluation and care, and orders the next actions. As a patient matches the definition for one or more of the populations for which we have developed a systems approach, the clinical team is alerted and prompted with orders appropriate to implement the related standard practices. As they round, they are shown

the status of each of their patients on each of the standard practices (Stead et al., In press). As they start the next cycle of system-supported care, they take corrective action as needed in addition to updating the plan and orders to reflect new information and trends.

To this point, our system development steps yield reliable execution on standard practices reflecting the literature and consensus. These practices may or may not actually be the right thing to do. Even if they are, they will get out of date as the biomedical knowledge base changes. In time, we expect our systems approach to practice to become self-correcting as we add indicators of good and bad clinical outcomes to the metrics of performance on the standard practices for each patient. Whenever the clinical team elects to vary from the standard practice, in effect it creates an experimental group. If outcomes of that group appear better, or even no worse, we will be able to do targeted clinical trials leading to change in the set of standard practices if appropriate. In addition, whenever clinical outcomes for a population deteriorate or diverge in the wrong direction from external benchmarks, we will know to reassess the standard set of practices for that population.

Example of Expert Management of System-Supported Practice

VUMC selected the ventilator management bundle as one of the test cases for our systems approach to practice. The following examples from that work are presented to highlight the gap between the available evidence and the set of standard practices needed to consistently produce the desired result. We also provide examples of decisions by the experts as they manage the cycles of system development and apply judgment within the resulting system-supported practice. We show how IT can decrease dependence on memory and provide a forcing function to help close the gap between intent and execution. Throughout the examples, we provide an indication of the number of people involved and the elapsed time.

We selected the ventilator management bundle as a test case for our systems approach to practice because of evidence of high morbidity and mortality associated with ventilator-acquired pneumonia (Bueno-Cavanillas et al., 1994; Girou et al., 1998); evidence linking specific practices to reduction in risk for (Ibrahim et al., 2001) or incidence of (Doebbeling et al., 1992; Thompson, 1994) ventilator-acquired pneumonia; and use of ventilators by several specialties in many units across our enterprise. Past VUMC initiatives had focused on tracking ventilator-acquired pneumonia and unit-specific practices to reduce the incidence. Our approach this time was different in that we started with three executive-level agreements. We would not focus on ventilator-acquired pneumonia. Instead, we would focus on cross-enterprise agreement on a bundle of well-defined standard practices

for ventilator management, on how we would measure performance, and on the processes we would use to quickly achieve consistent performance house-wide. These decisions sidestepped pitfalls such as clinical arguments about what does or does not constitute ventilator-acquired pneumonia and the tendency to say why a unit is unique instead of what units have in common. The constrained time horizon forced people to think of simple solutions instead of requesting complicated support systems to get better results without having to change what people do.

In this test case, the definition of the population was straightforward, a VUMC inpatient on a ventilator. Although aspects of ventilator management involve multiple information systems, nurse charting provides a single source for an up-to-date indicator that a patient is currently on a ventilator. We made the executive decision that we were ready to launch the effort in mid-December 2006 and assembled the core team just after the holidays. Since this effort was a cross-enterprise test case, the initial core team included the corporate strategy and nursing officers and the chief executive officer of the adult hospital. The chair of the Critical Care Committee, a physician, and the nurse director of the Surgical Intensive Care Unit, together with leaders from Clinical Improvement and Informatics, completed the team. Over the course of January, that team oversaw the compilation of the common fact base, obtained initial agreement of the medical directors of the nine intensive care units on the set of practices to include in the bundle, and identified the people to include in the cross-enterprise design day. The key decisions during this phase of the system development work included affirmation of the focus on the bundle of standard practices instead of the incidence of ventilator-acquired pneumonia; selection of goal-directed sedation monitored by the Richmond Agitation Sedation Score (RASS) (Thompson, 1994) as an alternative to sedation interruption since the latter is inappropriate for certain patients such as those with extreme burns; and preference for house-wide implementation of the bundle instead of unit by unit.

On the last Saturday in January 2007, 45 individuals from across VUMC participated in the cross-enterprise ventilator bundle design day. This group included medical and nursing leadership from each unit, post-graduate fellows, front-line nurses, pharmacy, respiratory therapy, infection control, nurse educators, informatics, evidence-based order set development, decision support and order entry, clinical documentation, business analytics, process reengineering, process audit, chief quality officer, and executives from the core team. Their objectives included a common understanding of the fact base; refined agreement on the set of practices; specific process steps and measures for each practice; and identification of the IT tools, education, and staffing needed for consistent execution. This design work was constrained to solutions that might be implemented house-wide

by mid-March. We were able to agree on cross-enterprise practice standards by decomposing high-level guidelines into components and agreeing on an approach to each component that is both supported by evidence and practical in our environment. For example, we replaced the UHC-recommended standard of oral care, defined to include everything from teeth brushing to supra- and subglottic suctioning, with three VUMC standard practices (oral swabs, teeth brushing, and hypopharyngeal suctioning). The more granular approach permits more focused accountability, performance measurement, and refinement over time. In addition, when the standard practice should change with patient condition, we made the criteria for branch points explicit. Practices requiring patient-specific variation ranged from stress ulcer prevention to goal-directed sedation. We agreed on which team role would be responsible for specific actions. For example, the physician should order and reassess the target RASS, and the nurse should assess the patient's condition against that target. We identified two ways our IT tools could support the clinical teams.

We would use a modular order set (Figure 4-2) to present the bundle of standard practices, together with definitions or patient-specific criteria directly in clinical work flow, and use exit checks for reminders if something was missed.

In addition, we would create a process control dashboard, as illustrated in Figure 4-3, with a line for each ventilator patient on a unit and a column for each element of the bundle, with a red, yellow, or green (gray scale in figure) square to indicate the status of the patient for that element.

Finally, we identified the teaching materials needed to support the change to the bundle of standard practices.

Over the course of February and March, work proceeded according to the time line from the design day. Since the cross-enterprise agreements were in place, the executives dropped off the core team to let the work proceed close to the action. Order sets were revised and education materials developed and distributed. However, we did not get traction until the process control dashboard was available in mid-May. At that point, any members of the team could see where action was needed as they walked onto the unit. As people began to question the many red squares on their unit, the core team was able to decide if the problem reflected a poorly defined standard practice, education, the documentation used to derive the status of a patient relative to a practice, or the algorithm used to calculate whether the status was acceptable (green), trending out of control (yellow), or unacceptable (red). By early September we felt we had reached a point of face validity and decided to launch a targeted education effort to close additional performance gaps.

All of our work to date has involved starting from the evidence base and developing the agreements and infrastructure to achieve consistent per-

(a)

Vanderbilt Medical Center
Hearts and Minds

EvidenceWeb
Order Set Display

Mechanical Ventilation Orders
Last modified: 2007-03-13 14:25:27

1. **VENTILATOR SETTINGS** CONTIN
   + **NURSING:** initiate ventilator associated pneumonia (VAP) weaning protocol (daily assessment of readiness to extubate)
2. **DVT PROPHYLAXIS**
3. **ICU Stress Ulcer Prophylaxis orders**
4. **SPECIFY TARGET RASS**
5. **ICU SEDATION PROTOCOL**

Nursing

6. **ELEVATE HOB** 30 degrees or greater
7. **mouth care q2h per VAP protocol** q2h per vap protocol
   + **NURSING:** Brush teeth q shift; oral suction swabs q2h; apply water -soluble mouth moisturizer PRN

(b)

ICU Stress Ulcer Prophylaxis orders
Last modified: 2007-03-13 13:43:07

With Gastric Access, (-) Gross Blood

1. **pepcid 20mg PT q12h; adjust for renal impairment** 20 mg per tube q12h

With Gastric Access, (+) Gross Blood

2. **LANSOPRAZOLE SOLU-TAB:PREVACID** 30 mg per tube q24h NOW (*Place tab in syringe with 10 ml water; shake gently and inject via enteral tube; flush with 5ml water*)

Without Gastric Access, (-) Gross Blood
***If TPN*:**

3. **pepcid 40mg q24h to TPN; adjust for renal impairment** 40 mg iv q24h (*Add to TPN Daily*)

***If NO TPN*:**

4. **pepcid 20mg iv q12h; adjust for renal impairment** 20 mg iv q12h NOW

(c)

Please select the target Richmond Agitation Sedation Scale (RASS) value for ZTESTWIZ, FEMALE19YR

Target RASS Value	RASS Description
0 Alert and Calm	
(•) - 1 Drowsy	Not fully alert, but has sustained awakening to voice (eye opening/contact **> 10 seconds**)
( ) - 2 Light Sedation	Briefly awakens to voice (eye opening/contact **< 10 seconds**)
( ) - 3 Moderate Sedation	Movement or eye opening to voice (**but no eye contact**)
( ) - 4 Deep Sedation	No response to voice, but movement or eye opening to physical stimulation
( ) - 5 Unarousable	No response to voice or physical stimulation

Submit Order Exit Without Ordering

FIGURE 4-2 (a) Ventilator management order set with a module for each element of the VUMC bundle of standard practices. (b) Expansion on selection of stress ulcer prophylaxis. (c) Expansion on selection of Target RASS.

Bed	Patient name	Age	LOS	Orders			Vent	SBT Scrn	SBT Trial	DVT	SUP	RASS Ord.	RASS Pt.	HoB	swab	teeth	hyS'x
3002B	T, V W	72y	6 d		flowsheet	MAR	v	F		v	v	-4	-4	30			
3003X	N, D	60y	17 d		flowsheet	MAR	v	F		v	v	0	-2	45			
3004B	T, P L	64y	34 d		flowsheet	MAR	v			v	v	-1	-1	30			
3005A	C, D E	61y	7 d		flowsheet	MAR				v	v	0	-1	30	v	v	
3005B	B, J	66y	7 d		flowsheet	MAR	v	F		v	v	-1	-3	30			
3006X	W, A A	20y	66 d		flowsheet	MAR	v			v	v	-1	-2	30			
3007X	W, L E	49y	9:14		flowsheet	MAR				v		0	-1	30			
3008X	P, J L	69y	50 d		flowsheet	MAR	v	F		v	v	0	0	30			
3009X	R, C	72y	15 d		flowsheet	MAR	v	F		v	v	-1	-2	30			
3011A	P, J E	88y	9 d		flowsheet	MAR				v	v	0	0	45	v	v	
3011C	J, W D	69y	2 d		flowsheet	MAR				v	v	0	-1	30			
3011D	P, P J	55y	10 d		flowsheet	MAR	v	P	P	v	v	0	-3	30			
3011E	R, R E	74y	9 d		flowsheet	MAR				v	v	0	0		v	v	
3011F	N, E Y	55y	3 d		flowsheet	MAR				v	v	-1	0	30	v	v	
3012A	S, J D	56y	14 d		flowsheet	MAR	v	F		v	v	0	0	30			
3012B	R, M	63y	10 d		flowsheet	MAR	v	F		v	v	-2	-2	30			
3013A	N, B D	60y	8 d		flowsheet	MAR	v	F		v	v	-3	-2	30			
3013B	H, S M	66y	16 d		flowsheet	MAR				v	v	0	-1	30	v	v	

FIGURE 4-3 Process control dashboard.

formance on standard practices. The next step will add outcomes such as time on mechanical ventilation, unplanned extubations, failed extubations, and complications (pneumonia, stress ulcer, and deep venous thrombosis) to the measures of process performance. This outcome feedback will in time provide the evidence to guide continued refinement of the standard practices.

Implications for Healthcare Workforce and Infrastructure Policy

The demise of expert-based practice is inevitable. The complexity of biomedical information and technology will increasingly overwhelm an individual expert's cognitive capacity. Specialization is not an answer because of the accompanying fragmentation. Fragmentation is incompatible with the personalization of care that is becoming possible with progress in genomics and systems biology. Even if its demise was not inevitable, we would want to move beyond expert-based practice. Other industries have shown that a standard process is the key to consistently producing the desired result. There is no reason to believe that health care can be an exception to this rule. A process that varies on a case-by-case basis accord-

ing to the opinion of individual experts will not consistently produce the desired outcome.

The move beyond expert-based practice is not straightforward. Health care differs from other industries in three ways that make transfer of approaches to standardization difficult. First, the manufacturing plants or services of other industries handle fewer inputs and outputs than their counterparts in health care. For example, a microchip fabricating plant has limited inputs that are translated into limited outputs through a limited number of manufacturing processes. Most healthcare facilities and services handle much greater variety. For example, an emergency department handles all comers, even if only to stabilize and transfer patients beyond their capability or to treat and return to primary care those patients whose problems are non-emergent. Highly specialized healthcare facilities have achieved consistent performance by limiting services to a few related clinical conditions and mimicking manufacturing by standardizing the complete process end-to-end. End-to-end standardization works when handling many instances of the same clinical condition, one after another. It does not scale up to handle a variety of clinical conditions at once. How might health care consistently produce the desired result in the face of this clinical variety?

Second, most other industries deal with physical systems while most of health care deals with biological systems. Each instance of a physical system is identical, produced from the same blueprint and behaving consistently according to the laws of physics. Variation is evidence of an error in the manufacturing process. To continue the analogy of a microprocessor plant, if a variation occurs, the error is identified, the process is corrected, and the variants are discarded. In contrast, biological systems are inherently variable. They evolve through random change in DNA sequence and survival of the fittest. An individual's environment and behavior affect his or her characteristics. Because of this variability, two individuals might present with the same condition, yet need different treatment. For example, the most effective drug might be safe for many, but hurt a few. This risk may or may not be known. Even if it is known, there may or may not be a way of testing individuals to see which group they are in. In addition, individual patients may place different values on the alternative outcomes. One might value cure enough to accept a significant risk while another might prefer to continue to cope with the illness rather than take the risk of treatment. How might health care consistently produce the desired result while accommodating biological variation, uncertainty, and differing value systems?

Third, other industries are able to isolate change and stage its introduction into routine production more systematically than health care. Model development and simulation minimize the need for production trial and error. Change can be isolated in major steps. For example if a new generation of chip becomes possible, the microprocessor factory can shut down

and completely retool to accommodate the changes. The rate of discovery in the biological sciences and the rate of introduction of new healthcare technology continue to increase. Yet new approaches are tested in production healthcare settings. Many of the changes are incremental, changing part of an approach to diagnosis or treatment. Many such changes occur in parallel. How might health care consistently produce the desired result while accommodating both experimentation and rapid change?

If health care did not differ from other industries, we could move beyond expert-based practice by agreeing on a standard practice for each condition and its use by all healthcare providers. Given the three major differences outlined above, such a simplistic solution cannot be expected to work. How then can health care achieve consistent performance, accommodating variety in clinical problems handled, variability in biology and values, and the rate of change in biomedical knowledge? We suggest that the answer involves standardization around a systems approach to practice, not around specific practices. Continuous system development and refinement through iterative cycles of the system development steps might yield local standard practices, consistent with global knowledge yet adapted to local resources and capabilities, changing evidence, and system performance. The linked cycles of system-supported practice permit flexing of standard practice for individual patients based upon expert judgment, but under the control of monitors that can warn of problematic trends in real time. Data reflecting the improvement or deterioration resulting from such flexing in turn provide evidence at the local level. Global correlation of local lessons in turn might feed back into the collective evidence base. Simply put, we still need the experts. Instead of spending the bulk of their time managing each individual patient as experiments with an *n* of one, they spend most of their time developing and iteratively refining the system of practice for their organization and working within the resulting system-supported practice. In both modes, whenever explicit evidence does not provide the next step, they make an expert judgment. In contrast to expert-based practice, this judgment takes place within a systems approach that turns the decision and the resulting outcome into information to guide the next iteration.

If correct, our suggestion to standardize around a systems approach to practice instead of around specific practices for specific patient conditions has three implications for healthcare workforce and infrastructure policy. First, we need to communicate more clearly to policy makers and payers the characteristics of health care that make moving beyond expert-based practice challenging. Without this understanding they will continue to ask for and pay for changes that are unlikely to produce the desired result. Similarly we need to help healthcare providers appreciate the synergy of a systems approach and the expert. The systems approach provides the con-

text and feedback for the expert. The systems approach does not replace or devalue the expert.

Second, we should call for health services and biomedical informatics research into techniques and technologies to support local development and iterative refinement of systems approaches to practice. For example, we might test approaches permitting "mass customization" of standard practices. If we try to define a guideline at such a high level that anyone can use it, many details must be left to expert interpretation. Instead we might define modules or components that are small and targeted enough to gain agreement on one approach. Local flexibility might then be achieved by mixing and matching components.

Third, we should call for direct payment to clinical and process experts for their work in the four system development steps. Since this work impacts all patients in their system, we can argue for payment at a multiple of payment for work with individual patients. Similarly, we should work to focus payment for work with individuals on the steps that require an expert—applying judgment within the system-supported practice or exerting technical skill. In parallel we could deemphasize payment for time spent working around the non-system. Collectively these changes would create strong economic incentives toward a systems approach to practice while highlighting a role for the expert that will stand the test of time.

THE PARTNERSHIP IMPERATIVE IN AN EVIDENCE-DRIVEN ENVIRONMENT

Marc Boutin, Executive Vice President, National Health Council

To begin, I'd like to give you a simple illustration of one of the challenges of looking at "the patient perspective." Imagine that you have just received a diagnosis of acute lymphocytic leukemia, a type of leukemia that progresses very quickly. Treatment can range from chemotherapy to radiation to a bone marrow transplant.

In one scenario, you are a 38-year-old parent who has three children at home under the age of 12. In another scenario, you are a 65-year-old individual who has recently retired from a career, with a husband or wife of 40 years who has also recently retired, and the two of you are looking forward to spending more time visiting your two grown children and three grandchildren. In yet another scenario, you are an 86-year-old widower with three children in their 60s and eight grandchildren.

Each of these patients has the exact same medical diagnosis on the surface, yet every person's circumstance is different, illustrating that a key challenge is to develop the evidence base that acknowledges that, even with identical diagnoses, a patient's life stage, underlying health, social support,

attitudes about health and illness, faith, culture, and other factors will greatly influence what is for each individual "appropriate treatment."

We've heard much about EBM from the point of view of many healthcare stakeholders, but what about the people the healthcare system is supposed to serve? It seems that we have an underlying assumption that, of course, all these parties exist to serve the patient and have the patients' best interest at heart, but does it really work that way? Is it possible for us to build an evidence base that takes into account the unique needs of each patient, delivering and ensuring the "right" health care for each person?

We know that when well used, in a strong provider-patient relationship, EBM can be a powerful tool to ensure the best possible medical outcome. EBM can indeed help close the quality chasm across geographic regions, treatment settings, and socioeconomic levels of patients. It can help us use resources where they are most effective. The challenge, however, is to balance our nation's urgent need to ensure quality care and use resources wisely, with the understanding that different patients react differently to different treatments and, just as importantly, have different priorities and personal values.

At the National Health Council (NHC) we frequently hear from patients whose chronic conditions require ongoing treatment to maintain their quality of life and enable them to remain productive members of society. The NHC has a broad and diverse membership, but representing the needs of patients is our primary focus. We have heard from many of our members that so-called EBM has been used to deny coverage to Medicaid patients in several states for treatments including asthma, epilepsy, and depression. This short-sighted view may save money for the payer in the near future, but it often later results in costly emergency room visits and hospitalizations, not to mention physical and/or emotional suffering for the patient, often accompanied by financial loss, all of which might have been prevented—or certainly lessened. We have all heard of similar cases in which the precepts of EBM have been distorted to look at short-term cost efficiency as the primary criterion.

If EBM is to be implemented systematically through a variety of mechanisms, it must be structured with the realization that what works for 80 percent of patients may actually cause harm to or be inappropriate for the other 20 percent. In other words, as we embrace an epidemiological view and use public health decision models, we should also remember and embrace the promise of personalized medicine. In the patient-centered world of personalized medicine, we allow individual patient data, in the hands of an individual health professional, to be given *equal* standing with aggregated public health data: as the IOM Roundtable has stated, "to account appropriately for individual variation in patient needs." *That* is our ideal.

We are encouraged and excited that many in the healthcare industry are coming together to create a healthcare system that is more consistently effective, safe, efficient, and affordable. Yet, as is often the case, many of these efforts have not really focused on the needs of the patient, or even on the simple concept that engaging patients more fully in their care can directly improve medical outcomes.

There are additional factors we must keep in mind as we consider how to go forward with EBM. One is that the quality of the evidence base is often not consistent—that is, some evidence is based on large, double-blind studies over long periods of time, while other research put forth as "evidence" is based on very small groups of as few as 20 patients in very short time frames. Also, of course we all can remember research results touted as strong evidence that were later discredited when new, more robust research was conducted. So we must remember that "all evidence is not equal."

Another factor to consider, which may be harder to grasp, is that if patients do not perceive a problem, they will not utilize the so-called solution to that problem. They may have many complaints about the way they receive health care, and we have all heard many of them, but the NHC's research among patients repeatedly shows that they do *not* think quality—or more specifically, lack of adherence to evidence-based guidelines—is the problem. So, if we want patients to be accepting of the concept of EBM, we must be willing to explain it and convince them it is something they need and something that will improve their health care and their health and well-being.

