Informed Consent for Pragmatic Trials — The Integrated Consent Model
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Learning health care systems hold great promise for improving medical care by systematically integrating the delivery of medical services with clinical research. In such systems, the generation of knowledge would be “embedded into the core of the practice of medicine,” leading to “continual improvement in care.” But is the goal of systematically integrating knowledge generation with health care delivery compatible with current research-oversight procedures — for example, when a comparative-effectiveness study compares two standard-of-care interventions?

In some pragmatic, randomized clinical trials comparing two commonly prescribed medications for an outpatient condition such as hypertension, the only material departure from clinical practice may be replacing the physician selection of treatment with a randomized selection. It seems unlikely that such a study can be seamlessly “embedded” in routine clinical care delivery if the traditional informed-consent process for research participation (with the usual complex, lengthy document) is required. But what are the alternatives?

A recent Department of Health and Human Services invitation for public comment specifically asked, “Should an IRB [institutional review board] be allowed to waive informed consent for research involving randomization of subjects to one or more standard of care interventions?”

One group has developed a sophisticated moral framework for evaluating the ethics of learning health care activities and argues, following others, that these principles yield a surprising result: in some pragmatic comparative-effectiveness trials, the fact of randomization need not be disclosed to patients, and thus no express informed consent for research participation is ethically necessary.

We share the goals of the learning health care movement and are deeply concerned about unnecessary regulatory obstacles to important research; however, we find the proposal to not disclose to patients the fact of randomization even in low-risk outpatient pragmatic trials (hereafter called the no-consent model) problematic for both ethical and practical reasons. We propose instead that the consent process itself should reflect the ideal of learning health care of integrating medical care and clinical research, and we propose an integrated consent model for some types of pragmatic, randomized clinical trials. Notably, such a model can reasonably be seen as compatible with existing regulations.

**The No-Consent Proposal**

In the no-consent model, patients would be unaware of the fact that they are in a randomized clinical trial. This cannot be accomplished without the physician actively concealing the patient’s inclusion in the study, much in the way that clinicians sometimes prescribe placebo treatments without patients’ knowledge. Imagine a patient asking why a particular treatment is chosen. Although in a narrow sense a physician can “accurately” say to the patient who is randomly assigned to a particular drug that “this drug is an effective drug that I commonly prescribe to treat high blood pressure,” an ordinary patient will not appreciate the artful choice of words. This lack of transparency would be intended. However, transparency is presumed in communications between physician and patient and between researcher and study participant. Are there sufficient reasons to override this presumption? We doubt this, for both ethical and practical reasons.

From an ethical perspective, the reasons in support of the no-consent model seem insufficient to overturn the presumption against concealment. First, the no-consent model incorrectly presumes that as long as welfare interests of patients are addressed, so are their autonomy interests: “Because the [pragmatic, randomized clinical trial] will have no adverse impact on patients’ clinical outcomes or experience, and imposes no nonclinical burdens and no more than minimal nonclinical risks, the study is presumably respectful of patients’ rights and dignity.”

This seems incorrect. We ordinarily judge that bypassing a person’s agency — unless the per-
son is incapable or not reasonably accessible — even for that person’s own good is unacceptable. Accordingly, the idea that “rights and dignity” are respected as long as the study participant’s welfare interests are not violated is mistaken.

Second, the no-consent model assumes that patients can have no reasonably “meaningful” basis for a preference between the randomized treatments and that this supports the no-consent proposal.9,10 This seems paternalistic in two ways. Even if patients do not have a meaningful basis for preferring A or B, they may have a meaningful basis for wanting to have a voice in the decision to participate in the randomized clinical trial. If a patient says, “I agree that there wasn’t a medical reason to choose A or B, but you should still have asked me,” it seems paternalistic to say to him that his complaint is unreasonable. It is unjustifiably paternalistic to hold that people have a right to exercise choice regarding research participation only when clinicians or ethicists judge them to have a meaningful interest in the matter. In addition, a patient may prefer drug A because, unknown to her doctor, she or a family member had a response to that drug in the past. This is not a meaningless basis of preference, and there may be other meaningful preferences that cannot be anticipated by the physician. Although under the terms of a pragmatic, randomized clinical trial the physician could use such information to over-ride the random selection of treatment,10 such a preference may not become known if the patient is excluded from the decision.

Third, there is very little benefit gained from concealing randomization. It is true that the no-consent model is simpler and far more efficient than the standard model of written informed consent. It would make possible studies that would otherwise be difficult to conduct under the standard model. But what if similar benefits could be obtained without actively concealing randomization? As we describe below, integrating usual clinical consent practices with an explanation of randomization would add very little burden while promoting the goals of a learning health care system even more fully.

