7
Clinical Trials of Information Interventions

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When a clinical decision support system (CDSS) passes the test of accuracy and is ready for clinical implementation, the need for replicable and generalizable measurement of practical impact emerges. It is increasingly acknowledged that measurement of system performance and impact represents the research component of informatics projects, and that such evaluations should guide the development of decision support technologies.[1,2] This chapter discusses the methodology for systematic evaluation of information interventions. It provides a framework for designing appropriate tests of the clinical impact of CDSS.

Several studies have demonstrated that computers are able to influence the behavior of providers, management of patients, and outcome of health care in many clinical areas.[3–8] Unfortunately, claims for computerized medical information systems seem to exceed the documented benefits. Many predictions about the computer revolution have not been realized, and the evidence arising from various clinical experiments is often controversial.[9–12] There is an increasing demand to provide convincing evidence of the benefits of clinical information services.[13–15]

The Practical and Scientific Need for Clinical Testing

Few medical questions have been more controversial than the clinical usefulness of computer systems. Early on in the development of clinical computing applications, it was suggested that the ability of computers to store information on patient history, physical findings, and laboratory data would assist in decision making, thereby freeing the physician to focus on other aspects of clinical care.[16] However, enthusiasm for the potential of the computer as an intellectual tool eroded quickly. For example, some studies indicated that a computer system for diagnosing abdominal pain generated more accurate information and reduced perforation rate.[17,18] Other studies concluded that the same system had no useful role in this diagnosis.[19,20]

Early computer system evaluations often assumed that more patient information meant better patient care. However, evaluation of techniques such as electronic fetal heart rate monitoring illustrate that this is not always the case. In the early 1970s, the common perception was that continuous heart rate monitoring can protect the fetus from prolonged intrauterine oxygen deprivation.[21,22] Subsequently, several controlled clinical trials failed to demonstrate any clinical benefit of this technology.[23–25]

Evaluators of clinical computer applications have repeatedly criticized insufficient demonstration of quality improvement. In a review of reports on clinical computer systems, over 75% of 135 articles were anecdotal, and only half of the remainder met basic scientific criteria for the conduct of clinical trials.[13] Piantadosi and Byar[14] concluded that a basic shift is required in how scientists view research concepts as opposed to research results; the former are generally not considered proper objects for review or dissemination. Similar issues have been raised in other areas of health sciences. For example, Tyson et al.[26] conducted a review of therapeutic studies in perinatal medicine and found only 10% of the reports presented conclusions of the investigators that were supported by the evidence they presented.

Some argue that medical information systems need not justify themselves in terms of improved patient outcomes because these systems are designed to influence primarily the providers of health care.[27] Therefore, only the change in the process of care has to be demonstrated (e.g., performance of clinicians). This argument is acceptable when the process of care affected has an obvious relationship to healthcare outcomes (e.g., certain cancer screening procedures). However, there are numerous aspects of health care for which the relationship between process and outcome is unclear (e.g., completeness of medical records).

Nevertheless, in order to compete for the resources of healthcare providers, system developers have to demonstrate the relevance of their computer programs to healthcare quality improvement and cost control.[28] Medical practice involves a tremendous amount of information processing: collecting patient data, sharing information with patients, decision making in diagnostics and therapeutics, documenting care, communicating with other healthcare professionals, and educating patients. Healthcare organizations invest on average only 2.6% of their operating budget in information technology, a marked contrast with the average 8% to 9% invested by the banking industry.[29] During the past decades, computer systems have become active ingredients of health services, but the assessment of the new information technology is still considered to be a controversial issue. Practitioners interested in applying the new technologies need information on the results of the clinical evaluation of computer systems.

The recurrent debate over healthcare reform and the intensive search for cost-effective methods to improve patient care, repeatedly highlight the need for adequate technology assessment of clinical information systems.

Although early evaluation studies focused on the accuracy of information generated by the computer system, newer studies tend to focus on differences in the process or outcome of care due to the computer system. Although health care is clearly an information-intensive service, the clinical value of computer applications is often questioned due to the lack of demonstrated clinical benefits. As healthcare organizations are actively searching for opportunities to improve their information systems through purchase or development, the example set by systems on the market is very important for practical and theoretical purposes as well.

