

The effect of sending advanced notification to trial participants two weeks before outcome data collection to improve retention: an embedded randomised controlled trial in the WORKWELL trial

Applicants

Lead applicant name, title and institution

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Co-applicant names, titles and institutions

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Host trial and SWAT registrations

The host trial (A randomised controlled trial of job retention vocational rehabilitation for employed people with inflammatory arthritis: the WORKWELL trial, funded by Arthritis UK) will be registered on the ISRCTN. This SWAT has been submitted to the MRC Northern Ireland Network for Trials Methodology Network [[reference number to be confirmed](#)].

Background: the pre-notification letter intervention

Many trials struggle with participant retention and completion of follow-up questionnaires. A recent UK study found that the median (IQR) retention rate across 151 trials was 89% (79%-97%) (Walters, et al., 2017). Reminders are generally an effective way of increasing response rates to questionnaires, with some evidence that pre-notification (contacting a participant to say that the trial team will be sending a questionnaire out soon) also provides some benefit, although it is not high certainty evidence (Edwards, et al., 2002). Therefore, there is no clear evidence as yet that pre-notification is effective for trial retention (Brueton, et al., 2014), nor whether any particular method (telephone, text, postcard, letter) of pre-notification confers any benefits over any other, although researchers have reported a lower odds of response following a postcard reminder than following a postal reminder to a survey (Sahlqvist, et al., 2011), albeit after rather than preceding the original questionnaire mailing.

There is also research on the content of contacts with participants, much of which relates to cover letters and post-reminders, although some relates to pre-reminders. Recent research on the content of cover letters has been performed by Duncan and colleagues (Duncan, Bonetti, Clarkson, & Ramsay, 2015) who developed a theory-based response letter intervention using Michie's Theoretical Domains Framework (TDF) (Michie, et al., 2005) and associated Behaviour Change Techniques (BCTs) (Michie, Johnston, Francis, Hardeman, & Eccles, 2008) (Abraham & Michie, 2008). Evidence on the effectiveness of this approach is still inconclusive (and also included as a SWAT idea within the PROMETHESUS project [SWAT24]).

It is therefore important to develop interventions, based on the evidence available, to investigate whether pre-notification improves questionnaire return rates in trials. Such pre-notifications should be developed using best current evidence in terms of mode of delivery and content, whilst practical considerations should, as ever, also be taken into account in the design and delivery.

Study area

Retention

Background: The WORKWELL host trial

NHS “usual care” for work problems for most people with inflammatory arthritis (i.e. rheumatoid arthritis (RA), undifferentiated inflammatory arthritis (UIA) or psoriatic arthritis (PsA) is limited. Referral to occupational therapy for vocational rehabilitation (VR) is often patchy or non-existent. WORKWELL is a pragmatic, multi-centre individually randomised controlled trial of job retention VR for employed people with inflammatory arthritis. The trial also involves cost-effectiveness and process evaluations.

Participants will be employed people with inflammatory arthritis who have concerns about continuing to work in future because of their arthritis. Participants (n=240) will be recruited from at least 18 Rheumatology out-patient and therapy departments in the United Kingdom (including sites in England, Wales, Scotland and Northern Ireland). Participants will be assigned to two groups (Control intervention group; WORKWELL intervention group) in equal numbers.

The Control intervention group will receive written self-help work information plus usual care. The WORKWELL intervention group will receive job retention VR plus the Control intervention. The WORKWELL intervention will be provided in each participating site by NHS occupational therapists or physiotherapists. Follow-up will be at 6 and 12 months post-intervention. At baseline, participants will be given the option of receiving a hard copy of the questionnaire by post and completed and returning this by post, or receiving an email with a link to an online questionnaire which they can complete and return electronically.

The primary outcome is presenteeism at 12 months, measured using the Work Limitations Questionnaire-25 (WLQ-25) (Lerner, et al., 2001). Secondary outcomes include: work measures, e.g. work activities limitations, perceived risk of job loss, absenteeism, job loss; contextual factors which may affect work status; health measures including health status (e.g. physical, mental, pain, fatigue, quality of life); and economic costs including health resource use.

Objective of this SWAT

To evaluate the effectiveness of a pre-notification letter or email for prompting completion and return of questionnaires at the 6 month follow up in the WORKWELL trial.

Methods

SWAT intervention

The SWAT intervention is a pre-notification communication sent two weeks before participants are due to be sent their 6 month follow-up questionnaire. Participants who elect to complete follow-up questionnaires online will be sent a personalised pre-notification in an email and those who elect to complete follow-up questionnaires in hard copy form and return by post will be sent a personalised pre-notification letter. Similar wording and layout will be used in the email and letter. The rationale for using a letter rather than a postcard is to use as consistent a form of pre-notification as possible

between those who have opted to complete postal and those who have opted to complete electronically, whilst maintaining the patient choice of mode of communication.

The text contained in the pre-notification has been informed by the theory and associated text used in the IQuad trial SWAT (SWAT 24) (Duncan, Bonetti, Clarkson, & Ramsay, 2015)].

