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Qualitative study investigating the underlying motivations of healthy participants in phase I clinical trials

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ABSTRACT

Objectives If patients are to reap the benefits of continued drug development, an understanding of why healthy participants take part in phase I clinical trials is imperative. The current study aimed to explore the nature of these underlying motivations which may, in turn, improve the overall participant experience and assist in the development of more effective recruitment and retention strategies.

Design This study used a qualitative design based on the theory of planned behaviour. Specifically, it explored healthy participants' underlying behavioural, control and normative beliefs which influence their participation in phase I clinical trials.

Setting This study took place at a company that specialises in conducting phase I and phase II clinical trials in the Australian state of Queensland.

Participants Participants (n=31) were either currently undergoing a phase I clinical trial or had previously taken part in a phase I clinical trial.

Results Results showed that the motivations were varied and not solely centred on financial gains. Reported advantages of participation included altruism, while inconvenience was most often reported as a disadvantage. Friends were reported as those most likely to approve, while one's mother was reported as most likely to disapprove. Having a suitable time frame/flexible scheduling and feeling comfortable taking part in the trial were both the most commonly reported facilitators, while inflexible scheduling/time commitment was the most commonly reported barrier.

Conclusions Practical implications included the need for organisations involved in clinical trials to be mindful of inflexible scheduling and exploring the possibility of making educational materials available to family members who may be concerned about the risks associated with participation. Overall, it is anticipated that the results of this study will improve the understanding of factors that influence phase I clinical trial participation which may, ultimately, help develop new therapeutics to improve patient health.

Strengths and limitations of this study

- ► Few, if any, prior studies have used a qualitative framework to explore the underlying beliefs of healthy participants in phase I clinical trials and no prior studies have applied a psychological theory-based decision-making model (ie, the theory of planned behaviour) to this context.
- ► Understanding the motivations of healthy volunteers to take part on phase I clinical trials is imperative if the volunteer experience is to be enhanced and recruitment and retention strategies are to be more effective.
- ► Qualitative study sample sizes are often small.
- ► Participants were self-selected so it is possible that they may have been more motivated and altruistic than the average clinical trial participant.

INTRODUCTION

Phase I clinical trials are often conducted on healthy participants (Please note that the terms 'participants' and 'volunteers' are used interchangeably throughout this article. While the authors prefer the term 'participant', consistency was maintained with the original research articles that are cited) and provide an opportunity for the general public to contribute to the advancement of medicine. A phase I trial provides important information regarding the drug's safety and includes preliminary assessments of the drug's tolerability, safe dosing levels, pharmacokinetics and pharmacodynamics.[1] In 2015 in Australia, 17%–19% of clinical trials were reported to be phase I trials.[2] A 2011 report by the Australian Government's Clinical Trials Action Group recommended that the level of knowledge and understanding of clinical trials in the Australian community needed to be raised as the current level was so low that it was inhibiting the development of new drugs.[3] The need to develop effective recruitment and retention strategies targeting healthy participants to meet the demand of these phase I trials is vital if patients are to reap the benefits of continued drug development.[2] An understanding of why healthy participants take part in these trials is, therefore, imperative.

Many studies have investigated the motivations for participation in the latter phases of clinical trials.[4–6] Typically, these trials do not recruit healthy participants, rather patients with the disease that the trial is targeting. These studies have found that the possibility of personal therapeutic benefit was the strongest motivator for participation.[6–9] As healthy participants are extremely unlikely to benefit in a therapeutic sense from taking part in a clinical trial (The exception may be some novel vaccine trials where the healthy participant may benefit medically from a publicly unavailable vaccine),[10] it is anticipated that their motivations are different from patient participants. A survey study conducted in Korea investigated the motivations of both patients (n=140) and healthy (n=151) participants[7] and found that the motivations for healthy participants were different from patient participants across all trial phases. Specifically, financial benefit was the most commonly cited motivation (85%) for healthy participants.

