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Patient-Centeredness in the Design of Clinical Trials

C. Daniel Mullins, PhD[1], Joseph Vandigo, MBA[1,], Zhiyuan Zheng, PhD[1,3], Paul Wicks, PhD[2]*

[1]*Pharmaceutical Health Services Research Department, University of Maryland School of Pharmacy, Baltimore, MD, USA;* [2]*PatientsLikeMe, Inc., Research & Development, Cambridge, MA, USA;* [3]*Surveillance and Health Services Research Program, American Cancer Society, Atlanta, GA, USA*

ABSTRACT

Evidence from clinical trials should contribute to informed decision making and a learning health care system. People frequently, however, find participating in clinical trials meaningless or disempowering. Moreover, people often do not incorporate trial results directly into their decision making. The lack of patient centeredness in clinical trials may be partially addressed through trial design. For example, Bayesian adaptive trials designed to adjust in a prespecified manner to changes in clinical practice could motivate people and their health care providers to view clinical trials as more applicable to real-world clinical decisions. The way in which clinical trials are designed can transform the evidence generation process to be more patient centered, providing people with an incentive to participate or continue participating in clinical trials. To achieve the transformation to patient-centeredness in clinical trial decisions, however, there is a need for transparent and reliable methods and education of trial investigators and site personnel.

Keywords: adaptive, Bayesian, patient-centered, pragmatic, trial design.

Introduction

Activated and engaged people are empowered to meaningfully participate in their health care [1]. When it comes to research, however, people generally participate passively in the learning process; participants usually are involved in clinical trials merely as human subjects rather than as engaged stakeholders. A more patient-centered approach to participant involvement in outcomes research has been proposed, which would lead to the empowerment of participants throughout the research process [2]. Study design elements of clinical trials intended for regulatory approval of drugs and health care technologies, however, traditionally do not reflect a patient-centered approach.

Meaningful participant involvement to help produce and disseminate relevant evidence for decision making is made more difficult when the clinical trial experience falls short of the participant's initial expectations. Individuals may feel comfortable with their participation initially, but they may become unsure of their involvement later as they progress through the trial. For instance, although participants in cancer trials are satisfied with their medical care, they are disappointed not to learn more about their disease through their involvement in research and they find that trial participation takes more time and effort than they thought it would [3]. As a result, the application of a patient-centered approach requires more than identifying people who are willing to participate in trials. Many people are, at least in theory, willing to participate in research if the study is convenient and if they are informed of study results [4].

There is no single answer to addressing the divide between expectations and the reality of clinical trial participation. Therefore, improvements to ensure that participants are truly providing informed consent must be implemented to address participant-related factors (e.g., mistrust of medical research, hard-to-reach groups, and lack of resources), contextual factors (e.g., cultural traditions), and research-related factors (e.g., likelihood of receiving placebo, risk of harm, and inconvenience of protocol) [5].

Patient-Centeredness through Clinical Trial Design

Patient-centered outcomes research is designed to "help people and their caregivers communicate and make informed health care decisions, allowing their voices to be heard in assessing the value of health care options" [6]. People increasingly want to be informed, empowered, and engaged with their medical management [7]. This attitude would carry over to clinical trial participation if many of the concerns regarding the fact that trials are not "patient centered" could be addressed. Providing better information to participants and incorporating alternative trial designs are ways to minimize these concerns. In this commentary, we discuss the potential for pragmatic, Bayesian, and adaptive trial designs to enhance patient centeredness within a clinical trial setting. There are characteristics specific to pragmatic, Bayesian, and adaptive clinical trials that offer potential improvements to the clinical

* *Address correspondence to:* Joseph Vandigo, Pharmaceutical Health Services Research Department, University of Maryland School of Pharmacy, 220 Arch Street, 12th Floor, Baltimore, MD 21201.

E-mail: jvandigo@umaryland.edu.

