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Does prospective acceptability of an intervention influence refusal to participate in a randomised controlled trial? An interview study

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ABSTRACT

Background: The generalizability of findings of Randomised Controlled Trials (RCTs) is undermined by low or biased recruitment. Reasons for participant refusal are infrequently reported in published literature.
Aims: To apply the Theoretical Framework of Acceptability (TFA) to: (1) explore patient-reported reasons for declining to participate in a RCT comparing a new service model (patient-initiated appointments) with standard care (appointments scheduled by clinician) for managing blepharospasm and hemifacial spasm; (2) to explore associations between decliners' perceptions of acceptability and non-participation.
Method: Eligible patients (n = 242) were approached to participate in the trial. Phase 1: decliners provided a brief reason for refusal. Reasons were analysed descriptively and reviewed against TFA constructs.
Phase 2: Consecutive decliners participated in short semi-structured interviews, to explore their reasons for refusal in more depth. Interviews were transcribed and analysed, with the TFA as a coding framework.
Results: Eighty-seven (36%) eligible patients refused trial participation; all provided a reason. From interviews with 15 decliners (17%), four key beliefs about acceptability were identified: happy with standard care (n = 41) (49%), anticipated burden of patient-initiated service, lack of confidence in ability to engage with new service and uncertainties about effectiveness of new service. Two themes reflected non-TFA factors: trial participation a low priority and burden of completing trial documentation.
Conclusion: Reasons for refusal trial participation included: (a) reasons directly associated with intervention acceptability, and (b) reasons associated with trial participation more broadly. The TFA facilitated identification of problematic aspects of the new appointment booking system which could be addressed to enhance acceptability.

1. Introduction

Rigorously conducted randomised controlled trials (RCTs) provide gold standard evidence for intervention effectiveness [1,2]. However, reaching the required sample size is often challenging, with 45–80% of RCTs failing to meet their target [3], thereby reducing the precision of their effect estimates and increasing the risk of Type II errors (false negatives). Other potential consequences include increased risk of sampling bias, reduced generalizability of findings, delays in trial completion and increased costs [4–7].

The Consolidated Standards of Reporting Trials (CONSORT) guidelines recommend authors report the number of individuals assessed for

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eligibility (including a breakdown of those not meeting eligibility criteria), the number that declined to participate or were excluded for other reasons, and the number of participants enrolled in a trial [8]. These guidelines suggest that reporting the numbers of decliners can provide insights into acceptability of an intervention [8]. However, whilst studies may report the number of decliners, the reasons for refusal are not always reported [9,10]. There has been a recent focus on advancing the methodology within clinical trials to boost recruitment of prospective participants [1,12]. Much of this research has focused on understanding the decisions around trial participation and exploring reasons for refusal [13–16].

Published reports of RCTs often include an assumption that poor recruitment is an indicator of low intervention acceptability but few studies have directly examined this assumption [9,17]. An overview of systematic reviews that claimed to define, theorise or measure acceptability of healthcare interventions, found that the concept of acceptability was poorly understood and often measured tatuologically with indicators such as "total trial dropout rate", "all cause-discontinuation (with reasons)" and "trial withdrawal rates" [17]. The review authors concluded that poorer intervention acceptability may explain low participation rates and high dropout rates in these trials, but no studies have tested this proposal empirically [17]. Better understanding of the relationship between eligible participants' anticipated acceptability of an intervention and their decision not to participate may help intervention developers design more acceptable interventions which, in turn, may improve recruitment and retention rates [8–20].

In the context of healthcare interventions, the Theoretical Framework of Acceptability (TFA) defines acceptability as: *"a multi-faceted construct that reflects the extent to which people delivering or receiving a healthcare intervention consider it to be appropriate, based on anticipated or experienced cognitive and emotional responses to the intervention"*. [17,21] The TFA consists of seven component constructs (Affective attitude, Burden, Perceived effectiveness, Ethicality, Intervention coherence, Opportunity costs and Self-efficacy) [17] that can be used to assess acceptability from the perspectives of intervention deliverers and intervention recipients either prospectively (prior to engaging with the intervention), concurrently (during the period of engagement with the intervention) or retrospectively (after the period of engagement with the intervention) [17].