It has been suggested that, without a financial incentive, recruitment of healthy participants would be a slow process, potentially thwarting the progress of new drug development.[11 12] Debate, however, surrounds the amount of financial incentive that should be offered. Higher incentives, for example, have been shown to encourage repeat or opportunistic volunteerism.[11 13] These sorts of volunteers, who are so heavily motivated by financial reward, can lose their ability to evaluate the risks, are more likely to take part in consecutive trials where the washout period is too short, or concurrently participate in more than one trial which increases their exposure to trial risks.[11–14] Abadie,[11] for example, found that every participant in their study said they had taken part in at least one trial that they considered to be very risky because the financial incentive was very attractive. In addition, financial incentives may encourage a bias towards participants from lower socioeconomic classes who may view the reimbursement more favourably than those from higher socioeconomic classes.[11 12] Indeed, in their study of the motivations of healthy participants in phase I clinical trials, Grady *et al*[15] found that 50% of their 1194 participants had annual incomes of below the national average and reported being unemployed at three times the national level.

Several qualitative studies based in the USA have investigated the experiences of participants in phase I clinical trials particularly in relation to serial participation and risk perception.[16–18] For example, a longitudinal interview study investigated how repeat participants weighed up the risks and benefits and included questions on their motivations to enrol.[18] As most trial participants in the USA are males and from minority groups, the financial incentive was often cited as the main motivation for serial participation. Another interview study examined emotion and risk in phase I participants and found that class and race were key factors in determining the emotional experience of risk.[16] For example, economic insecurity affected the emotional experience of risk when weighed up against the benefits. Monahan and Fisher[17] suggested that serial phase I trial participants can perceive themselves as entrepreneurs who are cleverly securing their financial futures and, in doing so, downplay the risks. While extremely rare, participation in phase I drug trials has resulted in severe illness and death of healthy participants. In 2006 in the UK, six healthy participants were hospitalised during a trial of drug TGN1412[19] and, in 2016 in France, one participant died and four fell ill during a trial of drug BIA 10-2474.[20] Independent investigations identified serious deficiencies in both of these trials. The TGN1412 trial, for example, was found to have poor record keeping and an underqualified physician.[19] The BIA 10-2474 trial was found to have breached the informed consent protocol by not updating the other participants on the status of one participant who was taken to hospital and later died.[20] While it is acknowledged that the clinical trial companies responsible for conducting these trials did not adequately protect their participants, these tragedies also drew attention to recruitment processes. Specifically, the recruitment processes highlighted the need to confirm that the information regarding the trial is well understood by potential participants, the impact of payment and the need to understand motivations for participation.[21] Very few studies, however, have specifically investigated underlying motivations of healthy participants.

In addition to the aforementioned qualitative studies which focused on serial participation and risk perception, Stunkel and Grady[22] conducted a literature review and identified only seven studies that investigated the motivations of healthy participants in phase I clinical trials. Two of these studies, however, investigated the motivations of subgroups of the population (ie, medical student and prisoners) (Please note that while it is unethical today to include prisoners in clinical trials, the study referred to in this manuscript was published in 1978, a time with different ethical guidelines) and, as such, cannot be viewed as generalisable to the population of clinical trial participants. The remaining five studies[10 15 21 23 24] were quantitative in nature and identified financial reward as the most reported motivation; however, each of the studies reported more than one motivation (eg, desire to help others, curiosity, receiving a full medical check-up).

In their recent survey study, Grady *et al*[15] investigated the characteristics, motivations and enrolment decision-making of 1194 healthy participants from phase I trials at Pfizer Clinical Research Units in the USA, Belgium and Singapore. The most common motivation was money with 58% of participants saying it was their primary motivation and 94% saying it was important or very important. Other factors were deemed by the cohort as being moderately or very important in their decision-making process. These factors were the staff's competence and friendliness (84% and 83%, respectively), the risks (81%), helping the development of new medicines and helping future patients (each 80%) and the time involved (73%). Of note, when the participants were presented with paired choices regarding motivations, the

risks associated with the trial and the potential side effects were reported as more important than the money.[15] Some clinical trial participants, however, report not being motivated by money at all.[10 21 24] Some studies, for example, have recognised the influence of other people in the decision-making process. Almeida *et al*,[10] for example, found that 88% of phase I participants consulted other people before making their decision regarding participation. Collectively, the results of the aforementioned studies highlight the varied nature of motivations for healthy participants in phase I trials. Investigating these motivations using a psychological decision-making model, such as the theory of planned behaviour (TPB),[25] will aid in understanding people's motivations.

