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Overall experiences of people with New Onset Type 1 Diabetes involved in a physical activity study

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Trial experience of newly diagnosed patients with Type 1 Diabetes

ABSTRACT

Objectives: Regular physical exercise may preserve beta cell function in newly diagnosed adults with Type 1 diabetes (T1D). However clinical trials to test this theory require the recruitment and retention of adults with new onset T1D, which can be challenging. We sought to determine the overall experiences of newly-diagnosed adults with T1D in an exercise study with the aim of understanding issues that influence the retention of trial participants in such studies.

Design: Qualitative methodology using individual face to face (n=6) and telephone interviews (n=14). Interview transcripts were thematically analysed using the Framework Method

Setting: The study took place at five participating UK hospitals.

Participants: Twenty participants in the Exercise for Type 1 Diabetes (EXTOD) study were interviewed to explore their study experiences and identify motivators and deterrents towards the study. Participants in control and intervention arms were interviewed, as were patients who had completed (n=16) and withdrawn (n=4) from the trial.

Results: Participants revealed barriers and facilitators to retention; the majority were generalisable to clinical trials of people with newly-diagnosed T1D. Lack of time, work pressures, level of health professional support, volume, clarity and consistency of information and feedback and a desire for knowledge about their condition were all cited as influencing factors to trial retention.

Conclusions: To our knowledge, this is the first qualitative study to examine the experience of being involved in an exercise trial by people with T1D . Findings suggest: appointments could be shorter, available outside of standard working hours and planned longer in advance; study information should be clear, consistent and offered in electronic and paper formats; questionnaires need keeping to a minimum; healthcare support and feedback needs providing regularly; thought is required around how to support participants in the non-exercising arm. These considerations may improve particiapant retention rates in new onset T1D studies.

Keywords: Type 1 diabetes; Exercise; Physical Activity; Trial Retention; Clinical Trials; Participants

Strengths and limitations of this study

- A qualitative, interview study was undertaken to explore, in-depth, the experiences of people with type 1 diabetes who were participating in an exercise study.
- The study was multi-site, taking place at five participating hospital trusts across the UK.
- Rigourous data collection and analysis techniques were undertaken, using the Framework approach.
- Participants were purposively sampled to allow for variation in the sample characteristics.
- To our knowledge, this is the first qualitative study to examine people with T1D experiences of being involved in an exercise trial.

INTRODUCTION

Type 1 diabetes (T1D) is a chronic autoimmune condition characterised by immune mediated destruction of insulin producing pancreatic beta cells [1]. Significant numbers of β cells are present at the time of diagnosis [2], but this continues to decline following diagnosis. Preservation of β-cell function is associated with improved glucose control, reduced risk of retinopathy and nephropathy and reduction in rates of hypoglycaemia of more than 50% [3]. Interventions that can preserve residual β-cell function in new-onset T1D are needed. Furthermore, therapies proven to preserve β-cell function in new-onset T1D can be taken forward into trials of T1D prevention.

In animal models of Type 1 and Type 2 diabetes (T2D), healthy humans, and in people with impaired glucose tolerance withT2D, regular exercise has been shown to preserves β-cell function [4]. For example, in people at risk of T2D, one hour of walking three times a week for eight months improved β-cell function by 60% [5] . These findings have not been tested in people with T1D and there is thus a need for a prospective clinical trial to test the hypothesis that exercise preserves β-cell function in people newly diagnosed with T1D.

The incidence rate of T1D is low, with 1 in 1000 affected and recruitment of people withT1D to clinical trials is challenging [6-8], with studies showing recruitment rates as low as 17% [6] . This means that retaining newly diagnosed patients with T1D who are recruited to studies is even more important. In studies of immunotherapeutic agents for T1D, drop out rates are 12-14% [9 10] ; however higher rates have been reported for exercise studies. In a meta-analysis of unsupervised exercise programmes, 20% of studies had a dropout of > 20%, 32% a dropout of 10–20%, and 48% a dropout of < 10% [11].

Barriers to participation in clinical trials are well documented [12], although no studies have looked at barriers to recruitment in patients with newly diagnosed T1D. There are very few studies that have

looked at how to improve retention rates of patients in a clinical randomized controlled trial (RCT). Those studies that have been done have concentrated on strategies to improve retention rather than barriers to retention [13]. No studies have looked at barriers to retention in patients newly diagnosed with T1D. We wished to address this important deficit by qualitatively exploring the experiences of people with newly diagnosed T1D who participated in the a recently completed exercise and T1DM study [14].

METHODS

Setting, access and recruitment

Study participants were from the EXTOD study, whose protocol has been described previously [13]. In brief, all patients aged between 16 and 60 years, diagnosed with T1D in the previous three months, from 19 UK hospital sites, were invited to participate. EXTOD had two phases. Phase 1 consisted of a qualitative study to determine attitudes and barriers to exercise in patients with newly diagnosed T1D. Phase 2 was a pilot RCT to assess uptake, intervention adherence, drop-out rates, and rate of uptake in the usual care group during a 12 month exercise intervention (where the participants came from for this study).

At the time of recruitment to the pilot RCT (phase 2) study, all patients received participant information leaflets and provided informed consent to potentially take part in a interview to explore their experience of being involved in the pilot RCT. Twenty participants from five participating sites (Birmingham, Leeds, Bristol, Gloucester, Taunton) were later selected using purposive sampling to ensure variety in terms of their key study characteristics [15]. Participants were sampled in relation to their age, gender, study arm (intervention/control) and study status (completed/withdrawn). Selected participants were sent a letter at the end of the pilot RCT , informing them that they would be contacted by the EXTOD team. This was followed, a week later, by a phone-call from a member of

the EXTOD team (nurse or doctor) to check they were happy to be interviewed. If willing, they were then telephoned by the researcher (CH), who has a nursing background and is an experienced qualitative researcher (though she had not previously undertaken any research in this area), to arrange a suitable time and date for her to undertake the interview. CH had had no contact with participants prior to this and participants were unaware of the researcher's background. All participants agreed to be interviewed.

This study had ethical approvals from The West Midlands and Solihull Research Ethics Committee (10/H1206/4).

Patient Involvement

The research question was derived from T1D patients attending clinic asking clinicians about any benefits and barriers to exercise, as they were aware that much work had been undertaken on this topic in T2D patients, but not in T1D patients. This led to the formulation of the research question and an application for funding to undertake this research. Patients were involved in the study design from the outset, as the researchers presented the study proposal to them, and asked for any comments relating to it. Issues relating to the conduct of the study, such as the potential burden of the exercise intervention to participants, were also discussed and any feedback was incorporated into the study design. Patients also contributed to the study conduct by sitting on the study management committee and helped with study oversight, including helping to develop approaches to improve study recruitment. Study finding were fed back to participants through an informal feedback evening where the findings were presented. In addition, a summary of findings was posted to participants.

Data collection

Participants at the hospital where the researcher was based (Birmingham) were given the option of being interviewed face-to-face at the hospital , or by telephone. The remaining participants were all interviewed by telephone, due to financial, time and travel constraints. All interviews were carried out with only the participant and CH present.

Interviews were carried out by CH, using a semi-structured topic guide (Table 1) that was developed in consultation with the EXTOD researchers. The interviews lasted between 20 to 50 minutes. No repeat interviews were conducted. Areas for discussion included levels of health professional support, information provided about diet and exercise and issues relating to recruitment and follow up. All interviews were digitally recorded and transcribed verbatim by a local transcription company.

