Debate

The quality case for information technology in healthcare

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Abstract

Background: As described in the Institute of Medicine’s Crossing the Quality Chasm report, the quality of health care in the U.S. today leaves much to be desired.

Discussion: One major opportunity for improving quality relates to increasing the use of information technology, or IT. Health care organizations currently invest less in IT than in any other information-intensive industry, and not surprisingly current systems are relatively primitive, compared with industries such as banking or aviation. Nonetheless, a number of organizations have demonstrated that quality can be substantially improved in a variety of ways if IT use is increased in ways that improve care. Specifically, computerization of processes that are error-prone and computerized decision support may substantially improve both efficiency and quality, as well as dramatically facilitate quality measurement. This report discusses the current levels of IT and quality in health care, how quality improvement and management are currently done, the evidence that more IT might be helpful, a vision of the future, and the barriers to getting there.

Summary: This report suggests that there are five key policy domains that need to be addressed: standards, incentives, security and confidentiality, professional involvement, and research, with financial incentives representing the single most important lever.

Background

"Indeed, between the health care that we now have, and the health care we could have, lies not just a gap, but a chasm." Crossing the Quality Chasm: A New Health System for the 21st Century[1].

When the Institute of Medicine recently assessed the current state of affairs in U.S. health care, they found it to be substantially lacking in key areas [1]. The report’s authors identified a multitude of quality issues to be addressed: complex care is typically uncoordinated, information is often not available to those who need it when it is needed, and as a result patients often do not get care they need, or alternatively do get care they do not need. A common theme underlying many of these quality issues has been under-investment in information technology in health care.

Discussion

Information technology in healthcare today

Payment issues, rather than clinical needs, have driven most investment in IT in healthcare. Thus, billing systems are generally much better than the clinical systems. Furthermore, while the exact figure varies depending upon the survey, healthcare has invested at least 50% less of its gross revenues in information technology than other information-intensive industries like banking [2–4]. Furthermore, while banking has international standards for
exchange of data, medicine does not. As a result, one can go to an automated teller in Tokyo or Moscow and withdraw money with a card, but going to a healthcare provider in one of these locations with a serious medical issue would be a rather different experience.

In other industries, companies have used excellent information technology as a competitive edge. For example, American Airlines derived substantial benefit from its SA-BRE system, which made it easy to determine which flights were available, and to make reservations [5]. Similarly, Federal Express with its tracking system has an enviably high level of reliability, which customers have perceived as extremely valuable [6].

Few similar examples exist in healthcare today. While a few organizations have what are perceived as "best-of-breed" information systems (LDS Hospital and Intermountain Health Care in Salt Lake City, Wishard Memorial Hospital and its affiliated clinics in Indianapolis, and Brigham and Women's Hospital and Partners HealthCare System in Boston, MA), [7–9] the reliability of these systems is nothing like that offered by the systems of companies outside of healthcare, for example Federal Express [10]. These organizations all have had good financial performance, which has given them an edge in their local markets, though their goal has not been to spread. In addition, all their information systems were "home-grown," and disseminating them has proved difficult even to small hospitals within their own networks. An exception has been the Veteran's Administration information system, which is an important model of integration. Information technology that results in better clinical quality has not played the same role it does in other industries for several reasons. One is that fee-for-service reimbursement did not reward efficiency. Another is that care delivery is so granular; much of it is delivered by not-for-profit organizations and there are not just a few dominant players as in other industries. Finally, in this unusual market, the healthcare IT vendors have had strong incentives to retain their customer base and avoid interoperability.

Nonetheless, excellent IT and high-quality health care are closely linked. All of the healthcare organizations mentioned above are recognized as quality leaders due to excellent clinical outcomes, which have been achieved in part because of their information systems. Furthermore, the organizations' information systems have several common threads: all provide near-immediate access to a wide array of information including nearly all clinical results; they are highly integrated; they provide clinical decision support; they have both inpatient and outpatient data with differing views for each; and they facilitate measurement.