Without true patient engagement and clear and honest communication about EBM, it is likely that many—maybe even most—patients will perceive that "the system" is out to limit their access to the care they need. *And* it is it likely to be much more complicated and expensive to implement than it needs to be. We believe the key is to protect and preserve the patient-provider relationship, so that it is on equal footing with public health and epidemiological evidence. The NHC wants to see us work together to address the needs of payers, industry, providers, and patients and their families alike.

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5

The Promise of Information Technology

INTRODUCTION

The Internet and other electronic information technologies have brought dramatic change to numerous sectors of the U.S. economy, including health care. Providers and patients now have a wealth of information literally at their fingertips. Discussed in this chapter is the work of two organizations that have developed information technology (IT) systems that help patients and providers find the information that is most relevant and actionable.

Rob Hayward, of the Centre for Health Evidence (CHE), notes that information overload makes it difficult for healthcare providers to easily integrate evidence into practice. For example, information sources such as journals each have their own way of organizing and presenting information, which is not easily adapted to clinical practice. Over the last decade, after working with many organizations and professional groups, CHE has developed a number of insights into technology that can serve as a conduit that links better information with better health outcomes. Key considerations include how to support information with convenience, and capacities for discrimination and integration into practice.

The changing healthcare information environment of consumers who are increasingly managing their own health care and health information is discussed by Peter M. Neupert, of Microsoft Health Solutions Group. Just as widespread access to the Internet has encouraged a more consumer-driven approach in industries such as banking, retail, and travel, consumers are being asked to take a more active role in their own health care. Consumers' vested interest in improving health outcomes will likely lead to a

growing role as a disruptive agent of change in health care—by demanding better information and tools to support their health decisions.

INFORMATION TECHNOLOGY TOOLS TO SUPPORT BEST PRACTICES IN HEALTH CARE

Robert Hayward, Centre for Health Evidence

A health informatics agenda is emerging that is preoccupied with evidence. After years of underinvestment in information systems, large-scale health infostructure initiatives have emerged in Western economies. National health reform plans in the United States, Canada, and Britain place evidence-based information systems among the top deliverables for this decade. Indeed, current policy ties this to an electronic health record for all Americans. Evidence-based medicine (EBM)? Policy makers have proclaimed that it can be beamed to the bedside.

The proponents of health informatics are quick to enthuse. Harnessing IT will improve health services because, of course, "better information begets better health." Yet how can better information yield better health? At least three things must happen. First, healthcare decision makers must discern better from worse information. Second, changes in knowledge must trigger changes in health practices. Finally, improved outcomes must result from altered practices. In short, better information begets better health through the medium of better choice.

If the starting point for better choices is better evidence, then the challenge of EBM boils down to at least three requirements. Evidence-based decision makers must be supported to do the following:

1. *Know what to do*—because best evidence about best practices informs decision making.
2. *Do what is known*—because they recognize problems, formulate questions, select resources, and apply knowledge appropriately.
3. *Understand what is done*—because health choices and outcomes are iteratively validated.

If, on the other hand, the starting point is the messy informational milieu of front-line clinicians, then even the most meritorious evidence is useless unless practitioners are supported with

- *Convenience*—because all the right information is available in the right place at the right time;
- *Discrimination*—because relevant and important information is filtered by the unique needs of community, group, and individual; and

- *Integration*—because evidence is embedded in work flow, its use is monitored, and effective evidence behaviors are correlated with health outcomes.

The CHE collaborates with health organizations, professional groups, and individuals to improve evidence convenience, discrimination, and integration at the point of decision making. A variety of Internet technologies have emerged. They have the following characteristics:

- *Simplicity*—with uncluttered, straightforward, and consistent presentation of information and an intuitive interface that requires a minimum effort to use without training
- *Accessibility*—with rapid access wherever healthcare decisions are made
- *Sensitivity*—to individual and group information preferences
- *Efficiency*—with important information resources organized under a single log-on to reduce the clinicians' total burden of information management

An iterative approach to developing "embedded evidence" systems has benefited from close collaboration with national and regional care societies, health professional organizations, and diverse healthcare institutions in Australia, Canada, and the United States. These have integrated evidence with practice for their members and clients. By attending to the common informational challenges experienced by busy clinicians, an approach to improving information literacy has emerged. This presentation highlights key lessons emerging from more than 10 years of observation involving over 29,000 front-line practitioners.

Knowing what to do at the right time and place is a huge challenge for practitioners, but their problem is not one of evidence access. There is vastly too much information to contend with, especially when using the Internet to address common clinical challenges. Instead, their challenge is one of information overload, interface chaos, and access fragmentation. Best evidence is increasingly aggregated in high-quality repositories, but presented by diverse publishers, each with unique ideas about how information should be organized and how search engines should function. The conscientious clinician struggles to navigate a plethora of products. Those products are not available in the various locations where decision makers guide health care. Many clinicians experience questions in information environments quite different from those in which they reflect on possible answers. The networks, sign-on protocols, resources, firewalls, hardware, and software may be incompatible on the ward, in the clinic, at the office, or at home. The clinicians' informational experience is particularly fragmented when it comes to health evidence, which may be differentially

licensed by individuals, groups, hospitals, professions, and universities. In sum, evidence access often does not translate to evidence availability when and where evidence is most needed.

Having evolved an information ecology that works for clinicians, the CHE now promotes and implements a Rule of Fives as a simple expression of what it means to deliver information convenience. A convenient decision support environment will have the following traits:

1. *Responsive*—because key sources of evidence are open, ready for searching within five seconds anywhere and anytime a clinical practice question arises
2. *Proximate*—because evidence repositories can be loaded and searched within no more than five mouse clicks from anywhere
3. *Guessable*—because it takes no more than five minutes to gain sufficient orientation to start using a decision support tool, without needing manuals, printouts, or help files
4. *Comprehensive*—because at least five distinct needs (e.g., communication, collaboration, evidence access, decision support, documentation, and news) are met
5. *Rewarding*—because users experience at least five practice-changing rewards per week of system use

If busy clinicians experience a decreased total informational burden, they will return and use a decision support environment consistently. If they use a resource consistently, then "capture" is achieved and it becomes possible to disseminate new information more effectively.

Many healthcare organizations are learning how to deliver evidence in a way that makes it more accessible. Indeed, there is no excuse today, given the quality of Internet services and the existence of high-quality evidence refineries, for not meeting the Rule of Fives. However, even when healthcare workers have rapid access to a smorgasbord of best evidence, information processing barriers can prevent that evidence from connecting with best practices. To apply evidence prudently in practice, clinicians must also be able to discern meaningful and answerable questions and to map them to different ways of knowing. They must know where to find the kind of evidence best suited to a particular way of knowing. Having found relevant material, they must then judge the believability, importance, and applicability of that evidence, before deciding whether it will do more good than harm to apply the evidence to a specific patient or population.

It is important to have access to reputable "external evidence" about what is known from the study of populations other than one's own, but practitioners and policy makers also need to be able to integrate that information with evidence from their own populations and settings. "Internal evidence" is increasingly a by-product of the administrative and clinical

data repositories supporting the work of healthcare organizations. These databases can be analyzed to better characterize the health risks, unique circumstances, pre-test probabilities, and patterns of health care that determine whether external evidence will deliver on its promise.

Equally important is the "personal evidence" that individual practitioners accrue over time. This experiential knowledge is rich with the practical details and know-how that ultimately determine whether external evidence can be applied in practice. Indeed, where researchers may best understand the science of health care, front-line practitioners best understand its application in context. The latest knowledge management products can empower practitioners to build, maintain, and work with collections of personal evidence in ways that encourage hypothesis generation about what works in health care. Ideally, these hypotheses would then make it back to health services researchers who would hone their research to improve the yield of actionable external evidence.

The CHE has found that the supporting evidence discrimination is about supporting, recognizing, gathering, and reflecting upon internal and personal evidence. Practitioners learn about discerning issues, asking questions, and positing appropriate rules of evidence and organizational change when they focus on the questions and data sources they know best. Moreover, by providing clinician groups with collaborative evidence management tools, "communities of inquiry" can emerge. Ultimately, these change the evidence culture of an organization and, over time, increase capacity for use of best external evidence.

The Nemours Foundation, which provides pediatric care in Delaware and Florida, offers an interesting case study. The Nemours hospitals and clinics committed to becoming evidence-based and embarked on a capacity-building initiative in collaboration with the CHE. An "InfoLink" clinician desktop was developed to integrate all clinical, decision support, communication, and collaboration IT. This emphasizes an information ecology that supports effective practice in office, clinic, hospital, and (for reflection) at home. Each practitioner group (e.g., emergency physician, surgeon, and orthopedic nurse) gets a different information environment with relevant, integrated, information resources. Quality resources are made actionable with shortcuts, integrated search engines, and a technology that embeds evidence access within digital health records. Clinicians can highlight any word or phrase, anywhere in any product, then select from a list of information needs. InfoLink then selects appropriate information resources, conducts a search, and presents decision support information in total compliance with the Rule of Fives. All this happens in a way that is optimized for one's specific clinical discipline and interest group. Currently, such instant access is emphasized for drug information, practice guidelines, patient information, and clinical references. Once a clinical care topic or issue is so identified, the "decision-making context" is shared among all available

evidence resources. The decision maker can switch to a particular product, with its search interface pre-loaded to address the issue at hand. InfoLink departs from the classic library model of evidence to organize resources in an evidence hierarchy of studies, synopses, summaries, syntheses, and systems. Most important are the systems, which present evidence in a way that is actionable within electronic medical records.

Another undertaking of the Nemours InfoLink initiative is to provide "information literacy" and "evidence literacy" training at the point of care. This is integrated into the online information environment, allowing clinicians to select topics and progress at a rate that meets their needs. The Users' Guides Interactive (http://www.usersguides.org) is linked to sources of evidence, allowing on-the-job learning about how to get the most from evidence repositories. This "embedded continuing professional development" proved essential to improving the use and application of best evidence in practice.

To support evidence discrimination, our experience suggests that at least five evidence services must be provided where and when healthcare decisions are made:

1. *Evidence selection*—because the most valid and clinically useful evidence repositories are filtered for user groups with specific health disciplines and interests
2. *Evidence synthesis*—because short, structured summaries of best evidence are offered for knowledge surveillance and maintenance of competence
3. *Evidence in context*—because the evidence application tools (e.g., algorithms, handouts, and risk assessment tools) are coupled with both clinical data sources and supporting evidence, all in a way that can be accessed as part of clinical work flow
4. *Evidence management*—because clinicians are able to record and organize questions as they arise, note evidence application issues, and selectively collaborate with colleagues to tap tacit knowledge about using evidence in context
5. *Evidence literacy training*—because decision makers are supported with embedded continuing professional development tools and resources that allow them to learn and improve their evidence literacy in practice

Working with organizations such as the Nemours Foundation, the CHE implements systems that monitor evidence behaviors. This involves recording and analyzing patterns of information use in practice. These data are used to help organizations apply a five-domain benchmark to track their path to an "evidence-based organization":

- *Level 1: Integrated information environment.* Clinical knowledge, communication, documentation, and decision support coexist in a single-sign-on clinical desktop.
- *Level 2: External evidence use.* Quality sources of external evidence are summarized and linked to healthcare work flow and decision making.
- *Level 3: Internal evidence use.* Locally relevant information about patients and populations is distilled from clinical and administrative data repositories and made available in actionable and integratable formats.
- *Level 4: Reflection in practice.* Individual and shared (communities of inquiry) tools support the recording of questions and collaborative seeking of answers.
- *Level 5: Change agency.* Embedded information literacy training and evidence literacy training support the emergence and empowerment of organizational change agents within the organization.

Informed choice is facilitated when information about health is connected with information about how to improve health. To attract clinician attention, a health information system must be ubiquitous, accessible, dependable, and credible. It must present all information—patient reported, clinician observed, and research derived—in a way that highlights its validity, importance, and applicability for individual patients. To retain clinician attention, a health information system must complement, not conflict with, the predominantly oral culture of information exchange in health care. The information tools must make it easier for decision makers to find and use high-quality information when reflecting with colleagues, consultants, and clients. Most importantly, information tools must decrease the clinician's total informational burden while easing communications with colleagues and participation in virtual learning and decision-making communities. Clinicians' work should be supported by an information culture that rewards explicit approaches to uncertainty and acceptance of just-in-time knowledge.

INFORMATION TECHNOLOGY TOOLS THAT INFORM AND EMPOWER PATIENTS

Peter M. Neupert, Microsoft

As a society, we are struggling to identify solutions to alarming trends in disease development, to the untapped potential of new medical discoveries, and to rapidly rising costs associated with health care. There is a growing role of the consumer as a disruptive agent of change in the broad

health ecosystem—driven by the need for better information and tools that support the decisions that we, as individuals, are now being asked to make about our health and the health of our families. The consumer needs to be better empowered with tools to make those choices. The availability, portability, and sharing and use of health information—through innovations in software—will be key to achieving this transformation.

A Decade of Changes

The past decade has been a time of unprecedented innovation in biological science that puts us at the threshold of an explosion in data about how our bodies work—right down to the molecular level. The next decade promises to increase that spectrum of data by a factor of thousands (Figure 5-1). Yet our healthcare system is not equipped to manage this volume of information and is struggling to derive value from potentially lifesaving data. The promise of personalized medicine is exciting, but that promise can be realized only if information is made available to the right people, at the right time, and in the right context.

The last decade has also been a time when consumers have connected themselves to a global information system—the World Wide Web—in unprecedented numbers, creating a society that has access to, and demands

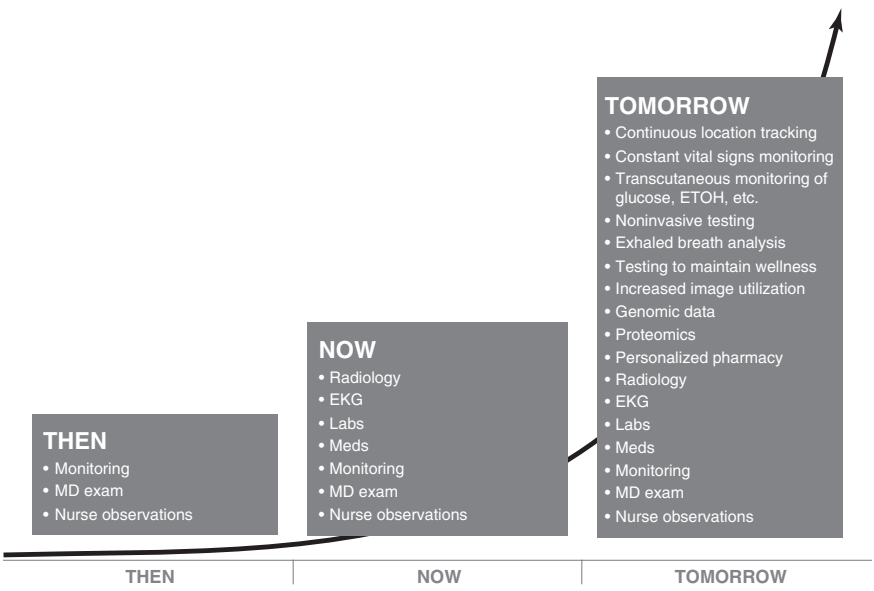

FIGURE 5-1 Data advances in medicine.

access to, up-to-date information around the clock. Accustomed to having online access to pricing and availability of products and services across other industries such as retail, travel, and financial securities, consumers are demanding to have a healthcare system that centers on their needs and the needs of their family: a system that supports individuals in the decisions we are now being asked to make about our health.

The Copernican Shift

Four hundred and seventy-seven years ago, Nicolas Copernicus stunned the world by challenging conventional wisdom and claiming that the Earth was not the center of the universe—that in fact the Earth and other planets revolved around the Sun. This required a significant mind shift for people and forced them to radically change centuries of thought that put Earth at the center of the planetary system.

The healthcare universe has traditionally revolved around the physician, the person that we as patients relied on implicitly to guide us and make decisions for us, to keep us alive and in good health; the person that served as our gatekeeper to health plans; the person that served as our liaison to pharmaceutical companies. Today's health information systems all center on the "facility"—whether it is the hospital, doctor's office, or insurance work flow. None of these systems creates a complete view of the consumer, and most are not accessible to the consumer.

The Copernican-like shift that we are experiencing today in health care is moving the patient to the center of this universe, requiring individuals to navigate the healthcare system and make decisions about their health as it relates to treatment choices, behavioral choices, and economic choices. Consumers are making this shift out of necessity. They can see that the system has gaps and that if they don't actively participate, they may be hurt or inconvenienced by those gaps.

This is a shift that has the potential to advance the trend toward personalized medicine, as consumers take more ownership and provide more input to their health and wellness plans. It is also a shift that has the potential to improve the economics of today's healthcare system.

Shifting Roles; Shifting Economics

The connected consumer is already demonstrating a demand for health information, with more than 8 million people per day doing health-related searches online, generating an online ad market in excess of $500 million in the United States (Figure 5-2).

The financial costs of treatment and support under current healthcare models continue to burden society, and are contributing to a shift

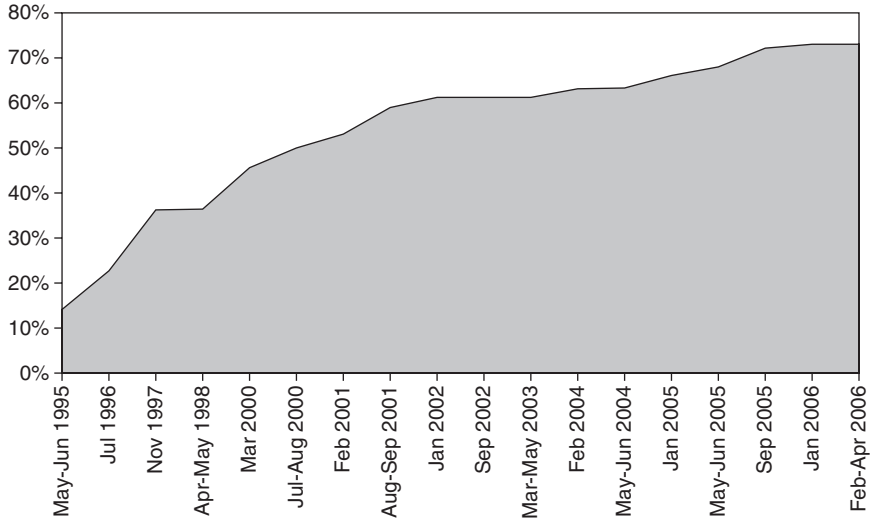

FIGURE 5-2 Percentage of U.S. adults online.
SOURCE: Pew Internet & American Life Project, March 2000-December 2006. All surveys prior to March 2000 were conducted by the Pew Research Center for People & the Press.

that sees more focus on prevention and wellness, and more focus on self-management—chronic care management that moves away from hospitals and specialty clinics and into the home environment, with support from family doctors and community institutions. The consumer is being asked to take on an increasing amount of responsibility as it relates to his or her health, and is asking in turn for best practices and actionable information that enables informed decisions around disease prevention and chronic patient care.

The opportunity for new forms of preventive care and home-based disease management requires new paradigms for payment and reimbursement. If we find them, we will free up human and economic resources across the healthcare system that today are overburdened. One of the challenges our health system faces centers on the fact that we spend billions of dollars annually looking for new treatment solutions or cures for disease, but collectively we do not spend significant dollars on measuring, evaluating, and determining best practices in our health delivery system. Clearly, part of the evidence base we need to build is on best practices of delivery.

This shift to the consumer will happen, irrespective of how health care is financed, as either a market-driven or a single-payer environment. The consumer understands that there are gaps in the system and that she cares

more about the outcome, has more to lose or gain, than other stakeholders in the system. With consumers as the driving catalyst for change, health services will have to compete for the dollars of the individual, resulting in a system that increasingly competes on quality of care; a system that is increasingly transparent; and a system that is forced to improve its access to and transfer of information.

EBM can no longer be a term that we talk about purely as it relates to the clinical community. Consumers too will want to understand what the evidence is and what it means to them. With so many different types of data being aggregated in so many different ways, by so many people, the key to enabling success rests on our ability to create knowledge and understanding from this information in ways that support improved quality and economics of health.

Pulling Even with Other Industries

The biggest barrier to achieving this kind scenario lies in the fragmented nature of our health system. Data are dispersed over a variety of facilities, providers, and even our own monitoring devices and home computers. The number of health data silos that have been created just in this country alone is mind-boggling and is working against a system that can deliver evidence-based care.

We are not the first industry struggling with fragmentation—in fact we might be the last. The consumer-centric model is one that other industries have had to adopt over the years in order to adapt to changing market needs, and health care is starting to catch up. Historically, the financial services industry was dominated by large institutions—banks, brokerage houses, and insurance companies—that dictated to consumers what they could get, how they could get it, when and where they could get it, and the price or commission they had to pay in order to enjoy the benefit of these services.