Table 1: Topic Guide for Interview Study

Openers	If I could start by asking you how long ago you took part in the study? How did you find the experience?
Diet and Exercise Information	How appropriate was the advice about diet and exercise in relation to its content and volume? Do you feel being recruited to the study so soon after diagnosis was a good thing or would you have preferred more time? When would have been an appropriate time? How well were able to take in the information you were given? Would it have been helpful to see the dietician again, or do you feel that once was enough? Did you refer to the study information booklet? If so, how helpful was the information booklet? Which sections of the booklet particularly helpful or unhelpful? Do you use the booklet as a reference guide now? Did any aspects of your diet change following looking at the information booklet? Can you think of any better ways in which the information could have been delivered?
Health Professional Support	How well supported did you feel in terms of the clinical support you received? Did you feel you more or less well supported through being on the trial? Do you feel being in the trial was better or worse in terms of the number of doctors/nurses you saw? Why? Were you happy seeing the same nurse all the way through the trial or would you have preferred more

	variety? Did you mind no longer seeing the nurse you saw when you were diagnosed? Do you mind not seeing these study doctors/nurses on a regular basis now? How well balanced were the follow up visits in terms of the health professional you saw? Would you have preferred more/less visits with a doctor/nurse etc...Or do you feel it was the right amount of time with each? Overall, how well supported by the doctors and nurses did you feel?
Recruitment and Follow Up	Where did you first hear about the trial from? Who approached you? What appealed to you about taking part in the study in the first place? What were your reasons? Was there anything that put you off taking part in the study? How easy to complete and understand were the questionnaires you received? During the trial you were required to have extra blood tests. How did you feel about having the extra bloods? How much did you feel the follow up visits were focused on you and how much did you feel they were focused on the trial and form filling etc...Was this appropriate or could it be weighted differently? Would you have preferred most of the follow up visits to have taken place face to face or over the phone? Can you describe whether being on the study affected your confidence levels in terms of undertaking exercise? What were your reasons for leaving the study? Why did you choose to continue/discontinue with the 5year FU as part of the study?
Motivational Interviewing (intervention group only)	How useful do you feel the extra support you were given by the nurse about managing your diabetes and exercising was? What were the pros and cons of talking to the nurse about this? Would it have been helpful to have weekly phone calls from the nurse to check on how you were getting on? Did the amount of exercise you undertook change as a result of these talks with the nurse or did it stay the same? Did the type of exercise you undertook change or stay the same following a) diagnosis and b) the intervention? How much physical activity were you carrying out before your diagnosis compared to a) during the study and b) now? Has your exercise levels been maintained post-study? Did you feel more or less confident about carrying out exercise following the intervention with the nurse? What more could have been done to encourage you to exercise? What sort of approach might have worked for you to help you to exercise? Some participants did not make their exercise target. Can you think how we could help them reach this target? What methods did you use to increase your exercise levels?
Future Development of Study	If there was one thing we could do to make the study easier for you to take part in what would it be? We are planning to undertake a larger scale study similar to the one you have taken part in. What sort of things would you change about the study that might make people want to take part in it more? Overall, what did you feel was good or bad about taking part in the study?

	Do you think you would be more or less likely to participate in clinical trials following this experience?

Data Analysis

Data analysis was carried out during the interview period to enable the interview process to be shaped by the emerging data themes and to identify when saturation had been reached. An inductive approach to data analysis was taken and themes were derived from the interview dataset. Data was coded by CH and was inserted into a framework analysis matrix Excel spreadsheet, to enable data ordering and synthesis, whilst retaining the meaning and feeling of the interviewees' words [16] . Themes were developed independently by reading and rereading the transcripts and through discussion with reseach team members (CH, PN and SG). The interviews were then analysed using thematic analysis [17]. Transcripts were not returned to participants to comment on during this process.

RESULTS

Participants

Twenty participants were interviewed;six face to face and fourteen by telephone (Table 2). Participants were recruited from all five participating sites; eleven were male, ages ranged from 19-55 and all were of white British ethnic orgin. Thirteen had been allocated to the intervention group and seven to the usual care comparator. Sixteen participants had completed EXTOD, whilst four had withdrawn for reasons including work commitments, a cancer diagnosis, and difficulties accepting their diabetes diagnosis.

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Table 2: Characteristics of participants

Participant	Gender	Centre	Treatment arm	Complete/with drew	Interview format
1	Female	Birmingham	Intervention	Completed	Telephone
2	Male	Birmingham	Control	Completed	Face to face
3	Male	Birmingham	Intervention	Completed	Face to face
4	Female	Birmingham	Intervention	Withdrew	Telephone
5	Male	Leeds	Intervention	Withdrew	Telephone
6	Female	Leeds	Control	Withdrew	Telephone
7	Female	Birmingham	Intervention	Completed	Face to face
8	Female	Birmingham	Intervention	Completed	Face to face
9	Male	Birmingham	Control	Completed	Face to face
10	Male	Birmingham	Control	Completed	Telephone
11	Male	Birmingham	Intervention	Completed	Telephone
12	Male	Taunton	Intervention	Completed	Telephone
13	Male	Gloucester	Control	Completed	Telephone
14	Female	Bristol	Intervention	Completed	Telephone
15	Male	Bristol	Control	Completed	Telephone
16	Male	Bristol	Intervention	Completed	Telephone
17	Male	Bristol	Control	Withdrew	Telephone
18	Female	Leeds	Intervention	Completed	Telephone
19	Female	Birmingham	Intervention	Completed	Face to face
20	Female	Taunton	Intervention	Completed	Telephone

Themes

The interviews yielded data on five main themes and these help formulate the barriers and fascilatators to trial participation (Table 3). These themes were: study paperwork; feedback; barriers to continued participation; coming to terms with diagnosis of T1D; effect of allocated arm.

Table 3: Facilitators and barriers to continued Clinical Trial Participation in People with Type 1 Diabetes Mellitus

Facilitators
• Consistency and continuity of health professional support • Clear, detailed and relevant information about diabetes and its management • Availability of both paper and electronic information and documentation • Reduction in volume of study documentation • Flexible access to trial facilities outside of normal working hours • Appointments scheduled in advance to allow for planning around work and social lives • Early feedback of trial findings
Barriers
• Time • Work pressure • Travelling to appointment • Length of visits • Length of study • Coming to tern with diagnosis • Being able to maintaining exercise levels • Being allocated to the control (non exercising arm)

Study Paperwork

Two main subthemes emerged within the 'study paperwork' theme; these were study information and study questionaires.

Study information

The volume, clarity and consistency of information provided were important in determining how well informed participants' felt about their diabetes and its management. Though a few participants felt they were given too much information, most felt that although there was a lot of information, it was useful, relevant and necessary so soon after diagnosis. Generally the information was cited as interesting, manageable and straightforward. Others spoke of how they valued the repetition of some information, as it meant they could fully absorb it.

'To be honest I thought it was perfect...I was sort of drip-fed information throughout the year really, and it was very good…After…The shock of being told you're Type 1 diabetic…I found it very good and the team was extremely helpful.' EXTOD 12

Most participants were happy receiving paper information, finding it easy to read and acknowledging that not everyone had Internet access. Others, especially younger participants, stated they would have preferred digital information, such as Apps, to access information faster. One participant suggested having a centralised webpage specific to the hospital's diabetes unit, with links to different diabetes resources on it. Participants supplemented the trial information with other resources, such as the 'Carbs and Cal' book [18]. Others used digital resources, such as the 'Carbs and Cal' or 'Fitness Pal' apps and online information [18].

