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Developing a clinical trial unit to advance research in an academic institution

Ivana T. Croghan [a,*], Steven D. Viker [a], Andrew H. Limper [a], Tamara K. Evans [a], Alissa R. Cornell [b], Jon O. Ebbert [a], Morie A. Gertz [a]

[a] Department of Medicine, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA
[b] Department of System and Procedures, Research and Education Unit, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA

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ABSTRACT

Research, clinical care, and education are the three cornerstones of academic health centers in the United States. The research climate has always been riddled with ebbs and flows, depending on funding availability. During a time of reduced funding, the number and scope of research studies have been reduced, and in some instances, a field of study has been eliminated. Recent reductions in the research funding landscape have led institutions to explore new ways to continue supporting research. Mayo Clinic in Rochester, MN has developed a clinical trial unit within the Department of Medicine, which provides shared resources for many researchers and serves as a solution for training and mentoring new investigators and study teams. By building on existing infrastructure and providing supplemental resources to existing research, the Department of Medicine clinical trial unit has evolved into an effective mechanism for conducting research. This article discusses the creation of a central unit to provide research support in clinical trials and presents the advantages, disadvantages, and required building blocks for such a unit.

1. Introduction

Research is defined as "the systematic investigation into and study of materials and sources in order to establish facts and reach new conclusions." *Good Clinical Practice* (*GCP*) is the basis for quality and human subject safety in all clinical research and provides guidance that must be strictly adhered to before, during, and after a research study is undertaken [1]. Unfortunately to quote Eisenberg, et al. "…over time, clinical trials in the United States have become too expensive, difficult to enroll, inefficient to implement, and ineffective to support the development of new medical products using modern evidentiary standards" [2]. This has been especially true in the current climate where funding has been reduced or completely eliminated for some research fields of study.

Clinicians are in a unique position to conduct patient-centered research and health care delivery improvements. Although physicians are adroit at identifying clinical questions, very few of these ideas ultimately result in research projects. The challenge in translating ideas to projects is due, in large part, to a lack of investigator research knowledge and an inability to execute research ideas, as well as unfamiliarity with the research landscape and its numerous regulations. In addition, physicians are hampered by the lack of time and competing demands. A review of investigators that received warning letters from the Food Drug Administration (FDA) as a result of site audits, found that failure of a principal investigator (PI) to supervise trials was the leading cause for the warning letters [3] (>37% of PIs audited in 2001 vs. 19% of PIs audited in 2000). [4]; other reasons cited included the coordinator's failure to complete all study duties, such as IRB submissions. All of these elements present critical barriers to conducting high quality research, which can contribute greatly to the advancement of the science and delivery of health care.

In an effort to continuously improve clinical trials administration and better serve patients, the Association of Academic Health Centers (AAHC) conducted a survey of its member institutions to gauge the nature and scope of clinical trials operations [5]. The results highlight the challenges facing academic institutions who wish to continue participating in rapidly evolving research practices. The greatest barrier for these institutions is the lack of systems and procedures and the suboptimization of resources [5].

Clinical researchers who have access to a supporting research infrastructure are able to increase their knowledge development, improve

Abbreviations: AAHC, Association of Academic Health Centers; CRO, Clinical Research Office; CTSA, Clinical and Translational Science Awards; CTU, clinical trial unit; DOM, Department of Medicine; FDA, Food and Drug Administration; GCP, Good Clinical Practice; IMARC, Information Management and Reporting Center; NIH, National Institutes of Health; PI, principal investigator; SCs, study coordinators.

* Corresponding author at: Mayo Clinic, 200 First St. SW, Rochester, MN 55905, USA.
E-mail addresses: croghan.ivana@mayo.edu (I.T. Croghan), viker.steven@mayo.edu (S.D. Viker), limper.andrew@mayo.edu (A.H. Limper), evans.tamara@mayo.edu (T.K. Evans), cornell.alissa@mayo.edu (A.R. Cornell), ebbert.jon@mayo.edu (J.O. Ebbert), gertz.morie@mayo.edu (M.A. Gertz).

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healthcare delivery, and more easily integrate these elements into clinical practice. The rapidly evolving clinical landscape consists of many complex and interdependent functions that are often isolated and lack integration within an institution. There is a great need for value-added resource(s) to provide expertise for complex trials; offer more oversight/guidance and in assistance in partnership with investigators, and to provide knowledge of study design, initiation, conduct, and outcomes.

2. Methods

Clinical trials units (CTUs) are specialized biomedical research units that can help to design and centrally coordinate clinical trials. Much like a core facility, CTUs can be "centralized shared resources that provide access to instruments, technologies, services and expert consultation to scientific investigators…" [6]. During a period in academia when clinician time and research funding are at a premium, a central CTU can be established with the purpose of providing assistance in the development, application, and implementation of industry- and investigator-sponsored clinical trials in compliance with Good Clinical Practice (GCP) and other ethics guidelines. The goal of the CTU is to provide resources and services to advance research and inform the clinical practice. This could be accomplished by having the CTU provide a focal point for clinical trials compliance or educational activities, standardize institutional policies, address clinical trials billing, or improve financial management of clinical trials.