With the advent of the Internet came the birth of the "self-directed consumer," and financial services institutions were forced to become more flexible, consumer-centric businesses. Transformation of the industry has enabled financial services organizations to provide a seamless experience for customers, consolidating their interactions across the industry with banking, lending, and brokerage services integrated into a single account.

I now cannot imagine a world in which I cannot log into my account and view my account balances, upcoming loan and bill payments, home mortgage balance, line of credit, all transfers, deposits, and other transactions. The industry leaders in financial services now provide customers with the information that they need to feel in control throughout the decision-making process.

Giving consumers more control and access to more information fosters customers that are more invested in their financial situation and are more invested in the institution that has helped them achieve their new level of confidence. The financial services organizations that are prospering today are the ones who responded to, and now understand, the self-directed consumer.

Solving Healthcare Fragmentation: The Strategic Role of Software

In looking at the challenges of the health ecosystem, any solution has to be broad enough to include stakeholders from across the spectrum of care, secure enough to promote trust, and open enough to encourage seamless adoption.

We believe that the individual is a possible change agent for healthcare fragmentation, and so the right solution is one that puts the consumer at the center of healthcare system, enabling consumers to be the aggregators of their information. A consumer-centric solution requires two things:

1. A private and secure data storage and sharing platform that will enable the seamless exchange of data between thousands of health applications and devices
2. An online solution tied to the platform that makes it easier for consumers to collect, persistently store, share, and act on their health data—private data that are entirely under their control

This platform needs to be inclusive of standards, and it needs to have the principles of privacy in place to earn the trust of consumers, while enabling the reuse of data. The same platform has to connect consumers with information from their physicians and extended care team, their health plans, pharmacies, and any number of devices that they use to track health and fitness behaviors.

Microsoft HealthVault Platform

Looking at consumer health needs and the industry's challenges, we developed and released in beta format, Microsoft® HealthVault™ in October of 2007. Microsoft HealthVault is a free Web-based platform designed to put people in control of their health data. It helps them collect, store, and share health information with family members and participating healthcare providers, and it provides people with a choice of third-party applications, services, and devices to help them manage things such as fitness, diet, and health. HealthVault also provides a privacy- and security-enhanced foundation on which a broad ecosystem of players—from medical providers and

health and wellness device manufactures to health associations—can build innovative new health and wellness management solutions to help put people in control of their and their family's health.

At Microsoft, we are committed to making it easy for users to import and export their data. We are not trying to lock anybody in. We are trying to be a catalyst for data liquidity in the broader health ecosystem, and we encourage folks to begin to start to think about that, and to start to make that happen. In developing HealthVault, we decided to make it free to users, and free to software developers, as the best way to spark innovation across the industry, and to encourage adoption and data liquidity.

The individual consumer is the aggregator, pulling the information together from across data sources such as dispersed patient records, prescription drug records, fitness and diet plans, and vital signs through external medical devices (blood pressure monitors, blood glucose monitors, etc.) that plug into the computer network. As controlled by the consumer, any part of this information may then be shared privately and securely with family member caregivers, with physicians and other health providers, or with anyone else the consumer chooses.

Many people want to be actively engaged in their everyday health, in monitoring and learning about what it is that can make them feel better, but without appropriate support systems, data today mostly get lost.

Eight years ago most people would not have imagined how different life would be today by being able to connect to people and to information, wherever you are, at any time. The long-term promise of HealthVault and its broad ecosystem of health partners is that having more data—and the software tools that allow us to gain insight from the data—will enable us, and the members of our extended care teams, to better understand the many real-life interactions and situations we encounter and to improve the everyday choices that we are making about our health.

Starting with Search

The beginning point for almost all consumer online experiences today starts with a search. Consumers start with searches because they have a need, and they are in the mode of "discover and learn" about that need. Studies show that between 65 and 70 percent of people start with a targeted search and from there access numerous online information sources.

To better fill this need, Microsoft has also developed HealthVault Search, a new Web search service that uses the storage capabilities of the HealthVault platform. HealthVault Search helps people discover answers to their health questions, learn more about topics important to them, confidentially store the information they discover, and act on that knowledge to improve their health and wellness. Furthermore, HealthVault Search in-

tuitively organizes the most relevant online health content, allowing people to refine searches more efficiently and with more accuracy.

Users want more than just to learn; they want to act to fix their need (Figure 5-3). We developed HealthVault Search as an entry point to the Microsoft HealthVault platform and as a way to ensure that consumers are finding the information they need, when they need it. In the context of the search experience, advertising is a key component of the content and is

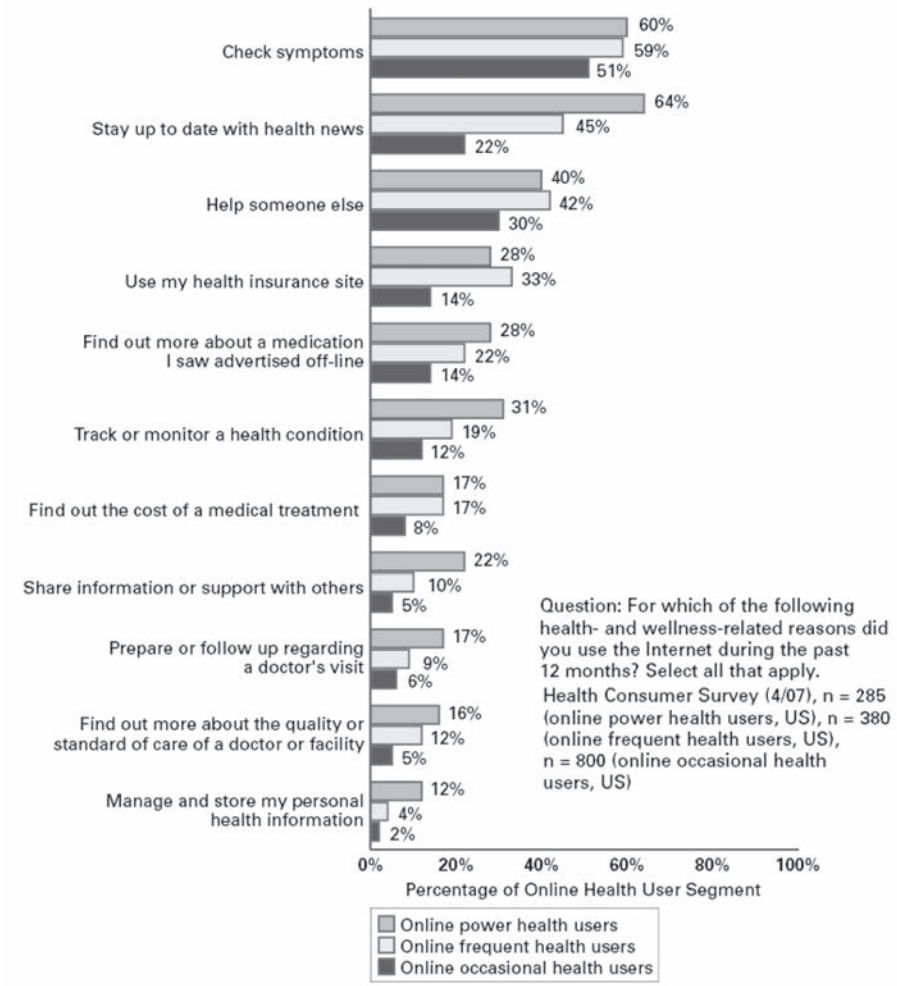

FIGURE 5-3 Online health users' reasons for leveraging the Internet.
SOURCE: Levy, 2007. Reprinted with permission from JupiterResearch, LLC.

actually a benefit to the consumer. However, advertisers need to help with the evidence around their claims if they want to be trusted by consumers. If advertisers can use their knowledge to communicate relevant information to consumers in a trusted and transparent way, ads will become part of the broader decision-making process.

Health search is a good business model and it can be used to create a platform of connecting consumers with data and with services, but it should never compromise the patient-physician relationship. Done in the right way, it can promote the sharing of information that individuals can use with their physicians to guide health decisions.

Protecting Your Health Data

We know that personal health information is some of the most sensitive data in people's lives. Assuring that confidential records are secured against theft, loss, or damage is crucial to earning and maintaining patients' confidence in the healthcare system and increasing their adoption of health IT, making them more likely to seek treatment and in turn live healthier lives.

In developing the Microsoft HealthVault platform and HealthVault Search application, we took an industry-leading approach to implementing privacy principles. The platform is underpinned by the following clear, strong, health privacy commitments:

1. The Microsoft HealthVault record you create is controlled by you.
2. You decide what goes into your HealthVault record.
3. You decide who can see and use your information on a case-by-case basis.
4. We do not use your health information for commercial purposes unless we ask and you clearly tell us we may.

Our HealthVault Search also sets a new industry benchmark for consumer privacy, as shown in Table 5-1.

Consumers can store and control an array of health information in their Microsoft HealthVault records, including prescription medication lists, health histories, hospital discharge summaries, lab results, fitness data, and HealthVault Search results. The technology is straightforward and makes it easy to confidently share health information with family, caregivers, or physicians. Simple information sharing among patients, physicians, and organizations will help promote greater efficiency, fewer errors, and better care.

TABLE 5-1 HealthVault Search Versus Other Health Search Options Online

HealthVault Search	Other Health Search
All traffic between users and search.healthvault.com is encrypted	Searching is not encrypted; traffic (including keywords) can be intercepted and read
Identifies users using cookies for 90 days	Will put a persistent identifier on a user's computer and use it to track users as they travel across the Web for years
We do not use behavioral targeting using information in HealthVault accounts	Will target ads based on past searches, past advertising responses, demographic information, time of day, etc.
We delete our server and application logs after 90 days	Keeps search information, including unique identifiers, for long periods of time
We do not keep track of individual query histories across sessions	Knows what you searched on over your past visits

Battling Health and Aging Trends

As our population ages and loads the system with a proportional increase in health issues, our current approach to managing health and delivering care is not sustainable from an economic standpoint. Today's health system is too focused on acute care and late-stage disease, addressing illness at an advanced stage, where treatment is extremely costly and often ineffective.

For the healthcare delivery system to continue to be viable there must be a radical shift to relieve pressure on strained and expensive human and infrastructural resources. This change will require a focus on personal prevention and wellness, a shift that will in large part be enabled by technologies available at low cost to the mass market. Enabling individuals to monitor and maintain their own health can take a great deal of the burden of healthcare delivery off the shoulders of medical practitioners, allowing them to focus on more valuable and complex care.

If people could more easily track and understand information such as their blood glucose levels and cholesterol levels—indeed, if that personal information was available at the press of a button—individuals might be more encouraged to take responsibility for their health before symptoms of illness appear. And we would have a new environment in which to motivate and educate users regarding behaviors and compliance.

As today's science evolves into tomorrow's technology, physicians will be able to determine a patient's level of disease risk based on an analysis of his or her genes or environmental factors. They will be able to develop a

personalized treatment plan and guide clinical trial participation and stratification based on a patient's genomic and biochemical makeup.

By integrating this with the other medical information, individuals can gain more insight and get actionable guidance toward their diets, proactive measures to improve their health, and the efficacy of medicines for them. However, they can only do this if they have the ability to access and derive meaning from this information.

The challenge does not lie in recognizing the potential for breakthroughs in health but in *realizing* this potential by providing the right tools to find the data that are relevant to you, extract information from the data, and convert that information to actionable knowledge.

Start of a Long Journey

Health care is a big and complex issue, and no single entity is going to fix it alone; a collaborative industry approach is the only way to get there. At Microsoft, our health vision is simple: We want to improve health around the world. We believe that a solution that puts consumers in control and positions them as agents of change is an important first step to achieving this vision, in partnership with stakeholders from across the health system. We hope that everyone will join us on what we know will be a long, but important journey.

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6

Transforming the Speed and Reliability of New Evidence

INTRODUCTION

The medical profession has long viewed randomized controlled trials (RCTs) as the best available evidence for determining whether specific medical interventions work. However, as previous chapters suggest, the speed and complexity with which new medical interventions and scientific knowledge are being developed often make RCTs difficult or even impossible to conduct. The capacity of healthcare informatics to collect, analyze, and include variability and comparison of data in health care is promising. Many healthcare practitioners are looking toward electronic medical records (EMRs) and clinical data registries as new sources of evidence because the information would be instantly accessible, include a broad cross section of the general population, and offer important longitudinal data often lacking in RCTs. In the area of drug development, a combination of regulatory and market pressures is making new sources of information even more critical. This chapter examines how electronic medical records and clinical data registries could be used to expand the evidence base in many areas, as well as the unique problems facing pharmaceutical companies as they begin to develop individually tailored medicines.

In his presentation, George C. Halvorson identifies many areas in which EMRs could greatly enrich research. For instance, massive data sets could be built that could be used to support structured clinical trials and track the longitudinal consequences of medical interventions. The data could also be used in new ways, finding unforeseen correlations. Health information technology can provide the large data sets, longitudinal data, and instant

data that will allow researchers to make the kinds of breakthroughs needed in the coming decades.

Eric D. Peterson notes that provider-led efforts to develop data registries could capture clinical information at major points and allow patients to be tracked over the long term. The data also could be used to generate new evidence and drive it into clinical practice more quickly. Professional societies such as the Society of Thoracic Surgeons, the American Heart Association, and the American College of Cardiology National Cardiovascular Data Registry all have rich data sets on patients with coronary disease, heart failure, and stroke. These data registries could capture standard data elements that could be linked, allowing cross-sectional and longitudinal information to be gathered from insurance claims or laboratory and pharmacy databases. The information could be used to track diseases, treatments, and outcomes.

In his paper, Steven M. Paul identifies the challenges that pharmaceutical companies face in using evidence to develop drugs that are tailored to individuals. In contrast, most pharmaceutical products today are developed as a one-size-fits-all product, but only about 50 percent of patients respond to any given drug therapy. A few drugs have been developed that are literally targeted to the molecular underpinnings of diseases. However, it will be difficult to develop such drugs for more complex and common diseases such as diabetes. In addition to the technical and scientific challenges that drug companies face, issues such as shorter patent lives of drugs, the slow Food and Drug Administration (FDA) approval process, and a lack of new molecules entering the pipeline are making the development of tailored drugs more appealing. The ability to use biomarkers in developing drugs has been helpful in reducing drug approval costs and shortening the process, but sustaining profitability becomes challenging when only a small subset of patients benefits from a drug.

ELECTRONIC MEDICAL RECORDS AND THE PROSPECT OF REAL-TIME EVIDENCE DEVELOPMENT

George C. Halvorson, Kaiser Permanente

The importance of the development and adoption of EMRs to functional improvements in the healthcare system and in patient health has been widely supported. This discussion focuses on the use of EMRs in medical research. Hopefully, there will be something in these comments that will be new or at least useful to some readers.

Kaiser Permanente (Kaiser) is currently spending about $4 billion putting its own EMRs and physician support tools in place. One of the ma-

jor reasons we are doing this entire EMR project is to facilitate medical research. We are doing it both to deliver better patient care and to do some serious medical research. We are committed to that agenda. However, I am not speaking just from Kaiser's perspective or our version of EMRs. Overall, as all caregivers manage to get data transferred from paper files into electronic records, I strongly believe that EMRs should and will revolutionize medical research. Done well, done adequately, compiled appropriately, and supported appropriately, EMRs should open up a Golden Age of healthcare research.

Think about the key advantages of the EMR for medical research—instant, comprehensive data. Instead of researchers' spending weeks, months, and years gathering pieces of data and pulling together sets of data, EMRs provide instant access to comprehensive data in real time. All patient medical information will be available electronically and true longitudinal data will be possible. Instead of data that are limited to the very narrow time frame of each study, if the database is constructed appropriately, data will go back years into history and extend indefinitely into the future.

Current medical research is built around very small numbers of patients—a couple of thousand patients here, a couple of thousand there—each in a very finite study. Using EMRs, the opportunity exists to have instant access to massive data sets comprised of millions and millions of patients' data. There is also great flexibility in data utilization with electronic data, and there will be a growing ability to use the data in various ways. With electronic data, studies can be reconfigured in ways that can't even be dreamt of when using a paper-based research system.

So how can this resource be used? In many ways. It will be ideal for highly structured clinical trials. In particular, classic clinical trials can be far better supported if the data are electronic. Also, electronic data could help with extended follow-up work for issues such as post-market tracking, and EMRs could be used to track progress and care results into the future. For example, if a patient has a stent put in, EMRs can help determine the consequences of that action, 3 years, 5 years, 15 years out, an impossible task using the time-limited, population-limited, classic paper-based research approach. Population health analyses can be carried out in whole new ways, with the prospect of identifying the impact of various kinds of care approaches on broad populations.

Unforeseen correlations will increasingly be detected, as it becomes possible to sort through electronic data sets and troll for correlations of age, ethnicity, or diabetes, for example, with other conditions. That type of statistical correlation searching and research cannot be done in any meaningful way with paper, but it can be done relatively easily if you put together the right electronic database. Just-in-time learning and treatment

searches also become possible with an EMR. A caregiver can identify what works for a given condition and what the most current patterns of treatment happen to be. There are all kinds of levels of electronic research that can be done in the context of current science. In the next wave of exciting research, DNA correlations will be commonplace, and it will be the norm to check a patient's genetics and reach some conclusions about patient care. Genomic and genetics research is developing in some exciting ways, as highlighted in several papers in this publication, and with electronic data, it will be possible to carry out this research much more broadly and much more effectively. Currently, such a project is under way at Kaiser, and a DNA database is being developed to support our research efforts.

Kaiser has conducted data file research using our electronic databases that illustrates the potential of EMR data. One analysis revealed that Vioxx was causing problems for a number of Kaiser patients and was conducted by sorting through our database. This original identification—conducted using a level 1 electronic database—was enough to trigger an alarm bell and lead to the initiation of an assessment process. However a level 1 database can only indicate that a percentage of patients are being harmed; the specifics of gender, age, ethnicity, and other conditions remained a mystery. Our new full EMR level 2 database, which is going into place now, will enable the additional step of identifying exactly which patients are harmed and which are benefited by a drug.

Kaiser has also initiated similar data work relative to both hormone replacement therapy and the follow-up care of patients that had heart stents. We identified the fact that there were some problems with particular stents. Again, this is the kind of results-based longitudinal data that can come from an EMR quickly and easily and be used to reach conclusions about approaches to care. The basic, rudimentary level 1 database provides one set of conclusions, but level 2 will allow researchers to drill down through the various layers of data and determine some additional findings and conclusions.

What does this mean for electronic data and EMRs in the future? Anyone who is going down the EMR pathway should begin with the end in mind and design data sets to support clinical trials. As EMRs are designed, medical research must be identified as one of the outcomes of the process so that the data fields and data sets necessary are included for that purpose. Likewise, data sets need to be designed to facilitate analysis of outcomes and care patterns. For example, relevant demographics should be built into the data set to enable evaluation of race, ethnicity, gender, economic status, and geography. From the outset, these types of capabilities must be built into the data set to allow that level of research over time.

Kaiser has spent significant time on this particular issue. We started with a dozen different ethnicities and then expanded to a couple of hun-

dred. We are now working backward to try to figure out what a workable number is—200 is too many. A broad category such as "Asian American" raises the fact that there are obvious differences between Korean Americans, Japanese Americans, and Chinese Americans. One category is not sufficient, yet a dozen is unmanageable. That is still a work in progress. The goal is to sort through all the data sets so you can say that these are relevant differences relative to ethnicity, behavior, and culture. Knowing that, we need to decide where we draw the definitional ethnic and racial line.

Some of these issues are going to be on a learning curve for a while, and they must be addressed as we move forward. Issues such as economic status, geography, and gender will all have to be part of our electronic research data set. Then—as a major next step—the data strategy should incorporate genetic components appropriately into the research agenda. Obviously, only a computer can do some of this work. It cannot be done effectively with paper files or stand-alone data sets. The computer is needed to create large data sets, longitudinal data, and instant data. If this work is done well, it could usher in the Golden Age of medical research.

Having said that, data must be widely available in order to truly reform health care in America. The key to real reform will be to focus the attention of the country on major and very specific healthcare opportunities. The standard model of reform right now, from a care delivery perspective, is highly disorganized. Our current approach is to do many separate and isolated projects all over the country and then hope that the cumulative impact of those local projects somehow magically adds up to better care. That model is not likely to work.

A second model proposed by quite a few people is to simply jump to conclusions about what might work and then micromanage bits and pieces of the care delivery process from the inside, to recruit more primary care doctors into local practice, for example, hoping that somehow more primary care doctors will result at some later time in a better set of healthcare outcomes for patients. That kind of reform model is also dependent on some categories of magical thinking and is somewhat unlikely to work to achieve real systematic reform.

Others think that financial approaches are needed and believe that micromanaging bits and pieces of caregivers' incentives will somehow result in improved health care. That model is also currently not well organized or focused enough to work.

