COORDINATING CENTER MODELS PROJECT*

A Study of Coordinating Centers in Multicenter Clinical Trials

I. DESIGN AND METHODS

Part 1 of 2

Prepared by the

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ABSTRACT

The Coordinating Center Models Project (CCMP) is a three-year, contract-supported project sponsored by the National Heart, Lung, and Blood Institute (NHLBI). The NHLBI sponsors a number of large multicenter clinical trials, each of which includes in its organization a coordinating center with responsibility for receiving, processing, and storing accumulating study data and performing other coordination functions. Multicenter clinical trials are complex operations expensive to design and carry out. Consequently, the functions of the coordinating center are also complex.

Coordinating centers and project offices of ten multicenter clinical trials, all sponsored by institutes of the National Institutes of Health, have participated in the data collection activities and the development and review of suggestions and recommendations emanating from the CCMP. A series of reports from the CCMP is in preparation. This first report deals with the design and methods of the project.

COORDINATING CENTER MODELS PROJECT

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I. DESIGN AND METHODS

by the
Coordinating Center Models Project Research Group*

1. INTRODUCTION

During the past 14 years the National Heart, Lung, and Blood Institute (NHLBI) has supported a number of large-scale multicenter clinical trials. Each of these trials involves, or has involved, treatment and follow-up of hundreds or, more often, thousands of individuals at a cost of many millions of dollars. Among the NHLBI trials, the number of participating clinical centers has varied from as few as five to as many as 53. Other typical centers included in the organizational structure of these clinical trials are the project office; one or more central units with responsibility for coding findings observed in documents such as electrocardiograms or X-ray films; one or more central laboratories; other centers with special tasks such as drug procurement and distribution; a coordinating center; and various administrative committees and review groups. Coordinating centers in multicenter clinical trials have traditionally played a major role in the success of such trials, beginning with the early planning stages and continuing throughout recruitment, application of the therapy or other test procedures, follow-up, closeout of patient follow-up, final analysis, and publication of findings. As recipient, editor, analyst, and custodian of the study

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*See page ii for membership of the Research Group and CCMP Committees.

data, the coordinating center has had vested in it a large responsibility for the conduct of the trial.

The role of the coordinating center in a multicenter clinical trial is a complex one. Although its unique function in the clinical trial organization is the central collection, storage, and analysis of accumulating study data, in many ways, as indicated by its name, this center is the focal point of the clinical trial. To serve the various functions assigned to it, the coordinating center must interact with all other centers participating in the clinical trial as well as with all of the various administrative and review committees.

Among the institutes of the National Institutes of Health (NIH) which sponsor multicenter clinical trials, NHLBI has by far the largest investment. According to cost data included in the 1975 NIH Inventory of Clinical Trials,[1] the 12 multicenter clinical trials sponsored by NHLBI during 1975 accounted for 83% of the total NIH support for multicenter trials during that year. The proportion of the total cost of a trial associated with the coordinating center is generally in the range of ten to fifteen percent.[2] Recognizing the important role of the coordinating center and the need for more research into coordinating center methodology as it relates to multicenter clinical trials, in June 1976 NHLBI awarded a three-year contract to the University of Maryland School of Medicine for "Development of a Coordinating Center Model for NHLBI Clinical Trials" and thereby initiated what has become known as the Coordinating Center Models Project (CCMP). Since 1963 the University of Maryland at Baltimore has housed the coordinating centers for several large clinical trials. Experiences in operating these coordinating centers have stimulated interest within that University in

research in the area of design, conduct, and management of multicenter clinical trials.

The authors of the Request for Proposals (RFP) which initiated the CCMP[3] anticipated that findings "will be utilized by NHLBI and its Coordinating Centers to improve the effectiveness of NHLBI's ongoing clinical trials, of future clinical trials, and of clinical trials generally." They indicated that the annual costs of NHLBI coordinating centers then totalled more than four million dollars with every prospect of increasing in the future because of inflation of the economy and "public resolve to deal finally and effectively with heart and vascular disease." The authors continued by stating that the project was expected to have "a significant and constructive impact" on:

- The planning, organization, administration, operation, and evaluation of coordinating centers;
- The interrelationships among NHLBI program offices, clinical centers, laboratories, coordinating centers, and advisory, executive, working, and review committees;
- A general understanding of the contributions of each of the principal disciplines brought to bear on coordinating center activities;
- The number of institutions that respond effectively to NHLBI's requests for proposals to establish coordinating centers;
- The body of knowledge dealing with the conduct of clinical trials and professional specialization and training in this area.

