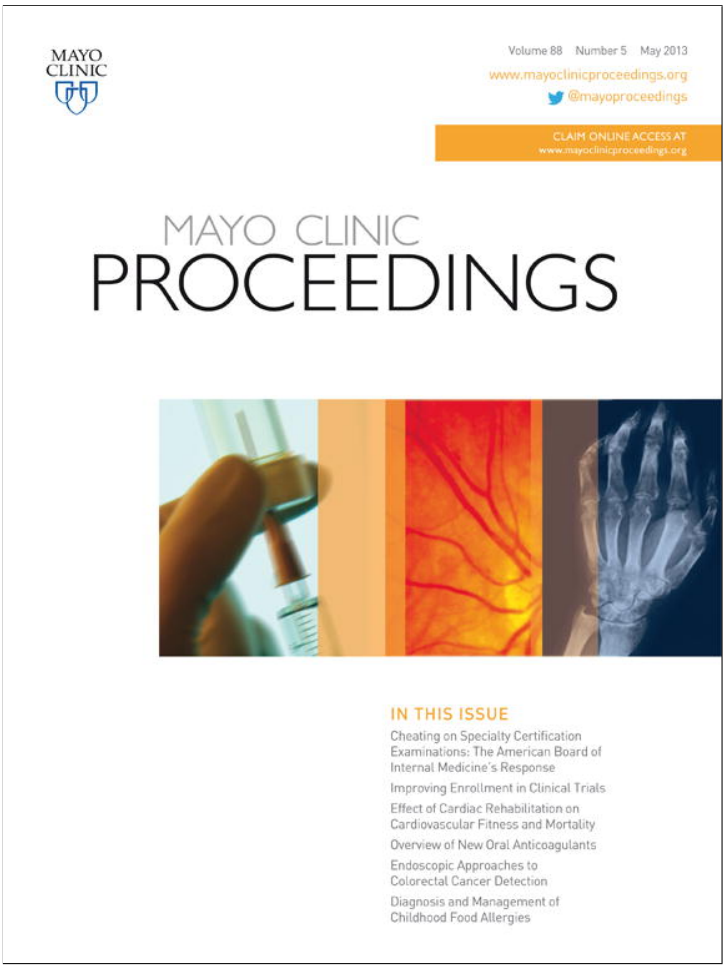

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Increasing Enrollment in Drug Trials: The Need for Greater Transparency About the Social Value of Research in Recruitment Efforts

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"Clinical trials and the consequent benefits to society are in jeopardy in the United States because of a decline in the ability to recruit patients in a timely manner to trials addressing key clinical issues."[1] So states a recent commentary in a leading medical journal, reflecting widespread concern in the research community about recruiting sufficient numbers of people into clinical trials. Anyone who cares about medical progress should share this concern.

What, then, is to be done about it? The authors, reflecting discussions at a US National Institutes of Health–sponsored workshop convened to address recruitment challenges, call for, among other things, a "national campaign to increase public awareness and participation in clinical trials" in hopes that it will establish research participation "as a valued contribution to the general public."[1] Bolstering their call is scholarship contending that people have an obligation to participate in clinical research.[2-4]

Designing Socially Responsible Campaigns in Support of Research

Although everyone should be deeply supportive of efforts to advance the goals of improved clinical care, coordinated campaigns to cultivate civic attitudes more sympathetic toward trial participation may do more harm than good in the long run if we do not take care at the outset to properly plan and carry out the campaigns. Campaigns presumably will seek to promote civic attitudes supportive of research by celebrating the promise of research to improve clinical care. Campaigns will need to back up such promises with research capable of doing that. Although there is an astonishing array of research currently under way that holds great promise to stimulate important clinical breakthroughs, not all research has the capacity to improve clinical care. Some drug trials, such as studies of "me-too" drugs that test whether a new drug to treat a particular condition is no worse than already approved ones, including lower-priced generic drugs that effectively treat the condition,[5] have little if any social value and thus violate one of the ethical prerequisites for clinical research.[6]

Unfortunately, neither the US Food and Drug Administration (FDA) nor institutional review boards (IRBs) have mechanisms that would prevent approval of drugs with dubious social value or alert research participants to the trials that study them. The FDA must review all drugs submitted for approval,[5] and it awards licenses to "noninferior" drugs. Although many, even most, noninferiority studies have important social value, FDA standards open the door equally wide for those that do not. For their part, IRBs are under a mandate to focus on the interests, rights, and welfare of the individual trial participant, not on the social value of any given experiment. Thus, research that does little, if anything, to bring the important contributions to society that support both the envisioned national campaign and claims that we have a duty to participate in research can quite easily pass regulatory muster.