What is likely to actually work to achieve real reform would be if the nation took a hard look at the fact that five medical conditions drive more than half of our healthcare costs. Americans could greatly improve the care infrastructure for patients with those five conditions, which should be viewed as a huge opportunity. If we focus on patients with those conditions and then work backward to align benefit sets, payment models,

structure, focus, attention, tools, data reporting, community priorities, and health education on those five conditions, the cost trajectory of American health care could be dramatically changed. Care could improve, and real and logistical pieces could be set in place that are directly aligned with the right outcome of real care reform and health care.

Healthcare reform in America has been approached backward—from the bottom up, starting with local bits and pieces. That whole agenda needs to be turned around. It is necessary to set a common goal—a practical and reasonable goal—and then to work backward, changing the total infrastructure as needed to align the functional system of care with that goal. Building the right electronic data sets and making medical research a direct tool of medical reform could result in massive improvements in healthcare delivery. What is most acutely needed is focus, followed by the development of these tools. I will end by saying, "Be well and if you are not well, be careful."

RESEARCH METHODS TO SPEED THE DEVELOPMENT OF BETTER EVIDENCE—THE REGISTRIES EXAMPLE

Eric D. Peterson, Duke University

The cycle of evidence development and adoption in medicine is far from ideal. Many current day care decisions must be made in the absence of empirical evidence, and where evidence exists, it is often incomplete. While RCTs have become the gold standard for therapeutic evaluation, such studies often determine treatment efficacy, measured only by short-term surrogate markers, rather than more meaningful long-term clinical events. Randomized trials tend to be carried out predominantly with younger, healthy patients who are treated under protocol conditions by highly trained specialists at leading medical centers. Thus, a full measure of their safety and effectiveness is realized only after the therapy reaches the market and is used in real-world patients and caregivers (Califf and DeMets, 2002). Even when good evidence is available, the speed and completeness of uptake of this information by clinicians is delayed and flawed by frequent errors of omission and commission (Balas, 2001).

Large-scale, provider-led clinical registries offer the potential both to augment medical evidence development and to speed evidence adoption into practice. A provider-led clinical registry can be defined as a clinician-organized network for collecting detailed patient information in a uniform fashion for a given population, often defined by a particular disease or medical treatment, and used for addressing research, quality assessment, and/or policy purposes. The concept for these registries can be traced back

to Eugene Stead, the first chairman of the Department of Medicine at Duke University. Forty years ago this year, he outlined the idea of a "living textbook of medicine," extolling physicians to routinely collect and record data on the treatment and outcomes of their patients in order to better care for those in the future (Pryor et al., 1985). The Duke Database for Cardiovascular Disease, the world's first longitudinal cardiovascular data registry, was spawned by these ideas and lives on in a number of national, collaborative, provider-led clinical data registries.

This paper outlines the desired operating and functional characteristics of an ideal clinical registry. We then take a more in-depth look at the leading edge of clinical registries as exemplified by those in cardiovascular disease. Through these registries we explore their current and future planned capacities, as well as their many applications for evidence development and dissemination. We end by discussing the challenges and opportunities faced by such registry efforts moving forward.

Characteristics of Ideal Clinical Data Registries

In a perfect world, data registries would accurately capture detailed clinical information at "key points and events" in a patient's life. Such data should be linkable within and among data sources, such that one could construct a longitudinal record of a patient's care and outcomes. For research purposes, these clinical data registries could also be supplemented when needed with other specialized information such as genomic, biomarker, and/or imaging information. This ideal registry should be readily accessible to researchers for scientific discovery; to outcomes researchers for studying healthcare delivery; and to frontline clinicians, giving them timely feedback on their care processes and outcomes to stimulate quality improvement.

Clinical registries should also have several important functionalities that have recently been summarized in an Agency for Healthcare Research and Quality supported *Users Guide to Registries Evaluating Patient Outcomes*. This document outlines good clinical practice policies for establishing or evaluating an existing registry, including the design and purpose, data sources, data elements, ownership and privacy issues, patient and provider recruitment, data collection and quality processes, and analysis and interpretation (AHRQ, 2007). Briefly, an ideal clinical registry should enroll representative patients, providers, and settings; collect information using standardized data elements and definitions; contain patient identifiers that allow linking of encounter records within and among data registries; have data quality and auditing systems in place to promote the accuracy and completeness of data entered; be flexible enough to allow rapid addition or deletion of variables to meet ever-changing clinical and research needs;

be analyzed by using state-of-the-art methodologies (Vandenbroucke et al., 2007); and be actionable, integrated with quality assessment and improvement efforts.

Size and Scope of Existing Cardiovascular Provider-Led Registries

While the characteristics and features of an ideal registry may seem futuristic, the majority of these features are now present or planned for by the major cardiovascular provider-led registries. Table 6-1 provides a brief description of the Society of Thoracic Surgeons (STS) National Cardiac Database, the American College of Cardiology (ACC) National Cardiovascular Data Registry (NCDR), and the American Heart Association (AHA) Get with the Guidelines programs (American College of Cardiology, 2007; American Heart Association, 2007; Society of Thoracic Surgeons, 2007). As demonstrated, the size and scope of these programs are quite substantial.

Current participation in these cardiovascular registries is voluntary, yet a growing number of external forces are beginning to provide strong incentives for clinician engagement. For example, one large healthcare insurer encourages registry participation by making involvement a condition for "premium provider status" (United Healthcare, 2007). Certain states have begun requiring registry participation as part of state-based certificate of need and quality assurance programs (Massachusetts Data Analysis Center,

TABLE 6-1 Selected Provider-Led Cardiovascular Clinical Data Registries

	Years of Data	No. of Sites	No. of Patients or Procedures
STS			
CABG	1990-2007	1,000	2,768,688
Valve	1990-2007	1,000	709,088
Thoracic	1999-2006	59	49,496
Congenital heart	1998-2006	59	84,072
AHA			
CAD	2000-2007	594	426,414
Stroke	2001-2007	1,040	494,815
Heart failure	2005-2007	397	130,489
ACC-NCDR			
Cath/PCI	1997-2007	971	Cath: 4,113,911 PCI: 2,003,719
ACS	2007	295	37,632
ICD	2005-2007	1,490	179,572

NOTE: ACS = acute coronary syndrome; CABG = isolated coronary artery bypass graft surgery; CAD = admissions for coronary artery disease; Cath = diagnostic coronary angiography; PCI = percutaneous coronary intervention; Valve = any valve procedure.

2007). Most recently, the Centers for Medicare and Medicaid Services (CMS) facilitated complete "voluntary" participation in an Implantable Cardioverter Defibrillator Device (ICD) Registry by requiring it as a condition for payment (CMS, 2007).

The scope of conditions and procedures covered by such registries is also rapidly expanding. For instance, within the past year, the ACC NCDR has launched three new registry efforts in ICD, carotid stenting, and acute coronary syndromes, and it is planning several more within the next few years, including congenital heart disease, cardiovascular imaging, and ambulatory cardiac care. The latter exemplifies the trend for many provider-led registries to expand beyond in-hospital settings and follow cardiac patients across the care continuum.

Modernization of Cardiovascular Provider-Led Registry Operations

Provider-led registries are also changing as we enter the electronic age of medical care. In particular, progress in five key areas is promoting the potential for more integrated and cross-purpose clinical registries. These include the standardization of data elements and definitions; the clarification of patient privacy rules; the development of new data harvesting technologies; the creation of longitudinally linked hybrid databases; and the growing collaboration among professional societies, insurers, and government regulators.

Data Standards Efforts

While the development of standards for medicine terminology has traditionally been elusive, cardiovascular clinical registries are now making great progress toward this goal. The AHA and ACC created a Data Standards Committee to develop cardiovascular (CV) elements and definitions that are used in all their society-based guidelines and registries. Similarly, the STS and ACC have worked to harmonize the nomenclature for their respective cardiac revascularization registries. Most recently, the National Heart, Lung, and Blood Institute sponsored a 2-day retreat to further institutionalize these standards across clinical trials and registries (U.S. Department of Health and Human Services, 2007).

Clarification of Patient Privacy Rules

In 1996, the U.S. Department of Health and Human Services issued the Health Insurance Portability and Accountability Act (HIPAA). While HIPAA was designed to protect misuse of patients' health information, (mis)interpretation of this complex ruling has created significant challenges

for registries and clinical research in general (Ness, 2007). More recently, the pendulum of HIPAA concerns appears to be swinging towards a more neutral position. Briefly, provider-led registries now are seen as compliant with HIPAA when using a business associate agreement with registry participants that permits data gathering and sharing for the purposes of quality assurance (Society of Thoracic Surgeons, 2007). Aggregated data within the warehouse can then be "de-identified" and used for research. In this manner, the burden and bias resulting from trying to gain informed consent from all patients in a registry can often be avoided (Alexander et al., 1998).

Data Harvesting Advances

Once data are more uniformly collected, it becomes possible to exchange among various electronic databases. Participants in clinical registries have traditionally entered clinical data using registry-specific software or, more recently, Web-based data capture systems. However, more and more hospitals already capture certain clinical data in the EMR. To capitalize on this, novel data harvesting and warehouse systems are now being developed that will permit providers to seamlessly map any existing stored patient information into a given clinical registry, thereby "pre-populating" the registry case report form and limiting redundant data entry. Additionally, data warehouses are moving toward the development of Web-based modular augmentation tools that will allow registries to rapidly collect new clinical information when needed. As such, registries are no longer locked into the usual 3-year or longer delay required for registry database upgrades. Rather, they now can respond nearly instantaneously to a new research, patient safety, or policy issue.

Longitudinal Linked Databases

Registries have traditionally collected cross-sectional information (e.g., in-hospital events) and have had limited functionality to study longitudinal patient outcomes. Yet longitudinal patient events (including hospitalizations, outpatient visits, and death) are routinely captured and stored in administrative claims databases such as those of Medicare or private insurers. To potentially access this valuable resource, the major CV provider-led registries are all currently working to link their clinical databases with claims sources. In a similar manner, the provider-led registries are also working together to develop a common standard for patient identifiers so as to facilitate cross-registry matching and analysis. These clinical claims and cross-registry hybrid analytic databases create unique research and quality improvement tools for future generations.

Collaborative Leadership

The above-noted progress is greatly facilitated when the major parties all work together. Whereas in the past, multiple registries competed to enroll similar patients, the field has recently consolidated, with the goal being to create one national, representative registry for each domain. Additionally, in 2006, the major cardiovascular provider organizations held a series of meetings with healthcare insurers and government agencies that resulted in a commitment by all parties to create the National Consortium for Clinical Databases to promote interregistry cooperation and collaboration.

Applications of Clinical Registry for Evidence Development

There are several means whereby clinical registries can augment evidence development (Box 6-1). These can be grouped into epidemiological investigations and those that specifically evaluate the effectiveness of medical therapeutics.

Epidemiological and Surveillance Studies

Clinical registries, if large, detailed, and representative, can be unique resources for national epidemiological and health services research. For

BOX 6-1
Means for Clinical Registries to Support Evidence Development

Epidemiological and Surveillance Studies
- Track disease conditions and medical treatments in community-based, "real-world" settings.
- Large longitudinal genomic studies.
- Conduct post-market evaluation of drugs and devices.
  - Study rare events, late outcomes, and "off-label indications."

Comparative Effectiveness Studies
- Support more efficient randomized clinical trials.
  - Identify patients and investigators; streamline data collection.
- Observational treatment comparisons.
  - Evaluate generalizability of trial findings in real world.
  - Examine clinical issues where RCT is either not possible or not feasible.

example, the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute provides an excellent source of information on cancer incidence and survival in the United States (National Cancer Institute, 2007). In a similar manner, cardiovascular clinical registries have been used to summarize national variability in disease treatment among providers (Peterson et al., 2006), disparities in care among specific patient subgroups (Blomkalns et al., 2005; Sonel et al., 2005), and temporal trends in treatments over time (Rogers et al., 2000).

Genomics Studies

Genomic association studies represent a cutting-edge potential use of clinical registries. Studies that attempt to link a given allelic variation such as a single nuclide polymorphism (SNP) to a disease state offer incredible potential to better predict patients' risk for disease, as well as their response to therapies (Damani and Topol, 2007). A major challenge with these studies is that a high number of statistical tests are often carried out on a relatively small patient sample. As a result, researchers run a high risk that any correlation between a given SNP and a phenotype may be spurious. Clinical registries, however, offer the opportunities to have detailed phenotypic and longitudinal outcomes information on a very large cohort of patients. If blood samples are routinely obtained, the potential to carry out more reliable genome-wide association studies, as well as to replicate promising SNP associations is enormous.

Post-Market Surveillance Studies

As noted earlier, the pre-market evaluation of drugs and devices is imperfect, limited in the total number and types of patients studied, the end points evaluated, and the duration of this evaluation. As a result, there are several recent examples where marketed therapies are subsequently found to be ineffective or unsafe. Clinical registries can be used to track the acute and long-term outcomes of therapies used in diverse patient populations, in on- and off-label indications, and under routine community clinical conditions and settings (O'Shea et al., 2004; Peterson et al., 2004). Such rich data sources can therefore uncover heretofore undiscovered rare side effects (Vioxx, Avandia) and drug-device (Eisenstein et al., 2007) and device-operator interactions (Al-Khatib et al., 2005).

Supporting Clinical Randomized Controlled Trials

Clinical registries also offer the ability to support the conduct of RCTs. During the study design phase, information from clinical registries can pro-

vide important information on the size of potential populations (informing inclusion-exclusion selection decisions), as well as expected clinical event rates in the study population (thereby facilitating sample size calculations to adequately power the RCT). During the enrollment period, comparison of trial versus registry populations can give a clue as to any patient selection bias that could limit the generalizability of trial findings. Registries also offer the potential to help augment assessments of long-term costs and cost effectiveness of a given therapy when used in routine clinical practice (Mark et al., 1995).

Beyond augmenting the design, conduct, and interpretation of RCTs, clinical registries could improve the actual efficiency of RCTs. Specifically, registries could be used to rapidly identify care providers who may be interested in being site investigators, as well as identify patients who are eligible for trial enrollment. In theory, the data collected for a registry could have a dual use in reducing the burden of data collected for a given trial. In the future, huge "practical clinical trials" may themselves be embedded within clinical registries (Tunis et al., 2003). In the extreme, qualified patients in a registry could be offered the option of trial participation. If interested, the patient would simply be randomized to one therapy or another, with all data collection and outcome assessment needed for the trial being conducted as part of routine registry operations.

Comparative Effectiveness

In situations where randomized treatment comparisons are not ethical or practical, or simply have not been conducted, observational comparative effectiveness studies of registry data provide a secondary source for evidence development. The potential need for evidence augmentation using existing databases is so great that some called for the formation of an entire new government agency to oversee comparative effectiveness studies (Wilensky, 2006), while Congress recently introduced a bill that would have provided up to $3 billion to fund this new agency over the next five years.

While the idea that comparative effectiveness studies may facilitate wiser and more efficient use of medical resources and has generated much excitement, the selection of one treatment versus another is almost never a "random event" in real life. Thus, observational comparison studies have the potential for selection biases as a major limitation. Fortunately, several statistical methodologies have been developed to adjust nonrandomized treatment comparisons for selection bias including multivariable regression modeling, propensity analyses, and instrumental variable analysis. Unfortunately, several studies have demonstrated that the analytic technique used for adjustment can impact study conclusions (Kurth et al., 2006; Stukel

et al., 2007), and there is no strong consensus about which technique is superior to another (Cepeda et al., 2003).

When the results of an observational treatment comparison confirm those available from a trial, one gains general assurance that the treatment is effective and safe even when used in broader patient groups (Peterson et al., 2003). However, discord between observational treatment comparison studies and RCTs can also prompt new insights. For example, one study of anticoagulants used in the care of patients with myocardial infarction from a large registry population demonstrated higher bleeding risks than those seen in the trial. Further exploration revealed that clinicians often gave their patients excessive doses of the medication in routine community care, which in part led to the unexpectedly high bleeding risks (Alexander et al., 2005). Thus, although both the trial and the registry were technically "right," they addressed separate questions. Within the controlled trial environment with its protocol-driven care, one effect was seen comparing these drugs. However, in community care, comparative risk benefit ratio of these two therapies was altered due to dosing errors.

Quality Assessment and Quality Improvement

This later point is indicative of a final important role that clinical registries can play, namely to ensure that evidence is fully and appropriately translated into clinical practice. The provider-led clinical registries were developed first and foremost as tools to support quality assessment and improvement. In this capacity, clinical registries have consistently uncovered issues of underuse, overuse, or misuse of proven therapies in routine clinical practice. Yet, beyond being solely a means to document provider performance problems, the registries themselves can be part of the solution. Specifically, coupled with timely feedback, clinical registries can supply providers with important information on areas where practice improvement is needed, as well as on how their care compares with peers.

The impact of such feedback on subsequent care and patient outcomes has been consistently demonstrated (Ferguson et al., 2003). Yet, the majority of these quality improvement (QI) studies employed time-series study designs and, thus, provide only indirect support that registry participation itself led to changes in care. More recent QI studies, however, actually employ cluster randomization at the participant level or other more rigorous designs to evaluate the impact of registry-based QI. In one study, surgeons participating in the STS national database randomized to receive a simple "call to action" and ongoing feedback led to significantly faster adoption of a guideline-based care process than by those not receiving this feedback (Ferguson et al., 2003).

Given this evidence of effectiveness, the tools used by registries to stimulate practice change also need to be refined. Many of the provider-led registries are now working on means of improving the QI process itself. Time delay between care delivery and provider feedback has been progressively shortened, with online, as well as hard-copy reports. Feedback reports are becoming more streamlined, customized, and individualized to the needs of the caregiver. Many such reports provide clinicians with multiple comparative benchmarks, as well as highlighting for the clinician specific care processes that need attention within his or her practice. Finally, provider-led registries are now supplying clinicians with specific tools to help show them not only "what" they are doing wrong, but "how" to practice better care.

The Future of Clinical Registries

Based on the promise and uses briefly described in this chapter, one might imagine that the future of provider-led clinical registries is extremely bright. Yet, this future is not without potential peril. In particular, participation in these registries remains largely voluntary and hospitals need to prioritize resources for registries in the face of shrinking clinical margins. Growing demands from government and insurers for collection of alternative performance assessment data threaten to further limit resources available for "optional" clinical registries. Additionally, an ever-litigious climate in medicine makes clinicians worry whether such clinical information may someday be "discoverable" and used against them.

The answers to these threats are not simple and will require a multilevel and persistent response. Clinicians need to make a strong case that clinical registries are best run and most valuable when they remain in the hands of clinicians. Such registries first were developed by clinicians to support discovery and ensure the quality of care. Practitioners who remain in the group most clearly understand what the most relevant research and practice issues are; they are directly responsible for the data collection and thus should be in control of the quantity and quality of the data collected; and they are the agents of change when new findings require it. While governments and insurers are charged with ensuring quality of care, clinicians are charged with delivering it. This last bit of logic has led external agencies to consider forgoing their external measurement systems and, instead, using provider-led clinical registries as their assessment tools. Such a development could lead to the assurance of clinician involvement in provider-led registries as well as the resources needed to run them. If so, the remaining challenges for provider-led clinicians will be to remain true to their research and QI roots, as well as to live up to the promise outlined above.

PRODUCT INNOVATION—THE TAILORED THERAPIES EXAMPLE

Steven M. Paul, Eiry W. Roberts, and Christine Gathers, Eli Lilly and Company

Introduction

Healthcare systems in the developed world currently face increasing challenges, coupled with unprecedented opportunities. In recent years, investments in biomedical research have resulted in a broad spectrum of advances in the areas of disease diagnosis and therapeutic intervention. As a result, clinicians and patients can now make choices among an expanded (and ever-increasing) array of options for the treatment of many common and chronic diseases, including mental illness, cardiovascular disease, and even some cancers. In addition to these therapeutic advances, evolving health information technology promises to deliver much improved access to information for clinicians, patients, and other stakeholders (including payers and governments) in the very near future. Such "real-time" access to information creates opportunities to facilitate more informed therapeutic decisions and to enable more rapid integration of complex information in a way that ensures improved efficiency and effectiveness in the delivery of health care to the population at large.

Despite these advances, however, the way in which health care is currently delivered by a large proportion of healthcare providers, and experienced by most patients, remains largely empirical. Therapeutic interventions are frequently applied in a "one-size-fits-all" approach, and the means by which individual patients are matched to therapeutic interventions often occurs by "trial and error." While it is important not to underestimate the impact of this historical approach to treating and managing many diseases, it is also clear that this rather empirical approach must evolve to embrace the principles of comparative effectiveness and evidence-based medicine. The ultimate goal, of course, is to provide healthcare decision makers (e.g., patients, clinicians, payers, and policy makers) with up-to-date, evidence-based information about treatment options so that they can make informed healthcare decisions. Virtually all stakeholders in the healthcare system today are demanding improved, more predictable, meaningful, and objectively demonstrable "health outcomes" from all types of medical interventions, including the use of biopharmaceuticals. Moreover, patients and clinicians are demanding better information about where and when to use—and when not to use—a given biopharmaceutical, including complete transparency in terms of its safety and efficacy. These heightened expectations, coupled with the explosion of technological advances in recent years, create a unique set of challenges and opportunities for the biopharmaceutical industry, particularly with respect to the discovery and development of new medicines.