Research Methods to Demonstrate Practical Impact

There is a growing demand for adequate technology assessment in the field of medical informatics.[13,14,30,31] Medical technology includes drugs, devices, and procedures used in medical care, as well as the organizational and supportive systems that provide such care. Technology assessment provides practitioners with information on alternative techniques. The pioneering report of Cochrane noted that many standard medical practices lack evidence of effectiveness.[32] Concerns of costs also stimulate efforts to assess the practical value of not only new, but also established, technologies. Some argue that the assessment of healthcare technologies should be an iterative process and that there is a need to continuously reassess existing technologies by combining evidence from all reliable sources.[32,33]

As Berwick notes, Deming's theory of continuous quality improvement depends on understanding and revising the production processes on the basis of data about the processes themselves.[34] Likewise, quality improvement efforts in health care depend on measurable quality objectives and appropriate interventions and changes in the process. Particularly, randomized controlled trials (RCTs) have direct relevance to healthcare quality improvement as they become increasingly important sources of information about the clinical value of various interventions (e.g., physician and patient education,[35] interventions to promote cancer screening,[36] computerized medical records,[37] and home care after hospital discharge[38]).

The concept of demonstrating quality improvement by measurements is accepted in the field of medical informatics. Clinical computer system designers often use benchmark tests, surveys, and historical control comparisons to indicate the quality improvement resulting from the use of the new system. However, benchmark tests only measure the technical performance of the computer programs. They do not provide useful data on the impact of the system on either the process or outcomes of care. On the other hand, surveys of users' opinions only provide indirect information about the difference the system made in patient care.

Comparison with historical controls (before-after study) is a popular method of evaluating clinical computer applications. The fact that computer

systems are often connected to a patient database further encourages the use of historical controls as a baseline for evaluation.[39] Although they may provide some useful information, analyses of databases or historical control groups of patients cannot replace planned clinical experimentation.[40] The greatest concern in using historical controls is that there may be a confounding bias introduced by the different time periods. Definitions of disease and diagnostic testing methods may change over time. In the database, data may be missing either because they were lost or not recorded. Furthermore, developing hypotheses after the collection of data often leads to unplanned multiple comparisons.[41] Excessive numbers of statistical tests can easily result in misleading statistical significance, but no practical significance.

Randomized controlled clinical studies can provide the most valid information about the efficacy of computerized information systems in patient care.[42] From 1985–1995, the number of randomized controlled clinical trials testing computerized information interventions increased an average of 50% annually.[42]

A review of clinical trials of clinical decision support systems provides strong evidence that some clinical decision support systems can improve physician performance.[43,44] However, the majority of studies assessing patient outcomes did not demonstrate significant improvements. In addition, there have been very few controlled studies of CDSS, which have a diagnostic, as opposed to a therapy focus.

User Satisfaction with Decision Support Systems

Measuring and managing users' attitudes toward various aspects of information systems is an important part of making computer systems successful. No clinical computer system can be successful without gaining the support of practitioners. The primary challenge of measurement is to find an appropriate control for comparison. Ideally, satisfaction should be measured before and after the introduction of the new decision-support system, and there should be an improvement in users' satisfaction. However, it is often challenging to develop a generic user-satisfaction instrument.

There are many complex beliefs, attitudes, and behaviors influencing computer use among healthcare professionals. A critical success criterion for how useful information systems are, is the way in which computer users react to various aspects of the system. If overall satisfaction levels are high, the user will adapt his/her activities to take advantage of the computer. The user may not cooperate and may become antagonistic toward the system if satisfaction is too low. Questionnaires or surveys are tools that can be used to assess user attitudes. The particular significance of surveys is their ability to measure the acceptance of the system and the satisfaction of the users. However, a system must be used appropriately before its impact can be

accurately measured. Inattention on the part of system developers to the specific clinical needs of end users may result in system underutilization or sabotage.[45,46]

Teach and Shortliffe[47] found that physician attitudes regarding computer-based clinical decision aids and a medical computing tutorial were generally favorable. Physician expectations about the effect of computer-assisted consultation systems on medical practice were also positive, although there were considerable differences among physicians. In addition, the tutorial produced a substantial increase in knowledge about computing concepts and a significant effect on physician demands.