Specific objectives of the project were stated to be:

- Formulation and elucidation of coordinating center policies, objectives, roles, responsibilities, and authority, both independently and as related to other study groups;
- Establishment of coordinating center cost and other management data for initiating, planning, operating, and evaluating clinical trials;
- Reduction in duplication of effort, relearning, and redevelopment of coordinating center technology and methods.

These goals imply a broad spectrum of tasks ranging from the compilation of basic management data to the exploration of much deeper philosophical issues which have implications for all collaborative research ventures.

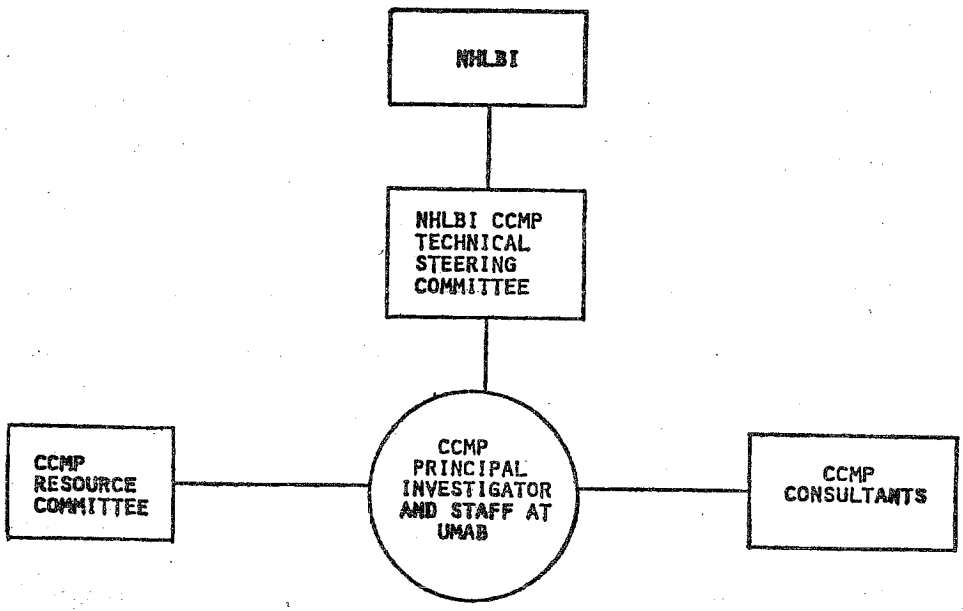
A topic much discussed during the early months of the CCMP was the definition of a "coordinating center model" as used in the RFP which initiated the project. The original proposal which was made in the response to the RFP and which survived those discussions was: 1) that a set of suggested procedures and recommendations be developed which would deal with coordinating center organization, management, and operation; 2) that these recommendations be presented in reports which would contain descriptive information, a discussion of the issues, supporting data and opinions, and the conclusions of the CCMP Research Group. The collection and summarization of descriptive data were considered to be extremely important, not only to support the conclusions of the CCMP but also to provide an information base since such data had not been compiled previously.

The intention of participants in the CCMP is that suggestions emanating from this project emerge as guiding principles, to be considered during the design and organization of a trial and its coordinating center, and not as rules or constraints to be imposed upon study centers and investigators. Since the CCMP Research Group cannot anticipate all situations which may arise, recommendations to be made in later reports from this project will be posed in general terms, to be modified, adapted, reshaped, or duly considered and rejected by those who are charged with meeting specific needs in future trials.

The purpose of NHLBI in sponsoring the CCMP has not been to evaluate existing coordinating centers or existing clinical trials. Data collected from coordinating centers by the CCMP Research Group has been used to describe these units as they have evolved with a long-term goal of developing historical norms to facilitate selection and evaluation of similar centers in future trials.

2. ORGANIZATIONAL STRUCTURE OF THE COORDINATING CENTER MODELS PROJECT

The organizational structure of the CCMP is depicted below.