'Being a bit of a technology geek, I went with the app which is the Carbs and Cals app…It will give you a particular breakfast, like Alpen…and then it will show you…the size of portion that you're supposed to have, and how much insulin you're supposed to take.' EXTOD 2

Study questionnaires

Most participants felt the study paperwork was too long and time-consuming, 'switching off' from it as a result, as it got in the way of work and personal lives. Much paperwork was questionnaires

relating to diet, exercise and quality of life that were completed at the study visit. Participants felt that although the paperwork was generally easy to complete and understand, it could also be repetitive, confusing and contradictory, containing irrelevant, non-specific questions, which were hard to relate and respond to.

'I remember always getting given the questionnaire sheet when I was having my bloods done. And I could just never fill it in. It used to be like – I used to say to my dad can you ask my questions and then I could do it, but it did go on for quite a while… And it was the same the second time I did it as well, and I was like I don't know what to put for these questions again. It seemed like I was doing the same thing.' EXTOD 19

Feedback

Some participants voiced disappointment at receiving little trial feedback, stating that the opportunity for feedback had incentivised them to join the trial, as a way of finding out about their diabetes and also that they wanted to learn more about the long term trial outcomes.

'It would be good to have some follow-up information...I wasn't quite sure how my fitness level was affected…And I never got to find out if it actually improved.' EXTOD 1

Barriers to continued participation

Seventeen of the 58 participants who were randomised into the original EXTOD study withdrew before the end of the study. We thus sought to understand why this might have happened.

Participants described practical barriers as the most likely reasons for dropping out. These included time and work pressures, dislike of blood tests, travelling to appointments, the long study duration, volume of visits and moving away.

'I'm not bothered for taking blood or doing injections or anything like that…But I can remember feeling bothered by that at the time. I think because I was very ill, really, still, and still quite fragile … I can remember that upsetting me…Because it was a study and because I didn't have to do it…If you volunteered to have a blood test and it takes a few times for them to take the blood, it's kind of like putting yourself through something difficult that you didn't really need to do.' EXTOD 6

The long study duration also deterred many participants, who felt it was too long to fully commit to, meaning they became less vigilant at attending appointments or completing study documentation due to the repetition involved.

'It's quite long. I think that was quite daunting. It turned out to not really be an issue, but because it's something that I could kind of blend into my lifestyle quite a lot. Because I suppose it didn't really require any prolonged visits to the clinic or anything because it was mostly just things that I could do myself. But initially that was a bit daunting because it's a year.' EXTOD 16

For most, committing to the EXTOD study had proved difficult, due to the time it required off work. This let to difficulties for participants in ensuring they could always attend appointments and sometimes proved costly, due to having to take unpaid leave for study visits.

"The time that you're having to have off work…Often it's unpaid leave so obviously that can be quite difficult." EXTOD 18

These time pressures had led to two of the interviewed participants withdrawing from EXTOD prior to completion. Solutions to these problems suggested by participants -who had both withdrawn and remained in the study - included offering more flexible appointment times and planning clinic visits further in advance so there was more time to plan around them.

'I left…Because I didn't have enough time…The study is of such a long duration and I just found that too challenging with work…If you had appointments at eight o'clock in the evening every time you

needed me then so be it…I have to do a hell of a lot of juggling in order to fit that sort of stuff in.' EXTOD 17

Coming to terms with diagnosis of T1D

Some participants spoke of how they had struggled to come to terms with their T1D diagnosis, with one participant citing this as their reason for withdrawing from EXTOD. For this participant, her difficulties coping emotionally with her diagnosis had prompted her doctors to advise her to withdraw.

"Don't think it kind of really sank in as to what I'd been diagnosed with... It had kind of hit me and I wasn't really dealing with having it…I wasn't taking my insulin and checking my levels as much…The doctors…Felt that it was best that I was taken off it." EXTOD 4

Effect of allocated arm

Some participants, who had been allocated the exercise intervention, spoke of difficulties maintaining the level of exercise expected of them, due to lack of motivation or the extra time it took.

'I think a year in it seemed to get a little bit "Oh God I've been doing this for a year now"…A year's a long time… Because towards the end as well, it was like you had to come in and then I had to do the gym thing, and it was kind of like…"oh this is getting really laborious".' EXTOD 2

Others, in the usual care comparator group, spoke of how this disincentivised them from remaining in EXTOD as they were not receiving the exercise benefits they had hoped for.

"The sort of people that…Take part…Are often similar to me in kind of quite wanting to do the exercise, and presumably about half of the time you get randomised into not doing the exercise. And I don't know whether that's off-putting as well." EXTOD 16

DISCUSSION

This is the first study to examine the experiences of people with T1D taking part in an exercise intervention trial. The findings have highlighted issues that should be considered when designing clinical trials involving this population group. Clinical trials which reflect the needs, wants and preferences of participants can lead to improvements in retention rates, statistical power and, in the longer term, to studies with more credible findings. The findings suggest that timing is an important consideration for many participants. Many may be offered trial entry shortly after their condition's onset and may be experiencing multiple health and lifestyle changes. This highlights the need for sensitive communication of information from health professionals when introducing clinical trials. The disappointment of some participants at being allocated the usual care group also highlights the need for a clear explanation of equipoise and other clinical trials terminology, so participants can make informed treatment decisions, minimising the potential for withdrawal rates after randomisation [19]. Additional measures that could help with this are offering the intervention at the end of the study or randomising more to the exercise arm than the control arm, to enable more participants access to the intervention.

The study has illustrated the need for the transmission of clear, relevant and useful information to clinical trial participants. Participants showed preferences for a wide-range of delivery modes, including paper formats, websites, apps and Internet forums. The use of appropriate, accessible media to convey information effectively and engage with participants is dependent on individual preferences and may be influenced by factors such as age, gender and income [20]. The popularity of Apps and multimedia technologies amongst participants indicates that these modes of information delivery should be incorporated specifically into trials with T1D participants, who are likely to be a younger, more technologically minded population group than trials with T2D participants. Future trial designs could offer paper and electronic information so participants' can utilise their preferred resource. Similarly, when collecting data, a range of methods could be employed, including paper documentation, spreadsheets, phone apps, emails and websites. Demonstrating versatility and

flexibility in data collection techniques may help motivate participants to complete study documentation that they might otherwise omit. The importance of providing regular study feedback to participants should also be considered, through letters, emails and presentations, so that their contribution is acknowledged and valued [21].

Finally, the interview findings highlighted that practicalities such as work pressures, time commitments and geographical location influenced participants' ability to commit to the trial. T1D onset usually occurs at a young age, with most people being diagnosed before 35 [22]. As a result, people with T1D are likely to have busy lives incorporating work, family and social engagements, making committing to a clinical trial difficult. This is verified by the commonest reason cited for the high dropout rate (29%) from EXTOD being time and work commitments. To rectify this, more flexible study visit times could be offered, with the option of attending outside normal working hours, such as evenings and weekends. Additionally, the provision of a timetable of scheduled appointments at the study outset would allow participants to plan for them. Improved hospital transport links could also facilitate ease of study attendance [23]. By incorporating a flexible approach to these practical barriers, participants will experience less difficulty in complying with study visits, improving retention rates. Consideration should also ensure that the exercise intervention can be integrated into people's lifestyles, without adding to their pressurised schedules. This could be done by providing a range of exercise options, in a range of locations and within a realistic timeframe, to minimise the likelihood of participants becoming over-faced by the extra commitment they have taken on.

