

CASE AND COMMENTARY

Can Consent to Participate in Clinical Research Involve Shared Decision Making?

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Abstract

Shared decision making honors patient autonomy and improves patient comprehension and therefore should be a part of every clinical decision a patient makes. Use of shared decision making in research informed consent conversations is more complicated due to diverse and potentially divergent investigator and patient interests, along with the presence of clinical equipoise. This article clarifies these different interests and discusses ways in which shared decision making can be applied in research. Provided there is transparency about competing interests, patient-centered and values-focused communication approaches embodied in shared decision making can support the ethical recruitment of patients for clinical research.

Case

Dr T is a rheumatologist and principal investigator in several clinical trials on biologic agents. One of her patients, Mr X, has rheumatoid arthritis that has not responded well to standard treatment. Dr T approaches Mr X about enrolling in a phase II trial, the purpose of which is to evaluate the efficacy, safety, and dose specifications of a new monoclonal antibody. Dr T explains the trial's design to Mr X, emphasizing the possibility that he would not receive the antibody if he is randomized to the placebo arm of the study. Dr T also explains that, if he does receive the antibody, Mr X could experience negative side effects and complications. Mr X agrees to participate in the trial.

About 2 weeks into the trial, during a follow-up visit, Dr T asks Mr X about his responses to the experimental agent. Mr X says, "Thank you, Dr T, for letting me try this treatment." Dr T explains that the antibody is neither a treatment nor (even anywhere near being) an approved clinical intervention. Dr T reminds Mr X of the trial's goals. Mr X responds, "I'm so lucky I have a doctor like you who can use research to help patients in ways other doctors can't. This new medicine is great."

Dr T wonders how to respond.

Commentary

Shared decision making is a pivotal way to uphold the foundational bioethical value of respect for patient autonomy.¹ Shared decision making involves eliciting patient preferences, aligning clinical care to those preferences, and ensuring that this process is made clear to the patient. Shared decision making thus improves patients' comprehension of their options, deepens the therapeutic alliance, and helps patients feel more comfortable that health care decisions match their goals of care.^{2,3,4}

Shared decision making can be an appropriate component of subject enrollment in clinical research studies, but the coexistence of a patient-centered approach with complicated investigator motivations—along with **clinical equipoise**—warrants an alternative approach to shared decision making. In this article, we summarize the basic approach to shared decision making and how it should be altered in the context of clinical research.

Practice vs Research

In clinical practice, shared decision making involves bidirectional communication between patient and clinician, in which both parties pursue high-quality care aligned to patient preferences, values, and goals of care.⁵ The clinician might have a personal preference for a particular approach, but this preference should be subordinate to the patient's direct clinical needs.

Clinical research brings different and often more complicated interests to the fore (see Table). These interests can be competing and affect the utility as well as the efficacy of shared decision making for the purpose of recruiting subjects for clinical studies.

Table. Interests of Clinical Practice vs Research Consent

Interests	Setting	
	Clinical Practice	Clinical Research
Public	<ul style="list-style-type: none">• Public health in general• Wise resource allocation• Suppression of transmissible diseases	<ul style="list-style-type: none">• Advancement of science
Institutional	<ul style="list-style-type: none">• Application of standard of care• Protection from legal risk by robust disclosure of risks benefits and alternatives	<ul style="list-style-type: none">• Grant funding• Prestige• Public trust
Clinician	<ul style="list-style-type: none">• Good health outcome for patient• Connection to patient• Good outcome metrics in eyes of institution	<ul style="list-style-type: none">• Patient safety and well-being• Good will between clinicians and investigator colleagues
Investigator	<ul style="list-style-type: none">• Not applicable	<ul style="list-style-type: none">• Grant funding• Prestige• Smooth enrollment of subjects

Patient	<ul style="list-style-type: none"> • Better health • More engagement • Understanding of risks, benefits, and alternatives • Connection to clinician 	<ul style="list-style-type: none"> • Altruism • Access to cutting edge therapies • Potential therapeutic misconception
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In contrast to clinical practice, an investigator enrolling a potential research subject is acting more on self-interest while also furthering the public interest in the advancement of science. She wishes to reach target enrollment smoothly, swiftly, and within budget. She seeks scientific discovery, career advancement, ample funding, and the like. The potential research subject might also have complicated interests at play in the decision to enroll in a research study. For example, the potential research subject may be motivated by altruism or the desire to access cutting edge therapies, and he may be subject to therapeutic misconception—the belief that he is sure to benefit therapeutically from research engagement.⁶ At times, the interests of investigators and potential research subjects can compete, such as when an investigator derives monetary or other less tangible benefits from enrolling subjects in a trial that might engender risks a subject would prefer to avoid.