This study applied the TFA to systematically investigate factors that may influence reasons for non-participation in a RCT that compared a patient-initiated service model with standard care (appointments scheduled by clinician) for two conditions: Benign Essential Blepharospasm (BEB) and Hemifacial Spasm (HFS). The aim of this study was to explore the reasons given by eligible patients for declining to participate.

2. Methods

2.1. Study design

This was a qualitative study embedded within a RCT. The RCT compared a patient–initiated treatment service model for BEB and HFS whereby patients scheduled their own repeat injections of botulinum toxin type A to standard care, where follow-up treatment was scheduled by the clinician. The protocol and results of the RCT are published elsewhere [22].

2.2. Ethical approval

The RCT and embedded qualitative study received full ethical approval from London - Queen Square Research Ethics Committee (Ref: 15/LO/0439). The trial was also registered on clinicaltrials.gov.uk (NCT02577224).

2.3. Participants

Inclusion criteria for the RCT can be found in Table 1. Patients were approached to participate in the RCT at their treatment clinic appointment. For this study eligible patients who declined to participate in the RCT were invited to participate in a semi-structured interview to explore reasons for declining.

2.4. Sample size

The semi-structured interview study aimed to recruit a minimum sample of 10 participants, between September 2015 and February 2016, with a stopping criterion of up to a further three participants to confirm data saturation had been reached [23].

2.5. Data collection

There were two phases to data collection.

2.5.1. Phase 1: recording reasons for declining to participate

Following standard practice for RCTs, patients declining to participate in the trial were asked to provide a brief reason for not participating in this study, which was recorded by the research team.

2.5.2. Phase 2: semi-structured interviews

Consecutive patients who declined to take part in the RCT were invited to take part in a short semi-structured interview with a researcher. Patients were informed that the interview would last no longer than 15 minutes and that the purpose was to gain an understanding of the reasons why some patients declined to participate in the trial. Written consent was obtained before the interview commenced. All interviews were conducted by the researcher (MS) and were digitally recorded and transcribed by a professional transcribing company. Transcripts were checked by the researcher for accuracy and any identifiable data removed.

A topic guide was developed by the primary researcher (MS) in collaboration with the research team. The topic guide included six open questions to explore the reason why patients did not want to take part in the trial (Table 2).

2.6. Analysis

2.6.1. Phase 1: recording reasons for declining to participate

Recorded reasons given for refusal to participate in the trial were analysed descriptively, by grouping the responses according to similarity. The groupings were then assigned labels and the labels were then reviewed against the TFA.

2.6.2. Phase 2: semi-structured interviews

All interview transcripts were analysed by applying principles of qualitative content analysis [24–26]. This approach has been widely applied to analyse interview data in the context of another theoretical framework [27,28]. Analysis was completed in two key steps:

Table 1
BEB and HFS Trial participant eligibility criteria.

Inclusion criteria	Exclusion criteria
Patient: - aged 18 or over - Consultant-led diagnosis of blepharospasm or hemifacial spasm - stable botulinum toxin treatment (i.e. receiving treatment over two previous cycles free of side effects) - has capacity to give informed consent	Patient: - has significant comorbidities - unable to communicate fluently in written or spoken English

Table 2
Reasons for refusal to particiapte topic guide.

Topic guide question
1. Would you mind telling me why you decided not to participate in this study?
2. Having read the information sheet, what did you like or dislike about the study?
3. What do you think about patients being able to book their own appointments?
4. What do you think about healthcare professionals deciding when a patient should receive treatment?
5. Do you think you would participate in other studies if they suited your needs better?
6. Overall, how acceptable do you find the current appointment booking service?

