



STUDY PROTOCOL

REVISED

An examination of the effects of a patient-designed-and-informed participant information sheet in comparison with a standard, researcher-designed information sheet on recruitment, retention and understanding: Protocol for a study-within-a-trial [version 2; peer review: 2 approved, 1 not approved]

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Abstract

Background: This protocol describes a double-blind, randomised non-inferiority study-within-a-trial (SWAT), comparing the effects of a patient-designed-and-informed participant information sheet with a standard, researcher-designed participant information sheet on recruitment, retention, decision certainty, participant information sheet understanding and likeability. The SWAT is part of a larger trial that aims to evaluate the feasibility and preliminary efficacy of a cognitive occupation-based programme for people with MS (COB-MS) on cognitive and daily functioning for people with multiple sclerosis.

Methods: During the study, 120 people with multiple sclerosis will be randomly allocated to one of the two groups, where they will either receive a standard participant information sheet or a patient-designed participant information sheet. Recruitment and retention will be analysed, as well as decision certainty, likability and understanding.

Discussion: Results will provide recommendations for recruitment, consent and retention for future trials, as well as shed some light on the factors influencing the understanding and likeability of a trial's participant information sheet. Recommendations will also be made regarding patient and public involvement in developing and/or aiding the development of participant information sheets.

Registration: SWAT: Northern Ireland Hub for Trials Methodology Research SWAT Repository Store ([SWAT105](#)). COB-MS trial: [ISRCTN11462710](#).

Open Peer Review

Reviewer Status

	Invited Reviewers		
	1	2	3
version 2 (revision) 30 Mar 2020	 report		
	↑		
version 1 24 Jan 2020	 report	 report	 report

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Keywords

Participation information, recruitment, retention, multiple sclerosis, public and patient involvement, PPI, SWAT

Any reports and responses or comments on the article can be found at the end of the article.

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REVISED Amendments from Version 1

The original version of this manuscript has been amended in light of initial reviewer comments and suggestions. Specifically, minor amendments have been made throughout in order to ensure clarity (e.g. rewording and the addition of further, though brief, elaboration). Only one major change was made to the manuscript – the editing of the ‘Background and rationale’, from approximately 750 words, to its current length, in light of reviewer commentary that this section could be more concisely expressed.

Any further responses from the reviewers can be found at the end of the article

Introduction**Background and rationale**

Recruitment is a critical process within research interventions, given its impact on statistical power, the validity of findings and investment of resources (Britton *et al.*, 1998; Wade *et al.*, 2009). Apart from advertisement materials, the participant information sheet (PIS) is the primary source of written information that potential participants engage with during the recruitment process. Indeed, it is crucial to ensure that potential participants understand both the broad and specific implications of the study to which they are consenting (McCaughey *et al.*, 2016). Though provision of a PIS is requisite as part of the informed consent process, in which case the PIS itself has been subject to ethical review, such ethical consideration does not necessarily account for *quality* of the PIS. Thus, it can be argued that just because the presentation of a PIS is not unethical, this does not ensure that it is appropriate.

Research indicates that understanding of the PIS is often poor amongst participants in health-related research (Khan *et al.*, 2014; McCaughey *et al.*, 2016). However, only a limited body of research has evaluated the effects of various manipulations to PIS development on recruitment and comprehension, yielding mixed results (e.g. Cockayne *et al.*, 2017; Knapp *et al.*, 2011; Manley *et al.*, 2015). As some of these manipulations can be costly with respect to both finances and time, future research is necessary to identify a practical, feasible means of enhancing PIS clarity and comprehension, as well as subsequent participant retention.

Having PIS design input from an individual eligible to participate in the intervention (e.g. living with the chronic illness), but without any personal bias involved with actually participating, may yield positive effects on recruitment and comprehension – that is, PIS development led by a *public and patient involvement* (PPI) member of the research team (not from a research background), who would otherwise be eligible to participate in the intervention. PPI is an effective means of enhancing the likelihood of a successful trial by involving people with lived experience of a particular condition as partners throughout the research process (Crocker *et al.*, 2018). In light of extant theory and research, a PIS developed in light of PPI may enhance trial understanding and recruitment (with respect to consent), as well as participant retention.

Objective

The objective of the current research (i.e. a study-within-a-trial; SWAT) is to compare the effects of two PISs designed to facilitate informed consent of potential participants – a (patient) PPI-designed-and-informed PIS in comparison and a standard, researcher-designed PIS on: recruitment, decision certainty, retention; understanding, readability, accessibility, likeability and decision to consent. The SWAT is part of a larger trial that aims to evaluate the feasibility and preliminary efficacy of an eight-session cognitive occupation-based programme for people with MS (COB-MS) on cognitive and daily functioning for people with MS (PwMS).

Methodology**Ethical statement**

Ethical approval was awarded by Galway University Hospitals on 13.08.2019 Ref: C.A 2231 and the study will be conducted at the National University of Ireland, Galway. All participants will take part in this study based on informed consent, in which they know their non-personalised data will be reported in published dissemination.