The sponsor, NHLBI, communicates with the Research Group at the University of Maryland through the CCMP Steering Committee which is comprised of the project officer for the CCMP and other NHLBI-designated representatives.

The Research Group is assisted and advised by special consultants and by the CCMP Resource Committee, a group whose membership contains representatives from the coordinating centers for six of the ten clinical trials studied, the CCMP project officer, the principal and co-principal investigators for the CCMP, and other individuals with clinical, statistical, and computer science expertise as well as experience in planning and conducting multicenter clinical trials (See page ii for a list of members of the CCMP organization). The Resource Committee members have played a major role in the project since they have reviewed the activities, facilitated the data collection efforts, and reacted to suggested procedures and recommendations as they have been developed by the Research Group.

3. STUDIES EXAMINED

The RFP which resulted in the creation of the CCMP designated that six of the multicenter clinical trials supported by NHLBI were to be studied under CCMP auspices. Since the RFP was issued, three other large multicenter trials have been initiated by NHLBI. Seven of these nine studies participated in the data collection activities of the CCMP and are listed in Part A of Table 1. Neither the Multicenter Investigation of Limiting Infarct Size nor the Beta-Blocker Heart Attack Trial was considered suitable for inclusion because the coordinating centers of those studies were in an early stage of activity. The CCMP Research Group considered a number of multicenter trials sponsored by other institutes of NIH for study. Those trials which participated in the data collection activities are listed in Part B of Table 1.

As indicated in Table 1, the ten trials reviewed vary considerably in size, whether size is measured in number of patients or number of collaborating centers. The study phase ranged from planning and protocol development to post closeout. Four of the ten studies were in the recruitment phase of activity; four others were in the treatment and follow-up phase. A later report from the CCMP will address the different demands on the coordinating center during each phase of a clinical trial.

Each of the clinical trials participating in CCMP activities has certain unique organizational and design features. The Lipid Research Clinics Coronary Primary Prevention Trial is a clinical trial of lipid-lowering medication which is part of the Lipid Research Clinics (LRC) Program. The coordinating center for this trial serves the total LRC Program, which consists of several additional large studies. The Coronary Artery Surgery Trial (CAST) is also a component of a larger study, the Coronary Artery Surgery Study (CASS). CAST is a randomized clinical trial of the effectiveness of coronary artery bypass surgery in comparison to medical treatment in prolonging life.

The Coronary Drug Project (CDP) is the oldest of the trials examined. This trial, for which patient follow-up is complete, compared the effectiveness of five lipid-lowering drug treatments with placebo in secondary prevention of myocardial infarction in men, that is, in preventing the recurrence of myocardial infarction among men who had already had at least one myocardial infarction prior to entry. An offshoot trial from the CDP, the Coronary Drug Project Aspirin Study, was a precursor of the Aspirin Myocardial Infarction Study. The latter study was designed to

TABLE 1

MULTICENTER CLINICAL TRIALS PARTICIPATING IN THE CCMP

PART A. NHLBI-SPONSORED TRIALS

Name	Abbrev.	Location of Coord. Ctr.	No. of Participating Ctrs.		No. of Patients	Coordinating Center Director	Project Officer (1978)	Study Phase (1978)
			Clinical	Other				
*Aspirin Myocardial Infarction Study	AMIS	Univ. of Md. Baltimore	30	4	4,524	William F. Krol, PhD	Wm. Friedewald, MD	Treatment and Follow-up
*Coronary Artery Surgery Trial	CAST	Univ. of Wash. Seattle	16	2	800+	Lloyd Fisher, PhD	Michael Mock, MD	Recruitment
*Coronary Drug Project	CDP	Univ. of Md. Baltimore	53	3	8,341	Paul L. Canner, PhD	Larry Friedman, MD	Post-Closeout
*Hypertension Detection and Follow-up Program	HDFP	Univ. of Texas Houston	14	5	10,940	C. Morton Hawkins, ScD	Gerald Payne, MD	Treatment and Follow-up
*Lipids Research Clinics Coronary Primary Prevention Trial	LRC-CPPT	Univ. of N.C. Chapel Hill	12	6	3,810	O. Dale Williams, PhD	Basil Rifkind, MD	Treatment and Follow-up
*Multiple Risk Factor Intervention Trial	MRFIT	Univ. of Minn. Minneapolis	20	4	12,866	Marcus O. Kjelsberg, PhD	Charles Kaelber, MD	Treatment and Follow-up
Study of Antenatal Steroid Treatment on Respiratory Distress Syndrome	RDS	Research Triangle Inst. Durham, N.C.	5	3	600+	Kenneth Poole, PhD	Bitten Stripp, PhD	Recruitment