1. *Deductive coding:* All transcripts were coded by (a.) reading participants' utterances that reflected evaluative responses about the new patient-initiated appointment service, (b.) considering their relevance to each of the definitions of the TFA constructs, and (c.) assigning the evaluative responses to one of the constructs (Table 3). Evaluative responses that were not deemed relevant to any of the TFA constructs were coded into an additional category, 'other factors' to ensure all responses about participants' decisions for declining to participate in the trial were captured. This deductive content analysis technique is appropriate for data analysis when the goal of the study is to validate an existing theoretical framework [29,30]. One researcher (MS) initially analysed all transcripts and two additional researchers (JF and MC) independently coded two randomly selected transcripts each for the assessment of inter-rater reliability, with the aim to independently code a minimum of 20% of the data.
2. *Generation of belief statements:* After all transcripts had been coded into relevant TFA constructs and the 'other factors' category, an inductive content analysis was applied to generate belief statements [27,28]. In this study, we define a belief statement as a concise summary label that incorporates all similar evaluative statements and provides detail about specific reasons for refusal to participate in the trial. For example, the following evaluating statements, '*I'm happy with the way the appointment system works'*, '*I'm happy with having my appointments booked for me'*, and '*I'm happy with the system as it is*', were grouped together to generate the belief statement 'I'm happy with the current system' representing the TFA construct, Affective attitude. All belief statements generated across transcripts within each TFA construct and the 'other' category were discussed with the research team. Differences in the grouping of the evaluative statements and in the wording of the belief statements generated were discussed until agreement was reached. All belief statements were then reworded to convey meaning that represented the majority of participant responses, using exact wording by the participants whenever possible. A frequency count for each belief statement was calculated across all interviews. The frequency counts refer to the number of participants who reported evaluative statements that reflect each belief statement. A participant may have reported more than one utterance that represents the belief statement, but each participant is counted once per belief statement generated.

Table 3
Definitions of the component constructs in the Theoretical Framework of Acceptability and 'other' category.

Theoretical Framework of Acceptability (TFA)	Definition
Affective Attitude	Anticipated Affective attitude: How an individual feels about the intervention, prior to taking part Experienced Affective attitude: How an individual feels about the intervention, after taking part
Burden	Anticipated burden: The perceived amount of effort that is required to participate in the intervention Experienced burden: The amount of effort that was required to participate in the intervention
Ethicality	The extent to which the intervention has good fit with an individual's value system
Intervention Coherence	The extent to which the participant understands the intervention and how it works
Opportunity Costs	Anticipated opportunity cost: The extent to which benefits, profits, or values must be given up to engage in the intervention Experienced opportunity cost: The benefits, profits or values that were given up to engage in the intervention
Perceived Effectiveness	Anticipated effectiveness: The extent to which the intervention is perceived to be likely to achieve its purpose Experienced effectiveness: The extent to which the intervention is perceived to have achieved its intended purpose
Self-efficacy	The participant's confidence that they can perform the behaviour(s) required to participate in the intervention
'Other' category	Utterances that answer the research question but do not necessarily reflect the TFA constructs (e.g. burden associated with trail documentation)

2.6.2.1. Inter-rater reliability. To assess the reliability of the researcher's coding (MS) two additional researchers (JF and MC) independently double-coded two transcripts in step 1 and step 2. Agreement was defined as the same part of the transcript coded into the same TFA construct or a conceptually synonymous non-TFA construct. Instances where text was coded into a TFA construct by one coder and was either not coded at all or coded into another TFA construct by a different coder, disagreement was registered. Percentage agreement was used to assess inter-rater reliability because the items (i.e. sentences in transcripts) may have been coded into more than one TFA construct [24]. Percentage agreement between 75 and 90% indicates an acceptable level of inter-rater reliability [25].

3. Results

3.1. Sample characteristics

Eighty-seven (35%) of 242 eligible patients invited declined to participate in the trial. Of these, 20 (23%) were approached to take part in the present interview study, and of these 15 (75%; 7 men and 8 women) consented to take part and participated in an interview. No further demographic characteristics were collected. The interviews lasted between 9 and 15 minutes and took place in the BEB and HFS treatment clinic at Moorfields Eye Hospital, London.

3.1.1. Phase 1: recorded reasons for declining to participate

Table 4 displays the reasons patients provided for declining to participate in the trial. The table also indicates whether the reason provided was associated with the intervention (and relevant TFA construct) or if the reason provided was associated with other factors. The most frequently reported reason for declining to participate was that patients were happy with the standard appointment service and did not want it to change, i.e. positive *affective attitude* about the standard service (41 participants, 49%). The second most commonly reported reason for declining to participate was a non-specific lack of motivation to take part in research (21 participants, 24%). Other reasons given for refusal were that it would not be practical for patients to book their own appointments (e.g. needing to book hospital transport for each appointment up to three months in advance) (7 participants, 8%).

3.1.2. Phase 2: semi-structured interviews

3.1.2.1. Inter-rater reliability. Inter-rater reliability for the deductive coding (step 1) was acceptable with 87% agreement between MS and JF

Table 4
Reasons given by patients approached to take part in the RCT for declining to participate.

