

Three Controlled trials of interventions to increase recruitment to a randomised controlled trial of mobile phone based smoking cessation support

Free C, London School of Hygiene and Tropical Medicine, Keppel St London WC1E

7HT

Hoile E, London School of Hygiene and Tropical Medicine

Robertson S, London School of Hygiene and Tropical Medicine

Knight R. London School of Hygiene and Tropical Medicine

Abstract 300 words

Background

Recruitment is a major challenge for trials but there is little evidence regarding interventions to increase trial recruitment. We report three controlled trials of interventions to increase recruitment to the Txt2stop trial.

Purpose

To evaluate:

Trial 1. the impact on registrations of a text message regarding an online registration facility.

Trial 2. the impact on randomisations of sending £5 with a covering letter to those eligible to join the trial.

Trial 3. the impact on randomisations of text messages containing quotes from existing participants.

Methods: Single blind controlled trials with allocation concealment.

Interventions:

Trial 1: a text message regarding our new online registration facility

Trial 2: a letter with £5 enclosed.

Trial 3: a series of four text messages containing quotes from participants.

The control group in each trial received standard Txt2stop procedures.

Results Trial 1: 3.6% (17/470) of the intervention group and 1.1% (5/467) of the control group registered for the trial, risk difference 2.5% (95% CI 0.6-4.5). 0% (0/470) of the intervention group and 0.2% (1/467) of the control group registered successfully online, risk difference -0.2 (95% CI -0.6-0.2).

Trial 2: 4.5% (11/246) of the intervention group and 0.4% (1/245) of the control group were randomised into the Txt2stop trial, risk difference 4.0% (95% CI 1.4-6.7).

Trial 3: 3.5% (14/405) of the intervention group and 0% (0/406) of the control group were randomised into the Txt2stop trial, risk difference 3.5 (95% CI 1.7-5.2).

Limitations There were no baseline data available for trial 1. Allocation of participant IDs in trials 2 and 3 was systematic.

Conclusion

Sending a text message about an online registration facility increased registrations to Txt2stop, but did not increase online registrations. Sending a £5 reimbursement for participants' time and sending text messages containing quotes from existing participants increased randomisations into the Txt2stop trial.

Introduction

Recruitment is a major challenge for most trials. A recent study found that only 31% of 122 (UK Medical Research Council and Health Technology Assessment funded) trials reviewed succeeded in recruiting 100% of target (1). Under-recruitment reduces study power, which could lead to the failure to detect modest but important clinical benefits of trial interventions. Failure to recruit within the target period and/or budget can have major research costs. This could potentially reduce funds available for other research (1). The Txt2stop randomised controlled trial will randomise 5800 participants to evaluate the effects of a mobile phone based smoking cessation support intervention (2). We aimed to recruit 5800 participants in 2 years (242 per month), but in the first 8 ½ months we only recruited 1058 participants. The proportion of eligible participants consenting in June 2008 was 35% (1058/3029) whilst the target was 50%.

There are a number of barriers to participation in randomised controlled trials. Potential participants may have limited knowledge of or trust in clinical trials (3). Potential participants may find randomisation and clinical equipoise difficult to understand or hard to accept. This may be because the language used to describe randomisation or clinical equipoise is unclear or inaccurate (4,5). Potential participants may also have concerns about uncertain treatment effects. Some may find randomisation hard to accept if they have a preference for a specific intervention or do not want to be allocated to the control group (6,7,8,9) Participation can be demanding: trial processes may be inconvenient or require additional time commitments and potential costs (3,10,11). In Txt2stop potential

participants reported concerns that Txt2stop might be a scam and that text messages to and from Txt2stop might result in high charges to their mobile phone bills, even though the study information stated no charges would be made. Trial protocols can cause problems for example if the trial regimen is difficult to follow or dull (11). Potential participants may be unwilling to accept additional procedures required for a trial such as tests, especially if they are invasive (12). Motivations to join a trial include altruism or participants may feel the trial offers a new treatment that is not generally available (4).

