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Two controlled trials to increase participant retention in a randomised controlled trial of mobile phone-based smoking cessation support in the UK.

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Ettore Severi^{1§}, Caroline Free^{2§}, Rosemary Knight², Steven Robertson², Philip Edwards² and Elizabeth Hoile²

¹Health Protection Agency, South East Region, 7th Floor, Holborn Gate, 330 High Holborn, London WC1V 7PP, UK,² London School of Hygiene and Tropical Medicine, Nutrition and Public Health Intervention Research Unit, Keppel Street, London WC1E 7HT, UK.

§ These authors contributed equally to this work

Contact: Ettore Severi – ettore.severi@hpa.org.uk

Background

Loss to follow up of study participants represents a threat to research validity. Many different methods have been tested to reduce such loss. Interventions designed to increase participants' awareness of benefits to society of completing follow up, and the impact of a telephone call from a senior female staff member requesting follow up have not previously been robustly evaluated.

Purpose: Trial 1 aimed to evaluate the effect on participant retention by increasing awareness of the benefits of participation to society.

Trial 2 aimed to evaluate the effect on trial follow up of a telephone call from a senior female clinical staff member.

Methods: Single-blind randomised controlled trials. Allocation to intervention or control group performed through minimisation in trial 1 and randomisation in trial 2. Allocation concealed. Trial 1's intervention was a fridge magnet and text message describing the benefits to society of completing follow up. Trial 2's intervention was a phone call from the study's principal investigator

Trial 1 controls received a text message not designed to increase awareness of the benefits to society of participation. Trial 2 controls received standard Txt2stop procedures.

Results: Trial 1: 49.8% (327/976) of the intervention group and 50.2% (329/974) of the control group returned the questionnaire within 26 weeks of randomisation, RR 0.99, 95% CI 0.88–1.12. 83.3% (813/976) of the intervention group and 82.2% (801/974) of the control group sent back the questionnaire within 30 weeks of randomisation, RR 1.01, 95% CI 0.97 – 1.05.

Trial 2: 31% (20/65) of the intervention group and 32% (20/62) of the control group completed trial follow up, RR 0.93, 95% CI 0.44 – 1.98.

Conclusions

Neither method (fridge magnet and text message describing participation's benefits to society, and a phone call from study's principal investigator) increased participant follow up in the Txt2stop trial.

Key words: randomised controlled trials; loss to follow up; benefits to society; female principal investigator; interventions.

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Introduction

Randomised controlled trials are considered to be the gold standard in evaluation as the randomisation process ensures the validity of the study results [pic][1]. Losses to follow up represent an important threat to the internal validity of randomised controlled trials, as those lost to follow up are likely to differ from those for whom follow up is completed [pic][2].

Only a 0% rate of loss to follow up ensures that no bias is introduced, so it is imperative that trials aim to achieve the highest possible follow up [2]. Large and differential losses to follow up pose a serious threat to the validity of trial findings. Sprague et al suggest that under five per cent loss to follow up will result in little bias, while a loss greater than 20% may represent a serious threat to study validity. The amount of bias introduced also depends on the differences between those who were and were not followed up and cannot be accurately determined[3].

Many trials fail to achieve high follow up, potentially wasting economic and intellectual resources. A review of participant recruitment and retention in randomised controlled trials (RCTs) in six major journals from 2009 showed that 48% of trials reporting a sample size calculation failed to achieve adequate numbers at outcome assessment, once those lost to follow up were excluded[4]. Economic and intellectual resources allocated to research studies are not limitless, and study validity compromised by excessive loss to follow up is a waste of valuable resources.

A wide range of interventions to increase response rates for postal, email and telephone questionnaires have been evaluated in randomised controlled trials, and they include questionnaire length, pre-notification, number of requests, the nature and style of questions, incentives, status of sender, and method of delivery [5].