Appendix 1 includes the reminder letter which will be replicated (in text-only format) in an email. The reminder letter (or email) will be personalised to include the (typed) name of the participant as there is some evidence that personalising may improve response rates in surveys (e.g. (McColl, et al., 2001)) (although this [SWAT 35] is one of the other interventions planned to be evaluated in the context of RCTs within the overall PROMETHEUS project).

Comparator

No pre-notification letter.

Outcome measures

Primary Outcome: Valid response for WORKWELL trial primary outcome (yes/no)

A valid response means usable outcome data for the primary outcome measure (WLQ-25 total score) obtained by any means, no more than 8 weeks (56 days) after the scheduled 6-month follow-up time-point.

Secondary outcomes:

1. Valid response for WORKWELL trial primary outcome (yes/no) without reminder (yes/no)
2. Number of reminders sent
3. Time to response [or ceasing follow-up] (days)
4. Costs per participant retained

SWAT recruitment and randomisation

All participants of the WORKWELL trial randomised to the WORKWELL or Control intervention except those who:

- have withdrawn from follow-up;
- are known to have died;

by the time-point 2-weeks prior to the planned mailing of the 6-month questionnaire (which will be at approximately 7 days prior to their 6-month time-point, according to CTU scheduling).

The SWAT randomisation will allocate eligible participants to either the SWAT intervention or Comparator in a 1:1 ratio and will be stratified by trial intervention arm (WORKWELL intervention or Control intervention) and chosen mode of response (electronic/postal), using block sizes of random length. A statistician not directly involved in the analysis (e.g. the SWAT CI) will create (and retain securely) the allocation list, and set up the randomisation system SealedEnvelope.com (or an alternative secure randomisation system delivered remotely by electronic means) in conjunction with Denise Forshaw (or a member of the Lancashire CTU Trial Team other than the Data Co-ordinator and Clerical Assistant managing the recruitment and delivery of the SWAT intervention)..

Allocation will be concealed from the Data Co-ordinator who, at the time-point 2 weeks prior to the scheduled mailing of the 6-month follow-up, will check participant eligibility (i.e. there is no record that WORKWELL trial participant has withdrawn from follow-up or died) and, having confirmed this, apply for the allocation from the randomisation system.

Sample size calculation

As is common with SWATs, we are limited to the host trial sample size and the proportion of this sample that are eligible for 6-month follow-up (i.e. have not withdrawn or known to have died). The WORKWELL trial recruitment target is 240 participants, and we expect a low rate of withdrawal or death (participants will need to be in work at the time of recruitment) of no more than 5% at 6-month follow-up, providing an approximate sample size of 228 for this SWAT.

A sample of 228 randomised in equal numbers to the two arms of this SWAT would provide 85% power to detect a 15% (or greater) differences in the percentage of valid response for the WORKWELL trial's primary outcome (assuming that the percentage of valid responses in the Control condition will be 75%). It is, however, expected that the effect on retention will be considerably less than 15%, hence the rationale for PROMETHEUS and the inclusion of the data from this SWAT in a meta-analysis of SWATs evaluating such pre-notification card/letter interventions, with the aim of achieving high power to detect realistic effects of such an intervention. For example, the PROMETHEUS overall target of 35000 participants in a meta-analysis of a particular intervention would provide approximately 90% power to detect a 2% increase in an already high 'retention percentage' (96% to 98%, OR=2.04) in line with the PROMETHEUS application form) or similar power to detect a 5% increase in a relatively low 'retention percentage' (from 75% to 80%) which is a more realistic effect (OR=1.33) than the 15% (OR=3.0) for which this individual SWAT is well-powered [2].

Analysis Plan

Baseline participant data, and the primary and secondary outcome measures will be summarised, using Frequency (%), Mean (SD) or Median (IQR), as appropriate) both overall and by SWAT group allocation

For the analysis of the effect of the intervention, all randomised participants will be included in the analysis.

Comparison of the primary outcome (valid response for WORKWELL trial primary outcome) between the pre-notification letter group and the no pre-notification group will use binary logistic regression, including the randomised group factor and adjusting for stratification variables (WORKWELL trial treatment allocation; chosen mode of response). Odds ratios and 95% confidence intervals for the between-groups difference in proportions completing the questionnaire will be estimated, and presented in conjunction with descriptive statistics of the number and percentage of respondents in each group. Analysis of the corresponding secondary outcome (valid response for WORKWELL trial primary outcome without reminder) will be performed using the same method.

Time to response will be compared between the groups using Cox regression, adjusted for WORKWELL treatment allocation and chosen mode of response. Data will be presented as a hazard ratio and related 95% confidence interval (CI); median time to response in each group will also be presented.

For the analysis of the difference in costs per participant retained (i.e. with a valid response for WORKWELL trial primary outcome) between those randomised to be sent the pre-notification and those randomised to not be sent the pre-notification, costs will include the direct costs of printing the pre-notification letter, envelopes and postage, and the cost of staff time spent administering the mail out (for example filling and labelling envelopes for those who choose to receive questionnaires by post, sending emails to those who choose to receive questionnaires electronically). We will present a crude analysis of the ratio of the estimated between-groups difference in costs, divided by the corresponding difference in proportions providing valid responses for WORKWELL trial primary outcome.