There are many potential interventions to increase participation in trials, and many are already used. Interventions may be designed to increase knowledge of or trust in clinical trials. Trial participants, for example, have stated that having contact with an existing trial participant made them more likely to join the trial (3). Interventions may make randomisation and clinical equipoise more understandable and acceptable. Researchers suggest piloting study information to check participants' understanding (5). In a trial of an intervention for prostate cancer testing and treatment there were increases in recruitment after the non- radical arm of a trial was redefined (6). Other interventions could reduce or compensate for the demands of participation such as by simplifying protocols or making trial participation more convenient. Interventions could increase the perceived personal and societal (altruistic) benefits of participation such as through monetary or non- monetary incentives, letters introducing the trial having a university letterhead or being signed by people with high status or through monthly newsletters. In the literature on survey participation, researchers suggest that due to 'social validation' people may be more willing to comply with a request if they believe that others have

already done so (13). Other interventions might simply remind potential participants about the trial.

Despite the high prevalence of recruitment problems and wide range of potential interventions there is limited evidence from randomised controlled trials regarding effective methods of increasing study recruitment (14). A systematic review of randomised controlled trials of interventions to increase recruitment identified fifteen eligible trials(14). Interventions involved, pre-warning participants, providing additional information, study design changes, changes to consent and incentives. Three trials of interventions (letter, postcard or telephone call) pre warning potential participants about a trial did not significantly increase the proportion of people joining a trial. Seven trials in the review evaluated providing additional information, of which two showed beneficial effects. One trial showed that presenting figures regarding drug A compared to drug B in terms of doubling the effect (rather than drug B compared to drug A halving effects) increased signed consents (15). Another trial showed that adding a questionnaire regarding home safety in a trial of a home safety intervention increased recruitment (16). There were two trials of study design. In one not having an untreated placebo arm for a trial of HRT did not influence recruitment, whilst a trial offering a patient preference arm increased recruitment (17,18). Two trials of changes in consent information had no significant impact on recruitment. There was one trial of monetary incentives, which increased completion of a pre trial questionnaire (19). The effective interventions described in this review were, however, not directly transferable to the Txt2stop trial.

Joining a smoking cessation trial involves being motivated to quit as well as being willing to join a trial. Thus, interventions to increase trial recruitment to a smoking cessation trial could also include interventions designed to increase the motivation to quit. The main reasons why smokers say they want to quit include better health, money savings, family pressure, concerns about the impact of smoking on children, the ban on smoking in public places, and pregnancy (20).

Background to the Txt2stop trial.

In the Txt2stop trial we recruit participants via adverts on radio stations, in newspapers, on the QUIT website and via flyers and posters in GP surgeries, pharmacies and smoking cessation services(2). Adverts direct participants to text a short code number (65151) if they are interested in obtaining further information about the trial. Research assistants based at the trial co-ordinating centre call participants who have sent a text message of interest in the study and ask eligibility questions. Eligible participants are daily smokers with a mobile phone, aged 16 or over and willing to quit in the next month. We send further information about the trial by post or email to eligible participants. Eligible participants send back a text message stating they consent or do not consent. Once consent is received the participant is called a second time (figure 1). The research assistants collect baseline data at this second call and an electronic link to the computer based randomisation program results in allocation to the intervention or control group.

We identified two points in the recruitment process where participants failed to progress either to randomisation or exclusion from the trial. Firstly, we were unable to contact

many potential participants who had sent us a mobile phone text message (SMS) to enquire about the trial, because they did not answer their mobile phones. In June 2008 there were 937 potential participants on the 'outstanding public interest' list (point A figure 1). Secondly, many eligible participants did not send a text message giving or refusing consent to randomisation. By June 2008, there were 1302 potential participants on the 'eligible' participants list (point B figure 1). These participants had been on these two lists for up to eight and a half months.

We generated three hypotheses to test in three controlled trials

- 1) An online registration facility would make trial participation more convenient for potential Txt2stop participants and increase registration to the trial.
- 2) Sending £5 with a covering letter to eligible participants to thank them for the time spent reading the study information and considering joining the trial would alleviate concerns about charges for text messages and increase randomisations to the Txt2stop trial.
- 3) Sending participants quotes from real participants regarding their reasons for quitting would equate to having 'contact' with a real trial participant, would help reassure potential participants that Txt2stop is not a scam and would remind potential participants of their own motivations for quitting resulting in increased randomisations to the Txt2stop trial.

