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TITLE

The effect of optimised patient information materials on recruitment in a lung cancer screening trial: an embedded randomised recruitment trial

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Mesh: embedded trial, study within a trial (SWAT), recruitment, randomised controlled trial

ABSTRACT

Background

Written participant information materials are important for ensuring potential trial participants receive necessary information to provide informed consent. However, such materials are frequently long and complex, which may negatively impact on patient understanding and willingness to participate. Improving their readability, ease of comprehension and presentation may assist with improved participant recruitment. The Systematic Techniques for Assisting Recruitment to Trials (MRC START) study aimed to develop and evaluate interventions to improve trial recruitment. This study aimed to assess the effectiveness of an optimised participant information brochure and cover letter developed by MRC START on response and participant recruitment rates.

Methods

A Study Within A Trial (SWAT), embedded in the EarlyCDT Lung Cancer Scotland (ECLS) trial, which aimed to assess the effectiveness of a new test in reducing the incidence of patients with late-stage lung cancer at diagnosis compared with standard care. Potential participants approached for ECLS were randomised to receive the original participant information brochure and accompanying letter (control group) or optimised versions of these materials which had undergone user-testing and a process of re-writing, re-organisation, and professional graphic design (intervention group). The primary outcome was the number of patients recruited to ECLS. The secondary outcome was the proportion of patients expressing an interest in participating in ECLS.

Results

2262 patients were randomised, 1136 of whom were sent the intervention materials and 1126 sent the control materials. The proportion of patients enrolled and randomised into ECLS was 180/1136 (15.8%) in the intervention group and 176/1126 (15.6%) in the control group (OR = 1.016, 95% CI, 0.660 to 1.564); the proportion of patients who positively responded to the invitation was 224/1136 (19.7%) in the intervention group and 205/1126 (18.2%) in the control group (OR = 1.103, 95% CI, 0.778 to 1.565).

Conclusion

Optimised patient information materials made little difference to the proportion of patients positively responding to a trial invitation or to the proportion subsequently randomised to the host trial.

Trial registration

ClinicalTrials.gov Identifier: NCT01925625, registered 15th August 2015
(<https://clinicaltrials.gov/ct2/show/NCT01925625>)

Study Within A Trial, SWAT-23, registered on 12th April 2016

Key words

Recruitment, patient information, research methodology, randomised controlled trial, Study Within A Trial (SWAT)

Background

Whilst randomised controlled trials are the gold standard for evaluating the effect of treatments, participant recruitment continues to be the biggest obstacle to their successful delivery (1–3). In the United Kingdom (UK), increasing numbers of people are approached to participate in trials (4). Despite this, the proportion of people who actually enrol is small and recruitment remains a challenge, with between 50% and 80% of all trials not meeting recruitment targets (2,5,6). Poor recruitment into a trial reduces the total sample size (limiting internal validity) and the proportion of eligible participants who are recruited (limiting external validity). Recruitment and retention are now the highest priority for methodological research in academic trials units in the UK (7), and systematic reviews have highlighted a clear need for recruitment interventions, especially those evaluated in ongoing trials where patients make real (rather than hypothetical) decisions about participation (8–10).

Although proper understanding of the trial is fundamental to valid participant consent, research suggests that trial participants can have insufficient understanding of some aspects, including the burdens and rewards associated with participation as well as their rights to revoke consent once enrolled (11,12). Furthermore, at the end of a trial participants may not know the name of the medicine being evaluated (13). Usually this information is provided in the form of a Participant Information Sheet (PIS); however, PISs are often long and complex, in part to meet the stipulations of research ethics committees. They may also lack visual appeal (14,15) with suboptimal formatting and writing of the information. These features can adversely affect prospective participants' willingness to engage with the leaflet so may go unread. When such leaflets are read, they may affect potential participants' understanding of a trial, which in turn can negatively impact on recruitment (and potentially retention). One way of improving the quality of the PIS is performance based user-testing. This is an iterative process that involves obtaining feedback from the target population for the PIS, expertise in writing for patients and graphic design and revising the material, which together aim to produce an optimised version of participant information materials.

The Systematic Techniques for Assisting Recruitment into Trials (START) study is a research programme, funded by the UK Medical Research Council (MRC) (16), which aimed to increase the evidence base for trial recruitment by developing a platform to advance the rapid and robust evaluation of recruitment interventions. Within START we have developed the methodological and reporting frameworks for embedding recruitment Studies Within Trials (SWATs) (17,18), and additionally developed two recruitment interventions (an improved PIS and a multimedia decision aid), which are being evaluated in a series of SWATs in multiple host trials, to determine their impact on participant recruitment within individual trials and across different trial contexts (19,20). Full details of the MRC START study are provided elsewhere (16).

This manuscript reports the fourth MRC START SWAT developing and evaluating optimised patient information materials (with improved readability and ease of comprehension) in a host trial evaluating a new test for screening lung cancer - the EarlyCDT Lung Cancer Scotland (ECLS) study.