PART B. TRIALS SPONSORED BY OTHER INSTITUTES OF NIH

Name	Abbrev.	Location of Coord. Ctr.	No. of Participating Ctrs.		No. of Patients	Coordinating Center Director(s)	Sponsor	Project Officer (1978)	Study Phase (1978)
			Clinical	Other					
Diabetic Retinopathy Vitrectomy Study	DRVS	Univ. of Minn. Minneapolis	13	3	826+	Glenn Bartsch, ScD	NEI	Philip Dern, MD	Recruitment
National Cooperative Gallstone Study	NCGS	George Wash. Univ. Bethesda, Maryland	10	7	900+	John M. Lachin, ScD Lawrence W. Shaw	NIAMDD	Sara Kalser, PhD	Recruitment
National Cooperative Dialysis Study	NCDS	Harvard Univ. Boston	3	5	200+	Raymond K. Neff, ScD	NIAMDD	Robert Wineman, PhD	Planning and Protocol Development

*Designated for review in the RFP for the CCMP

+Projected

test the effectiveness of aspirin in the secondary prevention of myocardial infarction.

The two largest clinical trials participating in the CCMP are the Multiple Risk Factor Intervention Trial (MRFIT) and the Hypertension Detection and Follow-up Program (HDFP). MRFIT was designed to test the effectiveness of intervening to modify three major risk factors - hypertension, hypercholesterolemia, and cigarette smoking - in reducing the risk of premature mortality. The primary goal of the HDFP is to compare the effectiveness of a systematic approach of sustained anti-hypertensive therapy with usual care as measured by total mortality among two groups of hypertensives in community-based populations.

The Respiratory Distress Syndrome Study is the youngest of the NHLBI-sponsored clinical trials reviewed. This clinical trial was designed to evaluate the efficacy of steroid therapy administered to mothers during labor in preventing respiratory distress syndrome in premature infants and to evaluate the side effects of such therapy.

The three clinical trials sponsored by other institutes within NIH participated in the CCMP with the knowledge and approval of the respective institutes. The Diabetic Retinopathy Vitrectomy Study, sponsored by the National Eye Institute, is testing the effectiveness of early versus delayed vitrectomy for preserving vision in eyes which have experienced diabetic vitreous hemorrhage. Both the National Cooperative Gallstone Study (NCGS) and the National Cooperative Dialysis Study (NCDS) are sponsored by the National Institute of Arthritis, Metabolism, and Digestive Diseases. The NCGS is evaluating the efficacy and safety of chenodeoxycholic acid in the dissolution of gallstones; the NCDS is comparing outcomes in

+Projected

patients with chronic uremia maintained on several different hemodialysis programs.

Information concerning management and operation of the different studies and their coordinating centers was obtained for review by the CCMP Research Group in several different ways. Both the project office staff and the coordinating center staff of each of the participating studies recorded information about the study on standardized self-administered forms. The data collection forms will be described in Section 5; copies of each are included in Appendix A. Information obtained on these forms was supplemented by meetings with project office staff, coordinating center staff, and clinical center personnel as well as by review of study documents such as manuals of operation, study forms, procedures manuals for the coordinating centers, and study publications.

4. PRINCIPLES OF OPERATION

Several principles have guided the design and conduct of the CCMP. These principles may be stated as:

- Systematic data collection and documentation of information obtained;
- Verification of information collected;
- Confidentiality of information collected;
- Review of findings and conclusions of the CCMP Research Group by the other groups and individuals involved in the project.

Systematic data collection, the first principle, was considered a necessary provision for minimizing both observer and responder bias. To

facilitate systematic data collection, standardized forms were developed. As noted above, copies of all forms are included in Appendix A.

