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The Technology Issue: New Tools to Tackle Old Problems

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In this issue of *Clinical Researcher*, the three articles that follow this page have been selected as the basis for a Home Study test that contains 30 questions. For your convenience, the articles and questions are provided in print as well as online (members only) in the form of a PDF. This activity is anticipated to take three hours.

Answers must be submitted using the electronic answer form online (members only, \$60). Those who answer 80% of the questions correctly will receive an electronic statement of credit by e-mail within 24 hours. Those who do not pass can retake the test for no additional fee.

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Maximize Your EHR Systems for Clinical Trials Operations

PEER REVIEWED | David M. Vulcano, LCSW, MBA, CIP, RAC
Candida Barlow, MSN, CTN, RN | Natalie F. Scully, PhD, CCRC, CCRA
Cynthia M. Soto-Azghani, BSN, RN, CCRC | Anthony Keyes, BS, PMP
Steven Ziemba, PhD, FACHE, CIP, CCRC, CPI

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At the Association of Clinical Research Professionals (ACRP) 2014 Global Conference, representatives from Epic, Cerner, and Allscripts were present to address many myths about electronic health record (EHR) systems. The results from 2014 were posted on the ACRP Online Community for Epic and Cerner. As it turns out, these systems are capable of tasks that many clinical research coordinators (CRCs) and others had believed the systems could not do.

LEARNING OBJECTIVE

After reading this article, participants should be able to describe how an electronic health record (EHR) system can assist researchers with patient safety, billing compliance, patient recruitment, and clinical trial metrics.

DISCLOSURES

David M. Vulcano, LCSW, MBA, CIP, RAC;
Candida Barlow, MSN, CTN, RN;
Natalie F. Scully, PhD, CCRC, CCRA;
Cynthia M. Soto-Azghani, BSN, RN, CCRC;
Anthony Keyes, BS, PMP;
Steven Ziemba, PhD, FACHE, CIP, CCRC, CPI:
Nothing to disclose

One overarching myth addressed was that the EHR companies are the ones to solve all our problems and hand the solutions to us, but it is not that easy, nor is it their place to solve problems at that level. An analogy is Microsoft Office, which comes with a powerful set of functional tools that must be customized at the institutional and personal level. Microsoft Corporation is not going to design and build an individual company's balance sheet in Excel, nor is the software manufacturer going to build an Access database and its front-end forms. Microsoft can provide the functionality and some basic training, but how that software is used is an institutional preference.

EHRs are arguably no different. Generally, the functionality desired by principal investigators (PIs) and CRCs is available, but is not used or promoted for a variety of reasons, ranging from not knowing it is there to not having developed it for use.

As a follow-up to the 2014 conference session, a 2015 session focused less on debunking the same myths and honed in on how to build the bridges in an organization and provide the business case for adding research functionality. Today, competing resources such as ICD-10 conversion and

meaningful-use attestations are taking priority, but nevertheless the business cases can be built for improved research functionality.

This article focuses on three core areas that will pay dividends: 1) Building a Business Case; 2) Strategies for Implementing a (Retroactive) Business Case; and 3) Building the External Support Network.

PART 1: Building a Business Case

“Executers create energy, they do not drain it.”

—paraphrased from “Execution,” by Larry Bossidy and Ram Charin

First, Mitigate Subject and Business Risks

PATIENT SAFETY

For nearly all EHRs, active alerts (see Figure 1) can be built to include notification to the research staff of any of their research participants who enter the emergency room, are seen in an outpatient clinic/satellite facility, or are admitted to the hospital (provided that the EHRs for the different facilities

are linked). This notification is particularly important, given that inpatient hospitalization meets the definition of a serious adverse event (SAE) (as found in ICH E6 1.50 from the International Conference on Harmonization).

In order to fully utilize these safety features, patients must be properly designated as participants in a research study and linked to the proper study. This should be done both through the EHR and in conjunction with a clinical trial management system (CTMS).

FIGURE 1: Example for Creating “Alerts” Within an EHR

Patient Safety Alert

- + This patient is on a CLINICAL RESEARCH TRIAL
- + Trial: Protocol Name
- + COMMENTS: Subject randomized to placebo or active factor X inhibitor
- + Contraindicated Medications: antithrombotics
- + National Clinical Trial #: NCTXXXXXXX
- + Primary Investigator: Name and Number
- + Research Coordinator: Name and Number
- + Research Department Main Phone:

Additional safety measures that should be added include hard stops and/or alerts for potential medication contraindications. All hospital medications, including those administered as part of a research study, are ordered almost exclusively through the EHR.

Inasmuch as strict adherence to the protocol is foundational to protect the safety of research participants and to ensure the integrity of scientific findings, deviations from the protocol must be fully identified, promptly reported, and documented accordingly. An EHR e-mail message can be utilized to alert the PI and study team to potential deviations to the protocol in real time, which may result in discovery prior to internal quality inspections or external monitoring.

Electronic research order sets can be specifically built to protocol specifications to prevent persons not involved in the study from inadvertently altering study orders. This not only saves valuable time, it also enhances safety by providing an electronic means of tracking protocol requirements

and preventing noncompliance. Mechanisms for building order sets vary among institutions and may require programming expertise. Some institutions may incorporate electronic order sets or “builds” as the expense of doing business, while other institutions relegate the build to each research team.

Each institution must decide if the utility of order sets should be internally supported or if research teams must secure their own expertise and/or funding. Research order sets and orders associated with research also play an important part in facilitating billing compliance. The additional function is institutionally dependent, based on whether the EHR is directly linked to billing modules.

BILLING COMPLIANCE

Billing compliance, especially when it involves the billing of federal payers, is a complex matter that creates many challenges (see Figure 2). Although entire conferences are dedicated to effective billing practices, participants remain confused on many counts. Even when the regulations and coverage decisions can be navigated correctly, it is difficult to implement a compliant billing system in a fast-paced and complex healthcare organization because of the many handoffs.

Any compliance officer in a healthcare-related entity should be well versed in the Stark Laws, False Claims Act, and Anti-Kickback Statute, as well as their penalties. Integrating research into this already complex system increases the risk for double-billing. Examples include billing Medicare for something for which the sponsor is paying the hospital and/or the research site/physician, billing

FIGURE 2: Billing Compliance and Work Effort Summary

Billing Compliance	Work Effort
Delineate standard of care vs. research	Increase study subject recruitment and retention efforts
Create charges in real time by automatically adding research billing codes and modifiers.	Improve accuracy of cohort discovery
Improve reimbursement collection	Automate source data collection and verification directly within the source
Manage potential fraudulent charges and decrease false claim submissions	Decrease potential adverse events for study subject; reduce care management time and possible length of stay

for nonreimbursable investigational products or for nonroutine care items, or billing Medicare when a sponsor agrees to pay for a clinical trial-related injury (which violates the Medicare Secondary Payor provisions).

There have been many well-documented cases in which providers have had to pay millions of dollars in fines and/or settlements due to inaccuracies in research billing. EHR systems often touch all points at the beginning of the billing cycle and personnel involved in the beginning of the billing cycle (such as clinical staff, coders, and others in charge of revenue integrity); therefore, the EHR is often that single source of all billing-related truths, including items significant to research-related billing.

HEALTHCARE SYSTEM ACCREDITATION

Hospital accreditation agencies such as the Joint Commission and Det Norske Veritas (DNV) Healthcare provide specific requirements for research operations (see Table 1). For research consent documents, the Joint Commission's standard (RI.01.03.05) and DNV's standard (PR.4) address the hospital's obligations independent of what the U.S. Food and Drug Administration (FDA) or Office for Human Research Protections (OHRP), both part of the Department of Health and Human Services, may require.

Both agencies also have standards that pertain to the management of investigational drugs. The Joint Commission's standards (MM.04.01.01 and MM.06.01.05) require a hospital-specific policy for investigational drug orders and management. Similarly, DNV's standard (MM.1) indicates that overall policies must include investigational medications/drugs that are not eligible for scheduled dosing times and provide general guidelines for what medication policies must include.

Specific tabs in the EHR can be utilized to easily identify research consents and medication records. For those nonhospital entities accredited by the Accreditation Association for Ambulatory Healthcare (AAHC), Section 19 puts forth requirements similar to those of the Joint Commission and DNV regarding documenting the informed consent process for research participants who are independent of FDA and OHRP requirements.

HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA) PRIVACY RULE AND NON-HIPAA PRIVACY AND SECURITY

Providers in the United States' healthcare delivery environments are no strangers to the privacy and security restrictions put forth by HIPAA. HIPAA is also intended to provide the parameters for the appropriate use and disclosure of health information for legitimate purposes, such as research. The process of releasing those data (usually pursuant to a signed authorization from the clinical trial participant) must be done in a HIPAA-compliant manner.

In a paper-based world, this introduces privacy risks for the patient and regulatory risks for the provider. Shifting the records with patient-identifiable protected health information (PHI), be they medical records or other paper source documents, into the EHR environment provides a secure storage mechanism that places the provider more in control of who is accessing that information.

The security of the subject's record may be ensured by issuing study monitors with their own user identification and password, so that their activity can be limited and tracked (even if they log in remotely) or by having them review the material over the shoulder of a staff person with access. Heads of organizations that have transitioned to EHRs would likely shudder to think that they would keep shadow paper copies of identifiable medical records of their patients. Arguably thus, the risk of a PHI breach to the research subject and the institution is no different if the PHI was on a medical record page or a research source document.

