

The Columbia Registry of Controlled Clinical Computer Trials

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ABSTRACT

Numerous reports on randomized controlled clinical trials of computer-based interventions have been published. These trials provide useful evaluations of the impact of information technology on patient care. Unfortunately, several obstacles make access to the trial reports difficult. Barriers include the large variety of publications in which reports may appear, non-standard descriptors, and incomplete indexing. Some analyzers indicate inadequate testing of computer methods.

The purpose of establishing a registry of randomized controlled clinical computer trials was to assist the identification of computer services with demonstrated ability to improve the process or outcome of patient care. A report collection, selection, information extraction, and registration method was developed and implemented. One hundred and six reports on computer trials have been collected. A large variety of computer-assisted interventions have been tested in the registered trials (40% reminder, 15% feedback, 14% dose planning, 14% patient education, 12% medical record). 76% of the registered reports were published in the United States and most of the remainder in various European countries. In reporting computer trial results, 77% of the authors did not use both the "computer" and "trial" keywords in the title or abstract of their papers. We conclude that a major obstacle to adequate computer technology assessment is inadequate access to the published results.

INTRODUCTION

Clinical evaluation of computer systems is an important information source for practitioners interested in applying the new information technology and for developers designing clinical computer systems. Insufficient demonstration of quality improvement has been repeatedly highlighted by analyzers of reports on clinical computer applications. In a review of such reports, over 75% of 135 articles were anecdotal, and only half of the remainder (16 articles) met basic scientific criteria for

the conduct of clinical trials [1]. Piantadosi and Byar 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. Their remark was that, "Curiously, computer algorithms are considered worthy of review and publication based largely on improvement in concept" [2]. Recently, Wyatt and Spiegelhalter stated that "only clinical trials can assess the impact of prototype medical decision-aids, but they are seldom performed before dissemination" [3].

Randomized controlled clinical trials of computer-assisted information services can provide the most reliable information about the value of computer systems. The primary advantage of such trials is the control of confounding bias through random assignment of a concurrent control group. Randomized controlled clinical trials can avoid the deficiencies of popular before-after evaluations (e.g., selection bias, nonstandard definitions, missing data, and multiple comparison [4]). There are several published reports on randomized controlled clinical trials of computer applications [5],[6],[7],[8]. Cochrane emphasized the need to summarize evidence derived from randomized controlled trials as distinct from other kinds of evidence [9]. Meetings of the Society for Clinical Trials have repeatedly emphasized the need for establishing registries of clinical trials.

Unfortunately, searches for the results of controlled clinical computer trials often lead to incomplete and inconsistent results. The terminology used by investigators and National Library of Medicine indexers is continuously changing [10]. The term "Clinical Research" was synonymous with "Clinical Trials" from 1966 until 1980. In 1980, "Clinical Trials" was established as a MeSH term to replace the "Clinical Research". In 1990, "Randomized Controlled Trials" became a MeSH term and in 1991 "Randomized Controlled Trial" was introduced as a publication type. Such arbitrary changes in terminology are not common knowledge. The indexing process for MEDLINE is entirely manual, introducing another source

of potential bias. Often articles are not explicitly identified as randomized controlled trials. The access to computer trials is particularly complicated by the lack of indexing. A significant number of periodicals in the field of medical informatics is not registered in the MEDLINE database (e.g., MEDINFO proceedings).

The primary goal of establishing the Columbia Registry of Computer Trials was to assist practitioners, clinical researchers, computer system developers, and health care administrators in comparing the effects of various computer-assisted information services on the process and outcome of patient care. To accomplish this goal, the experimental evidence, i.e. the results of randomized controlled clinical computer trials (computer RCTs) have been collected systematically. This paper provides a description of the registration method and an overview of the collected papers.