Theory of planned behaviour

The TPB is a well-validated decision-making model that is applied to predict intention and behaviour across a range of contexts. Broadly, the theory proposes that there are three constructs which together predict intention. These constructs are: (1) attitude (ie, how positively a behaviour is appraised); (2) subjective norm (ie, perceived social pressure to perform a behaviour); and (3) perceived behavioural control (PBC; ie, perceived ease of performing a behaviour). The theory purports that intention and PBC are the proximal predictors of behaviour. Influencing each of the three constructs are the associated underlying beliefs. Specifically, behavioural beliefs (ie, advantages and disadvantages of performing the behaviour) influence attitudes; normative beliefs (ie, whether specific others approve or disapprove) underlie subjective norm; and control beliefs (ie, barriers and facilitators) influence PBC. An investigation of the underlying beliefs regarding a behaviour can provide vital information on what motivates this behaviour[26] and can be important determinants of future research avenues, including intervention development.[27] Given that the results of this study may help inform the development of more effective retention and recruitment strategies for phase I clinical trials, the TPB framework was deemed appropriate.

To the authors' knowledge, no prior studies have applied the TPB underlying beliefs stage to healthy volunteers in phase I clinical trials. The TPB, however, has been found to be effective in predicting general volunteer behaviour in Australia.[28 29] For example, in the initial phase in their study, Greenslade and White[30] used the belief elicitation phase of the TPB to compare whether there were differences in the underlying beliefs of those who volunteered at an above average rate at a major Australian volunteer organisation and those who did not. Overall, the results of their study found that those who volunteered at above the average rate were less likely to believe that volunteering tied them down, involved boring tasks, that they had too little time to participate and that paid work and family and friend commitments would prevent them from volunteering.

The current study

The aim of the current study was to gain an in-depth understanding of the motivations of healthy participants to take part in phase I clinical trials. To the authors' knowledge, there are few qualitative studies that have explored these motivations. The current study, therefore, addresses a noteworthy gap in the literature by applying a psychological theory-based decision-making model (ie, the TPB) to gain an in-depth understanding of these motivations. It is anticipated that the results of this study will improve the understanding of factors that increase participant satisfaction of the trial experience. This knowledge may directly inform more effective recruitment strategies and increase retention rates in phase I clinical trials.

METHODS

Please note that the Standards for Reporting Qualitative Research guidelines[31] were used in this article.

Procedure

A bulk email invitation was sent to the Q-Pharm (Q-Pharm is a company located in Brisbane, Australia, that specialises in conducting phase I and II clinical trials) database and included the Participant Information and Consent Form (PICF). The PICF included that the study was a focus group/interview exploring healthy participants' underlying motivations for taking part in phase I clinical trials, that participation was voluntary, some sample questions and that the information recorded would be anonymous and confidential. With permission of the trial managers, potential participants undergoing a trial (who had already received the email invitation) were also approached during their confinement period or during an outpatient visit by the researchers. Care was taken to ensure that participants did not feel pressured to take part and participants were assured that their decision whether to participate would not impact their relationship with Q-Pharm or QUT.

Overall, there were 11 focus group discussions and four interviews which were conducted on Q-Pharm premises between October 2016 and April 2017. The focus group discussions comprised two to four participants (see table 1) and interviews were conducted when only one participant was available. For participants currently undertaking a clinical trial (n=22) the focus group/interview took place either during confinement or immediately after an outpatient visit. For participants not currently undertaking a trial (n=9), the focus groups were scheduled at a time/day that was convenient for them.

The focus groups/interviews were audiotaped, and lasted 20 and 50 min. At the start of the sessions, voluntary, written informed consent was obtained and demographic information (eg, gender, age) was collected. As the second author had many years of experience conducting focus groups on other disciplines and had no prior knowledge of the research in this specific area nor any affiliation with Q-Pharm, they were deemed most