Trial design

The current SWAT is a double-blind, randomised non-inferiority trial comparing the effects of a patient-designed-and-informed PIS with a standard, researcher-designed PIS on recruitment, decision certainty, participant retention, PIS understanding, PIS likeability and decision to consent. Both PISs are designed specifically for an MS cohort. The SWAT will be conducted in the context of a single-blind, cluster-randomised controlled feasibility and preliminary efficacy trial of the eight session COB-MS programme – a Cognitive Occupation-Based programme for people living with MS – in comparison with a treatment as usual, wait-list control group (i.e. the main trial). For further details of the study within which this SWAT will be conducted (from here on referred to as the ‘main trial’), see [ISRCTN1462710](https://www.isrctn.com/ISRCTN1462710).

Study setting

This is a community-based research study. Data will be collected in Ireland. The main study site is at NUI Galway; but data will be collected nationwide, dependant on the location of the participants.

Interventions

Two PISs were developed. A *standard, researcher-designed PIS* (SRPIS) was written by the post-doctoral researcher – from both the SWAT and the main trial – who has over 10 years’ research experience. The researcher wrote the PIS in light of templates from past trials for structure, making sure to include/address study background, procedure, eligibility, consent, funding/support and descriptions of both potential risks and benefits. A *PPI-designed-and-informed PIS* (PPIPIS) was developed by a PPI member of the research team – who was neither from a research or medical background, nor had experience in these fields – who would otherwise be eligible to participate in the intervention. The PPI member wrote the

PIS from a patient perspective, in light of what was deemed both necessary for potential participants to know and useful to know. The only restriction on PPIPIS development was that the PPI member was required to include/address study background, procedure, eligibility, consent, funding/support and descriptions of both potential risks and benefits. Following development of the PPIPIS, the document was further analysed, evaluated and subsequently approved as appropriate by other PPI members through discussion and agreement within a PPI focus-group; specifically: one other PPI member from the trial steering committee and an external PPI consultation group which was convened to discuss issues related to outcome measures and recruitment material, such as this. Notably, the PIS developers were blinded to each other's PIS and did not liaise or discuss the PISs during their development, both of which were submitted separately to the primary investigator (PI) for subsequent submission for ethical approval. Both PISs were accompanied by a PI-developed addendum regarding GDPR guidelines in order to ensure consistency in this context, for ethical purposes. See *Extended data*, for the two PISs, GDPR addendum and consent form (Dwyer, 2020).

Outcome measures

Recruitment will be measured dichotomously by whether or not the PwMS consented to participate in the main trial.

The Decisional Conflict Scale (DCS; O'Connor, 1995) is a 16 item questionnaire, answered via a five-point Likert scale, ranging from strongly agree (0) to strongly disagree (4), used to measure decision certainty, with respect to decision to provide consent to participate in this SWAT. The scale is established as valid and reliable with test-retest correlations and Cronbach's alpha of 0.78 (O'Connor, 2012).

Retention will be measured dichotomously by whether or not the PwMS completed participation in the trial. Notably, *level of retention* will also be measured by stages of completion, including (0–8) COB-MS sessions completed and (1–4) testing phases completed (i.e. on a scale of 1–12).

Understanding, readability, accessibility, likeability and decision to consent will be assessed via a six-item questionnaire, developed through discussion and agreement with a PPI focus-group, to be answered via six-point Likert scale, ranging from strongly disagree (0) to strongly agree (5):

1. The *Study Information Sheet* played a large role in my decision to participate in the study. (Decision to consent)
2. I was able to read the information presented in the *Study Information Sheet*. (Understanding)
3. I was able to understand the information presented in the *Study Information Sheet*. (Understanding)
4. The language used in the *Study Information Sheet* was accessible to me. (Understanding)
5. I knew I was going to consent participate before I was even presented the *Study Information Sheet*. (Decision to consent)

6. Overall, I liked *Study Information Sheet* that was presented to me. (Likeability)

Sample size

As the main trial is a feasibility study, a formal sample size calculation is not required. Instead, a pragmatic approach is adopted, based on an average recruitment rate for National Institute for Health Research (UK) funded randomised controlled trials (RCTs). A total of 120 PwMS will be recruited for the main trial; thus, the sample size for the SWAT will exceed 120 (i.e. accounting for 'consent decliners'), until saturation has been reached. See [Figure 1](#) for CONSORT flowchart of study participants.

Recruitment

PwMS will be recruited through advertisement in relevant outlets, including newsletters and other publications (e.g. monthly *MS Ireland* newsletter), MS-related websites, discussion boards and forums (e.g. *MS Ireland*), recruited occupational therapists, posters in relevant clinics around the Republic of Ireland (e.g. GP, primary care clinics, physiotherapy and neurology), radio and social media. Advertisements (see *Extended data*; Dwyer, 2020) will not provide detailed trial information that would contaminate or influence assimilation via the PISs. Individuals interested in participating will self-select through contacting the researchers by email or phone; and informed consent will be obtained prior to participation.

Interim analysis and stopping guidelines

There is no planned interim analysis. However, statistical analysis of descriptive data may be required in consideration of stopping guidelines for cases of unforeseen circumstances. Specifically, consistent with [Avery et al. \(2017\)](#), transparent reporting will be made around the decision-making process for stopping, amending or proceeding with the main trial and, likewise, the SWAT. As this is a SWAT embedded within a feasibility trial, stopping rules are distinct from those seen in a definitive trial and include two types of stopping guidelines – those specific unto the SWAT and those specific unto the main trial. The latter are relevant in this context, given that stopping the main trial prematurely would block assessment of participation completion and level of retention. The stopping rule specific unto the SWAT is recruitment of less than 70% during the recruitment phase set; protocol, including data collection period not tolerated by over 25% of participants. Stopping rules for the main trial also include: drop-out rate of participants during the COB-MS intervention is great than or equal to 50%; drop-out rate of occupational therapy participants greater or equal to 40%; serious adverse event(s) reported to the data monitoring committee (DMC) that are a direct result of the COB-MS and the DMC view require the stopping of the trial.

