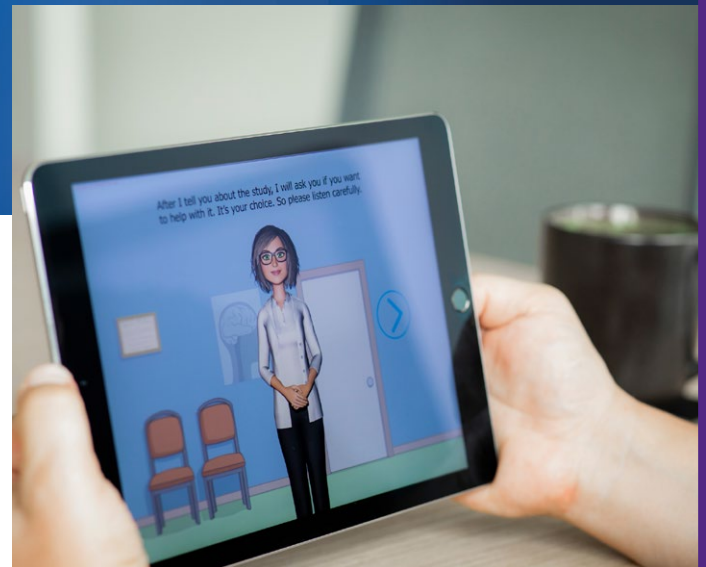


Making Clinical Trials More Patient-Centered Using Digital Interactive E-Consent Tools

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Abstract

Research participants are required to give their consent to participate in clinical trials and nonexempt government-funded studies. The goal is to facilitate participant understanding of the intent of the research, its voluntary nature, and the potential benefits and harms. Ideally, participants make an informed choice whether to participate; one that is based on having sufficient relevant knowledge and that is consistent with their values and preferences. Achieving this objective can be challenging, and as such, many scholars have declared the consent process flawed or "broken." Moreover, clinical trials are complex studies, and compelling evidence suggests that current consent processes are inadequate in achieving informed choice. E-consent offers a dynamic, engaging consent delivery mode that can effectively support making informed decisions about whether to participate in a trial.

Key Findings

- Many participants join trials without reviewing consent forms.
- Trial participants may feel hopeful and thus not register the risks.
- E-consent platforms offer an effective, well-received mode of decision support.
- Consenter (<https://www.consenter.org/>) provides decision support for clinical trials including people with limited cognitive capacity.

Participants are required by a regulation called the Common Rule to provide consent before participating in clinical trials and nonexempt federally funded human subject research.^{1,2} The regulations are intended to protect participants from enrolling in studies without adequately understanding the research purpose and that they personally may not benefit and could even be harmed. Typically, eligible individuals meet with a research representative who recites study information from a paper consent form and asks the potential participant if there are any questions or concerns before obtaining a signature.

This process is often insufficient to achieve informed choice among participants. Many factors contribute to the ineffectiveness of this practice. First, some people decide to participate in a study before the consent interaction.³ As such, they may be minimally engaged in the consent process. Other individuals may arrive to the study center with the consent form already signed. In the case of clinical trials, a participant's eagerness to realize a health benefit, even though one may not be achieved, may impede attention to the potential limitations and harms. Studies of the consent process have likewise demonstrated poor participant understanding of study procedures and outcomes.^{4,5} Further complicating the challenges to achieving informed consent, clinical studies and their accompanying consent processes have grown in complexity, particularly for multisite clinical trials.

