ORIGINAL ARTICLE

Three behavior change theory−informed randomized studies within a trial to improve response rates to trial postal questionnaires

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Abstract

Objectives: Our aim was to design and evaluate a novel behavior change approach to increase response rates to an annual postal questionnaire in three randomized studies within a trial (SWAT) and replicate the most promising SWAT.

Study Design and Setting: SWAT1 tested a trial logo sticker on questionnaire envelopes vs. no sticker; SWAT2 tested a theoretically informed letter sent with the questionnaire vs. a standard letter; SWAT3 tested a theoretically informed newsletter sent before the questionnaire vs. no newsletter. The SWATs were conducted within a large dental trial ($N = 1,877$ adults), and SWAT2 replicated in a different trial in a similar setting ($N = 2,372$).

Results: SWAT1 improved response rates by 1.4%, 95% confidence interval (CI) (-7.2%, 10.0%). SWAT2 improved response rates by 7.0%, 95% CI (1.7%, 12.3%). SWAT3 improved response rates by 0.8%, 95% CI (-5.1%, 6.7%). Replication of SWAT2 as the most promising SWAT showed improvement in response rates of 1.0%, 95% CI (-3.2%, 5.3%). Pooled results from SWAT2 showed an overall improvement in response rates of 3.4%, 95% CI (0.1%, 6.7%).

Conclusion: A theory-based behavioral approach to design interventions to improve trial response rates showed small but meaningful improvements. The approach presented here can be easily implemented and adapted to address other identified barriers to trial retention. © 2020 Elsevier Inc. All rights reserved.

Keywords: Attrition; Retention; Randomized controlled trials; Study within a trial; Behavioural intervention; Theoretical Domains Framework; Dentistry

1. Introduction

Randomized controlled trials (RCTs) are considered the gold standard in the evaluation of clinical effectiveness, but poor retention rates can have an impact on the robustness of the evidence found. Missing data in RCTs are a common problem that leads to reduced statistical power and can introduce bias if the participants providing data differ from those that do not respond. Methods to minimize attrition in trials have been identified by Clinical Trial Units' directors as one of the top priorities in trial methodology [1], although research in this field has been scarce compared with other areas of trial methodology like recruitment [2].

Different strategies have been used to improve the return of a questionnaire (such as provide financial incentives, increase the number and nature of reminders, and/or revise the content covering letter), but the current evidence supporting each strategy is weak [2,3]. There is no coherent evidence base to suggest how to implement specific strategies or to determine which of these strategies is more likely to be successful.

One way forward is to view the completion and return of a study questionnaire as a behavior, the target behavior being the patient returning the questionnaire. Developing behavior change interventions based on theory is strongly recommended by the Medical Research Council guidelines for developing complex interventions [4] because without clear and explicit theory to describe and understand mechanisms related to behavior, any interventions would not be generalizable. The theoretical domains framework (TDF) is

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What is new?

Key findings

- We tested three theory-informed interventions, as studies within a trial (SWAT) with the aim of improving response rates to an annual postal questionnaire. All three interventions (SWAT 1, 2, and 3) improved questionnaire response rates compared with the control groups; only SWAT 2, comparing a theoretically informed cover letter with a standard cover letter, showed a statistically significant improvement.

- We replicated SWAT 2 in a different trial with a similar population. Meta-analysis, including both SWAT 2 studies, found evidence of a small but significant benefit of using the theoretically informed cover letter.

What this adds to what was known?

- The evidence base on what works to improve retention in clinical trials is incoherent and lacks good evidence to demonstrate which strategies are likely to be more successful. We used a novel behavior change approach to develop interventions based on theory. This approach identified potential barriers to return of a postal questionnaire which could be mapped onto a behavioral change technique taxonomy.

- A theoretically informed cover letter improved response rates significantly.

- Replication of the cover letter intervention in a different trial increased strength of evidence.

What is the implication and what should change now?

- Using behavior change techniques in the written communication between trial offices and trial participants to address potential barriers to return of a postal questionnaire is a robust and replicable method to improve trial retention that can be easily adapted to different settings, it is inexpensive and easy to implement.

- Trialists aiming to improve trial retention can use this theory-informed, structured approach to design their interventions.

- The cover letter intervention can be replicated in other trials.

a tool for identifying the theoretical factors that might help or hinder behaviors [5]. The TDF collates similar constructs drawn from different psychological models into 14 theoretical domains (e.g., beliefs about consequences; knowledge). The approach has evolved to include systematic methodologies for identifying what specific behavior change techniques (BCTs) will overcome barriers [6].