The focus of biopharmaceutical research and development is currently shifting away from a sole preoccupation with traditional measures of "safety and efficacy" to more clinically relevant measures of "effectiveness" and to a better, more integrated understanding of benefit-risk for patients (i.e., providing "meaningful, improved patient health outcomes"). This more recent focus on health outcomes puts additional burden and complexity on biopharmaceutical research and development (R&D) when applied within the current R&D model, with a resultant increase in drug development time lines and overall costs. At the same time, the biopharmaceutical industry is experiencing unprecedented challenges to its fundamental business model, and some have even predicted the demise of the industry in its current form, given (1) decreasing R&D productivity overall, (2) the reliance that individual companies place on deriving profit from a small number of one-size-fits-all medicines, and (3) the large number of patent expirations looming for these medicines over the coming decade.

How might this tension between heightened expectations and demands on the part of consumers (patients, providers, and payers) and the enormous costs and risks inherent in biopharmaceutical R&D be reconciled? How does the well-recognized interindividual variability in drug response (for both efficacy and safety) among the general population complicate studies of comparative effectiveness of biopharmaceuticals, and how will it impact biopharmaceutical R&D in the future? How might the treatment and management of disease by biopharmaceuticals be best approached in an era of comparative effectiveness and EBM? Obviously, such challenges are multidimensional in nature and will require multiple interventions by all of the various stakeholders. We believe that to move forward successfully, the biopharmaceutical industry, with appropriate collaboration from all relevant stakeholders, must redouble its focus and reinforce its efforts to truly understand the needs of patients and to deliver new medicines that offer not only improved, but also meaningful, patient outcomes. As part of our commitment to this goal, we have recently developed and implemented a business model (for both R&D and commercialization) that we refer to as "tailored therapeutics." In short, tailored therapies give greater assurance that the "right drug" will be prescribed for the "right patient at the right dose and at the right time and with the right information and supporting tools." A critical success factor for delivering tailored therapeutics is our evolving and much greater understanding of the considerable heterogeneity that exists in the etiology and pathophysiology of disease and in the pharmacological response (both beneficial and adverse) to biopharmaceuticals. While many new tools (e.g., genomics, proteomics, computational approaches to disease state modeling) currently exist to explore the biological substrates of disease heterogeneity and the interindividual variability in the clinical response to biopharmaceuticals, the application of this technology

to predict the relevant health outcomes afforded by drugs remains a daunting challenge.

The rationale for how tailored therapies can potentially impact the discovery and development of biopharmaceuticals, as well as help to define and establish their comparative effectiveness in the marketplace, is outlined briefly below.

Challenges to the Current Drug Development Paradigm

Over the past 50 years, a large number of effective (and safe) medicines[1] have been introduced to treat and manage many acute (e.g., infectious diseases, myocardial infarction) and chronic (e.g., hypertension, diabetes) diseases. These drugs have beneficially impacted longevity, contributing to an ever-increasing life span, as well as to the quality of life in both developed and developing countries. Despite these successes, however, and the very significant, virtually unprecedented, advances in biomedical research that have been made over the past two to three decades, the number of new drugs approved by the FDA over the past 5 years has decreased dramatically (50 percent fewer drugs than in the previous 5 years). In 2007, for example, only 19 new molecular entities (NMEs) (including biologics) were approved by the FDA, the fewest number of new drugs approved since 1983 (www.fda.gov). This reduction in the introduction of new medicines is all the more troubling when one considers the enormous R&D investments currently made by the biopharmaceutical industry, now estimated to be in excess of $50 billion annually (Mathieu, 2007). In fact, it has been estimated conservatively that each new NME costs in excess of $1.5 billion to develop and introduce (Tufts Center for the Study of Drug Development, 2006). Diminished patent life, complicated by tougher regulatory requirements and enormous global pricing pressures, have all contributed to concerns about the viability of the current biopharmaceutical business model. Finally, it is widely expected that the use of generic drugs will dramatically increase over the next decade given the many scheduled near-term patent expirations. Demonstrating "comparative effectiveness" for a patent-protected drug versus a generic, in addition to monitoring a branded drug's safety profile in the post-marketing (generic) environment, will require considerably more resources and attention from the healthcare system.

Improving R&D productivity remains arguably the most important challenge facing the biopharmaceutical industry. The latter can be achieved by improving three of the most challenging elements of drug discovery and development: unit costs, cycle time, and most importantly, attrition. These

[1]Medicines are broadly defined to include traditional small-molecule drugs, bioproducts (proteins and peptides), and vaccines.

three dimensions of R&D "productivity" are intimately related to one another, and if each could be improved even modestly, R&D productivity would increase substantially, thus reducing the overall cost of developing a new medicine. A full discussion of R&D productivity is well beyond the scope of this paper. However, the challenges posed by the enormous attrition rates for drug candidates as they move through development must be underscored. Currently, about 50 percent of drugs in phase III (the final and most expensive phase of drug development) fail to make it to market, primarily because of unacceptable benefit-risk profiles. Phase II attrition (a phase in which safety is confirmed and efficacy is first established) is even more daunting: currently, 70 percent of potential new drugs entering phase II do not make it to phase III. Reducing the attrition of drugs that are in the late phase of development will be essential to improving R&D productivity. The use of biomarkers focused on the early identification of efficacy and/or safety signals, together with the use of markers focused on patient stratification strategies via a tailored therapy approach during late-stage clinical development, have already proven useful in this regard (and are discussed below). Importantly, the substantial late-stage attrition that characterizes drug development at present also complicates and confounds the timing and initiation of health outcome and comparative effectiveness studies, an essential "component" of future drug development and evidence-based medicine.

Tailored Therapies Enable a Paradigm Shift for Drug Development

For a variety of common diseases, only about 50 percent of patients will respond favorably to a given biopharmaceutical agent (Spear et al., 2001). Moreover, such response rates in individual patients are often highly variable in both their magnitude and their duration. In one sense, when it comes to "customer" expectations, there appears to be an "efficacy gap" for many marketed one-size-fits-all biopharmaceuticals. It is also important to emphasize that even if a patient experiences no (or little) therapeutic benefit from a given drug, he or she is still at risk for potential side effects and/or serious adverse events. Furthermore, several studies have shown that the burden of adverse drug reactions on the healthcare system is high, accounting for considerable mortality, morbidity, and extra cost (Lazarou et al., 1998). Side effects and/or serious adverse events in this context can often relate to the therapy's being inadvertently prescribed for the wrong patient or at the wrong dose for that patient. In many circumstances, interactions between concomitantly prescribed medicines also contribute heavily to the occurrence or severity of such events (often due to issues of competing or impaired drug metabolism). Most of these drug-drug interactions can be minimized or potentially avoided altogether.

Thus, individual differences in drug response (both good and bad) within the population of patients treated pose obvious challenges to drug development, as well as to the way medicines are used clinically and marketed by manufacturers. Such individual differences in treatment response also make it considerably more challenging to compare the effectiveness of one drug with another in a given class, since the benefit-risk ratio may differ dramatically for each agent (i.e., among subgroups of patients with the same disease). Thus, it is possible, perhaps even likely, that comparative effectiveness studies of drugs if carried out in large heterogeneous patient populations may miss subgroups of patients in whom a given drug may actually prove to be superior with respect to either its efficacy or its safety, or both. Identifying such subgroups especially in real-world situations will be essential for optimal utilization of any such drug and for establishing meaningful (evidence-based) comparisons between drugs (as well as with nonpharmaceutical interventions, for that matter).

Tailored therapy is an approach to optimizing the benefit and risks of a given drug for individual groups of patients. Tailored therapies exist across a continuum from the least tailored one-size-fits-all biopharmaceutical to the truly targeted therapy. The degree of tailoring possible will depend on a number of factors such as drug characteristics, underlying disease biology (e.g., genetics), available monitoring tools (e.g., diagnostic or imaging technologies), and a number of environmental variables (e.g., diet, culture). Currently, the most extreme examples of tailoring include a number of highly targeted cancer drugs (e.g., Gleevec, Herceptin) that work directly on the underlying biology or genetic etiology of the cancer itself. The predictability of a beneficial treatment response with such targeted agents, given that they work on the molecular underpinnings of the disease, is very high. Nonetheless, targeted drugs such as these are still fairly rare and exist at the extreme of the tailoring continuum. The term "personalized medicine" also broadly implies the ability a priori to match a particular therapy to an individual patient, often through pharmacogenomic approaches, which are used either to understand exposure at the individual patient level or to predict and/or measure efficacy or safety. As such, personalized medicines also represent a subset of the range of opportunities within the continuum of tailored therapies. In clinical practice, this type of personalized, pharmacogenomic approach has so far been very rarely applied (Lazarou et al., 1998) despite well-established genetic polymorphisms (e.g., SNPs) and available genotyping methods (Figure 6-1). The reasons for this are manifold, but include the lack of large prospective studies to evaluate the impact of genetic variation on drug therapy. Most importantly, the vast majority of the more common diseases are undoubtedly genetically complex and polygenic in nature (e.g., diabetes, obesity, hypertension, coronary heart

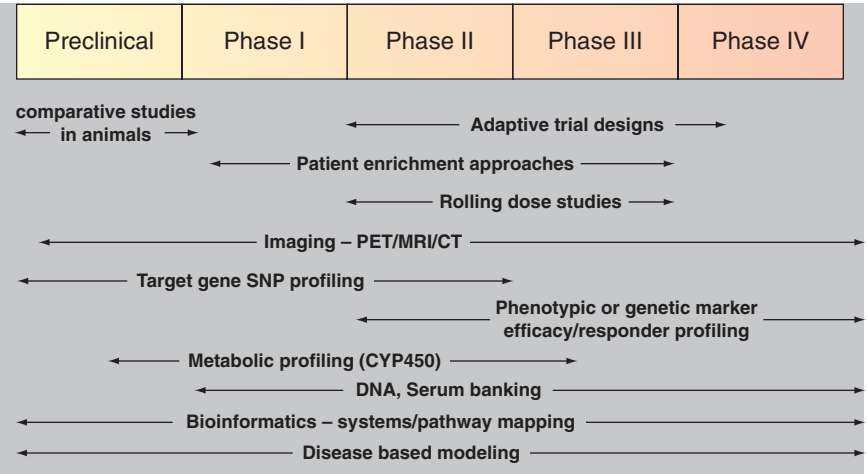

FIGURE 6-1 What are we doing differently?
NOTE: CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography.

disease), so whether targeted or more personalized drugs can routinely be developed for these disorders is far from certain (Need et al., 2005).

The concept of tailored therapies is certainly not new. For years, physicians have used biomarkers such as blood pressure or hemoglobin A_{1c} (HbA_{1c}) to monitor the effectiveness of antihypertensive and diabetes drugs, respectively. Compelling health outcome data exist for only a handful of biomarkers that allow physicians (and patients) to know the likely and predictable benefits of a given drug for a given patient. Two notable examples are the reduction in low-density lipoprotein cholesterol and HbA_{1c} resulting from treatment with hydroxymethylglutaryl-coenzyme A reductase inhibitors (statins) and certain antidiabetes medications (e.g., insulin), respectively. Both biomarkers are reliable predictors of beneficial health outcome (reduced morbidity and mortality) following treatment with these drugs. However, whether these biomarkers will afford the same degree of predictability for other cholesterol-lowering or diabetes medications is far from certain. This rather sobering possibility has recently been emphasized with the use of oral antidiabetic thiazolidenediones and other (non-statin) cholesterol-lowering agents.

The movement toward tailored (or "personalized") medicine has undoubtedly been accelerated by a whole range of new tools (see Figure 6-1).

Some of these tools aid the discovery and development of drug can-

didates, yet other emerging diagnostic and prognostic tools (e.g., genomics, imaging) will also ultimately benefit healthcare delivery. For example, in discovery, disease state modeling is utilized as a tool to compare new drug candidates with existing medicines in the marketplace. In essence, these models enable the selection of drug candidates that will demonstrate improved health outcomes. Other tools have impact that span all phases of development. For example, pharmacogenomics, or the ability to define genes or alleles that determine the response to drugs, is an exciting prospect for improving the predictability of tailored therapies. To date, there have been a few notable pharmacogenomic studies, particularly with respect to mutations or polymorphisms in drug-metabolizing enzymes (Evans and McLeod, 2003). These studies have proven highly informative in predicting the benefit, as well as the adverse event profile or liability of a number of important drugs. One of the most well known of these examples relates to the study of cytochrome P (CYP) 2C9 polymorphisms and their relationship to bleeding risk in patients treated with warfarin (Higashi et al., 2002). Research has led to the identification of two common polymorphisms of the CYP2C9 gene that appear to be associated with an increased risk of overanticoagulation and bleeding events among patients treated with warfarin. Discussions are currently under way at the FDA to consider the inclusion of these pharmacogenomic data in the prescribing information for warfarin, but even in this relatively well established case, there is much debate about the "clinical validity" and utility of the diagnostic test and the applicability of the data for dosing recommendations for warfarin therapy.

The focus of tailored therapies is on the predictability of the health outcome afforded by a given drug in an individual patient. In many circumstances, this may also involve an ability to determine whether there is sufficient exposure to the drug in any given patient to even create the opportunity for favorable clinical response. One such example includes the evaluation of the CYP2D6 genotype in psychiatric patients treated with antidepressants that are substrates of CYP2D6 (Meyer, 2004). Clearly in this population, genotyping can improve efficacy, prevent adverse drug reactions, and lower the cost of therapy overall. This knowledge has led to the recent, relatively broad, adoption of this approach in academic psychiatry units across the United States.

Beyond these relatively straightforward examples related to drug metabolism, however, clinical response for the vast majority of drugs is, as stated earlier, likely to be polygenic in nature, with multiple genes or alleles each contributing a small or very modest effect. The utility therefore of knowing these genes (i.e., to categorically predict the response to a given drug in an individual patient) is far from certain (Meyer, 2004). Moreover, for many drugs, nonbiological factors, including environmental factors (e.g., diet, exercise) that vary over time, may contribute as much or more

as genes to the ultimate effect of a drug. These caveats not withstanding, it is highly likely that a range of predictive tools will undoubtedly prove invaluable in tailoring therapies to individual patients or subpopulations of patients in the future (The Royal Society, 2005).

While the choice of the drug itself is essential, the dose, timing, and especially the duration of treatment are often critical in determining the ultimate health benefit for the patient. Thus, the broad concept of tailoring also includes various approaches to ensuring adequate compliance or adherence, including the use of biomarkers to assess the degree of drug efficacy (or lack thereof) and/or whether the patient is actually compliant with his or her treatment regimen to achieve optimal health outcomes. Again, in the real world—often in sharp contrast to the clinical trials required to establish safety and efficacy in the first place—such factors will in good measure determine the effectiveness and ultimate health outcome for any biopharmaceutical.

Impact of Tailored Therapies on Drug Development and Comparative Effectiveness

Tailoring therapies to the patients who will most benefit from them could improve R&D productivity by having an impact on the three important productivity levers (i.e., cost, time lines, attrition). For example, if one can identify a priori that the target or pathway under study is directly related to an important clinical outcome for at least a subgroup of patients with a given disease, then the "drug" can be tailored to impact that pathway and the attrition associated with drug candidates operating through that pathway should be reduced substantially. Moreover, if a subgroup of patients with any given disease or syndrome who are most likely to respond to a given drug can be identified using a biomarker, theoretically the number of patients (and thus the expense and cycle time) needed to demonstrate a clinically meaningful impact on efficacy and/or safety in late-stage clinical trials can also be reduced. We have used modeling to understand the relationship between response rate (relative to a placebo or a comparator) and sample size for clinical trials and have found that the use of a biomarker that increases drug response rates only modestly (20-30 percent) could dramatically reduce the number of patients required for late-stage clinical trials. The latter will therefore not only reduce the costs of expensive late-stage clinical trials, but also decrease the number of patients exposed to a drug that is unlikely to bring them benefit. Biomarkers can therefore also be used to avoid exposing patients who are most likely to have a serious adverse event or side effect (e.g., immunogenicity biomarkers for bioproducts). Moreover, attrition rates resulting from type II errors (false negative studies of active drug versus placebo or active comparators) will

be reduced by eliminating those patients who are unlikely to respond to a given drug and thus will reduce the statistical power (add to the "noise") inherent in any clinical study. Ideally, such biomarkers could also be used to stratify patients once the drug is approved and marketed. This, of course, is already the case with the targeted cancer agents cited above and in our view will eventually be the "rule not the exception" for the majority of drugs across the continuum of tailored therapies. Consequently, Lilly and other biopharmaceutical companies are employing biomarker strategies for virtually all drug candidates early in their development, first to help determine whether these drugs prove safe and efficacious—preferably in phase I or II (i.e., to reduce late-stage phase III attrition)—and then eventually to potentially stratify patient populations once the drug reaches the market. Lilly anticipates that some of these biomarkers will also eventually be validated and used as companion diagnostic or prognostic tests to increase the predictability of a beneficial response and to ensure the effectiveness of a given drug in real-world clinical settings. If successful, such an approach will dramatically increase the therapeutic benefit and thus the value proposition afforded by biopharmaceuticals in the treatment and management of disease.

In parallel with efforts focused on identifying the "right patient, right dose, and right time" for therapeutic intervention, it is imperative to utilize the principles of tailored therapeutics to improve relevant patient outcomes to establish comparative effectiveness among all treatment options. An equal effort must be focused on understanding which outcomes are relevant and value-added for patients, either at an individual or at a population level. Historically, much of the biopharmaceutical industry focus in this regard has been on the evaluation of clinical trial end points defined predominantly by the regulatory requirements to gain marketing approval. Although important, these end points are often far removed from the outcome measures that are meaningful to patients, providers, and payers. Such examples might include the distinction between the improvement in positive and negative symptoms observed in schizophrenic patients treated with antipsychotic drugs in pivotal clinical trials and the measurement of more valuable "functional-based" outcomes, such as whether the patient can maintain an independent living arrangement or maintain employment. If the biopharmaceutical industry is to deliver valuable medicines in the future, there needs to be increased collaboration across healthcare stakeholders to evaluate and "clinically validate" some of these important functional outcome measures so that they can be effectively incorporated into the development of new therapeutics, preferably even before approval and launch. Comparative effectiveness studies and their eventual adoption by providers and payers will thus need to consider all relevant and meaningful health outcomes.

Nonetheless, the tools currently being developed in support of tailored

therapies, if applied appropriately, could allow for the design of comparative effectiveness (Califf, 2004) studies that consider the biological (as well as nonbiological) substrates and heterogeneity of drug response, allowing for meaningful comparisons between drugs, or between drug and non-drug therapies, in subgroups of patients who are more likely to benefit from their use, as well as avoiding treatments (including drugs) of limited effectiveness. Only in such a setting where true confounders of outcome (such as those we have highlighted above) are recognized, fully understood, and taken into consideration, can comparative effectiveness assessments of biopharmaceuticals be truly informative and meaningful.

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7

Policy Changes to Improve the Value We Need from Health Care

INTRODUCTION

Almost every aspect of introducing more evidence into the healthcare system—from establishing electronic medical records (EMRs) to measuring quality care to revamping the reimbursement system—has complicated political and regulatory implications. Experts agree that the way these changes are presented to policy makers and the public will be critical for their acceptance. Moreover, a consensus on how to measure the value of healthcare services is needed to align evidence applications with overall healthcare goals.

In her paper, Donna E. Shalala draws on her experience as head of the Department of Health and Human Services in the Clinton administration in the 1990s to identify the political and regulatory challenges encountered in introducing evidence-based medicine (EBM) to the healthcare system. The way the political system is organized powerfully affects the quality of health care and the way it is delivered. Even when the evidence base is strong, it can be very difficult to make changes within the governmental system. It might not be realistic to expect Medicare or Medicaid to lead evidence-based efforts, particularly in terms of reforming the payment system. Drawing upon lessons learned in efforts to make childhood immunization universal in the 1990s, Shalala notes that successfully driving evidence through the healthcare system requires a very specific goal, consensus on the problem, and a public-private partnership on how to provide the solution.

Michael E. Porter's paper argues that fundamental to real reform is the improved ability to define and measure value in health care. Within the

field, however, there is a lack of consensus on a clear and shared goal—a confusion that is also reflected in many aspects of healthcare delivery, particularly in reimbursement policies. Delivering care of value is a goal that can unite the interests of all stakeholders; and defining and focusing on value is an important opportunuity to catalyze systemwide improvement in health care.

Porter defines value in healthcare delivery as patient outcomes achieved relative to the total cost of attaining those outcomes. The implications of measuring value for current approaches to process guidelines, outcomes measurement, and quality and safety improvement are discussed, along with some analytic challenges for the field. Consideration is needed on how to best measure health outcomes for multiple medical conditions and account for care received from many different specialists, and the long-term nature of the care. And an important first step is a more rigorous approach to defining and describing outcomes. In addition, the healthcare reimbursement model should be revamped to bundle reimbursements across medical conditions and cycles of care. Porter concludes that all stakeholders can contribute towards improvement in healthcare delivery by organizing their efforts around value as a central goal in health care.

