THE DESIGN AND EVALUATION OF A PROTOTYPE DATA MANAGEMENT AND ANALYSIS SYSTEM FOR CLINICAL INVESTIGATORS

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The CLINFO Project is an effort to identify the information processing activities and needs critical to clinical investigation (medical research involving human subjects which is aimed at improving diagnostic and therapeutic techniques) and to recommend how to satisfy these needs. To date the project (1) has determined that the most critical needs which can be met effectively using state-of-the-art computer technology lie in the areas of managing and analyzing clinical-research data collected by individual investigators, (2) has developed prototype minicomputer-based systems designed to satisfy these needs in the General Clinical Research Center (GCRC) setting, and (3) has installed, and is successfully operating, two prototype systems in GCRCs where they are being evaluated. The project is being conducted by computer scientists, clinical investigators and National Institutes of Health (NIH) staff members. It has involved several phases of activity, beginning with a determination of user requirements by means of informal and formal discussions and interviews. The present phases address the incremental and iterative design and development of a prototype, and the collection of detailed information about its utilization by diverse users at more than one site. If justified by user acceptance and estimated costs and benefits, the project will next specify a system appropriate for a large number of clinical researchers

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and will plan for its commercial development and distribution. This paper discusses the project's techniques for requirements analysis, design and evaluation, and describes early experiences with users.

BACKGROUND

The CLINFO project was initiated in 1972 to answer two fundamental questions, namely, (1) what are the information processing activities and needs of clinical researchers who investigate physiology and diagnostic and therapeutic techniques in GCRCs? and (2) what, if any, computer technology can meet the major needs of a variety of investigators at scattered geographic locations while being fiscally and otherwise acceptable to their institutions? To answer these questions in depth, the National Institutes of Health established a consortium comprising clinical investigators (T. G. Christopher, a nephrologist at the University of Washington, A. W. Nunnery, a pediatrician at the University of Oklahoma, and H. K. Thompson, Jr., a cardiologist at the Baylor College of Medicine), computer scientists (primarily G. F. Groner, N. A. Palley and N. Z. Shapiro at The Rand Corporation), and NIH staff members (W. R. Baker, Jr., and W. F. Raub at the Biotechnology Resources Branch, and W. R. DeCesare and his assistants at the GCRC Branch).

Although each of the participating clinical investigators had prior experience with computer technology and the computer scientists had prior experience with biomedical research, none of us had previously worked with the consortium members from other institutions. Although the consortium had some initial difficulties, the interdisciplinary approach has been instrumental to the success of the project because (1) expertise in medical research and in computer science and technology, in addition to NIH viewpoints, have been required and utilized throughout the project, (2) the viewpoints of the developers of any eventual computer system, as well as those of potential users, have been represented at all stages of the project to ensure that any computer system or systems recommended would be useful, acceptable and feasible, and (3) the medical and institutional diversity of the participating clinical investigators has helped to ensure the wide applicability of any recommendations. Finally, because of both the composition of the consortium and the investigative interests of its individual members, our approach has been to examine real-world problems in detail and then attempt to find or devise solutions rather than to start with existing solutions and try to mold problems to fit them.

REQUIREMENTS ANALYSIS

Our first steps toward determining user requirements were frequent and intense consortium discussions and visits to a number of clinical research centers where we observed and informally interviewed clinical research personnel (1). Although it was not always apparent, the early consortium discussions were aimed at developing good working relationships, a common terminology and compatible viewpoints. In the process, the computer scientists learned a great deal about the techniques, impediments and sociology of clinical research and the clinical investigators learned about the techniques and technologies of computer science. As the discussions progressed, we agreed upon specific objectives, priorities and methods of procedure, we formalized our understanding of clinical research impediments and we outlined tentative solutions. During the same period, we observed and informally interviewed more than 100 clinical research personnel at over a dozen clinical research centers. These visits were primarily intended to give the computer scientists first-hand knowledge of the scientific and operational details of clinical research. However, they were also invaluable in broadening the group's knowledge, filling in knowledge gaps, raising additional issues and testing hypotheses formulated in the consortium discussions.

We considered a large number of problem areas including clinical research center management, patient monitoring, medical records processing, research protocol generation and obtaining informed consent. Most of these were deemed inappropriate for detailed consideration or were deferred for one or more reasons: they were not critical problems for the clinical research we were considering, they would have to be solved more generally (i.e., outside of the research centers) before clinical research would be facilitated, it did not seem possible to formalize the problem in any general way at that time, or it did not seem appropriate to use computer technology in the problem area.