Although health information that has been de-identified according to HIPAA standards goes unregulated by HIPAA, there are still risks to be addressed. Large research datasets that otherwise could have been part of the EHR reside in the proverbial "locked filing cabinet" or in Excel spreadsheets and other database programs on laptops and USB "thumb" drives. The literature is full of incidents of lost research laptops.

Even if the data are de-identified, a business risk is still posed to the institution as well as the individual, given the ease of combining the information with other publically available datasets for what is known as "re-identification attack." Overall, having the research source data as part of the EHR protects not just the privacy of the subjects, but also the actual data, from potential breaches.

OTHER REGULATORY CONSIDERATIONS

FDA Form 1572 for investigational drug clinical trials and “The Statement of the Investigator Responsibilities” for investigational device clinical trials are, respectively, signed acknowledgements that investigators will adhere to FDA regulations regarding the conduct of investigational agents. Per 21 CFR 312 in the *Code of Federal Regulations*, investigators are required to delegate appropriate tasks to others based on their education, training, and qualifications.

The Delegation of Authority Log lists all persons to whom the PI has delegated significant trial-related duties (ICH E6 4.1.5). In some cases, discrepancies exist between the log and institutional policies for study team members. A CRC who is delegated medication dispensing responsibilities by the log may lack the credentialing necessary to enter medications in the EHR.

The log must be consistent with internal policy for the EHR to be fully effective. Depending upon the organization and the state it operates in, any activity documented by an unlicensed coordinator may need to be reviewed and signed by the appropriately credentialed and licensed staff to ensure that activity is not beyond the scope of services of the job description or licensure of the individual. Role-based security may be considered burdensome by study teams at first, but the safety, consistency, and transparency provided by EHRs ensure better alignment with institutional guidelines and protections.

Second, Capitalize on Business Opportunities

FEASIBILITY

EHR records support a vibrant environment for quick and accurate feasibility assessment for potential clinical trial offers. The skill set of information technology (IT) analysts decreases the work effort spent on behalf of the research staff by querying the existing data within an active EHR.

An accurate assessment of feasibility creates an environment of respect and trust among research centers and industry leaders. A researcher can submit the initial feasibility questionnaire to the IT analysts, or an automated process may be developed. Reports may be available in real time or by the end of the business day, depending on institutional policies and procedures.

TABLE 1: Accreditation Within Institutions Supported by Clinical Research Centers/Institutes

Policy or Process	American College of Surgeons (and Similar Organizations)	The Joint Commission/ AAAHC	Det Norske Veritas
Research Policies and Procedures	Specific to Type of Accreditation (Comprehensive Cancer Centers, Breast Centers, Stroke Centers, Trauma Centers, etc.)	Yes	Yes
Formal Screening Process to Identify Potential Patients	Specific to Type of Accreditation	No	No
Policy Related to Management of Investigational Drugs	Specific to Type of Accreditation	Yes	Yes
Policy Related to Documentation of Informed Consent	Specific to Type of Accreditation	Yes	Yes

The feasibility report provides accurate data regarding the center’s potential study subject pool. If the report does nothing else, it prevents institutions from accepting studies for which they cannot adequately recruit, not only saving these institutions time and expense, but also preventing them from gaining a reputation of being a “low enroller” or “zero enroller” in sponsor and contract research organization (CRO) databases.

Uploading EHR data to a cohort discovery tool, such as the National Institutes of Health (NIH)-funded i2b2 (Informatics for Integrating Biology and the Bedside) (see <https://i2b2.org/>), provides a fast and convenient way to identify a specific cohort of interest. A customized search for demographics, disease states, or lab values reveals the number of potential participants meeting the specified criteria. i2b2 searches millions of unique data elements at once without involving the use or disclosure of any PHI, and before an institutional review board (IRB) application is needed.

Based on the results, the investigator can make a more informed decision whether or not to proceed, saving countless hours, preventing studies “doomed to fail,” and greatly aiding in the selection of inclusion/exclusion criteria likely to make enrollment successful. In the past, this was possible only through IRB approval and exhaustive paper chart review. Once the decision is made to proceed with the study and IRB approval is obtained, the investigator can access PHI for the identified cohort.

CLINICAL TRIALS RECRUITMENT

Many practitioners attempt to recruit participants through an EHR’s patient portal. Participants receive a message through their portal indicating that they may be eligible for a study. Interested participants can consent online and complete the study questionnaire or other tasks related to recruitment.

The capability to engage the participant in the clinic is particularly exciting, given recent interest and funding opportunities for patient-centered outcomes research (PCOR). As IRBs are charged with the

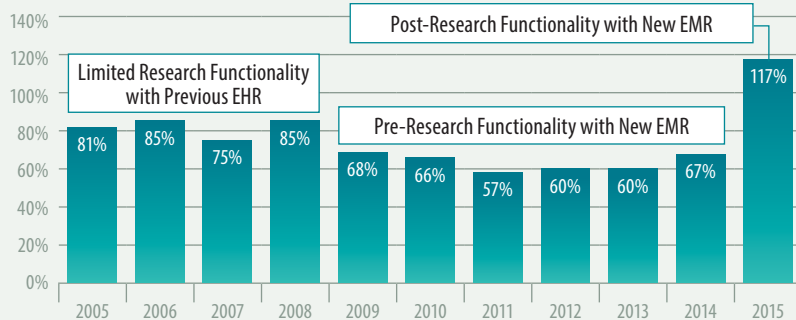
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CASE STUDY #1

Deaconess Clinic, a multispecialty group of more than 160 providers in Evansville, Ind., recently implemented surveillance and notification functionality for a long-term cardiovascular outcomes study. Using the study’s screening criteria, the EHR continuously monitored patients who were scheduled for upcoming appointments. The physicians’ daily appointment schedules were customized with “research-centric” views or columns to flag the appointments for selected patients who might qualify for the study. Physicians were then able to directly refer the patients to the study through the EHR; this is similar to how patients are typically referred to a specialist for an ancillary procedure. The research nurses were also alerted about the patient’s appointment in case the physician wanted to have the patient consented. As a result, 513 patient appointments were identified by the EHR, and 157 patient referrals were sent by 34 referring providers, more than tripling the targeted enrollment for the study. The impact on the research revenues due to this implementation was more than \$1 million over the course of the five-year study. Prior to this implementation, all studies were hitting only 57% to 67% of their enrollment targets. By building this functionality into their EHR, researchers were able to increase that percentage to 117% of their enrollment targets on a year-to-date basis (see graph below).

Average Enrollment Rate for Closed Studies 2005–2015



protection of research risks to human subjects, it will be essential to engage IRBs to assure that adequate informed consent and appropriate confidentiality measures are in place for this new era.

In the fast-paced emergency department setting, patients are not scheduled, and volume and acuity cannot be predicted as accurately as in other healthcare settings. An EHR’s built-in notification system can greatly aid the ability to identify participants by alerting the study team to a patient’s real-time presence via phone or e-mail after a certain diagnostic test/procedure (i.e.,

urinalysis) is ordered or a certain diagnosis made. Once the move to an EHR system is announced, research teams should petition leadership to have this type of functionality incorporated.

A paging communications workflow utilizing an order transmittal rule was built into the new EHR system to facilitate paging of emergency department study teams when an order for a certain test or medication is placed. A recent example utilizing an alert concerning any patient having a urine culture allowed the emergency department to enroll 90 participants in a kidney infection study much faster than anticipated. Once study enrollment was complete, the alert was simply inactivated.

A physician can also directly communicate with study teams by entering a nursing communication order. The order becomes a part of the EHR and documents that the provider has communicated with the patient and that the patient has given approval to be contacted by the study team. Because the order meets the order transmittal rule, an alert is sent to the study team.

Recruitment of study participants via EHR can also include direct notification of the physician. A significant challenge of recruitment involves simply maintaining provider awareness of active studies and their inclusion/exclusion criteria for screening. The potential exists for EHRs to maintain an active surveillance of scheduled patients and alert the provider to those who may be eligible for a study.

The applicability of this approach will vary by study. For example, an EHR may be able to discern all screening criteria for a prospective registry-based observational study, but only be able to provide high-level screening capabilities in the case of a randomized oncology treatment clinical trial (see Case Studies #1 and #2 for examples).

TRIAL METRICS

A benefit of EHR in the healthcare setting is the derivation of metrics from existing data. The monitoring of metrics is an important and useful practice in any business setting, though care must be exercised to focus on relevant metrics. Sometimes administrators simply need to ask, “How many clinical trial patients have we had?” or “How much revenue did this study bring?” or (after reading a bad press report) “Did we have anybody on that particular study in our hospital?”

Aspects such as productivity, efficiency, and even qualitative measures could also be utilized for more sophisticated inquiries and planning. Many clinical trial sites use a CTMS for such measures, but many sites do not have the benefits of such a robust system. For whatever reason, a number of sites unfortunately do not conduct metrics, and the end result is a poor awareness of their performance. This can be true for the site as a whole or for individual studies.

Reasons for not implementing metrics can vary, but a lack of time may certainly be one. The EHR can potentially automate the process, especially in the absence of a CTMS. Individual measures of study performance, such as enrollment rate, can be aggregated to provide a view of site performance. A dashboard can be developed for the site to monitor itself. In addition, data from different sites can be used to develop benchmarks for performance.