Txt2stop is a randomised controlled trial with 5800 participants that has been designed to evaluate the effect of mobile phone-based smoking cessation support on smoking rates at six months. Previous trials of smoking cessation support, particularly those using new technologies to deliver support, have experienced high and differential losses to follow up for long term outcomes [pic][6, 7]. One of our aims in the Txt2stop trial was to get high follow up. We followed up participants by any of the means they agreed to at the start of the trial, including post, email, and telephone calls to mobile, home or work numbers[8]. We used all the effective evidence-based methods that were feasible to introduce into the trial procedures, as identified in the systematic reviews by Edwards et al and Hoile et al. [pic][9, 10]. These included monetary incentives, posting correspondence by recorded delivery, pre-notification, follow-up contact, unconditional advance cash incentives, short, concise questionnaires, duplicate questionnaires sent at repeat follow-up attempts, mentioning that commitment to the trial implied an obligation to respond, mention of university sponsorship, personalised questionnaires, hand-written addresses on envelope, prepaid return envelopes with stamps instead of franking, an assurance of confidentiality and first class outward mailing.

We also tried to identify other interventions to increase follow up, and we evaluated their effectiveness in trials nested within the Txt2stop trial.

Edwards et al's systematic review of interventions to increase response to postal questionnaires includes 10 trials (with a total of 12 731 participants) that evaluate the effect of an appeal stressing the benefit to society if participants return a questionnaire: pooled odds ratio 1.09 (95% CI 0.92 to 1.29). The trials are affected by several design weaknesses: none of the ten trials give evidence of the randomisation methods, except Sletto 1940, where allocation is systematic [11]; there is no evidence that allocation of study arm was concealed from trial staff; and all the trials show evidence of selection bias [5]. The effects on follow up of interventions that outline trial participation's benefits to society remain uncertain.

Trials sometimes use a senior staff member to contact non-respondents with the aim of increasing follow up. Existing trials show no evidence of effect when a senior or well known person signs letters accompanying questionnaires: pooled odds ratios 1.05 (95% confidence interval CI 0.89 to 1.23) and OR 1.05 (95% CI 0.95 to 1.15) respectively[5]. It is plausible that more personal contact by telephone might have more influence, especially in a clinical trial where the call comes from a senior clinician or researcher. There is also no evidence of effect on response for the gender of the person requesting follow up for questionnaires (OR 1.07; 95% CI 0.72 to 1.58) but in one trial the odds of response decreased by over a half when the electronic questionnaire was signed by a man (OR 0.55; 95% CI 0.38 to 0.80)[5]. The effects of interviewer gender on follow up by telephone are not known.

We generated two hypotheses to test in two trials:

The first research hypothesis is that telling study participants that their participation in research could benefit society would increase follow up in the Txt2stop trial.

The second research hypothesis is that a telephone call from a senior female member of the team (clinical doctor) explaining the importance of follow up and asking participants to complete their participation would increase follow up in the Txt2stop trial.

Methods

We obtained ethical approval for these trials from the London School of Hygiene & Tropical Medicine Ethics Committee.

Trial 1: A randomised controlled trial evaluating the impact of an intervention providing information regarding the benefits to society of participation on participants' follow up.

This was a single-blind controlled trial, with those recording and assessing outcomes blind to the intervention.

The interventions:

The intervention group was sent written information on a fridge magnet by post (see fig1), between 16 and 20 weeks after randomisation into the Txt2stop trial, followed by a mobile phone text message (SMS) three days after the Txt2stop postal follow up questionnaire was sent. These aimed to sensitise participants by making them aware of the social benefits of remaining in the study for its full duration, regardless of smoking cessation status.

The initial sensitisation consisted of a message on a fridge magnet within a sealed envelope. The message said that medical research is important to society and pointed out that by taking part in Txt2stop, the participant was benefiting society

The text message said 'Be proud of yourself for helping medical research! Thank you for filling in the Txt2stop questionnaire.'

The control group received a text message reminding the participant the follow up was due three days after the Txt2stop postal questionnaire had been sent (week 23). The text message said 'Thank you for filling in the Txt2stop questionnaire.'

Eligibility criteria:

Existing Txt2stop participant [10].

Procedure:

Participants had consented to join the Txt2stop trial. They were able to withdraw at any time by texting 'stop' to the short code 65151. Consent for this trial was implicit by choosing to provide follow up or not. Any participant withdrawing from the Txt2stop trial was also withdrawn from this trial.

The participants were allocated to intervention or control through minimisation (using Minim software [12]) to balance four different characteristics affecting participant retention in Txt2stop: age, sex, Fagerstrom index and allocation to intervention or control group in Txt2stop. The allocation of the participants to intervention or control group was concealed from the investigators.