REGULATORY AND HEALTHCARE FINANCING REFORMS

Donna E. Shalala, University of Miami

Any discussion of incorporating EBM into the current healthcare system should include an examination of the role of government and regulatory agencies. This paper focuses on the political realities that must be faced in efforts to improve health care in this country.

The first issue to consider is whether discussions of cost savings and effectiveness should be separated. As government agencies try to institute reforms, one thing that has caused trouble in attempts to translate evidence into first-rate care is the suspicion among healthcare professionals that EBM is simply a budget cutting exercise. Part of the quality movement in medicine has tried to separate evidence-based care from cost cutting, implying that there is a kind of purity in doing the right thing and in making sure that available evidence is translated to the bedside.

As methods to incorporate better evidence into health care are considered, it must be remembered that the power of words cannot be underestimated. Those with knowledge of the history of attempts to get universal coverage—both from the debates over Social Security in the 1930s and of the Clinton Health Care Plan in the 1990s with the accusations of socialized medicine—know the power of words to transfer reform into something completely different. Whether reform efforts are labeled as socialized medi-

cine or viewed as an attempt to force a cookie-cutter approach that takes autonomy away from professionals, these are powerful words and images that have been used to derail attempts to introduce EBM and universal coverage in the United States.

The way the political system is organized powerfully affects the quality of health care and the way that it is delivered. Those who have suggested that universal healthcare coverage is needed before evidence can be incorporated into the system should note that even where we currently have a single payer or a large purchaser, this has still been extremely difficult. It seems logical that very large purchasers of health care such as Medicare, the Veterans Administration, or the military healthcare system should be able to put requirements in place that allow us to take EBM and transform the way care is delivered. However, even when the evidence base is very strong, it can be difficult to make these kinds of changes within the governmental system. Every step toward implementing change has a constituency and, usually, members of Congress who are particularly interested in those constituencies.

Therefore, another question that needs to be considered is whether we can expect Medicare to lead evidence-based efforts, particularly in terms of reforming the payment system. There already have been many attempts to bring EBM into the Medicaid and Medicare systems. In many cases, EBM was successfully integrated with policy outcomes, and the enormous purchasing power of the Medicare system was used to make changes. However, it is important to caution that with big changes, such as introducing large-scale demonstration projects, there can be a great deal of resistance from Congress. This resistance was sometimes fueled by individual professional groups and healthcare companies that were trying to protect not only their incomes, but also their way of doing things. While there is strong agreement that there should be a link between incorporating EBM into health care and being reimbursed for providing quality health services, there is no consensus in this country on how to do that.

With these points in mind, an examination of the ways in which EBM has successfully been incorporated into the system can help identify what political conditions are needed to make it happen. The last century of public health provides many strong examples of evidence being used to transform people's lives. They include such basic concepts as cleaner water, reliable sewage systems, and cleaner air. More recently, in the area of tobacco control and smoking cessation, the clear evidence that tobacco causes diseases exerted the necessary political pressure that changed behaviors and achieved results.

Another example of the overwhelming evidence that galvanized change is childhood immunization. As late as the 1990s, during the Clinton administration, half of the children in this country were not being immunized at

the right time. Because of the overwhelming evidence that immunization dramatically improves public health, one of President Clinton's main health priorities was to ensure that all children were receiving immunizations by age 3.

The fundamental problem in achieving universal immunization in this country has always been that a universal healthcare program is not in place. In fact, many thought it would be impossible without this. However, veterinarians in this country had already devised a tracking system and a method for immunizing every cow, sheep, dog, and kitten. If veterinarians could achieve this without universal health care, it could certainly be done for the children as well.

It took strong evidence and a powerful political and organizational movement to get 90 percent of the children in this country immunized. That meant winning the support of the states, professional groups, pediatricians, and health maintenance organizations; obtaining funding from Congress so the shots could be provided in doctors' offices, clinics, hospitals, and pharmacies at almost no charge; and developing an immunization tracking system.

This example illustrates that to have success in taking evidence and driving it through the healthcare system, we need a very specific goal, consensus on the problem, and a public-private partnership on how to provide the solution.

In the case of immunization, a sustainable system was created that remains in place to this day. However, it must be remembered that it was not very controversial; neither political party would lose contributions over offering immunizations. In addition, the government built in reimbursements and other incentives to ensure cooperation, such as denying enrollment in Head Start or child care centers without immunizations or withholding benefits from the Special Supplemental Program for Women, Infants, and Children.

Unfortunately, unlike immunization, clear answers do not exist for many of the problems currently at hand. In some cases, we have enough evidence to move forward, but the political climate surrounding these issues requires careful consideration of the consequences. It is safe to say that almost all healthcare professionals work toward what is best for their patients, but the interface between their livelihood, perceived underpayments, and the demands of EBM—including a patient's ability to shoot the messenger based on the research and to raise questions about the message—leads one to believe that this is far more complex than initially thought.

In this country we have a fragmented health system and fragmented research institutions. Many federal agencies are gathering and reviewing evidence, from the Agency for Healthcare Research and Quality (AHRQ) to the Centers for Disease Control and Prevention to the Department of

Defense (DOD) to the Veterans Administration (VA). In addition, the private sector is also doing this type of research, including all of the specialty boards and professional organizations, as well as insurance companies such as Aetna, WellPoint, United Healthcare, Humana, and Cigna. In fact, the private sector has more up-to-date usage information than many federal agencies. Many have suggested that the United States follow the lead of England and centralize this research and recommendations.

Before such a decision is made, the following questions should be asked: Should a system exist where the messenger is going to take all the shots? Can congressional protection be put in place for that messenger? When AHRQ's predecessor, the Agency for Health Care Policy and Research, tried to change practices in back treatment based on research, the back surgeons took it apart and the agency was almost disbanded. There are many instances where research almost brought an agency to its knees because a variety of interests weighed in on that particular piece of research.

Many agree that the best option would be to tithe every health plan in this country for this research in order to build a base of support. That funding would not necessarily be funneled to only one agency, but a base for research is crucial, given the billions of dollars that we spend on health care. Furthermore, it is crucial to politically protect the messengers, those who do the research and present it in a way in which it can be translated and used for patients.

Finally, is there a political will to make these kinds of changes? Every Republican and Democratic candidate for president speaks of the importance of information technology (IT). Why are EMRs not yet standard practice? Why is agreement lacking on what goes in that medical record? The DOD and the VA have required 6 months time to begin to come to agreement about what should be included in a medical record and about the interoperability of the system. While it is not an easy task, there certainly exists political consensus in this country on IT, as well as among presidential candidates on creating an agency for evidence-based research and the possibility of greater investments in research.

However, many raise the issue of political conditions for fundamental healthcare reform. In 1991 and 1992, when the Clinton administration was introducing its healthcare reform package, healthcare premiums were increasing and spending on drugs was going up faster (Figure 7-1). The growth in uninsured Americans is much more significant now than it was then. The increase in Medicaid spending is significantly less now. Other factors such as the rates of unemployment, inflation, and the federal budget deficit also are lower now than in the early 1990s.

Even so, Americans have not changed their minds over these last decades about the health system's need for reform. While there is agreement on the problem, Americans are not sure government ought to fix it.

HEALTH COSTS/UNINSURED	THEN	NOW
Increase in Premiums	14% (1990)	6.1% (2007)
Increase in Rx Drug Spending	14.7% (1990)	5.8% (2005)
Growth in the Uninsured	1.3 mil (1990)	2.2 mil (2007)
Increase in Medicaid Spending	27.1% (1991)	2.8% (2006)
ECONOMY		
Unemployment Rate	5.6% (1990)	4.6% (2006)
Inflation	5.4% (1990)	3.2% (2006)
Change in 1st Quarter State Tax Collections	-1.3% (1991)	5.8% (2007)
Federal Budget Deficit	$269 bil (1991)	$158 bil (2007 proj.)
POLITICS		
Control of Government	One party control until '95	Divided government
Presidential Leadership	#1 priority, Clinton proposes comprehensive overhaul (1993)	
THE PUBLIC		
% Saying Health System Needs Major Changes	54% (1991)	55% (May 2007)
% Picking Health as One of Top Two Issues Wofford/Thornburg vs. Today	50% (1991)	27% (August 2007)

FIGURE 7-1 The health reform context, then and now.

The Clinton administration of the 1990s alarmed many with a bold universal healthcare plan. People are not convinced that the president of the United States should be in charge of health care, with issues such as international security and the economy at the forefront of his or her mind.

Yet it helps to illuminate a principle of public policy. In our previous grand steps to introduce large-scale government solutions—in the 1930s with the creation of Social Security and in 1965 with the development of Medicare and Medicaid—there was agreement about the problem. During those periods there was also agreement about the solution; there was no serious private-sector or state alternative. There was debate about the delivery system, which is why Medicare is delivered by private insurers, but there was an agreement that the population to be served—the old and the sick—could not be served equitably by the private sector or other levels of government. Similarly, a private-sector alternative to Social Security did not exist either.

To make a grand social policy change such as providing universal health care, there must be consensus on both the problem and the solution. The mistake we made was that we assumed both existed, but alas, in

actuality, they did not. We had agreement only that there was a problem. This is similar to the challenge that faces the country today.

In the end, to bring research to bear on the way in which medicine is practiced in this country and the way in which we organize health care, the most self-interested people in our country must provide the leadership. Even though a number of presidential candidates intend to take on the issue, switching to an evidence-based system will require healthcare professionals' making the case as shrewdly as they possibly can.

DEFINING AND INTRODUCING VALUE IN HEALTH CARE[1]

Michael E. Porter, Harvard University

In any field, defining and measuring value is fundamental to progress. Improved performance and accountability are possible only when there is a clear and shared understanding of the goal, or "objective function," to use an economist's term. In most industries, participants contract freely and prices are set in open, competitive markets. The objective function is clear—making a profit. In healthcare delivery, however, the objective function is not so clear. Participant choices are constrained, prices are set or heavily influenced by government, and, in many cases, a public service mission and non-profit entities coexist with the profit motive.

Moreover, the profit motive is itself compromised in healthcare delivery by the current U.S. reimbursement structure in health care, as well as reimbursement practices in many other national systems. Prevailing reimbursement creates a disconnect between profits for system actors and value for patients because providers are rewarded for services, not patient results. System actors are also sometimes rewarded for shifting costs to others.[2] Such a divergence between profits and patient value makes defining, measuring, and reporting value even more essential to true improvements in care delivery.

Not surprisingly, there is confusion and lack of consensus about the appropriate objective function in health care. Many in the field talk about access as the objective. Others point to equity, community service, or better

[1]This article draws heavily on joint research with Elizabeth Teisberg (Porter and Teisberg, 2006). I am grateful to her for her fundamental contribution to the line of thinking discussed here. This paper also draws on subsequent research by Benjamin Tsai, Saquib Rahim, and Jennifer Baron at the Institute for Strategy and Competitiveness at Harvard Business School. Jennifer Baron, Sachin Jain, Joan Magretta, Michael McGinnis, and Elizabeth Teisberg provided helpful comments.

[2]The same is true for health plans, who can profit through shifting costs and restricting revenues to providers, patients, or the government without actually offering patient outcomes or true efficiency.

population health. Still others define the goal as patient satisfaction, quality, safety, or care that is consistent with medical evidence. Nearly all actors identify cost containment and achieving an operating surplus as among their principal aims. The Institute of Medicine's own definition of goals for the healthcare delivery system includes no less than six elements: safety, effectiveness, patient centeredness, timeliness, efficiency, and equity (IOM, 2001). In addition to the existence of multiple goals, different actors in the system define the objective function differently, a sign that the participants may be working at cross-purposes.

I believe that many of the difficulties in improving healthcare delivery stem from confusion and disagreement about defining, measuring, and rewarding value. The primary objective for healthcare delivery should be value for patients, measured by patient health outcomes per dollar expended to achieve those outcomes. Value is the only goal that unites the interests of all the parties in the healthcare system. Improving value is also fundamental to achieving all the other goals, such as expanding access and improving equity.

Defining Value

Value in any field must be defined around the customer, not the supplier. Value must also be measured by outputs, not inputs. Hence it is patient health *results* that matter, not the volume of services delivered. But all outcomes are achieved at some cost. Therefore, the proper objective is the value of health care delivery, or the patient health outcomes achieved relative to the total cost (inputs) of attaining those outcomes. Efficiency, as well as other objectives such as safety, are subsumed by value.

Health outcomes refer to the set of *objective* outcomes, not just patient perceptions of outcomes which can be biased toward the service experience. There is not just one outcome of care for any health condition, but multiple outcomes that jointly constitute value. Patient circumstances and preferences will affect the weighting of these outcomes to some degree, a subject discussed later.

The costs of achieving outcomes refers to the *total costs* involved in care, not just the costs borne by any one actor or for any particular treatment or episode.[3] Hence, shifting costs across parties by, for example, raising patient co-payments for prescription drugs, does not add value but simply changes who pays. The mismeasurement of costs works against true value improvement, and is endemic in healthcare delivery in every country,

[3]We treat non-economic costs of care, such as the patient's discomfort, anxiety, and time, as part of patient outcomes. See below.

especially in the United States, because of the way that services are organized and paid for.

Value for patients improves when equivalent outcomes are achieved at a lower cost, or better outcomes are achieved at comparable (or lower) cost. Yet outcomes and costs are not independent. A powerful lever to reduce costs is to improve outcomes, such as through early detection that limits the complexity of care, less invasive treatment, faster recovery, or less need for subsequent care. The power of quality improvement to drive down costs is greater in health care than any other industry I have encountered, because of the basic truth that better health is inherently less expensive than poor health.[4] That so many actors in health care treat cost containment as the goal, instead of patient value, has severely handicapped the rate of value improvement.

Access to health care is a basic goal of any healthcare system, but access per se does not constitute value. Access provides the opportunity for value to be created by the delivery system, but is not in and of itself the goal. If outcomes were universally measured, it would quickly become clear that the value of care is highly variable, even for patients with access. Improving value holds the key to expanding access to care in a way that is affordable.

Equity in health care for all individuals and groups is another desirable goal, but again equity itself is not value. Equitable care that is poorly delivered leads to a system in which everyone has equal access to suboptimal outcomes. Discussions of equity also tend to focus on inputs, not outputs. The best way to improve the equity of care, and perhaps the only way, is to measure value, ensure transparency of value, and reward value. Only in this way will the value delivered for every patient count, including individuals who are currently poorly served.

Measuring Value

Value in healthcare delivery is largely unmeasured, a striking fact about healthcare delivery not only in the United States but around the world. Failure to measure value is the most serious self-inflicted wound of the medical profession and the broader provider community, because it has slowed innovation and brought about micromanagement of physician practice.

Measuring value depends first and foremost on properly measuring *health outcomes*. The chain of causality that determines outcomes is illus-

[4]This does not imply, for example, that all efforts at prevention will lower costs or even improve value. However, focusing on outcomes as a way to reduce long-term costs will spur innovations in better and more cost-effective forms of prevention as well as other value improvements.

trated in Figure 7-2, which embodies Donabedian's important distinction between process and outcome (Donabedian, 1966). Patients have some initial or preexisting conditions. Services are delivered through processes of care delivery that reflect medical knowledge and are affected by patient initial conditions. The care delivery process should strongly influence the outcomes achieved.

Some of the current challenges in measuring value are highlighted by Figure 7-2. First, there is a great deal of confusion about the distinction between processes and outcomes. There has been a proliferation of protocols, evidence-based guidelines, and practice standards that are used to measure "quality" and serve as the basis of pay-for-performance initiatives (Fonarow et al., 2007). Many participants in the healthcare system, and most quality measurement systems in health care, confound processes and outcomes or treat processes and structures as if they were outcomes.

While structural factors, protocols, guidelines, and practice standards are partial predictors of outcomes, they are not outcomes themselves (Brook et al., 2000). Adherence to these types of measures is an imperfect indicator of outcomes.

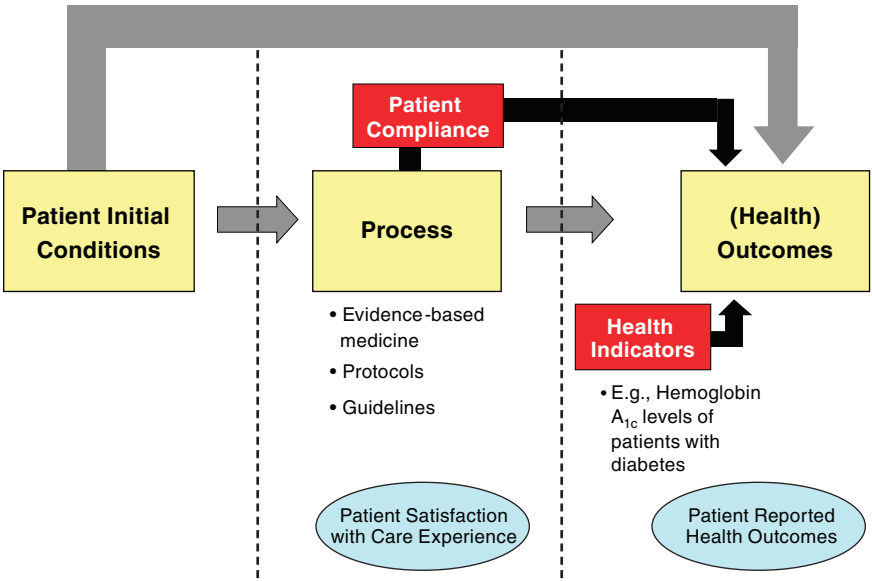

FIGURE 7-2 Measuring value in health care.
SOURCE: Michael Porter, 2007.

Process guidelines are invariably incomplete and omit important influences on the value of care (Krumholz et al., 2007). Practice standards often fail to adapt care sufficiently to individual patient circumstances—standardized processes do not guarantee standardized outcomes. Experience also shows that providers following identical guidelines achieve different results. Process guidelines also fail to cover the full cycle of care that actually determines value. Thus, process measurement alone will not assure that results will improve for all patients.

Moreover, process guidelines can slow innovation, because agreeing on guidelines is inevitably slow and invariably political. Medicine is constantly being refined, and guidelines can lag best practice or, conversely, lead to undue attention to processes that have yet to be definitively proven with a sufficient body of evidence. For example, best practice in treatment of post-menopausal women with estrogen has changed several times in the last decade alone, as new evidence has become available about the risks and benefits of the treatment for particular patient subpopulations.

Process control alone, then, is a risky and ultimately flawed approach to improving outcomes and increasing patient value. In any complex system, attempting to control behavior without measuring results will tend to limit progress to incremental improvement. Without a feedback loop involving the actual outcomes achieved, providers are denied the information they need to learn and to improve their care delivery methods. Process control is a tempting shortcut because processes are easier to measure (and less controversial) than outcomes, but there is no substitute for measuring *both* (Birkmeyer et al., 2006).

Another important distinction is that between *health indicators* and outcomes as shown in Figure 7-2. Indicators, such as hemoglobin A_{1c} levels used in diabetes care as biological markers of blood sugar control, should be highly correlated with actual outcomes such as acute episodes and complications (de Lissovoy et al., 2000). However, such biological indicators are still predictors of results, not results themselves. To improve value in healthcare delivery, it will also be necessary to measure true outcomes and not rely solely or even predominantly on such indicators.

Figure 7-2 also includes *patient compliance* as an essential factor contributing to health outcomes. There is compelling evidence that patient compliance with recommended preventive measures, preparations for treatment (e.g., weight control, muscle strengthening), and treatments themselves has a major influence on outcomes. Yet there is a glaring absence of systematic measurement of patient compliance, a major gap in measurement. Focusing on adherence to provider practice guidelines without measuring compliance merely obscures the link between process and outcomes. Failing to measure compliance also absolves providers (and health plans) of responsibility to treat compliance as integral to care delivery.

There has been growing attention to patient satisfaction in health care, but sometimes in a way that obscures true value measurement. Figure 7-2 separates two roles of patient satisfaction in measurement: patient satisfaction with the process of care (including hospitality, amenities, etc.) and patient reporting of the results of care. There has been a tendency to rely too heavily on patient surveys in quality improvement programs, and surveys have focused mostly on the service experience. These surveys rarely cover patient compliance, a major gap. Many surveys also fail to address what is most important for value measurement, the actual health outcomes as perceived by the patient. Generic patient satisfaction surveys also fail to capture the specific aspects of health status relevant to each patient's particular medical conditions, which are usually the most important outcomes.

While the service experience can be important to good outcomes, it is the outcomes themselves that constitute value. In the absence of true results measurement, patients will tend to default to friendliness, convenience, and amenities as proxies for excellence in healthcare delivery. Providers cannot rely too heavily on service satisfaction surveys as measures of outcomes, or the value delivered.