Many of the challenges to clinical trial retention in people with T1D are similar to the challenges facing the general population who are recruited to clinical trials [24-28]. The issues and challenges participants faced, such as the long study duration, difficulties completing documentation and time pressures, are also likely to be challenges for the general clinical trials population, including T2D. However, this study has identified that although many of these trial related issues are not specific to T1D populations, the reasons for these issues are likely to be different. For example, people with T1D

or T2D may report that time pressures prevent them from committing to a clinical trial. However, whilst for the T1D participant, time pressures may stem from work priorities, the T2D participant time pressures may stem from regularly caring for grandchildren. By understanding more about the reasons behind these barriers to trial recruitment and retention, trials can be designed to accommodate and facilitate the wants and needs of these different groups. The average age of participants entering clinical trials is over 50 years of age [26 29]. This contrasts with the randomised EXTOD participants, whose mean age was 32 years. This younger age-group is likely to face more difficulties in adhering to rigid time schedules and appointments due to added work, family and social pressures. This is important for clinicians and researchers to acknowledge, allowing them to design T1D studies that will facilitate trial recruitment and retention, by offering more flexible appointment times, out-of-hours services and realistic, manageable exercise schedules. These practical solutions are important considerations for retaining participants in clinical trials and must be valued if rich and full trial datasets are to be obtained. When considering study design, thought must be given to how to increase recruitment, as well as how to make the study experience appealing to participants once they have consented. By paying attention to the participant's perspective, the chances of retaining participants for the study duration will increase, improving trial outcomes and participant satisfaction with trial entry.

Strengths and limitations

The interview participants were selected from five UK hospitals, increasing the transferability of the findings to a range of settings. Participants were purposively sampled, stratifying them according to age, gender, randomisation arm and whether they had completed or withdrawn from the study. This enabled a diverse and comprehensive collection of narratives to be gathered and analysed, enhancing the trustworthiness of the findings. However, although 12% of EXTOD participants recruited were non-White, none of the participants recruited to the qualitative study were non-White. This lack of representation is due to our exclusion of ethnicity as a criterion in our purposive sampling. Although, we did not purposefully exclude non-White participants from the sample, the likely reason for their

lack of inclusion is because T1D is far more common in White populations than other ethnic groups [30]. Additionally, many of the geographical locations we recruited from had a White population of over 84% [31-33]. Despite this, including ethnicity in our purposeful sample could have ensured that non-White populations were represented. In addition, due to the interview participants being situated around the UK, most interviews were conducted by telephone. However, where possible, participants were given the choice of being interviewed face-to-face or by telephone, allowing them to choose the setting they found most relaxing, thus increasing opportunity for open dialogue between interviewees and researcher. The fairly even split between participants choosing face-to-face and telephone interviews suggests that providing a choice of setting may increase recruitment and retention to trials, giving participants the opportunity to select their most comfortable environment.

CONCLUSION

To our knowledge, this is the first qualitative study to examine T1D participants' experiences of being involved in a clinical trial. Although people may be initially motivated to enter clinical trials for reasons such as altruism and a desire for information, practical factors such as work and time constraints, study duration and financial difficulties often act as deterrents for remaining on trials. Though these issues in themselves are not unique to the T1D population, the *reasons* for these issues are likely to be different. These reasons need considering when designing T1D clinical trials, to ensure that appropriate modifications are built into the trial design to enable people withT1D to participate with minimal disruption to their lives.

The study findings have highlighted that differences do exist between T1D participants and the general clinical trials population. Firstly, the younger age of people with T1D at recruitment may make it harder for them to commit to clinical trials due to increased work, family and social pressures; this was verified by study participants. Secondly, the study has indicated that using multimedia technology might benefit T1D participants, who are used to handling information electronically. It has highlighted that to increase retention to T1D trials, improvements to trial design are required. This can

be done through providing flexible access to services, clear and relevant study information, documentation and feedback, as well as consistent healthcare support.

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COMPETING INTERESTS STATEMENT

None declared.

REPORTING GUIDELINES

The COREQ reporting guidelines were followed.

DATA SHARING STATEMENT

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

All authors (CH, PN, RA, AD, KS, AK, SG) contributed substantially to conception and design, or acquisition of data, or analysis and interpretation of data. All authors drafted or revised the article critically for important intellectual content. All authors gave final approval of the version to be published.

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Table 1: COREQ Checklist for manuscript ID bmjopen-2018-022353

Checklist number	Item	Description	Location in manuscript (page number)
1	Interviewer/facilitator	Which author conducted interview/focus group	Page 6
2	Credentials	What were the researcher's credentials	Page 1
3	Occupation	What was their occupation at the time of the study	Page 6
4	Gender	Was the researcher male of female	Page 6
5	Training	What experience or training did the researcher have	Page 1, page 6
6	Relationship established	Was a relationship established prior to study commencement	Page 6
7	Participant knowledge of researcher	What did participants know about the researcher	Page 6
8	Interviewer characteristics	What characteristics were reported about the interviewer (bias, assumptions, interest in research topic)	Page 6
9	Methodological orientation and theory	What methodological orientation was stated to underpin the study (grounded theory, content analysis etc...)	Page 9
10	Sampling	How were participants selected?	Page 3, 5, 18
11	Method of approach	How were participants approached e.g.face to face, telephone etc..	Page 5-6
12	Sample size	How many participants were in the study?	Page 5
13	Non-participation	How many participants refused to participate/dropped out?	Page 6
14	Setting of data collection	Where was the data collected: home, clinic, workplace?	Page 7

15	Presence of non-participants	Was anyone else present besides the researcher and participants?	Page 7
16	Description of sample	What are the important characteristics of the sample? E.g. demographics.	Page 9-10
17	Interview guide	Were questions, prompts, guides, provided by the authors? Was it pilot tested?	Pages 7-8
18	Repeat interviews	Were repeat interviews carried out? If yes, how many?	Page 7
19	Audio/visual recording	Did the research use audio/visual recording to collect the data?	Page 7
20	Field notes	Were field notes made during/after the interview	Pages 7-8
21	Duration	What was the duration of the interviews/focus groups?	Page 7
22	Data saturation	Was data saturation discussed?	Page 9
23	Transcripts returned	Were transcripts returned to participants for comments/correction?	Page 9
24	Number of data coders	How many data coders coded the data?	Page 9
25	Description of the coding tree	Did the researcher provide a description of the coding tree?	Page 9
26	Derivation of themes	Were themes identified in advance or derived from the data?	Page 9
27	Software	What software, if applicable, was used to manage the dataset?	Page 9
28	Participant checking	Did participants provide feedback on the findings?	Page 9
29	Quotations presented	Were participant	Pages 11-15

		quotations presented to illustrate the themes/findings? Was each quotation identified e.g. participant number?	
30	Data and findings consistent	Was there consistency between the data presented and the findings?	Pages 11-19
31	Clarity of major themes	Were the major themes clearly presented in the findings?	Pages 11-15
32	Clarity of minor themes	Is there a description of diverse cases or minor themes?	Pages 10-15

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A qualitative study of barriers to clinical trial retention in adults with recently diagnosed Type 1 Diabetes

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Trial experience of people with newly diagnosed Type 1 Diabetes

A qualitative study of barriers to clinical trial retention in adults with recently diagnosed Type 1 Diabetes

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ABSTRACT

Trial experience of people with newly diagnosed Type 1 Diabetes

Objectives: Regular physical exercise may preserve beta cell function in newly diagnosed adults with Type 1 diabetes (T1D). However clinical trials to test this theory require the recruitment and retention of adults with new onset T1D, which can be challenging. We sought to determine the overall experiences of newly-diagnosed adults with T1D in an exercise study, to understand issues that influence the retention of trial participants in such studies.

Design: Qualitative methodology using individual face to face (n=6) and telephone interviews (n=14). Interview transcripts were thematically analysed using the Framework Method

Setting: The study took place at five participating UK hospitals.

Participants: Twenty participants, aged 19-55 years, in the Exercise for Type 1 Diabetes (EXTOD) study were interviewed to explore their study experiences and identify motivators and deterrents towards the study. Participants in control and intervention arms were interviewed, as were people with T1D who had completed (n=16) and withdrawn (n=4).