Whenever possible, CCMP personnel who were selected to conduct interviews and discussions with staff members of the individual studies and coordinating centers were chosen from those who had no prior or current involvement in the particular study. This procedure was followed to minimize the possibility of introducing bias into the findings. For example, the principal investigator of the CCMP is a member of the CASS Policy Advisory Board. By virtue of that role, he did not participate in the CCMP visit to the CAST coordinating center. The visit was made by two members of the CCMP Research Group who had no role in either the larger study (CASS) or the clinical trial (CAST).

In recognition of different points of view among those questioned and interviewed, verification of information was carried out whenever possible. For example, general descriptive information for each study was first obtained from the study project officer. Information supplied by that individual was verified by the director of the respective coordinating center who corrected, amended, or amplified it if he thought appropriate. Substantive differences in the factual information supplied were reconciled by the Research Group when necessary by noting the differences and discussing them with the project officer and the coordinating center director.

Even some information originally considered by the CCMP Research Group to be factual or "hard" proved to be surprisingly amenable to differing interpretations. For example, total annual expenditures of the coordinating center during each year of operation was considered to be a straightforward request. However, expenditures may be interpreted

differently by the individuals in the sponsoring institute who disperse the funds, the director of the coordinating center who is responsible for use of the funds, and the individuals in the parent institution business office who receive the funds and account for their use.

Safeguards to preserve confidentiality were regarded as an important aspect of the data collection process. Forms completed by staff of the project offices and coordinating centers contained both factual information and subjective evaluations which are not available through public channels of communication. Anonymity of the providers of sensitive information has been and will continue to be preserved in presentations or publications of findings from the CCMP. Completed data collection forms are stored in locked files; access is limited to personnel in the CCMP Research Group.

The collaborative nature of the CCMP produced some of the problems common to many collaborative ventures. One of these concerned the equitable distribution of credits and recognition accruing from the project. A group authorship policy was adopted for all publications and presentations resulting from work done under the aegis of the Coordinating Center Models Project. Individuals associated with the project have been identified in each paper and report, but individual members of writing teams have not been singled out for special recognition.

A two-stage editorial review procedure has been implemented for reports, publications, and presentations prepared by the CCMP. The first review is carried out by those members of the Research Group not actually involved in preparing the specific paper or report. After suggestions resulting from this review are incorporated, the document is sent simultaneously to the members of the Resource Committee and the Steering Committee for second level review and comment. One member of

each committee is designated as primary reviewer for a given paper or report. Suggestions made by these two groups are considered in preparing a draft to be circulated for final editorial review by all data contributors.

5. INFORMATION COLLECTION METHODS

5.1 Data Collection Forms

The CCMP Research Group developed standard self-administered data collection forms to be completed by individuals in each of the clinical trials studied. Completion of these forms provided the major portion of the information acquired by the Research Group. Some of the forms were completed by the study project office staff or similar individuals; others were completed by the directors and other personnel of the coordinating centers. Table 2 lists the forms and indicates whether the staff of the project office or the coordinating center were responsible for completing each one. Copies of the forms are appended (Appendix A).

TABLE 2

ASSIGNMENT OF RESPONSIBILITY FOR COMPLETING CCMP DATA COLLECTION FORMS

Name of Form	Responsibility for Completion: Proj. Off.	Coord. Ctr.
General Study Information	X	
General Study Information Review		X
Project Office Information	X	
Funding Summary	X	
Coordinating Center Budget Summary		X
Activity Analysis	X	X
Coordinating Center Information		X
Data Processing Systems		X
Coordinating Center Expenditures		X

The General Study Information Form, as its name implies, was designed to collect descriptive information on the design and organization of participating studies. After this form was completed by project office staff, a copy of the completed form was incorporated in the General Study Information Review Form for review, and revision if necessary, by the director of the coordinating center. Substantive changes made by the coordinating center director were forwarded to the project officer for corroboration to assure the validity of data reported

The Project Office Information Form was completed by the project officer with major responsibility for the study. Its purpose was to collect descriptive information about the project office staff and their activities. The Funding Summary Form was completed under the supervision of the project officer. This form requested information on expenditures by year and by type of study center for all centers and on coordinating center annual budget requests. The Coordinating Center Budget Summary Form provided for independent categorization of budget items for one or two budget periods by the coordinating center director for comparison with information supplied by project office staff.

