Developing Responsible Policies for Recruitment into Clinical Research. *By Amy McGuire, JD, PhD*

Scientific progress depends on the successful recruitment of human subjects to participate in medical research. However, it has been shown that most eligible patients do not participate in clinical trials. There are several reasons why this may be the case. In this essay, we will examine some particularly salient barriers to patient participation and possible solutions.

Patient Notification

First, enrollment in research is largely dependent on physicians notifying their patients that trials exist for which they are eligible. Various studies demonstrate that many physicians do not inform eligible patients about research opportunities for a variety of reasons, including: the physicians' lack of awareness of ongoing trials, lack of time to introduce the issue, and financial/resource constraints. Physicians may also have concerns about the effect of inviting patients to participate in research on the physician-patient relationship. Further, they may feel uncomfortable with the dual role of physician-investigator, randomization, and the uncertainty regarding clinical trial outcomes. [1,2]

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Each of the concerns that influence physicians' decision to suggest clinical trials to patients merit responsible exploration and investigation. Some creative solutions have been suggested and warrant further consideration. For example, improving and continuing to develop a national trial registry may help address some of the logistical barriers to recruitment into clinical trials. This would facilitate awareness of ongoing trials and could be used as a resource to stimulate dialogue about research participation between physician and patient. Of course, sensitivity to patient access to this information must be a priority. Both physician and public education are essential components of this effort.

Education and public dialogue may also be helpful in addressing some of the concerns about the dual role as a physician-investigator. It is critical that we train physician investigators in techniques, such as establishing guidelines, to better manage the ethical challenges that may arise. This will help them balance professional obligations to patients and the responsibility to promote scientific progress.

Interest and Motivation

A second reason why eligible individuals may not participate in research is because of lack of motivation or interest on the part of potential subjects. Motivation to participate in research depends largely on whether the potential subject is a patient or a healthy volunteer.[3] Although there is an assumption that altruism is what motivates subjects to participate in research, studies suggest that patients may be more motivated by the hope of benefit, either for themselves, their offspring, or others who may be suffering from the same disease or disorder. [4] Whether or not there is actually a potential to benefit from participation in even Phase 1 clinical trials is currently under debate.[5] Regardless of whether the hope for benefit is realistic or the product of false hope, it acts as a strong motivator for participation and must therefore be studied and addressed responsibly. Because there is no potential for healthy volunteers to directly benefit from research participation (other than the psychological benefit of knowing that they are helping others), it is frequently more difficult to recruit healthy volunteers into research studies than to recruit affected patients. Thus, it is imperative that we explore strategies for recruiting healthy controls and that we revisit some of our moral assumptions about issues such as compensation for participation.

Studies also suggest that distrust is one of the main reasons why individuals, particularly specific subsets of the population, are reluctant to participate in medical research.[6] Unless we work to restore trust in research through public education, transparency, and the ethical conduct of research, these subsets of the population will continue to be excluded from important research studies and they, as a group, will suffer. We cannot adequately address disparities in healthcare until we attend to this culture of distrust.

To increase trust and boost enrollment in research, we must develop comprehensive guidelines for ethical recruitment practices. There is currently no clear conceptual framework for situating policy discussions about recruitment into medical research. Rarely is recruitment defined or even distinguished from other research activities, such as the informed consent process or the more general process of enrollment.

A coherent conceptual model is an essential first step to any policy development. In order to engage in a policy discussion regarding recruitment, we must clearly articulate what recruitment is and develop a common vocabulary for our discussions. Although it is a necessary first step, this is often the most challenging aspect of any policy development endeavor.

Inconsistent Recruitment Policies

A brief review of the institutional policies available online for the top twenty-five U.S. medical schools receiving the most NIH research grant money in 2004 suggests that few of these institutions have a coherent policy on recruitment. Most consist of piecemeal guidance scattered throughout general investigator handbooks or institutional policy for human subjects research. Combing through these extensive guidance documents, one can find tidbits of policy on topics related to recruitment, such as incentives to physicians for enrolling subjects into research studies, the equitable selection of subjects, the ability to contact potential subjects from disease registries and patient databases, appropriate advertisements, payment to subjects, and various recruitment practices. However, without one comprehensive policy on recruitment, it is difficult for investigators and

institutional review board (IRB) members to know what constitutes unethical or impermissible conduct relating to subject recruitment.