Results: Participants revealed barriers and facilitators to retention; the majority were generalisable to clinical trials of people with newly-diagnosed T1D. Coming to terms with a diagnosis of T1D, lack of time, work pressures, level of health professional support, volume, clarity and consistency of information and feedback and a desire for knowledge about their condition were all cited as influencing factors to trial retention.

Conclusions: To our knowledge, this is the first qualitative study to examine the experience of being involved in an exercise trial by people with T1D . Findings suggest: appointments could be shorter,

available outside of working hours and planned longer in advance; study information should be clear, consistent and in electronic and paper formats; questionnaires need minimising; healthcare support and feedback needs providing regularly; thought is required around how to support non-exercising arm participants. These considerations may improve participant retention rates in new onset T1D studies.

Keywords: Type 1 diabetes; Exercise; Physical Activity; Trial Retention; Clinical Trials; Participants; Adults; Diagnosis

Strengths and limitations of this study

- A qualitative, interview study was undertaken to explore, in-depth, the experiences of people with type 1 diabetes who were participating in an exercise study.
- The study was multi-site, taking place at five participating hospital trusts across the UK.
- Rigourous data collection and analysis techniques were undertaken, using the Framework approach.
- Ethnicity excluded as a purposive sampling criterion resulting in only White participants being represented.
- To our knowledge, this is the first qualitative study to examine people with T1D experiences of being involved in an exercise trial.

INTRODUCTION

Type 1 diabetes (T1D) is a chronic autoimmune condition characterised by immune mediated destruction of insulin producing pancreatic beta cells [1]. Significant numbers of β cells are present at

the time of diagnosis [2], and preservation of β-cell function is associated with significant benefits for people with T1Ds. Interventions that can preserve residual β-cell function in new-onset T1D are needed.

In animal models of Type 1 and Type 2 diabetes (T2D), healthy humans, and in people with impaired glucose tolerance withT2D, regular exercise has been shown to preserves β-cell function[3]. These findings have not been tested in people with T1D and there is thus a need for a prospective clinical trial to test the hypothesis that exercise preserves β-cell function in people newly diagnosed with T1D.

The EXTOD (Exercise for T1D) study was a pilot study undertaken to explore whether exercise can preserve beta cell function in adults newly diagnosed with T1D. In designing this study, we had to bear in mind that the incidence rate of T1D is low, and recruitment of people withT1D to clinical trials is challenging [4-6]. Other studies have shown recruitment rates as low as 17% [4] . This means that retaining people with newly diagnosed T1D who are recruited to studies is even more important. In studies of immunotherapeutic agents for T1D, drop out rates are 12-14%[7-8] ; however higher rates have been reported for exercise studies. In a meta-analysis of unsupervised exercise programmes for people with T2D, 20% of studies had a dropout of > 20%, 32% a dropout of 10–20%, and 48% a dropout of < 10% [9].

Barriers to participation in clinical trials are well documented [10], although no studies have looked at barriers to recruitment in people with T1D. There are very few studies that have looked at how to improve retention rates of people with T1D in a clinical randomized controlled trial (RCT). Those studies that have been done have concentrated on strategies to improve retention rather than barriers to retention [11]. No studies have looked at barriers to retention in people newly diagnosed with T1D. We wished to address this important deficit by qualitatively exploring the experiences of people with newly diagnosed T1D who participated in a recently completed exercise and T1D study [12]. Here we report our findings from a qualitative study of barriers to clinical trial retention in adults with recently

diagnosed T1D. We have not reported other findings from the EXTOD study, which are reported separately[13,14].

METHODS

Setting, access and recruitment

Study participants were from the EXTOD study, whose protocol has been described previously[12] . In brief, all people aged between 16 and 60 years, diagnosed with T1D in the previous three months, from 19 UK hospital sites, were invited to participate. The EXTOD study explored the barriers and benefits of exercise in adults with newly diagnosed T1D. The hypothesis being tested by the EXTOD study was that exercise preserved beta cell function in adults recently diagnosed with T1D. EXTOD had two phases. Phase 1 consisted of a qualitative study to determine attitudes and barriers to exercise in people with newly diagnosed T1D[13]. Phase 2 was a pilot RCT to assess uptake, intervention adherence, drop-out rates, and rate of uptake in the usual care group during a 12 month exercise intervention (where the participants came from for this study).

At the time of recruitment to the pilot RCT (phase 2) study, all people with T1D received participant information leaflets and provided informed consent to potentially take part in an interview to explore their experience of being involved in the pilot RCT. Of the 60 participants who took part in the pilot RCT, twenty participants from five participating sites (Birmingham, Leeds, Bristol, Gloucester, Taunton) were later selected using purposive sampling to ensure variety and diversity in terms of their key study characteristics[15]. Participants were sampled in relation to their age, gender, study arm (intervention/control) and study status (completed/withdrawn) to ensure that an even spread of participants across the key characteristics were sampled. Similarly the sites were selected to allow a purposeful sampling of geographical areas participating in the EXTOD study (teaching hospitals versus district general hospitals). Selected participants were sent a letter at the end of the pilot RCT , informing them that they would be contacted by the EXTOD team. This was followed, a week later, by a phone-call from a member of the EXTOD team (nurse or doctor) to check they were happy to be interviewed. If willing, they were then telephoned by the researcher (CH), who has a nursing

background and is an experienced qualitative researcher (though she had not previously undertaken any research in this area), to arrange a suitable time and date for her to undertake the interview. CH had had no contact with participants prior to this and participants were unaware of the researcher's background. All participants agreed to be interviewed.

This study had ethical approvals from The West Midlands and Solihull Research Ethics Committee (10/H1206/4).

Patient Involvement

The research question was derived from people with T1D attending clinic and asking clinicians about any benefits and barriers to exercise, as they were aware that much work had been undertaken on this topic in people with T2D, but not in people with T1D. This led to the formulation of the research question and an application for funding to undertake this research. People with T1D were involved in the study design from the outset, as the researchers presented the study proposal to them, and asked for any comments relating to it (approximately seven people with T1D were involved). Issues relating to the conduct of the study, such as the potential burden of the exercise intervention to participants, were also discussed and any feedback was incorporated into the study design. People with T1D also contributed to the study conduct by sitting on the study management committee and helping with study oversight, including helping to develop approaches to improve study recruitment (three people with T1D were involved). Study findings for phase 2 of the study were fed back to participants through an informal feedback evening where the findings were presented. This was well received by the participants. In addition, a summary of findings was posted to participants.

Data collection

Participants at the hospital where the researcher was based (Birmingham) were given the option of being interviewed face-to-face at the hospital , or by telephone. The remaining participants were all interviewed by telephone, due to financial, time and travel constraints. All interviews were carried out with only the participant and CH present.

Interviews were carried out by CH, using a structured topic guide (Table 1) that was developed in consultation with the EXTOD researchers. The interviews lasted between 20 to 50 minutes. No repeat interviews were conducted. Areas for discussion included levels of health professional support, information provided about diet and exercise and issues relating to recruitment and follow up. All interviews were digitally recorded and transcribed verbatim by a local transcription company.

Table 1: Topic Guide for Interview Study

Openers	If I could start by asking you how long ago you took part in the study? How did you find the experience?
Diet and Exercise Information	How appropriate was the advice about diet and exercise in relation to its content and volume? Do you feel being recruited to the study so soon after diagnosis was a good thing or would you have preferred more time? When would have been an appropriate time? How well were able to take in the information you were given? Would it have been helpful to see the dietician again, or do you feel that once was enough? Did you refer to the study information booklet? If so, how helpful was the information booklet? Which sections of the booklet particularly helpful or unhelpful? Do you use the booklet as a reference guide now? Did any aspects of your diet change following looking at the information booklet? Can you think of any better ways in which the information could have been delivered?
Health Professional Support	How well supported did you feel in terms of the clinical support you received? Did you feel you more or less well supported through being on the trial? Do you feel being in the trial was better or worse in terms of the number of doctors/nurses you saw? Why?

