What the Patient Should Order

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Open global standards, workflow integration profiles, and related processes have been developed through consensus-based procedures. Although these standards and profiles should be augmented with additional therapeutic area–based content standards, they are available now to enable the use of electronic health records to directly support clinical research concurrent with patient care. Improving the exchange of information and integrating workflow between research and health care are inherently necessary to accelerate the pace of informing clinical decisions based on current research findings and for an efficient, cost-effective health care system to improve the quality of patient care.

INTRODUCTION
When one needs health care, it is the expectation—or at least the hope—that this care will be based on current knowledge of the optimal procedures and therapies. Unfortunately, the time required to gather information about the effectiveness and safety of potential new procedures or drugs and to translate this knowledge into accepted treatments has been estimated to be approximately 17 years (1). Indeed, the clinical research process is antiquated (2), but health care–associated issues also contribute to the delay in translation. To improve this situation, clinical information must flow more easily into research data that can be readily aggregated to provide a sufficiently large set for reliable analyses to inform health care decisions. This cycle of health care providing data for research and research informing health care will become more important and challenging in the future, as volumes of clinical genomics information become available to enable personalized health care. Of even greater importance is that relevant processes must be reengineered to enable clinicians to provide care to patients while simultaneously supporting research. Finally, patients and clinicians must be confident that the research data will be used appropriately, maintaining privacy while contributing to safer and higher-quality care.

Specific key issues that must be addressed to close this 17-year gap in translation include the following: (i) privacy concerns (real and perceived), (ii) the need for global data interchange standards and standards-based technology, (iii) the need to streamline data entry and access (entering data just once to serve multiple purposes), and (iv) the integration of clinical care and clinical research workflows. Several excellent initiatives provide opportunities to link health care and research more closely through improved information exchange. It is critical to build awareness about how to evaluate, support, and leverage these initiatives to shorten the delay between research and new health care options (Fig. 1). In this Commentary, I discuss the four key issues described above, with the goal of guiding the evaluation of health care initiatives and research projects for their potential contributions to a more efficient and higher-quality health care system.

PRIVACY CONCERNS
Privacy concerns related to health care data are important and are addressed through various means, including the security of data storage systems, the U.S. Health Insurance Portability and Accountability Act (HIPAA), and privacy initiatives in other countries. From the standpoint of clinical research, it is unfortunate that insurance companies typically have access to information from medical records before a manufacturer of a biopharmaceutical product or device or a regulator, particularly with regard to safety. Hence, we see statements from patient privacy activists such as the following: “Your right to decide who can see and use your sensitive, personal health information was eliminated in 2003. See how.” Or: “Today, laws governing access to health records expose employees to the possibility of employment discrimination. Thirty-five percent of Fortune 500 companies admitted to looking at employees’ health records before making hiring and promotion decisions” (3). Unfortunately, such statements can deter potential patients from participating in research studies that could contribute to improving health care. There are additional regulations to protect those who participate in clinical research studies, including those of oversight committees (such as institutional review boards), the Code of Federal Regulations, and the International Conference on Harmonisation (ICH) Good Clinical Practices.

Clinical research relies on people who are willing to participate in studies that provide information about the effectiveness and safety of methodologies, biopharmaceutical products and devices, as well as the influence of environmental factors. Participants can be healthy individuals or patients with particular problems. Patients with chronic disorders, especially those with unsatisfactory treatments, are frequently amenable to having their medical information contribute to a better understanding of their disorder and the development of improved treatments. They sign informed consent forms for this purpose. In addition, the data that are used in clinical research studies do not typically include direct patient identifiers and are aggregated in such a way that identification of a particular person is essentially impossible. For those suffering from debilitating diseases, the opportunity to receive a safe and effective treatment is paramount. The research system must not abuse their confidence, and the use of data from systems such as electronic health records (EHRs) must not compromise the privacy of these data. This condition is a core requirement in the work of the Health Information Technology Standards Panel (HITSP) and other initiatives.