Randomisation

PwMS participants will be randomly allocated to one of two study arms (i.e. SRPIS and a PPIPIS), using 1:1 allocation, via randomised block permutation (i.e. two randomised blocks of four and six per block). Randomisation will be conducted through a purpose-designed computer-generated system. Specifically, one researcher with statistical expertise will conduct the randomisation based on the sequence and type of randomisation

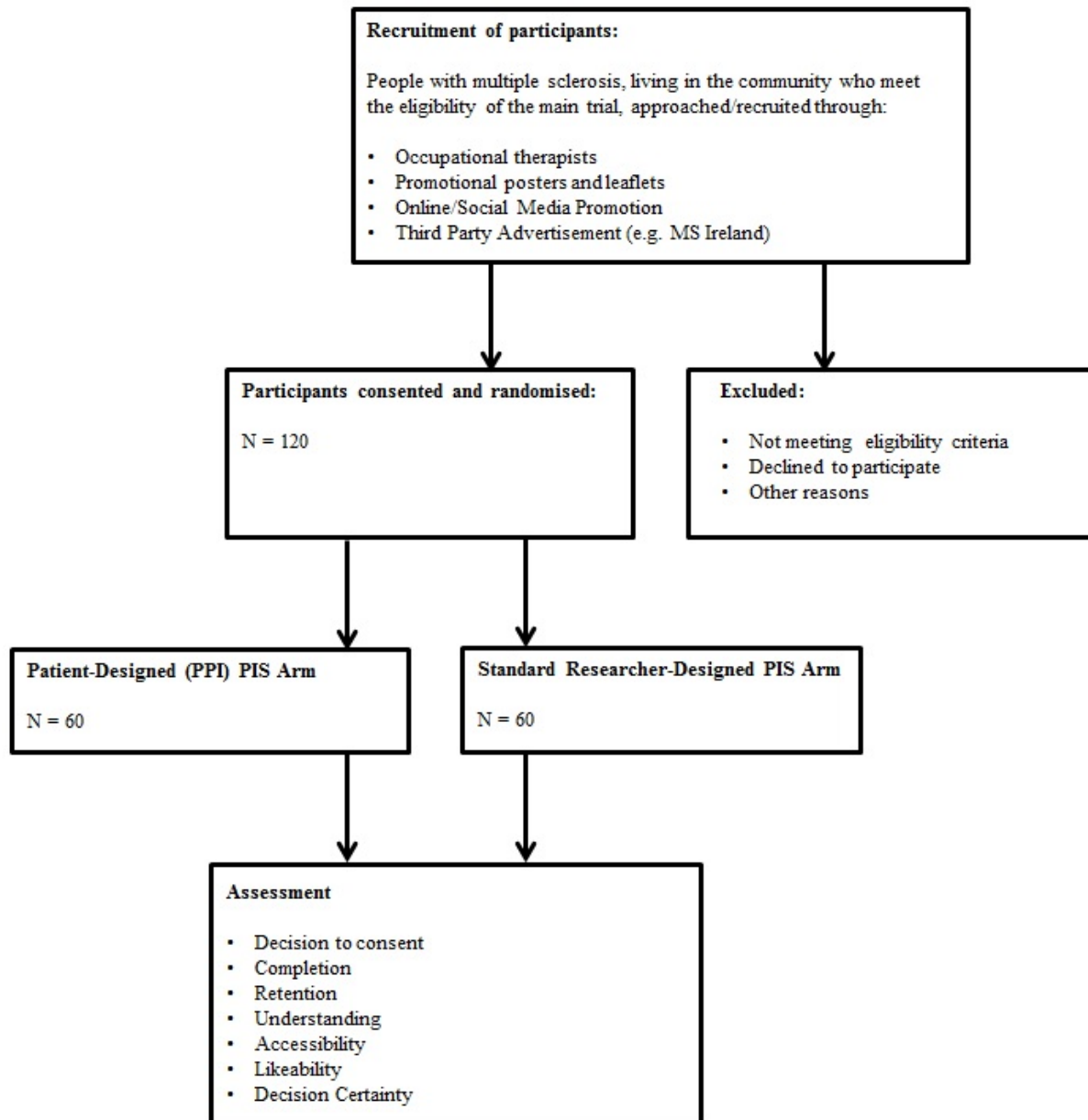


Figure 1. CONSORT flowchart of participants.

described above. A second researcher, blind to the sequence, will collate the names of potential participants' in light of a 'first-come-first-serve' basis regarding expression of interest in the study, and address information packs to potential participants based on the code yielded from the randomisation process. The code consists of a four digit, non-repeating string which cannot be 'guessed' by the blinded researcher. A third researcher will recode the data upon imputation, resulting in the blinding of the initial researcher, who will analyse the data.