Table 1 Summary of participant groups

Group number	Group type	Participants (n)	Participant age and gender
1	Focus group discussion	2	*45 M, 19 M
2	Focus group discussion	2	47 M, *24 F
3	Focus group discussion	3	25 F, 29 F, 39 F
4	Focus group discussion	2	23 M, 23 F
5	Focus group discussion	2	19 M, 46 F
6	Focus group discussion	3	32 M, 33 M, 43 M
7	Focus group discussion	3	26 M, 31 M, 34 M
8	Focus group discussion	2	61 F, 32 M
9	Interview	1	39 M
10	Interview	1	19 M
11	Focus group discussion	4	20 F, 20 F, 24 F, 26 F
12	Interview	1	32 M
13	Focus group discussion	2	68 F, 69 F
14	Interview	1	69 F
15	Focus group discussion	2	62 F, 63 F

*45 M means a 45-year-old male; 24 F means a 24-year-old female.

suitable to conduct the focus groups. As such, the second author led eight of the focus group discussions while the first author observed and took notes which were included in the data analysis. The first author led the remaining seven discussions when the second author was unavailable, making every effort to conduct the focus groups in a similar manner. An independent transcriber was used as each audio tape became available, allowing for data analysis to take place in parallel to data collection. The transcriptions were stored on a password-protected computer folder to which only one researcher (the second author) had access.

Materials

A structured question guide, adapted from the standard TPB belief elicitation questions,[32] was used (see online supplementary appendix A). The questions were open ended and identified accessible underlying behavioural beliefs (eg, 'What do you think would be the disadvantages of volunteering for a Phase 1 clinical trial?'), normative beliefs (eg, 'Consider the people important to you, who are they and would they approve of you volunteering for a Phase 1 clinical trial?') and control beliefs (eg, 'What factors may make it easier for you to volunteer for a Phase 1 clinical trial?'). Probes were used when it was necessary to clarify responses or to gain more information. Member checking was used to ensure responses were interpreted by the researchers as intended. At the end of the interview/focus group, participants were asked if there was anything further they would like to add.

Participants

Participants (n=31; 16 female, 15 male) were aged 19–69 years (*M*=37.0 years; *median*=32 years). Sixteen participants had completed/were completing an undergraduate degree, while the remainder had completed high school (n=9), Technical and Further Education (TAFE) (n=5) or a postgraduate degree (n=1). Sixteen participants were working full time or part-time, with the remainder classifying as either students (n=6), students working part-time (n=5) or retired (n=4). Thirteen participants had taken part in a more than one phase I clinical trial while the remaining participants (n=18) had taken part/were taking part in their first phase I clinical trial. The types of phase I clinical trials undertaken by participants ranged from 2 or 3 months-long drug or parasite challenge studies with overnight or half-weekly confinement periods through to vaccine trials conducted on an outpatient basis spanning 6–12 months. The reimbursement for participation in each phase I clinical trial varied with the length of each study. All participants received a coffee voucher to compensate them for their time in attending the focus group/interview.

Patient and public involvement

This study only involved healthy members of the public who were currently, or had previously, taken part in a phase I clinical trial. The development of the research was informed by a desire to understand healthy participant motivation to enable clinical trial agencies to better meet the needs of healthy volunteers. No patients took part in this study. The results of the study have not been disseminated to the study participants in accordance with our ethical approval. Each participant, however, received an information sheet containing the contact details of the research team, should they wish to be informed of the study's results.

Data analysis

The interviews and focus group discussions were transcribed verbatim, excluding any identifying information. The transcriptions were supplemented with notes taken by the second author who observed the focus group discussions. The analysis was manual and broadly followed the six stages of thematic analysis identified by Braun and Clarke[33]: familiarisation with the data, coding, searching for themes from the codes, reviewing themes, defining and naming themes and writing up the themes. Importantly, the coding and theme development took place in the context of a theory-led approach[34] within the behavioural, normative and control belief categories

from the TPB. A cyclical process was used where the data were coded and recoded as new themes emerged until no new themes could be established.[35] Data collection was halted when no new themes were emerging. At the end of the data analysis, a content analysis was conducted on each theme and subtheme to identify the most common responses.

The analysis was primarily conducted by the second author who was experienced in analysing qualitative data. In the early stages of data analysis, a student assisted by independently coding the data. Data analysis occurred in parallel to data collection and updates were sent to the coauthors at several time points (specifically when n=17, n=26 and n=31). At each of these time points, the coauthors reviewed the analysis and provided feedback.