OPTIMIZATION OF WORKFLOWS FOR CRCs AND CLINICAL RESEARCH ASSOCIATES (CRAs)

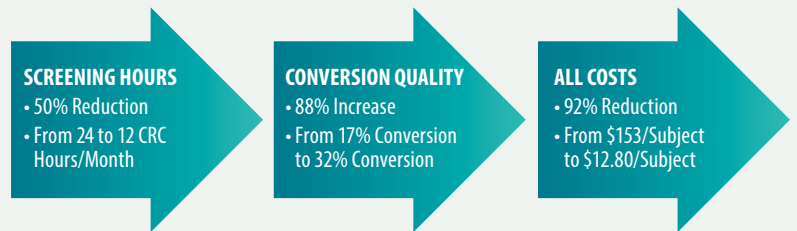
CRCs often have to abstract data from EHRs to enter into case report forms (CRFs). Conversion to EHRs makes this task easier. While this is generally a standard feature of EHR functionality that does not need extra builds above and beyond those required for normal operation, sometimes there are internal obstacles that slow down CRC access to the EHRs (see Case Study #2 for an example of the improved efficiency).

To also enhance the utility of EHR in research studies, it would be beneficial if data could be uploaded from the EHR into the electronic CRFs (eCRFs). This is technically feasible, and has been demonstrated in pilot studies by the Clinical Data Interchange Standards Consortium (CDISC); however, it has not been adopted by sponsors and sites in any meaningful manner.

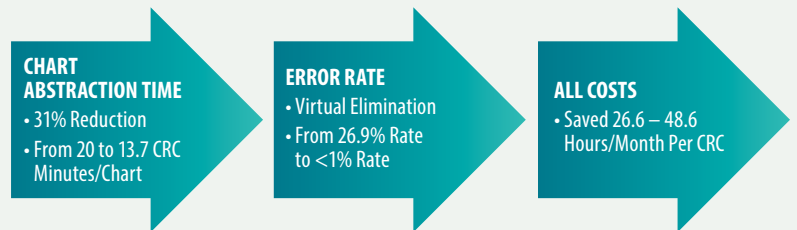
The upload would have to be managed by the department in charge of health information management to ensure security and accuracy of information, as well as to ensure that only minimal necessary information is uploaded. The data upload would ensure accuracy of data, reduce time needed for data entry (especially “double entry”), and allow CRC efforts to be focused on data verification and completion of additional elements prior to submission of eCRFs.

CASE STUDY #2

An unpublished case study conducted within another large healthcare system identified the following study metrics related to screening utilizing a manual vs. an automated EHR process. A significant finding was that the screening process timeframe was cut in half and the weekly labor effort was significantly decreased after implementation of an automated screening process.



The same case study demonstrates that there is significantly improved quality and cost savings when a CRC can realize the full functionality of the EHR’s search features. Note that CRCs whose duties include higher amounts of chart abstraction will realize more productivity advantages here than will their counterparts who perform more clinical procedures.



The use of tablets and other mobile devices is now possible for many EHRs. This may increase functionality in active settings, where sitting at a desktop is neither practical nor optimal.

Although tablet use may involve providing a custom build to the EHR system instead of creating separate eCRFs on the tablet, there are also technologies that can enable an eCRF to be automatically completed within the user’s current application, saving the need for double entry or manual uploads from the EHR. Again piloted by CDISC and again not yet widely utilized, the “remote form for data capture” technology promises to be the one of the most influential tools for integrating the workflow processes of clinical care and clinical research.

As part of the protocol monitoring process, monitors or CRAs may be required to review records, but it is often challenging to isolate only the records of subjects in the clinical trial. Monitors have either had to look over the shoulder of a research staff member (which is not the most optimal use of the research staff’s time) or been subjected to a security background check (requiring them to give their Social Security Number) in order to be granted direct electronic access.

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Given the lost productivity and high costs of travel, any investment in remote monitoring sessions can be seen as a win-win scenario for sponsors/CROs and sites.

Setting up a system to support remote monitoring of EHR data is feasible (and is often done for peer or legal review), and the costs can be shared with the sponsor or CRO. Given the lost productivity and high costs of travel (typically \$700 or more in direct travel costs for a two-day monitoring session), any investment in remote monitoring sessions can be seen as a win-win scenario for sponsors/CROs and sites.

CLINICAL “BLUE RIBBON” MANDATES

Achieving certain quality designations, whether mandated or voluntary, is an important focus of leadership in healthcare organizations. Programs responsible for designating Centers of Excellence or other national and international designations have become industries unto themselves.

To earn many of these “blue ribbons,” be they in clinical areas (such as cancer, stroke, or trauma) or for professionals (such as the American Nurses Credentialing Center’s MAGNET Recognition Program), the institution must be engaged in varying degrees of research. While some of the research requirements are very onerous, many can be accomplished with simple utilization of existing health data.

Before EHRs became available, data collection, processing, abstraction, analysis, storage, and transmission was an expensive manual process, even for retrospective research, due to the onerous task of digging through medical records. With the right capabilities, the EHR can be a powerful and inexpensive source of easily extracted and analyzed data that meet these requirements.

PART 2: Strategies for Implementing a (Retroactive) Business Case

“The best time to plant a tree was 20 years ago . . . the second best time is now.”

—Chinese proverb

WORK WITHIN THE SYSTEM THAT IS GREATER THAN THE RESEARCH DEPARTMENT

Regarding the conversion to EHRs, David Blumenthal, one of the architects of the Health Information Technology for Economic and Clinical Health

(HITECH) Act and the former National Coordinator for Health Information Technology, stated, “These IT implementations are rare, once-in-an-organization’s-lifetime opportunities . . . [to clean up messy systems and to make fundamental decisions about workflow and governance]. I just wish more organizations would take advantage of them.” Blumenthal also stated that the implementation of health IT is “not a technical project, it’s a social change project,” meaning that the IT department is not just downloading software and clicking “I Accept” the Terms and Conditions.

Many of the challenges faced by research staff result from their not having a voice at the table when decisions are being made about EHR systems that directly or indirectly affect the staff. Most hands-on users of the EHR system are not in senior-level decision-making positions; thus, there exists an inherent disconnect that is linked only by the voices at the table, either in person or by proxy.

Given the higher priorities and louder stakeholders at hand, it seems that research staff have to be assertive and invite themselves in order to have a place at the table. Assuredly, one of the best ways to have one’s voice heard over the myriad of other demands is to personally be there to give it; therefore, research staff should find out when these meetings are to be held and/or who is in charge of the agenda.

Alternatively, a list of research needs can be inserted into status reports to make sure the research department has a voice (see other sections in this article that reference Physician Champions and discuss parallels for synergizing voices). Having a spot on the written plan, even if that spot has low priority and results in no action, is arguably better than not having a spot on the plan, as somewhere, somebody is evaluated on that plan.

Other challenges include not knowing whom to ask for answers or solutions. It is not uncommon, especially in large organizations, for several IT personnel to respond to an inquiry by saying that the EHR system “can’t do that” and for the next person (IT or otherwise) to respond by showing that it could have been done all along. Persistence here often pays off, and these systems often can do what is wanted (as-is or with some tweaking).

Clinical staff who best know the functionality and/or an operator who best understands the business impact can be valuable resources

to overcoming challenges. IT personnel work hard, yet are unfamiliar with the specific needs of end-users. Effective partnerships—including detailed requests, engaged IT personnel, and strong working relationships—are key to overcoming many challenges.

FIND ONE OR MORE PHYSICIAN CHAMPION(S)

The implementation of an EHR likely represents a significant capital investment by the institution, based on input from leaders across many departments. Finding a voice and forum to convey needed changes can be difficult in even the most accommodating firms. Individuals in firms without an existing or effective change-control process may be relegated to simply discovering creative workarounds.

Enlisting a Physician Champion (especially one who is computer savvy) is often the best, and perhaps only, way to affect positive changes. A strong case with sufficient documentation and justification is still required, but a Champion will get the message to those in a position to act and follow through. An advocate who is both a respected clinical leader (knowing what is needed) and an acknowledged business leader (knowing what is possible) can present the message strongly and to the right individual(s), who are empowered to make selections of vendors and/or who have the authority to allocate resources.

FIND PARALLELS TO MAKE RESEARCH NEEDS EASIER TO ASSIMILATE

Often, the research-related requests for EHR functionality are not necessarily unique. A request may often be stigmatized because it comes from the research office when, in fact, with little to no creativity there is existing functionality that can be piggybacked. For example, a research department's request to split bills between a research sponsor and the patient's payor could be met with unnecessary obstacles, although the request could involve simply finding out how bills may be split for routine-care procedures, such as a hysterectomy (which insurance covers) and a tummy-tuck (which is cosmetic and often not covered) during the same hospital stay.

Once a research staffer has found a parallel, it is much easier to add research to existing policies and practices than to try to define a whole new

process for research. Simple things such as notifying research staff of subsequent care a patient/subject receives and ensuring the availability of custom order set functionality, processes for remote viewing of medical records, functionality of pop-up warnings, etc., are all items utilized in routine care from which the research staff can benefit.

Shifting the request from something like “for research, because we're different, we need to add...” to something like “you know how we accommodate for [nonresearch activity that the EHR already supports], well this is essentially the same thing” could make all the difference.

IDENTIFY RESEARCH FUNCTIONALITY GURUS/SUPER-USERS

For the successful implementation of EHRs, end-users need to be appropriately trained on the basic functionality of the EHR system being utilized (identifying patients, obtaining results, accessing information, etc.). Additional job-specific training is needed (e.g., how to enter billing codes/insurance information for personnel in the billing department and how to dictate notes/write orders/transfer charts for personnel in the clinical area).