Reasons given by patients for declining to take part	Number (%)	Reason associated with the intervention or other factors?	TFA Construct/Other category belief statement
Happy with current scheduled appointments - wouldn't want to change the system	41 (49)	Intervention	Affective Attitude
Not practical to book own appointments e.g. needs to book transport or leave from work well in advance	7 (8)	Intervention	Perceived Burden of participating in intervention
Patient is thinking about stopping treatment in near future	1 (1.1)	Intervention	Perceived Effectiveness
Demands of multiple healthcare appointments for self and/or family members would make taking part burdensome	8 (9.2)	Other factors	Trial participation considered burdensome
Patient does not have time to fill in long questionnaires	5 (5.7)	Other factors	Burden of completing trial documentation
Elderly & frail - physically unable to fill in long questionnaires	3 (3.4)	Other factors	N/A
Patient doesn't want to take part in research	21 (24)	N/A	N/A
No reason given	1 (1.1)	N/A	N/A
Total no. Of patients refused	87 (100)		

and 80% agreement between MS and MC. There was 100% agreement for the generation of belief statements (step 2) between MS and JF on two transcripts, and 85% agreement between MS and MC on the generation of belief statements in an additional two transcripts.

3.1.2.2. Theoretical Framework of Acceptability. Participants' utterances were coded into five of the seven TFA constructs. Table 5 presents example quotes for each of the TFA constructs and the inductive belief statements generated within each construct, along with the frequency of each belief statement.

3.1.2.2.1. Affective attitude. The majority of participants (n = 9) expressed a positive attitude towards the standard booking system, represented by three belief statements (Table 5). The positive belief statements suggest that the standard service was perceived as acceptable. Within the belief statement, *'I like the current model'* participant 2 said:

> *"I like to have three months which is what I was told I should have. I like it to be booked for the next one, when I come here, it's in the diary and I know where I am." (Participant 2)*

3.1.2.2.2. Burden. Five belief statements were generated within the construct of burden. Two of the belief statements represented high anticipated burden associated with the new service. Two participants reported that '*it would be difficult to fit other appointments around my eye appointment'* indicating that the patient-initiated service was perceived as unacceptable. It seems the flexibility of the patient-initiated appointment booking system was perceived as making appointment times less predictable. For example, participant 7 said:

> *"I know when I've got this appointment, so I can work round it, if I don't know when this appointment is, it'd make it more difficult to book other appointments." (Participant 7)*

One belief statement however included evaluative responses suggesting *'low anticipated burden associated with the new service'*. Here, patients believed that the patient-initiated service offered greater flexibility to patients including the opportunity to schedule their treatment as and when they needed it:

> *"I liked the flexibility that you're offering, that people can come along as soon as they feel the need of further treatment." (Participant 3)*

The remaining two belief statements represented burden associated with the standard service, including the belief statement *'it's very difficult to change a booked appointment.'* This suggests that there were aspects of the standard service that may be considered less acceptable:

> *"It's very difficult to make another appointment or to change something." (Participant 5)*

3.1.2.2.3. Intervention coherence. Three belief statements were generated within the construct of intervention coherence, with two indicating a lack of understanding of the patient-initiated service '*how will they know I need or do not need an appointment'* and '*it doesn't make sense to me that patients book their own appointments'*:

> *"It means you turn up and it doesn't give the staff the opportunity to plan and prepare. It will be extra work for the staff. If I just call on the telephone you can't see me so how will they know that I need or do not need an appointment?" (Participant 13)*

> *"I don't understand that bit about patients booking their own appointments, doesn't really make sense to me." (Participant 14)*

Only one participant in the sample understood the rationale for the patient-initiated service, reflected in the belief statement *'patients can book their treatment when they need it'*.

3.1.2.2.4. Perceived effectiveness. Participant responses represented three belief statements indicating uncertainties about the effectiveness of the patient-initiated service, '*timing of the booking systems may not be effective for everyone', 'it won't work as its difficult to get an appointment in the current system'*, and *'it's a good idea as long as there is availability of appointments.'* For example, participant 2 anticipated that the timings of the appointments in the patient-initiated service may not suit everyone, and thus believed that standard care would be more effective:

> *"I mean some people might feel they ought to come in more often, others might leave it too long, and that's why I think it's best to stick to the health professional being the ones to say, you know we need to see you in … you know whatever time." (Participant 2)*