Objectives

We aimed to evaluate the effectiveness of optimised patient information materials on the numbers of participants responding to the initial invitation to participate and the numbers ultimately enrolled to the ECLS trial.

Methods

We report the development of the evaluation of the recruitment intervention in line with the guidelines for reporting embedded recruitment SWATs, which adapts Consolidated Standards of Reporting Trials (CONSORT) for recruitment SWATs (18). The checklist of items for reporting recruitment SWATs is included as an additional file.

Trial design: the ECLS host trial

Lung cancer is the world's leading cause of cancer-related mortality and a major source of morbidity (21). ECLS aimed to assess the effectiveness of a new test (EarlyCDT-Lung test) in reducing the incidence of late-stage lung cancer at diagnosis, compared with standard clinical practice (22). Half of those enrolling were randomised to be offered the EarlyCDT-Lung test, a simple blood test to detect 7 autoantibodies to aid in the risk assessment and early detection of lung cancer. The other half also had their blood taken, but this was not tested as part of the trial. Intervention participants who had a positive test were followed up with an x-ray and serial computer tomography (CT) imaging six-monthly for 24 months. Control participants received standard care. ECLS aimed to recruit 10,000 participants from Glasgow and surrounding areas in Scotland, UK at the time of the current study. Recruitment into ECLS occurred between August 2013 and August 2016.

In ECLS potentially eligible individuals were identified from general practice (GP) medical records through an electronic medical record search undertaken by the Scottish Primary Care Research Network (SPCRN), which was established in 2002 as a framework to co-ordinate national research activity in primary care. The SPCRN was also responsible for accessing patient details, determining eligibility and mailing trial invitations, which consisted of a GP-signed letter and a participant information booklet. Those responding positively to the invitation could opt into the trial using a posted reply slip, SMS (text) message, email or telephone. Those meeting the trial eligibility criteria and providing consent were recruited. The eligibility criteria were: patients aged 50 years to 75 years; willing and able to give informed consent for participation in the trial; and current or ex-smokers with at least a 20 pack year history (e.g. smoking at least 20 cigarettes per day for 20 years). If patients had less than a 20 year pack history, they had to have a first-degree relative with a history of lung cancer. The ECLS trial team did not have access to patients' details until they independently contacted the trial team.

Participants who did not respond to the initial invitation letter were sent a reminder letter, written and designed by the ECLS study team, to determine whether they had received the trial invitation and whether they were interested in taking part. However, this follow up process was only introduced seven months after the start of recruitment.

Trial Design: the embedded recruitment SWAT

Recruitment into the SWAT took place over a 5-month period (February-June 2014) until the target sample size of the SWAT was reached. The SWAT adopted a randomised controlled trial design. Patients identified as potentially eligible for the ECLS trial (from GP lists) were individually randomised to either:

- a) Control participant information brochure (PIB): the original ECLS PIB and covering invitation letter (see Appendices 1 and 2)
- b) Intervention PIB: the user-tested PIB and covering letter (see Appendices 3 and 4).

The recruitment trial included all patients identified as potentially eligible for the ECLS host trial: there were no additional inclusion or exclusion criteria. The ECLS trial team led on the implementation of the SWAT in their host trial, with methodological input from the START team. Author ST was a co-investigator on both ECLS and MRC START and proof read the control PIB in his role on ECLS before START began. ST played no role in the development of the START ECLS PIL. No other member of the ECLS team was part of the START team.

The control intervention - PIB

The control PIB was developed by the ECLS host trial team, based at Tayside Clinical Trials Unit (TCTU). This was presented as a booklet of 32 pages in length, and approved by The East of Scotland Research Ethics Committee REC1 on 16th April 2013, reference 13/ES/0024, as part of the ethics application for the ECLS study. Unlike most participant information leaflets in trials which tend to be written as plain text documents, the control PIB was a coloured document formatted by a professional design company and included photos (Appendix 1). The accompanying GP letter was on a single A4 sheet with tear-off reply slip and contact details on the reverse (Appendix 2).

One of the MRC START investigators (ST) proof-read the content of the control PIB in his former role as the Assistant Director of TCTU and a co-investigator on ECLS. ST's role in the control PIB did not extend beyond proof-reading, with all other work undertaken by the wider ECLS team. None of the other MRC START investigators were involved in the development of the original PIB.

The recruitment intervention

A revised PIB and accompanying GP letter were developed using the performance based user-testing process. This was an evidence-based (23), expert-led process that consisted of optimising the readability, appearance and navigation of the PIB and letter. The majority of the content of the original PIB was retained, but re-written and re-designed based on the feedback from the user-testing process. This process was led by author PK from the START team, who has significant experience and expertise in writing for patients, with user-testing being undertaken by Luto Research Limited (Leeds, UK). Healthy volunteers with a similar age, educational and employment socio-demographic profile as the sample for ECLS were recruited for the performance-based user-testing. Individuals who had participated in any healthcare trial or user-testing in the preceding six months were excluded. An iterative user-testing process was followed (24–27), which involved

objectively evaluating the ability of patients to locate and understand key information contained in the PIB and letter.