ADOPTION OF GLOBAL DATA INTERCHANGE STANDARDS AND STANDARDS-BASED TECHNOLOGY
The word “standards” elicits both positive and negative reactions. Standards might pertain to meeting certain quality requirements (high standards). Conversely, they might bring to mind rigidity and thus the misperception that they inhibit innovation or stifle creativity. “Standards do not stifle innovation or competition. Rather, they’re the foundation for both. The standardized electrical plug and socket have not prevented anyone from producing new, interesting and innovative appliances. Instead, they have meant that anyone in the country can buy a gadget safe in the knowledge they’ll be able to power it.” This quote comes from an article on why innovation needs standards, referencing in particular the World Wide
Web Consortium (W3C) (4). The example provided rings true anywhere and raises another issue. When thinking of standards, there is a tendency to consider one’s own company or geographical area. In clinical research, however, there is a need to think globally. Adopting a proprietary or a country-specific standard might be counterproductive, especially in the global arenas of health care and research; in fact, the terms seem to be oxymorons. For this reason, the standards development activities in health care and clinical research involve organizations that develop global standards, such as the International Standards Organization (ISO), Health Level Seven (HL7), and the Clinical Data Interchange Standards Consortium (CDISC), which have realized that there is more value in collaboration than in the creation of competing standards and that substantial benefits can be afforded by an improved link between health care and research through the use of global standards that enable innovation (5).

Specifically, there is value (opportunity for innovation) that can be gleaned from data interchange standards, which afford the opportunity to redirect a researcher’s or clinician’s attention to more important and interesting work, because the mundane aspects of formatting data to move it from one system to another are already agreed on and addressed. In terms of cost and time savings, clinical research standards have been found to decrease the overall non-value added time and resources for a study by 60% and the study startup time by 70 to 90% (6). In addition, such standards allow for latitude in the study design; it is simply the data structures and definitions that should be standardized (behind the scenes), so that information can be exchanged from system to system efficiently, without loss of meaning (semantic interoperability).

In clinical research studies that involve hundreds of different clinical sites, data from these centers must be integrated into a common database so that a sufficiently large sample can be analyzed. When clinical research data are on paper or in portable document format (PDF) files rather than in a standard electronic form, such analyses are inhibited, if not impossible. When the U.S. Food and Drug Administration (FDA) receives data from various manufacturers in proprietary formats, FDA researchers cannot readily make comparisons across treatments for a given disorder. Moreover, they cannot use certain tools for their review of such a submission, because such tools cannot be used with data that do not adhere to the standard format.

Indeed, data interchange standards improve the quality and accessibility of important information. As Kwak and Dickerson observed, “New systems that are built on standards for interoperable electronic and personal health records create new opportunities for building solutions to the problems that health care services face today. And, such standardization also empowers patients to have more control over their own health care” (7). The feasibility, practicality, and value of personalized health records will be enhanced by global standards, so that information from a variety of sources can populate an individual’s record automatically.

In summary, standardization of research and health care information technologies (HITs) in accordance with an accepted set of open global standards will allow clinicians and researchers to choose from a variety of technologies that best fit a given activity, confident that such standards-based technologies will work together appropriately and provide the data needed for multiple purposes. For example, an EHR should provide information for assessing the quality of care, public health reporting, clinical research, and patient safety in addition to supporting individual patient care.

**STREAMLINING DATA ENTRY AND ACCESS**

It is crucial that EHRs or health information technologies support the entry of information only once, for multiple downstream purposes. If a patient has a disease associated with an outbreak or a serious adverse event, this information should be reported to the appropriate parties. Relevant data can also contribute to an aggregated clinical research database for analyses to inform future health care decisions or, in the case of the FDA, to populate a cross-study database to improve its evaluation of the safety and efficacy of a new medical product or therapy. All of this information is a subset of health care data. Hence, if the data are entered initially in an EHR, there is an opportunity to use these data for other beneficial purposes, in addition to patient care. Unfortunately, technology that uses
proprietary standards or is not based on open standards does not support data exchanges (whether they are between health care systems or among health care systems and research or reporting systems) without excessive time and effort. When standards are not used, data sharing requires extensive mapping of data elements to enable cross comparisons. Such mapping—to attempt to match up data, after the fact, when it is not collected in the same format and may include slightly different definitions for each element—is non-value added work that is time-consuming, tedious, and inherently error-prone. Conversely, developing technology based on open global standards facilitates data sharing, streamlines these processes, and broadens the selection of technologies that support the entry of data once for multiple downstream purposes and of tools that can facilitate data exchange (i.e., tools that can “talk to each other”).