Participant responses also reflected two belief statements about their prior experience of treatment effectiveness under the standard service: *'the current system works for me'* and *'I don't want to change anything; it works out perfect for me*'. Participant 14 indicated the standard service is acceptable:

> *"For the last 3 to 4 years I've been coming for my appointments and they have been booked for me. I think this system works well. Not sure how it would work if patients start booking their own appointments …. I think this system works better. I think it's better for the doctor to decide, they know about the condition." (Participant 14)*

3.1.2.2.5. Self-efficacy. Two belief statements were generated within the construct of self-efficacy, which focuses on the participants' confidence that they can perform the behaviours required to participate in the intervention. The belief statements indicate the patient-initiated service was viewed as unacceptable due to a *'lack of confidence with engaging in the new service'*. For this belief statement Participant 6 expressed:

> *I would not like to change my appointments as I am not so confident that I would book an appointment myself in good time. (Participant 6)*

Table 5
Reasons for refusal coded into the relevant TFA constructs including belief statements per construct and frequencies per belief statement.

Construct	Example quote	Belief statement[a]	Total Frequency per belief statements (out of 15)[b]
Affective attitude	I like to have three months which is what I was told I should have. I like it to be booked for the next one, when I come here, it's in the diary and I know where I am (Participant 2)	I like the current model **(+)**	3
	I'm quite happy with the way it is … I'd like to stay as I am (Participant 6)	I'm happy with the current system **(+)**	4
	I am very happy. In my mind 10 weeks' time I will come in. I like knowing when my appointments are (Participant 9)	I like knowing when my appointment is booked **(+)**	2
BurdenIntervention coherence	I know when I've got this appointment, so I can work round it, if I don't know when this appointment is, it'd make it more difficult to book other appointments (Participant 7) It would be more stressful having to call up to make an appointment, but when I know that I'm coming in, it's in the diary on the day I'm going. Is it easier for me to manage? (Participant 9) I liked the flexibility that you're offering, that people can come along as soon as they feel the need of further treatment (Participant 3) It's very difficult to make another appointment or to change something (Participant 5) it' a long way to travel to my appointments … because of the walk to the bus stop or … And go on the bus and then the train and then the bus and it's a difficult journey (Participant 4)	**High anticipated burden associated with the new service:** It would be more difficult to fit other appointments around my eye appointment **(−)**	2
	It would be more stressful having to call up to make an appointment, but when I know that I'm coming in, it's in the diary on the day I'm going. Is it easier for me to manage? (Participant 9)	It would be more stressful to make my own appointment **(−)**	2
	I liked the flexibility that you're offering, that people can come along as soon as they feel the need of further treatment (Participant 3)	**Low anticipated burden associated with the new service:**The new service has better flexibility (low perceived burden) **(+)**	2
	It's very difficult to make another appointment or to change something (Participant 5)	**Burden associated with standard care:** it's very difficult to change a booked appointment **(−)**	2
	it' a long way to travel to my appointments … because of the walk to the bus stop or … And go on the bus and then the train and then the bus and it's a difficult journey (Participant 4)	It's a long way to travel to attend my appointments **(−)**	2
	It means you turn up and it doesn't give the staff the opportunity to prepare it will be extra work for the staff and this is the other point when I say plan. If I just call on the telephone you can't see me so how can you … how will they … know I need or do not need an appointment? (Participant 13)	**Lack of understanding of patient-initiated service:** How will they know I need or do not need an appointment on the phone? **(−)**	1
	I don't understand that bit about patients booking their own appointments, doesn't really make sense to me (Participant 14)	It doesn't make sense to me patients booking their own appointments **(−)**	2
	The patient booking service will be good for some as people can come along as soon as they feel the need for further treatment, instead of having to wait until their scheduled appointment. (Participant 3)	**Understanding of patient-initiated service:** Patients can book their treatment when they need it (+)	1
Perceived effectiveness	I mean some people might feel they ought to come in more often, others might leave it to long, and that's why I think it's best to stick to the health professional being then to say, you know " we need to see you in … you know whatever time" (Participant 2)	**Uncertainties about the effectiveness of the patient-initiated service:** Timing of the booking system may not be effective for everyone **(−)**	2
	I don't think it will work because I come in every roughly 10 weeks and sometimes even with 10 weeks you can't get in (Participant 4)	It won't work as its difficult to get an appointment in the current system (−)	1
	I think that's good as long as when you ring to book there are places (Participant 3)	It's a good idea, as long as there is availability of appointments (±)	2
	I am very happy because I'm working and in terms of the symptoms they more or less get it right. (Participant 13)	**Perceived effectiveness of standard care:**The current system works for me (+)	5
	When I used to go round there it'd be like every three months, every four months, sometimes nearly five months. It was really bad like. Since I've been coming round here I was coming the same again and then I see this young lady and she's done it totally different, and she's been telling me to come every two months to see how it works out. It's been working out perfect, y'know, so I don't really want to change anything, rock the boat like. I don't want to change anything, its two months and it works out perfect for me. (Participant 12)	I don't want to change anything it works out perfect for me **(−)**	2
Self-efficacy	I would not like to change my appointments as I am not so confident that I would book an appointment myself in good time (Participant 6)	Lack of confidence with engaging in the new service **(−)**	1
	I have other appointments made with other problems that I've got, and I can fit them around it instead of having to worry all the time and whether I get them in to the right dates and things (Participant 7)	I would worry about booking my appointment around booking other appointment **(−)**	1

