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An Ethnographic Study of Collaborative Clinical Trial Protocol Writing

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Abstract

Clinical trial protocol documents play an important role in clinical research. However, clinical protocol writing remains a complex and relatively un-studied process. Protocols are often written by teams of people, yet little prior research has captured the problems or analyzed the collaboration support needs of protocol writers. Here we present the results of an initial ethnographic study into the clinical trial protocol writing processes at a representative cooperative clinical trial group funded by National Cancer Institute (NCI). We analyzed the collaborative nature of the writing process, identified common problems, derived information and communication support needs of collaborative clinical protocol writers, and provided recommendations to streamline the process. We believe that this paper contributes useful implications for the design of future collaborative clinical protocol writing tools.

Keywords

Clinical Protocols, Needs Assessment, Cooperative Behavior, Group Processes, Collaborative Writing

Introduction

Protocol documents are essential for carrying out clinical trial research. These documents are large and complex, containing comprehensive information on many aspects of the conduct of clinical trials, including specifications of good medical practices, disease-specific clinical knowledge, statistical considerations, patient eligibility, and treatment specifications. The validity, accuracy, and coherency of the document can have a huge influence on the treatment administration and on the interpretability of the research results. If we wish to improve the quality of clinical trial protocols, we should improve the clinical trial protocol writing process. Unfortunately, very little prior research has looked into this writing process to uncover how different sections are created and integrated into one consistent protocol. As van der Lei pointed out, there has been little study of the clinical trial protocol writing process[1].

In the United States, a large number of clinical trial protocols are developed through the clinical trials cooperative group program.[2] Cooperative groups include researchers, institutions, and cancer centers throughout US, Canada, and Europe. They place more than 22,000 new patients into cancer research trials each year [2]. These cooperative groups follow standard protocol development processes and use a group of geographically distributed experts, to design and conduct large-scale trials in multi-institutional settings. This sort of collaboration adds challenges for informatics researchers aiming to streamline and improve the protocol development process [3].

Without studying the collaborative process, it is hard to design and build "human-centered" tools that might help clinical trial protocol writers. We must first understand who is involved in the collaborative protocol writing process, what their roles and responsibilities are, how they collaborate and coordinate their work, what their tool support needs are, etc. Some medical informatics tools have been designed to support clinical trial protocol authoring [4,5,6], but these tools are designed for a single clinical trial protocol author, and are inappropriate for the collaborative protocol development process. Our long term goals include building more appropriate tools that do match the natural collaborative protocol writing process, and will therefore be more readily accepted by real-world users. In general, medical informatics system designers sometimes omit the important first step of a careful study of users and current work practices. In our work, we aim to avoid such a mistake, and therefore have carried out a lengthy study of the real-world collaborative protocol-writing process at the Southwest Oncology Group (SWOG). In this paper, we describe some of the problems from this study and their implications for the design of collaborative protocol writing systems.

Study Methodology

SWOG is a major adult cooperative cancer research group funded by the NCI. It is committed to high standards in clinical trial protocol development and opens about 30 new protocols every year. Protocol development within SWOG is a collaboration among study statisticians, physicians leading the scientific effort (clinical researchers), individuals responsible for protocol editing and coordination (protocol coordinators) and an individual who coordinates all protocol development (protocol manager). The statistical center for the group is in Seattle, Washington; the protocol coordination occurs at the Southwest Oncology Group Operations Office in San Antonio Texas; and clinical researchers can be from any one of hundreds of SWOG affiliated institutions in the United States.

We selected SWOG as a representative organization for our study of the protocol writing process. Our ethnographic study at SWOG included both interviews and observational studies.

Interviews

We conducted ten in-person interviews with SWOG personnel. We recruited our study subjects through word-of-mouth and email invitations. To cover the diversity of expertise in the clinical protocol writing process, we selected three statisticians, three protocol coordinators, three clinical researchers, and one protocol manager.

We conducted a one-hour interview with each subject. We inquired about their previous clinical protocol writing experiences, the activities they are involved in, and their responsibilities. Below are some selected questions from our interviews. These questions help us to understand real scenarios in the collaborative writing process.

1. What are the major steps in the writing process?
2. Who are involved in each step and what is their work?
3. What is the most difficult part of the writing process?
4. What tools or assistance do protocol writers get?
5. What are writers' unmet needs?
6. How do protocol writers coordinate the group work?
7. What is the protocol review process like?