Aims We aimed to evaluate by controlled trial:

- 1) the impact on trial registrations of sending a text message to potential participants about our new online registration facility
- 2) the impact on randomisations and consents to be randomised into the Txt2stop trial of sending £5 with a covering letter to eligible participants to thank them for the time spent reading the study information and considering joining the trial.
- 3) the impact on randomisations and consents to be randomised into the Txt2stop trial of sending a series of four text messages containing quotes from existing participants

Methods

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

Trial 1: A randomised controlled trial of sending a text message regarding the newly available online registration facility.

This is a single-blind randomised controlled trial with those assessing outcomes blind to the intervention.

The interventions

Control group. Participants in the control group received the normal trial procedures, which involves research staff calling their mobile number to register them for the trial (no text message).

Intervention group. The intervention was a single text message:

‘Thanks for your interest in Txt2stop, the smoking cessation programme. We have tried to contact you but with no luck. You can now register your details at www.txt2stop.org. We will continue to try to speak to you.’

Eligibility criteria

This was a pragmatic trial, so we included all participants on the ‘outstanding public interest list’ for the Txt2stop trial (point A on figure 1).

Procedures

Participants had consented to find out more about the Txt2stop trial by texting in their interest. They were able to withdraw at any time by texting ‘stop’ to the shortcode 65151. Consent for this trial was implicit by choosing to receive, read or stop messages.

The participants were randomly allocated using a web based random number generator to the intervention or control group. Allocation was concealed and outcome assessors were blinded.

Outcome

The main outcome for the study was registration to the Txt2stop trial at two weeks by eligible participants (point B figure 1). Secondary outcomes were: registration using the online facility by two weeks by eligible participants; completed registrations at two

weeks, including both eligible and ineligible participants and all completed registrations at 2 weeks using the online registration facility.

Sample size

A sample size of 937 gives a 90% chance of detecting an absolute difference of 4.5% in registrations (6.5% in the intervention group compared to 2% in the control group) at a two-sided $\alpha = 0.05$.

Trial 2: A controlled trial to evaluate the impact on consent to join the Txt2stop trial of sending £5 with a covering letter to those eligible to join the trial to thank them for their time spent reading about the trial and considering joining.

This is a single-blind controlled trial with those assessing outcomes blind to the intervention

The interventions

Control group. Participants received the normal trial procedures. Eligible participants are sent the study and consent information sheets by post or email (according to their preference) immediately after registration. This information was not resent during the trial.

Intervention group. Participants received a letter containing study and consent information and a £5 note to thank them for their time spent reading the study

information and considering joining the trial. They had previously been sent study and consent information immediately after registering for the trial.

Eligibility criteria

This was a pragmatic trial, we included all participants who were currently eligible for the Txt2stop trial (point B figure 1) who had not yet stated whether they consented to join the trial, and had provided a postal address at registration.

Procedures

Participants had consented to receive information about the trial from us by texting 'smoke' to the shortcode 65151 from a mobile phone. They were able to withdraw at any time by texting 'stop' to 65151. Consent for this trial was implied by either choosing to keep or return the £5 note. The control group was sent the letter with £5 at the end of the trial.

The data manager placed registration ID numbers of participants in ascending numerical order and alternate participants were allocated systematically to the intervention or control group. The ID numbers were not linked to any names or other personally identifying information so allocation was concealed. The consent SMS messages were collected by the automated computer system. Follow up was at 2 weeks to assess whether or not the participants had been randomised into the Txt2stop trial (point C on figure 1).

Outcomes

The outcome for the study was randomisation into the Txt2stop trial within 2 weeks. A secondary outcome was consent to be randomised into the Txt2stop trial within 2 weeks.

Sample size

A sample size of 491 gives an 81% chance of detecting an absolute difference of 6% in conversions to consented status (8% in the intervention group compared to 2% in the control group) at a two-sided $\alpha = 0.05$.

Trial 3

This is a single-blind controlled trial with those assessing outcomes blind to the intervention group.

The interventions

Control group. Participants in the control group received the normal trial procedures.

Intervention group. The intervention is a series of four text messages over one week containing quotes from existing participants, e.g.