Four rounds of user-testing were undertaken with ten volunteers in each round. The combined mean age of volunteers across the four rounds was 63 years (range: 51-75 years); 50% were female; 37.5% had completed their education at the UK minimum age (14-16, depending on participant age), 42.5% completed education at 18, and 20% had higher education (graduates); 52.5% were retired, 42.5% were employed and 5% were unemployed. At each round, volunteers were presented with a single version of the PIB and invitation letter, which they were then asked to read. Then each volunteer was asked to find information in the PIB or letter, using 20 structured questions (24,25). Seventeen of these questions focused on the PIB and three focused on the invitation letter. To test the organisation of the information, volunteers were asked to identify the answer in the PIB or letter; to test understanding they were asked to provide the answer in their own words. The questions focused on:

1. The ECLS trial's nature and aims
2. The process and meaning of consent in ECLS
3. ECLS trial procedures
4. Safety, efficacy and nature of the intervention being evaluated in ECLS

Round one involved testing the control ECLS materials, consisting of a 32 page A5 booklet in colour and a two-sided A4 participant invitation letter, which contained an overview of the study on one side and contact details of the ECLS trial team on the other with a tear off slip. Rounds two to four involved versions of the optimised information materials. After rounds two to four revisions were made to the materials in response to the obtained user-testing data. If volunteers had difficulty with understanding, it signified a need to revise the wording, and if they had difficulty finding an answer, it signified a need to amend the document's organisation or navigation. Table 1 below lists the main changes made to the PIB following user-testing, which is also attached as (Appendix 3).

Table 1: Changes to the content and structure of the PIB

Changes to content	Changes to the form and structure
Added NHS Scotland logo to front page	Reduced length from 32 to 30 pages
Shortened 'foreword' by 50%, and changed heading to 'Introduction'	Moved 'contents' page from page 4 to page 2, and added trial team contact details at bottom
Changed all but one of the six photographic images, to reflect more demographic diversity	Trial team contact details moved from back page to page 27
Added a trial flow-chart of the participant pathway in the centre of the booklet	Made contents list clearer and more spread out
Added summary circles of text throughout the booklet	Use of short sentences, plain English, bullet points throughout
New back page, with the same image as front page (map of Scotland) with NHS logo	

Optimisation of the PIB also involved professional graphic design by a company with significant expertise in designing patient communication materials (Appendix 3).

The changes to the accompanying invitation letter were: letter was shortened, removal of content duplicated in the PIB; 'bullet points' were added; and a 10 point summary of the ECLS trial was printed onto the reverse of the letter; tear off reply slip was placed at the foot of letter, so that letter text was retained. Appendix 4 shows the changes made to the invitation letter.

Outcome measures

The primary outcome was the number of patients recruited into the ECLS trial. The secondary outcome was the proportion of patients expressing an interest in participating in ECLS.

Sample size calculation

The recruitment trial was powered to detect a significant improvement in recruitment rate into ECLS, defined as an absolute increase of five per cent above baseline. Baseline response rates for the first five ECLS practices were around 20% (December 2013), although patient ineligibility and difficulties contacting some people reduced the 20% response rate to a recruitment rate of approximately 14% in later practices. For a baseline of 20% recruitment, a sample size of approximately 2000 patients was estimated to provide at 80% power and alpha 0.05 for a 5% minimally important increase in recruitment between intervention PIB and the control PIB.

Randomisation

Potential participants identified from GP lists as eligible were randomly allocated to receive the control PIB or intervention (user-tested PIB) and GP covering invitation letter at a 1:1 ratio using the recruitment tracking software developed by the Health Informatics Centre, University of Dundee and the Tayside Clinical Trials Unit.