Decision-support modules built into the Health Evaluation through Logical Processes (HELP) system are described in more detail in Chapter 8. HELP is a clinical information system developed at LDS Hospital that includes a computer-based patient record, alerts, reminders, and other decision-support aids. Gardner and Lundsgaarde measured the attitudes of physicians and nurses who used the HELP system through a questionnaire with fixed-choice questions supplemented with free-text comments.[48] The respondents did not feel that computerized decision support decreased their decision-making power, nor did they feel that expert computer systems would compromise patient privacy or lead to external monitoring. The results of the survey indicated that experience with a system was the best way to break down attitudinal barriers to the use of that system. Although surveys and questionnaires can provide direct evidence of user attitudes toward CDSS, they are only an indirect measure of the behavioral impact of these systems.

Randomized Controlled Clinical Trials of Decision-Support Services

Because medical practice requires the efficient management of information, providing information to physicians is increasingly recognized as a clinical intervention designed to influence the process and/or outcome of patient care.[40,49] The quality of care is expected to be improved by the advanced methods of decision support. However, the benefits have to be demonstrated by appropriately controlled clinical measurements. There are many types of randomized clinical trials (e.g., parallel designs, factorial designs, cross-over trials), but the basic principles are the same: prospective and contemporaneous monitoring of the effect of a randomly allocated intervention. It is widely accepted that clinical trials represent a design superior to before-and-after studies (vulnerable to changes, over time, that are unrelated to the effect of the intervention) or matched control studies (a much less reliable method of obtaining comparable groups of subjects). Today, drugs, surgical procedures, alternative care delivery techniques, and

computerized decision-support services are evaluated in randomized controlled trials. For example, Pozen et al.[50] tested a predictive instrument to reduce admissions to the coronary care unit. They found that the instrument had the potential to reduce coronary care unit admissions by 250,000 for acute ischemic heart disease.

As necessary as RCTs are, they also have limitations. RCTs can test only specific hypotheses about selected aspects of computer systems. For instance, no single RCT can answer the question as to whether an integrated hospital system is good or bad. Selected information systems can be good for certain types of patients, indifferent for others, and only potentially useful for a third group of patients. Experimental evaluations of clinical computer applications (computer-assisted services) need to identify the specific conditions to be treated, specific interventions to be tested, and specific outcome variables to be measured. If this is done, the results can be specific, interpretable, and useful for practical purposes.

A surprisingly high proportion of trials are performed in outpatient facilities, particularly in primary care, while relatively few trials evaluated hospital information systems. This finding is in contrast to the large sums of money spent on information systems for inpatient care.

Although clinical trials are rapidly gaining acceptance in technology assessment, the methodology of such trials does not seem to be common knowledge. Several techniques commonly used in drug trials are irrelevant in testing computerized information interventions (e.g., blinding to the intervention, placebo), while other aspects are more critical (e.g., detailed description of sites, technical specification of intervention). The evaluated effect can be either a change in the process of care (e.g., increased or reduced use of certain drugs) or in the outcome of care (e.g., lower rate of infections). A particular weakness of many trials of computer systems is the lack of evaluation of patient outcome. It is certainly understandable that many information service trials evaluate the effect on care processes, since their main intent is to influence the process through the provision of accurate and timely information. However, documenting decreased side effects or other outcome measures, such as lower complication rates, could probably convince more clinicians as to their usefulness.