The fourth form completed by project office staff was the Activity Analysis Form. This form was constructed to permit determination of responsibility for each of a large number of activities performed within a study organization. Of particular interest were those activities performed totally or in part by individuals within the coordinating center. This form was also completed independently by coordinating center staff without knowledge of the response provided by the project office staff so that comparisons of perceptions of responsibility could

be made.[4] Discrepancies in preception regarding assignments were resolved by consultation between the project officer and coordinating center director.

The three remaining forms - the Coordinating Center Information Form, the Data Processing Systems Form, and the Coordinating Center Expenditures Form - were all completed by coordinating center personnel. The Coordinating Center Information Form was used to collect information on the interaction between the coordinating center and the parent institution, organization of the coordinating center, staffing of the coordinating center, and assignment of responsibility for certain tasks within the center. The Data Processing Systems Form was designed to collect extensive information on the data processing systems at the coordinating center, including descriptions of computing facilities; the number, qualifications, and assignments of data processing personnel; and details of selected data processing operations. The Coordinating Center Expenditure Form was used to record coordinating center expenditures within specified categories during each year of operation.

Individuals supplying information were asked to forward to the CCMP Research Group study documents such as manuals of operations, study forms, study publications, organization charts, available descriptions of procedures, and sample reports of various types. Documents supplied have provided an important source of information supplemental to the completed forms.

5.2. Interviews

One or more visits were made to six of the seven coordinating centers in NHLBI-funded studies listed in Table 1. The CDP coordinating center was not visited because it was in the post-closeout phase of

operations and staffing was minimal. One series of visits was made by a member of the CCMP Research Group with expertise in management to document administration of the coordinating centers and factors within the parent institutions which affected administration of the centers. This individual prepared a written report following each visit which was reviewed by the center director. In all cases but one the project officer was also interviewed; written summaries of those interviews were also submitted for review by the individuals interviewed. A report from the CCMP will incorporate findings from these interviews.

Another series of visits was conducted by members of the Research Group with experience in coordinating center management and operations. The emphasis of discussions during these visits was on recommendations for future clinical trials and future coordinating centers on the basis of the experience of members of the coordinating center staff. Information reported on the data collection forms was reviewed and discussed during the interviews if clarification or amplification was necessary. Any special tools or procedures used to manage the centers were discussed; for example, one center has developed a multi-level system of assigning and reviewing priorities for data processing tasks which might be adapted for implementation in other studies. Recommendations developed from these discussions will be included in subsequent reports from this project.

5.3. RFP Content Evaluation

An evaluation of the ten RFPs issued by NHLBI from 1969 through 1977 for coordinating centers to participate in multicenter trials was carried out using a form designed by the CCMP Research Group for that purpose. The goal of this evaluation was to characterize those RFPs and

to identify deficiencies in information provided which might be remedied in future RFPs. Later reports will discuss the evaluation and present recommendations which arose from it. A copy of the RFP Content Evaluation Form is appended (Appendix B).

5.4. Clinical Trials Bibliography

A bibliographic resource for clinical trials has been developed in parallel with data collection and other activities. Compilation of a bibliography of published papers and unpublished documents which deal with many aspects of clinical trial design, methods, management, and operations was undertaken to provide a reference resource to be used by the CCMP Research Group during the course of the project and to be distributed to other interested parties on completion. Useful information in this area is often difficult to locate since much of it either is identified in information retrieval systems such as Index Medicus by keywords not germane to clinical trials or is unpublished. The procedures used for identifying papers and documents for inclusion and a description of the classification, storage, and retrieval system will be included in another report devoted to the bibliography.

5.5 Other Information Sources

Other pertinent information was obtained through conversations with individuals active in multicenter clinical trial organizations, in clinical centers, and in coordinating centers not participating in the formal data collection activities. CCMP workshops devoted to special topics, the Annual Symposia on Coordinating Clinical Trials, and the 1977 NIH National Conference on Clinical Trials Methodology provided for stimulating discussions and exchanges of developing ideas.

6. GOALS

The goals of the CCMP as defined by the Research Group and the other participants are the following:

- Description of existing coordinating centers and the environment within which they function;
- Identification of organizational and operational difficulties common to most centers and studies reviewed;
- Development of recommendations to aid future coordinating centers and clinical trials to organize, manage, and operate efficiently;
- Development of mechanisms to facilitate communication and transfer of technology among multicenter trials.