However, if individual personnel are familiar with only their “piece” of the system, no one will have the overview necessary to know how tasks within the EHR are inter-related, find more efficient ways to perform tasks, or identify potential “gaps” in the system. The super-user or EHR guru needs to have a high level of computer literacy, be able to communicate information in an understandable way to end-users to facilitate their learning, be able to understand difficulties and identify solutions, and be a leader and champion for the implementation of the EHR.

If the user groups have someone who can be a super-user, the system will be easier for those with limited computer literacy to implement. The super-user also needs to be comfortable and confident enough about his or her abilities to search out answers or solutions from blogs, other super-users, or EHR representatives. If an institution does not have an identified super-user, it would be best to identify one right away, even if that person temporarily has to be you, the reader.

If individual personnel are familiar with only their “piece” of the system, no one will have the overview necessary to know how tasks within the EHR are interrelated, find more efficient ways to perform tasks, or identify potential “gaps” in the system.

→ HOME STUDY

*The Technology Issue:
New Tools to Tackle Old Problems*

PRESENT YOUR NEEDS AS A SOLID BUSINESS CASE

Business can improve only to the extent that performance improves. Two factors come into play in this regard. The first is knowledge of the quality of existing performance, and the second is the ability to act on that knowledge. The use of EHRs in clinical research can fulfill both of these factors.

In the first case, the ability to collect and aggregate data into meaningful metrics provides the ability to develop an awareness of one's performance level. In the second case, EHR capabilities can be utilized to act on and improve such measures, both quantitatively and qualitatively. Individual study performance, enrollments, staff performance, and participant compliance are examples of measures that can add value to a busy clinical research site.

The business case (see Table 2) for the use of EHR for research enhancement, site performance, and metrics development also incorporates an indirect aspect. This is the relationship of a research department within the overall healthcare organization. Simply put, hospitals and healthcare systems have expectations of their departments in terms of efficiency, cost reduction, and improved performance. By extension, decisions about reductions in departments may be based on these aspects, especially for healthcare systems operating on thin margins.

That said, an additional challenge faced by research sites is the need to educate leadership about the business of research, which is an area with which many healthcare leaders may not be familiar. The use of EHRs in research is a means to address these concerns of healthcare leadership relevant to research. Again, the usefulness of EHR in this regard involves the development, implementation, and utilization of practical metrics.

TABLE 2: Resources to Support the Business Case of EHR Support in Clinical Research

Benefit of IT Solution	What/How to Measure
1. Transparency Related to Clinical Documentation	<ul style="list-style-type: none"> • Decrease deviations related to clinical standard of care. • Promote provider awareness within health system. • Comply with responsibilities related to accreditation/licensure requirements.
2. Awareness of Investigational Drugs/ Devices	<ul style="list-style-type: none"> • Prevent medication/device-related errors. • Comply with requirements related to protocol adherence.
3. Emergency Use of Unapproved Drugs/Devices	<ul style="list-style-type: none"> • Monitor drugs given/devices used and study subjects receiving drugs/implants prospectively; currently, tracking can be done only retrospectively, thus increasing potential harm to patients.
4. Humanitarian Use Devices	<ul style="list-style-type: none"> • Monitor devices used, number of devices implanted, billing and revenue reimbursement related to Humanitarian Use Devices, and benefit to health system as a whole for access to advanced device practices for underserved patient populations.
5. Identification of Study-Related Procedures That are Not Standard of Care (SOC) Per the Protocol	<ul style="list-style-type: none"> • Identify research-related costs and differentiate between SOC and research billing to ensure investigational billing compliance. • Monitor patients effectively who are on clinical trial protocols; decrease administration of contraindicated medications and/or procedures related to clinical care outside a clinical trial protocol. • Justify SOC/non-SOC decision to sponsors/auditors using historic data for justification.
6. Billing for Hospital Services Pursuant to the Clinical Research Protocol	<ul style="list-style-type: none"> • Monitor orders for procedures and treatment plans as indicated within the protocol for research SOC treatment vs. investigational care treatment. • Comply with billing and reimbursement requirements.
7. Centers for Medicare and Medicaid Services Coverage of Routine Costs in Qualifying Clinical Trials	<ul style="list-style-type: none"> • Monitor (decreased) coding/billing errors, improve the turn-around time, and decrease the work involved in retrospectively monitoring claims related to clinical trial patients. • Decrease potential fraudulent billing related to research subjects.
8. Prediction of Enrollment for Clinical Trials	<ul style="list-style-type: none"> • Decrease inappropriate acceptance of clinical trials when the facility does not have the required study patient population. • Decrease cost burden associated with acceptance of protocols for which providers cannot enroll patients. • Decrease regulatory burden and work effort for unproductive clinical trials.
9. Increase in Clinical Trial Compliance	<ul style="list-style-type: none"> • Decrease deviations related to study-subject safety and protocol compliance. • Comply with protocol procedures and orders.
10. Documentation of Clinical Research Source	<ul style="list-style-type: none"> • Assure compliance with ICH E6 (Good Clinical Practice) related to essential documentation in clinical research trials. • Increase documentation efficiencies (i.e., ability to sign research related records electronically, decreasing clinical research coordinator work effort and improving investigator oversight, etc.). • Assure HIPAA compliance related to PHI. • Assure human subject protection and safety.
11. Identification of Human Subjects Research	<ul style="list-style-type: none"> • Increase quality of recruitment pool based on improved inclusion/exclusion screening. • Decrease pre-screen failures and screen failures.
12. Response to Allegations of Research Misconduct	<ul style="list-style-type: none"> • Provide transparent auditing system to track clinicians and providers who are investigators or who provide patient care for clinical trial protocols. • Monitor ongoing SOC with respect to transparency for clinicians and providers who are not part of the clinical research team.

PART 3: Building the External Support Network

“Be the change you want to see in the world.”

—Gandhi

ENSURE THAT IMPLEMENTATION IS IN THE HANDS OF IMPLEMENTATION EXPERTS

People generally agree that if you do something right the first time, you save time and money that would otherwise be spent in redoing the work. While CRCs are generally seen as jacks of all trades, even computer-savvy CRCs rarely have experience in EHR implementation and functionality. As stated above, there should be an identified super-user, who will likely be a CRC, but the super-user role should not be confused with the implementer role.

There are generally expert implementers (or at least identified/trained implementers) within the IT staff, project management personnel, and/or nursing informatics specialists charged with the migration of functionality. Assuming that research is on their punch-list, let them do the job that they do best instead of trying to change a CRC or PI into an EHR implementer. Taking a CRC out of a revenue-generating role to learn how to be an EHR implementation expert is unlikely to be time well spent.

FIND ONE OR MORE HELPLINE(S)

All EHR vendors have technical support (online or in-house) and even some research functionality support available for implementation, troubleshooting, and maintenance of the system. In addition, a number of online communities (blogs, forums) are available through the different EHR vendors (as well as independent organizations). Many vendors have live meetings that have research-specific breakout sessions. Even if a user cannot go to the meeting, he or she can ask an attendee to pick up the materials or ask the vendor to send them.

SHARE TRAINING/TIPS WITH OTHERS

Sometimes EHR support forums may be nonexistent or inaccessible to the research staff, either by omission or by institutional design. Instead of (or as a supplement to) vendor-supplied assistance, most professional societies (such as the ACRP) have discussion forums that can provide help from peers in similar positions.

Further, institutions are partnering to share best practices. Effective change realized in one place is often easily duplicated elsewhere. Research professionals with an interest in and a working knowledge of EHRs must continue to build bridges among peer institutions and alongside other forums. These mavens can advance the cause in many ways, such as by volunteering to be leaders, conducting solution-finding sessions at local professional chapter meetings and conferences, or writing grants for implementation through the NIH or the Clinical and Translational Science Awards (CTSA) program, among other examples.

Conclusion

In the book “Management: Ready Aim Fire,” Anthony La Russo states, “. . . managers can find that they have set a long term path for their organization by making a series of decisions focusing on numerous separate short term problems.” He goes on to state, like so many others, that you have to initiate the change you need rather than wait for your organization to evolve (look what waiting for evolution did to the dinosaurs). Thus, although people often state that “someone needs to fix this” and “someone needs to lead this effort,” they frequently forget that they are “someone” as well.

It is up to clinical research operators to make their needs known, struggle to the top of the list, and lead the change in their organization. By presenting a solid business case, you can differentiate your needs from those of others who cannot articulate the value of the investment to the organization.

Research professionals must work within their own institutions to build and maximize EHR benefit(s) and spread their success stories across the broad research landscape. This must be done to enhance the benefit and safety of all research participants, to meet the scientific and ethical responsibilities of research professionals, and to derive maximum benefit and efficiency among research teams.

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David M. Vulcano, LCSW, MBA, CIP, RAC, is an AVP and the Responsible Executive for Clinical Research at Hospital Corporation of America in Nashville, Tenn.

Candida Barlow, MSN, CTN, RN, is director of clinical research at St. John Clinical Research Institute in Tulsa, Okla.

Natalie F. Scully, PhD, CCRC, CCRA, is a clinical research oversight specialist at the Texas Heart Institute in Houston, Texas.

Cynthia M. Soto-Azghani, BSN, RN, CCRC, is a clinical skills specialist and adjunct faculty at Tyler Junior College in Tyler, Texas.

Anthony Keyes, BS, PMP, is employed at the Johns Hopkins University School of Medicine in Baltimore, Md.