One area that did seem promising was the organization, exploration and analysis of research study data collected by individual investigators. Many researchers explained that although they had to surmount great difficulties in collecting data about human subjects, the tools and techniques for extracting useful information from their data were so primitive and time consuming that many questions which their data theoretically answer were never addressed. Although the problems and approaches described to us differed in detail, they were thematically similar. Generally clinical investigators collect time-oriented, but sparse, data about

individual patients; they explore them by looking at sets of data values for groups of patients; they examine changes over time for individual patients or patient groups; they create subsets of patients who have common characteristics; and, once they have organized the interesting data, they analyze them using fairly simple, standard techniques. These activities, as described, were sufficiently formalized and general that it seemed feasible to develop a computer system or package to assist a significant number of clinical researchers with their activities.

An examination of existing computer systems and software packages demonstrated the feasibility of providing assistance in this problem area. However, it also showed that existing systems and packages were inappropriate because they dealt with only a small part of the problem, they required too much programming by the user, they were too expensive, and/or they were not usable outside a single institution. Preliminary design efforts indicated that although there were outstanding computer science problems that had not been previously addressed, the chances were good that a useful system could be developed, and that, because we were primarily concerned with handling only modest amounts of data, the resulting system would have a reasonable cost.

We had, thus, come to the preliminary conclusions that clinical research is impeded because of difficulties in managing and analyzing research data, that these difficulties are critical and widespread, and that it would be feasible to develop a computer-based system for assisting with these activities. These findings were substantiated by requests that the NIH was receiving from clinical research centers for programmable calculators and computers to be used for data analysis.

To verify our conclusions and to determine computer system design parameters, we conducted an in-person, questionnaire-based interview of 90 investigators at 23 General Clinical Research Centers (2,3). We asked each investigator about his background and research interests; how much data of what types he collected; how he organized, explored and analyzed his data; what difficulties he had doing this; what experiences he had had in using or attempting to use programmable calculators and computers; and how computer-based assistance with his data management and analysis activities might benefit his research. The interviewed investigators told us that, aside from obtaining financial support, their greatest difficulties were in organizing and analyzing their data; because they were GCRC users they were already obtaining beds for their research subjects and adequate assistance in collecting samples, controlling their patients' diets, and other medical aspects of their work. Investigators

claimed that if they had a readily accessible, well designed data management and analysis computer system, together with especially trained support personnel, this would reduce their nonproductive time, provide greater insight into their research, reduce the duration of their research studies and increase their publishable results.

One striking result of these interviews was that although nearly everyone we talked with had nominal access to a computer center, very few investigators used it. They often lacked appreciation for what computers could do for them (partly because the computer center generally showed little interest in them and provided little in the way of user services), and when they attempted to use computers they encountered many administrative, sociological and technical difficulties. On the other hand, many investigators were making extensive, effective and comfortable use of programmable calculators owned by their project or center; these calculators are useful for data analysis but not data organization and often require the data to be reentered each time they are analyzed.

The survey also demonstrated a great deal of commonality among the investigators who use the General Clinical Research Centers. Nearly all investigators record their data in laboratory notebooks

and in patient "flowsheets" (showing variables versus time), create subsets of patients, graph their data and perform simple statistical analyses. Eighty percent of the interviewed investigators have 75 or fewer subjects on a study and record a total of fewer than 100,000 data values throughout the course of a study.

The survey substantiated our earlier finding that computer technology, if applied to assisting individual investigators in the collection, organization and analysis of their research data could meet the major needs of a variety of investigators at scattered geographic locations. It demonstrated that technology could be introduced most successfully if it were placed under the administrative control of the clinical research center and if it were accompanied by personnel who would operate the hardware and educate and assist users. Furthermore, the survey results emphasized that a computer system for clinical investigators would have to be specially designed to meet their needs without requiring much from them in the way of programming, special technical skills or non-productive effort. Also, survey results, together with a technical analysis, indicated that because of their sufficient capabilities, small physical size, low cost and apparently satisfactory reliability, it would be feasible to base such a system on a minicomputer.