Inclusion and exclusion criteria

Inclusion and exclusion criteria are based on the main trial. Notably, however, though the inclusion/exclusion criteria are

presented within the PISs, eligibility will not be confirmed until after completion of the SWAT. Thus, it cannot be ensured that participants will meet the main trial's inclusion/exclusion criteria. Though the main trial's criteria for eligibility are not relevant to the SWAT, records of eligibility and reasons for ineligibility will be recorded. Inclusion criteria for the main trial include:

- 1) aged 18 years of age or older;
- 2) fluent in written and spoken English;
- 3) have a diagnosis of multiple sclerosis (consistent with the McDonald Criteria for the Diagnosis of Multiple Sclerosis [Thompson *et al.*, 2018]);

- 4) cognitive difficulties, as shown by a score of >22 on the *Multiple Sclerosis Neuropsychological Screening Questionnaire* (Benedict *et al.*, 2004)
- 5) are clinically stable (i.e. not having an active relapse);
- 6) can provide informed consent;
- 7) no neurologic history other than MS, including evidence of current dementia;
- 8) no history of major depressive disorder, schizophrenia, or bipolar disorder I or II;
- 9) no history of diagnosed substance use or dependence disorder;
- 10) not currently undergoing any other form of cognitive rehabilitation; and
- 11) living in the community.

The exclusion criteria for the main trial are: (1) cognitive impairment that would affect reliable participation or capacity to give informed consent; (2) are incarcerated or institutionalized; and (3) significant neurological condition or organic brain damage (unrelated to MS).

Procedure

Consistent with the recruitment strategy discussed above, all individuals interested in participating will self-select through contacting the researchers by phone or email. The duration of the recruitment period for both the main trial and SWAT is eight months. Potential participants will be sent a randomly allocated PIS in the post to consider before making their decision to participate in the main trial. Participants will also be sent a consent form for the main trial and the outcome measures relevant to this SWAT. Following verbal consent and screening via telephone, SWAT data and written consent will be collected by another member of the research team (i.e. an assistant psychologist trained in psychological assessment), who will have phoned in advance to organise a home visit for the main trial's baseline assessment (i.e. within three months of receiving their randomly allocated PIS). Consenting participants may choose not to complete some aspects or all of the self-report SWAT outcome measures and, at the same time, remain in the main trial, in which case, partial response or non-response to the self-report SWAT outcome measures will be treated as missing data. Consistent with the protocol for the main trial, those who decline to participate in the trial will be asked, with informed consent, to provide the reasons why they have declined to participate in the main trial. These data will include the measures identified in this SWAT protocol. Those who consent to participate in this 'decliner cohort' will be asked to complete the measures already sent to them and return them completed to the research team. Those who do not consent to participate in the 'decliner cohort' will be thanked for their time and consideration. Rates of all forms of consent will be recorded. See [Table 1](#) for SWAT schedule, consistent with SPIRIT guidelines.

Analysis

Statistical analysis will be conducted through two chi-square tests of independence, which will be performed to examine the relationship between source perspectives (i.e. SRPIS and

PPIPIS) on both consent and trial completion (i.e. retention). A series of analyses of variance will be conducted to examine the effects of source perspective on level of retention, understanding, readability, accessibility, likeability, decision certainty and decision to consent regarding the two different PISs. Statistical significance will be determined at the .05 level. Descriptive statistics and correlations will be reported for all measures. Sub-group analyses will be conducted if warranted by the planned analyses to aid interpretation of the statistical findings (e.g. differences between: main trial completers and non-completers; or low and high scorers on the DCS).

Data management and monitoring

A FAIR Data Management Plan (Wilkinson *et al.*, 2016) will be used for this SWAT, which ensures that all data are *findable, accessible, interoperable* and *reusable*. That is, collected anonymised data will be made openly available, where possible, in an ethical manner; and ensures that appropriate data management is conducted during all phases of the study. Upon collection, data will be imputed to an electronic file and stored on an encrypted, password-protected, hard drive. All hard copies of data will be kept securely in a locked cabinet at the study site. Confidentiality of all data and individual results will be protected at all times and anonymisation will be used throughout the study. Names or other personal identifiers will be securely stored separately from other data, identified by code, to ensure blinding. The statistician will analyse cleaned, depersonalised data. Blinded researchers, including the statistician, will only have access to cleaned, depersonalised data sets. Participants will be aware of and have consented to these processes in advance of participation. All data collection and storage will be conducted consistent with GDPR guidelines.

PPI

PPI in research refers to the involvement of people with lived experience of a particular condition (e.g. MS) as partners throughout the research process and is often an effective means of enhancing the likelihood of a successful trial (Crocker *et al.*, 2018). Consistent with PPI practice, both the main trial and this SWAT have a PPI member as part of the research team for their entire durations. There are two PPI members on the trial steering committee and an external PPI consultation group has been convened to discuss issues – outcome measures and recruitment material. To reiterate, SWAT outcomes were in part developed through discussion and agreement with a PPI focus-group; and the one PPI research team member devised the PPI-developed PIS. Furthermore, both recruitment and dissemination of results will be aided through PPI through lay knowledge translation in the community.

Safety

No harm is expected to come to participants from taking part in the SWAT. If any harm does occur, it will be recorded and reported to the Principal Investigator and relevant Ethics Committees.

Study status

At the time of submission of this protocol, recruitment has commenced.

Table 1. Study-within-a-trial schedule.