The setting in which the trial is conducted is critical to the representativeness of the trial. For example, the guidelines of the Nordic Council on Medicines recommend that the selection of a site for the trial has to be dependent on the potential risks involved to ensure satisfactory safety for the subjects.[51] It is a reasonable expectation that the site of a trial should represent the actual settings where the intervention will ordinarily be applied, otherwise, the generalization of the results are questionable. Many RCTs have tested the effect of various interventions on the practice patterns of residents in large academic centers. It is frequently assumed that the effects will be identical when board certified physicians are subjected

to the same intervention in a nonacademic environment, a hypothesis which has never been evaluated.

In health services research, randomization often assigns patients to groups through their healthcare providers. Major textbooks on clinical trials describe a large variety of randomization techniques.[52] The common feature of these techniques is that the patient is the unit of randomization. In health services research, it is often the provider who is directly targeted by the intervention. Therefore, the provider should be the unit of randomization and patients or encounters are randomized only through their providers. Our studies documented that only one-third of the trials on computer systems used an appropriate randomization technique.[53] The use of provider as a unit of randomization works well and could be more widely used in health services research. However, the number of providers has to be sufficient to ensure representativeness of not only the patient sample, but also of the provider sample. It is difficult to accept trials that randomize through a small number of provider units (e.g., patients of one hospital are in the study group while patients of another hospital are in the control group). In most cases, trials that randomize through less than six provider units should not be accepted as valid sources of evidence.

Columbia Registry of Medical Management Trials

Improving quality of care is not only a professional and ethical concern of physicians, but also the most important challenge facing a healthcare organization today.[34] Advanced computer techniques promise significant improvement in the quality of care through increased use of appropriate procedures and reduced use of unnecessary and potentially harmful procedures. Cochrane[54] emphasized the need to summarize evidence derived from randomized controlled trials as distinct from other kinds of evidence and to organize critical summaries by specialty or subspecialty of all relevant randomized controlled trials.

Various trial registries have been established in an attempt to improve access to published reports. Many of these registries deal with perinatal care, management for AIDS, or cancer treatment (e.g., the Oxford Perinatal Database,[55] the AIDS Clinical Trials Information Service, and the National Cancer Institute (NCI) Cancer Control Intervention Studies[56]). Some review papers contain valuable bibliographies of clinical trials.[57] However, clinical trials testing medical management interventions, a broad area critical to health-care quality improvement and cost control, have not been the focus of any known registry.

The purpose of organizing the Columbia Registry of Medical Management Trials is to support practitioners and researchers with the best available controlled evidence on the practical value of clinical interventions changing the delivery of health services. The registry is used to facilitate

access through improved MEDLINE indexing, to develop meta-analyses and reviews, and to analyze the trial methodology in health services research. Examples of the interventions within the scope of our registry include patient education, reminders/prompts, feedback, computer-aided diagnosis-making, and computerized records. There are approximately 1,800 reports on randomized controlled trials in the registry.

Specific eligibility criteria have been developed for inclusion/exclusion of reports in the Columbia Registry of Medical Management Trials. The design of the report is the first aspect evaluated. The study must be a prospective, contemporaneously controlled clinical trial with random assignment of intervention. Trials using allocation systems similar to a random number table (e.g., alternating encounters, alternating days of the week) are also eligible. Reports that do not meet this basic criterion (e.g., nonrandomized trial groups, review articles) are not included in the registry. Second, there should be an information management intervention in the study group with no similar intervention in the control group. Often, the control group simply receives the current standard of care, as compared with the experimental intervention used in the trial. The third criterion is that the effect of the intervention on the process and/or outcome of patient care must be measured. Planned or ongoing trials are not included in the registry because they do not meet this criterion.

The Columbia Registry of Medical Management Trials serves as a valuable resource for information system developers and practitioners by systematically collecting and rearranging the knowledge from these trials into a format that can be used by practitioners and others making healthcare decisions. This knowledge engineering is accomplished in several steps. First, the trials are located by using a systematic approach to search MEDLINE, which is likely to outperform conventional searches. Each search consists of a study design concept and an intervention or effect concept. The study design concept is the same for each search and includes the following terms: random (truncated textword), group (truncated textword), random allocation (textword and MeSH), randomized controlled trial (publication type) and clinical trial (publication type). The intervention or effect concept changes depending on specific interventions or effects. Subsequently, critical information is abstracted from the registered trials, and the practical messages of such studies are made available to those who need them. The same executive summary can be used to implement organizational changes, further healthcare quality improvement, conduct meta-analyses, or write literature reviews.

