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ORIGINAL ARTICLE

Patient preferences for personalized (N-of-1) trials: a conjoint analysis

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Abstract

Objective: Despite their promise for increasing treatment precision, Personalized Trials (i.e., N-of-1 trials) have not been widely adopted. We aimed to ascertain patient preferences for Personalized Trials.

Study Design and Setting: We recruited 501 adults with ≥2 common chronic conditions from Harris Poll Online. We used Sawtooth Software to generate 45 plausible Personalized Trial designs comprising combinations of eight key attributes (treatment selection, treatment type, clinician involvement, blinding, time commitment, self-monitoring frequency, duration, and cost) at different levels. Conditional logistic regression was used to assess relative importance of different attributes using a random utility maximization model.

Results: Overall, participants preferred Personalized Trials with no costs vs. $100 cost (utility difference 1.52 [standard error 0.07], $P < 0.001$) and with less vs. more time commitment/day (0.16 [0.07], $P < 0.015$) but did not hold preferences for the other six attributes. In subgroup analyses, participants ≥65 years, white, and with income ≤$50,000 were more averse to costs than their counterparts (P all $<$ 0.05).

Conclusion: To optimize dissemination, Personalized Trial designers should seek to minimize out-of-pocket costs and time burden of self-monitoring. They should also consider adaptive designs that can accommodate subgroup differences in design preferences.

Keywords: N-of-1 trials; Conjoint analysis; Multi-morbidity; Patient-centered care; Heterogeneity of treatment effects; Discrete choice

1. Introduction

The age of personalized health and patient-centered care [1], particularly as they relate to chronic disease management [2], has ushered in a renewed interest in a decades-old methodology—Personalized Trials (also known as N-of-1 trials or single-person trials) [3,4]. Unlike parallel-group randomized controlled trials that randomly assign patients to different treatments to understand the effects of treatments in a population, Personalized Trials randomize treatments across time within each patient to determine the relative benefits and harms of the treatments for that one patient [5]. In this way, Personalized Trials are the foundational design for a truly patient-centered comparative effectiveness method [6]. In fact, a recent working group suggested that Personalized Trials may provide the strongest evidence in the hierarchy of evidence-based medicine for informing individual patients' treatment decisions [7,8]. Historically, in introducing evidence-based medicine, Guyatt and others described these Personalized Trials as the pinnacle of the evidence-based design pyramid [9].

In prior research, Personalized Trials have led to valuable changes in treatment, cessation of treatment, or confirmation of the efficacy of the original treatment [10–12]. However, other than isolated pockets of activity, Personalized Trials are conducted infrequently in clinical practice [8,13,14]. In postmortem assessments as to why

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What is new?

Key findings

- Patients held the strongest preferences for Personalized Trial prototypes that minimized out-of-pocket costs and required brief daily monitoring.
- Design features such as blinding, treatment type, and overall trial duration did not significantly influence patient preferences for Personalized Trials.
- There was particular aversion to cost amongst white, lower income and older participants compared to their counterparts.

What this adds to what was known?

- This is the first study to use conjoint methodology to assess preferences for Personalized (i.e., N-of-1) Trial designs.
- This study will help inform the design and marketing of the next generation of Personalized Trials aimed at patients with multiple chronic conditions.

What is the implication and what should change now?

- Personalized trial designers and public health officials should consider ways to limit out-of-pocket costs associated with Personalized trials and consider facilitating brief self-monitoring with mHealth.

Personalized Trials never became standardly used designs, proponents concluded that they were insufficiently appealing to patients or clinicians to justify the cost and effort needed to design and implement them [8,13]. Personalized Trial design specifications are mostly driven by clinicians or researchers [5,14]. Yet, there are a number of options for design features or design attributes (e.g., cost, blinding, duration) that could influence patient acceptability and demand [5]. A better understanding of the circumstances under which patients would be interested in conducting Personalized Trials could foster a wider adoption in the use of this methodology [5,15].

Conjoint analysis is a well-established market research technique for assessing consumer preferences. It involves asking consumers to choose between hypothetical products that differ along a number of "attributes." Each of these attributes is defined by a set of characteristics called "levels." For example, a car can be described by attributes such as color and price. Levels for color can include black, white, and blue. The choices respondents make between hypothetical products can then be analyzed to determine how changes in these attributes can impact overall product acceptability [16–18]. We aimed to use conjoint analysis to elicit patient preferences for Personalized Trial designs and to understand the ways in which Personalized Trial attributes (e.g., cost, blinding, trial duration) contribute to the overall acceptability of these trials. The results would allow researchers and clinicians to incorporate patient preferences when designing the next generation of Personalized Trial prototypes such that they will be attractive to patients. Although conjoint analyses have been widely used in the fields of psychology, economics, and marketing, and more recently in public health, they have infrequently been used to inform clinical trial design [18].

2. Methods

2.1. Stakeholder engagement

An essential component of our methodology was the development of a "collaboratory" or a networked format that includes social processes such as collaboration techniques, formal and informal communication, and agreement on norms, principles, values, and rules by a group of stakeholders relevant to the design and implementation of Personalized Trials in clinical practice [19]. The collaboratory's 30-member team included patients with multiple comorbidities, clinicians with and without experience conducting N-of-1 trials, health care administrators, scientists, methodologists/statisticians, ethicists, and experts in dissemination. Our collaboratory met quarterly from July 2014 to September 2017 to review study design, conduct, analysis, interpretation, and dissemination of findings. Collaboratory meetings were conducted by phone and in person and were scheduled to maximize the availability of all participants. This allowed for a transparent process and helped improve the relevance of the study design and approach.

2.2. Recruitment

We conducted a cross-sectional survey of 501 individuals with two or more chronic conditions.

Participants were recruited from a general population panel maintained by the Harris Poll Online (HPOL), which includes several million online members. The panel was recruited from a multitude of sources (e.g., targeted emails sent by online partners, social media, news, and telephone recruitment of targeted populations). Each recruitment source was carefully vetted through a rigorous interviewing and testing process and then monitored for response quality on an ongoing basis. For the present study, the HPOL panel was actively screened to identify a nationally representative group of adults with two or more chronic conditions. These sampling procedures have been widely used and allow for rigorous, scientifically acceptable practice without spending considerable time and energy assembling large and comprehensive samples [20].