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ORIGINAL ARTICLE

A patient-focused, theory-guided approach to survey design identified barriers to and drivers of clinical trial participation

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Abstract

Objectives: Despite clear evidence showing that many clinical trials fail or are delayed because of poor patient recruitment, there is surprisingly little empirically supported guidance for trialists seeking to optimize their trial recruitment strategies. We propose that the challenges of recruitment can be better understood and addressed by thinking of research participation as one or more behaviors, subject to the same forces as other human behaviors. In this article, we describe an adaptable, behavioral theory-driven approach for designing pretrial surveys of the barriers and drivers relevant to trial participation. Instead of proposing a single survey instrument intended to be used uniformly across many situations, we propose that tailored surveys be informed by a common comprehensive, theory-guided development approach that ensures all domains potentially guiding participation are considered.

Study Design and Setting: We used the Theoretical Domains Framework (TDF), which organizes over 100 constructs known to be associated with behavior and behavior change into 14 domains that describe determinants of professional and patient health behaviors, to inform the development of tailored surveys about barriers to and drivers of clinical trial participation. After searching the literature for barriers and drivers to trial recruitment relevant to each of the TDF domains, we developed separate surveys for members of two national health charities (Canadian Breast Cancer Network, Huntington Society of Canada) to exemplify how the approach can be adapted across settings. We conducted think-aloud interviews with members of each group to maximize the clarity and usability of the surveys, elicited opinions about which barriers/drivers were relevant for each patient group, and identified additional barriers/drivers. Interviews proceeded iteratively with changes incorporated into subsequent interviews. Here, we describe our two target patient groups, as well as our process of modifying, adding, and deleting barrier/driver items for each group and across theoretical domains.

Results: We interviewed 8 women with a history of breast cancer from the Canadian Breast Cancer Network (48−65 year old) and 11 Huntington Disease community members (9 women) from the Huntington Society of Canada (26−70 year old). After the iterative development interviews, the breast cancer group had identified 38 barriers/drivers thought relevant to their participation in clinical trials across 12 TDF domains. The Huntington group identified 47 items across 13 TDF domains.

Conclusion: Our patient-focused and theory-guided approach was able to identify a more comprehensive range of barriers to and drivers of trial participation than existing published tools. Our approach is also more broadly adaptable than such tools, in that it uses a theoretical framework and in-depth piloting to generate a set of items tailored to each specific clinical area, rather than a single set of items intended to be applicable to all situations. This theory-guided approach also enables more specific recruitment strategies to be developed

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once domain-specific barriers are known, potentially optimizing participation for a given trial and helping build a cumulative evidence of barriers/drivers and strategies for addressing them.

Keywords: Clinical trials; Recruitment; Trial participation; Patient engagement; Surveys

1. Introduction

Encouraging clinical trial participation (a participant-centered term) and recruitment (a study-centered term) remains a central and enduring challenge for health research. Participation rates are consistently low for both public and private research enterprises [1,2]. In the United States, 40% of National Cancer Institute−funded clinical trials have been shown to be discontinued, nearly half because of participation issues [3]. One systematic review showed that 44% of trials funded by the UK National Institutes of Health Research failed to meet their participation targets [4]; similar results have been found for cardiovascular trials [5] and primary care trials [6]. In the private sector, things may be even worse; 80% of industry-funded trials are reported to not meet participation targets [7]. The costs associated with poor participation are substantial, and include wasted resources, opportunity costs, delayed innovation, potentially biased results, potentially reduced public trust, and ethical problems associated with exposing participants to risk without any scientific gain [8].

The literature on trial recruitment strategies provides surprisingly little guidance to trialists seeking to increase participation in their trials. Considerable work has been conducted, but several reviews have found many studies with questionable methodological quality [9−14]. Many of the tested strategies are context-specific and not always feasible, sustainable, or (in some cases) ethical. The most recent Cochrane systematic review on the topic [12] (68 randomized trials with over 74,000 participants) identifies only two relatively minor strategies that evidence suggests clearly increase recruitment (telephone reminders to people not responding to postal requests, open rather than blinded trials). Recent international initiatives have sought to address this lack of guidance and include efforts to systematize the registration, conduct, and reporting of recruitment strategy trials nested within primary clinical trials [15−17]. Priority setting exercises have also identified key unanswered research questions, including how recruiters can more effectively communicate with potential participants [18], what information should be provided to potential trial participants, how best to deliver information about trials, and what barriers exist to involvement in trials [19]. These priorities have informed this study.