From a practical perspective, the no-consent proposal unintentionally reduces the collaborative spirit of the learning health care model. Even if periodic and general educational efforts are made to inform patients about the occasional use of pragmatic, randomized clinical trials in the learning health care system, it seems doubtful that such efforts would be sufficient to bring about a genuine cultural change of patient expectations. In fact, if patients generally came to understand that concealment of randomization sometimes occurs, they would often have reason to be uncertain. Almost any treatment recommendation could be part of a randomized clinical trial. The uncertainty about whether their doctors are actively concealing information could erode trust. Furthermore, concealment of randomization deprives patients of an opportunity to actively — that is, by agreement — promote the “common purpose of improving the quality and value of clinical care and health care systems.”10

InTEGRATED CONSENT

We propose a model for informed consent when a pragmatic trial is testing commonly used treatments that in ordinary practice involve only brief verbal consent and that have been independently validated through well-controlled clinical trials. In such instances, we recommend a consent process that itself reflects the integrated model of learning health care.

When prescribing a treatment, physicians discuss its rationale, any alternatives, and their likely consequences (including both potential benefits and likely side effects) and obtain the patient’s agreement.13 In most cases, no written consent or form is necessary, and often only a brief discussion is needed. We assume that the pragmatic, randomized clinical trial would undergo customary IRB review, but the consent would simply incorporate the fact of randomization into the usual clinical discussion about treatment (see box).

Once a decision is made by the patient to enroll in the pragmatic, randomized clinical trial, the physician does what she would ordinarily do in the course of her practice — that is, document the clinical interaction. She would record the fact that the consent conversation took place (“We discussed the rationale, the risks and benefits of both options,” and so on), that there was agreement, and that a treatment (A or B) was chosen — including the process of random selection. She would also
check a box so that the patient’s outcomes are sent to the trial database.

This procedure recapitulates in the consent conversation the reality of an integrated clinical care–research process that is the pragmatic, randomized clinical trial. From an ethical point of view, this process is both necessary and sufficient: necessary for the reasons we have outlined above, and sufficient because virtually all the patient’s welfare interests are in line with what he would receive in ordinary clinical care and the only unusual element — that of randomization — is integrated into the clinical consent conversation.

This modified clinical consent procedure makes transparent to the patient the essential research component rather than actively concealing it. The increase in the amount of time and burden to the physician and the patient, as compared with the ordinary practice of clinical consent, should be minimal. The integrated consent model also provides an opportunity for the patient to actively collaborate in a learning health care activity.

INTEGRATED CONSENT AND EXISTING REGULATIONS

The proposed model does not include all the elements of informed consent required by U.S. federal regulations (e.g., it lacks explicit statements regarding voluntariness and confidentiality, because the context renders them unnecessary). However, the model satisfies the four regulatory requirements for alteration of informed consent. First, the kinds of pragmatic, randomized clinical trials that we describe above present research risks that are not greater than minimal. Second, the alteration would not adversely affect the rights or welfare of study participants, because the traditional, lengthy consent process offers no greater protection of the rights and welfare of patient–study participants than our integrated model. The third requirement — that the research cannot “practically” be carried out without the alteration — can be met to the extent that the unique value of the learning activity in a learning health care system requires highly integrated clinical and research elements. Standard consent practices for research participation would substantially burden ordinary clinical care so that the type of data targeted by a pragmatic, randomized clinical trial would be impracticable to collect. That is, if standard informed-consent processes for randomized clinical trials are required, no busy primary care office would be able to accommodate this practice in its existing day-to-day routine of patient care. This loss of the ability of the trial to mirror the everyday delivery of patient care would compromise the primary scientific benefit of a pragmatic trial — its generalizability to the actual, frontline practice setting. Fourth, patients could easily be informed of any pertinent information after the study, if appropriate.

CONCLUSIONS

A well-developed learning health care system would integrate clinical research with medical care, including the use of pragmatic, randomized clinical trials. Such trials can be designed so that the main distinguishing feature is that they replace “clinician’s uncertainty with randomization” in the selection of treatment. When such randomized clinical trials involve validated, widely used treatments that ordinarily require only verbal consent, the traditional approach to informed consent for research participation is ethically unnecessary and may in fact compromise the integrity of such studies, whose main rationale derives from the close integration of everyday health care delivery and research. The

Suggested Script for Disclosing Randomization in a Pragmatic, Randomized Clinical Trial.*

"[As we’ve talked about, you have high blood pressure. . . . We’ve already tried exercise and diet, and unfortunately they have not worked. . . . I can treat you with drug A or drug B. They’re both approved by the Food and Drug Administration, and I commonly use either one of them in patients to control high blood pressure; they are both taken once a day and they have similar side effects, which are . . . ]

But honestly, we doctors really don’t know if one is better than the other. So our hospital is doing a study by randomly (like a flip of a coin, so that we can obtain an unbiased answer) giving patients one or the other drug and then comparing results over a period of 1 year. You might remember that ours is a learning health care system and this means that we do the study as part of providing care, so there won’t be any special procedures or visits. And if at any point you or I think it would be good to try another medication instead, we can do that. So unless you have a preference for drug A or B, I’d like to include you in the study.

[Do you have any questions?]"

* Material similar to what is in the brackets would need to be discussed in ordinary clinical conversation. Only unbracketed portions are information added to disclose randomization.
solution, however, is not to jettison research consent altogether but to take the integration of medical care and clinical research to the informed-consent process itself. The integrated consent model, by incorporating the key research element in pragmatic, randomized clinical trials into a familiar clinical conversation, satisfies the requirements of both clinical and research ethics.

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