STUDY PROTOCOL

Protocol for a factorial randomised controlled trial, embedded within WHiTE 8 COPAL, of an Enhanced Trainee Principal Investigator Package and Additional Digital Nudge to increase recruitment rates [version 1; peer review: 2 approved]

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Abstract

Recruitment remains an issue when conducting randomised controlled trials (RCTs) with a significant proportion of studies failing to reach their target sample size. Studies evaluating interventions to improve recruitment aimed specifically at recruiters to the trial are limited in number. This factorial RCT will evaluate the effectiveness of an educational intervention to trainee principal investigators and a positive reinforcement intervention via an email nudge on increasing recruitment. The targeted recruiters will be in 20 centres nationally recruiting to one large orthopaedic randomised controlled trial, WHiTE 8 COPAL. Centres will be randomised via minimisation to one of four groups. The primary outcome is recruitment rate in the first six months that a centre is actively recruiting, with data being analysed via a Poisson regression model. Results will be presented as adjusted incidence rate ratios with 95% confidence intervals. Secondary outcomes relate to the feasibility and logistics of running the interventions. We will also collect feedback regarding the educational programme set out for the trainee principal investigators. The study started in August 2018 with the anticipation of the primary objective endpoint by October 2019. The results of this study will be used to inform the design of future RCTs, particularly in orthopaedics in the UK, where the role of Trainee Principal Investigators is now a consistent one across different trials.
Trial registration: 11600053, ISRCTN, 20/08/2018; SWAT 67, Northern Ireland Hub for Trials Methodology Research SWAT repository, 01/10/2017.

Keywords

Trainee Principal Investigator, TPi, Nudge, Swat, Recruitment, Education

Open Peer Review

Reviewer Status ✓ ✓

	Invited Reviewers	
	1	**2**
version 1 published 22 Jul 2019	✓ report	✓ report

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

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Introduction

Randomised controlled trials (RCTs) are considered the gold standard when evaluating the efficacy and effectiveness of health care interventions. Unfortunately, a significant number of well-designed RCTs struggle with the recruitment of participants and subsequently fail to reach their target sample size[1].

Several hypothetical and real-life studies on methods to improve participant recruitment to RCTs have been conducted with mixed results, with only a minority targeting recruiters to the trial[2–5]. The results of a survey of clinical trials units in the UK concluded that priorities for evaluation included training site staff, methods of communication with patients and incentivising site staff[6].

The aim of this real-life study is to assess the effects of targeting healthcare professional recruiters with an educational intervention with or without positive reinforcement on participant recruitment. This study within a trial (SWAT) will test two different methods of enhancing recruitment: introducing an enhanced trainee principal investigators (TPI) package, and personalised email nudges (see *Extended data*[7]) to healthcare professionals involved in patient recruitment. The SWAT will be implemented in a large, UK, multicentre orthopaedic RCT, the WHiTE 8 COPAL trial. The interventions have both been used in current orthopaedic trials, but their effects on recruitment have previously not been investigated.

Interventions

This will be a multicentre, 2×2 factorial RCT run between August 2018 and October 2019 with random allocation of the recruiting centre to one of four groups:

Group 1: Enhanced TPI package.

Group 2: Use of a personalised email nudge to each recruiter.

Group 3: Enhanced TPI package and use of a personalised email nudge to each recruiter.

Group 4: Usual practice (neither the enhanced TPI nor personalised email nudge).

Full details of each intervention have been provided as *Extended data*[7] and are summarised in Table 1. The consent to participate as a TPI and interventions will be implemented by the

Table 1. Summary of additional activities in each intervention group.

Activity	Usual practice	Enhanced TPI	Email nudge
Identify TPI for the trial	Through local Principal Investigator	Through local Principal Investigator	
Training of TPI regarding how to perform their role once centre is activated for recruitment	Local Principal Investigator TPI Manual	Local Principal Investigator WHiTE 8 Research Fellow via 1:1 telephone induction TPI manual Induction summary presentation	
Training TPI regarding the WHiTE 8 trial and consenting procedures	Local Principal Investigator	Local Principal Investigator WHiTE 8 Research Fellow via 1:1 telephone induction WHiTE 8 consent flow diagram and protocol provided	
Peer-support of TPI		Monthly contact by WHiTE 8 Research Fellow WHiTE 8 Research Fellow can be contacted by TPI as required by SMS/WhatsApp/Email	
Digital information provided to TPI	TPI Manual	Induction agenda TPI manual and new TPI checklist Induction summary presentation WHiTE 8 consent flow diagram and protocol TPI contact information consent form	
Identifying patients for the trial	Trauma meeting	Trauma meeting	
Confirmation of randomisation	Automated email to recruiting centre		Automated email to recruiting centre Additional personalised email to express gratitude and encourage further recruitment within 72 hours of randomisation

TPI, trainee principal investigator

White 8 Research Fellow (author N.A.). Consent materials are also available as *Extended data*[7].

Sample selection

As in many SWATs, a power calculation was not undertaken as the number of participating sites is fixed and driven by the needs of the host trial. All WHiTE centres planned to be recruiting to the WHiTE 8 trial will be included, except the centre in which N.A. is based. We anticipate a minimum of 20 centres being involved in recruiting. Trial interventions will only be discontinued if the host trial (WHiTE 8 Copal) is discontinued.