Statistical methods

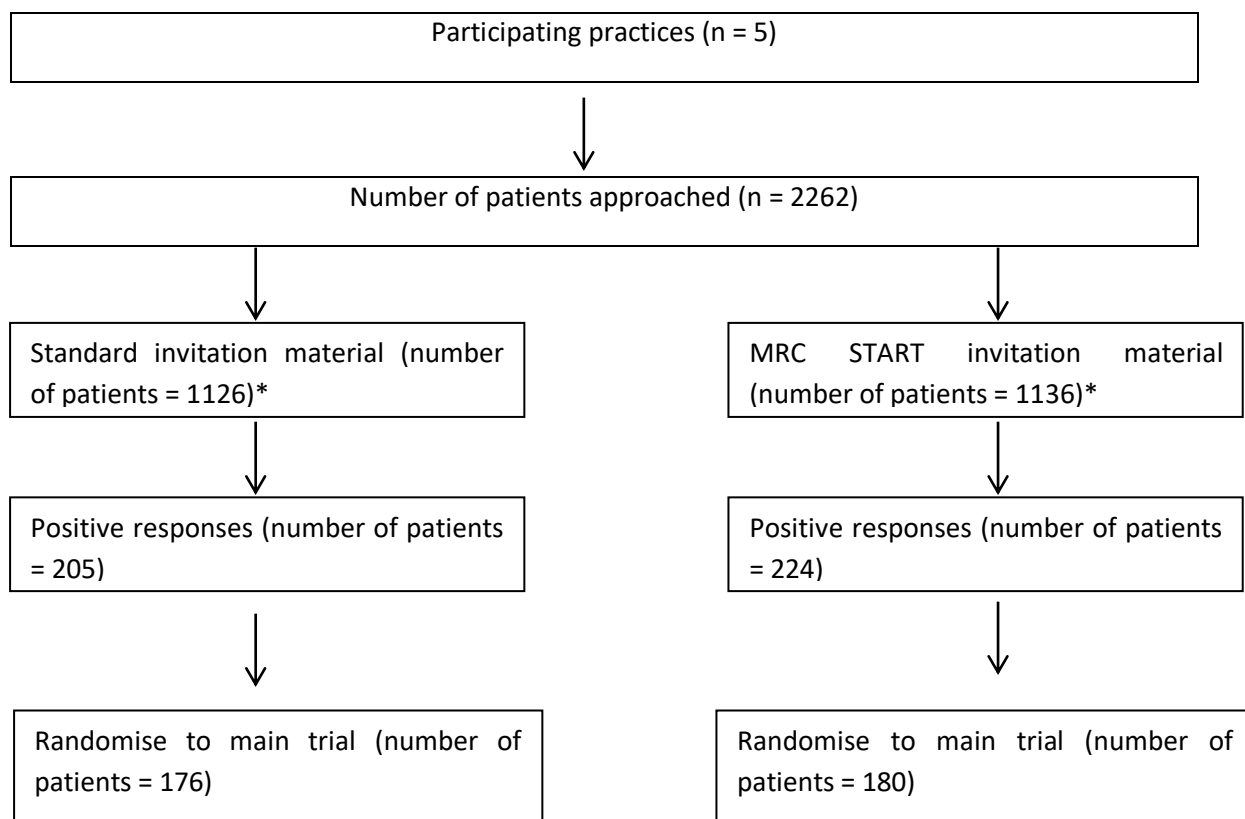
Analyses were conducted in line with a standard statistical plan developed at Barts and the London Pragmatic Clinical Trials Unit.

We initially described outcomes separately by arm for patients who expressed an interest in the study and those who were recruited into ECLS. We then compared these using logistic regression. Analyses followed the intention-to-treat principle and were conducted in Stata, version 14 (Stata Corp., College Station, TX, USA). An independent statistician (VM) who conducted analyses remained blind to allocation until the analyses were complete.

Results

A total of 2262 patients were randomised for the SWAT, of whom 1136 were sent the intervention PIB and 1126 were sent the control PIB. For the primary outcome, the proportion of patients enrolled and randomised into ECLS (the host trial) was 180/1136 (15.8%) for those sent the intervention PIB and 176/1126 (15.6%) in the control PIB group (OR = 1.016, 95% CI, 0.660 to 1.564). Figure 1 outlines the recruitment flowchart for the SWAT.

Figure 1: Flowchart of participant response and recruitment. Based on the 'guidelines for reporting embedded recruitment trials', which adapts Consolidated Standards of Reporting Trials (CONSORT) for embedded recruitment trials (18)



*Patients from two of the five practices also received a reminder following the initial invitation. The same reminder letter was used regardless of what invitation they originally had.

For the secondary outcome the proportion of patients who responded positively to the invitation and expressed an interest in trial participation was 224/1136 (19.7%) for patients sent the intervention PIB and 205/1126 (18.2%) in the control PIB group (OR = 1.103, 95% CI, 0.778 to 1.565).

Harms

We did not measure potential harms, such as perceptions of increased pressure to participate in patients receiving the intervention PIB.

Discussion

Summary of main findings

We evaluated the effectiveness of optimised patient information materials on improving recruitment into a lung cancer screening trial. Being sent the optimised patient information materials made little difference to the proportion of patients positively responding to a trial invitation, or to the proportion being randomised.

Strengths and limitations

We systematically developed optimised patient information materials based on an established and published process (24–27); according to a published protocol (28); and report our findings in line with best practice guidance for reporting recruitment SWATs (18). This SWAT was fully powered and used an *a priori* sample size calculation, unlike most SWATs – including those conducted in as part of the MRC START project - which set sample sizes on convenience (29).

In line with the statistical analysis plan, we undertook the analysis according to the initial randomisation. However, although in the SWAT all the initial invitations were correctly sent as per random allocation to the intervention or control PIB, the ECLS team sent out further reminders in two practices to patients who had not responded, in the intervention as well as in the control arm of the SWAT, which were not optimised or randomised. The use of these reminders was a capacity decision and at the time of the SWAT not all patients were sent reminders; this was because sending out more fresh invitations through newly recruited general practices led to a better recruitment return than reminding non-responders. However, since the reminder letters were not randomised, their use may have diluted the effect of the recruitment intervention, although this effect is mitigated because we aimed to identify differences in proportions between the intervention and control groups, rather than absolute levels. This highlights some of the issues with undertaking recruitment SWATs, including difficulties in aligning the SWAT and host trials (30).