We propose that the challenges of trial participation can be better understood and addressed by reframing research participation as involving one or more behaviors (e.g., signing consent forms and engaging in study activities), by one or more groups of actors (e.g., patients and recruiters [20]), that should be subject to the same forces as other human behaviors. When faced with similar challenges in the study of complex health interventions, implementation science moved to capitalize on frameworks, theory, and methods from the behavioral sciences to design more effective, theory-informed strategies to influence decision-making and behavior [21]. The reasoning was that without clear and explicit theory to describe and understand relevant mechanisms determining the behavior of actors in the health system, interventions would inevitably be hit and miss. This approach has since been used to guide science and improve practice across a wide range of complex health interventions [22−24]. The trial participation literature to date has largely lacked these tools and this perspective [25,26], instead leaving decisions about how to engage people in research to individual trialists and anecdotal expertise within the trial teams. Under such circumstances, it is much more difficult to develop a cumulative science that describes why participation is so low in some studies and what recruitment strategies are more effective [21].

One framework that can provide us with specific tools to help optimize trial participation is the Theoretical Domains Framework (TDF) [27−29], which organizes over 100 constructs known to be associated with behavior and behavior change into 14 domains. These domains can be used to group barriers and drivers of professional and patient health behaviors into categories for which effective change strategies are known [30]. Efforts to describe barriers and drivers related to trial participation typically only touch on a small number of these domains. For example, one scale of 39 items includes 32 focused on two TDF domains (social influences on participation and beliefs about the consequences of participation), with 11 domains not represented [31]. Because the TDF combines the breadth of lessons from many theories and literatures about human behavior change, it may be more comprehensive in assessing barriers than other techniques. Furthermore, the approach has evolved to include systematic methodologies for identifying what specific strategies can overcome the kinds of barriers represented within each domain [29,30,32]. By systematically describing the relevant barriers to participation to specific trials in terms of this framework, we may be able to more effectively design and report strategies that overcome these barriers and increase participation. Recent work has started to explore the applicability of this framework using other methods and stakeholder groups [20,33−36].

Patient pretrial surveys are often used as a means to assess feasibility of recruitment for upcoming clinical trials [31,37,38], in part by assessing barriers to and drivers of participation in a broader sample of the target population

What is new?

Key finding

- We report a tailorable, theory-guided, and patient-focused approach to developing pretrial surveys that identify barriers to and drivers of participation in clinical trials.

What this adds to what was known?

- Our approach can help design surveys of patient populations that more systematically identify challenges relevant to participation in specific trials and can suggests ways to overcome these challenges.

What is the implication, what should change now?

- Consistent use of a systematic and theory-informed approach to designing pretrial surveys will advance the science of clinical trial recruitment and more efficiently lead to strategies that overcome trial-specific barriers to participation.

than can be addressed with more qualitative approaches. Existing tools to guide such surveys typically prioritize common issues over study-specific ones. Here, we describe a generalizable approach for developing surveys informed by the TDF. Several advances will be achieved. First, the approach will enable us to query patients about a much broader and more comprehensive range of factors related to participation than existing tools in the literature included [31,39]. Second, the approach can help trialists design interventions that specifically target the relevant barriers [30,40]. Third, our approach engages patient opinions and perspectives from the outset, consistent with an increasing realization that patient involvement is essential at all phases of trial development [41]. Finally, by using a theory-informed pretrial survey development approach across multiple conditions and trials, we will facilitate accumulation of knowledge around how best to optimize clinical trial participation.

2. Objective

To design a comprehensive, tailorable, patient-focused, and theory-guided approach for designing pretrial surveys about barriers to and drivers of clinical trial participation.