Improving the Quality of Dentistry (IQuaD) is a trial based in the United Kingdom that used annual postal participant questionnaires to collect patient-reported outcomes over 3 years. The first-year questionnaire had poor response rates. To address this, a novel behavior change approach was designed and evaluated in three randomized studies within a trial (SWATs) [7] with the aim to increase response rates to the postal questionnaires issued in IQuaD. We also aimed to test the most promising intervention in a second trial, INTERVAL [8], and pool results from both studies.

2. Material and methods

2.1. Setting

The IQuaD trial used a split-plot design [9,10] and recruited 1,877 participants from 63 dental practices across Scotland and the North East of England from February 2012 until July 2013. IQuaD is described using the PICO framework as follows:

Population—Adults with good oral health who are regular attendees to the United Kingdom's National Health System primary care dental services.

Interventions and comparisons—Providing no scale and polish or 12-month was compared with the standard 6-month scale and polish. Personalized (intervention) vs. standard oral hygiene advice (comparison) was also compared.

Outcome—IQuaD's primary clinical outcome was bleeding on probing (collected through clinical examination). Patient-reported outcomes for the trial, including the primary patient-reported outcome, a 7-point self-efficacy scale, were collected from participants via an annual postal questionnaire during a 3-year follow-up from randomization.

The questionnaires were issued centrally by the trial office based in the Centre for Healthcare Randomised Trials, at the University of Aberdeen. Questionnaires were issued with a cover letter using a semiautomated process; if not returned within 3 weeks of issue of the first questionnaire, a reminder letter and second questionnaire were sent.

Replication was performed in the INTERVAL study [11], an individual randomized, parallel arm trial that randomized 2,372 participants from 50 dental practices in Scotland, England, and Northern Ireland from July 2010 until July 2014. Following the PICO framework:

Population—Adults with good oral health who are regular attendees to the United Kingdom's National Health System primary care dental services.

Interventions and comparison—24-month or risk-based recalls (interventions) were compared with 6-month recall (comparison).

Outcome—The primary clinical outcome was bleeding on probing (collected through clinical examination). Patient-reported outcomes for the trial, including the primary patient-reported outcome, an oral health–related quality of life scale (OHIP [12]), were collected from participants via an annual postal questionnaire during a 4-year follow-up from randomization.

The questionnaires were issued central by the trial office at the University of Dundee. The same reminder system used in IQuaD was adopted in INTERVAL.

2.2. Participants

IQuaD participants were on average 48 (Standard Deviation (SD) = 16) years old, 65% were female, they were regular attenders to the dentist, and had overall a good oral health [9].

INTERVAL participants were also regular attenders to the dentists and with overall good oral health. They were on average 48 (SD = 15) years old, 60% were female.

The three SWATs theory-informed development strategy is described as follows.

2.3. Intervention development

- Stage 1: Interview of trial staff to assess their perceptions of potential barriers for questionnaire response.
- Stage 2: Identification of potential modes of action using the TDF. Those were mapped onto BCTs that are known to (or likely to) change theoretical constructs within these domains [6]. The BCTs also had to be feasible to operationalize in a letter or other printed format.
- Stage 3. Development of three interventions deliverable by mail to trial participants (by creating text or using prompts) that translate the domain targets and techniques.
- Stage 4. Validating the written content (backward translation exercise). Supplemental tables 1-3 list the potential mode of action and BCTs used in each intervention and their operationalization.

2.4. The studies within trials

2.4.1. SWAT1: the sticker trial

Participants due to be issued the annual follow-up questionnaire at year 1 (March 2013 – August 2013) were randomized using simple randomization via an automated, central randomization service in a 1:1 participant randomized 2-arm parallel trial to receive the questionnaire either in a A4 brown opaque envelope with the IQuaD trial logo sticker added to the top left corner (intervention group) or envelope with no sticker (control group). To implement the randomization, a random list was computer-generated by an independent statistician. The sticker with the IQuaD logo provided official credentials as well as a prompt to

remind participants of the trial. SWAT1 aimed to test if the addition of the sticker could prompt opening of the envelope and subsequently return the questionnaire. The intervention's image is presented in Appendix 1.