Trial experience of people with newly diagnosed Type 1 Diabetes

	Were you happy seeing the same nurse all the way through the trial or would you have preferred more variety? Did you mind no longer seeing the nurse you saw when you were diagnosed? Do you mind not seeing these study doctors/nurses on a regular basis now? How well balanced were the follow up visits in terms of the health professional you saw? Would you have preferred more/less visits with a doctor/nurse etc...Or do you feel it was the right amount of time with each? Overall, how well supported by the doctors and nurses did you feel?
Recruitment and Follow Up	Where did you first hear about the trial from? Who approached you? What appealed to you about taking part in the study in the first place? What were your reasons? Was there anything that put you off taking part in the study? How easy to complete and understand were the questionnaires you received? During the trial you were required to have extra blood tests. How did you feel about having the extra bloods? How much did you feel the follow up visits were focused on you and how much did you feel they were focused on the trial and form filling etc...Was this appropriate or could it be weighted differently? Would you have preferred most of the follow up visits to have taken place face to face or over the phone? Can you describe whether being on the study affected your confidence levels in terms of undertaking exercise? What were your reasons for leaving the study? Why did you choose to continue/discontinue with the 5year FU as part of the study?
Motivational Interviewing (intervention group only)	How useful do you feel the extra support you were given by the nurse about managing your diabetes and exercising was? What were the pros and cons of talking to the nurse about this? Would it have been helpful to have weekly phone calls from the nurse to check on how you were getting on? Did the amount of exercise you undertook change as a result of these talks with the nurse or did it stay the same? Did the type of exercise you undertook change or stay the same following a) diagnosis and b) the intervention? How much physical activity were you carrying out before your diagnosis compared to a) during the study and b) now? Has your exercise levels been maintained post-study? Did you feel more or less confident about carrying out exercise following the intervention with the nurse? What more could have been done to encourage you to exercise? What sort of approach might have worked for you to help you to exercise? Some participants did not make their exercise target. Can you think how we could help them reach this target? What methods did you use to increase your exercise levels?
Future Development of Study	If there was one thing we could do to make the study easier for you to take part in what would it be? We are planning to undertake a larger scale study similar to the one you have taken part in. What sort of things would you change about the study that might make people want to take part in it more? Overall, what did you feel was good or bad about taking part in the study?

	Do you think you would be more or less likely to participate in clinical trials following this experience?

Data Analysis

Data analysis was carried out during the interview period to enable the interview process to be shaped by the emerging data themes and to identify when saturation had been reached. For example, some participants in the early interviews spoke of how they had struggled to come to terms with their new T1D diagnosis. As a result subsequent interviews explored this area in more depth, focusing on the impact this had on their experience of participating in the EXTOD study. An inductive approach to data analysis was taken and themes were derived from the interview dataset. The pre-determined topic areas set out in the topic guide (Table 1) such as 'health professional support' and 'recruitment and follow-up' guided the analysis process as much of the data collected focused on these topic areas, enabling the researchers to elicit information that was relevant to the study question. Data was coded by CH and was inserted into a framework analysis matrix Excel spreadsheet, to enable data ordering and synthesis, whilst retaining the meaning and feeling of the interviewees' words[16]. Themes were developed by CH by reading and rereading the transcripts and these themes were then agreed during discussions with reseach team members (CH, PN and SG). The interviews were then analysed using thematic analysis[17]. Transcripts were not returned to participants to comment on during this process.

RESULTS

Participants

Twenty participants were interviewed; six face to face and fourteen by telephone (Table 2). Participants were recruited from all five participating sites; eleven were male, ages ranged from 19-55 and all were of white British ethnic orgin. Thirteen had been allocated to the intervention group and seven to the usual care comparator. Sixteen participants had completed EXTOD, whilst four had

withdrawn for reasons including work commitments, a cancer diagnosis, and difficulties accepting their diabetes diagnosis.

Table 2: Characteristics of participants

Participant	Gender	Centre	Treatment arm	Complete/with drew	Interview format
1	Female	Birmingham	Intervention	Completed	Telephone
2	Male	Birmingham	Control	Completed	Face to face
3	Male	Birmingham	Intervention	Completed	Face to face
4	Female	Birmingham	Intervention	Withdrew	Telephone
5	Male	Leeds	Intervention	Withdrew	Telephone
6	Female	Leeds	Control	Withdrew	Telephone
7	Female	Birmingham	Intervention	Completed	Face to face
8	Female	Birmingham	Intervention	Completed	Face to face
9	Male	Birmingham	Control	Completed	Face to face
10	Male	Birmingham	Control	Completed	Telephone
11	Male	Birmingham	Intervention	Completed	Telephone
12	Male	Taunton	Intervention	Completed	Telephone
13	Male	Gloucester	Control	Completed	Telephone
14	Female	Bristol	Intervention	Completed	Telephone
15	Male	Bristol	Control	Completed	Telephone
16	Male	Bristol	Intervention	Completed	Telephone
17	Male	Bristol	Control	Withdrew	Telephone
18	Female	Leeds	Intervention	Completed	Telephone
19	Female	Birmingham	Intervention	Completed	Face to face
20	Female	Taunton	Intervention	Completed	Telephone

Themes

The interviews yielded data on five main themes and these help formulate the barriers and facilitators to trial participation (Table 3). These themes were: study paperwork; feedback; barriers to continued participation; coming to terms with diagnosis of T1D; effect of allocated arm.

Table 3: Facilitators and barriers to continued Clinical Trial Participation in People with Type 1 Diabetes Mellitus

Facilitators
• Consistency and continuity of health professional support • Clear, detailed and relevant information about diabetes and its management • Availability of both paper and electronic information and documentation • Reduction in volume of study documentation • Flexible access to trial facilities outside of normal working hours • Appointments scheduled in advance to allow for planning around work and social lives • Early feedback of trial findings
Barriers
• Time • Work pressure • Travelling to appointment • Length of visits • Length of study • Coming to tern with diagnosis • Being able to maintaining exercise levels • Being allocated to the control (non exercising arm)

Study Paperwork

Two main subthemes emerged within the 'study paperwork' theme; these were study information and study questionaires.

Study information

The volume, clarity and consistency of information provided were important in determining how well informed participants' felt about their diabetes and its management. Though a few participants felt they were given too much information, most felt that although there was a lot of information, it was useful, relevant and necessary so soon after diagnosis. Generally the information was cited as interesting, manageable and straightforward. Others spoke of how they valued the repetition of some information, as it meant they could fully absorb it.

'To be honest I thought it was perfect...I was sort of drip-fed information throughout the year really, and it was very good…After…The shock of being told you're Type 1 diabetic…I found it very good and the team was extremely helpful.' EXTOD 12 (Male, Taunton)

Most participants were happy receiving paper information, finding it easy to read and acknowledging that not everyone had Internet access. Others, especially younger participants, stated they would have preferred digital information, such as Apps, to access information faster. One participant suggested having a centralised webpage specific to the hospital's diabetes unit, with links to different diabetes resources on it. Participants supplemented the trial information with other resources, such as the 'Carbs and Cal' book[18]. Others used digital resources, such as the 'Carbs and Cal' or 'Fitness Pal' apps and online information[18].