3. Methods

3.1. Setting

Clinical Trials Ontario (CTO) is an independent, not-for-profit organization established with support from the government of Ontario to improve the environment for the conduct of clinical trials. As part of this mandate, CTO identified as a priority working with various health charity and patient groups to design and administer online surveys to patients about their knowledge about, attitudes toward, and participation in clinical trials and clinical research. A half-day, in-person meeting held in Toronto in March 2018 was attended by executives from 6 Canadian patient organizations, with the goal of sharing information about patient attitudes toward clinical research, describing the groups' efforts to understand these attitudes, and discussion of barriers and drivers of clinical research participation specific to and common across the different patient groups. After this meeting, two patient groups (the Canadian Breast Cancer Network, Huntington Society of Canada) agreed to participate in the theory-guided survey development process to identify a standard, theory-guided approach to identifying barriers and drivers to clinical research participation via online surveys. The study group felt that these two clinical conditions varied in terms of gender prevalence and relative availability of trials (Breast Cancer often has many trials recruiting, Huntington disease (HD) relatively few), such that they would teach us more about how to tailor these surveys for different clinical areas. The results of these surveys will be reported separately.

3.2. Item identification and design

We identified an initial bank of items by drawing from a range of highly cited or recently published scales and reviews on the topic [31,37,39,42–47]; while relatively few of these focused primarily on patient-focused methods and items, we chose to emphasize factors that were potentially reportable by participants. When seeking to standardize the item format, it became clear that some items (e.g., ''my health is good'') could be rated as either a driver to participate (i.e., I'm able to participate) or a barrier (i.e., I'd rather be doing other things while I'm able), which prevents simple agree/disagree response options. To maintain simple, consistent response options throughout the survey, the study team settled on a 5-option assessment, with each item phrased as a statement and the respondent asked to indicate if the item would push them ''toward'' or ''away'' from participating and indicating whether it would push them ''a little'' or ''a lot'' (''no effect'' as the other alternative). This approach enabled all respondents to label each item as a barrier or a driver, without doubling the number of responses required.

After making this design decision, for clarity, each item was phrased as a sentence fragment starting with ''If'' or ''my belief/sense that'' as the case warranted. The study team (which included executives from each patient organization) went through several iterations to merge similar items and reword for clarity. (See appendix for more details).

3.3. TDF domain assignment

Draft items were assigned to the 14 domains of the TDF-2 [28]. Two independent raters assigned items to domains, with consensus resolving disagreements; where agreement could not be reached, a third reviewer with expertise in use of the TDF resolved disputes. Where a domain was not represented by any item, the study team chose not to develop new domain-specific items, instead leaving it to the interviewees to propose any relevant new items. Items from existing scales were chosen if they could clearly be worded as barrier or driver. All additional items proposed by interviewees were assigned to domains, i.e., there were no items identified that raters felt could not be assigned to a domain.

3.4. Interviewees

A convenience sample of participants was identified by executive members of the two patient organizations (Canadian Breast Cancer Network, Huntington Society of Canada). Patients and family members with lived experience of the relevant conditions were approached by the organizations. Participants were provided with the interview guide before the scheduled interview date. Interviews were planned to continue until saturation of newly identified barriers/drivers was reached.

3.5. Interviewing process

Interview guides were piloted sequentially, first focusing on the breast cancer survey, then on the Huntington survey. Interviews had 3 goals: 1) to maximize the clarity and usability of the full planned survey, 2) to obtain opinions about the relevance of the barriers/drivers identified in the survey, and 3) to elicit additional relevant barriers/drivers. Interviews used a ''think aloud'' approach [48], which requires interviewees to verbalize thoughts as they read instructions, interpret questions, and provide answers to the survey. The approach is recommended for self-completed questionnaires, providing detailed insights into how the reader is interpreting and interacting with the survey [48]. Two interviewers took notes throughout the sessions, and these formed the basis of discussions between study team members between sessions. Interviews were audio recorded to enable review as necessary.

The pilot survey was divided into 3 sections. The first measured experience and demographics (personal experience with illness and previous experience with research participation, age, sex, education, income, employment, and ethnic background). The second section included 12 items modified from the objective knowledge component of the Quality of Informed Consent scale [49], which measures objective knowledge about key elements of clinical trials. Detailed description and analysis of these components will be the subject of separate work and will not be discussed further here.

