

Professional Obligations

Summary: To examine the ethical obligations relating to the protection of human subjects of clinical investigators and of other members of the research team or those who advise patients concerning research participation; and to analyze the ways in which these obligations differ from and overlap with the obligations of clinicians providing clinical care.

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Background: An inherent tension and conflict of commitment has been described in the role of the physician-investigator. The conflict arises out of a division of loyalties for the physician-scientist, most noticeably between the physician's traditional commitment to the patient's best medical interests and the scientist's commitment to the interests of science and society. Nurses and other members of the clinical and research teams are also subject to similar tensions and conflicts created by simultaneous allegiance to both the patient and the research.

Little systematic attention has been devoted to characterizing the obligations of clinical investigators engaged in research with human subjects. The professional integrity of investigators as a source of protection of research subjects has been neglected, owing in part to the emphasis on regulation of research by IRBs. Additionally, the focus on the obligation of investigators to obtain informed consent as the key ethical protection for research subjects has led to the relative neglect of other important obligations relating to the recruitment, screening, monitoring, and discharge of research subjects.

When clinical research is intertwined with clinical care, there is an inherent tension for patient care to be confused with and compromised by scientific investigation.

Accurate ethical analysis of the obligations of investigators and other professionals who support the research enterprise depends on understanding how clinical research differs from, though overlaps with, clinical care. Despite important differences between research and patient care, when research subjects are patients recruited because they have a medical condition under investigation, it is often presumed that the ethics of the physician-patient relationship should govern the conduct of clinical research. For example, The Declaration of Helsinki, the leading international code of ethics for clinical research, fails to provide clear and consistent guidance on the obligations of investigators as distinct from physicians providing medical care.

As clinical research is increasingly conducted at a variety of sites and in societies with differing standards of medical care, questions arise about whether or not background access to health care has any influence on the obligations of investigators to research participants.

Objectives:

- (1) To identify and analyze ethical conflicts and tensions in the roles of clinical investigators and members of the clinical research team.
- (2) To delineate and develop a systematic account of the obligations of investigators, research coordinators, and research nurses concerning the protection of research participants.
- (3) To examine critically the proper role of physicians in recruiting their patients for clinical research.
- (4) To characterize the obligations of physicians in advising their patients concerning participation in clinical research.
- (5) To examine the basis or and limits of an obligation to offer treatment for conditions uncovered or developed while participating in research.

Methodology: The process of clinical research from the initial formulation of a research question to the completion of a study will be analyzed to determine the key responsibilities of professionals relating to the protection of research subjects. Relevant literature on research ethics as well as ethics literature on

role responsibilities and obligation will be surveyed and examined critically. To address conflicts in the role of study coordinators, the Department convened focus groups of study coordinators from a variety of research settings.

Results: The Department undertook an initial inquiry into professional integrity in clinical research that examined tensions between the identities and roles of the investigator as physician and as scientist. It was argued that professional integrity and protection of subjects during the course of research depend on understanding the differences between clinical research and clinical care and the ways in which pursuing rigorous science has the potential to compromise the well-being of research subjects. Recognizing that conflicting loyalties between patient care and scientific investigation are not limited to physician-investigators, the Department examined the role of study coordinator. Study coordinators, often but not always nurses by profession, are responsible for coordinating many aspects of research studies, most typically including recruitment of subjects and monitoring. Some study coordinators present information to subjects as part of the informed consent process and many obtain the subject's signature as an indication of consent. In some cases, study coordinators have a long term relationship with subjects, either because of the nature of the research and/or based on a previous clinical relationship. Little is known about the strategies study coordinators use to recruit subjects into studies, nor about how their relationship with a subject might influence their interactions with subjects and their multiple responsibilities. The Department approached this question in a collaborative project with colleagues from the National Human Genome Research Institute and the University of North Carolina by conducting 7 focus group discussions with study coordinators from academic medical centers, the NIH, and the private sector. We developed discussion vignettes for focus group participants in an effort to better describe the role of the study coordinator, and the influence of study coordinator relationships with subjects, principal investigators, sponsors, and others. The result of this work was the identification of three separate potentially conflicting 'advocacies' that study coordinators balance and support, advocacy for the 'patient' in research, advocacy for the 'subject' of research, and advocacy for the research itself.

The Department examined the responsibilities of physicians as advisors to patients considering participation in clinical trials. The ethical analysis emphasized the role of treating physicians in helping patients understand the differences between clinical care and participation in a clinical trial.

Future Directions: Planning is underway for conceptual research on the obligations of investigators conducting clinical research in developing countries to provide care for the health needs of research subjects that are not related to the research. This project began with a presentation by the Department on this topic at human subjects research conferences in Ghana and Uganda in March 2002. Research on this topic will be lead by the Department with collaboration from

conference participants. Discussions are continuing through an NIH-wide working group examining the issue in the context of HIV research.

The Department is in the early stage of undertaking a more comprehensive ethical analysis aimed at answering the question of what ethical obligations investigators have for providing health care to research participants outside the scientific design of the research. A philosophical framework for answering this question will be developed and current views of the responsibilities of investigators will be examined critically. Additionally, it is anticipated that empirical research will be conducted on the perceived role conflicts of physician-investigators aimed at elucidating their understanding of tensions between scientific investigation and patient care and the strategies they use to manage these conflicts. Drawing on this research, the Department's textbook on the ethics of human subjects research will contain a chapter on the professional obligations of investigators.

Publications:

1. Miller FG, Rosenstein DL, DeRenzo EG. Professional integrity in clinical research. *Journal of the American Medical Association*. 1998;280:1449-54.
2. Davis A, Hull S, Grady C, Wilfond B, Henderson G. The Invisible hand in clinical research: the study coordinator's critical role in human subjects research. *American Journal of Law, Medicine & Ethics*. 2002, in press.
3. Chen DT, Miller FG, Rosenstein DL. Clinical research and the physician-patient relationship. *Annals of Internal Medicine*, in press.