Value and the Concept of Quality in Health Care

An important corollary to defining the value proposition in health care is the definition of quality. In health care, the whole notion of quality has become a source of confusion and sometimes a distraction from genuine value improvement. Quality ought to refer to patient outcomes. Quality relative to cost determines value in health care, as it does in any field.

In health care, however, most quality initiatives are focused on processes of care and compliance with evidence-based guidelines. For example, of the 71 Healthcare Effectiveness Data and Information Set measures, the most widely used quality measurement system, only six are outcomes or health indicators and the balance are process measures. Of the comprehensive collection of quality measures found in the National Quality Measures Clearinghouse, the overwhelming majority are not outcomes (AHRQ, 1999). The quality movement in health care is on a dangerous path by trying to measure and control physician practice directly, rather than measuring outcomes. While outcome measurement is difficult, process measurement is not a substitute.

There has also been a tendency to equate safety and quality. The proliferation of safety initiatives is laudable, and has produced genuine improvements for patients. However, safety is just one aspect of quality and not necessarily the most important aspect. To say it another way, doing no harm is important, but improving the degree of recovery or the sustainability of recovery are just as important, if not more so. As I will discuss below, too

much focus on safety instead of overall outcomes and value may lead to incremental process improvements affecting safety, rather than rethinking the overall delivery of care to improve total outcomes including safety.

The Unit of Value Creation

To understand value in any field, the unit for which value is measured should conform to the unit in which value is actually created. The unit of value creation should define organizational boundaries in care delivery, which is a central tenet of organizational theory. In health care, however, both measurement and organizational structure are misaligned with value creation. In fact, one of the principal reasons why value is mismeasured in health care, or not measured at all, stems from faulty organizational structures for healthcare delivery.

Patient value is created by the integrated care of a patient's medical condition over the full cycle of care, rather than by a single specialist or by a discrete intervention (Porter and Teisberg, 2006). A medical condition is an interrelated set of patient medical circumstances best addressed in an integrated way. Care for a medical condition, such as breast cancer, diabetes, inflammatory bowel disease, asthma, or congestive heart failure, will normally require the involvement of multiple specialties. The definition of a medical condition *includes the most common co-occurrences*, or diseases that occur together. Caring for the medical condition of diabetes, for example, needs to integrate the care for hypertension and vascular disease. Value for the patient is created by the combined efforts to care for the patient's medical condition, not by any one specialty.[5] True accountability for value is inherently *shared* among the providers involved.

The unit of value creation in health care delivery—care for a medical condition encompassing the cycle of care—collides with the way delivery is currently organized in the United States and in virtually every other country. Instead, care should be organized into Integrated Practice Units (IPUs).[6] A patient may be cared for by more than one IPU at the same time, which greatly simplifies the coordination challenges compared to today's structure in which each specialist or intervention for each medical condition must coordinate with all the others involved in the patient's care. Health care today is organized by facility (e.g., hospital, clinic), by specialty, and/or by discrete intervention (e.g., imaging, surgery, office visits). This means that both out-

[5]Note that the set of specialties required to care for a medical condition may differ across patient populations.

[6]The IPU structure dramatically reduces the complexity of coordination and facilitates the true medical integration of care.

comes and processes tend to be mismeasured. Also, faulty organization of care creates many hurdles to actually achieving excellent outcomes.

Measurement today usually focuses on the individual providers or specialists, despite the fact that the intervention of one provider is not the sole or even the primary determinant of the overall outcomes. Measurement focuses on the discrete intervention, despite the fact that the intervention is one of many that determine outcomes. Measurement covers short episodes, which tells an incomplete story in understanding the overall outcome. For example, mortality measures often track mortality after surgery or for the duration of the patient's stay, but not after a short post-discharge period. Outcomes from a few discrete interventions, or in a few medical conditions, tend to be used as proxies for the overall outcomes of the provider.

Current organizational structure in healthcare delivery makes it difficult to measure value correctly. Indeed, this is one of the most important reasons why it is poorly measured, or not measured at all. Providers, particularly, have a tendency to measure only what is under their direct control in a particular intervention, even if this is not what actually determines value. What is measured is what is easy to measure, rather than what matters for outcomes. What is measured is also what is billed, even though the unit of reimbursement is misaligned with overall value.[7] Or, measurement is centered for the hospital or facility as a whole, even though this unit of analysis has little relevance for value delivered.

Gathering long-term, longitudinal data on outcomes is surely challenging, but the cost of doing so is unnecessarily high because of the current organizational structures and practice patterns. If practice structures were realigned to cover the care cycle, the cost of long-term outcome measurement would fall dramatically. Moreover, the assumption of joint responsibility for outcomes would be natural.

All these observations also apply to measuring costs. To understand the true costs of heath care delivery, one must measure the costs of all the interventions and services involved in determining the outcome. Today each unit or department is seen as a separate revenue or cost center; no one measures the cost of the entire care cycle. Entities such as rehabilitation centers and counseling units are all but ignored in cost analysis. Many costs, such as those borne by the patient or within primary care practices, are not counted in measuring procedure-centric care. Treating drugs as a separate cost, for example, only obscures the overall value of care. All costs must be included to measure the total cost of delivering outcomes, and overall value.

While the unit of value creation is the medical condition over the cycle of care, a given patient may have *multiple medical conditions*. This often

[7]For these reasons, the use of claims data in outcome measurement can be misleading unless it aggregates claims at the medical condition level.

occurs, for example, in older patients who might have congestive heart failure and breast cancer and osteoarthritis of the hip. Such patients are best cared for by integrated practices for each condition that coordinate with each other. Value is best measured for each medical condition, with the presence of other medical conditions a risk factor in each one. In this way, it is possible to compare one patient's results with others, and measure how well a provider deals with complicated patients. The alternative, defining a different measure of value for each patient, defeats the whole purpose of measurement.

Measuring Health Outcomes

Outcomes are the core of value in healthcare delivery. There is growing attention to measuring outcomes, which is a most welcome development. However, the practice of outcome measurement suffers from a number of problems. One of these is a tendency to look for a single ideal outcome measure for a given medical condition. Often, the measure chosen is one which is easy to agree upon and/or easy to measure. However, there is never one outcome measure in any field or endeavor, and health care is no exception.

For every medical condition, there are multiple outcomes that collectively define patient value. One commonly measured outcome is survival or death. This is just one outcome, albeit an important one. Outcomes related to safety, such as the incidence of medical errors along with their consequences, are an additional type of outcome measure. To think holistically about outcome measurement for a medical condition, outcomes can be can be conceptualized in a hierarchy, with the most fundamental outcomes, survival and patient health, achieved at the top, and other outcomes arrayed in a natural progression, such as those related to the nature and speed of the recovery process and those related to the sustainability of the results. Although there is not time to explore the details in this discussion, it should be possible to characterize the set of outcomes for a medical condition in a fashion that lends to objective and quantitative outcome measurement.[8]

For many patients, trade-offs may exist among individual outcomes. For example, a more complete recovery could require treatment with a greater risk of care-induced illness. Or, more complete recovery could require treatment that is more discomforting. Where there are trade-offs, individual patients may differ in the weight they place on different levels of the hierarchy, and on specific measures. The discomfort of treatment willingly endured will be affected, for example, by the degree and sustainability

[8]See Michael E. Porter, "What Is Value in Health Care?" Working paper, Harvard Business School, Boston, MA, 2008.

of health achieved. For example, cosmetic considerations may weigh heavily against risk of recurrence, such as in the choice of the amount of the breast resected for breast cancer patients, or long-term sustainability of recovery may matter less to older patients. A complete understanding of all aspects of such an outcome hierarchy matters more, not less, when different groups of patients value individual outcomes differently.

Thus, the first step to a systematic approach to value improvement is a disciplined approach to defining and describing the total set of outcomes. In most fields, including medicine, progress in improving value is iterative and evolving. Excellent performance on one quality attribute leads to attention on improving others (although improvements may also occur simultaneously). Over time, innovations seek to relax trade-offs among quality dimensions.

In healthcare delivery, the concept of an outcome measures hierarchy emphasizes that progress can be made at different rates at different levels. As survival rates improve, for example, more attention can be focused on the speed and discomfort of treatment. Once effectiveness in recovery reaches an acceptable level, attention can shift to relaxing trade-offs between effectiveness and risk of complications, as in cancer therapy. By measuring the entire outcome hierarchy, such improvement is not only encouraged but made more transparent and systematic. And viewing outcomes in a hierarchy reveals opportunities for dramatic value improvements in existing therapies as well as in the development of more cost-effective therapies that address disease earlier in the causal chain. This is a potential source of great optimism for the future in terms of cost containment.

Some Analytic Challenges

If we posit a hierarchy of outcome measures for a medical condition, this raises the question of how the importance of each one should be determined. Also, should the set of outcome measures be aggregated to determine an "overall" outcome? These are important questions, which can easily derail outcome measurement. They have led to the effort to monetize outcomes by, for example, calculating the value of human life or measuring the monetary benefits of improved productivity. If outcomes can be monetized, they can be aggregated and directly compared to costs to determine benefit-cost of value.

Seeking to monetize individual outcomes is tempting, but unnecessary and even misleading and distracting in value measurement. Monetizing even tangible outcomes such as improved survival is fraught with complexity, and often arbitrary. Monetizing more subjective or intangible outcomes is problematic. How should less arduous or less discomforting treatment be monetized? How should cosmetic or appearance improvements be valued?

With multiple outcomes, as we have noted, the value and weights will also vary by patient.

Attempting to calculate a single aggregate outcome measure for all patients, or for each patient, is not the right approach to outcome measurement, at least given the current state of practice. Instead, the focus should be on improving the set of outcomes (and value) in the sense that some outcomes improve without sacrificing others. For this purpose, outcomes need not be monetized, and individual outcome measures need not be aggregated.

Similarly, factoring initial health state into outcome measurement is an important issue. Because a patient's initial conditions affect the outcomes that can be achieved, measuring initial conditions is needed and outcomes must be stratified based on the important initial conditions or risk-adjusted. Several efforts to gather and report outcomes have failed because inadequate risk adjustment led to resistance and rejection by the medical community (Porter and Teisberg, 2006). Even in its current imperfect state, however, getting on with understanding the relevant initial conditions and adjusting for them is essential to improving value itself. For example, the lack of case adjustment methods is a root cause of the underpayment of providers for more complex cases, both in the United States and elsewhere. Flawed reimbursement for complex versus simpler cases has many adverse consequences for value, ranging from inadequate care to excessive fragmentation of "profitable"services.

Finally, the task of appropriately measuring costs requires close attention. Cost measurement needs to follow some essential principles, including: measuring the full costs of care, not the portion of costs borne by any one actor or the portion of costs taking any one form (e.g., drugs, tests, office visits); endogenizing costs borne by employers or families; aggregating costs for medical conditions over the cycle of care, by aggregating the costs of all the interventions involved; measuring the actual costs, not charges; aligning the unit of reimbursement with the unit of value—which will require a shift to bundled reimbursement models for medical conditions, in which all physician fees, services, facilities, and drugs over the care cycle are included in a single price; and varying prices according to patient initial conditions.

Summary

Value must be the fundamental goal of any healthcare system. Measuring value, and improving it, must become the driving force for every participant in the system. Today, in the U.S. healthcare system and in systems around the world, value is measured incompletely, if at all, which is the single biggest weakness standing in the way of healthcare improvement. The fact that healthcare delivery is not organized around value impedes

excellent care and drives up its cost. The fact that reimbursement is not aligned with value cripples the process of value improvement, and renders the profit motive a destructive force rather than a value driver.

Proper measurement of value is the single most powerful lever for improving healthcare delivery. While current organizational structures and practice standards surely create obstacles to value measurement, there are promising efforts to overcome these obstacles. While current measurement efforts are highly imperfect, at least the process of measurement has begun. Health plans, providers, employers, and government policy can all contribute to making measurement of value in health care a reality. If all actors in health care were to embrace value as the central goal, and work together to achieve good measurement, the resulting improvements in healthcare delivery would break the current logjam that threatens the nation's human and economic health.

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Appendix A

Meeting Agenda

Evidence-Based Medicine and the Changing Nature of Health Care

The National Academy of Sciences Building
2100 C Street, N.W.
Washington, D.C.

Monday, October 8

9:20 a.m. **Introduction of the Program**
Mark B. McClellan, M.D., Ph.D., Senior Fellow and Director, Engelberg Center for Health Care Reform, Leonard D. Schaeffer Chair in Health Policy Studies, Economic Studies, The Brookings Institution
Elizabeth G. Nabel, M.D., Director, National Heart, Lung, and Blood Institute, National Institutes of Health

9:30 a.m. **What Forces Are Driving the Need for Better Medical Evidence?**
Chair: *Denis A. Cortese, M.D.*, President and Chief Executive Officer, Mayo Clinic

Relationship Between Health Care and the Evidence Base: Current Profile
Elliott S. Fisher, M.D., M.P.H., Professor of Medicine and Community and Family Medicine, Center for the Evaluative Clinical Sciences, Dartmouth Medical School

How the Pace of New Health Product Introduction Affects the Need for Evidence
Molly J. Coye, M.D., M.P.H., Founder and Chief Executive Officer, Health Technology Center

How the Pace of New Insights into Genetic Variation Affects the Need for Evidence
David M. Altshuler, Ph.D., M.D., Director of Medical and Population Genetics, Broad Institute

Impact of the Evidence Shortfall on Health Care Costs, Public Budgets, and the Economy
Peter R. Orszag, Ph.D., Director, Congressional Budget Office

10:30 a.m. QUESTIONS AND DISCUSSION

10:50 a.m. BREAK

11:10 a.m. HOW CAN PATIENTS AND PROVIDERS CONTEND WITH THE CHANGES?
Chair: *Michael M. E. Johns, M.D.*, Chancellor, Emory University

Practical Front-Line Challenges and the Future of Expert-Based Care
William W. Stead, M.D., McKesson Foundation Professor of Medicine and Biomedical Informatics, and Associate Vice Chancellor for Strategy and Transformation, Vanderbilt University

The Patient-Physician Partnership in Fostering an Evidence-Driven Environment
Marc Boutin, Esq., Executive Vice President, National Health Council

Information Technology Tools That Support Best Practices by Healthcare Providers
Robert Hayward, M.D., M.P.H., F.R.C.P.C., Associate Professor, Departments of Medicine and Public Health Sciences, and Director, Centre for Health Evidence, University of Alberta

Consumer-Accessible, Web-Based Health Information to Empower Patients
Peter M. Neupert, M.B.A., Corporate Vice President, Health Solutions Group, Microsoft Corporation

12:10 p.m. QUESTIONS AND DISCUSSION

12:30 p.m. LUNCH BREAK

2:00 p.m. **What's Needed to Transform the Speed and Reliability of New Evidence?**
Chair: *John W. Rowe, M.D.*, Professor, Department of Health Policy and Management, Columbia University Mailman School of Public Health

Electronic Health Records and the Prospect of Real-Time Evidence Development
George C. Halvorson, Chairman and Chief Executive Officer, Kaiser Foundation Health Plan, Inc., and Kaiser Foundation Hospitals

Research Methods to Speed the Development of Better Evidence
Eric D. Peterson, M.D., M.P.H., Professor of Medicine, Duke Clinical Research Institute

Biopharmaceutical and Medical Device Development: Tailored Therapies Meet Evidence-Based Medicine
Steven M. Paul, M.D., Executive Vice President, Science and Technology, and President, Lilly Research Laboratories, Eli Lilly and Company

2:45 p.m. **Questions and Discussion**

3:00 p.m. **How Can Policy Changes Improve the Value We Get from Health Care?**
Chair: *John K. Iglehart*, Founding Editor, *Health Affairs*, and National Correspondent, *New England Journal of Medicine*

What Is Value in Health Care?
Michael E. Porter, Ph.D., Bishop William Lawrence University Professor, Harvard Business School

Regulatory and Financing Reforms Necessary for Effective Health Care
Donna E. Shalala, Ph.D., President, University of Miami

3:30 p.m. **Questions and Discussion**

4:00 p.m. **Closing Remarks**
Mark B. McClellan, M.D., Ph.D.
Elizabeth G. Nabel, M.D.

Appendix B

Biographical Sketches of Principals

David M. Altshuler, Ph.D., M.D., is a clinical endocrinologist and human geneticist whose laboratory aims to characterize and catalogue patterns of human genetic variation and, by applying this information, better understand the inherited contribution to common diseases. He was a leader in the SNP Consortium and International HapMap Consortium, public-private partnerships that created genome-wide maps of human genetic diversity that now guide the design and interpretation of genetic association studies. His research has contributed to identifying the role of common genetic variants in type 2 diabetes, prostate cancer, age-related macular degeneration, and systemic lupus erythematosis. Dr. Altshuler is a Distinguished Clinical Scientist of the Doris Duke Charitable Foundation and a Clinical Scholar in Translational Research of the Burroughs Wellcome Fund. He is a member of the American Society of Clinical Investigation, and serves on advisory boards at the National Institutes of Health, Doris Duke Charitable Foundation, and the Wellcome Trust as well as editorial boards of *Annual Review of Genomics and Human Genetics*, *Current Opinions in Genetics & Development*, and *Science Magazine* (Board of Reviewing Editors).

Marc Boutin, Esq., is the Executive Vice President at the National Health Council, an umbrella organization representing approximately 100 million people with chronic conditions. The Council promotes health care for all people, the importance of medical research, and the role of patient-based groups. Throughout Mr. Boutin's career, he has been highly involved in health advocacy, policy, and legislation. He has designed and directed numerous strategies for issues ranging from access to health care to can-

cer prevention. Before joining the Council, Mr. Boutin served as the Vice President of Government Relations and Advocacy at the American Cancer Society for New England and was a faculty member at Tufts University Medical School. In addition to senior government relations positions at Easter Seals and the Massachusetts Association of Health Boards, he was a civil rights litigator.

Denis A. Cortese, M.D., is President and CEO of Mayo Clinic, chair of the Mayo Clinic Board of Governors, and a member of the Board of Trustees. He is a professor of medicine and a former director of the Pulmonary Disease subspecialty training program. Dr. Cortese was a chair of the Clinical Practice and a member of the Board of Governors in Rochester before moving to Mayo Clinic in Jacksonville, Florida, in 1993. From 1999 to 2002 he served as CEO of Mayo Clinic and Chair of the Board of Directors at St. Luke's Hospital, both in Jacksonville. Dr. Cortese relocated back to Rochester and assumed his current position in February 2003. His major research interests have been in interventional bronchoscopy, including appropriate use of photodynamic therapy, endobronchial laser therapy, and endobronchial stents. He is a former president of the International Photodynamic Association, a member of the Institute of Medicine (IOM) and chair of the Roundtable on Evidence-Based Medicine. Dr. Cortese received the Ellis Island Award in 2007.

Molly J. Coye, M.D., M.P.H., is Founder and CEO of the Health Technology Center (HealthTech), a non-profit education and research organization established in 2000 to advance the use of beneficial technologies in promoting healthier people and communities. Dr. Coye has extensive experience in both the public and private sectors having served as Commissioner of Health for the State of New Jersey and Director of the California Department of Health Services, in addition to heading the Division of Public Health at the Johns Hopkins School of Hygiene and Public Health, leading marketing and product development for interactive health communication and disease management at HealthDesk Corp, serving as Executive Vice President for the Good Samaritan Health System, and directing the Lewin Group's West Coast office. She is on the Board of Trustees of the American Hospital Association, Aetna, Inc., and the Program for Appropriate Technology in Health. She was also a founding board member of the California Endowment, the largest private healthcare philanthropy in California.

Harvey V. Fineberg, M.D., Ph.D., is President of the Institute of Medicine. He served as Provost of Harvard University from 1997 to 2001, following 13 years as Dean of the Harvard School of Public Health. He has devoted most of his academic career to the fields of health policy and medical deci-

sion making. His past research has focused on the process of policy development and implementation, assessment of medical technology, evaluation and use of vaccines, and dissemination of medical innovations. Dr. Fineberg helped found and served as president of the Society for Medical Decision Making and also served as consultant to the World Health Organization. At the IOM, he has chaired and served on a number of panels dealing with health policy issues, ranging from AIDS to new medical technology. He also served as a member of the Public Health Council of Massachusetts (1976-1979), as chairman of the Health Care Technology Study Section of the National Center for Health Services Research (1982-1985), and as president of the Association of Schools of Public Health (1995-1996). Dr. Fineberg is co-author of the books *Clinical Decision Analysis, Innovators in Physician Education,* and *The Epidemic That Never Was,* an analysis of the controversial federal immunization program against swine flu in 1976. He has co-edited several books on such diverse topics as AIDS prevention, vaccine safety, and understanding risk in society. He has also authored numerous articles published in professional journals. Dr. Fineberg is the recipient of several honorary degrees and the Joseph W. Mountin Prize from the U.S. Centers for Disease Control and Prevention. He earned his bachelor's and doctoral degrees from Harvard University.