Building the "pyramid" of clinical information systems begins with a master patient index and results retrieval. These building blocks are necessary before higher level applications are introduced. One especially important higher-level application is computerized physician order entry, in which providers write orders including prescriptions using computers [11]. Computerization of ordering is important because most actions in health care follow an order; computerizing this process allows provision of real-time decision support to providers, for example implementation of guidelines and critical pathways. Another application that is extremely important for delivering decision support is a program called an event monitor, which sits over a database and can provide notification when an important event is found (for example, a markedly elevated serum sodium level) [12]. Even more challenging than computerizing ordering or building an event monitor, especially in the inpatient setting, is computerizing the medical record, especially capturing of notes in real time. Outpatient electronic medical records, in contrast, are relatively easier to implement and many examples of well-developed outpatient records exist [13]. Many benefits can be realized with the addition of each of these building blocks.

Unfortunately, the industry norm in U.S. clinical information systems includes only the base of the pyramid, if that. While most hospitals now do have both a master patient index and results retrieval available for some tests for individual patients who had tests done at a specific institution, views across institutions are rare, and many results are not incorporated. Building a master patient index is challenging in the U.S. because of the absence of a unique identifier, and building and maintaining such an index is laborious. Many lab tests are performed at "outside" laboratories, and because of this lack of integration such results are generally unavailable via the information system, as may be the case with unusual tests like electroencephalograms. While images of a variety of types including radiographs and electrocardiograms can now readily be displayed,[14] such images are typically not yet accessible to providers.

More important, most hospital systems provide little or no clinical decision support to providers. Clinical decision support takes many forms – including passive display of information such as the last digoxin level and potassium in a patient receiving digoxin; reminders – for example, that a mammogram is due; alerts – that the hematocrit is falling rapidly or that the patient has an allergy to the prescribed drug; and guidelines – suggestions about orders in a patient with a suspected myocardial infarction. Asking providers to deliver today's complex care without such assistance is like asking a commercial pilot to fly with no instruments, given the vast array of informa-
tion and knowledge that providers must handle. One reason that such clinical decision support is infrequently delivered is that today’s subsystems – for example, the laboratory and pharmacy systems – do not have good interfaces and thus cannot readily communicate with each other. This lack of communication makes extracting important information and providing clinical decision support vastly more difficult than it needs to be [15,16].

Furthermore, the inpatient and outpatient systems in most healthcare systems are disconnected. Rarely can providers access outpatient medical information from the inpatient setting, or vice versa. Yet this information is absolutely pivotal to providing safe, efficient medical care; after all, a patient’s allergies are the same both inside and outside the hospital. Covering for another physician’s patient panel is vastly easier, safer and more efficient when their medical record – especially their problems, medications, and test results – can be instantly accessed. Transfers from acute care to long-term care or home-care are also problematic; often little information is transferred with the patient. In general, outpatient care is much more fragmented than inpatient care, and would likely benefit even more from computerization and communication of information than inpatient care.

The lack of electronic information also limits quality reporting. Most organizations report externally for both inpatients and outpatients using only claims data, as required by state and federal agencies; this is sometimes supplemented by chart review. These claims data lack clinical detail, so that reports on Pap smear rates do not take into account, for example, whether a woman has had a hysterectomy [17]. Internally, organizations generally have information that is somewhat better, although this information is often sharply limited. For example, organizations may assess the rates at which groups of patients (e.g. with congestive heart failure) are compliant with a few guidelines using chart review.

**How quality improvement is currently done**

Quality improvement in healthcare today is going on at many levels, but is generally poorly coordinated. Organizations, practices, hospitals, and insurers all have programs intended to improve quality, but many of these programs overlap, and most are of marginal impact.

While the science of quality improvement has grown dramatically in recent years, many relatively ineffective approaches remain the workhorses of change, especially with regard to physician behavior. In particular, education continues to be a mainstay, and is often carried out through lectures and newsletters. While this kind of passive education clearly plays some role, studies repeatedly demonstrate that its effect is modest and wanes rapidly when discontinued [18].