Equipoise

Diverse and potentially competing interests are not the only reason shared decision making in the research context differs from that of clinical practice. The existence of clinical equipoise—ie, uncertainty about the relative therapeutic benefit of every arm of a trial—alters the role of shared decision making when consenting a potential subject to participate in clinical research. In the clinical setting, expected outcomes of a diagnosis or treatment are reasonably well known and can be aligned to patient goals of care. By contrast, the validity of clinical research requires clinical equipoise. In the presence of equipoise, it is not clear how the decision at hand will or will not further the research subject’s values and goals. This uncertainty must be clear to the patient to avoid therapeutic misconception and thus to orient the patient to valid interests in study participation, such as altruism, curiosity, and trust in the investigator. Without clarifying that uncertainty exists as to the relative superiority of any given treatment, it would be easy for the investigator’s personal interests (such as monetary incentives for subject recruitment or pursuit of career advancement) to swamp the larger subject-centered values that more properly should motivate recruitment and the subject’s personal decision about whether or not to participate.

The key differences between investigators’ and subjects’ interests and the existence of clinical equipoise inform the approach to shared decision making in the research context. We will summarize the basic structure of shared decision making and how its application changes in informed consent conversations with potential clinical research subjects.

Shared Decision Making in Research

In clinical practice, shared decision making generally involves 3 components: (1) assessing health literacy in order to properly clarify the decision at hand, (2) discussing risks and benefits, and (3) explicating how different options align with a patient’s personal context and overall goals.⁷

Assessing health literacy is an essential first step in the shared decision-making process to determine the appropriate language to convey options, risks, and benefits in a manner the patient understands. It is the clinician's responsibility to translate the language of medicine into the vernacular. If 2 parties in a conversation are speaking different languages, the conversation goes nowhere. Once patient and clinician share a common language, only then can the conversation move towards a meaningful discussion of the available options. Perhaps the most pivotal part of shared decision making is what follows—eliciting the patient's preferences and values and explaining how potential decisions and outcomes align with these preferences and values.

In the research context, consent to be a research subject can involve shared decision making, but the process is modified to address the different interests of subjects and investigators as well as the existence of equipoise. The major steps of the process are as follows:

1. Assess the health and research literacy of the potential research subject.
2. Disclose physician interests in the proposed study.
3. Discuss patient motivations for participation.
4. Translate research methodology and technical language into the vernacular.
5. Explain potential risks and benefits of both placebo and intervention.
6. Assist the patient in picturing how the decision to either participate or not participate in the study would fit into his or her lifestyle.
7. Allow the patient to decide whether to enroll as a human subject.

In discussing clinical research, there are multiple health and research literacy issues that need to be made clear before a potential research subject can truly consent. For example, the investigator must assess potential research subjects' understanding of their own medical condition before discussing their comprehension of a proposed experimental intervention for that condition. Research terminology may be opaque to potential research subjects. Do they understand what *randomization* or *phase II trial* mean? Explaining these complicated concepts in lay language is essential.

Following the health and research literacy assessments, the clinical investigator should disclose relevant personal interests to the potential research subject, including whether the investigator is paid to recruit potential subjects for a clinical trial or has stock in the company funding the study.

After addressing health and research literacy, as well as disclosing potential **conflicts of interest**, the next step is an open and honest conversation about the potential research subject's motivations. This is a crucial step in the shared decision-making process for research consent because of the opportunity to clarify important misconceptions and resolve conflicts of interest. Once motivations and interests of both parties have been made clear and misconceptions corrected, if both the potential research subject and the investigator are comfortable moving forward in the consent proceedings, the next step is to explain what a "study" really means.

Only after motivations and study design and concepts have been made transparent should the conversation shift towards describing potential risks (ie, side effects) or benefits (ie, potential therapeutic outcome based on mechanism of action) of all arms of the study—in this case, the placebo and intervention. Physicians partaking in shared decision making with potential research subjects are presented with the challenge of

both accurately conveying what is known so far about the experimental intervention(s) and clarifying that significant uncertainty regarding the efficacy of the intervention(s) inherently still exists.