Observational Studies

We observed communication patterns of the clinical protocol development process by tracking a portion of email communication and by observing the SWOG protocol review committee (PRC) meetings. We collected over 70 emails over a five-month period containing comments and questions about a single ongoing protocol writing effort. We also collected comments from the PRC and statisticians concerning about 25 other on-going protocol writing efforts. These documents resulted in a database of over 1200 individual comments. In general, over a period of about a year, we collected documents and email messages containing protocol drafts, protocol review comments, organizational protocol development policy, standards, and protocol writing guidelines from SWOG.

Study Results

These interviews and observation study data give us an understanding of the protocol writing process. Below we describe a protocol writing model, its collaborative nature, common problems in the writing process, and our recommendations for solving these problems.

A Writing Model

A simple model for protocol writing consists of the following four steps in order: (1) submit an initial proposal, (2) generate the first complete draft, (3) iteratively review and revise the drafts, and (4) submit final draft to the NCI for approval. However, the details within step #3 are quite complex. There are many participants that may wish to review a protocol, and SWOG has established processes that describe how reviewing and revising should occur and who should carry out which activities. Figure 1 shows two tables listing some of the activities and participants in the protocol writing process. Although some of the links between participants and activities are obvious (e.g., a protocol manager tracks the development process), other relationships are dynamic and complex. In this paper, our focus is not on these workflow details, but rather on the collaboration challenges resulted from the complex workflow and implications for system design.

Activities	*Participants*
Create an initial draft	Statisticians
Edit a draft	Clinical experts
Comment on a draft	Organizational protocol coordinator
Resolve controversial comments	Protocol managers
Incorporate comments	Organizational protocol review committees (PRC)

Figure 1 - Typical activities and participants in collaborative protocol writing

Collaborative Protocol Writing

There are several characteristics of clinical trial protocol writing that affect the collaboration among participants. First, protocol writers are a fairly loosely coupled team. They are affiliated with different organizations and are spread apart geographically. In addition, the team is often dynamically formed by the organization; team members may not have known each other prior to working on a particular protocol.

Second, due to their variable schedules, protocol writers usually work asynchronously. They rely on emails to coordinate group work and to distribute protocols. For better coordination, SWOG and most cooperative groups adopt a "single scriber strategy",[10] where only one writer (in SWOG's case, the protocol coordinator) actually changes the protocol document and releases new versions. Others engage in discussion of the ideas, and only send comments and suggested changes to the single scriber.

Third, protocol writers have widely different backgrounds and areas of expertise. For example, clinical researchers are responsible for scientific validity, statisticians for the statistical basis of the design, and protocol coordinators for using current standards of wording

Finally, assembling a clinical trial protocol requires collecting information from a variety of heterogeneous sources. These sources include old protocols, published studies, organizational protocol standards or policies, and conversations among clinical trial experts in emails, telephone calls, or fax materials. Thus, protocol writers need to manipulate many sources, and have a broad collaboration with multiple parties.

Problems and Recommendations

We observed a number of problems in the protocol writing process. These affect the efficiency of the process, and we hope they can be alleviated with appropriately designed tools for improved communication. Thus, we both describe the problems, and provide our recommendations for solutions.

Insufficient Communication

Protocol writers use email as their most used communication method. Although email has advantages for asynchronous collaborators, it also has limited support for the sorts of communication needed by protocol writers. The inefficiency of email in protocol writing is reflected in the following ways:

- Forwarding emails with attachments of protocol drafts introduces work with a high cognitive load. A protocol coordinator must track these versions and keep straight who is working on what. If a protocol coordinator receives many attachments from many collaborators on several different protocols, she can become overwhelmed.
- During the writing process, there may be many conversations and debates, but standard email clients do not provide good support for threaded discussions. Therefore, it is hard to track the topics and the idea flow in emails.
- The single scribe model can lead to the protocol coordinator becoming the hub for all communication. Rather than reviewers or clinical researchers contacting each other directly, questions and comments are often relayed indirectly through the protocol coordinator. Problems result from this structure: some questions are asked repeatedly, perhaps by different participants; some answers conflict with each other, and the participants may not notice this conflict. Also, there is no good mechanism to notify participants when their questions or comments have been resolved, or to help them be aware of specific questions that may be addressed directly to that participant. The following example comment highlights these problems.
- *"Hello A, Just an update, I had sent the draft to X and Y as you requested. I have heard back from Y but not X. I don't know what the situation with X is, I'm going to go ahead and incorporate Y's comments and send you a draft back within the next couple of days. Did Z have any further comments regarding the draft? Thanks, B"*
- It is difficult for protocol writers to find out "who knows what I don't know" and "where to get more information or help". As mentioned above, protocol writers might not be familiar with each other; they also do not know each other's schedule or availability when they need help.