METHODS

The following eligibility criteria have been specified and used in the collection and registration of reports: (1) prospective, contemporaneously controlled clinical trial with random or quasirandom assignment of intervention; (2) computer-assisted intervention in the study group and no similar computer assistance in the control group; and (3) a direct effect on the process and/or outcome of patient care was measured.

In collecting eligible reports, efficient retrieval from the reference databases of bibliographic citations is critical. Recall is defined as the percentage of total number of relevant references in the database that were retrieved. Precision is defined as the percentage of total number of references retrieved that were relevant references [11]. In developing the search strategy of registration, a high rate of recall, with a corresponding low precision, was targeted in order to obtain completeness.

Numerous search strategies have been combined to collect eligible trial reports and to develop the registry:

- Extensive MEDLINE (CD-PLUS) search by using numerous search strategies. Obviously, this approach results in a high rate of recall and a corresponding lower rate of precision. Through the use of several search strategies, trial reports were retrieved and the search strategy has been repeatedly redefined. In this process, MeSH keyword and textword (including truncated word) searches have been combined.

- Manual search of the proceedings of American, International, and European Medical Informatics Associations. These proceedings are not referenced in the MEDLINE database. The search of proceedings can help to locate results presented in leading national and

international meetings. The manual search of proceedings has been restricted to publications in English, French, and German.

- Systematic hand search of the reference lists of retrieved trial reports and review papers. This search resulted in finding several additional reports. Furthermore, manual search of books and monographs has been performed in the area of medical computer applications (e.g., Lecture Notes in Medical Informatics, IFIP/IMIA books).

- Ad hoc methods, informal contacts have been used to obtain further and unpublished trial results (e.g. correspondence, E-mail, meetings). Personal contacts were expected to turn up a small but significant proportion of trial reports on file.

- In addition, extended intervention searches have been performed in the MEDLINE database. By using the above methods, specific information services can be identified as tested in clinical practice (e.g. alerts to physicians, recalling letters to patients). An extended intervention search is defined as the retrieval of trials testing the same or similar information services without considering computer assistance. This type of search offers important advantages: a) Virtually all trials testing a specific service can be located and the benefits of computer-assisted services can be compared to the effect of similar but non computerized services; b) reports on computer trials can be located when neither MeSH nor textword search can identify an eligible report.

Retrieval of reports was followed by a registration process. The search strategy of this project was designed to provide high rate of recall. The corresponding low rate of precision required the gatekeeper role of registration. The decision on inclusion or exclusion was based on a search for facts unambiguously excluding the report from further analysis (e.g. randomization was interpreted by the authors as random sampling and not as a method of treatment allocation). When no such evidence was found, the report was registered. The application of eligibility criteria was liberal. The process was not expected to exclude reports on behalf of future reviewers. Papers reporting ongoing clinical computer trials have also been collected and included.

When the title and abstract of a retrieved report left open the question of eligibility, the copy of the full report was obtained for further detailed analysis. When it was unclear from the report whether or not a controlled trial had been conducted, the authors were contacted. Either as a result of the clarification or without it, if necessary, a decision was made concerning the inclusion of the report in the register. Again, the above listed eligibility criteria were used to make the final decision.

Information extracted from the reports was attached to the photocopy of reports and filed. The continuous increase in the number of published computer trial reports and the planned addition of reports on trials testing identical but non computer-assisted information services urge the organization of a computerized database. Particularly, trial reports can be connected in various ways. Investigators can publish several reports on the same trial. Different reports can describe different aspects of the same trial. Various trials can evaluate the same or similar intervention. The same outcome variable can be observed in evaluating substantially different interventions (e.g. change in the efficiency of cancer screening as a result of reminding physicians or patients). The registration of non computer assisted information services can make the evaluation of information services more comprehensive (e.g., reminder printed by a computer or prepared by a research assistant). Access to reports requires text word search including truncated words, Boolean searches including parenthetical grouping, import of downloaded records from bibliographic databases, and export of data files in ASCII format. The INMAGIC Textbase Software was selected for the development of the Columbia Registry database.