DESIGN APPROACH

While we had dealt with our original broad questions reasonably well, we were also convinced that several more detailed questions would have to be answered before computer technology could be successfully placed in the hands of many clinical investigators. What specific functions should be provided to meet the needs of most researchers at most clinical research centers? In an interactive system, what should the human/terminal interface look like in terms of languages provided, graphics, etc.? What personnel are required? What are appropriate operating procedures? What hardware can be most effectively purchased, installed and maintained? Given that a system can be developed, is it worthwhile to make it widely available? To what degree would it be accepted by users? What are its costs and benefits? What needs does it leave unmet?

To obtain answers to such questions, we proposed to develop a prototype system and to install copies of it at two or three clinical research centers where it would be used and evaluated by a variety of investigators. A prototype would provide a concrete testbed and design vehicle that both users and designers could relate to. If we could develop a prototype that was sufficiently utilized, we would be able to learn about its costs and benefits and, if successful, we would have a good basis from which to develop specifications for a more widely available system. Although this approach was expensive, it would be less expensive in the long run,

and would have a greater chance of success, than prematurely providing computer systems to users. The NIH concurred with this approach.

Our overall plan included installing prototype systems (under the purview of two of the original consortium members--Drs. Thompson and Christopher) at two clinical research sites and providing personnel (called "system managers") to support the systems and collect evaluation data there (4). At each site we would learn about requirements for hardware, software, operating procedures and personnel; overall acceptance; and costs and benefits. Based on user reactions and our own observations, we would change the prototype system and procedures so that at all times they would embody, to as large an extent as practical, the specifications that we are in the process of developing. If the prototype operated successfully and was well received at the first two sites, a stable version would be installed and evaluated at a third site that is not biased because of the presence of one of the original project participants. The third site would provide a good test of the specifications developed at the first two; if successful there, we would reexamine our experience and the available and predicted technology,would solidify our specifications and would plan for the commercial development of a system that meets the specifications.

Prior to selecting computer hardware, we designed, and had reviewed by clinical investigators and computer scientists, an initial functional description of the CLINFO prototype system (5). Our design assumed the following series of activities during the life of a clinical research study (6):

- As a study protocol is designed, the investigator decides what data are to be collected, at what rate and in what volume.

- As the study progresses, data are collected and entered (i.e., recorded) in a file that contains all the data collected about patients on the study. Considerable care is taken to ensure the validity of those data.

- The investigator reviews and summarizes the data as the study progresses. Part of summarization is the selection of patients with particular characteristics, the review of data from a particular patient, and the review of particular parameters from all patients on the study. In addition, there is a need to review data collected for a particular patient (or a group of patients) at a particular point in time or at different but related times. The summarizations are generated by transcribing data from a

variety of sources (e.g., the file of study data) to a tabular form which is more convenient for review and analysis. Also, the investigator wants to perform mathematical and statistical analyses upon and produce reports, plots and graphs from, his data.

- After the investigator has collected data for several studies, he may want to perform retrospective studies which abstract patients and their data from existing studies.

- Data recording is performed primarily by data clerks, nurses and technicians; data analysis is performed primarily by investigators, fellows and other especially trained staff members.

We concluded that the CLINFO prototype should be designed to support these activities by providing an online, interactive computer system which:

- Protects the privacy of both the patient and investigator.

- Allows the investigator to describe the contents of a computer-based "study data file."

- Provides for data entry into the study data file and several forms of data screening and encoding.

- Allows the investigator to extract from the list of all patients in the study those patients who have particular characteristics.

- Allows for the creation of tabular arrays of data called "worksheets" from a variety of sources, in particular from the investigator's computer-based study data file.

- Allows the investigator to perform one of a number of mathematical and statistical analyses upon, and produce simple reports, graphs and plots from the worksheets.

- Protects the investigator's data from loss due to computer malfunction.

- Allows for the transformation of worksheets into a form compatible with a simple programming language. Regardless of what functions are provided by the system, each investigator will need to develop computer programs to

meet his own unique needs. The Basic programming language was selected because it is both easy to use and powerful, and because it is widely used.

- Provides for the automatic collection of data required for evaluation of the prototype.

- Provides an operating environment for the prototype system which allows the addition of features which are not part of the original design.

The hardware selected was a Data General Eclipse S/200 minicomputer, a number of data storage and other peripherals, four alphanumeric display terminals for users and two hardcopy devices, to be attached to the terminals. This configuration, exclusive of terminals and hardcopy devices, costs approximately $90,000.