Steven Ziemba, PhD, FACHE, CIP, CCRC, CPI, is an associate director at Marshfield Clinic Research Foundation in Marshfield, Wis., and chair of the Association Board of Trustees for ACRP.

eSource and Risk-Based Monitoring: A Favorable Union for Future Clinical Trials

PEER REVIEWED | Neha Sharma, MSc, MA

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The growing cost of drug development is paving the way for newer technologies in clinical research. Taking its cue from success stories of automation across other industries, the pharmaceuticals sector's acceptance of the Cloud, "big data," and analytics stands as a testimony to changing times.

The focus now is on risk-based monitoring (RBM) for enabling early risk identification and mitigation while aiding targeted actions for sites requiring attention. RBM looks at issues at the root level, and uses technology for challenging the status quo. The need for 100% source data verification (SDV) is being challenged, and innovative ideas to reduce SDV are being explored.

The use of electronic source (eSource) technology can potentially catalyze clinical trials transformation via RBM.

This paper will explore how eSource provides a solution to labor-intensive SDV practices and accelerates data review, and offers some factors to consider for eSource deployment. It highlights how eSource maximizes the utilization of monitors' capabilities to channelize source data review (SDR) for RBM. Lastly, it covers some of the players offering eSource technology and services.

Background

As per Medidata's infographic on RBM released in July 2014, trial monitoring represents 30% of the cost of conducting a clinical trial, with 85% of the monitoring time being spent on SDV. However, these extensive efforts and costs linked to SDV result in less than 3% of data being updated to any significant degree.

With these facts in place, industry was still expected to spend \$7.5 billion on SDV in 2014.¹ With the goal of encouraging the industry toward effective transformation, the U.S. Food and Drug

Administration (FDA) published three back-to-back guidance documents for pushing technology adoption in clinical trials. This included guidance for RBM in August 2013,² guidance for use of eSource in September 2013,³ and guidance for regulatory submission using standardized study data in February 2014.⁴

With this support and push for disruptive innovation, technologies like Cloud-based data storage and its solutions (e.g., eSource) are being extensively explored in the life sciences sector. With the Cloud, since software resides on a web-based server shared with virtual resources vis a vis desktop, the efficiency gains are higher. Costs related to information technology expenditure and inefficiencies of manual paper processes are eliminated, though security is enhanced.

Since paper-based data collection fails to provide similar control, Cloud-enabling eSource solutions can be a boon for a regulated industry like clinical research. Companies like Eli Lilly and Johnson & Johnson are already adopting the Cloud to empower their scientists across the globe, while building capabilities for data-crunching functions.⁵

In addition to paper case report forms (CRFs), use of computerized systems for capturing data and recording some source data electronically during clinical investigation has been common. As per the FDA, source data include all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical investigation used for reconstructing

LEARNING OBJECTIVE

After reading this article, participants should be able to discuss how eSource can enable effective risk-based monitoring for clinical trials.

DISCLOSURES

Neha Sharma, MSc, MA:
Nothing to disclose

and evaluating the investigation (electronic source data are data initially recorded in electronic format). Examples include, but are not limited to, clinical data initially recorded in electronic health records (EHRs) maintained by healthcare providers and institutions, electronic laboratory reports, digital medical images from devices, and electronic diaries completed by study subjects.³

The traditional data entry mechanism by which site coordinators transcribed data from source documents to a database drove the need for SDV and posed challenges to real-time data review. The following sections of this article will briefly review the factors that led to the modern focus on eSource.

Issues of Delayed Data Review and Data Cleaning—eSource Offers Solutions

Following a patient's visit, conventional data review and cleaning methodologies are data entry-dependent. Sites typically take three to five days for data transcription from source document to CRF. This creates a first level of dependency and delay in data review in terms of data availability. With onsite monitor visiting site every four to six weeks, a second level of data cleaning delay occurs for already-available data in the database. Since the data are reviewed weeks after a patient visited the site, follow up for data issues becomes a big challenge that delays the overall data-cleaning process.⁶

For eSource solutions with real-time data entering a database, the eCRF itself becomes the source. Since patient data are directly fed into an eCRF, any discrepancies or missing data can be corrected in the patient's presence. This implies that the need for performing transcription checks via SDV can be eliminated for studies in which eSource is used. High-quality data and cost efficiencies related to query management can also be achieved through the decreased effort devoted to data cleaning by data managers and monitors.

Impact of eSource on Changing Role of Onsite Monitors

Based on guidance provided by FDA on RBM and eSource, pharmaceutical companies are taking measured steps. The vision of conducting trials that are focused on maximizing the right usage of resources and technology is coming to fruition. Onsite monitors are being retrained to think differently and drop age-old habits.

The need for transitioning monitoring activities from being seemingly futile clerical efforts to being value-added uses of skills is being mandated. With less effort spent on data transcription, the focus of monitoring can be easily shifted to SDR. Onsite monitors can now review data patterns aimed at identifying risks early; their reviews and analyses of trends, key risk indicators, and signals can help investigators better conduct their trials. All of this helps channelize site monitoring efforts based purely on the site's risk profile, which is a successful realization of one of the core RBM goals.

Management of discrepant data as a result of incorrect transcription, noncompliance to data entry guidelines, and other factors is traditionally under the purview of data managers; with eSource, the scope of data manager review would also change. The dynamics of these changes are also of substantial interest in the overall scheme of RBM, and should be considered for future discussions.

Convergence of eSource and RBM

It can be seen by previous discussions that the needs of RBM can be fulfilled by eSource in many ways, and that for problems related to delayed data review, 100% SDV, and more, eSource with its multiple benefits offers the key. Some key features of eSource that make it an extremely powerful tool involve how it:

- enhances significance of onsite visits by collecting patient data while the patient is onsite;
- aids flagging and cleaning of data issues while data are being entered;
- significantly decreases the human error element by removal of the data transcription step;
- provides a solution to sites for adopting RBM by not only reducing, but by eliminating the need for SDV;
- enables real-time analytics and trend review to help trial leaders make informed decisions;
- provides a common area for data review to multiple stakeholders in a study;
- allows integration of lab results and medical records for quick decisions;
- can be easily customized to be accessible via web; and
- complements RBM execution and cost savings for sponsors.

Taking its cue from success stories of automation across other industries, the pharmaceuticals sector's acceptance of the Cloud, "big data," and analytics stands as a testimony to changing times.

→ HOME STUDY

The Technology Issue:
New Tools to Tackle Old Problems

The traditional data entry mechanism by which site coordinators transcribed data from source documents to a database drove the need for SDV and posed challenges to real-time data review.

eSource thus provides the pharmaceuticals industry with an answer to one of its biggest pain points related to cost implications of frequent monitoring visits for 100% SDV, thereby improving trial budgets. It can enable availability of real-time data for central monitor review and be a boon for data analytics. eSource enables a holistic review of data coming from multiple sources, thereby helping clinical project managers assess and mitigate risks from several functional areas at one go.

Growing Acceptance of eSource Among Stakeholders

Lack of effective change management has been an impeding factor for the pharmaceutical sector in its RBM implementation. In an environment where the roles of clinical trial stakeholders are changing and performance is the driver, eSource is seen as one of the best options for making life easier. Site coordinators and monitors are able to effectively manage queries in a patient's presence at sites, thereby reducing follow ups, and eSource further minimizes the probability of errors through pop-up alerts that call the user's attention to potentially bad entries to the database.

The use of eSource is particularly helpful for investigators who have to remember the trial designs of various projects they are working on. Meanwhile, onsite monitors can focus more on building site relationships and SDR. With site performance being linked to a monitor's performance index, eSource offers great relief to monitors who are already dealing with the increased expectations of RBM.

To assess whether eSource is beneficial in a real-world setting, a study was conducted using RBM and direct data entry (DDE) methodologies. It was reported that usage of eSource at a particular site resulted in a huge saving of effort in onsite monitoring, as compared to studies that were using paper CRFs. Protocol compliance and issue tracking was also improved, as issues identification and correction was faster.⁷ An overall saving of 70 labor hours was reported by the clinical sites when they replaced paper CRFs and EDC with DDE.⁸

Considerations for Effective eSource Implementation

Having discussed how eSource enables RBM and its growing acceptance as a research tool, it is still essential to weigh out the benefits offered by eSource versus its ability to enhance patient safety and data integrity.

For trials using eSource, FDA guidance stresses the need for clearly defining the data originators, the modalities of source data capture, and what the data element identifiers are for each data element in a trial's data management plan, so that all of these elements may be referenced during audits and inspections. Integration of crucial parameters like instruments, data standards, control files, and validated data integration methodologies that are all compliant with 21 CFR Part II of the *Code of Federal Regulations* enables smooth set up of eSource; however, constraints for successful implementation must also be examined in advance.

A few considerations for successful deployment of eSource would include:

- Correct selection of eSource from a gamut of solutions based on a trial's needs and this solution's capability to export data in a format that easily integrates into EDC
- Validation of data sources (instruments, medical devices, databases) used at sites for regulatory compliance
- Incorporating electronic prompts, flags, and data quality checks for data accuracy and effective data collection (for data capture systems not having inherent checks, mapping of data element identifiers between the system and the eCRF and design of edit checks are needed to minimize data loss during data entry)
- Effective controls for role-based user access to systems and overall trial to ensure all user activities are date and time stamped

Meanwhile, agreements that describe how study information will be shared among investigative sites and third parties will need to be defined in the planning stage. During the conduct of the study, configuring the trial database to report only the data specified in the protocol will help with the data review process.⁹

With regulations favoring eSource and the array of benefits that eSource offers (including its value in facilitating RBM), various players are trying to seize opportunities existing in market. Discussed next are some of the ideal features of eSource and current players in the market offering these services.