Description of existing coordinating centers is essential for reliable projections of the needs of coordinating centers in future clinical trials. By combining information from different centers, a composite description of existing coordinating centers will be developed. For example, the cost of operating coordinating centers is of concern both to sponsoring agencies and to directors of such centers. No data have previously been compiled from a group of operating coordinating centers in multicenter clinical trials which would permit realistic projections for new studies. Information obtained and summarized by the CCMP Research Group may be useful in guiding planning and management of future studies and coordinating centers.

Among anticipated useful outcomes of the comparative description of existing coordinating centers are identification of problems common to all or most of the centers and suggestions for solutions. At present one center may have implemented a rational procedure which obviates a problem common to most other centers but may not have communicated the solution to others.

An important component of description will be a management analysis by function. For example, knowledge of the responsibilities which are routinely assigned to coordinating centers should be valuable to someone organizing a new center; in one sense, a coordinating center is defined by its responsibilities. At another level, it is desirable to know which responsibilities of the coordinating center are commonly delegated to staff members with certain types of expertise; for example, those responsibilities usually assumed by statisticians in most centers, those assigned to programmers, etc. At still a different level, the distinguishing responsibilities of each center or committee in the clinical trial organizational structure and the role the coordinating center plays in fulfilling the responsibilities of each one will be useful items of descriptive information.

The interaction among various individuals at different centers required to carry out the CCMP has itself contributed to communication among existing coordinating centers. A series of technical reports will present the descriptive findings, analysis and interpretation of findings, and recommendations and suggestions emanating from the synthesis of information. These reports will be available from the National Heart, Lung, and Blood Institute and from the CCMP Research Group. In addition, some of the findings will be compiled in a format suitable for publication and submitted to appropriate journals, e.g., Controlled Clinical Trials.[5]

When the CCMP was initiated in 1976, responsibility for organizing and conducting the Annual Symposia on Coordinating Clinical Trials was delegated to the CCMP Research Group. These symposia were initiated in 1973; the fifth one was held in Arlington, Virginia, on May 25 and 26, 1978. These annual meetings have provided a forum for exchanges of

ideas and information among personnel involved in coordinating clinical trials, including both members of the staff of coordinating centers and representatives of agencies which sponsor such trials. The CCMP Research Group has used the annual symposia as a means of communicating preliminary findings from the project to the coordinating center community. An introductory presentation of the design of the CCMP was made at the fourth annual meeting in 1977;[6] at the fifth symposium in 1978 four presentations of preliminary findings were made.[2,4,7,8] It is anticipated that additional presentations of CCMP findings will be made at the Sixth Annual Symposium on Coordinating Clinical Trials to be held in Boston in May 1979.

7. COMMENT

The need for investigation and evaluation of activities associated with the design and conduct of clinical trials has been noted by Grizzle,[9] Gordon,[10] the National Commission on Digestive Diseases[11]; and by Meinert and Hawkins.[12] The difficulty of giving proper attention to such methodologic activities while conducting clinical trials has also been discussed by the latter authors. Increasing attention is being devoted to the multicenter clinical trial as an evaluation tool. Freiman et al[13] developed criteria for evaluating the design and conduct of clinical trials and applied them to a number of ongoing and completed studies. Meinert[14] has suggested standards for publications from multicenter trials.

Attempts are being made by both sponsoring agencies and investigators involved in clinical trials to provide more opportunities for discussion

and exchange of information among individuals participating in the conduct of clinical trials and the management and operation of coordinating centers. The increasing attendance at the Annual Symposia on Coordinating Clinical Trials and the unexpectedly large turnout at the 1977 NIH National Conference on Clinical Trials Methodology indicate a growing interest in and concern for improving methods for carrying out all aspects of multicenter clinical trials. The Coordinating Center Models Project is itself the result of recognition by the National Heart, Lung, and Blood Institute of the need for research into methods for managing and operating coordinating centers in multicenter clinical trials. A professional society and journal for individuals involved or interested in clinical trials, although still under development, should fill some of the communcations needs which must be met if methods for planning and conducting these studies are to improve.

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