What's Needed for Informed Consent

Shared decision making in the research context, conducted as above, supports high-quality informed consent conversations and thus leads to true subject comprehension and better alignment of enrollment decisions to subject values.

Revisions to the Common Rule, a federal law that protects human research subjects—including by obtaining informed consent—support the use of shared decision making in informed consent conversations. Effective January 2019, the Common Rule was revised in an effort to promote respect for the autonomy of human subjects. These revisions to the Common Rule include intensified requirements that subjects be armed with “the information that a reasonable person would want to have in order to make an informed decision.”⁸ Researchers are now required to present not only why someone might choose to participate, but also why someone might choose not to take part in a study.⁸ Furthermore, the Common Rule now specifies that informed consent should not “merely provide lists of isolated facts.”⁸ The US Department of Health and Human Services has defined “key information” that should be included at the beginning of any consent documentation^{8,9} and specified that basic information be provided, including the purpose and duration of a study and the procedures involved as well as reasonable and foreseeable risks, discomforts, and benefits. Each of these features of informed consent can easily be built into the shared decision-making process outlined above, particularly steps 5 to 7.

Traditionally, informed consent forms have consisted of dozens of pages of densely typed text that is not linguistically accessible to or understood by the majority of research subjects.^{10,11} A signature at the end of an informed consent form, therefore, often does not guarantee **true informed consent**. Although recent amendments to the Common Rule aim at improving the informed consent process, the changes do not encompass the wording of consent forms or the order of documentation. The inclusion of shared decision making in research informed consent, by contrast, would address this unmet need.

Comprehension

Coming back to the case at hand, assuming that Dr T has not done so already, she should start with the first step in shared decision making for informed consent: the assessment of Mr X's health and research literacy. No matter how carefully and thoroughly Dr T feels she has described Mr X's role in the study, all of this talk is for naught if Mr X doesn't understand the goals of the conversation. Then we suggest that Dr T disclose her personal interests in the clinical trial if she has not already done so, in part so that Mr X could weigh whether this disclosure affects his interest in participation. Once Dr T and Mr X agree on the goals of the conversation and transparency about mutual interests has been ensured, the two should discuss the necessary study details—including the consequences of agreeing or refusing to participate in the study—even if this means covering some of the same ground. Mr X should be able to describe in his own words what he understands his role in this research to be; this teach-back method has been shown to enhance understanding.¹² In the event that Mr X cannot articulate the inherent risks and benefits of participation in the experimental study despite Dr T's

clarifying and reiterating them, then the only appropriate course of action is disenrollment from the study.

Achieving baseline understanding is essential to informed consent. From the information provided, Mr X appears not to understand what randomization entails, what phase of research he is participating in, and what *treatment* means in this context. Each concept should be clarified, as should Mr X's motivations for participation. Now that their informed consent conversation has been tailored to Mr X's health and research literacy, undertaken with transparency about interests, and focused on aligning a decision about enrollment with Mr X's goals and values, both Mr X and Dr T can be confident that Mr X's decision to participate in research comports with the federal standard for outstanding clinical research.

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Editor's Note

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Conflict of Interest Disclosure

Benjamin Moulton has worked for the nonprofit Informed Medical Decisions Foundation, which merged into the nonprofit Healthwise. Both nonprofit organizations produced and disseminated patient education materials, including patient decision aids. As chief executive officer of Informed Decisions, LLC, he provides policy advice to both nonprofit and for-profit organizations. His clients have included ACP Decisions, the Informed Medical Decisions™ Program at Massachusetts General Hospital, and EBSCO Health. Glyn Elwyn has edited and published books by Oxford University Press and Radcliffe Medical Press that provide royalties on sales, and he owns copyright in measures of shared decision making and care integration—namely, CollaborATE, IntegRATE, ConsiderATE, CoopeRATE, ToleRATE, and Observer OPTION(5) and Observer OPTION(12). In addition, he has in the past provided consultancy for organizations, including Emmi Solutions, LLC; National Quality Forum; the Washington State Department of Health; and SciMentum, LLC. He is the founder and director of &THINK, LLC and SHARP NETWORK, LLC, and serves as an advisor or consultant for Access Community Health Network, Chicago; EBSCO Health; Bind; PatientWisdom, Inc; and Abridge AI, Inc. The other authors had no conflicts of interest to disclose.

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