Ideal Features of eSource and Current Players

The FDA and other regulatory agencies consider it of utmost importance that eSource technology provides substantial data element identifiers for use in any examination by audit trail of eCRF

data, and that it provides information allowing for the reconstruction and evaluation of the clinical investigation for which it was used. Companies building eSource solutions are wise to align their business plans to the specifications cited in the aforementioned FDA guidance documents.

Some of the ideal features that companies developing eSource solutions should keep in mind include the functionality needed to capture data during patient visits and to facilitate remote monitoring and real-time data review access. Data integration capabilities for data coming from multiple sources could be of immense value for overall data analysis.

eSource solutions providing final analysis datasets as per standard formats (e.g., in a study data tabulation model) would help save time and efforts during end game activities. Today, with data presentation being about pie charts and histograms, solutions offering graphical reports for data visualization and analytics in mobile/tablet handsets could be considered icing on the cake.

Currently, Clinical Ink¹⁰ and assisTek¹¹ are among the companies that offer eSource solutions in the market. With increasing awareness of the potential demand for the tool, the number of players who will be developing and marketing eSource services is expected to rise. As the industry continues to gain clarity on the practical usage of eSource, there also comes the need to constantly monitor upcoming solutions for better and enhanced features.

Conclusion

For successful completion of clinical trials, among the most important parameters are timely entry and review of data; if these can happen at the time of a patient's visit, the workload of monitoring visits and data cleaning efforts can be reduced. With eSource enabling DDE, the need for paper records and SDV can also be reduced drastically.

This paper discussed how efficiencies gained through the use of eSource can enable effective implementation of RBM by way of reduced SDV and targeted monitoring of variables that "actually" matter. With data transcription being almost eliminated, real-time monitoring of data can be achieved with ease.

Furthermore, the transition from manual and effort-intensive activities to more streamlined processes paves the way for role repurposing on the clinical trials team. This paper also discussed how the role of monitors is about to undergo a paradigm

shift from its nature as experienced when following traditional data review methods. The shifting of the focus of reviews from SDV to SDR for monitors, and a focus on overall risks and trend analysis for data managers, will be crucial for successful RBM.

While realizing the potential of eSource and its benefits, this paper also highlighted important factors that need to be considered while implementing eSource. Lastly, some ideal features of eSource and players currently offering eSource products in the market for cost-effective, data-driven, and effectively operated clinical trials were discussed.

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Neha Sharma, MSc, MA, (sharmaneha90@gmail.com) is a manager for risk-based monitoring with Tata Consultancy Services Ltd in Mumbai, Maharashtra, India.

For eSource solutions with real-time data entering a database, the eCRF itself becomes the source. Since patient data are directly fed into an eCRF, any discrepancies or missing data can be corrected in the patient's presence.

The Rise of Electronic Data Capture and its Greatest Obstacle

PEER REVIEWED | Colton Castle, MS | April Bell, MS, CCRC | Patricia Gwartz, PhD

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Advancement in healthcare-related technologies has resulted in a groundswell of information contained in patient health records. Electronic data abstraction systems have allowed medical professionals to analyze and apply vast bodies of information comprehensively. In the field of clinical trial management, electronic data capture (EDC) has become vital to this process.

Over time, EDC yields benefits in cost, trial duration, and the capacity to utilize remote monitoring. As a result, EDC usage in clinical trials has increased dramatically in the last decade. However, EDC implementation can prove costly, and often causes temporary disruptions to workflow and productivity.

EDC implementation must evolve to become less costly and more user-friendly before EDC usage reaches ubiquity in clinical trial management.

The Problem Created by Technology

Clearly, EDC has become the industry standard for information analytics in clinical trial management. Virtually all clinical trials begun in the last decade employ EDC in some capacity. However, EDC continues to struggle against a familiar (but significant) obstacle in terms of implementation and, as a result, most investigational sites still utilize paper-based data capture systems. What difficulties continue to plague investigational sites and sponsors, preventing the paradigmatic implementation of EDC?

To begin to consider the answer to this question, one must recognize that the healthcare industry is experiencing a “big data” revolution. In the minds of healthcare professionals, this means that the exorbitant amount of data management

necessary for comprehensive patient care has outstripped current methods of analyzing and adapting that information in useful ways.¹

Traditionally, a patient’s health record has included a detailed medical history, a list of concomitant medications and dosing, family history, laboratory test results, etc. This body of information swelled significantly with technological advancement in medical imaging, and promises to continue increasing exponentially as genomic sequencing becomes common practice in western medicine^{1,2} As an example, including clinical text and imaging data, Beth Israel Deaconess Medical Center in Boston, Mass. currently generates 20 terabytes of new health record data per year for an active patient population of 250,000.³ Following the current trend, the volume of data storage necessary for hospitals and clinics to maintain will continue to escalate considerably with the advent of new technologies.

Quality patient care now requires a complex and costly system of analytics to comprehensively process and interpret this vast body of information in meaningful ways. Information analytics on this scale has only been made possible through the rise of electronic systems, particularly the electronic health record (EHR).¹

In 2009, the Health Information Technology for Economic and Clinical Health (HITECH) Act authorized incentives to physicians willing to adopt EHR methods.⁴ According to a 2014 data brief from the Centers for Disease Control and Prevention, the percentage of office-based physicians who employed any kind of EHR methodology in their practice increased from 18.2% in 2001 to 48.3% in 2009, and 78.4% in 2013.⁴ From another viewpoint, office-based physicians’ use of a holistic EHR system in their practices rose dramatically from 10.5% in 2006 to 48.1% in 2013⁴ (see Figure 1).

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LEARNING OBJECTIVE

After reading this article, participants should be able to explain the driving forces behind the increasing prevalence of electronic data capture in clinical trial management, and to examine reasons why many investigational sites still depend on paper-based data capture.

DISCLOSURES

Colton Castle, MS;
April Bell, MS, CCRC;
Patricia Gwartz, PhD:
Nothing to disclose

The growing need for complex information analytics will soon necessitate systemic EHR use in every field of the healthcare industry.

The Rise of Electronic Data Capture

The field of clinical trial management has experienced a similar groundswell in electronic system implementation in the past decade. In the same manner that EHR represents the most vital component of electronic system utilization in primary care settings, EDC epitomizes this progress in clinical trial management.

In 2005, only 24% of trials incorporated EDC in their trial management system. The prevalence of EDC system use rose dramatically in the following years.⁵ In 2012, 75% of clinical trials were likely to use EDC. This represents a yearly increase of 15% of clinical trials converting from traditional paper-based data capture to EDC.⁵

Why has clinical trial management evolved to incorporate the same kinds of electronic systems utilized in other healthcare fields?

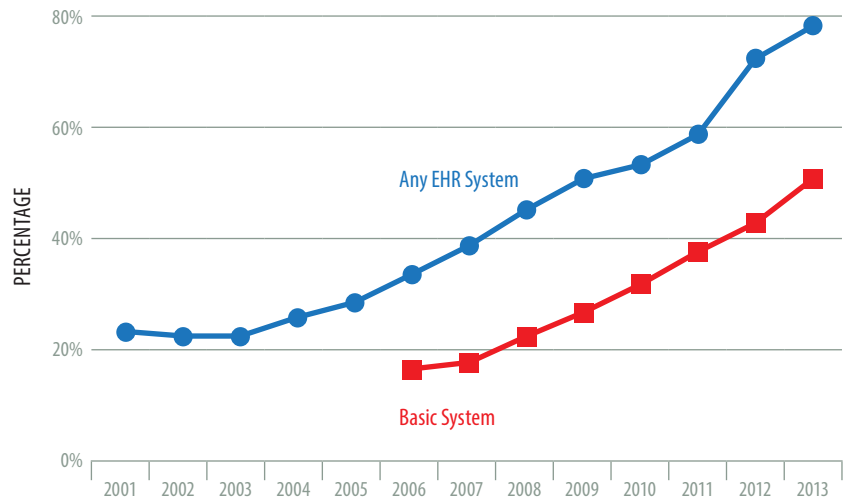
One consideration is that clinical trial cost represents a significant deterrent to medical innovation. Achieving investigational product approval is both a costly and time-consuming process and, as a result, reducing the monetary burden of clinical trials is vitally important to improving the efficiency of global healthcare innovation.

Research and development (R&D) for a new chemical or biological entity can exceed \$1 billion and require 10 to 15 years from R&D to U.S. Food and Drug Administration (FDA) approval.⁶ Only 333 new drugs and biologics achieved FDA approval in the United States from 2000 to 2010 and, of those, just two out of 10 produced enough revenue in marketing to compensate for R&D costs.⁶

Electronic-based systems in clinical trials have the potential to alleviate some of this burden and, in doing so, benefit both the sponsor and the consumer. Shorter, less costly trials have motivated sponsors to incorporate EDC into their studies at a dramatically increasing rate. EDC reduces clinical trial costs by decreasing the number of mistakes in data collection and management, shortening the average study duration, reducing the financial burden of trial queries, reducing data collection and monitoring costs, and streamlining database processing.⁷

Green (2015) analyzed data from four different clinical trials—one each in Phase I, Phase II, Phase IIIa, and Phase IIIb—to perform a detailed cost comparison of EDC vs. traditional paper-based data capture (Phase IIIa trials are conducted before a New Drug Application is submitted to the FDA, and IIIb trials are conducted after, but prior to marketing approval). The research included 228 investigational sites and 8,264 subjects over the course of 54 months.⁸ Green compared cost metrics in three areas: approved EDC budgets

FIGURE 1: Percentage of Office-Based Physicians with EHR Systems



Source: Compiled from Chun-Ju, et al. (2001–13)

in each clinical trial, estimated costs for a paper model, and implementation and EDC costs applied under a level 2 technology transfer and enterprise relationship pricing model (this model projects cost savings associated with research sites internalizing EDC software use and performing their own electronic case report form [eCRF] design and data management, rather than outsourcing these responsibilities to the software vendor).