Randomisation

The WHiTE centres will be randomised by minimisation on a rolling basis as sites become activated to one of the four groups to balance key baseline characteristics. Self-reported site feasibility questionnaires completed by the recruitment centres will be used to collect the information required for the minimisation. Minimisation will be based on the following factors:

1. Cluster size (number of intracapsular hip fractures presenting in the previous year, cut at the median <300 or ≥300)

2. High vs Low recruiting centres (<9 or ≥9 per month based on previous RCTs run within WHiTE Cohort)

3. Co-recruitment to WHiTE 5 (yes/no) (Another RCT using the same patient population running at a few of the recruitment sites)

This randomisation will be performed using specialist computer software, MinimPy (Saghaei and Saghaei, 2011). This is an open trial and participating sites, the data analyst nor trial team will be blind to allocation.

Outcomes

The primary outcome is the total number of patients recruited in the first 6 months from a site opening to recruitment to the WHiTE 8 COPAL trial.

The secondary outcomes are: conversion rate from screened population collected monthly from the central recruitment database (coordinated by the Oxford Clinical Trials Research Unit); and the time taken to implement each intervention from commencing recruitment in each centre.

The trainee's perspective of their role will be collected through the TPI survey (available as *Extended data*[7] at the end of the SWAT in each centre. The Research Fellow will keep a record of the time taken delivering the TPI education intervention and a log of communication for peer-support during the period of the SWAT to inform future implementation.

Ethical issues

The University of York Health Sciences Ethics Committee has approved this study within a trial. Ethics Approval ID: HSRGC/2018/266/C. Substantive protocol amendments will be sought approval through then university ethics committee.

Trial registration

This SWAT is registered with ISRCTN (11600053) and is embedded in the WHITE 8 Copal trial (ISRCTN 15606075).

This SWAT is also registered to the SWAT repository store as part of the Northern Ireland Hub for Trials Methodology Research (SWAT 67).

Data analysis

Analysis will be conducted in STATA v15 on an intention-to-treat basis, including all sites in the group they were originally allocated to regardless of deviations based on non-compliance. Statistical significance will be assessed using logistic regression two-sided statistical tests at the 5% significance level. The trial will be reported to CONSORT guidelines, and a flow diagram will present the progression of sites through the trial.

Baseline data relating to the sites (including the minimisation factors) will be summarised for the four groups as randomised and as analysed to assess whether possible loss-to-follow-up has introduced selection bias. Continuous data will be presented using descriptive statistics (e.g., mean, standard deviation, median, minimum, maximum), while categorical data will be given as counts and percentages. No formal statistical comparison of baseline data will be undertaken between the four groups.

The number of participants recruited per site will be summarised. A Poisson regression model, containing the two interventions (Enhanced TPI and Email Nudge) and the minimisation factors (cluster size, and number recruited per month will be included in their continuous form) will be undertaken. Adjusted incidence rate ratios (IRRs) and associated 95% confidence intervals (CIs) will be obtained from this model. The presence of an interaction between the two interventions will also be tested by including an interaction term in the model.

Feasibility outcomes, such as the time required to run the education intervention and communication time and methods used for the peer support aspect of the intervention, will be reported descriptively.

A data monitoring committee will not be used as this a trial involving recruiters and patient safety will not be affected by conducting this trial. No formal auditing of trial procedure will take place.

Discussion

If successful, we would like to show that these can be feasibly implemented in future RCTs with additional benefit of reaching targeted sample sizes within the planned recruitment timeline due to increased recruitment rates.

Plans for dissemination

Results of this study will be form part of a PhD thesis, published in a peer-reviewed journal, presented at conferences and be shared with recruiting centres and clinical trials units.

Data availability

Underlying data

No underlying data are associated with this article.

Extended data

Open Science Framework: Protocol for a factorial randomised controlled trial, embedded within WHiTE 8 COPAL, of an Enhanced Trainee Principal Investigator Package and Additional Digital Nudge to increase recruitment rates. https://doi.org/10.17605/OSF.IO/FZ4JH[7].

This project contains the following extended data:

- Extended SWAT Protocol
- Nudge email 1
- NUDGE MATRIX
- TrainingPackage_V1_2017-03-14 (trainee principal investigator manual)
- Consent for contact
- Enhanced TPi Induction Agenda ver1.0apr18
- New TPI Checklist
- SWAT Participation info ver3apr18
- TPI Induction Presentation
- TPi_Follow_up_Survey

Reporting guidelines

Open Science Framework: SPIRIT checklist for article 'Protocol for a factorial randomised controlled trial, embedded within WHiTE 8 COPAL, of an Enhanced Trainee Principal Investigator Package and Additional Digital Nudge to increase recruitment rates'. https://doi.org/10.17605/OSF.IO/FZ4JH[7].

Grant information

The author(s) declared that no grants were involved in supporting this work.