We chose an extended version of Basic as our prototype implementation language, even though it is not necessarily the best programming language in which to implement the eventual system. We chose Basic because we thought it was sufficiently powerful to do the job, because we could use an interactive language to develop and modify the prototype quickly and easily, and because it provides a single programming language for both prototype developers and users. The prototype software was

designed to be highly modular for efficient development and modification and so that it could be run on a small computer.

From the user's viewpoint (7,8), the prototype is prompt oriented, i.e., the user is generally presented with several choices and he selects one by typing a number, a letter or a word. This approach was selected in order to make the system easy to learn to use and easy to remember how to use. To provide a system which can be used by diverse investigators, yet which can be individualized for particular investigators, the data stored on the system are organized into studies which are described by "schemata." A schema is a user-defined description of his data, i.e., it contains the names, characteristics and organization of his variables. Data are generally stored in a three-dimensional study data file in which they are organized by patient, variable and time and from which they can be retrieved into two-dimensional worksheets. Worksheet data may be plotted and analyzed, and the results of analyses may be stored in worksheets for further processing.

Although we could have completed the development of a full-blown prototype prior to testing and evaluation, we decided instead to take an incremental, iterative approach. We did this because we wanted feedback based on users' experience with a concrete system

as soon as possible, and because we wanted to discover any administrative or operational problems early. We decided to develop the software in a number of "releases," the first three of which (numbered -1, 0, and 1) would be used by only project personnel, carefully selected clinical research personnel, and all qualified users, respectively. Release 1 was to incorporate nearly all of our initial design, Release 2 was to be a modification based on feedback from users at the first clinical research site, and Release 3 was to incorporate experience at all of the participating clinical research sites. Included in our evaluation plans were methods for directly and indirectly obtaining user reactions to the prototype.

EVALUATION APPROACH

The evaluation is based on four plans which are designed to collect information which can be used to enhance the utility of the prototype and to estimate its benefits (4). Although our investigation is based on the scientific method, the evaluation plans should not be equated with scientific experiments. This is primarily because they seek answers to a large number of questions concerning differences in the use of the system as a function of medical specialty and over time at each site, and because the prototype is to be changed in response to our findings. Thus, the number of variables which will be examined will far exceed the sample

size. As a result, even though we expect that substantial progress can be made toward meeting our objectives, many of the conclusions will not be statistically supportable.

Evaluation Plan 1 seeks to define the adequacy of the system features with respect to their utility and user interaction, the potential need for additional features, and the system capacity in terms of amounts of data and numbers of simultaneous users. Example questions are: What is the extent of use of features such as those related to performing simple descriptive statistics, graphing and tabulating data, and subsetting data? How might the system be organized to minimize the interaction required to accomplish frequently performed tasks? How many patients, variables and data values should the system accommodate for each study?

Evaluation Plan 2 examines organizational and operational implications in terms of the need for personnel having particular characteristics; such environmental factors as number, type and location of terminals and hours of system availability; and operational procedures, for example, for ensuring the security of data. Questions are: How much training of what types is required for which users? What is the need for system availability during hours other than 7 a.m. to 7 p.m. on weekdays? How often should

file backup tapes be made and how long should they be kept? What are the appropriate qualifications and job description for the system manager?

Evaluation Plan 3 attempts to evaluate costs and benefits of the prototype system. We are particularly interested in costs to users in terms of time and frustration, and system operating costs such as those for maintenance and supplies. We are attempting to estimate the benefits in terms of investigator's time saved for other activities, improved quality and quantity of research, cost reduction and minimization of invalid data analyses. To do a precise assessment of benefits, particularly regarding the impact of the system on clinical research, would require both more data and a longer time span than is possible in the present project. Thus, the primary focus of this plan is on short-term benefits.

Some evaluation data are collected automatically as the CLINFO prototype system is used. The remaining data are collected through interviews, observations and from records kept by the system manager. In almost all cases of manually collected data there are data collection instruments and forms to promote consistency and completeness in data recording. Evaluation data are forwarded to the project's computer scientists who organize and analyze them

with the assistance of their CLINFO system. As data are collected, users are identified by codes (rather than by recognizable identifiers) and any sensitive information is deleted prior to sending data from a clinical research site to the computer scientists. Of course, reported results are statistical and do not identify individual users or patients.