Few knowledgeable people would contend that research of questionable social benefit does not exist, that all clinical research, by definition, is important. Over the period from 1990 to 2002, the FDA approved over 1000 new drugs. More than 75% of them were found to have "therapeutic qualities similar to those of one or more already marketed drugs."[7] Given this outcome, it is no surprise that physicians are discriminating consumers of science who question, if not dismiss out of hand, some research in favor of other research,[8] revealing the discrepancy that exists in both the quality and value of research.

Many in the public are already aware of this discordance in the importance of drug trials. Many others, however, including many potential research participants, have no basis

Mayo Clin Proc. ■ May 2013;88(5):442-445 ■ http://dx.doi.org/10.1016/j.mayocp.2013.03.001
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by which to discern the importance of a clinical trial. This heterogeneity in the public shows why we must be cautious with campaigns to tout drug trials as activity that promotes our collective well-being. On the one hand, campaigns touting all research in general may just generate cynicism on the part of some who are knowledgeable about the discrepancies in social value among trials. On the other hand, those same campaigns could favorably dispose those members of the public who lack much knowledge about clinical research to enrollment in trials that, truth be told, deserve less, not more, public support.

These considerations show how campaigns that are poorly conceived could create a backlash injurious to trials investigating innovative approaches to conditions that lack effective treatment, raising the stakes for correctly mounting the recommended campaigns. One way to assure a campaign's effectiveness and simultaneously avoid backlash may be to wed campaigns to efforts that will help the public do what most physicians already do, distinguish research that deserves broad support from research that does not.

Although we normally do not worry about the public's ability to be discerning about campaigns promoting charitable giving and volunteerism, clinical research is different. We need to keep in mind those who will struggle to understand the merits of much clinical research. After all, credible physicians and nurses who patients look to for their needed medical care will recruit patients to the clinical trials in the same settings in which the patients get their medical care. Although most patients will appreciate the importance of a trial that is testing a novel approach to a disorder that lacks effective treatment, how many will understand the relative importance of trials of "me-too" drugs that will compete with effective generic drugs, let alone understand the value of trials conducted so that sponsors can extend lucrative marketing rights or provide sales forces with additional study data to make their sales pitches to physicians more persuasive? Under no stretch of the imagination do these latter kinds of studies deserve broader public support.

Promoting Transparency About a Clinical Trial's Social Value

We owe the public honest disclosure about why any given trial is being conducted so that they understand the extent to which a trial, if completed, could promote the common good. The informed consent process is one way to provide this disclosure to prospective research participants. A clear declaration could be made in informed consent forms that states whether a trial is investigating a way to potentially eventually improve current medical care and explains why it does or does not have the potential to do so. The Figure illustrates how a declaration might be made in an informed consent form. Research institutions could implement this proposed reform on a voluntary basis. All that would be required is for investigators to declare to IRBs what the potential social value of a clinical trial is, along with supporting information.

There will be major challenges, no doubt, in developing the kind of reporting system envisioned herein. Investigators already feel overburdened with IRB paperwork. Also, scientists typically do not like to be placed in the position of publicly challenging the validity of another's work, and many may see a reporting system as doing just that. The system is not meant to question the scientific validity of others' work, and this should become clear to researchers as they grow accustomed to the proposed system of disclosure. That system is meant to answer a simple question: What promise does a clinical trial hold for improving the lot of patients? Our current surrogate markers for the social worth of drugs—government approval and marketability to prescribing physicians—at times miss this most basic mark. A social value reporting system would address this deficiency. This essay is not meant to fully explicate the proposed system. That effort is probably best left to a trusted professional society or societies that would take responsibility for developing the system and ensuring both that it could be implemented locally and that it is not burdensome.