RESULTS

Based on the experience of numerous searches

Table I. MEDLINE search strategy

<ol style="list-style-type: none"> 1. EXPLODE CLINICAL TRIALS (MeSH) (a) 2. EXPLODE COHORT STUDIES (MeSH) (b) 3. CLINICAL TRIAL (publication type) 4. PROSPECTIVES\$ (text word) 5. RANDOM ALLOCATION (MeSH) 6. RANDOM\$ (truncated word) 7. CLINICAL TRIAL (text word) 8. CONTROLLED TRIAL (text word) 9. CONTROL GROUP (text word) 10. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 11. EXPLODE MEDICAL INFORMATICS (MeSH) 12. COMPUTE\$ (truncated word) 13. MICROCOMPUTE\$ (truncated word) 14. 11 OR 12 OR 13 15. 10 AND 14 (a) CLINICAL RESEARCH (MeSH) was used between 1966-79 (b) PROSPECTIVE STUDIES or FOLLOW-UP STUDIES (MeSH) was used between 1966-89. EXPLODE function was not used for these terms.

during the development, the combined search strategy was refined and implemented. A set of specific computerized and systematic manual search procedures has been developed to collect new experimental evidence as it becomes available. In addition, a MEDLINE search strategy was developed for the purposes of registration and continuous updating (Table I).

Currently, 106 reports on randomized controlled clinical computer trials are registered. The first report was published by Peck et al. in 1973 [5]. Their paper, entitled "Computer-assisted digoxin therapy", was published in the New England Journal of Medicine. During the 80's the average rate of increase in the number of published trial reports was over 50% annually (Fig. 1). The drop in the number of registered reports from the most recent years is another sign of difficulties in retrieval. The analysis of reference list in papers retrieved by other methods proved to be a very valuable source of reports but this method could not cover the most recent years. More trial reports

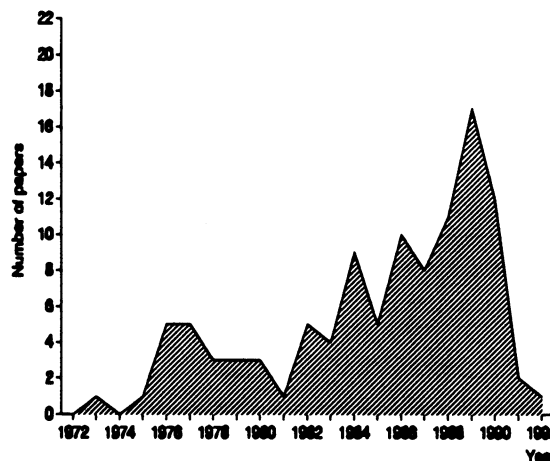


Figure 1 Trend of publication

have been published in Medical Care than in any other journal (18). We found 11 randomized controlled clinical trial reports in various SCAMC proceedings. Seventeen percent of the registered reports were published in periodicals, monographs, and proceedings not referenced by MEDLINE.

The source of registered trial reports was also analyzed (Fig. 2). 80 reports on randomized controlled trials of computer-assisted information services have been published by researchers from the United States. The University of Indiana was the largest producer of trial reports (12). However, 25 trials have been performed in other countries and some of them were not published in English. This indicates the variety of sources which can cause difficulties in retrieving reports on computer trials.