2.4.2. SWAT2: the theory-informed letter trial

Participants receiving year 1 or year 2 follow-up questionnaires (December 2013-August 2014) were randomized via an automated, central randomization service in a 1:1 participant randomized 2-arm parallel trial to receive either the standard cover letter (control group) or theoretically informed letter incorporating BCTs in the text of the letter (intervention group). A centralized computerized system automatically randomized letters/newsletters using simple randomization. By including selected BCTs in the theoretically informed cover letter, the aim was to encourage questionnaire return. SWAT2 was replicated in the INTERVAL trial, and it is freely available in the SWAT repository.

2.4.3. SWAT3: the theory-informed newsletter trial

A newsletter was developed to incorporate some of the BCTs used in the theoretically informed letter in SWAT2 (available in Appendix 2). Participants due to receive a newsletter informing them about the progress of the trial at year 2 follow-up (January 2015 – July 2015) were randomized via an automated, central randomization service in a 1:1 participant randomized 2-arm parallel trial to receive the newsletter either 2 weeks before first issue of their postal questionnaire (intervention group) or not receive a newsletter (control). Owing to ethical constraints, all participants were required to receive a newsletter, so participants randomized to the control group received the newsletter after the SWAT intervention, either with a reminder (if they had not replied to the first questionnaire sent) or after return of their questionnaire to the trial office. Owing to the enforced design of this SWAT, as well as testing whether the BCTs incorporated in a different format to the cover letter (i.e., a newsletter) encouraged return of questionnaires, we were able to test a second research question: does the timing of delivery of a newsletter affect response rates? The intervention group received the newsletter before the first questionnaires and the control group received it with the second (reminder) or after return of the first questionnaire.

2.5. Outcome

We measured the response rate as returning a questionnaire within the reminder period, that is, at least 6 weeks after the questionnaires were sent. For SWAT3, the response rate was measured at 3 weeks—after that, participants in the control group who had failed to reply to the first questionnaire received a newsletter.

2.6. Sample size

Samples sizes were calculated based on the number of available participants at the time of conducting each SWAT. For SWAT1, a total of 500 participants (250 participants per arm) would allow us to detect an 11% difference in response rates between arms, assuming 65% response rate at baseline and an α of 0.05. For SWAT2, 1,100 participants would be sent annual questionnaires from 1st Jan 2014 to end July 2014. A sample of 550 per group would allow a difference of 8% (65% to 73%) to be detected with 80% statistical power at the two-sided 5% significance level. For SWAT3, 1,091 participants would have questionnaires sent from 1st Jan 2015 to end July 2015. A sample of 545 per group would allow a difference of 8.2% (60% to 68%) to be detected with 80% statistical power at the two-sided 5% significance level. We assumed a lower baseline response rate of 60% for SWAT 3 because as of November 2014, 60% were returning their year 2 questionnaires.

The sample size calculation for the replication of SWAT2 in INTERVAL was the same as the one used for the original SWAT2 in IQuaD.

2.7. Statistical analysis

Results were analyzed using an intention-to-treat framework and comparing the overall response rate in intervention and control arms for each SWAT separately. We used a two-sample test of proportions for large samples to calculate the difference of proportions confidence interval (CI) [13]. We implemented this in Stata 15 using the command *prtest*.

To obtain pooled results of SWAT2 interventions from IQuaD and INTERVAL, we have followed the Cochrane Collaboration guidance on meta-analysis which states that "Meta-analysis is the statistical combination of results from two or more separate studies." [14]. Therefore, a fixed-effect meta-analysis was calculated using the Mantel-Haenszel method. Analyses were carried out in Stata 15 [15].

2.8. Ethical approval

The East of Scotland Research Ethics Committee approved SWAT2 on the 16th of December 2013 and its replication on the 21st of August 2015. SWAT3 was approved by the same committee on the 22nd of December 2014. SWAT1 did not require any ethical approval.

3. Results

3.1. Studies within trial results

3.1.1. SWAT1: the sticker trial

Supplemental Figure 1 summarizes the flow of participants in SWAT1. In SWAT1, 258 participants were randomized to the sticker arm and 259 to the no sticker. The addition of the IQuaD trial logo sticker did not significantly improve the response rate [51.9% vs. 50.5%, difference +1.4%, 95% CI (−7.2% to +10.0%)] (Table 1).