Recommendations: To solve these sorts of problems, it would be helpful to keep a persistent log of threaded discussions for a protocol and also to provide some mechanism for automatic notification. Instead of using email attachments to distribute copies of the protocol, there should be a shared file space for all participants. Also, threaded discussions within the writing group should be shared in a knowledge pool instead of being kept in private emails. We recommend a design that enhances the "awareness" of participants—an understanding of the activities of others and the work context. For example, if a protocol writer or reviewer wishes to ask a question, she should be aware whether or not an appropriate expert is available, and could perhaps make direct contacts.

Inefficient Protocol Review Process

Protocol review is an important step in the writing process to ensure the quality of the protocol document. Currently, reviewers often print out the protocol document, write comments on a separate sheet or in a separate document, and then email these comments to the protocol coordinator. Comments are communicated separately from the protocol documents. Therefore, to specify a comment, reviewers must include extra text to specify precisely the context for their comment. As an example, to suggest a change of four words, a reviewer wrote:

> *"...sec 2, second paragraph, first sentence, suggest 'over the use of single agents' instead of 'over the sequential use of them' since we decided against a cross-over."*

All participants who work with such comments, must access multiple artifacts simultaneously: the comments, the older document version, a newer document version, and any personal notes or responses to the comment. The protocol coordinator (the single scriber) might take one of following action in response to a comment: modify the protocol, forward the questions to appropriate people, respond to the comment via a separate email, or search for standards or old protocols that include the answer. This complexity makes it difficult for protocol editors to process comments efficiently.

Recommendations: A web-based collaborative reviewing system is a potentially promising solution. Such a system could support threaded comments so that reviewers and writers could see each other's reactions more immediately. Collaborative annotation technology could be applied to allow protocol reviewers to make in-line comments, so that their comments are attached directly to the appropriate context in the document. While email could still be used, a collaborative tool should also support more direct communication, reducing the number of email attachments distributed among participants.

Poor Version Control Support

To avoid confusion caused by multiple versions, current SWOG practice is for the protocol coordinator (the single scriber) to keep the current version of a protocol electronically, whereas all past versions of the protocol document are saved as hard copies. This makes it difficult for users to find information from previous document versions, and as a result, each protocol has relatively few released versions. In addition, when a new version of the document is produced, the editor must announce to the collaborative team what changes have been made, which problems or issues still remain, and who still needs to work on which sections. Thus, information about versions is buried in email, making it difficult to track at a later date if there are problems. In our short-term observational study, there was one instance where

collaborators were working on the wrong version. However, when this does happen, the cost in wasted time is high.

Even when there is no confusion about versions, the extra communication overhead can be expensive and frustrating. Below is an example of an email message that shows both the need to explain what is in a new version, and an example of the difficulty in getting prompt responses from participants:

> *"Hello A, Attached below is the latest version of the protocol. I am also forwarding the suggestions made by the stat center, that I have already incorporated. I never heard from X. Please feel free to call/email with further comments and suggestions, B"*

Recommendations: A protocol document repository with version control is a promising solution. Such a system could provide shared access to all versions of a protocol under development. A single source of protocols could ensure that everybody gets the appropriate version at any moment. Also, these versions could be directly annotated or linked to information about which comments or issues have been resolved.

Ineffective Group Coordination

Because people working with SWOG belong to different organizations, they usually have separate, additional work beyond the effort of protocol development. For example, a clinical researcher might also be a professor; he has clinical, mentoring, and administrative duties, in addition to research. Protocol writing is rarely a top-priority job; therefore, it is often difficult to schedule protocol-writing tasks. Because of competing outside tasks, participants may quickly send an email response, and then move on to other duties without paying close attention or noting a lack of response from the recipient. Participants place more urgency and priority on protocol writing only when protocol deadlines are enforced.

A significant complication of this issue is that the participants involved in protocol development have different levels of status. There is a hierarchy where the clinician researcher is usually treated as the highest-level authority. Thus, it is often hard or impossible for others (e.g., protocol editors) to make demands on these researchers.

Recommendations: An ideal solution to this problem is to facilitate automatic coordination by providing group awareness and shared feedback among protocol writers. Instead of relying on explicit reminders, group awareness could enable protocol writers to naturally notice each other's work. In a separate manuscript, we provide examples of how awareness mechanisms might work for a collaborative protocol-writing system.[11].