Does this study have the potential to improve health care?

The Jane Doe Research Institute voluntarily participates in the Clinical Trials Social Value Rating System, which evaluates the potential of clinical studies to contribute to important medical advances. Reviewers have determined that this trial has the potential to make the following contributions to medical care:

Initials: _____

FIGURE. Example of wording about the potential social value of a trial for inclusion in informed consent forms.

Critics may raise various concerns about the proposal. Some may contend that such a system is not needed because consent forms always contain information about "why a study is being done." Although it is true that consent forms identify the stated purpose of a study, eg, to test whether a drug is safe or effective, anyone familiar with clinical research knows that consent forms basically ignore the broader social merits of research. When readers with limited knowledge of research read terms like *effective* in informed consent forms, they may simultaneously infer important social value on the trial. This inference is understandable when one considers that forms are routinely silent about broader contextual information regarding drug research, such as the fact that, for example, a study is placing volunteers at risk to prove that a drug is "effective," ie, not inferior to its competitors, so that the company conducting the trial can try to capture a share of a multibillion dollar market. There are important reasons why such information should be disclosed,[9] and research participants themselves report that they would like to have such information.[10] The fact is, however, that current informed consent practices can obscure and even inflate, not reveal, the potential social value of clinical trials. The system being proposed herein could help remedy that problem.

Some may worry that the proposed system will paint types of trials, such as postlicensure phase 4 studies or noninferiority studies, in a negative light, but the information to be disclosed in consent forms under the proposed system will refer only to an individual trial. For example, the new disclosure would show how a phase 4 trial that is a head-to-head comparison of approved drugs to assess superiority would provide great social value. It would also reveal the limited, if not trivial, social value for other kinds of drug trials. For example, it would make more transparent how a "seeding trial" enrolls participants so that physicians will become familiar with the study drug before FDA approval and thus be more likely to prescribe it following FDA approval.[11]

Were this proposal to be adopted, we have to recognize that it will not be a panacea for all the ills of our drug testing system. First of all, the envisioned disclosures will have little influence on the decisions of many prospective trial participants because they will not pay much attention to the information being disclosed,[12] nor would it necessarily or easily deter sponsors from trying to conduct unimportant drug trials. The system will, however, change a status quo in great need of change. It will provide important information to those people who will choose to include it in their deliberations about whether to volunteer for a trial. Equally, if not more, important, it will increase awareness within research institutions about the social importance of the research they conduct. Many research institutions tout the "world-class" and "cutting-edge" nature of their research. The proposed disclosures would make transparent to researchers, IRB members, and others the amount of research at the institution that lives up to those claims. At those institutions where much of its research rates high in terms of social value, people will quickly understand that assertions about world-class and cutting-edge research is not empty sloganeering but substantive claims backed up by impressive amounts of research. This will support a sense of pride and commitment to the success of the institution's research mission. At those institutions where a considerable portion of the research rates low in terms of social value, dialogue might ensue about whether the institution wants to require some minimal level of social value, in addition to regulatory approval and sponsorship, for the research it conducts. Both of these would be direct and positive outcomes of the proposed system.

Conclusion

Increased participation in clinical trials will not materialize in the absence of the public's trust in research. So, as those of us in the research community contemplate campaigns to promote civic attitudes that research participation is a valued contribution to the general public or embrace talk that people have an obligation to participate in research, we need to consider how we best merit the public's trust. Otherwise, campaigns to promote positive civic attitudes toward research, let alone talk of an obligation to participate in it, seem premature.

Transparency is central to showing how we warrant the public's trust,[13] so it behooves us to promote greater transparency in the research setting. Joining the social value reporting system proposed herein with campaigns to increase civic attitudes conducive to the volunteerism clinical research requires is a way to

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increase transparency and thus support for the clinical research that has brought us some of the most important social advances in history.[14] The transparency that will result from the proposed system will also let prospective trial participants judge for themselves whether a particular trial is deserving of their trust and support. This information seems little to give in return to, and wrong to withhold from, those who make clinical research possible in the first place.

Grant Support: This work was supported in part by the National Center for Advancing Translational Sciences, National Institutes of Health, through grant UL1 TR 000002.

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