3.1.2. SWAT 2: the theory-informed letter trial

Supplemental Figure 2 summarizes the flow of participants in SWAT2. In SWAT2, 596 participants were randomized to the intervention letter and 596 to the standard letter. The overall response rate in IQuaD for the intervention group was 72% and for the control group 65%. There was a +7.0% 95% CI (+1.7% to +12.3%) difference in the response rate between groups favoring the intervention (Table 1).

3.1.3. SWAT3: the theory-informed newsletter trial

Supplemental Figure 3 summarizes the flow of participants in SWAT3. 558 participants were randomized to the intervention group and 532 to the control group. The response rate at 3 weeks was 49% vs. 48% with no significant increase [difference +0.8%, 95% CI (−5.1% to +6.7%)].

The prenotification newsletter did not significantly increase the overall response rate at 6 weeks [66.7% vs. 69.4%, difference −2.7%, 95% CI (−8.2% to +2.8%), *P*-value = 0.34], compared with sending the newsletter with reminder questionnaires.

3.2. Replication of SWAT2 and meta-analysis

For SWAT2 replication, there were 957 INTERVAL participants randomized to the intervention letter and 910 to the standard letter. The response rate in INTERVAL was 67% for the intervention letter group and 66% in the standard letter group. There was a +1% difference (95% CI

Table 1. Randomized studies within trial results by randomized arm

Study within a trial	Response rate intervention group % (n/N)	Response rate control group % (n/N)	Proportion difference between response rates (95% confidence interval) (%), *P*-value
SWAT1 (sticker vs. no sticker)	51.9% (134/258)	50.5% (131/259)	1.4% (−7.2% to 10.0%), 0.75
SWAT2 (intervention letter vs. usual letter)	71.8% (428/596)	64.8% (386/596)	7.0% (1.8% to 12.3%), 0.009
SWAT3 (newsletter vs. no newsletter)	49.1% (274/558)	48.3% (257/532)	0.8% (−5.1% to 6.7%), 0.79

−3.2% to +5.3%, *P*-value = 0.65) between groups favoring the intervention.

Meta-analysis of the results of INTERVAL and IQuaD found a risk difference of +3.4% in favor of the intervention letter (95% CI (+0.1% to +6.7%), *P*-value = 0.044) (Figure 1), showing a small but statistically significant benefit from the intervention letter when compared with the standard letter.

4. Discussion

We conducted three theory-informed randomized SWAT using a novel behavior change approach to determine the effect on response rates to an annual postal questionnaire. All three interventions improved questionnaire response rates compared with the control groups. Only SWAT2, comparing a theoretically informed cover letter with a standard cover letter issued with the questionnaire, showed a statistically significant improvement. SWAT2 was replicated in a different RCT recruiting participants in a similar setting. Our meta-analysis, including both studies, found evidence of a small but statistically significant benefit of using the theoretically informed cover letter.

To our knowledge, this is the first time a theory-informed intervention using a validated behavioral framework to improve retention has been tested across multiple randomized controlled SWAT. This methodology provides trialists with a framework that is easily adaptable to address different barriers to trial retention. Our structured approach to intervention development aligns with the Medical Research Council guidelines [4] for developing complex interventions; we interviewed IQuaD trial team members to investigate potential barriers and facilitators to retention and planned our interventions to address those, embedding BCTs in each intervention. Our results suggest the BCTs used addressed some of the barriers to return of questionnaires.
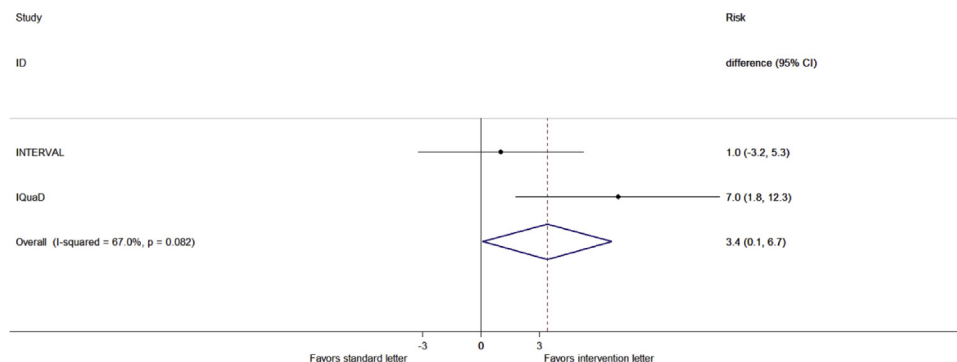
Barriers to return questionnaires may vary throughout a trial's lifetime. The newsletters (SWAT3) were sent at a different follow-up time point (second year of follow-up)

than the theoretically informed cover letter (SWAT2) (mostly first year of follow-up, with a smaller number issued in year 2). We observed a difference in response to the intervention cover letter in SWAT2 between year 1 and year 2 questionnaires (not published, information available on request). Further research should investigate the best timing to optimize behavior change interventions in improving trial retention.