The retrieval of trial reports referenced in

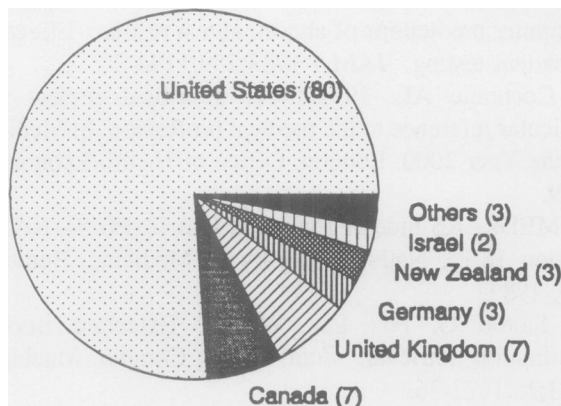


Figure 2 Geographic distribution

MEDLINE is complicated by several factors. The MeSH terminology is continuously developing and access to the trial reports is improving. However, retrieval of earlier published reports remains difficult (Table I). Changes in MeSH terminology repeatedly highlight the importance of using relevant keywords in titles and abstracts (Table II). These words could provide adequate support for the retrieval of reports on computer trials. The data from our Registry suggest that the use of critical terms has been inconsistent in publishing trial results. In addition, some scientific journals do not publish abstracts. Other journals require abstract only for certain papers but not for others and trial reports are published in both categories. Such inconsistencies in editorial policies decrease the efficiency of textword searches.

A large variety of computer-assisted interventions have been tested in the registered trials. Forty per cent of the reported trials evaluated various types of reminder messages i.e., information which is supposed to be known but often not considered. Half of these trials tested methods reminding patients (e.g., reminders to encourage influenza vaccination [12]). The other half tested methods recommending appropriate actions for physicians (e.g., alert report on digoxin intoxication [6], expert system consultation [13]). Delayed, cumulative feedback methods were tested by 14 % of trials (e.g., feedback to encourage generic drug prescribing [14]). Education and rehabilitation methods were described in 14% of the registered trial reports (e.g., education lesson for patients with rheumatoid arthritis [15]). A similar percentage of trials tested computer assisted dose planning and drug administration methods (e.g., insulin dosage decision-making [7], Bayesian dosing program for phenytoin [16]). The effect of computerized medical records was analyzed in 12 % of trials (e.g., medical record summary system [17]). Nine trials tested miscellaneous computer-assisted

interventions (e.g., computer predictions of abnormal test results [8]).

Table II Use of keywords

	"COMPUTER"	
	Yes	No
Yes	35	13
"TRIAL"		
No	52	7

DISCUSSION

A randomized controlled clinical computer trial can demonstrate the specific effect of a specific information service on the quality of care. No single trial can answer the question that an integrated hospital information system is good or bad. In fact, complex information systems provide a large variety of services. The registration of computer trials demonstrates that numerous information services have been tested in a large variety of clinical situations. However, certain types of computer-assisted information services are clearly underrepresented.

It has long been suspected that reviews of studies published in the biomedical sciences are based on a biased sample of studies [18]. This biased sampling can have a potentially serious effect on the synthesis of trial results. The tendency of publishing only significant findings is called the file drawer problem [19]. Scientists may be discouraged from submitting negative results. Consequently, never published and considered reports fill the file drawers. Although a higher percentage of unpublished reports have negative findings, negative studies are no less important than those with positive results. The acceptance rate of negative studies was 11% at one large scientific meeting, while 57% of the positive abstracts were accepted for presentation [20]. This bias against the null hypothesis may lead to distorted estimation of effect sizes. Complete collection of trial reports is needed to eliminate selection bias.

The demonstrated inconsistencies of the reporting process are obstacles preventing researchers, system developers, and practitioners in obtaining the needed evidence. Without the complex procedures developed and

implemented in our project reviewers may have access to only selected studies. These facts repeatedly indicate the need for complete retrieval, registration, and quantitative reviewing.

The results of this registration will be made available by periodic publication of the results, as they become available. In addition, dissemination is planned via the e-mail list MHCARE_L@MIZZOU1.MISSOURI.EDU ("Managed Health Care and Information Management"). The authors would appreciate any information leading to the capture of unpublished or unindexed trials reports. The Columbia Registry of Controlled Clinical Computer Trials is an ongoing effort to collect, review, and disseminate the best available evidence.

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