A leading expert on informed consent at the National Institutes of Health, Dr. Christine Grady, wrote in a *New England Journal of Medicine* report that the classic consent interaction is outdated.⁶ Although

John Wilbanks, chief commons officer at Sage Bionetworks, a biomedical research organization, punctuates this sentiment by stating that, "Informed consent has not been implemented as a relationship, but instead as a single-point transaction that must be completed to enroll participants."⁷ McNutt and colleagues support this critique with evidence that potential participants spend little time reviewing consent forms.⁸ Particularly concerning are data from Lee and colleagues indicating that participants in environmental health studies failed to understand the risks of the research in which they enrolled.⁴ Accordingly, Dr. Gail Henderson has posed the question, "*Is Consent Broken?*" based on the challenges of consenting participants for genomic sequencing research.⁹ The concerns raised by this collective evidence persist and call into question whether study participants are adequately informed.

Commentaries by bioethicists often highlight clinical trials as studies that present the greatest challenges to an effective and efficient consent process.¹⁰ When consenting to participate in clinical trials, patients frequently misunderstand key information in the consent process, including the rationale and design of the study.⁵ This misunderstanding can lead to difficulty with recruitment and higher drop-out rates.¹¹ Globally, 90 percent of trials fail to achieve timely recruitment of their targeted population¹² and participant dropout rates average 30 percent for Phase 3 trials.¹³ Given this, recruitment and retention of eligible participants are critical to the success of clinical trials; problems with either can lead to time extensions, underpowered studies, and even early study termination.¹⁴ Ensuring that potential participants have a good understanding of the clinical trial through better informed consent procedures can address these recruitment and retention challenges.¹⁵⁻¹⁷

Lentz and colleagues report professional consensus that the current informed consent process for clinical trials needs to improve to enhance participants' understanding.¹⁸ One important improvement is greater retention of participants. To address the deficits, the Clinical Trials Transformation Initiative published recommendations to improve trial consent by including a tiered consent process that

provides critically relevant information customized for decision making about trial participation.¹⁸ Consistent with the initiative's efforts, the Department of Health and Human Services, in recognizing the need to improve the consent process for clinical studies, updated the Common Rule to include a requirement for a clear, concise, and focused summary of key information.¹

Drs. Grady⁶ and Henderson⁹ both articulate how technology is advancing research methods and clear communication practices, calling for opportunities to develop concise novel approaches to improve informed consent. Addressing this call, Grady and colleagues conducted a randomized trial comparing a short concise consent to standard consent within a multinational trial on the timing of starting antiretroviral therapy in HIV-positive adults and found the longer consent form provided no additional benefits.¹⁹ Kim and Kim also tested a simplified clinical trial consent form for its effect on understanding and thus the efficacy of consent information. They found the simplified form to be associated with higher levels of objective and subjective understanding.²⁰ Turbitt and colleagues similarly found a streamlined consent process to be equivalent to standard consent for participating in a genome sequencing study.²¹ This evidence reinforces Agency for Healthcare Research and Quality guidance that information should be delivered in a way that is simple, clear, and concise.²²

In addition to responding to how information is presented, decision science recognizes individual factors that are also at play when making a decision to enroll in a clinical trial. These cognitive and affective factors have been shown to impede understanding that a clinical trial comes with no guarantee of a positive health outcome. Specifically, several common factors—such as optimism and hope for health gains,²³ challenges in understanding probabilities,²⁴ and limited health literacy—adversely affect decision making.²⁵ Further, personal relevance and tailored presentation of information can affect health decision making.²⁶ The offer of participation in a clinical trial is often a novel opportunity for potential participants who have no prior experience to inform their decision. Decision support tools can address many

of these factors, such as using plain language and low health literacy standards.

Evidence from a Cochrane review supports the use of decision aids as an effective way to optimize informed consent for clinical trials.²⁷ Decision aids for health-related topics improved several patient reported outcomes: understanding of options and consequences, more realistic expectations, more active participation, and greater decisional satisfaction. Based on these outcomes, Juraskova and colleagues tested the efficacy of a decision aid to enroll in clinical trial or not.²⁸ They found that those who received the decision aid had higher knowledge after deciding to enroll in the trial than those who received standard consent materials. Additionally, those who received the decision aid had lower decisional regret. Higher trial knowledge and less regret suggest the benefits of a decision tool that includes key consent information and allows participants to clarify their values by comparing risks and benefits of participation. Innovative ways to convey information and assess understanding may be effectively presented within this format.