The third section focused on the barriers and drivers to participation in a clinical trial. Instructions asked the interviewee to imagine they were being asked to participate in a clinical trial investigating how well a new treatment works for breast cancer. The section included ~40–45 items (exact number varied as the survey instrument evolved). Our strategy for adding or deleting items during the interview phase was designed to be simple and inclusive of as many distinct issues as possible. Suggestions from interviewees about modifications, additions, and deletions due to lack of relevance for the clinical area were discussed by the study team and implemented between interviews. Interviews proceeded until saturation was achieved, i.e., no new barriers/drivers were being identified.

After completion of the breast cancer survey piloting, the second HD survey was piloted in the same way, with the exception that the starting set of items was the final set identified after the breast cancer piloting. Minor wording differences necessitated by the different clinical conditions were made, study team members with specific expertise in HD were asked to comment, and interviews on a new set of interviewees proceeded as above. All individual interviews were conducted by teleconference or Zoom videoconferencing with two members of the research team (KC and NH or JCB).

3.6. Analysis

Frequencies summarized demographic and disease experience variables collected for our two sets of interviews. Theme analysis included a deductive approach of identifying, clarifying, and assigning new items suggested by interviewees to theoretical domains, which were then incorporated into subsequent iterations of the survey. Two coders (JCB and KC) agreed on the assignment of new items to domains, with the consensus from a third coder (JP). Given that the initial list of items was extracted from several scales that usually were not guided by behavioral theory, and given that many existing scales address only a few domains, we examined how well this combined list covered the 14 theoretical domains of the TDF framework. We also collated the items in each of the final surveys in terms of the number falling into each domain.

4. Results

Table 1 describes our two samples of interviewees. Because this was a largely self-selected sample focused on obtaining opinions about the survey, we did not press individuals if they chose not to complete demographic and experience questions; hence, some of these data are missing. We were able to interview 8 female breast cancer survivors from 7 different provinces, ranging in age from 48 to 65 years, who had been identified through previous interactions with the Canadian Breast Cancer Network.

Table 1. Demographic and experience of interviewees

Variable	Breast cancer ($N = 8$)	Huntington disease ($N = 11$)
Province		
Ontario	2	7
Other	6	4
Sex		
Female	8	9
Male	0	2
Age (range, mean)	48–65 y (56 y)	26–70 y (37 y)
Missing	5	0
Survey responses for		
Self	8	3
Family member	0	8
Confidence in explaining what a clinical trial is to a friend/family member		
Completely confident	2	9
Somewhat confident	5	2
Not very confident	0	0
Not at all confident	0	0
Missing	1	0
Approached to participate in any kind of research study about [Breast Cancer; Huntington Disease]		
Yes	7	7
No	1	3
Don't know/can't remember	0	1
Actually participated in any research study about [Breast Cancer; Huntington Disease]		
Yes	7	7
No	1	4
If Yes, how long ago was your main participation (range)	2 mo–10 y ago	1 y–19 y ago
Missing	2	5

Most (7/8) participants indicated having been approached about, and 7/8 indicated that they had participated in at least one research study in the past, this participation having taken place anywhere from 2 months to 10 years ago. Most (7/8) indicated that they were somewhat or very confident that they could explain what a clinical trial was to a friend or family member. We also interviewed 11 HD community members (9 women, 7 from Ontario), 3 of whom indicated that they were positive for the HD gene mutation and were answering for themselves, the other 8 indicating that a family member had the gene mutation and were answering based on the experience of the family member. Only 7/11 indicated they had been approached about research participation, and 7/11 indicated having participated in a research study. However, all indicated that they were somewhat or very confident that they could explain what a clinical trial was.

Table 2 summarizes the distribution of items into domains across the two final lists (BC and HD); for comparison, this distribution is also provided for 3 previously published survey instruments that informed our initial list of items [31,39,42]. Our two lists included items that fell into 12 (BC) and 13 (HD) of the 14 TDF domains, with only minor differences in the number of items falling under each. The three previously published scales that were developed without patient input or a theoretical domains framework included items that fell into 4, 7, and 4 theoretical domains.