'Being a bit of a technology geek, I went with the app which is the Carbs and Cals app…It will give you a particular breakfast, like Alpen…and then it will show you…the size of portion that you're supposed to have, and how much insulin you're supposed to take.' EXTOD 2 (Male, Birmingham)

Study questionnaires

Most participants felt the study paperwork was too long and time-consuming, 'switching off' from it as a result, as it got in the way of work and personal lives. Much paperwork was questionnaires relating to diet, exercise and quality of life that were completed at the study visit. Participants felt that although the paperwork was generally easy to complete and understand, it could also be repetitive,

confusing and contradictory, containing irrelevant, non-specific questions, which were hard to relate and respond to.

'I remember always getting given the questionnaire sheet when I was having my bloods done. And I could just never fill it in. It used to be like – I used to say to my dad can you ask my questions and then I could do it, but it did go on for quite a while… And it was the same the second time I did it as well, and I was like I don't know what to put for these questions again. It seemed like I was doing the same thing.' EXTOD 19(Female, Birmingham)

Feedback

Some participants voiced disappointment at receiving little trial feedback, stating that the opportunity for feedback had incentivised them to join the trial, as a way of finding out about their diabetes and also that they wanted to learn more about the long term trial outcomes.

'It would be good to have some follow-up information...I wasn't quite sure how my fitness level was affected…And I never got to find out if it actually improved.' EXTOD 1(Female, Birmingham)

Barriers to continued participation

Seventeen of the 58 participants who were randomised into the original EXTOD study withdrew before the end of the study. We thus sought to understand why this might have happened.

Participants described practical barriers as the most likely reasons for dropping out. These included time and work pressures, dislike of blood tests, travelling to appointments, the long study duration, volume of visits and moving away.

'I'm not bothered for taking blood or doing injections or anything like that…But I can remember feeling bothered by that at the time. I think because I was very ill, really, still, and still quite fragile

… I can remember that upsetting me…Because it was a study and because I didn't have to do it…If you volunteered to have a blood test and it takes a few times for them to take the blood, it's kind of like putting yourself through something difficult that you didn't really need to do.' EXTOD 6(Female, Leeds)

The long study duration also deterred many participants, who felt it was too long to fully commit to, meaning they became less vigilant at attending appointments or completing study documentation due to the repetition involved.

'It's quite long. I think that was quite daunting. It turned out to not really be an issue, but because it's something that I could kind of blend into my lifestyle quite a lot. Because I suppose it didn't really require any prolonged visits to the clinic or anything because it was mostly just things that I could do myself. But initially that was a bit daunting because it's a year.' EXTOD 16 (Male, Bristol)

For most, committing to the EXTOD study had proved difficult, due to the time it required off work. This let to difficulties for participants in ensuring they could always attend appointments and sometimes proved costly, due to having to take unpaid leave for study visits.

"The time that you're having to have off work…Often it's unpaid leave so obviously that can be quite difficult." EXTOD 18(Female, Leeds)

These time pressures had led to two of the interviewed participants withdrawing from EXTOD prior to completion. Solutions to these problems suggested by participants -who had both withdrawn and remained in the study - included offering more flexible appointment times and planning clinic visits further in advance so there was more time to plan around them.

'I left…Because I didn't have enough time…The study is of such a long duration and I just found that too challenging with work…If you had appointments at eight o'clock in the evening every time you needed me then so be it…I have to do a hell of a lot of juggling in order to fit that sort of stuff in.' EXTOD 17(Male, Bristol)

Coming to terms with diagnosis of T1D

Some participants spoke of how they had struggled to come to terms with their T1D diagnosis, with one participant citing this as their reason for withdrawing from EXTOD. For this participant, her difficulties coping emotionally with her diagnosis had prompted her doctors to advise her to withdraw.

"Don't think it kind of really sank in as to what I'd been diagnosed with... It had kind of hit me and I wasn't really dealing with having it…I wasn't taking my insulin and checking my levels as much…The doctors…Felt that it was best that I was taken off it." EXTOD 4(Female, Birmingham)

Effect of allocated arm

Some participants, who had been allocated the exercise intervention, spoke of difficulties maintaining the level of exercise expected of them, due to lack of motivation or the extra time it took.

'I think a year in it seemed to get a little bit "Oh God I've been doing this for a year now"…A year's a long time… Because towards the end as well, it was like you had to come in and then I had to do the gym thing, and it was kind of like…"oh this is getting really laborious".' EXTOD 2(Male, Birmingham)

Others, in the usual care comparator group, spoke of how this disincentivised them from remaining in EXTOD as they were not receiving the exercise benefits they had hoped for.

"The sort of people that…Take part…Are often similar to me in kind of quite wanting to do the exercise, and presumably about half of the time you get randomised into not doing the exercise. And I don't know whether that's off-putting as well." EXTOD 16(Male, Bristol)

DISCUSSION

This is the first study to examine the experiences of people with T1D taking part in an exercise intervention trial. The findings have highlighted issues that should be considered when designing clinical trials involving this population group. Clinical trials which reflect the needs, wants and

preferences of participants can lead to improvements in retention rates, statistical power and, in the longer term, to studies with more credible findings. The findings suggest that timing is an important consideration for many participants. Many may be offered trial entry shortly after their condition's onset and may be experiencing multiple health and lifestyle changes and struggling to come to terms with their diagnosis of T1D. This highlights the need for sensitive communication of information from health professionals when introducing clinical trials to adults with T1D, as they may be experiencing tensions between not wanting to 'become' their new illness or allow it to govern them, whilst reconciling that they need to be adaptable to their illness if they are going to feel well again[19-20]. The disappointment of some participants at being allocated the usual care group also highlights the need for a clear explanation of equipoise and other clinical trials terminology, so participants can make informed treatment decisions, minimising the potential for withdrawal rates after randomisation[21] . Additional measures that could help with this are offering the intervention at the end of the study or randomising more to the exercise arm than the control arm, to enable more participants access to the intervention.

The study has illustrated the need for the transmission of clear, relevant and useful information to clinical trial participants. Participants showed preferences for a wide-range of delivery modes, including paper formats, websites, apps and Internet forums. The use of appropriate, accessible media to convey information effectively and engage with participants is dependent on individual preferences and may be influenced by factors such as age, gender and income[22]. The popularity of Apps and multimedia technologies amongst participants indicates that these modes of information delivery should be incorporated specifically into trials with T1D participants, who are likely to be a younger, more technologically minded population group than trials with T2D participants. Future trial designs could offer paper and electronic information so participants' can utilise their preferred resource. Similarly, when collecting data, a range of methods could be employed, including paper documentation, spreadsheets, phone apps, emails and websites. Demonstrating versatility and flexibility in data collection techniques may help motivate participants to complete study documentation that they might otherwise omit. The importance of providing regular study feedback to

participants should also be considered, through letters, emails and presentations, so that their contribution is acknowledged and valued[23].

Finally, the interview findings highlighted that practicalities such as work pressures, time commitments and geographical location influenced participants' ability to commit to the trial. T1D onset usually occurs at a young age, with most people being diagnosed before 35[24]. As a result, people with T1D are likely to have busy lives incorporating work, family and social engagements, making committing to a clinical trial difficult. This is verified by the commonest reason cited for the high dropout rate (29%) from EXTOD being time and work commitments. To rectify this, more flexible study visit times could be offered, with the option of attending outside normal working hours, such as evenings and weekends. Additionally, the provision of a timetable of scheduled appointments at the study outset would allow participants to plan for them. Improved hospital transport links could also facilitate ease of study attendance[25]. By incorporating a flexible approach to these practical barriers, participants will experience less difficulty in complying with study visits, improving retention rates. Consideration should also ensure that the exercise intervention can be integrated into people's lifestyles, without adding to their pressurised schedules. This could be done by providing a range of exercise options, in a range of locations and within a realistic timeframe, to minimise the likelihood of participants becoming over-faced by the extra commitment they have taken on.