Notes.

[a] Belief statements with **(+)** indicate a positive reflection of the TFA construct (e.g. for the construct of Affective attitude- I'm *happy with the current system*). Belief statements with **(−)** indicate a negative reflection of the TFA construct (e.g. for the construct of Burden – *it's very difficult to change a booked appointment*). Belief statements with (±) indicate a neutral reflection of the TFA construct (e.g. for the construct o Perceived effectiveness – *It's a good idea, as long as there are availability of appointments)*.

[b] Total number of belief statements refers to the number of participants who reported a view that reflects each belief statement in table. A participant may have reported more than one quote in line with the belief statement, but each participant is counted only once per belief statement.

3.1.2.3. Other factors associated with reasons for declining to participate. Participant responses in the interviews also reflected three further factors not associated with the acceptability of the intervention: (1) the burden of completing trial documentation, (2) trial participation considered a low priority, and (3) a non-specific lack of motivation to take part in research. The participant quotes associated with these belief statements are presented in Table 6.

4. Discussion

This study is the first to have applied the Theoretical Framework of Acceptability (TFA) to examine the reasons given by eligible patients for refusing to participate in a RCT evaluating the effectiveness of a novel patient-initiated treatment service for BEB and HFS compared to a standard clinician-determined treatment service [22]. The TFA was applied to determine whether anticipated (lack of) acceptability of the new service was a driver of refusal to participate. The findings from this study suggest that underlying reasons for refusal to participate in this trial can be differentiated between reasons directly associated with the acceptability of the intervention, and factors associated with specific trial processes.

4.1. Summary of findings

The four most commonly reported acceptability-related reasons for refusing to participate in the RCT were: a preference for standard care, anticipated burden associated with the new service, lack of confidence in being able to engage with the new service, and uncertainties about the effectiveness of the new service. These findings were in line with the brief reasons given by other patients who refused to take part in the trial, and who did not take part in the semi-structured interviews. The most common reason for refusal (the documented reasons from all decliners) being that they were happy with the standard care system and did not want to change the approach to booking their treatment appointments. Satisfaction with the standard care service could explain why some participants in this study may have understood the potential benefits of the patient-initiated service. Previous research has also suggested that reasons for not taking part in a range of clinical trials included preference and familiarity of standard care treatment options and the lack of confidence in the effectiveness of an alternative intervention [11,15,16,31].

Two belief statements reflected further factors not associated with the acceptability of the standard care or the patient-initiated treatment service but with taking part in the research process: (1) study participation was considered a low priority and (2) the anticipated burden of completing trial documentation. These beliefs are similar to findings reported in a qualitative study that explored the reasons for refusal in a range of studies that were part of the National Institute of Mental Health Program [32]. Reasons reported in that study included protocol-related issues (e.g. duration of intervention, duration of follow up) and lifestyle issues (e.g. inability to participate during work hours, burden of travelling to clinical centre [32].