Challenging Integration of Heterogeneous Input

A clinical trial protocol is a clinical research design as well as an operational manual; therefore, it must satisfy experts from different backgrounds and disciplines. For example, a protocol must have valid statistical considerations, good medical practice descriptions, and ethical considerations for patients. It must also serve as a detailed manual for health care providers. Thus, a clinical protocol must integrate knowledge from heterogeneous information sources in a consistent manner. These knowledge sources include: 1) authorized clinical knowledge and statistical knowledge from the clinical researcher and the statistician; 2) available updates on drug information from pharmaceutical companies; 3) critiques of the written protocol from the Protocol Review Committee (PRC), Institutional Review Boards (IRB), and the Cancer Therapy Evaluation Program (CTEP); and 4) current health care policy and standard practice, usually from CTEP. All these knowledge sources comprise important input for the protocol. Integration of these heterogeneous sources is a challenge for protocol writers.

Recommendations: To achieve a coherent integration of heterogeneous inputs, a system might be developed for knowledge-based consistency checking. Such a system could provide semi-automatic methods for improving the consistency of the protocol.

Difficult Knowledge Retrieval

Many parts of a clinical trial protocol come from old knowledge or standards defined by SWOG. However, there is no support for efficient retrieval and maintenance of such valuable knowledge. Usually, a new protocol is related to other protocols: some share the same patient population; some share the same drug information; and some are a direct follow-up to a prior successful study. Currently, retrieval of all these relevant documents depends on a protocol editor's good memory and information retrieval skills. This leads to variability and inefficiencies during protocol writing.

Recommendations: To solve this problem, it would be useful to provide a clinical trial design library with reusable and sharable guidelines, templates, and standard wordings. This library could be provided as a single source of information accessible by all protocol writers. Such a library would also need to be equipped with version control mechanism because standards are continually evolving. It could potentially solve problems resulting from heterogeneous information sources.

Implications for System Design

Clinical trial protocol writing is a complicated multi-user work process. Traditional decision support tools for trial design did not satisfy the needs of protocol writers, especially in the aspects of group communication, protocol version control, knowledge reuse, information integration, and group work coordination. All these greatly affect the efficiency of the protocol development process. Based on this analysis, we summarize the unmet needs of clinical trial protocol writers:

- Awareness of the shared workspace and individual contributions to the protocol under development
- A sharable repository of clinical trial protocols and comments with version control support
- A reusable knowledge library for protocol standards with version control support
- An efficient collaborative reviewing tool

Currently, email systems, instant messengers, and other modern communication tools are readily available. However, these generic tools cannot by themselves provide the communication support for the practice of clinical trial protocol writing that we observed. For example, Shortliffe et al. demonstrate that emails are only effective for collaborative work after participants have

shared background knowledge and have met face-to-face [12]. Given our analysis and the findings above, we believe that we can now do an improved job of designing systems that more appropriately meet the users' needs. In a separate manuscript, we report on our preliminary development of a system that meets some of these needs [11].

Summary and Discussion

In summary, we consider major problems in the clinical trial protocol writing process to be insufficient communication, inefficient protocol review processes, poor version control support, a lack of easily accessible reusable knowledge, ineffective group coordination, and the challenge of integrating heterogeneous information sources. All of the above problems could contribute to clinical trial protocol errors and delays [13].

For informatics, the main result of our ethnographic study is the demonstration of the collaborative richness and complexity in a medical domain. We suggest that groupware tools that support user awareness and improved work coordination are the right approach for this domain. However, these cannot be appropriately designed or built until we have first understood the work setting, including the user roles, activities, and the work processes that connect the participants. More generally, we believe that this lesson in understanding the details of collaborative work is of value in many medical settings that involve technology and collaboration [14].

We acknowledge some limitations of our study. First, individuals work in many different ways. Our selected study subjects may therefore not have provided a complete picture of the writing process. Second, our study has been limited to a single organization: SWOG. However, because SWOG is representative of NCI cooperative groups, we believe that most of our results can be generalized to other cooperative groups.

As multidisciplinary collaboration in both clinical and research settings is becoming a common aspect of contemporary health care, strategies to enhance inter-professional interactions can facilitate collaborations. With this study, we detailed the collaborative nature of the clinical trial protocol writing process, and we provide recommendations for solutions to existing problems in this collaborative process. We hope these suggestions can inform the design of future clinical trial protocol writing systems.

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