Timepoint	Study period			
	Pre-intervention	Intervention	Post-intervention	Post-main trial
	$-t_1$	t_0	t_1	t_2
Self-selected enrolment	X			
Allocation	X			
Verbal consent	X			
Intervention		X		
Signed consent			X	
Assessments				
<i>Recruitment</i>			X	
<i>Retention</i>				X
<i>Understanding</i>			X	
<i>Likeability</i>			X	
<i>Decision to consent</i>			X	
<i>Decision certainty</i>			X	

Discussion

Early pilot studies have shown that COB-MS training may lead to improvements in daily living and cognitive functioning in people with MS (Reilly & Hynes, 2018). However, these findings require replication with a larger participant pool; and, as such, any barriers to recruitment and retention should be avoided. Past RCTs have found recruitment of MS participants to be slow, with low uptake rates (Carter *et al.*, 2015; Cooper *et al.*, 2011). Complicated or jargonistic PISs may hinder patient's understanding of the study (Parker *et al.*, 2018). By involving people with MS in the design of MS-specific PISs, it may increase understanding and, in turn, both recruitment and retention (Crocker *et al.*, 2018). If a patient-informed PIS is found to be an effective way of increasing recruitment, then the current SWAT protocol could provide a beneficial template for future clinical research in MS. Overall, results from this SWAT may provide useful recommendations for recruitment, consent and retention for future trials, as well as shed some light on the factors influencing the understanding and likeability of a trial's participant information sheet.

Dissemination

Findings of the SWAT will be submitted for publication in a peer-reviewed journal and presented at both national (Ireland) and international conferences. This SWAT's knowledge exchange plan also includes accessible outlets of dissemination for lay audiences, such as through PPI-oriented national meetings and other local level presentations and fora, social media, as well as NUI Galway communications, with an aim of targeting the research community and both PPI and funding bodies. Study results will be submitted for appropriate dissemination within six months of final data collection.

Data availability

Underlying data

No data are associated with this article.

Extended data

Open Science Framework: An examination of the effects of a patient-designed-and-informed participant information sheet in comparison with a standard, researcher-designed information sheet on recruitment, retention and understanding: Protocol for a study-within-a-trial. <https://doi.org/10.17605/OSF.IO/DGZBQ> (Dwyer, 2020)

This project contains the following extended data:

- PISs-GDPRAddendum-ConsentForm.docx (document containing patient information sheets, GDPR addendum and consent forms)
- TrialAdvertisements.docx (document containing advertisements for the trial)

Data are available under the terms of the [Creative Commons Zero "No rights reserved" data waiver](#) (CC0 1.0 Public domain dedication).

Reporting guidelines

Open Science Framework: An examination of the effects of a patient-designed-and-informed participant information sheet in comparison with a standard, researcher-designed information sheet on recruitment, retention and understanding: Protocol for a study-within-a-trial. <https://doi.org/10.17605/OSF.IO/DGZBQ> (Dwyer, 2020)

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Open Peer Review

Current Peer Review Status:   

Version 2

Reviewer Report 30 March 2020

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Vivian Welch 

School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Canada

Responses to peer review are excellent.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Systematic reviews and health equity.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 09 March 2020

<https://doi.org/10.21956/hrbopenres.14067.r27169>

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Erik Lundstrom

Uppsala University, Uppsala, Sweden

Eva Isaksson

Karolinska Institutet, Solna, Sweden

General comments

This manuscript addresses an important field: improvement of the patient information sheet to increase recruitment and retention in clinical trials. It is obvious that the authors know their field, given the

information in the introduction and the length of the manuscript.

My main concern is that it is not clear what the primary outcome is? See methods.

Overview

- The manuscript would be much better if it could be shorter, especially the introduction.
- Don't use so many abbreviations.
- I can't find the two participant information sheet (PIS) (am I missing something?). It would be good to find a link early in the text.
- Generalisability - can the result of this study be used in other study groups or other diagnosis?
- How is the cognitive status of this patients? Can this affect the result of this study or the content in the PIS?
- Did the PPI member that were designing the PPIPS had MS so that they could relate to specific questions and feelings in the information? That part is not clear. Maybe you should describe it more thoroughly.

Title

A little wordy. Is it possible to shorten?

Maybe: Comparing standard information with patient-designed sheet: Protocol for a study-within-a-trial.

Abstract

Background: It is a little hard to know how large the larger study is, just adding n=... would help. "The SWAT is part of a larger trial (n=...)"

"Methods: During the study, 120 people with multiple sclerosis will be randomly allocated to one of the two groups, where they will either receive a standard participant information sheet or a patient-designed participant information sheet."

Question: Are they randomly allocated 1:1?

"Recruitment and retention will be analysed, as well as decision certainty, likability and understanding."

Question: What is the primary outcome? How are the recruitment analysed? And I wonder, would you really expect higher recruitment and retention? I would be surprised if you get +2-3% more recruitment.

"Discussion: Results will provide recommendations for recruitment, consent and retention for future trials, as well as shed some light on the factors influencing the understanding and likeability of a trial's participant information sheet."

Question: This is a very strong statement. It might provide recommendations on recruitment. But also on consent, and retention?

Introduction

It is obvious that the authors know their field. Well written. But too long; approx. 750 words, including objective. Suggestions: Reduce to max 350 words.

Methodology

Trial design: OK, but please tell us how large the main study is.

My main concern is that I don't get what is the primary objective for this study.

1. Is it recruitment? If so, what would be regarded as a success? 1%, 2%, 5%, 10%.
2. Retention? If so, what would be regarded as a success?
3. Also you mentioned a questionnaire. What would you expect to be a success or a relevant difference?

