Ethical Considerations in Conducting Pragmatic Trials in Oncology

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Pragmatic trials evaluate interventions in real-life scenarios, which differ from explanatory trials that control for numerous factors and variables to best determine causal associations. Each approach has advantages and disadvantages. Conducting pragmatic research trials while maintaining the tenets of the ethical conduct of research can sometimes be challenging, particularly regarding informed consent. In this column, distinctions between pragmatic and explanatory trials are discussed from an ethical view.

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Pragmatic trials capture the essence of an intervention in real-life scenarios and time, and may differ from explanatory trials, which focus on the efficacy of an intervention via ideal clinically orchestrated methods (Gaglio, Phillips, Heurtin-Roberts, Sanchez, & Glasgow, 2014; Schwartz & Lellouch, 2009). Schwartz and Lellouch (2009) defined pragmatic trials as analyzing outcomes of interventions between subjects who choose which intervention to participate in. In comparison, explanatory trials test causal associations or the efficacy of an intervention under controlled conditions (Gaglio et al., 2014; Schwartz & Lellouch, 2009; Thorpe et al., 2009).

Pragmatic trials can also take the form of randomized, controlled trials, which compare a new therapy to standards of care (Kalkman, van Thiel, van der Graaf, et al., 2017; McKinney et al., 2015). Pragmatic trials usually have larger samples, occur in varied settings, and boast high external validity, whereas explanatory trials are more controlled, have smaller samples, and claim higher internal validity (Patsopoulos, 2011).

Research ethics can sometimes be challenging to uphold when conducting pragmatic trials. By defining the constraints of the research protocol according to ethical guidelines, the natural setting of the pragmatic trial can be compromised. For example, the process of obtaining informed consent with forms that must include specific criteria can disclose information to participants that could compromise the study, or, in some cases, the trial can be compromised by the participants knowing they are part of the study (McKinney et al., 2015). In addition, the informed consent content and process can lead to a biased sample because of select groups who agree to participate and who may not be a comprehensive representation of the targeted population (Kalkman, van Thiel, Zuidgeest, et al., 2017), therefore limiting external validity (Patsopoulos, 2011). A growing argument among researchers conducting pragmatic trials is for the use of alternate consents, such as integrated consent (a combined consent process for clinical procedures and research), broadcast consent (notifications about trials are distributed, and patients are given the opportunity to ask questions; no written informed consent exists), or complete waivers of consent (Kalkman, van Thiel, Zuidgeest, et al., 2017). Another approach gaining popularity is staged-informed consent, in which individuals within a cohort sign one consent to be randomized to a trial, and those randomized to the intervention arm are given a second consent that details the intervention (therefore reducing crossover and contamination from those not randomized to the intervention). At the end of the study, the entire cohort receives the