The 1950 participants who joined Txt2stop between 1 March and 1 June 2009 were included in the trial.

Outcome:

The outcome of the study was completed follow up at 26 and 30 weeks from randomisation.

Sample size:

The study was powered for the primary outcome measure. If the real difference in follow up at 26 or 30 weeks was 85% versus 80%, there was an 80% chance that a trial with 1900 subjects, 950 per group, would achieve $2P < 0.05$.

Trial 2: A randomised controlled trial of one telephone call from the study principal investigator to increase participant follow up within a randomised control trial.

This was a single-blind controlled trial, with those recording and assessing outcomes blind to the intervention.

The intervention:

The intervention group received a phone call from the study principal investigator (female senior clinician and researcher), who invited participants who were at least 6 weeks overdue in providing a cotinine sample to complete follow up. The control group received the standard Txt2stop procedures.

Eligibility criteria:

Enrolled in Txt2stop, and therefore aged 16 years or over; daily smoker; willing to quit in the next month; owns a mobile phone; resident in UK [10].

Procedure:

Participants had consented to join the Txt2stop trial. Consent for this trial was implicit by choosing to provide follow up or not. Any participant withdrawing from the Txt2stop trial was also withdrawn from this trial. The sample was made up of all participants in Txt2stop who were more than six weeks overdue for follow up. Allocation to intervention or control group was performed through computer generated randomisation and was concealed from the investigators.

The study principal investigator contacted participants by telephone in April 2009.

Outcome:

The study outcome was completed follow up for the Txt2stop trial.

Sample size:

The study was powered for the primary outcome measure. If the real difference in follow up at 35 weeks was 85% versus 43%, there was a 80% chance that a trial with 127 subjects, 65 in intervention and 62 in control group, would achieve $2P < 0.05$.

Results

Trial 1: 1950 participants were included in the trial. As shown in table 1, the baseline characteristics of the trial 1 population were similar to those of the Txt2stop population, with analogous proportion of participants in terms of sex, age, ethnicity, education, employment and level of nicotine dependence (Fagerstrom index). Twenty six weeks after randomisation, 33.5% (327/976) of participants who were sent the fridge magnet and text message describing benefits to society posted the questionnaire back, compared with 33.8% (329/974) of participants who did not receive the intervention describing benefits to society. The risk ratio for response to the fridge magnet was 0.99 with a 95% confidence interval between 0.88 and 1.12. The effect modification by the different allocation within the Txt2stop intervention and control groups was tested and the P value for the test of homogeneity was 0.92 showing no interaction.

Thirty weeks after randomisation, 83.3% (813/976) of participants who were sent the fridge magnet and text message describing benefits to society posted the questionnaire back, compared with 82.2% (801/974) of participants who did not receive the intervention describing benefits to society. The risk ratio for response was 1.01 (95% CI 0.97 to 1.05). The effect modification by the different allocation group within the Txt2stop trials was tested and the P value for the test of homogeneity was 0.83 showing no interaction.

Trial 2: 127 participants were included in the analysis. As shown in table 1, the baseline characteristics of the population in trial 2 were similar to those of the population in Txt2stop in regard to sex and ethnicity. The trial 2 population was generally younger and slightly more educated than the Txt2stop population, with a lower proportion of manual workers, and fewer participants who had serious nicotine dependence.

Thirty one percent (20/65) of participants who received the phone call from the study principal investigator completed follow up by sending cotinine samples, compared with 32% (20/62) of those who received the Txt2stop normal procedures. The risk ratio was 0.95 (95% CI 0.44 to 1.98).

Discussion

Information describing the benefits to society, via written information on a fridge magnet, and a subsequent a text message, did not increase study follow up at 26 weeks or 30 weeks after randomisation. A single phone call from a female senior clinician/researcher did not increase participant follow up. These interventions had no additional effect on follow up when evaluated within a trial where all other interventions known to increase follow up (as identified by Edwards et al and Hoile et al) were already implemented.

The impact of the intervention describing the benefits to society of completing follow up may have been reduced, since follow up letters in the standard Txt2stop follow up procedures already described these benefits to some extent. The Txt2stop standard procedures included telephone calls from trial assistants who could be male or female. The senior female clinician researcher was not the only female member of staff calling participants.