A limitation of our study is that we were unable to gather data to assess any moderators of the effect of the intervention, such as age, gender, ethnicity or socioeconomic status, which may have provided additional information on the impact of the intervention in different groups. It was not the aim of the study to undertake qualitative interviews with patients sent the trial information, so we were not able to explore the wider impact of optimised patient materials beyond recruitment rates. There are also a number of different ways in which the intervention PIB was optimised ([we were evaluating a particular way of producing a PIB, rather than any single change to the PIB](#)), thus in the absence of a process evaluation, [or series of trials of individual PIB changes](#), it is difficult to determine whether any single change or different combination of changes may have been more effective. The user-testing process may have had a positive impact in its own right by improving readability and ease of comprehension and therefore may have led to better engagement with the trial; however, we did not assess this.

In comparison with the materials used in many clinical trials, the original PIB was high quality, using colour photographs and developed by a highly experienced trials team. Additionally, the original PIB was proof-read by an ECLS co-investigator who was a START co-investigator. Thus it may not have been representative of the typical PIB developed by trial teams. This may have limited the potential additional benefit of the user-testing process, and may explain the lack of difference between the intervention and control groups. [However, our current findings with an odds ratio of 1.016, \(95% CI, 0.660 to 1.564\) are in line with those of the three other SWATs undertaken as part of START, where the odds ratios of the user-tested versus control leaflets were: 1.01 \(95% CI 0.71–1.45\) \(31\); 1.12 \(95% CI = 0.78 to 1.61\) \(19\); and 1.63 \(95% CI = 1.00 to 2.67\) \(19\). Therefore, all current SWATs to date have found little or no effect of the intervention PIB compared with the control PIBs, suggesting that proof reading of the control PIB by a START co-investigator did not significantly impact on the control leaflet in this current SWAT. The latest Cochrane review also undertook a meta-analysis of these SWATs with an overall risk difference estimate of 1% \(95% CI = -1% to 3%\). The START ECLS](#)

[risk difference is 0% \(95% CI = -3% to 3%\) so entirely consistent with the other three.](#) Trialists now routinely involve patients and the public to assist with developing information leaflets for patients, which may reduce the relative benefits of user-testing.

In this SWAT 'harm' could include reduced recruitment in the intervention PIB group. We therefore evaluated a two-tailed hypothesis for the primary and secondary outcomes, which accepted that sending the recruitment intervention to potential participants could cause benefit or loss to recruitment for the host trial. Although patients not being recruited presents a loss to the host trial, for the patient, not being enrolled into the trial may not be harmful as they may have made an informed decision to not participate. The results demonstrate that the recruitment intervention was not effective for increasing response and randomisation rates.

Comparison with existing literature

This SWAT adds to the small but emerging literature on the effects of modified information on trial recruitment. In the Cochrane review of recruitment interventions (9), three trials explored the impact of supplementary written material on recruitment and found little evidence of benefit. As part of MRC-START programme, this manuscript is the fourth SWAT evaluating the effects of optimised participant information materials on trial recruitment in different trial contexts (19,31). [This will enable us to determine the effectiveness of the intervention within each individual host trial and across different trial contexts and patient populations, using a meta-analysis. We are taking this approach since recruitment interventions may impact differently according to the specific contexts, trial interventions, and patient populations. In this specific SWAT, we tested the intervention in the context of a screening trial. Previous SWATs of the same intervention have been undertaken in a falls prevention trial \(31\), and in two trials delivering telehealth interventions for patients with cardiovascular disease and depression \(19\).](#) These trials have shown small increases in the numbers of patients positively responding and enrolling; however such increases were not statistically significant. This SWAT shows similar results in a small but statistically non-significant increase in response and recruitment rates. In this SWAT, the proportions of patients responding in both intervention (19.7% response; 15.8% enrolled) and control groups (18.2% response; 15.6% enrolled) were higher than in our previous trials; for example, the Healthlines Depression recruitment SWAT achieved recruitment rates of 6.3 % in the intervention group versus 4% in the control group (OR = 1.63, 95 % CI = 1.00 to 2.67) (19). This may have been a consequence of the use of reminder letters in both the intervention and control groups. All current SWATs of this enhanced PIB intervention have been compared with original PIBs developed by highly experienced host trial teams based within UKCRC accredited Clinical Trials Units, which have some of the most experienced teams delivering trials in the UK. It may be that the optimised leaflets may be found to be more effective if compared with leaflets developed by less experienced trial teams [in the UK or elsewhere.](#)

Implications for recruitment research

As part of the START programme we have undertaken a series of SWATs of optimised participant information materials to determine their overall effectiveness within individual trials and across different trial contexts.

In START we have demonstrated the feasibility of developing and evaluating recruitment interventions in multiple ongoing trials. Future research should focus on reducing uncertainty around the effect of existing interventions used to improve recruitment (such as telephone

reminders) and developing and evaluating new interventions to support trial recruitment, especially those interventions targeting the education and training of trial recruiters, which has been highlighted as a priority topic around recruitment into trials (32,33). Improving the evidence base around recruitment has the potential to increase recruitment rates and increase the proportion of trials delivering on time.