RESULTS

Table 2 summarises the findings categorised into each of the TPB underlying belief categories along with sample supporting quotes. For the behavioural beliefs, there were three most commonly reported advantages: money, altruism and the opportunity for self-development (ie, taking part in a valuable learning experience, the opportunity to expand one's social network and taking part in a valuable life experience). Inconvenience, encompassing time requirements and the pretrial restrictions were most often reported as a disadvantage by the majority of the participants. For the normative beliefs, friends were reported as those most likely to approve, while one's mother was reported as most likely to disapprove. For the control beliefs, having a suitable time frame/flexible scheduling and feeling comfortable taking part in the trial were both the most commonly reported facilitators. Relatedly, inflexible scheduling/time needed was the most commonly reported barrier.

DISCUSSION

The aim of the current study was to explore the underlying motivations of healthy participants who take part in phase I clinical trials. Overall, the findings strongly support the suggestion that the motivations of healthy participants in phase I clinical trials are varied and that participants are motivated by more than financial reasons. Below, the findings are discussed for each of the TPB underlying belief categories (ie, behavioural, normative and control).

Behavioural beliefs

Money and altruism were reported as the main advantages to take part in clinical trials by the same number of participants (n=12). Previous quantitative studies consistently found financial reward to be the strongest motivation, with altruism(Please note that altruism was defined differently in the previous studies. For example, it has been defined as the desire to help others,[21] helping the future of clinical trials[7] and progressing medicine.[10 15] In the current study, each of these definitions was included in the theme of altruism) the second strongest motivation.[7 10 15 21 24] Ferguson,[21] however, found that the number of participants who reported financial reward and the desire to help others as 'highly relevant' and 'relevant to some extent' were approximately the same when these two scale anchors were combined. The prospect of self-development was also a key advantage in the current study. This theme was divided into the three subthemes of (A) valuable learning experience; (B) opportunity to expand social network; and (C) valuable life experience. Given that over half of the participants in the current study (n=17) were university students or had completed tertiary education, their desire to learn may be a greater motivating factor than those without a tertiary education. Previous quantitative studies have similarly found that the opportunity to learn was an important motivator[36] as well as the opportunity for expanded social contact.[21]

Inconvenience, divided into the two subthemes of (A) time requirements and (B) pretrial restrictions, was reported by the majority of the participants (n=25) as the primary disadvantage of participation. Inconvenience has also been raised in previous literature, particularly for understanding why healthy participants are likely to take part when it is unlikely that they will gain any therapeutic benefit and they find the trial inconvenient.[10] Interestingly, Greenslade and White[30] found that those who volunteered at an above average rate were less likely to view the time requirements associated with participation as an excuse for not volunteering. Regardless, clinical trial organisations may benefit from implementing methods that could both increase efficiency and reduce participant inconvenience. Organisations may consider providing more flexible times for participant visits, conducting home or 'off-site' visits, or providing the participants with remote 'tele-health' measures to record their medical procedures and trial progress. Finding ways to make these measures compliant with current trial protocols and government regulations will require imaginative thinking and adaptive language.

Normative beliefs

While there was a variety of important others reported as approving and disapproving (eg, spouse, other family, father, flatmate), friends were reported as most likely to approve and one's mother was reported as the most likely to disapprove. The university students, in particular, believed their friends would approve because they would relate to the importance of the financial reward. Many participants reported that their mother would disapprove as they would worry about possible side effects and potential illnesses that may result from the trial. Despite this perception, this belief was not strong enough to prevent this study's participants from taking part in the trial. Given the average age of the participants in the current study was 37 years, this result is unsurprising. Almeida *et al*[10] similarly found that, while 80% of their study's participants reported that important others advised that they should not participate, they still took part in the study. It may,