In trial 1, the participants were allocated to intervention or control group through minimisation to avoid imbalances within the Txt2stop allocation groups. The data manager performing the minimisation was blinded to the coding of the baseline characteristics and the allocation was therefore concealed.

The control group received a text message very similar to the text sent to the intervention group, but without any comment describing benefits to society. This text message was sent because SMS messages have been shown to work as effective reminders for appointments and medications reminders [13, 14]. Several days of strike of the Royal Mail service during three weeks in October and November 2009 [15] seriously affected the Txt2stop questionnaire return. The strike is likely to have decreased the return of questionnaires in the early phase. During the strike, it is possible that some post may have been lost by Royal Mail and attempts to obtain the data for a second time may have been less effective than the first request. There is no reason to expect that the strike would have differentially affected follow up between the intervention and control group, and so the strike may have affected the precision of the result but is unlikely to have influenced the direction of effect. These trials were pragmatic and, apart from the interventions tested, used the existing Txt2stop procedures.

There is no evidence that either describing the benefits to society of trial participation to participants or a call from a female senior researcher influence follow up when other evidence based methods to increase follow up are already employed.

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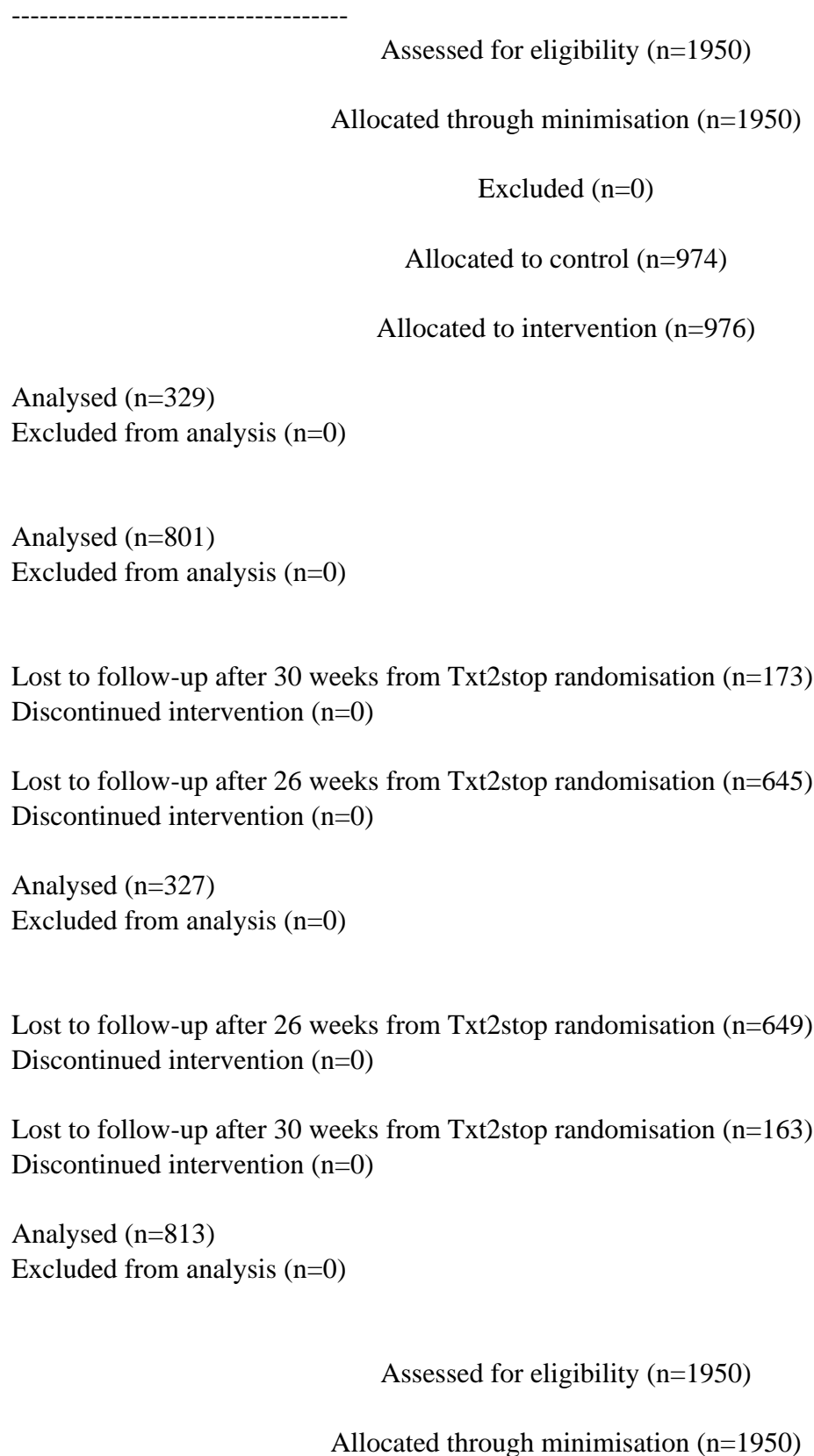
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Table 1: Characteristics of trial participants