The Clinical and Translational Science Awards (CTSA) given through the U.S. National Institutes of Health (NIH) National Center for Research Resources to medical research institutions across the United States are intended to create a national consortium with the goal of transforming clinical and translational research. Key elements of the CTSA include collaborative studies and community engagement, which are intended to “foster collaborative partnerships and enhance public trust in clinical and translational research to facilitate the recruitment of research participants from the community” (8). This concept will derive success from agreement on global and open data interchange standards to facilitate information sharing within and across institutions. In addition, it is becoming incumbent on researchers from academia and industry alike to provide a minimum set of information openly to the public. This includes registering clinical studies through clinicaltrials.gov or the World Health Organization International Clinical Trials Registry Platform and posting summary results at the end of a study. This transparency is being encouraged not only nationally by the U.S. government but globally by the editors of science journals. Many feel that research projects supported by government funds should use open standards to enhance efficiency and ensure that both positive and negative results are made available to the public.

The typical process for reporting adverse events for monitoring the safety of an approved product is now done on paper and submitted by fax. This reporting process can take more than 30 min; hence, most adverse events go unreported, because during this amount of time a clinician can see another patient or two. This situation can easily translate to insurance companies having more rapid access to safety information than regulators, researchers, or manufacturers of biopharmaceutical products or devices. How can such reporting be encouraged and facilitated? New standards-based initiatives, such as the development of an integration profile (described in the next section), should substantially decrease the time required to report outbreaks to the Centers for Disease Control (CDC) and adverse events to the FDA and manufacturers.

INTEGRATING THE WORKFLOW BETWEEN CLINICAL CARE AND CLINICAL RESEARCH

Privacy, security, global standards, and standards-based technology are all important for improving the link between research and health care and for providing reassurance to patients who are considering the possibility of participating in research. However, largely because the research process is so cumbersome, the majority of clinicians who participate in a clinical trial once never do so again, resulting in many studies that are either carried out overseas or take longer than necessary.

Three key goals form the core of recent initiatives that aim to link clinical research and health care: (i) to collect or enter data only once, for multiple downstream purposes (thus eliminating transcription, which takes time and decreases quality); (ii) to make it easier for clinicians to care for their primary patients while supporting clinical research needs (integrating workflow); and (iii) to improve patient safety, adhering to privacy and electronic record–keeping regulations. The following initiatives deserve mention because they are making recognizable progress toward a closer link between health care and research.

Collaboration among standards development organizations (SDOs). The collaboration between HL7 and CDISC was formalized in 2001 and is based on an agreement to harmonize clinical research and health care standards. In addition, HL7 has been working with other health care standards organizations globally [including the ISO technical committee for health care standards and the Comité Européen de Normalisation (CEN)] to bring disparate standards together. As a result of such collaborations, there is now a Joint Initiative Council (with members from HL7, CDISC, ISO, CEN, and the International Health Terminology SDO) that is invested in ensuring harmonized global standards for health care and research. A collaborative information model called the Biomedical Research Integrated Domain Group (BRIDG) model has been developed with stakeholders from CDISC, the National Cancer Institute, NIH, the FDA, and HL7 to address the domain of protocol-driven research in the context of the health care reference information model, and a suite of clinical research standards have been published (by CDISC) to support standards-based data interchange from research protocol through analysis and reporting (9). These standards apply broadly to protocol-driven research of various types—academic, government, and regulated research.

eSource in clinical research. For quite some time, there were major concerns about conducting research studies using “eSource” data: information that was captured initially in a permanent electronic record and then used for a clinical study. “Permanent” in the context of this definition implies that any changes made in the electronic data are recorded via an audit trail. In this scenario, data are not entered onto paper first. Clarification of process guidelines that facilitate the use of eSource technologies (such as EHRs or eDiaries) for research, in the context of relevant global regulations, was a goal of the eSource Data Interchange (eSDI) initiative, which was launched through the FDA with CDISC convening a volunteer team. The resulting eSDI document (10) includes 12 requirements for clinical research processes using eSource (including three scenarios for EHRs) to ensure that regulations are met in research conducted with eSource data. Much of this document is now referenced in guidelines written by the European Medicines Agency for its field auditors.