Don't get me wrong. I do think this is important, but I think that this intervention is too weak. Or is the study explorative? I'm totally OK with that.

In short: What would be a statistical significant and clinical relevant difference between the groups?

Is the rationale for, and objectives of, the study clearly described?

Partly

Is the study design appropriate for the research question?

No

Are sufficient details of the methods provided to allow replication by others?

No

Are the datasets clearly presented in a useable and accessible format?

No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Stroke. Clinical research, both observational and randomised.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to state that we do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 18 Mar 2020

Christopher Dwyer, National University of Ireland, Galway, Galway, Ireland

Many thanks for your comments. We considered each in turn and, have amended the manuscript in light of these considerations. Other comments and questions we answer here.

My main concern is that it is not clear what the primary outcome is? See methods.

All outcome measures are 'primary', given the exploratory nature of this non-inferiority SWAT.

The manuscript would be much better if it could be shorter, especially the introduction.

The introduction has been edited to strengthen clarity and is now shorter.

Don't use so many abbreviations.

This is stylistic in nature; also given that the use of acronyms enhances the flow of prose-reading and shortens the manuscripts length, we have not cut any acronyms.

I can't find the two participant information sheet (PIS) (am I missing something?). It would be good to find a link early in the text.

Please see 'Extended data'.

Generalisability - can the result of this study be used in other study groups or other diagnosis?

Given that the intervention manipulation does not regard MS, then yes, it is somewhat generalisable. However, this reasoning is speculative and we recommend replication in other cohorts in order to observe whether there is some effect of using a MS cohort on such PIS manipulation.

How is the cognitive status of this patients? Can this affect the result of this study or the content in the PIS?

Participants will have cognitive difficulties; but, consistent with the PISs (again see 'extended data'), such difficulties would not extend to compromising ability to 'provide informed consent'. However, given the prospective nature of this protocol, we cannot be sure that such cognitive difficulties will not affect the results of the study (let alone the protocol); thus, this comment will surely be considered in the results paper.

Did the PPI member that were designing the PPIPS had MS so that they could relate to specific questions and feelings in the information? That part is not clear. Maybe you should describe it more thoroughly.

"A PPI-designed-and-informed PIS (PPIPIS) was developed by a PPI member of the research team - who was neither from a research or medical background, nor had experience in these fields - who would otherwise be eligible to participate in the intervention."

Title

A little wordy. Is it possible to shorten?

Maybe: Comparing standard information with patient-designed sheet: Protocol for a study-within-a-trial.

Though the title might be considered long, we believe the existing title ensures accuracy and clarity.

Abstract

Background: It is a little hard to know how large the larger study is, just adding n=... would help. "The SWAT is part of a larger trial (n=...)"

"Methods: During the study, 120 people with multiple sclerosis..."

Question: Are they randomly allocated 1:1?

Yes, amended.

"Recruitment and retention will be analysed, as well as decision certainty, likability and understanding." Question: What is the primary outcome? How are the recruitment analysed? And I wonder, would you really expect higher recruitment and retention? I would be surprised if you get +2-3% more recruitment.

Recruitment is assessed dichotomously – consent or no consent. All outcome measures are 'primary', given the exploratory nature of this non-inferiority SWAT, which is also why it's inappropriate to 'expect anything' in this context – there are no specified hypotheses.

"Discussion: Results will provide recommendations for recruitment, consent and retention for future trials, as well as shed some light on the factors influencing the understanding and likeability of a trial's participant information sheet." Question: This is a very strong statement. It might provide recommendations on recruitment. But also on consent, and retention?

The results – be they positive, negative or neutral will indeed provide information regarding manipulation of PISs and their effects on recruitment, retention, consent, etc. Of course, like all research, replication of results will be necessary; however, this SWAT will contribute to this area of study.

Introduction

It is obvious that the authors know their field. Well written. But too long; approx. 750 words, including objective. Suggestions: Reduce to max 350 words.

The introduction has been edited to strengthen clarity and is now shorter.

Methodology

Trial design: OK, but please tell us how large the main study is.

"Methods: During the study, 120 people with multiple sclerosis..."

My main concern is that I don't get what is the primary objective for this study.

"The objective of the current research (i.e. a study-within-a-trial; SWAT) is to compare the effects of two PISs designed to facilitate informed consent of potential participants – a (patient) PPI-designed-and-informed PIS in comparison and a standard, researcher-designed PIS on: recruitment, decision certainty, retention; understanding, readability, accessibility, likeability and decision to consent."

Is it recruitment? If so, what would be regarded as a success? 1%, 2%, 5%, 10%.

With respect to the primary outcomes, again all outcome measures are 'primary', given the exploratory nature of this non-inferiority SWAT. We are not concerned with feasibility standards in this SWAT, such as overall recruitment success. The SWAT is a comparison study.

Retention? If so, what would be regarded as a success?

See response directly above.

Also you mentioned a questionnaire. What would you expect to be a success or a relevant difference?

Don't get me wrong. I do think this is important, but I think that this intervention is too weak. Or is the study explorative? I'm totally OK with that.

Again, the study is exploratory. A 'relevant difference' will be determined at the .05 level of statistical significance. This has been added for clarity.

In short: What would be a statistical significant and clinical relevant difference between the groups?

See above.

With respect to the reports regarding the rationale, objectives, design, methods and datasets, we hope our responses have provided clarity and answer the questions arising from your review.

Competing Interests: No competing interests were disclosed.