All analyses will be performed in Stata (V14 or later); tests will be two-sided and use a 5% significance level.

A meta-analytic framework will be undertaken by the PROMETHEUS team to explore variability across host trials. Proportions of participants responding in each trial of a pre-notification card/letter/text intervention will be entered into a meta-analysis, and the heterogeneity of the intervention effect across trials will be assessed using the I^2 statistic. If substantial heterogeneity is demonstrated (I^2 of 50% or greater), we will explore differences between trials that might explain that variation. The power of any such analyses may be limited if there are small number of trials, but in such an instance we will explore this issue qualitatively using data collected on the trial, the patient population, and the trial context.

Project timetable

Date	Action
31st August 2018	Peer review of WORKWELL SWAT protocol
17th September 2018	Documentation for the SWAT agreed & signed off
17th September 2018	Submission to REC of application
1st May 2019	Set-up of SWAT project, randomisation system etc.
1st July 2019	Recruitment to the SWAT begins
1st March 2021	Recruitment to the SWAT ends
31st May 2021	Data cleaning and submission of data set to PROMETHEUS team
31st May 2021	Collation of results and analysis, begin write up of trial level paper

Level of funding required

We estimate the proposed SWAT will cost £4761 (100% of directly incurred costs only). This comprises staff costs to randomise and to collect and manage the SWAT data (Data Co-ordinator, UCLan), send out the pre-notification card/letter/email (Clerical Assistant, UCLan) and analyse the data (Research Associate, Manchester) and consumables costs (randomisation system fees – SealedEnvelope, up to 250 randomisations using stratified randomisation; attendance at conference, most likely MRC Trials Methodology Conference in 2021, to present results).

UoM		Cost (£)
Research Associate (Statistics)	Grade 6, 5 days	1,101
Conference fees & travel		750
TOTAL Manchester		1,851
UCLan		
Clerical Assistant (Clinical Trials)	60 hours	960
Data Co-ordinator	60 hours	1,140
Randomisation Fees		810
TOTAL UCLan		2,910
TOTAL		4,761

Expertise of team

Chris Sutton is an experienced trials statistician with an interest in embedded trials to improve retention. He is the Manchester CTU lead on PROMETHEUS and has prior experience of an embedded feasibility trial of methods of requesting participant information from General Practices.

Sarah Cotterill has expertise in intervention trials that draw on behaviour science, and she has recently led an embedded trial to improve retention in a cohort study.

Denise Forshaw is an experienced Trials Manager, co-ordinating the Trial Management and Data Management Team in Lancashire CTU at UCLan, and has recently led an embedded feasibility trial of methods of requesting participant information from General Practices.

Sarah Rhodes is a statistician (Research Associate) with experience in embedded trials, including the embedded trial to improve retention in a cohort study led by Sarah Cotterill.

Alison Hammond is a Professor in Rheumatology Rehabilitation with an interest in trials methodology, and is the Chief Investigator for the WORKWELL Trial.

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Appendix 1:WORKWELL pre-notification letter

WORKWELL 6m Questionnaire pre-reminder letter v1 16 .7.18 IRAS ID

	<p>WORKWELL Trial Data Co-ordinator Lancashire Clinical Trials Unit Brook Building, Room BB418 University of Central Lancashire Preston PR1 2HE</p>
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Date:

Dear [Insert participant name]

Re: WORKWELL: Testing work advice for people with arthritis.

We are really grateful to you for taking part in the WORKWELL Trial which is comparing two different forms of work advice to see which better helps people with arthritis reduce their work problems or stay in work. A year is a long time to commit to a research study such as WORKWELL and we hope that providing the monthly sickness absence information and completing the questionnaires is not proving too much for you. No matter how much you use the work advice information or whether your work problems have improved or not, your contribution remains valuable and we will learn a lot from the data you provide.

This is just a reminder that we will be sending you the second questionnaire in the study in a fortnight's time. This will take you about 15 – 30 minutes to complete. If you indicated that you preferred to complete the questionnaire online, the link to the online questionnaire will be sent to you by email.

We would be grateful, when you receive the questionnaire or link to the online, if you would complete the questionnaire and return it within **two weeks**. If you require any further help or information about the study, or have decided you no longer wish to continue taking part, please phone the WORKWELL Trial Office by on 0161 295 XXXX or 0161 295 2120, or by email to XXXXX@salford.ac.uk or m.lowe2@salford.ac.uk.

Once again, thank you for continuing to take part. Your help is very much appreciated.

Best wishes

[Insert Alison's e-signature here]
Professor Alison Hammond
Professor in Rheumatology Rehabilitation
Health Sciences Research Centre
University of Salford

[Insert Rachel's e-signature here]
Dr. Rachel O'Brien
WORKWELL Trial Manager
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