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PubMed Abstract | Publisher Full Text | Free Full Text

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http://www.doi.org/10.17605/OSF.IO/FZ4JH

Open Peer Review

Current Peer Review Status: ✔ ✔

Version 1

Reviewer Report 05 September 2019

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✔ **Kath Star**
Centre for Healthcare Randomised Trials (CHaRT), Health Services Research Unit, University of Aberdeen, Aberdeen, UK
Victoria Bell
The Centre for Healthcare Randomised Trials, University of Aberdeen, Aberdeen, UK

This is an interesting and well designed trial and the outcomes will be of interest to many involved in running clinical trials.

There are a few suggestions/areas for consideration by the authors:

- The manuscript would benefit from the addition of a description of the role of a TPI should be included (as stated in section 1.3.2 of the extended protocol)
- Have the authors considered additional timepoints for follow up? Recruitment fatigue can often affect long-running studies and it would be interesting to determine whether the intervention has longer-lasting effects.
- Feasibility and resource use are an important aspect of the study and should be included in the secondary outcomes.
- Have the authors considered performing a formal cost analysis? It would be interesting to understand the cost/benefit of the intervention.
- There are a number of acronyms referring to the studies hosting or associated with EnTraP – WHiTE, WHiTE 8, WHiTE 8 Copal, WHiTE 5 - that we found confusing and detracted from the description of the study. Section 1.3.1 of the extended protocol explains the relationship between these studies well, and it would be useful to include this for the reader to understand the context of the host trial.
- In the extended protocol the study is referred to as EnTraP and it would be beneficial to include this in the article to refer to e.g. 'the *EnTraP* Research Fellow'.

- Will education and experience of the sites staff be mentioned or evaluated when analysing the results as this can impact on recruitment.

The extended protocol submitted as extended data still has some comments and tracked changes the authors may want to remove before indexing.

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?
Partly

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

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Trial management and design

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.

Reviewer Report 03 September 2019

https://doi.org/10.5256/f1000research.21652.r52423

Mike J. Clarke
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Struggling or failing to achieve their target recruitment, and therefore, failing to have adequate statistical and clinical power, is a problems for many clinical trials. It contributes to research waste and slows down our ability to resolve important uncertainties in health and social care.

This is a well reported protocol for a SWAT (Study Within A Trial) that will be embedded in the WHiTE 8 COPAL randomised trial. The SWAT will investigate ways to increase recruitment in the clinical trial. I think it should be indexed and I wish the authors well with the conduct and analysis of the SWAT. It might be helpful to add a reference to a more general article about SWAT to help readers who would like to find out more (e.g. Education section – Studies Within A Trial (SWAT). (2012)[1]; or Smith V, Clarke M, Devane D, *et al*. (2013)[2]; or Treweek S, Bevan S, Bower P, *et al*. (2018)[3]).

The methodology study has been registered as SWAT 67 (go.qub.ac.uk/SWAT-SWAR) and is also registered as ISRCTN11600053. It will be a factorial, cluster randomised trial in which recruiters at each of

the 20 sites for WHiTE 8 COPAL will be allocated to one of four groups. The two interventions in the factorial design are the introduction of an enhanced trainee principal investigators' (TPI) package and personalised email nudges, which are sufficiently different to meet the criteria for the good use of a factorial trial design. There is an adequate summary of the interventions in the body of the article. The use of minimisation to allocate the centres to one of the four groups is an appropriate strategy to help achieve balance, especially with such a relatively small number of units being randomised. Apart from my concern below, the minimisation variables seem reasonable. However, might variables 1 (cluster size) and variable 2 (monthly recruitment in previous randomised trials in WHiTE COPAL) be so closely correlated that they will serve as a single variable only? For instance, my presumption would be that the smaller centres (i.e. <300 cases) would have the lower recruitment (i.e. <9/month), and the larger centres would have the higher recruitment.

My concern is with the primary outcome, which is the number of patients recruited in the first six months after a centre opens. My concern is that there might be such wide variation in these numbers that, with perhaps five centres in each of the four allocation groups (or ten in each of the groups testing each of the two interventions) that underlying differences between the centres might dominate the final results. I realise that cluster size will be used in the minimisation and in the analysis but this seems to be dichotomous around a median of 300 cases in the previous year which, depending on the distribution of the cluster sizes, might be too simplistic a split. For example, if there are three sites with less than 50 cases in the previous year, or three with more than 500 cases, these might highly skew the data if, by chance, all three at the low or at the high end are randomly allocated to one of the interventions. It would be reassuring to know that the centres are not so heterogeneous or, if they are, that a finer level of adjustment than below and above 300 will be used in the analysis.

In summary, this is an important study. It will provide evidence relevant to other orthopedic trials, that may help future researchers to boost recruitment (if one or both interventions are effective) or to re-direct SWAT to other areas if they are not. Its relevance is also likely to extend beyond clinical trials in this setting, by contributing to the overall evidence base on interventions to boost recruitment, which have been shown to be so lacking in the Cochrane Methodology Review (reference 2 in this manuscript).

References

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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: I am one of the people responsible for the SWAT initiative and my departments hosts the SWAT repository.

Reviewer Expertise: Clinical trials; systematic reviews; research methodology.

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.