Conclusions

We evaluated the effectiveness of optimised patient information materials on recruitment into a trial of a screening test for lung cancer. Optimised patient information materials did not increase the proportion of patients positively responding or being randomised. This SWAT adds to the evidence base around trial recruitment and will contribute to a future meta-analysis of the effectiveness of optimised information materials, [as part of the MRC-funded START project, and as part of the Cochrane systematic review of recruitment interventions, which is led by a member of our team.](#) Further interventions addressing identified priorities for recruitment research should be developed and evaluated using SWATs.

Abbreviations

List of abbreviations used

PIB – Patient Information Brochure

PIS – Patient Information Sheet

ISRCTN – International Standard Randomised Controlled Trial Number

RCT – Randomised Controlled Trial

NRES – National Research Ethics Service

MRC START – Medical Research Council Systematic Techniques for Assisting Recruitment to Trials

NHS – National Health Service

OR – Odds Ratio

CI - Confidence Interval

Declarations

Ethical approval and consent to participate

Ethics approval was obtained to undertake ECLS from the UK National Research Ethics on 16 April 2013, using the recruitment method outlined above (East of Scotland Research Ethics Service REC 1, REC reference 13/ES/0024).

Consent for publication

This manuscript does not report individual patient data thus it was not necessary to obtain consent to publish from individual participants.

Availability of supporting data

The data for this study is available on reasonable request to Prof Peter Bower, the corresponding author.

Competing interests

One of the MRC START investigators (ST) did proof-read the content of the control PIB in his former role as the Assistant Director of TCTU and a co-investigator on ECLS.

All other authors declare that they have no competing interests.

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Authors' contributions

The following are or were members of the ECLS trial team: Shaun Treweek (ST), Roberta Littleford (RL) and Stephanie Gallant (SG). ST is a Co-investigator of the MRC START programme and Co-investigator of the ECLS trial, participated in the design and coordination of the SWAT and reviewed the protocol.

The following were members of the MRC START team: Peter Bower (PI), Peter Knapp, Adwoa Parker, Jo Rick, Sandra Eldridge, Vichithranie Madurasinghe, David Collier (DC) and Paul Wallace. PB is the Principal Investigator of the MRC START programme. PK is a Co-investigator of the MRC START programme and led the user-testing and graphic design for one of the optimised PIB. AP drafted the manuscript. JR was the MRC START study manager. SE is a Co-investigator of the MRC START programme and prepared the standard analytic plan and reporting guidelines as part of the MRC START programme which was used to inform the statistical analysis and reporting of the SWAT. VW prepared the analytic plan and reporting guidelines as part of the MRC START programme and undertook the statistical analysis. All authors read and approved the final manuscript.

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References

1. Bower P, Wallace P, Ward E, Graffy J, Miller J, Delaney B, et al. Improving recruitment to health research in primary care. *Fam Pract* [Internet]. 2009 Oct;26(5):391–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19549623>
2. Sully BG, Julious SA, Nicholl J. A reinvestigation of recruitment to randomised, controlled, multicenter trials: a review of trials funded by two UK funding agencies. *Trials*. 2013;14(1):166.
3. Carlisle B, Kimmelman J, Ramsay T, MacKinnon N. Unsuccessful trial accrual and human subjects protections: an empirical analysis of recently closed trials. *Clin Trials* [Internet]. 2015;12(1):77–83. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25475878>
4. National Institutes of Health. About NIH [Internet]. Vol. 2015. National Institutes for Health; 2015. Available from: <http://www.nih.gov/about/>
5. CenterWatch. State of the Clinical Trials Industry 2009: A Sourcebook of Charts and Statistics. Lamberti MJ, editor. CenterWatch; 2009. 548 p.
6. Walters SJ, Bonacho I, Bortolami O, Flight L, Hind D, Jacques RM, et al. Recruitment and retention of participants in randomised controlled trials : a review of trials funded and published by the United Kingdom Health Technology Assessment Programme. 2017;1–10.
7. Smith CT, Hickey H, Clarke M, Blazeby J, Williamson P. The trials methodological research agenda: results from a priority setting exercise. *Trials*. 2014;15(1):32.
8. Watson JM, Torgerson DJ. Increasing recruitment to randomised trials : a review of randomised controlled trials. *BMC Med Res Methodol*. 2006;9:1–9.
9. Treweek S, Lockhart P, Pitkethly M, Cook JA, Kjeldstrom M, Johansen M, et al. Methods to improve recruitment to randomised controlled trials: Cochrane systematic review and meta-analysis. *Bmj* [Internet]. 2013;3(2). Available from: <http://bmjopen.bmj.com/content/3/2/e002360.full.pdf+html>
10. Treweek S, Bevan S, Bower P, Campbell MK, Christie J, Clarke M, et al. Trial Forge Guidance 1: What is a Study Within A Trial (SWAT)? *Trials*. 2018;19(139).
11. Jenkins VA, Anderson JL, Fallowfield LJ. Communication and informed consent in phase 1 trials: a review of the literature from January 2005 to July 2009. *Support Care Cancer* [Internet]. 2010;18(9):1115–21. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=20204418>
12. Fortun P, West J, Chalkley L, Shonde A, Hawkey C. Recall of informed consent information by healthy volunteers in clinical trials. *QJM*. 2008;101(8):625–9.
13. Griffin JM, Struve JK, Collins D, Liu A, Nelson DB, Bloomfield HE. Long term clinical trials: how much information do participants retain from the informed consent process? *Contemp Clin Trials* [Internet]. 2006 Oct;27(5):441–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16798101>
14. Sugarman J, McCrory DC, Hubal RC. Getting meaningful informed consent from older adults: a structured literature review of empirical research. *J Am Geriatr Soc*. 1998;46:517–24.