4.2. Implications

This study provides evidence that the reasons for eligible patients refusing to participate in a RCT may in part be due to perceptions about the (lack of) acceptability of the interventions being tested and in part about the (lack of) acceptability of the trial research procedures. The current findings demonstrate that using the TFA to guide the analysis of qualitative data leads to conceptually coherent insights with practical relevance. Future studies could maximise these benefits by using the TFA constructs to develop more focused topic guides or questionnaires to explore the factors associated with reasons for refusal to participate, ideally within the pilot and feasibility phase of the intervention development cycle [33]. TFA-informed interview topic guides could explore the acceptability, from potential participants' perspectives, of the control and experimental interventions being evaluated and the study methods used to evaluate them. This would provide key information about how the intervention content or materials, or trial processes, could be modified to enhance acceptability, which, in turn, may increase the numbers who consent to participate in the main trial [9,11].

In terms of patient-initiated services for blepharospasm, where symptoms return after a period of time and patients need further treatment, consideration needs to be given to minimise the burden associated with patients booking their own appointments, including ways in which confidence in engaging with the new service can be enhanced. The findings from this study also suggest that participants may not have fully understand the purpose and benefits of the patient–initiated service, which potentially impacted on perceived effectiveness. This may have been due to ambiguous or unclear detail in the patient information sheet provided to potential participants, which may have created a lack of trust in the patient-initiated service. However, clinical staff involved in the trial did answer patient queries about the patient–initiated service when recruiting participants and reassured patients that they could access an urgent appointment when needed. Future trials could go further by ensuring all patient-facing study materials are clearer and point out the potential benefits of the intervention. This could be achieved by including patients in all stages of trial design and asking for feedback on materials as well as pilot testing materials to ensure they are clearly understood [34,35]. With regard to the potential burden associated with taking part in a trial, researchers should consider the amount of contact and documentation, including printed questionnaires and telephone follow-up calls, participants are expected to engage with.

4.3. Strengths and limitations

A key strength of this study is that it is one of the few studies to have collected and analysed qualitative data on reasons for declining to participate in an RCT. This study is also the first to have explored factors associated with the reasons for declining to participate in a trial by applying a multi-construct theoretical framework to determine if those reasons are associated with anticipated intervention acceptability [17].

The study has some limitations. Interviews were completed with a convenience sample of 15 patients representing 75% of those who initially consented but only 17% of all patients approached. At face value there is a substantial risk of selection bias as we do not know whether non-participants differ in their perceptions of acceptability. However, the belief statements that emerged from the interview sample are similar to the brief reasons reported by the much larger sample of participants that declined to participate in the RCT, providing some assurance that the range of views captured in the interviews are indicative of the wider population.

Another limitation to consider includes the structure of the topic guide. Whilst the analysis of the interview data was informed by the TFA, the topic guide did not reflect all constructs within the TFA and two constructs were not reported by participants (i.e. opportunity costs and ethicality). This was a decision made by the trial team to keep the length of the interviews to a minimum and not burden participants declining to participate in the RCT. Furthermore, given that the TFA is a relatively new framework, we did not want to confine patients to only providing reasons reflecting the TFA constructs. Thus, the use of open questions ensured that participants were able to express their reasons without being confined to the TFA constructs and allowed for the emergence of reasons unrelated to acceptability and which were categorised within 'other factors'.

5. Conclusion

This study has investigated patients' reasons for declining to participate in a RCT of a new patient–initiated treatment service for

Table 6
Reasons for refusal coded into "other factors" including belief statements per construct and frequencies per belief statement.

	Example quote	Belief statement	Total Frequency per belief statements (out of 15)[a]
Other Factors	It was having a commitment to you know, have to sort of record things (Participant 2)	Burden of completing trial documentation	1
	I've got other health issues just at the moment and I'm going to be going to the hospital backwards and forwards (Participant 2)	Trial participation considered a low priority	2
	It's because I've got family problems and would not be doing what you want me to do (Participant 8)		
	I just don't want to take part (Participant 1)	I don't want to take part in research	2

Notes.
[a] Total number of belief statements refers to the number of participants who reported a view that reflects each belief statement in table. A participant may have reported more than one quote in line with the belief statement, but each participant is counted only once per belief statement.

Benign Essential Blepharospasm (BEB) and Hemifacial Spasm (HFS) compared to standard care. Two types of reasons can be differentiated: those associated with intervention acceptability, and those associated with trial procedures. This study indicates that the Theoretical Framework of Acceptability (TFA) can be successfully applied to generate understanding of the perceived problematic aspects of new interventions and trial processes and where intervention designers could concentrate their efforts to improve patient acceptability.

Declaration of competing interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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