Table 2 Summary of the Underlying Beliefs

Behavioural beliefs	Themes	Subthemes	Supporting quotes
Advantages	Money (n=12)		'The financial benefits are nice.' (M)
	Altruism (n=12)		'The contribution you can make to medicine in the future.' (F)
	The opportunity for self-development (n=11)	Valuable learning experience (n=5) Opportunity to expand social network (n=4) Valuable life experience (n=2)	'I'm really curious about how things work and drugs work and that sort of thing and you know if I have to use myself 'a guinea pig' well then okay.' (F) '…all the other 7 people like they were all pretty cool and we all sort of got to know each other pretty well.' (M) 'I think it's a good life experience. It's a story it's you know it's a wedding story.' (M)
	Receive a full medical check-up (n=2)		'You actually get like they medically test you to make sure that you're fit to do the trial. So it kind of comes with it that you get tested and you could find out that you have some other issue that's underlying that wasn't there but they find out about it. I guess that's a benefit.' (M)
Disadvantages	Inconvenience (n=25)	Time requirements (n=14) Pretrial restrictions (n=9)	'It was actually for fiveweeks it was from Wednesday to Saturday we were in here. And then we had to come back at seven on the Sunday morning again for bloods. So that was quite a long.' (F) 'Some of the restrictions they have before you come in. Like you can't exercise before you go in and stuff like that.' (F)
	Possible side effects (n=5)		'I get scared that maybe when I'm older and I get some random like disease or something. I don't know I feel like it would be hard to trace back to this.' (M) 'Maybe there is a slight risk that something could go wrong.' (F)
	Medical procedures (n=2)		'…lots of blood tests and stuff.' (M)
Normative beliefs			
Approve	Friends (n=14) Spouse/partner (n=8) Other family (n=7) Mum (n=4) Flatmate (n=4) Father (n=3)		'Yeh my friends are OK with it, most of them are uni students though so they see the $ sign.' (F) 'My partner is usually against it, but I can usually talk him around.' (F) 'My brother was supportive.' (F) 'Yeah and my mum was quite positive about it, she was like yeah go for it. You know like I heard good things about that.' (M) '…oh the person I live with, flatmate really, she's …she thinks it's really cool and she's got no issues.' (M) 'My dad would (approve) but everyone else, no.' (M)
Disapprove	Mother (n=12) Spouse/partner (n=7) Other family (n=7) No-one (n=5) Friends (n=4) Father (n=3)		'Only my mother is the one that directly disapproves. Because she feels that I'm going to get sick one day.' (M) '…my partner doesn't like it but that's his problem.'(F) 'Family is not (for it), just because they don't have enough information really.' (M) 'No I had nobody, nobody in family, friends anybody…nobody that I've spoken to has been anti it at all.' (F) '…one of my friends was concerned about my reasons behind it.' (F) 'I think my dad would also be quite worried if he knew.' (F)

Continued

Table 2 Continued

Behavioural beliefs	Themes	Subthemes	Supporting quotes
Control beliefs			
Facilitators	Suitable time frame/ flexible scheduling (n=9) Feeling comfortable (n=8) Low risk (n=3) If participant believes their contribution can make a difference (n=3) Easy access to information about trial (n=2)		'Yeah I think the timeframe for me is something. It's got to fit in with what you're doing…' (M) 'Definitely what would encourage me is a, just a longer timeframe between the start of the advertising and the start of the trial that would help definitely.' (M) 'I think once you've done a trial you sort of feel comfortable to do more.'(M) 'You know reading the information that you're given and I felt it was going to cause maybe a long term problem or issue then I might think twice about it.' (M) '…it was kind of good in that, you know if you're looking at it as in you're making a difference or whatever.' (M)
Barriers	Inflexible scheduling/time commitment (n=13) Possible side effects (n=6) Being inoculated (n=5) Lots of restrictions (n=4) Invasive method of drug delivery (eg, tube down throat) (n=2) Lots of selection criteria (n=1) If it is hard to find information on the internet (n=1) Needing a car (n=1)		'And it's just a time thing with me, I think if it took too much time or if it was too much involvement I would probably yeah not be involved.' (F) '(If) I felt it was going to cause maybe a long term problem or issue then I might think twice about it.' (M) 'If they injected you with some kind of disease it would probably put me off it' (F) 'So like if it's got a lot of restrictions it's definitely less attractive maybe I wouldn't do it.' (F) 'If it means really invasive but I can't see how a trial would be that apart from the tube down the throat which I will not do. I couldn't, I'd gag too much to have that done.' (F) 'When it starts getting super requirements…the list passes like 20 things you can't do.' (M) 'That you kind of need a car.' (F)

therefore, be worthwhile for clinical trial organisations to make educational materials available to family members/significant others (and parents in particular), to include them in the informed consent process (possibly through eConsents(eConsents refers to electronic consenting of trial participants using an array of digital elements and process efficiencies)), or give them the opportunity to talk with the clinical trial team. Having this information may encourage a higher level of support for trial participation from significant others, resulting in higher levels of participation.