The other main strategies for changing physician behavior include feedback, financial incentives, rationing and penalties [19]. Feedback – when given at all – is typically aggregate and retrospective. Sometimes providers do get lists of patients who are out of compliance for a certain measure such as mammography, but these lists, while useful, are often inaccurate because they are based on claims data, and they cover only a tiny proportion of the issues that might be addressed. Financial incentives (e.g. capitation) and rationing (e.g. formularies) clearly work, but are presented by physicians, and can be hard to implement. Penalties create even more resentment, and are generally counterproductive.

A more effective approach to changing physician behavior appears to be provision of real-time education and feedback while providers are delivering care using clinical decision support. Such decision support improves decision-making and adherence to guidelines, [20] and is generally well-accepted by providers. It is most effective if delivered in concert with other behavior changing approaches, including education and retrospective feedback.

Another highly effective approach for improving quality is to use industrial quality improvement techniques to address and retool specific processes, generally with multidisciplinary teams [21]. Many of the processes within medicine were never consciously designed. Judicious introduction of IT into many of these processes may be helpful.

**How quality is currently measured**

Today, most quality measurement within organizations is done using claims data, which lack clinical detail. Cases are aggregated using diagnosis-related groups (DRGs) which are assigned post-hoc and may not accurately represent patients’ clinical presentations. The outcomes most frequently assessed are mortality, length of stay, and charges (though increasingly costs are being measured as well). For most conditions, mortality is sufficiently low to be meaningless, and even for conditions with higher mortality organizations often do not perform severity adjustment because of the difficulty of doing so, although increasingly good adjusters are becoming available [22]. Length of stay can be decreased with enough focus and effort, and it is useful for cost reduction efforts, but is hardly a comprehensive quality measure.

The variables most amenable to change are process measures, and many have been associated with improved long-term outcomes [23–25]. Examples include door-to-needle time in patients with suspected myocardial infarction, use
of appropriate antibiotics in patients with community-acquired pneumonia, and use of beta-blockers in patients with cardiac ischemia. However, such process measures are difficult or impossible to extract from claims data, and costly chart review is typically needed in today's system. As a result, most organizations measure only a few of these at one time, because of the high cost of doing so. Moreover, for complications or adverse events, the standard is to rely on self-report by providers, which dramatically underestimates the frequency of these events [26].

Even among institutions which are leaders in quality measurement, the current state of the art is to compare crude outcomes by condition from claims data, typically using resources such as the University Hospital Consortium database which includes information like length of stay and morbidity and mortality data [27]. Such comparisons can be useful and result in identification of problems that can be addressed in an organization (for example if high mortality is identified in patients with community-acquired pneumonia), but these comparisons often aggregate disparate groups of patients, involve long lag times and lack clinical detail. In addition, the data may or may not be used by those actually delivering care.

The recent interest in quality by payors and regulators has resulted in a multitude of requests for quality data, which is overwhelming the limited resources of quality managers in most organizations, especially as most call for process data which organizations do not have at hand. Typically, healthcare has devoted a tiny fraction of its overall revenues to quality measurement and management, so that it is not surprising that there is little reserve.

The evidence on quality and IT

While increasing the use of IT in healthcare would result in benefits in several domains, the quality benefits will probably be some of the largest. In particular, this would improve the likelihood that processes will be successful, and would allow delivery of evidence-based decision support to providers, narrowing the gaps between evidence and practice.

Many studies now show that computerization of reminders and prevention guidelines improves adherence [28]. Reminders are especially important in the care of chronic conditions, which represent a large proportion of expenditures [29]. Management of these conditions requires tracking on the part of patients as well as excellent communication between providers and patients regarding tracking and deviations; this will be made dramatically easier with IT.

It will also be possible to improve safety in a variety of ways by increasing the use of IT; [30] including introducing checks for problems, highlighting and communicating information about key abnormalities to providers so they receive a rapid response, and facilitating communication between providers. Communication between patients and providers is also vitally important for safety, especially outside the hospital. In one study of outpatient adverse drug events, a large proportion of events could have been prevented or ameliorated with better communication between patients and providers [31].

Compared to direct improvement, quality measurement is even more profoundly affected when information is stored electronically in medical records, which are vastly richer than claims databases. It becomes possible to routinely find patients with certain conditions, to ask questions about their recent laboratory values, and even to go through their notes to look for certain issues, like new problems [32,33].