A major source of data about how and when the CLINFO prototype system is being used and by what categories of users is a transaction log. This is a comprehensive log of user-system interactions that is collected automatically on magnetic tape as the system is used. Transaction logs are analyzed to determine the overall degree and duration of system utilization each day and to determine the degree to which system features are utilized by principal investigators, fellows, technicians and other categories of users. Those logs can also be used to establish the correspondence between sequences of interactions and both user problems and system errors.

The system manager at each site keeps records which include costs for supplies and services, descriptions of all hardware and software failures, reports summarizing his allocation of time to various duties, summaries of user progress, and descriptions of all user-initiated requests for modifications to the system. In addition, the system manager records all system hardware or software

behavior which might be considered unusual.

In addition to the CLINFO personnel normally at each site, a CLINFO "system representative," who is one of the computer scientists, visits each site at regular intervals. Among his duties is interviewing each user before he begins to use the system and after he completes a research study using it. The pre-use interview is based on a questionnaire intended to elicit background information, expectations for the use of CLINFO and a description of a study to be investigated using it. The post-use interview elicits information about the completed study, including its data volume, problems encountered using CLINFO, and the costs and benefits perceived by the user.

PRELIMINARY RESULTS

It is currently November 1976 and our design, development and evaluation efforts are scheduled to be completed in about one year. CLINFO prototype systems have been operating at the Baylor College of Medicine and the University of Washington since January 1976 and September 1976,respectively. Software development has been on schedule throughout the project; Release 2 was distributed in October. The hardware has been acceptably reliable. Although we

have little objective evaluation data at this point, the prototype appears to meet the major needs of a variety of medical specialists at both sites. At the first site, system utilization has risen to about 200 user hours a month. Because of these early positive indications and because a third site must be activated soon if we are to learn much from it, it has already been decided to install a prototype system at a third clinical research site. The planned installation date there is early 1977.

We have already learned a great deal from user feedback. Consequently, we have made major changes in the system design even though the original design accommodated users' needs reasonably well. The units of time quantization initially provided by the prototype were too restrictive so we had to change it to provide for times ranging from minutes to years. The prototype was originally designed such that users would store original (by their own definition) data in the study data file, retrieve them and then compute and store derived results in worksheets. Because of the flexibility and power of the study data file, users want to store derived data there also and so we have subsequently provided for this. Users have asked us to change our implementation

priorities. For example, we have added nonparametric statistical tests and frequency counts, have provided for data sorting much earlier than planned, and have deferred the implementation of more complex analyses such as two-way analysis of variance and step-wise linear regression. Whereas we were initially unsure about the general utility of computer-based procedures to assist with radioimmunoassays, users have convinced us of the widespread need for such procedures. Users have also suggested numerous detailed changes in the system's design and, as a result, it has become more convenient to use. Fortunately, because it was our initial intent to develop a prototype system that could be easily modified, and we designed the software with this in mind, it has not been difficult to accommodate these changes.

Our experience has also resulted in changes to the hardware specifications. Although the minicomputer hardware, together with storage cabinets and a work table, can fit into a room 14-foot square or so, it is sometimes difficult to find this amount of space in a hospital and to provide the required air conditioning, and power. We initially provided two user terminals with hardcopy devices and two without; however, utilization of particular terminals suggested and users' stated needs further confirmed a strong requirement for recording the system's output on paper. Now each user

terminal is provided with a hardcopy device. The prototype produces (30 x 60 resolution) scatterplots and histograms on the display terminals and the hardcopy devices can draw lines between graphed points at higher resolution. These features are used extensively but we are still uncertain about the need for more expensive, line-drawing graphics terminals. Such terminals, together with compatible hardcopy devices, certainly would be well received but it is not clear that they are justified at their present cost.

The system manager, who introduces the system to users, answers their questions, writes special-purpose programs for them, and operates and maintains the system, clearly has an essential role. However, although the present system managers are very busy, we do not yet know how large a job this will be when our evaluation efforts end, the software becomes more powerful, and the hardware becomes simpler. The system representative performs the necessary functions of giving the system developers first-hand knowledge of users' needs, providing users and on-site project personnel with new information and insights, and transferring information from one CLINFO site to another. These functions may become less important as the system becomes more stable, but they become more important as the number of users and the number of sites grow.

In conclusion, we feel the project has been successful to date and that this can be attributed to multidisciplinary requirements analysis, step-by-step prototype development, and multi-site, multi-user system evaluation. During the next year, we look forward to continued evaluation, particularly of costs and benefits; development of specifications for a system useful to a broad segment of the clinical research community; and planning for its commercial development and distribution.

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