15. Cox AC, Fallowfield LJ, Jenkins VA. Communication and informed consent in phase 1 trials: a review of the literature. *Support Care Cancer* [Internet]. 2006;14(4):303–9. Available from: <http://www.springerlink.com/content/q5n24622w415r26x/fulltext.pdf>
16. Rick J, Graffy J, Knapp P, Small N, Collier DJ, Eldridge S, et al. Systematic techniques for assisting recruitment to trials (START): Study protocol for embedded, randomized controlled trials. *Trials*. 2014;15(1).
17. Rick J, Graffy J, Knapp P, Small N, Collier D, Eldridge S, et al. Systematic techniques for assisting recruitment to trials (START): study protocol for embedded, randomized controlled trials. *Trials* [Internet]. 2014;15(1):407. Available from: <http://www.trialsjournal.com/content/15/1/407>
18. Madurasinghe VW, Sandra Eldridge on behalf of MRCSG, Gordon Forbes on behalf of the SECG. Guidelines for reporting embedded recruitment trials. *Trials* [Internet]. 2016;17:27. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4714476/>
19. Man MS, Rick J, Bower P. Improving recruitment to a study of telehealth management for long-term conditions in primary care: two embedded, randomised controlled trials of optimised patient information materials. *Trials*. 2015/07/19. 2015;16:309.
20. Bower P, Collier D, Eldridge S, Graffy J, Kennedy A, Knapp P, et al. A multimedia intervention to enhance recruitment to clinical trials in primary care and community settings: process of development and evaluation. *Trials*. 2013;14(Suppl 1):P90.
21. Dela Cruz CS, Tanoue LT, Matthay RA. Lung Cancer: Epidemiology, Etiology, and Prevention. Vol. 32, *Clinics in Chest Medicine*. 2011. p. 605–44.
22. Sullivan FM, Farmer E, Mair FS, Treweek S, Kendrick D, Jackson C, et al. Detection in blood of autoantibodies to tumour antigens as a case-finding method in lung cancer using the EarlyCDT®-Lung Test (ECLS): study protocol for a randomized controlled trial. *BMC Cancer*. 2017;
23. Raynor DK, Dickinson D. Key principles to guide development of consumer medicine information--content analysis of information design texts. *Ann Pharmacother*. 2009/03/26. 2009;43(4):700–6.
24. Knapp P, Raynor DK, Silcock J, Parkinson B. Performance-based readability testing of participant materials for a phase I trial: TGN1412. *J Med Ethics* [Internet]. 2009;35(9):573–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19717698>
25. Knapp P, Raynor DK, Silcock J, Parkinson B. Performance-based readability testing of participant information for a Phase 3 IVF trial. *Trials*. 2009;10(1):79.
26. Knapp P, Raynor DK, Silcock J, Parkinson B. Can user testing of a clinical trial patient information sheet make it fit-for-purpose?-a randomized controlled trial. *BMC Med*. 2011;9(1):89.
27. Raynor DK, Knapp P, Silcock J, Parkinson B, Feeney K. “User-testing” as a method for testing the fitness-for-purpose of written medicine information. *Patient Educ Couns*. 2011;83(3):404–10.
28. Rick J, Graffy J, Knapp P, Small N, Collier DJ, Eldridge S, et al. Systematic techniques for assisting recruitment to trials (START): study protocol for embedded, randomized controlled trials. *Trials*. 2014;

29. Adamson J, Hewitt CE, Torgerson DJ. Producing better evidence on how to improve randomised controlled trials. *BMJ* [Internet]. 2015;351(h4923). Available from: <http://www.bmj.com/bmj/351/bmj.h4923.full.pdf>
30. Graffy J, Bower P, Ward E, Wallace P, Delaney B, Kinmonth A-L, et al. Trials within trials? Researcher, funder and ethical perspectives on the practicality and acceptability of nesting trials of recruitment methods in existing primary care trials. *BMC Med Res Methodol* [Internet]. 2010 Jan;10:38. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2873514&tool=pmcentrez&rendertype=abstract>
31. Cockayne S, Fairhurst C, Adamson J, Hewitt C, Hull R, Hicks K, et al. An optimised patient information sheet did not significantly increase recruitment or retention in a falls prevention study: an embedded randomised recruitment trial. *Trials*. 2017;18(144).
32. Healy P, Galvin S, Treweek S, Whiting C, Maeso B, Williamson PR, et al. Prioritising recruitment in randomised trials: the priority study- an Ireland and UK priority setting partnership. *Trials*. 2017;18((Suppl 1)):032.
33. Bower P, Brueton VC, Gamble C, Treweek S, Tudur Smith C, Young B, et al. Interventions to improve recruitment and retention in clinical trials: current practice and future priorities. 2014;