Finally, electronic records can be linked with public health surveillance. The events of September 11 underscore the obvious need to improve these links [34].

The financial case for IT and quality

Overall, disappointingly few studies have examined the financial case for IT and quality, and doing so is methodologically challenging. But in other industries, investment was made because it made sense, and not because of randomized controlled trials.

That being said, some data are available, although most relate to individual features or applications. For example, in a randomized controlled trial Tierney et al. found that use of computerized physician order entry as compared to paper ordering resulted in 12.7% lower charges (p=0.02) and 13.1% lower costs (p = 0.02) [7]. They believed that many of the benefits were seen because of delivery of computerized decision support at the time of ordering. Our group found that implementation of computerized physician order entry resulted in a 55% decrease in the serious medication error rate [35].

In other non-clinical domains, for example in the evaluation of electronic claims processing vs. manual processing, electronic processing will clearly have benefits, although relatively few data are available. Similarly, changes that result in greater efficiencies in patient and specimen movement, as well as decreased work for staff, will likely be highly beneficial, although the impact is difficult to measure.

To assess the overall costs and benefits of an electronic medical record system, Kian [36] constructed a cost-bene-
fit model for a hypothetical computer-based patient record system planned for the M.D. Anderson Cancer Center, and predicted that over a 10-year period, the total costs would be $54.5 million and the total benefits would be $129.7 million. In the ambulatory setting, Renner performed a study of a 40-physician ambulatory care medical group and estimated a net present value for the EMR system of $279,670 [37].

Less direct evidence comes from a recent study suggesting that organizations that invest more in IT are more efficient [38]. The “most wired” hospitals had lower median expenses per discharge and greater productivity, as measured by full-time equivalent staff (FTE) per adjusted occupied bed, paid hours per adjusted discharge, and net patient revenue per FTE. However, differences in clinical outcomes were less clear: in cardiovascular disease and obstetrics, the “most wired” appeared to perform better, but were similar with the nation’s average across the other 4 categories studied.

Taken together, these data suggest that benefits can be demonstrated for specific applications and domains. However, many benefits will take time to be realized, and may accrue across a sufficiently broad range of areas that it will be hard to attribute them directly to changes in IT. Nonetheless, the aggregate data do suggest that better IT in healthcare, as in other industries, is associated with greater efficiency and will be associated with higher quality as well.

**How recent changes including the internet affect the equation**

Several recent changes in information technology make rapid adoption of IT in healthcare especially attractive. One is that the cost of computer processing continues to decline. Another more profound change is the Internet, which essentially represents an inexpensive, broadly distributed platform that is ubiquitously available, even to small or geographically remote sites. This makes it possible to distribute information and knowledge at very low costs. This will affect the delivery of software and data for quality improvement, measurement, and research. For example, in one large on-going study, investigators have set up an approach in which identifiable data remain local due to privacy issues, but analyses are conducted centrally using deidentified data. Mirrored code is sent out to individual sites via the internet to minimize programming burden [39]. Finally, handheld devices will increasingly allow extension of desktop systems and will be used for many routine tasks such as capturing vital signs or administering medications.

**Vision of quality improvement**

The high-quality health care information systems of the future will be vastly different from those of today. Longitudinal medical records will allow tracking of patients’ conditions and medications so that providers in emergency rooms and hospitals will have detailed information at their fingertips. Clinicians will document using structured tools that allow capture of patient symptoms, clinical findings, and the physician’s assessment. The interdisciplinary teams that manage patients with chronic conditions will be able to track their panels, and seamlessly exchange information. When patients are admitted to a hospital, they will be tracked from the instant they enter the hospital until they leave. Because diagnoses will be entered early, guidelines will be made available to providers. It will be easy to see where a patient physically is at any time, where they are in their hospital course, what their treatment is, and whether guidelines are being followed.

In one controlled trial simply posting the expected length of stay for patients by condition resulted in a decreased length of stay, [40] and this sort of thing will be done routinely in a variety of clinical situations. Both patients and providers will have a better sense of what will occur and when, and this will result in higher satisfaction in both groups. When patients leave the hospital, their information will go with them to the team responsible for post-hospital care. This system will include safety nets that are not present today (so that if a patient does not arrive in clinic after a hospitalization, someone will go looking for them). Such nets are conspicuously absent in today’s system.