Reviewer Report 04 March 2020

<https://doi.org/10.21956/hrbopenres.14067.r27170>

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Emmy Racine 

School of Public Health, University College Cork, Cork, Ireland

Patricia M. Kearney 

School of Public Health, University College Cork, Cork, Ireland

Overall comments

Thank you for the opportunity to review this protocol. I have conducted this review under the supervision of Professor Patricia Kearney, School of Public Health, University College Cork. The protocol describes the study rationale and design of a Study Within A Trial (SWAT). This SWAT will be conducted within a larger trial that aims to evaluate the feasibility and preliminary efficacy of a cognitive occupation-based programme for people with MS (COB-MS). The purpose of the SWAT is to compare a PPI designed Patient Information Sheet (PPIPIS) to a standard, researcher-designed Patient Information Sheet (SRPIS). The outcome measures include trial recruitment and retention along with decision certainty, understanding, readability, accessibility, likeability and decision to consent.

The study addresses a relevant and important research question. Although, PPI is increasingly emphasized as an essential component of health research, evidence on the impact of PPI is piecemeal and inconclusive.

Comments by section:

Abstract

Background: This paragraph provides the reader with a summary of the SWAT instead of providing background on the study context. I suggest rephrasing this paragraph to include the key points from each of your paragraphs in the introduction section of your paper. Then state the study objective. This will clarify what the knowledge gap is and how you aim to address it.

Methods: How will decision certainty, likeability and understanding be analyzed? What are the data collection and analysis procedures?

Discussion: As is, this paragraph does not reflect the same points that you make in the discussion section of the paper. I suggest rephrasing this paragraph to reflect the key points that you put forward in the discussion.

Introduction

In the introduction, the authors draw on a range of literature and the study objective is clear. However, the introduction is quite long. You have included the key information that the reader needs to know but there is some overlap between paragraphs and the knowledge gap you are trying to address could be made more explicit. I suggest you re-phrase the Introduction so that each paragraph outlines the key points that the reader needs to know (e.g. PIS, Why PIS are important, PPI, What we know about PPI (e.g. Cockayne *et al.*¹, Crocker *et al.*²), what we don't know about PPI- knowledge gap, study objective). Some of the references to existing literature could be moved to the discussion.

Other suggestions for the Introduction:

- Paragraph 1: 'primary source of written information'- I suggest inserting the word 'written' here as potential participants often receive verbal information from the study team before they consent to participate.
- Paragraph 1: What do you mean by 'quality' here? Do you mean easy to understand?
- Provide SWAT definition/explanation and explain to the reader why SWATs are important.

Methods

Ethical statement: Word missing from first sentence, suggest adding- 'the study will be conducted at the...'

Trial design: decision to consent is mentioned twice in the first sentence.

Intervention: As it is currently written, you explain the SRPIS first and then describe the PPIPIS. I think this order makes sense but in the rest of the paper (including study objective) you refer to the PPIPIS first and SRPIS second. Please ensure that the order is consistent throughout the paper.

Outcome measures: The six-item questionnaire is not an objective measure of readability, understanding, likeability etc. I understand that this questionnaire cannot be changed as study recruitment has already started but I think you need to justify why you did not choose an objective measure and highlight in your discussion that this is a limitation of the study.

Procedure: Rephrase 5th sentence, it is currently too long and difficult to understand. Also, will the same researcher phone all potential participants? This is important as previous studies have shown that the researchers' manner/approach can influence the persons decision to participate.

PPI: Suggest moving the definition of PPI to the Introduction and keeping this paragraph as an explanation of the PPI activities within this particular study.

Discussion

The discussion should include:

- The strengths and limitations of the study. You don't need to go into too much detail but show that you are aware (i.e. strength-important research question that adds to the evidence base for PPI, limitation- six-item questionnaire is not an objective measure).
- Add some more information on the transferability of findings. You mention that the current SWAT protocol could provide a template for future clinical research in MS. Is the PPI-PIS designed specifically for use with PwMS or is there potential for it to be adapted in studies with other populations?

Dissemination:

The knowledge exchange plan is well thought out. The results of this SWAT will be of interest to members of the research community (especially those interested in PPI), PPI contributors and funding bodies. Well done!

References

1. Madurasinghe VW, Sandra Eldridge on behalf of MRC START Group and Gordon Forbes on behalf of the START Expert Consensus Group: Guidelines for reporting embedded recruitment trials. *Trials*. 2016; **17**: 27 [PubMed Abstract](#) | [Publisher Full Text](#)
2. Crocker JC, Ricci-Cabello I, Parker A, Hirst JA, et al.: Impact of patient and public involvement on enrolment and retention in clinical trials: systematic review and meta-analysis. *BMJ*. 2018; **363**: k4738 [PubMed Abstract](#) | [Publisher Full Text](#)

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?

Yes

Are the datasets clearly presented in a useable and accessible format?

Not applicable

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 18 Mar 2020

Christopher Dwyer, National University of Ireland, Galway, Galway, Ireland

Many thanks for your comments. We considered each in turn and, have amended the manuscript in light of these considerations. Other comments and questions we answer here.