For the 38 items in the BC survey, the number of items per domain ranged from 0 items (Intentions and Behavioral Regulation) to 7 (Beliefs about Consequences and Social Influences). For the 47 items in the HD survey, the number of items per domain ranged from 0 items (Intentions), to 10 (Beliefs about Consequences). More details on each of the individual survey item sets can be seen in the Appendix.

5. Discussion

We sought to develop a comprehensive, tailorable, theory-informed, and patient-focused approach to assessing

Table 2. Distribution of survey items into TDF domains

TDF domain	Moorcraft 2016 (15 B/Ds)	Kurt 2017 (25 B/Ds)	Frew 2010 (39 B/Ds)	Breast cancer survey (38 items)	Huntington disease survey (47 items)	Example items
Knowledge	4	1		1	2	BC, HD item: My belief that I would learn more about my condition if I participated.
Skills		1		2	2	BC, HD item: If I find the trial documents hard to understand.
Social/professional role and identity		1	6	2	2	BC, HD item: My belief that participation is part of my role as a good citizen
Belief about Capabilities				4	4	BC, HD item: My belief that participating would give me a sense of control over what is happening to me.
Optimism				1	1	BC, HD item: My hope that participation would help find a cure.
Belief about Consequences	8	5	16	7	10	BC, HD item: My hope that participation will help me with my condition.
Reinforcement		1		4	5	BC, HD item: If I would gain access to new study drugs.
Intentions				0	0	
Goals	1			4	5	BC, HD item: My belief that participation would interfere with other goals of mine.
Memory, Attention, and Decision Processes				1	1	BC, HD item: If the investigators provided telephone reminders about study appointments.
Environmental Context and Resources		8		4	4	BC, HD item: If I think there is a substantial time commitment.
Social Influences	2	8	16	7	9	BC, HD item: If my physician

(*Continued*)

Table 2. Continued

TDF domain	Moorcraft 2016 (15 B/Ds)	Kurt 2017 (25 B/Ds)	Frew 2010 (39 B/Ds)	Breast cancer survey (38 items)	Huntington disease survey (47 items)	Example items
						thought I should participate.
Emotion			1	1	1	BC, HD item: My worry about unknown side effects.
Behavioral Regulation				0	1	HD item: My belief that trial participation would help me plan how to manage treatment better.

barriers to and drivers of clinical trial participation, to facilitate the design of pretrial surveys that identify all factors likely to affect participation. Questionnaires that assess barriers to and drivers of trial participation exist, but often do not reflect the full range of issues identified when qualitative methods are brought to bear [50, 51]. In contrast, qualitative approaches to assessing barriers and drivers exist, but are necessarily limited in the number of patients reached, and are rarely informed by behavioral theory, theory that can help design more effective design behavior change interventions [30].

Our results show that existing scales assessing barriers to participation in clinical trials have tended to focus on issues that fall into only a handful of TDF domains but not always the same domains. One recent systematic review identified a range of scales that together cover most (but not all) domains [43]. By selecting items from a variety of scales and using pilot interviews to identify new, study-specific items, however, nearly all domains were addressed in our surveys. This suggests to us that there is likely a broader range of factors relevant to participation than is reflected in any existing generic tool or scale. Indeed, qualitative research in the area often identify issues that would seem not to be captured by these scales [52,53];exploration of whether the qualitative studies incorporate more TDF domains than scale development studies is an interesting area for further study.

Across our two clinical areas, only one theoretical domain (Intention) ended up not being represented by any items. Rather than being an indication that it is not relevant to trial participation, given that intention to engage in a behaviour is known to be a strong determinant of conduct of the behavior [54], we think this finding stems from the hypothetical nature of this initial study. We initially identified such an item from this domain, but it was deleted for lack of clarity as interviewees found it difficult to determine intention when considering a generic hypothetical trial, as opposed to a real, imminent one. Future implementations of this survey approach conducted for specific, imminent trials should consider including and examining Intention items.