Much of the quality improvement that is done will revolve around refinement of specific processes, for example the process of getting a patient through a cardiac catheterization, the medication process, or the process of dealing with diabetic outpatients with poor glycemic control. Teams will have not only the information they now have, but also detailed time data, information about how often processes fail or are delayed, and information about the outcomes of processes. They will also have better outcome data, which patients will provide.

Patients will be a much more active part of care. They will have much more information and control, and will interact with the healthcare system outside of visits much more than is usual today. Self-management will be the norm for chronic conditions [41]. All of this will be facilitated by IT: by patient websites that allow them to interact with their providers, by integrated networks within healthcare organizations, and by electronic records that are the backbone for these functions. Thus, diabetics will enter glucose and blood pressure results on their website, receive suggestions regarding changes in management to improve
their control, and be notified when they are overdue for preventive measures like eye or foot exams.

**Vision of quality measurement**

Quality measurement depends even more on use and integration of information technology than does quality improvement. In the future, it will become routine to measure quality on an on-going basis for many conditions and processes, and this measurement will take place as care is provided and be integrated into the fabric of routine care. For example, for a patient with a myocardial infarction, the time they are first seen by emergency technicians, the time they arrive at the emergency department, and the time they get to the catheterization laboratory will all be routinely logged. In addition, the time when many key medications were given will be recorded, as will a number of key historical and physical findings. Nurses and physicians will chart using tools that capture key data in structured format. This will facilitate both clinical care and research, so that, for example, patients with cardiogenic shock can be rapidly identified and offered the opportunity to participate in controlled trials.

Gathering these types of data will then dramatically facilitate process improvement, because it will be possible to address issues of variation, and to determine where delays and suboptimal outcomes are occurring. Risk-adjusted comparisons within and among institutions will be possible, which will allow overall improvement like that which has been achieved by a few isolated groups such as the Northern New England Cardiovascular Collaborative [42].

**Barriers to change**

Perhaps the most difficult and problematic barrier to adoption of quality-related IT is that incentives for adopting such changes are lacking under the current reimbursement system. For example, under fee-for-service reimbursement there is no financial incentive for hospitals to reduce adverse event rates. Even under prospective or capitated reimbursement, justifying investment in technology that will result in longer-term benefit may be hard for capital-strapped organizations. In contrast, technologies like magnetic resonance imaging scanners result in billable services and hospitals have had no trouble making these investments.

An additional issue with the current reimbursement system is that providers are not reimbursed for care that occurs outside encounters. Reform of the payment system to reward such care is badly needed [1]. Also, support for collecting quality measurement data is necessary [43].

Legal issues relating to this area also represent an important barrier. For example, the Stark laws make difficult

some collaborations that would be beneficial, for example for an integrated delivery system to support implementation of electronic records in affiliated physician offices.

Another problem has been that information systems are highly complex, and provide uncertain return on investment. Because of the complexity of information systems, an organization will generally be best off developing a long-term relationship with one or a few vendors because of issues relating to connectivity. Because of this, the approach of vendors in this domain has been to develop non-standard software, and to hold tightly to its client base. Making a transition from one vendor to another today is difficult because of the lack of standards.

A further key issue is the wide array of healthcare organizations and the highly disparate nature of groups, ranging from solo practitioners and small hospitals to large hospitals and large integrated delivery systems. A solution that is effective in a large hospital may not work in a much smaller one. However, the internet should make it possible to deliver applications to a wide array of even geographically remote sites at low cost.

A further barrier relates to privacy, confidentiality and security of health information. Today's laws regarding these issues relate mainly to a paper world and are inadequate [44]. While the Health Insurance Portability and Accountability Act (HIPAA) begins to address some of the relevant issues, much remains to be done. Thus, while additional legislation is needed, it must be crafted in ways that make a revolution in healthcare information possible, and do not paralyze this revolution [45]. Specifically, it might become extremely difficult to do clinical research if new legislation is too restrictive; to address many issues, access to large populations is critical. Technically, it is feasible today to ensure data safety, but much work is needed in this domain to develop laws and regulation that adequately balance privacy concerns with the quality benefits that may be realized through use of health information [46].