This approach could be cost-effective because it allows for the sharing of knowledge and expensive resources within an institution. As in clinical practice, where the care model is moving toward a team-based "clinical care team," a centrally-located CTU could act as a "research team." This infrastructure could provide scientific mentorship, protocol development, and study coordination services. Following the team-based model, stakeholders with various research skills and knowledge would collaborate to form a first-class research team. The CTU research team would support research investigators by providing mentorship, protocol development, regulatory services, and the use of highly-trained research coordinators; this research team has available institutional resources to manage and complete a research study across the disciplines and organizational divisions within an institution.

2.1. Building on existing infrastructure

In 2006, in reaction to fluctuations in funding, the Mayo Clinic Department of Medicine (DOM) undertook an informal process of "sharing" study coordinators (SCs) in an effort to balance resources. At the same time, investigators who had prior success in attaining research funding, found that the reduced funding resulted in lost resources to pay for well-trained study coordinators, thereby hampering completion of the research projects. The "shared-resource" model linked investigators who had quality trained staff, but no funds with investigators who had funds but lacked quality trained staff. Staffing of SCs was temporarily shared between the investigators. This model created a win–win for all involved due to reduced financial burden and increased job stability for the study coordinators. Although this partnership was successful, the long-term stability was threatened by relentless changes in the funding landscape. Indeed, even the program funded by the National Institutes of Health (NIH) Clinical and Translational Science Awards (CTSA) have undergone a shift in funding direction in recent years [7].

In 2009, the DOM provided financial resources to develop a Clinical Research Office (CRO). The mission of the CRO was to provide the four general medical divisions within the DOM with the resources to increase academic productivity. The CRO operated with the "shared-resource" model. In addition to providing experienced and trained study coordinators, the CRO provided scientific mentorship for coordinators and investigators, as well as regulatory guidance statistical resources and manuscript support to assist investigators in the development and implementation of research ideas. Each of the four divisions supported this infrastructure through financial contributions and administrative oversight. First author publications for one of these four divisions increased from 99 in 2012 to 157 in 2014. The annual participant satisfaction survey indicated that participating investigators were very pleased with the services and requested continued access to this resource. On the heels of this success, demand for these services from other areas within the organization greatly increased.

In 2014, the DOM formally expanded services to the remaining nine DOM divisions (N = 13) through the establishment of the clinical trial unit (CTU). The CTU was designed to supplement, not replace, existing research units that served specific divisions/investigators (including the DOM CRO as well as other departmental research units). The purpose of this expansion was to fulfill a need for service to investigators who lacked research resources but had funding available. The CTU, unlike the CRO, is funded through a fee-for-service model. The charge-back system was designed to offset the operational costs of the unit and its associated support staff to conduct research studies. Investigators who access CTU services are billed at an hourly rate based on the amount and type of work completed. This financial model offers a competitive advantage to investigators, as their study is supported by highly-trained personnel, for only the hours worked on their specific project. The CTU eliminates the need for an investigator to hire, train, or terminate individuals as their research funding fluctuates. It also removes the burden from the investigators to pay for back-up support while the primary coordinator is on vacation, leave, or participating in continued education for coordinators. The centralization of these functions within the CTU allows investigators to be assigned study staff with the proper training needed in the study and to begin enrolling patients faster for competitive enrollment studies. It also eliminates the burden to the PI for administrative and supervisory oversight for the CTU staff assigned to him/her for the duration of their study. This effort has resulted in an overall reduction of personnel expenses for studies.

The fee-for-service approach of the CTU is based on a well-established process which takes into consideration the average pay for the individual staff members as well as the overall operating costs of the CTU. The financial goals of the CTU are to recover the costs associated with its operation, not to make a profit. Funding is sourced from internal support rather than external awards (such as Federal, Pharmaceutical or Foundation) that are limited due to the current political/economic climate. Recovering costs and sourcing funds internally contribute to the strength and long-term sustainability of the program.

2.2. Key elements for optimal clinical trials infrastructure

Research infrastructure provided through a team-based model is critical to the sustainability and growth of clinical research. The CTU can operationalize this goal by compiling a "research team" which is experienced and knowledgeable in interacting with key stakeholders (Table 1). The success measures that can be derived from the implementation of such a central clinical research unit are defined in Table 2. While electronic health records, standard nomenclature, and data standards are critical for efficiency in the research environment [2], these elements alone will not improve or simplify the research process for novice investigators. Lack of or limited knowledge and access to basic research support resources will have a greater impact on research success than innovation of programs. Fig. 1 presents key resource elements that should be considered and incorporated into a CTU. Fig. 2 illustrates the basic reporting structure of the CTU in its current state.

3. Results

Within this section, we present three scenarios. The scenarios are compilations of previously encountered real situations. For simplicity, we have excluded study complexities such as investigator time, drug/