'XXX XXX from Kilburn quit in the Txt2stop trial. 'I decided to quit smoking as although I feel fit and healthy at the moment I became worried about my long term health, in particular my fear of getting cancer in later life.' to join text I consent to 65151 or if not interested text I do not consent to 65151.

Eligibility criteria

This was a pragmatic trial, we included all participants who were currently eligible for the Txt2stop trial (point B figure 1) who had not yet stated whether they consented to join the trial, and for whom we did not have a postal address.

Procedures

Participants had consented to receive messages from us by sending a text message 'Smoke' to the short code 65151 to find out more about the Txt2stop trial. They were able to withdraw at any time by texting 'stop' to 65151. Consent was implied by choosing to receive, read or stop messages.

The data manager placed the ID numbers of participants in increasing numerical order and alternate participants were allocated systematically to the intervention or control group. The ID numbers were not linked to any personal or identifying data and therefore allocation was concealed. Follow up was at 2 weeks to assess whether or not the participants has consented to join the txt2stop trial. The consent SMS messages were collected by the automated computer system, the allocation was unknown to investigators retrieving outcome data.

Outcomes

The outcome for the study was randomisation into the 'Txt2stop 'trial within 2 weeks. A secondary outcome was consent to be randomised into the Txt2stop trial within 2 weeks.

Sample size

A sample size of 811 gives an 85% chance of detecting an absolute difference of 4.5% in consenting to join the trial (6.5% in the intervention group compared to 2% in the control group) at a two-sided $\alpha = 0.05$.

Statistical analysis

All sample size calculations and analyses were conducted in STATA version 11.0. Analysis was conducted based on intention to treat. We estimated the risk difference and 95% confidence intervals of full registration or consenting to join the trial at 2 weeks using Fisher's exact test.

Each potential participant took part in only one of these three trials.

Results

Trial 1. 937 participants were included in the trial. There were no baseline data regarding participant characteristics. 3.6% (17/470) of participants who were sent the text message regarding the new online registration facility were registered successfully (i.e. registered and were eligible) for the trial within two weeks, compared with 1.1% (5/467) of the control group. The risk difference is 2.5% (95% confidence intervals 0.6-4.5). None of the intervention group registered successfully online, compared with 0.2% (1/467) of the control group, risk difference -0.2 (95% confidence intervals -0.6-0.2).

4.5% (21/470) of the intervention group and 1.5% (7/467) of the control group attempted to register for the trial (eligible and ineligible participants), risk difference 2.9% (95% confidence intervals 0.7- 5.0). Of these combined eligible and ineligible registrations, 0.6% (3/470) of the intervention group and 0.4% (2/467) of the control group, risk difference 0.2 (95% confidence intervals -0.7-1.1), registered online. The remainder registered by phone.

Trial 2: 491 participants were included in the trial. The mean age of participants was 35.8 years (SD 10.8) for the intervention group and 36.2 years (SD 11.1) for the control group

4.5% (11/246) of participants sent the letter with £5 were randomised into the Txt2stop trial compared to 0.4% (1/245) of those who were not sent anything. The risk difference is 4.0% (95% confidence intervals 1.4-6.7).

5.3% (13/246) of participants sent the letter with £5 gave their consent to be randomised into the Txt2stop trial, compared with 0.4% (1/245) of the control group. The risk difference is 4.9 (95% confidence intervals 2.0-7.7). Participants were free to keep the money whether or not they joined the Txt2stop trial. Three participants returned the £5 stating that they had done so as they had decided not to join the Txt2stop trial. Other potential participants that did not join Txt2stop kept the £5.

Trial 3: 811 participants were included in the trial. The mean age of participants was 33.4 years for the intervention group (SD 9.2) and 34.1 years for the control group (SD 9.4). 3.5% (14/405) of those sent the series of text messages containing quotes were randomised into the trial, and none of the 406 people in the control group were randomised into the trial. The risk difference is 3.5 (95% confidence intervals 1.7-5.2). 4.2% (17/405) of those sent the series of text messages containing quotes gave their consent to join the trial, and none of the 406 people in the control group gave their consent to join the trial at two weeks. The risk difference is 4.2 (95% confidence intervals 2.2-6.1)

Discussion

A text message telling potential participants that we had been trying to contact them, and that they could now use our new online registration facility increased registrations to the trial, but did not increase online registrations. Sending a letter with £5 to thank participants for their time increased randomisations into the Txt2stop trial. A series of four SMS messages containing quotes from existing Txt2stop participants increased randomisations into the Txt2stop trial.