Identifying practical, simpler ways to respect persons' self-determination and choices led Dr. Grady to observe that information technology may be an effective way to provide informed consent with minimal intrusion into the lives of potential participants.⁶ Digital informed consent, broadly referred to as "e-consent," is a technology-based patient-engagement tool that typically presents consent information using multimedia components and may also include a digital signature. E-consent aims to improve understanding among potential participants in clinical trials and subsequent trial retention.

Recent studies demonstrate the benefits of e-consent when compared with the standard informed consent process. Rowbotham and colleagues conducted a randomized controlled trial comparing an e-consent that combined a video, standard consent language, and an interactive quiz with a paper consent. They demonstrated that the interactive e-consent improved understanding of study procedures in, and the risks of a chemotherapy trial.²⁹ Kraft and colleagues conducted a randomized study assessing

three multimedia e-educational aids compared with standard text aids to understand medical practice research.³⁰ Dual-channel approaches, animated videos, and slideshows with voiceover were significantly more effective than single-channel techniques in achieving participant understanding of the research. Similarly, an observational study by Fanaroff and colleagues comparing video- to text-based consent for multicenter trial enrollment found that the sites that implemented video consent more rapidly enrolled the first participant and enrolled older and more ethnically diverse participants than the sites using text consent.³¹ E-consent platforms can also be readily translated into other languages extending accessibility to more diverse participants. Tenaerts and colleagues cite advances in e-consent, such videos or dual channels that combine visuals with voiceover, followed by quizzes as some of the most striking improvements in clinical trial consent over the past decade.³²

The Food and Drug Administration has published guidance on the use of e-consent in clinical studies, including clinical trials.³³ Some platforms allow for electronically signing and enrolling in trials, which can be an added benefit. Regardless, e-consent comes with challenges in verifying that participants have the capacity to consent and that participants are the person they claim to be.

Despite recent advances, the challenge of achieving informed consent from research participants with cognitive impairment remains. Individuals with cognitive impairment have a difficult time retaining novel information communicated verbally without prompts. They may also have short attention spans. Although e-consent platforms offer novel ways to convey key information to achieve informed consent, clinical investigators need evidence to determine approaches that are most effective. One randomized study of a hypothetical clinical trial compared standard paper consent to e-consent paired with a digital, interactive education tool for adults with intellectual impairment associated with fragile X syndrome.³⁴ The digital tool included dual-channel delivery of information, interactive elements to illustrate the main concepts of consent and a quiz to check for understanding. Use of the tool by

adults with fragile X syndrome was shown to result in enhanced understanding among a subgroup of participants. The combination of e-consent elements (dual-channel information, interactive elements and a quiz) is likely to be the driving factor enhancing understanding³⁴ though individual elements may be more impactful for certain individuals. Research is needed to examine the e-consent process relative to the standard consent process for individuals with cognitive impairments as well also those without including the user experience. Future studies should examine the impact on e-consent on a range of measures including the understanding but also the ability to reason and make informed decisions as a result of increased understanding. Our research has found that higher functioning individuals with fragile X syndrome were more likely to understand the concrete elements of the trial and higher understanding was a significant predictor of appreciation (i.e., one's ability to link the decision to one's one situation).³⁴ The digital tool, Consenter, has since been updated and its capacity expanded. It is available through RTI International as a customizable decision tool to achieve informed consent for clinical trials enrolling those with intellectual impairment participants as well as those without cognitive challenges (<https://www.consenter.org/>).

Updated expectations to improve consent and recent evidence, coupled with innovative technological advancements, highlight the promise of e-consent to improve the consent process for clinical trials. Further, e-consent responds to the call for technology that is minimally intrusive and individualized while conforming with consent regulatory requirements.¹

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