Many of the challenges to clinical trial retention in people with T1D are similar to the challenges facing the general population who are recruited to clinical trials[26-30]. The issues and challenges participants faced, such as the long study duration, difficulties completing documentation and time pressures, are also likely to be challenges for the general clinical trials population, including T2D. However, this study has identified that although many of these trial related issues are not specific to T1D populations, the reasons for these issues are likely to be different. For example, people with T1D or T2D may report that time pressures prevent them from committing to a clinical trial. However, whilst for the T1D participant, time pressures may stem from work priorities, the T2D participant time pressures may stem from regularly caring for grandchildren. By understanding more about the reasons

behind these barriers to trial recruitment and retention, trials can be designed to accommodate and facilitate the wants and needs of these different groups. The average age of participants entering clinical trials is over 50 years of age[28-31.] Whilst there is growing evidence that T1D is diagnosed throughout adult life[32,33] the mean age of the randomised EXTOD participants was 32 years, suggesting that trial retention considerations should focus on needs of younger adult populations. This younger age-group is likely to face more difficulties in adhering to rigid time schedules and appointments due to added work, family and social pressures. This is important for clinicians and researchers to acknowledge, allowing them to design T1D studies that will facilitate trial recruitment and retention, by offering more flexible appointment times, out-of-hours services and realistic, manageable exercise schedules. These practical solutions are important considerations for retaining participants in clinical trials and must be valued if rich and full trial datasets are to be obtained. These considerations may also have some relevance for T2D populations, with the average age of onset for this disease getting younger[33,34]. When considering study design, thought must be given to how to increase recruitment, as well as how to make the study experience appealing to participants once they have consented. By paying attention to the participant's perspective, the chances of retaining participants for the study duration will increase, improving trial outcomes and participant satisfaction with trial entry.

Strengths and limitations

The interview participants were selected from five UK hospitals, increasing the transferability of the findings to a range of settings. Participants were purposively sampled, stratifying them according to age, gender, randomisation arm and whether they had completed or withdrawn from the study. This enabled a diverse and comprehensive collection of narratives to be gathered and analysed, enhancing the trustworthiness of the findings. However, although 12% of EXTOD participants recruited were non-White, none of the participants recruited to the qualitative study were non-White. This lack of representation is due to our exclusion of ethnicity as a criterion in our purposive sampling. Although, we did not purposefully exclude non-White participants from the sample, the likely reason for their lack of inclusion is because T1D is far more common in White populations than other ethnic groups[35].

Additionally, many of the geographical locations we recruited from had a White population of over 84%[36-38]. Despite this, including ethnicity in our purposeful sample could have ensured that non-White populations were represented. In addition, due to the interview participants being situated around the UK, most interviews were conducted by telephone. However, where possible, participants were given the choice of being interviewed face-to-face or by telephone, allowing them to choose the setting they found most relaxing, thus increasing opportunity for open dialogue between interviewees and researcher. The fairly even split between participants choosing face-to-face and telephone interviews suggests that providing a choice of setting may increase recruitment and retention to trials, giving participants the opportunity to select their most comfortable environment.

CONCLUSION

To our knowledge, this is the first qualitative study to examine T1D participants' experiences of being involved in a clinical trial. Although people may be initially motivated to enter clinical trials for reasons such as altruism and a desire for information, practical factors such as work and time constraints, study duration and financial difficulties often act as deterrents for remaining on trials. Though these issues in themselves are not unique to the T1D population, the *reasons* for these issues are likely to be different. These reasons need considering when designing T1D clinical trials, to ensure that appropriate modifications are built into the trial design to enable people withT1D to participate with minimal disruption to their lives.

The study findings have highlighted that differences do exist between T1D participants and the general clinical trials population. Firstly, despite T1D increasingly being diagnosed in adult life, the younger adult age of people with T1D at recruitment may make it harder for them to commit to clinical trials due to increased work, family and social pressures; this was verified by study participants. Secondly, the study has indicated that using multimedia technology might benefit T1D participants, who are used to handling information electronically. It has highlighted that to increase retention to T1D trials, improvements to trial design are required. This can be done through providing

flexible access to services, clear and relevant study information, documentation and feedback, as well as consistent healthcare support.

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COMPETING INTERESTS STATEMENT

None declared.

REPORTING GUIDELINES

Trial experience of people with newly diagnosed Type 1 Diabetes

The COREQ reporting guidelines were followed.

DATA SHARING STATEMENT

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

All authors (CH, PN, RA, AD, KS, AK, SG) contributed substantially to conception and design, or acquisition of data, or analysis and interpretation of data. All authors drafted or revised the article critically for important intellectual content. All authors gave final approval of the version to be published.

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Table 1: COREQ Checklist for manuscript ID bmjopen-2018-022353

Checklist number	Item	Description	Location in manuscript (page number)
1	Interviewer/facilitator	Which author conducted interview/focus group	Page 6
2	Credentials	What were the researcher's credentials	Page 1
3	Occupation	What was their occupation at the time of the study	Page 6
4	Gender	Was the researcher male of female	Page 6
5	Training	What experience or training did the researcher have	Page 1, page 6
6	Relationship established	Was a relationship established prior to study commencement	Page 6
7	Participant knowledge of researcher	What did participants know about the researcher	Page 6
8	Interviewer characteristics	What characteristics were reported about the interviewer (bias, assumptions, interest in research topic)	Page 6
9	Methodological orientation and theory	What methodological orientation was stated to underpin the study (grounded theory, content analysis etc...)	Page 9
10	Sampling	How were participants selected?	Page 3, 5, 18
11	Method of approach	How were participants approached e.g.face to face, telephone etc..	Page 5-6
12	Sample size	How many participants were in the study?	Page 5
13	Non-participation	How many participants refused to participate/dropped out?	Page 6
14	Setting of data collection	Where was the data collected: home, clinic, workplace?	Page 7

15	Presence of non-participants	Was anyone else present besides the researcher and participants?	Page 7
16	Description of sample	What are the important characteristics of the sample? E.g. demographics.	Page 9-10
17	Interview guide	Were questions, prompts, guides, provided by the authors? Was it pilot tested?	Pages 7-8
18	Repeat interviews	Were repeat interviews carried out? If yes, how many?	Page 7
19	Audio/visual recording	Did the research use audio/visual recording to collect the data?	Page 7
20	Field notes	Were field notes made during/after the interview	Pages 7-8
21	Duration	What was the duration of the interviews/focus groups?	Page 7
22	Data saturation	Was data saturation discussed?	Page 9
23	Transcripts returned	Were transcripts returned to participants for comments/correction?	Page 9
24	Number of data coders	How many data coders coded the data?	Page 9
25	Description of the coding tree	Did the researcher provide a description of the coding tree?	Page 9
26	Derivation of themes	Were themes identified in advance or derived from the data?	Page 9
27	Software	What software, if applicable, was used to manage the dataset?	Page 9
28	Participant checking	Did participants provide feedback on the findings?	Page 9
29	Quotations presented	Were participant	Pages 11-15

		quotations presented to illustrate the themes/findings? Was each quotation identified e.g. participant number?	
30	Data and findings consistent	Was there consistency between the data presented and the findings?	Pages 11-19
31	Clarity of major themes	Were the major themes clearly presented in the findings?	Pages 11-15
32	Clarity of minor themes	Is there a description of diverse cases or minor themes?	Pages 10-15