Abstract

Background: This paragraph provides the reader with a summary of the SWAT instead of providing background on the study context. I suggest rephrasing this paragraph to include the key points from each of your paragraphs in the introduction section of your paper. Then state the study objective. This will clarify what the knowledge gap is and how

you aim to address it. Methods: How will decision certainty, likeability and understanding be analyzed? What are the data collection and analysis procedures? Discussion: As is, this paragraph does not reflect the same points that you make in the discussion section of the paper. I suggest rephrasing this paragraph to reflect the key points that you put forward in the discussion.

The Abstract has been amended to more accurately reflect the Background section. Given the length of the response regarding methods in the abstract, we have chosen to leave such discussion until the outcome measures and analysis sections. Finally, the discussion section of the Abstract has been amended to include further implications of the SWAT; and as a result, the Abstract and Discussion are now consistent.

Introduction

In the introduction, the authors draw on a range of literature and the study objective is clear. However, the introduction is quite long. You have included the key information that the reader needs to know but there is some overlap between paragraphs and the knowledge gap you are trying to address could be made more explicit. I suggest you re-phrase the Introduction so that each paragraph outlines the key points that the reader needs to know (e.g. PIS, Why PIS are important, PPI, What we know about PPI (e.g. Cockayne *et al.*¹, Crocker *et al.*²), what we don't know about PPI- knowledge gap, study objective). Some of the references to existing literature could be moved to the discussion.

The introduction has been edited to strengthen clarity and is now shorter.

Other suggestions for the Introduction:

Paragraph 1: 'primary source of written information'- I suggest inserting the word 'written' here as potential participants often receive verbal information from the study team before they consent to participate.

'Written' has been added to 'primary source of information' to enhance clarity.

Paragraph 1: What do you mean by 'quality' here? Do you mean easy to understand?

Yes, by quality, we mean easy to understand; but, we also mean readability and likeability – other factors considered throughout the protocol. However, it would not be appropriate to introduce these concepts yet at this point, from the standpoint of ensuring logical 'flow'.

Provide SWAT definition/explanation and explain to the reader why SWATs are important.

In an effort to keep the introduction as succinct and concise as possible, we chose not to define or elaborate on SWAT – we deemed explanation of the acronym sufficient for the protocol.

Methods

Ethical statement: Word missing from first sentence, suggest adding- 'the study will be conducted at the....'

Amended.

Trial design: decision to consent is mentioned twice in the first sentence.

Amended.

Intervention: As it is currently written, you explain the SRPIS first and then describe the PPIPIS. I think this order makes sense but in the rest of the paper (including study objective) you refer to the PPIPIS first and SRPIS second. Please ensure that the order is consistent throughout the paper.

Amended.

Outcome measures: The six-item questionnaire is not an objective measure of readability, understanding, likeability etc. I understand that this questionnaire cannot be changed as study recruitment has already started but I think you need to justify why you did not choose an objective measure and highlight in your discussion that this is a limitation of the study.

Given that readability, understanding and likeability are different from person to person, self-report was deemed the most appropriate method of assessing these. Though these are subjective from the participants' perspectives (as are all self-report measures) the measure is objective from a data analysis perspective (i.e. through examination of a quantitative measure). With respect to using an *established* measure, the DCS was the only measure known to our research group that addressed our targeted outcomes. The questionnaire was purpose-built to address other outcomes of interest.

Procedure: Rephrase 5th sentence, it is currently too long and difficult to understand. Also, will the same researcher phone all potential participants? This is important as previous studies have shown that the researchers' manner/approach can influence the persons decision to participate.

Amended.

PPI: Suggest moving the definition of PPI to the Introduction and keeping this paragraph as an explanation of the PPI activities within this particular study.

Amended.

Discussion

The discussion should include:

The strengths and limitations of the study. You don't need to go into too much detail but show that you are aware (i.e. strength-important research question that adds to the evidence base for PPI, limitation- six-item questionnaire is not an objective measure).

As this is a protocol, we have deemed this inappropriate for this manuscript - given the prospective, exploratory nature of this non-inferiority SWAT, we are as of yet unaware of its strengths and weaknesses. Upon conducting the study and applying the protocol, strengths and weaknesses will be discussed, alongside study findings.

Add some more information on the transferability of findings. You mention that the current

SWAT protocol could provide a template for future clinical research in MS. Is the PPI-PIS designed specifically for use with PwMS or is there potential for it to be adapted in studies with other populations?

Amended – implications of MS-specific PIS manipulations are now addressed (but not thoroughly elaborated, given the prospective nature of the protocol).

Dissemination:

The knowledge exchange plan is well thought out. The results of this SWAT will be of interest to members of the research community (especially those interested in PPI), PPI contributors and funding bodies. Well done!

Many thanks for your comments!

Competing Interests: No competing interests were disclosed.

Reviewer Report 24 February 2020

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Vivian Welch 

School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Canada

This is a well-written, well-reasoned and clear protocol for a study within a trial to assess whether a patient/public designed participant information sheets is preferred by participants and/or leads to better retention for a clinical trial.

The methods are well-described in sufficient detail for replication. The protocol is available on the open science framework already and anonymized data will be made available according to FAIR principles.

My only comment in writing up the trial is that the rationale for the decisional conflict scale to focus on the SWAT rather than the main trial was not clear until later in the protocol, where the authors state that since eligibility is assessed after the SWAT.

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?

Yes

Are the datasets clearly presented in a useable and accessible format?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Systematic reviews and health equity.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 18 Mar 2020

Christopher Dwyer, National University of Ireland, Galway, Galway, Ireland

Many thanks for your comments.

Competing Interests: No competing interests were disclosed.