Several studies documented that, regardless of the complexity of the search process, some eligible reports will remain unretrieved. Therefore, clinical trial registries grow not only through the inclusion of new publications, but also through the discovery of eligible studies published earlier. The developers of the Oxford Perinatal Database also noted that there is no "gold standard" available to judge the completeness of a registry.[55]

TABLE 7.1. Information intervention categories.

Information Intervention Categories	Number of Reports (% Positive)
Patient Focus	
Computer-assisted interactive patient education, instruction and therapy	19 (74)
Patient prompt/reminder	15 (80)
Patient-computer interactive information gathering	2 (100)
Provider Focus	
Provider prompt/reminder	19 (100)
Computer-assisted treatment planner	19 (79)
Provider feedback	19 (68)
Computerized medical record and information access	19 (74)
Prediction	6 (83)
Computer-assisted diagnosis	4 (50)
Total*	98 (85)

* Some reports test several interventions.

The synthesis of trial results helps the identification of most effective information services. Table 7.1 shows the percentages of positive trials for different types of information interventions that are included in the registry.

The number of randomized controlled trials as the ultimate evidence on the practical difference made by a specific intervention is rapidly expanding. Meta-analysis is the use of statistical techniques to integrate results of separate, but similar, clinical trials. Instead of providing a qualitative assessment of a few studies, meta-analysis promises a systematic and quantitative synthesis of all available studies. Systematic collection procedures are designed to avoid the well known deficiencies of the conventional "pick-and-choose" approach.[58]

Research synthesis of evidence from several randomized controlled clinical trials always raises the question of clinical efficacy. Vote-counting is an established method of expressing the success rate of a particular intervention.[59] When the number of successful trials is very high in a particular category, then the intervention is likely to make a difference. The particular advantage of vote-counting is that information on the success or failure of the intervention is available from virtually all trial reports. Obviously, vote-counting does not consider the magnitude of effect. Primary research reports not providing enough information to calculate effect size estimates usually contain information about the direction of the effect. On the other hand, meta-analyses using the popular odds-ratio methods can specify the magnitude of the effect, and are likely to discover additional categories of effective interventions.

Diversity, a frequent concern in research synthesis, can be an advantage as well as a disadvantage. Trials pooled together are always somewhat

different in their sites, samples, interventions, and effect variables. A diversity of sites and samples (within the stated pooling criteria) can help document an intervention's success under a variety of circumstances. Diverse interventions can also help to reflect the natural variability of use in different healthcare organizations. For example, it would be unreasonable to demand separate testing of physician reminders for every single clinical procedure. Successfully applying a particular information intervention in a variety of settings and disease conditions increases the generalizability of results and the intervention's practical value.

As discussed in Chapter 2, computerized decision support requires representation of clinical knowledge in Boolean production rules or other tightly organized structures (e.g., expression in probabilities, knowledge frames). To represent the data from clinical trials, into a form that can be used in CDSS, requires knowledge engineering, and the structuring of such evidence is becoming an important trend in knowledge engineering. As the amount of published scientific evidence grows, finding the right report is no longer sufficient. The report has to be supplemented with the abstraction of the specific information to meet the needs of clinicians, researchers, and policy makers. Conventional abstracts by the investigators provide useful synopses, but often lack detail and standardization. An analysis of 150 trial reports led to the development and validation of a quality scoring system which can be used as an itemized checklist to portray the methodological quality of health services research trials.[53]

Effective Information Interventions

Randomized controlled trials confirm that four generic information interventions that are active components of computer systems can make a significant difference in patient care (patient education, treatment planning, physician and patient reminders).[60] To manage care and improve quality, computer systems of primary care should incorporate these effective information services.