We propose that recruitment strategies will be more effective when they take into account the specific environments and characteristics of the trial, sometimes necessitating differences in approach even between sites within the same study. We make the analogy with the complex interventions often the subject of the study in the implementation science literature. Graham's Knowledge to Action framework [55] seeks to characterize the process of implementing these complex interventions to effect practice change. The model emphasizes adapting knowledge to local contexts, assessing barriers to change, and developing implementation interventions specifically tailored to addressing those barriers. We propose that our approach to trial barriers survey development can help trialists better assess how to develop recruitment strategies that are specifically tailored to address local barriers to trial participation.

This approach is a departure from the existing survey literature, which has focused on creating indices of generic barriers common across many clinical situations. Instead of proposing a single instrument intended to be used uniformly across many situations, we are proposing that tailored surveys be informed by the same comprehensive, theory-guided framework. Whether by 1) starting with the current list of barriers/drivers and adding/deleting relevant ones based on patient interviews, 2) taking a different existing set of barriers, assigning them to domains and considering how the missing domains might suggest new barriers, or 3) using a TDF-focused interview guide to identify barriers (e.g., [56]), we propose that using this framework-guided approach can have several benefits. First, it has the potential for a much broader utility than any individual scale that might be modified or discarded because some individual items are inappropriate. Second, because the approach involves a framework that is designed to facilitate implementation, there is potential to provide

guidance based on existing literature about how most effectively to intervene with barriers stemming from specific domains [30]. As only one example, understanding that trial participation may interfere with other goals of the potential participant can suggest clear, theoretically supported interventions to address the barrier (e.g., aligning participation with goals), and interventions less likely to be successful (providing additional information and knowledge about the trial) [57].Third, the approach can help provide a common language and organization around categories of barriers/drivers that involve common mechanisms, which can facilitate a more cumulative science that is currently fragmented and not guided by theory. Finally, the approach can facilitate the science of recruitment by linking the results to the likely mechanisms leading to the results, as opposed to focusing on categories of intervention (e.g., modifying information and changes in trial conduct) that do little to help understand when and where a certain type of mechanism is likely to work [12].

This work is exploratory and therefore has a number of limitations. First, we did not conduct a systematic review of existing recruitment barriers tools, instead opting to focus on the most recent and/or highly cited of these. In future work, we plan to conduct such a review to explore coverage of TDF domains, frequency of individual barriers, and identify any additional classes of barriers not addressed by the TDF. Second, the surveys involve respondents making decisions about what would and would not affect hypothetical participation behaviors; future work will have to explore the extent to which such hypothetical decisions mimic real-world participation behaviors, perhaps informed by a novel framework describing the conditions under which hypothetical decisions will predict real-world decisions [58]. Third, this initial work involved only small samples from two specific patient groups, samples that included primarily older, well-educated women; exploration of the approach on more diverse samples is warranted, as is the exploration of the whether barriers/drivers identified in more diverse settings and with more diverse participant groups can be equally well categorized by the theoretical domains.

Fourth, our sample sizes ended up to be determined by resources and availability of participants rather than detailed assessments of saturation, and so we cannot be certain that more items would have been identified with more interviews. Fifth, the instructions provided about the hypothetical ‘‘trial’’ were generic by design (e.g., ‘‘a clinical trial investigating how well a new treatment works for breast cancer’’); it is likely that studies using this approach would be able to provide a more detailed description of the target study, which would both suggest new barrier/drivers and change the frequency of endorsement of the different items. Sixth, we do not yet know whether such surveys will result in better participation rates. We note, however, that this TDF approach to assessing barriers is successfully used in the implementation science literature and is credited with improving our understanding of how resulting implementation interventions work [29]. Finally, the TDF has been criticized for being an individual-level-only framework, not giving enough emphasis on organizational and environmental issues that can affect behaviors such as study participation. We are planning further work that will assess whether additional domains based on organizational, health system, and societal-level factors (e.g., the Consolidated Framework for Implementation Research [59]) might improve the approach, as has been discussed elsewhere [60].

6. Conclusion

Our new approach for developing pretrial surveys of the determinants of study participation based on the TDF provides an approach to comprehensively and prospectively identify barriers to and drivers of the success of clinical trials and help trialists optimize participation in their trials based on behavioral theory.

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Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinepi.2020.12.013.

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