Sample sizes in individual SWATs might not be large enough to detect small but meaningful improvements in response rates. Replication is a key element in conducting SWATs and we recommend that other researchers implement these interventions and report their results so these can be included in meta-analyses. To facilitate that process, SWAT 2 has been registered on the SWAT repository (SWAT 24; https://w3.abdn.ac.uk/hsru/iquad/Public/DownloadPage.aspx). SWATs 1 and 3 are available as Appendices in the present article. Researchers replicating these interventions are encouraged to use their data to start or update meta-analyses. Any improvement in the response rate to follow up postal questionnaires can be worthwhile, particularly if the changes leading to the improvement are inexpensive.

It is challenging to quantify costs and resources used in the context of running an SWAT. Although the SWATs presented here were reasonably quick and inexpensive to implement, we have not presented costs of implementation (e.g., cost opportunities of trial manager time preparing amendments for ethics approval, programmer time to set up randomization of participants) and cost-effectiveness. We recognize that these are important factors when making decisions in a trial, and this is a common limitation in SWATs across different areas [16].

Appropriate planning to prevent retention problems (instead of reacting to them) and stop/go criteria, like those considered in pilot studies, could help trialists conducting SWATs. Decisions about what interventions to select, how to take them forward, when to look at the data, and whether to stop earlier in case of potential harm must happen quickly during a busy, real-life trial. Here, SWAT3 presents an example of a challenge in which decisions had to be

Study ID		Risk difference (95% CI)
INTERVAL		1.0 (-3.2, 5.3)
IQuaD		7.0 (1.8, 12.3)
Overall (I-squared = 67.0%, p = 0.082)		3.4 (0.1, 6.7)

Favors standard letter ← -3   0   3 → Favors intervention letter

Fig. 1. Meta-analysis results of standard letter vs. intervention letter (SWAT2) risk differences for patient questionnaires' response rate in IQuaD and INTERVAL represented in a forest plot. SWAT, studies within a trial.

made within the constraints of ethical recommendations, all participants had to receive a newsletter. As a result, we had to measure response rates in SWAT3 earlier than expected and earlier than SWAT1 or SWAT2.

Trial retention is recognized as one of the most challenging and important problems in the conduct of RCTs, and addressing it is a research priority for different stakeholders [2]. However, research in this field is scarce with Brueton et al. identifying the need to test different methods to improve retention [3]. The most recent Cochrane review for strategies to improve retention found no evidence that the behavioral/motivational strategies used were either more or less effective than standard information for retaining trial participants (relative risk: 1.08; 95% CI: 0.93 to 1.24, P-value = 0.31) (273 participants; [17,18]). However, these strategies were implemented before the main trial started, as a prevention measure and without investigation of potential barriers and facilitators to retention in their contexts. We believe our behavioral approach represents a more robust strategy to improve trial retention.

Our SWAT3 showed no evidence of a significant improvement in response rates for a prenotification theory-informed newsletter compared with no newsletter. This contrasts with results from a previous study that reported a modest but significant improvement in response rates (1.6%) when comparing a prenotification newsletter with no newsletter [19]. However, the study targeted a different population (older women at risk of hip fracture), and the baseline response rate was already high (94.6%), making a comparison with our study challenging.

In conclusion, we have shown that using BCTs that address perceived barriers and facilitators to the return of a postal questionnaire can improve retention, but replication across similar and different settings is essential.

CRediT authorship contribution statement

Beatriz Goulao: Methodology, Software, Formal analysis, Writing - original draft, Visualization. **Anne Duncan:** Conceptualization, Methodology, Investigation, Project administration, Writing - original draft, Visualization. **Ruth Floate:** Investigation, Project administration, Writing - original draft. **Jan Clarkson:** Conceptualization, Methodology, Writing - original draft, Supervision. **Craig Ramsay:** Conceptualization, Methodology, Writing - original draft, Visualization, Supervision.

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Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinepi.2020.01.018.

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