Interactive patient education can help patients improve their health through health promotion, educational information on the management of medical conditions, and computerized instruction. Seventy-four percent of the patient education studies were successful. Chapter 11 includes descriptions of some of these patient education studies.

A large number of studies employed the use of computer algorithms to assist in drug dosing decision making (e.g., aminoglycoside,[61] insulin,[62] digoxin,[3] phenytoin,[63] sodium nitroprusside,[64] lidocaine,[65] propranol,[66] and amitriptyline[67]). For example, the first known trial of a decision-support system compared the effect of computed digoxin dosage to that of unaided physician judgment.[3] The results indicated that the computer slightly outperformed the physician and that the correlation between predicted and measured serum digoxin concentrations was closer in the computer-assisted

patient group. Overall, 79% of the computer-assisted treatment planner studies were successful.

Reminders represent one of the primary techniques of delivering messages generated by clinical decision support systems. Reminder messages recommend specific action at the time of decision-making. Computers can scan each patient's record to identify tests and other procedures that are due. The main function of the computer system is the identification of eligible patients and triggering the use of a particular clinical procedure.

Several controlled experiments have demonstrated that physicians respond to computer-generated reminders by performing the recommended interventions (e.g., influenza immunization, mammography). For example, patients of physicians who received reminders on the encounter forms were significantly more likely to have a mammogram ordered for them.[67] Procedures frequently targeted by the provider prompt/reminder trials included cancer screening[36,68] (stool occult blood, sigmoidoscopy, rectal examination, mammography, breast examination, Papanicolaou test, pelvic examination) and vaccinations (influenza,[69] pneumococcal,[70] tetanus,[71] and infant immunizations[72]). All of the physician reminder studies and 80% of the patient reminder studies were successful.

The syntheses of trial results from the registry have already led to several practical and significant observations. For example, our meta-analyses of randomized controlled trials testing physician reminders concluded that this is a highly effective information intervention, but the results vary depending on the targeted clinical procedure (e.g., cancer screening versus immunization).[73,74] These and other studies have demonstrated that computers can help to make patient care more consistent by reminding physicians to order or perform recommended procedures. Many systems show significant and beneficial impact in selected clinical areas, particularly health maintenance. In addition, 95% of the studies in our systematic review of the acceptability and effectiveness of computerized patient education interventions reported positive results.[75]

Value of Noncomputerized Information Interventions

Originally, the Columbia Registry of Medical Management Trials was designed to include only trials using some form of computer intervention. Once the first 100 trials had been registered, it became clear that noncomputerized information interventions could be equally valuable.

Patient education provides an example of how noncomputerized information interventions can be effective. Educating patients about good chronic care, needs to be based on scientifically sound evidence. Patient education involves more than telling people what to do or giving them instructional material to read. The growing number of randomized clinical trials testing patient information makes the casual, ad hoc, and opinion-based

approach to patient education unacceptable. People easily slip in opinions when they are describing what should be included in the education of patients. Generalization of clinical trial results appears to be a better option than just relying on opinion. There are many education topics that are definitely useful for patients, and educators should choose them over contents that have never been shown to be beneficial.

A systematic review of 170 studies involving the education of 25,970 patients with diabetes, asthma, or congestive heart failure documents that far more clinical evidence is available on patient education beyond simply confirming that education is generally useful. Numerous successful randomized controlled trials link various educational contents and methods to improved health status, social functioning, and satisfaction.[76] This systematic review has led to the development of evidence-based patient education checklists for diabetes, asthma, and congestive heart failure. The evidence base from the randomized controlled trials of patient education could be combined with information technologies to increase access to education through new approaches. Packaging of informational messages, for easier and more effective prompting, as well as alternative delivery techniques, should be analyzed in future randomized controlled trials.

Obtaining good data is the basis for decision making about the value of diagnostic and other decision support systems. As more CDSS reach the implementation stage, RCTs of their effectiveness, as an information intervention, will be possible. Registries of RCTs will be able to provide the data needed to answer questions about the value of particular CDSS, the value of CDSS in particular settings, and the value of CDSS for particular purposes.

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