Control beliefs

A range of facilitators and barriers was reported. Suitable time frame/flexible scheduling was the most commonly reported facilitator to trial participation and the related concept of inflexible scheduling/time needed was the most commonly reported barrier. Perhaps, unsurprisingly, Grady *et al*[15] found that the time requirements were rated as less important in the decision-making process among the unemployed than the employed participants. The results of the current study, however, were based on the responses from participants who were mostly employed and/or studying (n=27). Clinical trial facilities and the trial sponsors therefore need to be mindful of this finding when scheduling trials as it is clearly of utmost importance to participants and, in particular, participants who work or study. While maintaining high safety standards, the clinical necessity of repeated, and daily or twice-daily outpatient visits needs to be considered as the frequency of these visits may affect recruitment rates. Providing flexibility for clinical attendance around scheduled time points would still provide participants with options to comply with the trial protocols.

Feeling comfortable was reported as an important facilitator. Encouragingly, many participants in the current study reported trusting the medical expertise of the staff members who were involved in their phase I trial procedures. Trials perceived as having a low risk, participant belief that they can make a difference and easy access to trial information were also reported as facilitators by a few participants. Additional barriers reported by a few participants were possible side effects, being inoculated (ie, affected by the investigational agent) and having substantial lifestyle restrictions both pretrial (eg, no alcohol in the trial lead time) and while on trial (eg, during confinement).

Strengths and limitations

Few prior studies have used a qualitative framework to explore the underlying beliefs of healthy participants in phase I clinical trials nor have they applied a psychological theory-based decision-making model (ie, the TPB) to this context. Qualitative study sample sizes are often small and the participants are self-selected so it is possible that participants may be more motivated and altruistic than the average clinical trial participant. It is also acknowledged that 4 of the 15 discussions were interviews in which the participant may have provided different responses to those they may have provided had they been part of a focus group. While the results of this study were compared with previous studies, these comparisons should be reviewed with caution given the previous studies were quantitative in nature. Finally, while it is acknowledged that differences in trial schedule, medical procedures and reimbursement are likely to influence motivations (ie, first-in-human drug trials with lengthy confinement, multiple lifestyle restrictions and extensive clinical sampling are usually compensated far higher than a vaccine trial), it is beyond the scope of this study to investigate these potential differences.

Future research

As this study is based on the initial, underlying belief elicitation phase of the TPB, it would be worthwhile assessing a broader endorsement of the beliefs in a larger survey study. These qualitative and quantitative findings could then inform the development of effective strategies for recruitment and retention, especially in regard to communicating the rationale of trial scheduling and lifestyle restrictions to potential participants. Future research could also investigate whether there are differences in the motivations of younger and older participants as the study participants in the current study were more likely to believe that their friends would approve as they would similarly be motivated by financial reward. Building on the quantitative work of Chen e*t al*,[37] a qualitative study could similarly explore whether there are differences in motivations for the different trial designs, medical procedures and the underlying clinical utility of the trialled drug

CONCLUSION

The current study employed a qualitative approach to explore the motivations of healthy participants taking part in phase I clinical trials. Results showed that the motivations of healthy participants are varied and not just dominated by financial gains, thereby providing valuable information to the ethical debate surrounding financial incentives. Overall, it is anticipated that the results of this study will improve the understanding of factors that influence phase I clinical trial participation. Specifically, practical implications include the need for organisations involved in clinical trials to be mindful of inflexible scheduling and explore the possibility of making educational materials available to family members who may be concerned about the risks associated with participation. These factors may then be used to develop more effective recruitment and retention strategies which will, ultimately, help develop new vaccines and therapeutics to improve patient health.

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Contributors KJM, SLE and PMG conceived the study idea. KMW provided theoretical (TPB) expertise and guidance to develop the study's design. CSG and KMW developed the focus group interview guide. CSG and KJM conducted the focus groups. PMG provided access to participants. CSG analysed the data with regular input from KJM and KMW. CSG drafted the manuscript with regular input from KJM and KMW. SLE and PMG critically reviewed the draft manuscript. All authors approved the final manuscript.

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