Green's calculations project a significant and definitive cost reduction in each clinical trial phase associated with EDC implementation (see Figure 2).⁸

In a separate study, Jeannic, et al. (2014) retrospectively analyzed the study-related costs of 27 trials from 2001 to 2011, in which 16 utilized paper-based data capture and 11 employed EDC.⁷ Calculating total study expenditure as an estimate of labor-related and logistical costs, the researchers showed that the mean expense per patient was significantly less in the EDC trials (\$497 compared to \$1,509 for paper-based trials, for a 67% reduction in cost per patient).

Moreover, the authors demonstrated that trials employing EDC resulted in a significantly shorter study duration when compared to their traditional counterparts. EDC trials required an average of 31.7 months from the opening of the first center to database lock compared to 39.8 months for paper-based trials, despite a longer median projected duration (27 months for EDC-based and 24 months for paper-based trials)⁷ (see Figure 3).

Benefits to Monitoring

EDC yields these tremendous benefits in clinical trial efficiency, in part by decreasing the time and cost necessary for monitoring. In the course of clinical trials, sponsors usually contract clinical research associates (CRAs), more commonly known as monitors, to perform source data

EDC implementation must evolve to become less costly and more user-friendly before EDC usage reaches ubiquity in clinical trial management.

HOME STUDY

The Technology Issue:
New Tools to Tackle Old Problems

In the same manner that EHR represents the most vital component of electronic system utilization in primary care settings, EDC epitomizes this progress in clinical trial management.

verification (SDV) and other examinations of investigational sites. The traditional paradigm requires CRAs to travel to sites and monitor each individual site in person.^{9,10} This process is both costly and time consuming.

In order to decrease the time and cost burden, risk-based monitoring (RBM) is now the standard of practice. RBM is a method of SDV that allows monitors to focus their energies on data points that represent the most important risks to data quality, subject safety, and sponsor investment (such as trial endpoints, institutional review board approvals, investigational product accountability, etc.).^{9,10} However, this method prevents a CRA from performing 100% SDV.

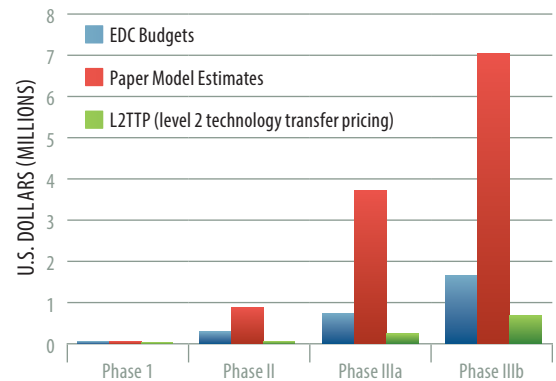
EDC presents the opportunity for remote monitoring. This process saves time and reduces cost for clinical trial sponsors by eliminating the need for onsite monitoring, and it increases overall data quality by allowing for timely, more complete SDV.¹⁰ Mealer, et al. (2013) compared analytics between remote monitoring and traditional onsite monitoring in two national clinical trial networks. Their analysis included five hospitals and 32 subjects (16 per arm of the study). In comparison of time consumed per data value monitored, the researchers calculated a mean duration of 0.39 minutes for remotely monitored data points versus 0.5 minutes for conventional. In analyzing time consumed per CRF verified, the authors observed an average of 3.6 minutes compared to 4.6 minutes for data points monitored onsite (see Figure 4). The researchers also cited 99% SDV for remotely monitored trials.¹⁰

Plagued by Paper: Overcoming a Classic Obstacle

EDC offers the exciting possibility of streamlining clinical trial management, resulting in shorter, less costly studies. However, in spite of the numerous potential benefits of utilizing EDC, clinical research has failed to keep pace with the technological advance of other healthcare fields. Clinical research did not even begin to incorporate electronic systems for record storage and data capture until the 1990s.¹¹ Currently, most investigational sites still incorporate some kind of paper-based data capture.

What obstacle has caused clinical research to lag behind the technological curve set by the rest of the healthcare industry, and why do most clinical trials still employ paper-based data capture?

FIGURE 2: Cost Comparison of EDC vs. Traditional Trials



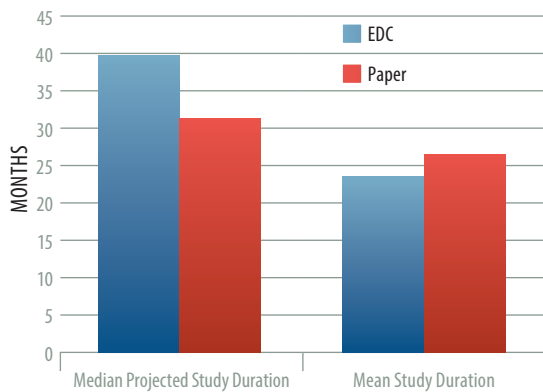
Source: Data compiled from Green (2001)

Perhaps clinical research professionals can learn from the obstacles that other healthcare professionals have overcome in their utilization of electronic systems. Historically, implementation has represented the greatest obstacle to ubiquitous use of electronic systems in healthcare, particularly in primary care settings. This challenge seems to inhibit clinical research management in the same way, in terms of its efforts to incorporate EDC and electronic systems.

Though EHR and EDC represent two markedly different tools to solve specific problems related to their own unique and respective fields, both systems must overcome this analogous obstacle. Similar to EHR, the difficulties of transitioning to EDC in clinical trial management are front-loaded, and the benefits only offset these deterrents over time. For EHR, the most notable of these challenges include high acquisition costs and temporary loss of productivity due to personnel training.¹² In the realm of clinical research, these two obstacles bifurcate; acquisition cost exclusively concerns the sponsor, whereas loss of productivity primarily relates to the investigational site and only secondarily to the sponsor.

The financial burden represents a prominent challenge faced by the healthcare field's implementation of EHR.¹³ Adoption of EHR software and hardware is the biggest concern. A 2002 study of a 280-bed acute care hospital estimated the seven-year cost of implementing EHR to be about \$19 million USD.¹⁴

Research into the financial implications of EHR use in the outpatient setting shows similar results. Researchers estimate a cost of \$50,000 to \$70,000 to implement EHR in a three-physician clinical office.¹⁵ However, as EHR technology has improved and its use become more conventional, implementation costs have declined dramatically. A 2010 study of EHR expense in the clinical setting estimated implementation costs of \$14,000 for a six-physician outpatient office and about \$19,000 for offices of three physicians or fewer.¹⁶

FIGURE 3: Study Duration in EDC vs. Traditional Trials

Source: Data compiled from Jeannic, et al. (2014)

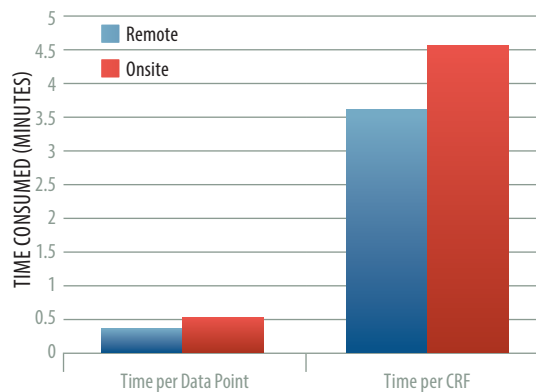
Even after adoption and implementation of EHR systems, maintenance of those systems can still be extremely costly. Maintenance expenses include hardware replacement and upgrade, ongoing training for end-users, and technical support.¹² A 2005 study examining 14 separate clinical practices estimated the ongoing costs of maintaining EHR systems to be about \$8,412 per year.¹⁷ The study calculated that 91% of this cost resulted from hardware replacement, vendor software maintenance and support, and personnel compensation.

EHR incorporation can also cause a loss of productivity. Productivity loss encompasses any disruption in workflow caused by EHR implementation. These disruptions may present as a temporary loss of productivity in the implementation phase, or as a continuing loss of productivity due to lack of compliance with system use. These problems can result from software and hardware installation time consumption, necessary end-user training and technical support (both initial and ongoing), and the extensive time involved in converting existing paper records into an electronic format.¹²

Wang, et al. (2003) performed a five-year cost-benefit analysis of overall productivity in clinical offices implementing EHR systems. The researchers observed a 20% loss of productivity during the first month of EHR use¹⁸; however, this effect leveled out over time. The study noted a 10% loss of productivity in month two, 5% in month three, and virtually no loss of productivity by month four. Moreover, a 2011 study estimated that adopting EHR in 26 primary care practices required an average of 134.2 hours for training alone.¹⁹

The Future of Information Analytics

As technology advances, the need for electronic systems in clinical research will continue to increase. Following the trend of history, developments in healthcare technology will result in exponentially greater volumes of medical data and the need for sophisticated ways of abstracting those data.