The policies that do exist rarely move beyond the legally required boilerplate to provide substantive guidance on challenging issues related to subject recruitment. For example, most institutions have a policy that echoes the federal mandate for an equitable selection of subjects,[7] but few specify what this means, acknowledge the challenges of recruiting certain subsets of the population into research, or provide support or guidance for how to accomplish this important goal. They generally leave it to the IRB to determine when the selection of subjects is equitable in the context of a given study. Without institutional guidance on how to evaluate or accomplish this, however, IRBs are left only with the subjective judgments of their members. This perpetuates inconsistency among IRBs, creating disparities in the ethical assessment of research protocols and causing much frustration and cynicism among investigators.

On some issues, there is more institutional guidance, but the policies that exist vary by institution. For example, the Health Insurance Portability and Accountability Act's (HIPAA) Privacy Rule has caused much debate regarding who can contact potential subjects about research opportunities and under what circumstances. This presents a challenging dilemma. On the one hand, it is important to protect patient privacy and to limit third parties, including non-treating physicians, access to patient records and to patients themselves as potential research participants. If patients receive phone calls or letters from people whom they do not know about a research opportunity related to their specific medical condition, they might feel that their privacy has been breached, perpetuating distrust in the medical profession and discouraging their participation in research. On the other hand, requiring the treating physician to contact patients about potential research opportunities may introduce undue influence and create confusion about the physician's role. Patients may become unsure whether the physician is acting as a *caregiver* protecting and promoting the patient's health-related interests, a *scientist* interested primarily in generating generalizable knowledge, or an *agent* of the investigator with no particular interest of her own. A review of institutional policies suggests that there is much variation on this topic, ranging from institutions that allow direct contact from the primary investigator to those that require that the treating physician make contact to those that suggest the use of a third party intermediary. These discrepancies can be confusing to both investigators and IRB members and reflect a lack of social consensus about this important issue.

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Conclusion and Recommendations

I believe that in order to eliminate disparities in healthcare and to increase enrollment into clinical research, it is essential that we work together to accomplish the following aims. First, we must address the culture of distrust that exists among certain groups and work to build trust through ethical research practices, public education, and a policy of transparency. Second, it is essential that current and future policy development be grounded in a coherent conceptual model that defines and distinguishes the various phases of research, including recruitment, informed consent, enrollment, participation, and post-trial treatment and follow-up care. This conceptual model should help build a common vocabulary that is generally accepted and widely adopted. Third, we must clearly identify what issues related to subject recruitment are ethically controversial or create a significant barrier to research participation. We must then address these issues responsibly through public dialogue, empirical study, and policy development. Fourth, potential subjects, investigators, institutions, and federal policymakers must all work together to develop comprehensive policy guidance that is responsive to this public dialogue and empirical research. All stakeholders should have a say in defining the issues and developing the policy to address them. Finally, as we begin to address these concerns, public and physician education and institutional infrastructures that can provide guidance and support will be important aspects of successful implementation. Only by working together in a coordinated effort can we begin to accomplish these five aims. ●

References

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Table 1. Clinical trial challenges and recommended policy solutions

Challenges	Potential policy-based solutions
- Low patient interest and motivation to participate due to a history of abuses and/or lack of awareness of advantages of participation -Inadequate support for or monitoring of recruitment and enrollment efforts focused on subsets of the population -Lack of an updated and "robust" national registry of clinical trials	**Aim 1.** Develop policy which helps to build trust by establishing ethical research practices, public education, and a policy of transparency
- Lack of awareness regarding clinical trials and what they entail -Inconsistent understanding of the distinction between recruitment, consent, and enrollment	**Aim 2.** Establish a coherent conceptual model that defines and distinguishes the various phases of research, thereby creating a common vocabulary for those conducting and participating in clinical trials
-Inconsistencies in physicians' willingness and policies regarding patient notification of eligibility for a clinical trial -Physician concerns and discomfort regarding randomization, potential "loss" of patients to the trial, discomfort with dual role of physician-investigator or lack of awareness of trials by the physician	**Aim 3.** Identify and address through open dialogue, public education, empirical study and policy development the ethically controversial issues and barriers to participation in clinical trials
-Inconsistent recruitment guidelines within and between research institutions.	**Aim 4.** Encourage the participation of potential subjects, investigators, institutions, and federal policymakers in the development of comprehensive policy guidance responsive to the public dialogue and empirical research accomplished in **Aim 3.**
-Lack of guidance on how to interpret national policies (e.g. HIPAA), creating inconsistent interpretations by individual institutions -Lack of objective ways to measure and support adherence to guidelines and requirements regarding diversity in recruitment to clinical trials	**Aim 5.** Increase public and physician education and build institutional infrastructures that can provide consistent guidance and support to those involved with clinical trials.