Elliott S. Fisher, M.D., M.P.H., is Professor of Medicine and Community and Family Medicine at Dartmouth Medical School and Director of the Center for Healthcare Research and Reform within the Dartmouth Institute for Health Policy and Clinical Practice. At Dartmouth, he was a founding director and is now Senior Associate of the VA Outcomes Group, teaches in the Clinical Evaluative Sciences Master's program, and is the Principle Investigator for the Dartmouth Atlas of Health Care. His research focuses on exploring the causes of the two-fold differences in spending observed across U.S. regions and healthcare systems—and the consequences of these variations for health and health care. Dr. Fisher's work demonstrating that higher-spending regions and health systems do not achieve better outcomes or quality has had a major impact on current thinking about health care and healthcare reform. He has served on the National Advisory Council of the Agency for Healthcare Research and Quality and was recently elected to the IOM.

George C. Halvorson was named Chairman and CEO of Kaiser Foundation Health Plan, Inc. and Kaiser Foundation Hospitals, headquartered in Oakland, California, in March 2002. He has more than 30 years of healthcare management experience and was formerly president and CEO of HealthPartners, headquartered in Minneapolis. He is the author of widely acclaimed books on the U.S. healthcare system including the recently

released *Health Care Reform Now!* Mr. Halvorson also wrote *Strong Medicine and Epidemic of Care*, which Warren Buffet said was "by far the clearest explanation of how we have gotten to where we are in health care, and what is likely to happen." He serves on a number of boards, including those of America's Health Insurance Plans, where he is the 2007-2008 chairman, and the Alliance of Community Health Plans. He is the current president of the Board of Directors for the International Federation of Health Plans and a member of the Harvard Kennedy School Healthcare Delivery Policy Group. Mr. Halvorson also serves on the IOM Roundtable on Evidence-Based Medicine and on the Commonwealth Fund Commission on a High Performance Health System.

Robert Hayward, M.D., M.P.H., F.R.C.P.C., is a practicing general internist, and a leading expert in health informatics and clinical decision support. He is Assistant Dean, Health Informatics, Faculty of Medicine and Dentistry, at the University of Alberta and Director of the Centre for Health Evidence, where he leads a team of health information specialists and healthcare practitioners to develop information tools that bring evidence to the bedside for improved healthcare decision making. He serves a number of initiatives, including lead faculty for both SEARCH Canada (information and evidence literacy for middle management) and CHSRF EXTRA (information literacy for healthcare executives), the Evidence-Based Medicine Working Group, and the Users' Guides to the Medical Literature. He is editor of *JAMA*'s Users Guides Interactive and has established industry-academic bridges to bring ideas, expertise, and products from research to implementation. Dr. Hayward's current research initiatives include (a) appraisal and assessment of decision support, (b) presentation of health evidence to clinicians at the point of care, (c) appraisal and implementation of clinical practice guidelines, and (d) virtual learning communities.

John K. Iglehart has held two editorial leadership positions in the world of health policy making for the last 25 years. He has been editor of *Health Affairs*, a bimonthly policy journal that he founded in 1981 under the aegis of Project HOPE, a not-for-profit international health education organization. *Health Affairs*, a peer-reviewed, multidisciplinary journal, has made its mark by translating health services research and analysis into content that is more accessible to members of Congress and other key participants in federal and state health policy making. Over this same period, Iglehart also has served as national correspondent of *The New England Journal of Medicine*, for which he has written more than 100 essays called Health Policy Reports. Before 1981, he served for 2 years as a vice president of the Kaiser Foundation Health Plan and director of its Washington, D.C., office.

Iglehart held a variety of editorial positions from 1969 to 1979, including the editorship of *National Journal*, a privately published weekly on federal policy making. He is a member of the IOM and served on its Governing Council (1985-1991); is an elected member of the National Academy of Social Insurance; and serves on the Advisory Board of the National Institute for Health Care Management and the Editorial Board of *Morbidity and Mortality Weekly Report*.

Michael M. E. Johns, M.D., assumed the post of Chancellor for Emory University on October 1, 2007. Prior to that, starting in 1996, Dr. Johns served as Executive Vice President for Health Affairs; CEO, The Robert W. Woodruff Health Sciences Center; Chairman of the Board, Emory Healthcare; Co-Chairman of the Board, EHCA, LLC; and Professor, Department of Otolaryngology, Emory University School of Medicine. As leader of the health sciences and Emory Healthcare for 11 years, Dr. Johns engineered the transformation of the Health Sciences Center into one of the nation's pre-eminent centers in education, research, and patient care. From 1990 to 1996, he was Dean of the Johns Hopkins School of Medicine and Vice President of the Medical Faculty at Johns Hopkins University, after having served, beginning in 1984, as professor and chair of Otolaryngology-Head and Neck Surgery and as Associate Dean for Clinical Affairs. He is a member of the IOM and has served on many IOM committees and as both a member and Vice Chair of the IOM's Council. Dr. Johns also is a Fellow of the American Association for the Advancement of Science.

Mark B. McClellan, M.D., Ph.D., a Senior Fellow at the Brookings Institution, became the Director of its Engelberg Center for Healthcare Reform in July 2007. The Center will study ways to provide practical solutions for access, quality, and financing challenges facing the U.S. healthcare system. Dr. McClellan also is the Leonard D. Schaeffer Chair in Health Policy Studies. He has a highly distinguished record in public service and in academic research. He served as administrator for the Centers for Medicare and Medicaid Services (2004-2006), commissioner of the Food and Drug Administration (2002-2004), member of the President's Council of Economic Advisers, and senior director for health care policy at the White House (2001-2002). In these positions, he developed and implemented major reforms in health policy. In the Clinton administration, Dr. McClellan was deputy assistant secretary of the Treasury for economic policy (1998-1999), supervising economic analysis and policy development on a range of domestic policy issues. He is a member of the IOM, a Research Associate of the National Bureau of Economic Research, and a Visiting Scholar at the American Enterprise Institute.

J. Michael McGinnis, M.D., M.P.P., is a Senior Scholar at the IOM, leading its initiative on evidence-based medicine. From 1999 to 2005, he served as Senior Vice President and founding Director of the Health Group, and as Counselor to the President, at the Robert Wood Johnson Foundation (RWJF). From 1977 to 1995, he held continuous appointment as Assistant Surgeon General, Deputy Assistant Secretary for Health, and founding Director, Disease Prevention and Health Promotion, through the Carter, Reagan, Bush, and Clinton Administrations. Programs and policies created and launched at his initiative include the Healthy People process on national health objectives, now in its third decade; the U.S. Preventive Services Task Force, now in its fourth iteration; the Dietary Guidelines for Americans (with USDA), now in its sixth edition; the RWJF Health & Society Scholars Program; the RWJF Young Epidemiology Scholars Program; and the RWJF Active Living family of programs. His international service includes appointments as Chair of the World Bank/European Commission Task Force on post-war reconstruction of the health sector in Bosnia (1995-1996) and State Coordinator for the World Health Organization smallpox eradication program in Uttar Pradesh, India (1974-1975). He is an elected member of the IOM, Fellow of the American College of Epidemiology, and Fellow of the American College of Preventive Medicine. Current and recent Board memberships include the Nemours Foundation Board of Directors, the IOM Committee on Children's Food Marketing (Chair); the NIH State-of-the-Science Panel on Multivitamins in Chronic Disease Prevention (Chair); the Health Professionals Roundtable on Preventive Services (Chair); the FDA Food Advisory Committee/Subcommittee on Nutrition; and the Board of the United Way of the National Capital Area (Chair, Resource Development).

Elizabeth G. Nabel, M.D., is Director of the National Heart, Lung, and Blood Institute at the National Institutes of Health. Dr. Nabel oversees an extensive national research portfolio to prevent, diagnose, and treat heart, lung, and blood diseases. As a cardiovascular physician-scientist, she has made substantial contributions to the understanding of the molecular genetics of vascular diseases, and has delineated the mechanisms by which cell cycle and growth factor proteins regulate the proliferation of vascular cells in blood vessels, a process important for the development of atherosclerosis and other cardiovascular diseases. Her vascular biology laboratory has characterized the role of cell cycle inhibitors on vascular proliferation and inflammation, and this research has opened up new avenues for therapeutic targets in the vasculature. More recently, she has studied the genomics of cardiovascular disease including the premature aging syndrome, Hutchinson-Gilford Progeria Syndrome. An elected member of the American Society for Clinical Investigation and the Association

of American Physicians, Dr. Nabel has received numerous awards for her scientific accomplishments and several honorary degrees. She is a member of the IOM and serves on its governing Council.

Peter Neupert is Corporate Vice President for the Health Solutions Group at Microsoft Corp. and is responsible for Microsoft's collaboration with the healthcare ecosystem to address global infrastructure issues of significant scale. Under his strategic direction, the Health Solutions Group is developing applications and solutions for clinical and business requirements of healthcare professionals in the enterprise, and which enable improved personal health management for consumers. Neupert served as president and chief executive officer of Drugstore.com Inc. (1998-2001), and as chairman of the board of directors (1999-2004). He led Drugstore.com to become a top online retail store and information site for health, wellness, beauty, and pharmacy products. He served on President Bush's Information Technology Advisory Committee (2003-2005) where he co-chaired the Health Information Technology subcommittee and helped drive the 2004 report *Revolutionizing Health Care Through Information Technology*. In 2000, he received an Ernst & Young Entrepreneur of the Year award for his work at Drugstore.com. Neupert is a member of the IOM Roundtable on Evidence-Based Medicine and sits on the Pacific Health Summit Advisory Board, as well as the boards of infiLearn.com and Cranium, Inc.

Peter Orszag, Ph.D., is Director of the Congressional Budget Office. Previously, he was the Joseph A. Penchman Senior Fellow and Deputy Director of Economic Studies at the Brookings Institution. While at Brookings, he also served as Director of the Hamilton Project, which provides a platform for scholars to offer proposals for promoting broad-based economic growth; Director of the Retirement Security Project, which focuses on promoting retirement security; and Co-Director of the Tax Policy Center, a joint venture with the Urban Institute providing analysis of tax issues. In 1997 and 1998, Dr. Orszag served as Special Assistant to the president for Economic Policy and Senior Economic Adviser at the National Economic Council. In 1995 and 1996, he was Senior Adviser and Senior Economist at the President's Council of Economic Advisers. His main areas of research have been pensions, Social Security, budget policy, higher education policy, homeland security, macroeconomics, and tax policy—topics on which he has published widely in academic journals.

Steven M. Paul, M.D., is Executive Vice President, Science and Technology, and President, Lilly Research Laboratories of Eli Lilly and Company. Dr. Paul's research activities have established an important role for specific neurotransmitter receptors in mediating the central actions of various neuro-

active drugs. Among his many contributions has been the delineation of the role of receptors for the inhibitory neurotransmitter GABA in mediating the behavioral effects of benzodiazepines, barbiturates, short-chain alcohols, as well as a novel class of neuroactive steroids. He is currently working on new therapeutic approaches for Alzheimer disease and his laboratory has recently discovered a novel monoclonal antibody directed at the amyloid β-peptide which is currently in clinical development as a potential therapy for Alzheimer disease. Dr. Paul has authored or co-authored over 500 papers and invited book chapters. He serves on the editorial boards of several scientific journals and has served on several NIH extramural and intramural committees. Dr. Paul is a member of the executive committee of PhRMA's Science and Regulatory committee and is currently its chairperson. He is a member of the IOM and served on its Board on Neuroscience and Behavior. He is a member of various other professional and honorary societies and is a recipient of many scientific honors.

Eric D. Peterson, M.D., M.P.H., is a Professor of Medicine in the Division of Cardiology and the Associate Vice Chair for Quality at Duke University Medical Center. He is also an Associate Director and Director of Cardiovascular Research at the Duke Clinical Research Institute. Dr. Peterson is a leader in quality research, with over 255 peer-reviewed publications in the field. He is also the Principal Investigator for the Society of Thoracic Surgeons National Cardiac Surgery Database, Data Coordinating Center for both the American College of Cardiology's National Cardiac Database and the American Heart Association's (AHA's) Get With the Guidelines Data. He participates on multiple national committees including Chair of the AHA's Quality of Care and Outcomes Research Interdisciplinary Working Group, the Veterans Administration's Quality Enhancement Research Initiative Executive Committee, the National Quality Forum Technical Advisory Panel for Priorities, Goals and a Measurement Framework: Efficiency and Episodes of Care, and the IOM Committee on Redesigning Insurance Benefits, Provider Payments, and Accountability Programs to Promote Quality of Health Care Delivery. Dr. Peterson is also a Contributing Editor of the *Journal of the American Medical Association*.

Michael E. Porter, Ph.D., is the Bishop William Lawrence University Professor at Harvard Business School. A leading authority on competitive strategy and the competitiveness of nations and regions, his work is recognized in governments, corporations, non-profits, and academic circles across the globe. Professor Porter's core field is competition and strategy, and this remains the focus of his research. His ideas have also redefined thinking about competitiveness, economic development, economically distressed areas, and the role of corporations in society. He is the author of 17 books

and numerous articles. Professor Porter has recently devoted considerable attention to understanding and addressing the problems in health care evident in the United States and abroad. His book, *Redefining Health Care* (with Elizabeth Teisberg), develops a new framework for understanding how to transform the value delivered by the healthcare system.

John W. Rowe, M.D., is Professor in the Department of Health Policy and Management at the Columbia University Mailman School of Public Health. From 2000 until his retirement in late 2006, he served as Chairman and CEO of Aetna, Inc., one of the nations leading healthcare and related benefits organizations. From 1998 to 2000, Dr. Rowe served as President and CEO of Mount Sinai NYU Health, one of the nations largest academic health care organizations. From 1988 to 1998, prior to the Mount Sinai-NYU Health merger, he was President of the Mount Sinai Hospital and the Mount Sinai School of Medicine in New York City. Before joining Mount Sinai, Dr. Rowe was a Professor of Medicine and the founding Director of the Division on Aging at the Harvard Medical School as well as Chief of Gerontology at Boston's Beth Israel Hospital. He has authored over 200 scientific publications, mostly on the physiology of the aging process, including a leading textbook of geriatric medicine, in addition to more recent publications on healthcare policy. He has received numerous honors and awards for his research and health policy efforts regarding care of the elderly. Currently, Dr. Rowe leads the MacArthur Foundation's Initiative on An Aging Society. A member of the IOM, he also chairs its Committee on the Future of Health Care Workforce for Older Americans.

Donna E. Shalala, Ph.D., is Professor of Political Science and president of the University of Miami. She has 25 years of experience as an accomplished scholar, teacher, and administrator. In 1993, President Clinton appointed her U.S. Secretary of Health and Human Services (HHS) where she served for eight years, becoming the longest serving HHS Secretary in U.S. history. In that position, she directed the welfare reform process, made health insurance available to 3.33 million children through the approval of the State Children's Health Insurance Program, raised child immunization rates, led major reforms of the Food and Drug Administration's drug approval process and food safety system, revitalized the NIH, and directed a major management and policy reform of Medicare. President Shalala has numerous honorary degrees and a host of other honors. She is a director of Gannett Co., Inc.; UnitedHealth Group, Inc.; and the Lennar Corporation. She also serves as a Trustee of the Henry J. Kaiser Family Foundation and is a member of the IOM and previously served on its governing Council.

William W. Stead, M.D., is Associate Vice Chancellor for Strategy and Transformation and Director of the Informatics Center at Vanderbilt University. In this role, he functions as Chief Information Architect for the University. As an undergraduate at Duke University (1960s), he was a member of the team that developed the Cardiology Databank, one of the first clinical epidemiology projects to change practice by linking outcomes to process. As a faculty member in Nephrology, he was the physician in the physician-engineer partnership that developed the Medical Record, one of the first practical computer-based patient record systems. He helped Duke build one of the first patient-centered hospital information systems and led two prominent academic health centers at Duke (1980s) and Vanderbilt (1990s), through both planning and implementation phases of large-scale integrated advanced Information Management Systems Projects. His Vanderbilt team created informatics techniques for linking information into clinical workflow, overcame the barriers to technology adoption, and reduced the cost and time required to implement enterprise-wide information technology infrastructure. Dr. Stead is Founding Fellow of the American College of Medical Informatics and American Institute for Engineering in Biology and Medicine, and an elected member of the IOM and the American Clinical and Climatological Association.

Appendix C

IOM Roundtable on Evidence-Based Medicine Roster and Background

Denis A. Cortese (*Chair*), President and CEO, Mayo Clinic
Adam Bosworth, Founder President and CEO, Keas
David R. Brennan, CEO, AstraZeneca PLC
Carolyn M. Clancy, Director, Agency for Healthcare Research and Quality
Helen Darling, President, National Business Group on Health
James A. Guest, President, Consumers Union
George C. Halvorson, Chairman and CEO, Kaiser Permanente
Carmen Hooker Odom, President, Milbank Memorial Fund
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Institute of Medicine Roundtable on Evidence-Based Medicine *Charter and Vision Statement*

The Institute of Medicine's Roundtable on Evidence-Based Medicine has been convened to help transform the way evidence on clinical effectiveness is generated and used to improve health and health care. Participants have set a goal that, by the year 2020, 90 percent of clinical decisions will be supported by accurate, timely, and up-to-date clinical information, and will reflect the best available evidence. Roundtable members will work with their colleagues to identify the issues not being adequately addressed, the nature of the barriers and possible solutions, and the priorities for action, and will marshal the resources of the sectors represented on the Roundtable to work for sustained public-private cooperation for change.

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The Institute of Medicine's Roundtable on Evidence-Based Medicine has been convened to help transform the way evidence on clinical effectiveness is generated and used to improve health and health care. We seek the development of a ***learning healthcare system*** that is designed to generate and apply the best evidence for the collaborative healthcare choices of each patient and provider; to drive the process of discovery as a natural outgrowth of patient care; and to ensure innovation, quality, safety, and value in health care.

Vision: Our vision is for a healthcare system that draws on the best evidence to provide the care most appropriate to each patient, emphasizes prevention and health promotion, delivers the most value, adds to learning throughout the delivery of care, and leads to improvements in the nation's health.

Goal: By the year 2020, 90 percent of clinical decisions will be supported by accurate, timely, and up-to-date clinical information, and will reflect the best available evidence. We feel that this presents a tangible focus for progress toward our vision, that Americans ought to expect at least this level of performance, that it should be feasible with existing resources and emerging tools, and that measures can be developed to track and stimulate progress.

Context: As unprecedented developments in the diagnosis, treatment, and long-term management of disease bring Americans closer than ever to the promise of personalized health care, we are faced with similarly unprecedented challenges to identify and deliver the care most appropriate for individual needs and conditions. Care that is important is often not delivered. Care that is delivered is often not important. In part, this is due to our failure to apply the evidence we have about the medical care that is most effective—a failure related to shortfalls in provider knowledge and accountability, inadequate care coordination and support, lack of insurance, poorly aligned payment incen-

tives, and misplaced patient expectations. Increasingly, it is also a result of our limited capacity for timely generation of evidence on the relative effectiveness, efficiency, and safety of available and emerging interventions. Improving the value of the return on our healthcare investment is a vital imperative that will require much greater capacity to evaluate high-priority clinical interventions, stronger links between clinical research and practice, and reorientation of the incentives to apply new insights. We must quicken our efforts to position evidence development and application as natural outgrowths of clinical care—to foster health care that learns.

Approach: The IOM Roundtable on Evidence-Based Medicine serves as a forum to facilitate the collaborative assessment and action around issues central to achieving the vision and goal stated. The challenges are myriad and include issues that must be addressed to improve evidence development, evidence application, and the capacity to advance progress on both dimensions. To address these challenges, as leaders in their fields, Roundtable members will work with their colleagues to identify the issues not being adequately addressed, the nature of the barriers and possible solutions, and the priorities for action, and will marshal the resources of the sectors represented on the Roundtable to work for sustained public–private cooperation for change.

Activities include collaborative exploration of new and expedited approaches to assessing the effectiveness of diagnostic and treatment interventions, better use of the patient care experience to generate evidence on effectiveness, identification of assessment priorities, and communication strategies to enhance provider and patient understanding and support for interventions proven to work best and deliver value in health care.

Core concepts and principles: For the purpose of the Roundtable activities, we define evidence-based medicine broadly to mean that, *to the greatest extent possible, the decisions that shape the health and health care of Americans—by patients, providers, payers, and policy makers alike—will be grounded on a reliable evidence base, will account appropriately for individual variation in patient needs, and will support the generation of new insights on clinical effectiveness.* Evidence is generally considered to be information from clinical experience that has met some established test of validity, and the appropriate standard is determined according to the requirements of the intervention and clinical circumstance. Processes that involve the development and use of evidence should be accessible and transparent to all stakeholders.

A common commitment to certain principles and priorities guides the activities of the Roundtable and its members, including the commitment to the right health care for each person; putting the best evidence into practice; establishing the effectiveness, efficiency, and safety of medical care delivered; building constant measurement into our healthcare investments; the establishment of healthcare data as a public good; shared responsibility distributed equitably across stakeholders, both public and private; collaborative stakeholder involvement in priority setting; transparency in the execution of activities and reporting of results; and subjugation of individual political or stakeholder perspectives in favor of the common good.