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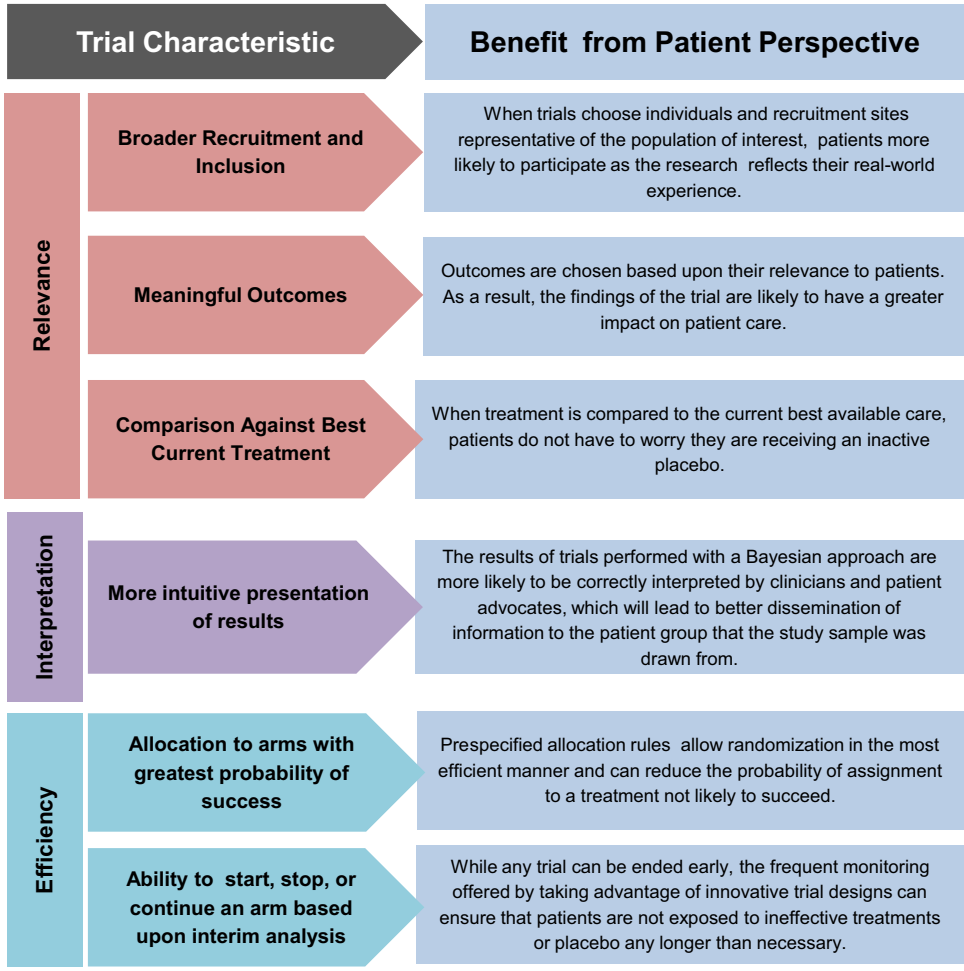

Fig. 1 – Means by which trials designs can promote recruitment and retention in clinical trials by improving the patient experience.

trial process, which frequently is neither patient centered (in terms of the evidence generated, population studied) nor patient friendly (in terms of meeting information needs). The goal is to consider the viewpoint of participants, rather than trialists or other stakeholders, and to supplement the wealth of literature on these trial designs that document the benefits to other, nonparticipant, stakeholders. Figure 1 illustrates these characteristics and their corresponding benefits in terms of relevance, transparency, and efficiency from the perspective of the patient.

Pragmatic Trials

Traditional trials recruit highly selected patients seen in specialist environments and meet rigorous inclusion/exclusion criteria such as being free of comorbidities, which might confound the results of the experiment. In contrast, pragmatic trials support the generation of evidence that might be considered more relevant to the real-world decision making of participants [8]. Pragmatic trials recruit from various clinical settings and include study participants who reflect the real-world population affected by the condition the treatment aims to address. This means that the participants most likely to benefit from a treatment will be represented in the study and the effect observed in the trial more closely represents what a typical person could expect to experience. Pragmatic trials frequently also support the utilization of outcome measures that are more relevant to participants. Incorporating outcomes that are meaningful to participants increases the likelihood that once the results of a study are made available, people will benefit from the knowledge gained. For example, if a study examines only changes in laboratory values or clinical indicators, it will be unable to help a person decide whether a treatment is right for him or her if that individual is concerned with quality-of-life issues. Where nothing prevents patient-reported outcomes from being used in traditional trials, historically these types of measures were relatively uncommon or perceived as less important than laboratory values. This is also not to suggest that pragmatic, Bayesian, and adaptive trials are prohibited from using laboratory values and clinical indicators; they are simply in a position to support the use of outcomes relevant from a patient perspective. Individuals participating in a pragmatic clinical trial likely will receive the current criterion standard of care or the innovative treatment; no patient receives an inactive comparator (placebo) unless there truly are no comparator interventions in use, such as in trials in which there is no equipoise between no therapy and the experimental therapy. Consequently, the study results will more accurately inform decisions in the real world in which people and their clinicians typically have to make a choice between therapeutic options.