| Variable | Txt2stop population N (%) | Trial 1 population N (%) | Trial 2 population N (%) |
|------------------|---------------------------------|--------------------------------|--------------------------------|
| Sex | | | |
| female | 2605 (44.9) | 883 (45.3) | 60 (47.2) |
| male | 3195 (55.1) | 1068 (54.8) | 67 (52.8) |
| Age (years) | | | |
| <30 | 1572 (27.1) | 573 (29.4) | 64 (50.4) |
| 30-45 | 2716 (46.8) | 897 (46.0) | 50 (39.4) |
| >45 | 1512 (26.1) | 480 (24.6) | 13 (10.2) |
| Ethnicity | | | |
| white | 5136 (88.5) | 1771 (90.8) | 109 (85.8) |
| black | 240 (4.1) | 62 (3.2) | 6 (4.7) |
| asian | 253 (4.4) | 61 (3.1) | 8 (6.3) |
| other | 134 (2.3) | 45 (2.3) | 3 (2.4) |
| unknown | 37 (0.6) | 11 (0.6) | 1 (0.8) |
| Age left school | | | |
| <=16 | 2538 (43.8) | 985 (50.5) | 54 (42.5) |
| >16 | 3262 (56.2) | 965 (49.5) | 73 (57.5) |
| Employment | | | |
| manual | 1789 (30.8) | 523 (26.8) | 28 (22.0) |
| non manual | 2539 (43.8) | 679 (34.8) | 45 (35.4) |
| N/A unknown | 1472 (25.4) | 748 (38.4) | 54 (42.5) |
| Fagerstrom index | | | |
| <=5 | 3488 (60.1) | 1154 (59.2) | 59 (46.5) |
| >5 | 2312 (39.9) | 796 (40.8) | 68 (53.5) |

Figure 1: Trial 1 flow chart (a fridge magnet and a text message to increase participant's retention in Txt2stop)

Figure 2: Trial 2 flow chart (a telephone call from the study principal investigator requesting follow up in Txt2stop)



Excluded (n=0)

Allocated to control (n=974)

Allocated to intervention (n=976)

Analysed (n=329)

Excluded from analysis (n=0)

Analysed (n=801)

Excluded from analysis (n=0)

Lost to follow-up after 30 weeks from Txt2stop randomisation (n=173)

Discontinued intervention (n=0)

Lost to follow-up after 26 weeks from Txt2stop randomisation (n=645)

Discontinued intervention (n=0)

Analysed (n=327)

Excluded from analysis (n=0)

Lost to follow-up after 26 weeks from Txt2stop randomisation (n=649)

Discontinued intervention (n=0)

Lost to follow-up after 30 weeks from Txt2stop randomisation (n=163)

Discontinued intervention (n=0)

Analysed (n=813)

Excluded from analysis (n=0)

Assessed for eligibility (n=127)

Allocated through randomisation (n=127)

Excluded (n=0)

Allocated to control (n=62)

Allocated to intervention (n=65)

Analysed (n=20)

Excluded from analysis (n=0)

Lost to follow-up at all self reported outcomes (n=42)
Discontinued intervention (n=0)

Lost to follow-up at all self reported outcomes (n=45)
Discontinued intervention (n=0)

Analysed (n=20)
Excluded from analysis (n=0)