FIGURE 4: Efficiency of Remote vs. Onsite Monitoring

Source: Data compiled from Mealer, et al. (2013)

As it pertains to clinical research, EDC will certainly play an important role in the future of clinical trial management. Clinical trial cost represents one of the foremost concerns of the industry, and EDC offers significant potential benefits in that realm. However, the difficulty of implementing EDC systems still deters many investigational sites and sponsors from seeking these benefits.

The industry must find practical ways to alleviate the burden of implementing EDC for both site and sponsor and, in so doing, tread the path cut by the rest of the healthcare industry into a brave new era of medical innovation.

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Colton Castle, MS, (coltoncastle@gmail.com) is a clinical research coordinator at the University of North Texas Health Science Center's Office of Clinical Trials in partnership with the Center for Disease Control's Tuberculosis Trials Consortium.

April Bell, MS, CCRC, is a Certified Clinical Research Coordinator at the University of North Texas Health Science Center.

Patricia Gwirtz, PhD, is a professor and associate dean at the University of North Texas Health Science Center and UNTHHealth.

The Technology Issue: New Tools to Tackle Old Problems

OPEN BOOK TEST

This test expires on June 30, 2017

(original release date: 6/1/2016)

Maximize Your EHR Systems for Clinical Trials Operations

1. Electronic health record (EHR) systems can support organizational compliance by:
 - A. Identifying if the patient is on a research study, the study name, and contact information
 - B. Ensuring security of patient's medical record in a non-HIPAA compliant manner
 - C. Manually adding modifiers/codes to the patient's account for billing
 - D. Providing unlimited access to medical records with an audit trail for monitors
 2. Patient safety is enhanced with the use of EHRs through the:
 1. Creation of medication alerts
 2. Use of messages to PI/study team about protocol deviations
 3. Identification of the EHR super users
 4. Use of vouchers sent to study subjects
 - A. 1 and 2 only
 - B. 1 and 4 only
 - C. 2 and 3 only
 - D. 3 and 4 only
 3. The EHR can also facilitate study participant safety by:
 - A. Identifying potential study participants for recruitment and enrollment
 - B. Making it easier to submit materials to the institutional review board
 - C. Incorporating electronic research order sets to prevent individuals from altering study orders
 - D. Ensuring clinical studies adhere to the HITECH Act
 4. The EHR can aid billing compliance in clinical research through:
 - A. Generating an accurate study budget
 - B. Identifying procedures that are standard of care as opposed to investigational
 - C. Identification of staff time and indirect costs
 - D. Enabling easier charge capture
 5. Regulatory compliance can be facilitated through the use of EHR in clinical research via which of the following?
 - A. Assurance of compliance with ICH E6 and HIPAA
 - B. Creation of more policies on regulatory compliance
 - C. Reduction in how often the Compliance Officer audits a study
 - D. Reports of deviation to OHRP if a section of the protocol is not followed exactly
 6. What is a potential relationship between the EHR and Delegation of Authority Log that could prove inconsistent?
 - A. The PI should not sign the Delegation of Authority Log until the study has been set up in the EHR.
 - B. Roles delegated on the Delegation of Authority Log may differ from access levels permitted in the EHR.
 - C. All research studies with a Delegation of Authority Log should be in the EHR.
 - D. Only study team members with access to the EHR should be listed on the Delegation of Authority Log.
 7. EHRs capitalize on business opportunities by:
 - A. Creating easily identifiable research consents and medication records
 - B. Supporting an environment for quick and accurate feasibility assessments
 - C. Allowing transparency related to clinical documentation
 - D. Reducing investigator ability to make informed decision whether or not to proceed with the trial
 8. Clinical trial metrics can be obtained from an EHR on all of the following except:
 - A. How many patients participated in research studies
 - B. What studies were charged to research not insurance
 - C. How many research exams were done by a particular department
 - D. Feedback provided by patients in follow-up surveys
 9. Which of the following is not true according to the article?
 - A. Most EHR systems cannot support research functionality.
 - B. There are often online support communities (blogs, forums) available supported by the EHR vendors as well as independent of them.
 - C. It is technically feasible to upload data from the EHR into an eCRF.
 - D. Research functionality competes with other functionality needs such as "Meaningful Use" and standards conversions for the necessary resources.
 10. What key resource do the authors recommend identifying to affect positive change?
 - A. Physician Champion
 - B. Creative workarounds
 - C. EHR vendor representative
 - D. Senior-level information technology personnel
- eSource and Risk-Based Monitoring: A Favorable Union for Future Clinical Trials**
11. What percentage of a monitor's time is spent on source data verification (SDV) during an onsite visit?
 - A. 30%
 - B. 50%
 - C. 75%
 - D. 85%
 12. The desire to do what drives the need to conduct SDV?
 - A. Utilize a monitor's full potential during onsite visits
 - B. Effectively transcribe data from source documents to database
 - C. Build better relationships with site staff
 - D. Follow the regulations correctly
 13. What dependency is created while using conventional data-cleaning methodologies?
 - A. Delay in conducting remote visit
 - B. Delay in conducting onsite visit
 - C. Delay in data availability and cleaning
 - D. Delay in submitting reports to clinical project manager

Find the most current online test at www.acrpnet.org/homestudy, including any revisions made after publication of this issue of *Clinical Researcher*.

- 14.** Which activity helps in channelizing the site monitoring activities based on a site's risk profile?
- Thorough review of data through remote monitoring
 - SDV
 - Source data review (SDR)
 - Review of patient profiles
- 15.** eSource enables effective risk-based monitoring (RBM) implementation by near elimination of which human activity for site monitors?
- Onsite monitoring visits
 - Remote review of data
 - Telephonic contacts to site
 - Data transcription step from source to eCRF (database)
- 16.** How does eSource help clinical project managers in mitigation of risks?
- By making it easier to conduct data analytics
 - By providing holistic review for data from multiple sources
 - By providing ready reports for decision making
 - By reducing onsite monitoring visits
- 17.** With eSource, monitors can now focus on which two value-added activities?
- Building site relationships and SDR
 - SDV and remote monitoring
 - Patient data review and remote monitoring
 - SDV and patient data review
- 18.** What helps in effective data collection and data accuracy while setting up eSource?
- Effective quality control checklist being used by data entry operator
 - Electronic prompts, flags, and data quality checks
 - Reports and visualizations
 - Help by quality assurance personnel at site
- 19.** What helps in ensuring activities are date and time stamped?
- Audits
 - Controls for role-based user access
 - Inspections
 - Data entry
- 20.** What characteristics will provide regulatory agencies with confidence about study quality when reviewing studies using RBM?
- Audits and inspections
 - Documentation of role access
 - Subject data element identifiers and ability to re-construct clinical investigation
 - Frequent meetings on overall status of trials using eSource
- The Rise of Electronic Data Capture and its Greatest Obstacle**
- 21.** What phenomenon has led to the need for electronic record keeping systems to organize and abstract patient health records in healthcare?
- The HITECH Act
 - The "Big Data" revolution
 - HIPAA
 - The Affordable Care Act
- 22.** What caused the upswing in electronic health record utilization by office-based physicians, beginning in 2009?
- The HITECH Act
 - The "Big Data" revolution
 - HIPAA
 - The Affordable Care Act
- 23.** From 2005 to 2012, the likelihood of clinical trials to utilize electronic data capture (EDC) increased by how much yearly?
- 5%
 - 8%
 - 10%
 - 15%
- 24.** Three beneficial factors that motivate sponsors to incorporate EDC into their clinical trials are:
- Reduced cost
 - Easy implementation
 - Shortened trial duration
 - Prospect to conduct remote monitoring
- 1, 2, and 3 only
 - 1, 2, and 4 only
 - 1, 3, and 4 only
 - 2, 3, and 4 only
- 25.** In what three ways can EDC reduce clinical trial costs to the sponsor?
- Increasing the likelihood of investigational product approval
 - Decreasing mistakes in data collection and management
 - Resolving data queries more efficiently
 - Streamlining database processing
- 1, 2, and 3 only
 - 1, 2, and 4 only
 - 1, 3, and 4 only
 - 2, 3, and 4 only
- 26.** EDC potentially offers more efficient and cost-effective prospects for clinical trial monitoring. What novel approach to monitoring does EDC make possible?
- Risk-based monitoring
 - Source data verification
 - Remote monitoring
 - Enhanced monitoring
- 27.** If EDC offers so many benefits, why do many investigational sites still depend on paper-based data capture?
- EDC becomes less cost-effective over time
 - EDC produces more data collection errors
 - EDC is difficult to implement
 - EDC complicates the monitoring process
- 28.** Which obstacle represents the primary concern of the sponsor in implementing EDC systems?
- Loss of productivity
 - Increased trial duration
 - High acquisition cost
 - FDA data security concerns
- 29.** Which obstacle represents the primary concern of investigational sites in implementing EDC systems?
- Loss of productivity
 - Increased trial duration
 - High acquisition cost
 - FDA data security concerns
- 30.** Which three factors often cause a loss of productivity in the process of implementing EDC systems at investigational sites?
- End-user training
 - Lack of user compliance
 - Software/hardware installation
 - Regulatory complications
- 1, 2, and 3 only
 - 1, 2, and 4 only
 - 1, 3, and 4 only
 - 2, 3, and 4 only