Functional profile for EHRs in clinical research (EHRCR). This profile details functional specifications for the use of EHRs in research. The EHRCR Functional Profile Working Group spearheaded the effort; two HL7 Workgroups, one specializing in EHR standards and the other devoted to clinical research, took the profile through the ballots and comment reso-
lution process. It became an American National Standards Institute (ANSI) standard in 2009 and is now being used as a reference by the Certification Commission for Health Care Information Technology in developing certification criteria for EHRs used in clinical research.

Streamlining workflow through an integration profile. Working with Integrating the Healthcare Enterprise on an initiative to improve the way in which information is shared between health care and clinical research, CDISC developed a simple but powerful integration profile that enables EHRs to support research, safety reporting, and other use cases without excessive burdens on EHR vendors. This work, which was launched on the basis of the eSDI described above and a subsequent pilot, leverages the requirements set forth in the eSDI document. The profile, called retrieve form for data capture (RFD), simply “pulls” a form into the EHR environment at the appropriate time and pre-populates certain fields from information in the EHR (11). The form can be a clinical research case report form, a safety reporting form, a disease outbreak report form, or a disease registry form. The RFD is now being used for clinical research studies (12) and has supported safety reporting for adverse drug events (ADE) through a project called ASTER (ADE Spontaneous Triggered Event Reporting), postmarketing surveillance in Japan, and the reporting of flu outbreaks to the CDC. In the case of RFD, use of an open standard that supports a process that integrates adverse event reporting into EHRs reduced reporting time from more than 30 min to 30 s (13). The RFD is endorsed by EHR vendors for its value, its facilitation of research at sites, and its ease of implementation (14).

Interoperability specifications. The Health Information Technology Standards Panel has been developing interoperability specifications (ISs) to support various use cases and capabilities of EHRs. Each IS identifies existing standards (and gaps) and provides relevant specifications for that use case or capability. As of late 2008, an EHR clinical research initiative was approved, and ANSI convened a workgroup to prioritize the first use case in this space (15). The workgroup comprised representatives from numerous organizations that are considered stakeholders in clinical research, and the first priority was to develop an IS to support the exchange of a core set of data from EHRs to clinical research systems. With funding from ~40 organizations and the help of numerous volunteers, the EHR clinical research-related work of the Health Information Technology Standards Panel is proceeding, and the team is developing an IS in accord with the standards that were identified in the first step of the process as follows: (i) a form of the HL7 standard called the Clinical Document Architecture (CDA)/Continuity of Care Document (CCD) to provide an eSource document; (ii) the RFD for workflow integration/processing of information between EHR and research; and (iii) the CDISC Clinical Data Acquisition Standards Harmonization (CDASH) standard, which identifies a core set of data elements that are needed across essentially all clinical research studies. This Health Information Technology Standards Panel IS for clinical research should be available by the end of 2009.

CONCLUSIONS

Much work remains, but the path is being paved for research to inform health care decisions more effectively and efficiently (Fig. 2). The base clinical research standards (open and global) are available, although further refinements and augmentation are in order, particularly in the areas of efficacy-related common terminologies or ontologies toward semantic interoperability. The steadily increasing collaboration of SDOs is an encouraging trend. And there is now recognition by governments that EHRs are critical to improving the quality of health care. It is incumbent on all clinicians, scientists, and policy-makers to ensure that these EHRs/HIT applications support open global standards that will enable the use of valuable health care information for knowledge enhancement, not only for patient care but also for clinical and translational researchers, which will in turn increase the opportunity for patients to receive care that is based on current research. Understanding this concept as patients—and we are all patients—is critical to efficient, cost-effective, and higher-quality health care.

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COMMENTARY

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