**Policy Implications**

To achieve the changes mentioned earlier, at least five policy areas are especially important: standards, incentives, security and confidentiality, professional involvement, and research. Development of a National Health Information Infrastructure – as discussed by Detmer in the accompanying paper – could dramatically facilitate progress in all these domains [47].

**Standards**

An absolutely pivotal early step is establishment of national standards for key medical domains, including messaging, problems and conditions, laboratory and radiology data, medication data, and pathology results
have targeted are actively considering adopting these practices, and this is likely a result of their activities [52]. Payors can adopt contracting and reimbursement strategies that reward organizations that use IT more effectively – for example, submitting claims electronically. Regulatory agencies can ask for quality measurement data that are meaningful, standardized and are more readily gathered electronically.

**Security and confidentiality**

Security and confidentiality in information technology also represent an urgent concern. The Health Insurance Portability and Accountability Act (HIPAA) begins to address this area, [53] but has many problems which will need to be resolved, specifically concerning the nature of the boundaries regarding what is permissible and what is not; if interpreted broadly, HIPAA could make clinical research nearly impossible [47]. More legislation will be needed to strike an effective balance.

**Professional involvement**

Physicians, nurses, pharmacists and other types of health care providers all need to become more involved in advocating for and developing IT in healthcare and electronic medical records. This is an issue both at the local level (within institutions and among community practitioners) and for professional and organizational leadership groups. While some groups such as the American Academy of Family Physicians have led in this area with their work on electronic medical records, more often such professional groups are behind in this area. To deal with this, more attention, including funding, will need to be directed at this area. To be effective, development and implementation of new information technologies must speak to the minute-to-minute needs of all types of providers.

**Research**

Finally, while a great deal is known about what works regarding using IT to improve quality, much remains to be learned, especially regarding implementation and dissemination of systems. Key questions remaining include how best to deliver clinical decision support, how much adjustment of guidelines is needed for local implementation to be successful, how clinical information systems can best be implemented and disseminated – especially to small hospitals and community-based providers, how patients can best be involved more than they are, and the role of the Internet and other new technologies in this revolution.

**Summary**

Healthcare in the U.S. today is inefficient, error-prone, and of variable quality. Information technology has the potential to substantially improve care by bringing decision support to the point of care, by providing vital links
and closing "open loop" systems, and by allowing routine quality measurement to become reality. Achieving this potential will be challenging, and is far from guaranteed, but it is possible. If it is to occur, substantial investment will be needed to galvanize this change, probably in large part from the federal government, with development of a national health information infrastructure representing the most important piece of the puzzle.

Competing interests
Dr. Bates has received honoraria for speaking from the Eclipsys Corporation, which has licensed the rights to the Brigham and Women's Hospital Clinical Information System. The hospital no longer has a financial relationship with Eclipsys. Dr. Bates is a coinventor on Patent No. 6029138 held by Brigham and Women's Hospital on the use of decision support software for medical management, licensed to the Medicalis Corporation. He holds a minority equity position in the privately held company Medicalis which develops web-based decision support for radiology test ordering, and serves as a consultant to Medicalis. He is also a consultant and serves on the advisory board for McKesson MedManagement, a company which assists hospitals in preventing adverse drug events. He is on the clinical advisory boards for Zynx Inc., which develops information technology. And Voltage Inc. which compiles information on compliance for drug companies. He is a consultant for Alaris, which make intravenous drug delivery systems.

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References
19. Eisenberg JM: Doctors' Decisions and the Cost of Medical Care, Ann Arbor, MI, Health Administration Press 1986

Page 8 of 9 (page number not for citation purposes)
47. Detmer DE: It is about health: Securing a National Health Information Infrastructure. Unpublished Work 2002
52. The Leapfrog Group for Patient Safety: Rewarding Higher Standards. [www.leapfroggroup.org]5-4-2002

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