These trials were pragmatic and apart from the interventions tested used the existing Txt2stop trial procedures. There is no baseline demographic data for trial 1 as Txt2stop does not have any baseline data for potential participants on the 'outstanding public interest' list. The only baseline demographic data for participants in trials 2 and 3 is age as age is the only demographic data collected to assess eligibility for the Txt2stop trial. The method of allocation for trial 2 and 3 was systematic. The participant IDs were not linked to any personal or identifying data so allocation was, however, well concealed. The trial participants had been on the 'outstanding public interest list and 'eligible but not consented list' for Txt2stop for up to eight and a half months so a low recruitment rate from these 'old' lists was anticipated. The impact of these interventions on recently registered participants is unknown, as the numbers were too small to stratify the analysis based on how long participants had been on the lists. The recruitment rate in the control groups in each of the trials was lower than anticipated in each of the sample size calculations. Although the effect estimates were statistically significant the absolute percentage difference between the intervention and control groups were lower than those described in the sample size calculations. In trials 2 and 3 the number of participants

consenting and being randomised is not the same as there can be delays in getting hold of participants who text in their consent to take them through the randomisation procedure. Following the completion of these trials, we introduced the interventions into the Txt2stop recruitment procedures. These interventions were implemented alongside other changes to increase Txt2stop recruitment such as: repeating the most effective adverts, refining recruitment processes and modifying study letters. The Txt2stop trial recruitment was complete in June 2009, over four months ahead of target. Sixteen percent 913/5800 of all randomised participant registered using the on line facility. The proportion of eligible participants consenting at the end of recruitment was 55% (5800/10627), five percent above target.

These trials describe three novel and effective means of increasing recruitment to the Txt2stop trial. The mechanism of action for the text message regarding the availability of online registration was not through increased use of the online registration facility. The message may have worked by reminding potential participants that Txt2stop was trying to call them, and making them more receptive to answering their mobile phones when next called by Txt2stop. Those in the control group, who registered online, could have independently sought out the Txt2stop website www.txt2stop.org and discovered the online registration facility. The additional cost of sending an SMS message for each eligible participant registered was £1.94 for the SMS messages, based on a cost of £0.05 for each SMS message sent. The intervention also took 15 minutes of data manager's time. Reimbursing participants for their time in considering joining a trial may be relevant to recruitment to other trials. The additional cost for each additional person

randomised was however high £121.5 (not taking into account postage, stationary and staff time for sending out letters). The control group did not receive an additional letter and so part of the intervention may have worked by reminding participants about Txt2stop. Sending potential participants quotes from existing participants about their experiences of being in the trial may be relevant to other trials. The cost was £5.80 for each additional person randomised for the SMS messages, based on a cost of £0.05 for each SMS message. The intervention also took less than an hour of data manager's time to send out the messages. We did not evaluate whether the text messages with quotes worked by increasing motivation to quit, through social validation, by reducing the concerns about Txt2stop being scam or by providing some 'contact' with an existing participant or a combination of these potential mechanisms. SMS messages have been successfully used to remind patient about appointments and remind them to take medicines (20, 21). It is likely that the interventions used in these trials acted at least partly as reminders. A reminder would be cheaper than some of the interventions described and should be evaluated. Future trials should evaluate the effect of quotes from existing participants delivered via other media (print, email). The impact of sending vouchers to thank people for their time by email, which would avoid postage and stationary costs, could also be evaluated.

A stronger and broader evidence base regarding interventions to increase recruitment is required to address highly prevalent recruitments problems and maximise the health benefits achieved through trials. This paper provides evidence regarding three interventions, but to date many potential interventions have not been evaluated. Future

interventions could target potential participants or collaborators. Interventions could be designed to increase the potential participants' knowledge of and trust in trials or to increase understanding and acceptability of randomisation and clinical equipoise. Interventions could aim to reduce the demands of participation such as by limiting the inconvenience, time costs and procedures involved in participation and increase the perceived personal and societal (altruistic) benefits of participation. Researchers and funders should embed future trials of recruitment interventions within existing research.

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