Figure legends

Table 1: Changes to the content and structure of the PIB

Figure 1: Flowchart of participant response and recruitment. Based on the 'guidelines for reporting embedded recruitment trials', which adapts Consolidated Standards of Reporting Trials (CONSORT) for embedded recruitment trials (18)

Additional files

Additional file 1

- File format: Microsoft Word document
- Title of data: Table 1: Changes to the content and structure of the PIB
- Description of data: an overview of the changes made to the components of the recruitment intervention

Additional file 2

- File format: . Microsoft Word document
- Title of data: Figure 1: Flowchart of participant response and recruitment. Based on the 'guidelines for reporting embedded recruitment trials', which adapts Consolidated Standards of Reporting Trials (CONSORT) for embedded recruitment trials (18)
- Description of data: an overview of the flow of patients in the embedded trial

Additional file 3

- File format: Microsoft Word document
- Title of data: Checklist of items for reporting embedded recruitment trials. Based on the 'guidelines for reporting embedded recruitment trials', which adapts Consolidated Standards of Reporting Trials (CONSORT) for embedded recruitment trials.

- Description of data: Checklist for reporting embedded recruitment trials

Additional file 4

- File format: Microsoft Word document
- Title of data: Appendix 1: Original patient information brochure
- Description of data: Original patient information brochure

Additional file 5

- File format: Microsoft Word document
- Title of data: Appendix 2: Original accompanying GP letter
- Description of data: Original accompanying GP letter

Additional file 6

- File format: Microsoft Word document
- Title of data: Appendix 3: Optimised patient information brochure
- Description of data: optimised patient information brochure

Additional file 7

- File format: Microsoft Word document
- Title of data: Appendix 4: Optimised accompanying GP cover letter
- Description of data: Optimised cover letter

Appendix 1: Original patient information brochure



**EARLY LUNG CANCER
DETECTION STUDY**

**WE NEED
10,000
PEOPLE**

**FROM TAYSIDE & GLASGOW
TO TAKE PART**

**ECLS
STUDY**



ECLS Study

**Early Cancer detection test - Lung Cancer
Scotland**

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All our contact details are on the back page.



Appendix 2: Original accompanying GP letter

Send on GP headed note paper



[insert date]

Dear [insert name]

Important new study to help find lung cancer earlier

We are writing to tell you about a study to help find lung cancer earlier. Our practice is asking all patients aged 50 to 75 who smoke or have smoked in the past to think about taking part.

Lung cancer kills more people than any other cancer. Most cases are picked up late when the chance of surviving is low. We know that finding lung cancer early can save lives. A new blood test may pick up very small cancers before they make people feel ill or can be found on chest X-rays. We want to find out if the test saves lives and what people think about the test. If you take part, you will help us to find this out.

We have enclosed a brochure telling you more about the study. Please read this and think about taking part. If you would like to find out more about the study, or if you do not want us to contact you again, please fill in the reply slip and post in the FREEPOST envelope. Your details will **only** be used for the researchers to contact you about the study.

You can find out more about the study by visiting the study website www.ecisstudy.org or contact us using the contact details overleaf. Agreeing to find out more about the study does not mean you have to get involved. You can leave the study at any time you choose.

Thank you for taking the time to read this letter.

Yours sincerely

[insert GP signature]

General Practitioner

PTO for Reply Slip and other contact details

Enc. ECLS Participant Information Brochure, v1.2, 1st May 2013

Freepost Envelope

For more information about the ECLS study please
contact us by any of the methods below quoting reference: { insert number}

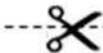
Email: info@eclsstudy.org

Phone: [01382 xxxxxx](tel:01382xxxxxx)

Text: [eclsgo](sms:eclsgo) {insert number} to 0778 620 2820

Website: www.eclsstudy.org

Or please complete the reply slip below and return in the FREEPOST envelope:



ECLS Ref No: [insert number]

Name: [insert name]

Yes, I would like to find out more about the study.

My contact details: Day time number:

Mobile number:

Email address:

No, please don't contact me again

Appendix 3: Optimised patient information brochure

NHS
SCOTLAND

**EARLY LUNG CANCER
DETECTION STUDY**

**WE NEED
10,000
PEOPLE**

**FROM TAYSIDE & GLASGOW
TO TAKE PART**

**ECLS
STUDY**

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If your blood test is negative.....	17
Non-Test Group	18
Possible benefits & disadvantages of taking part..	19
Other study information	21
What do I do now?.....	27

And then...

If you are interested in taking part, please return the reply slip at the foot of the letter from your GP.

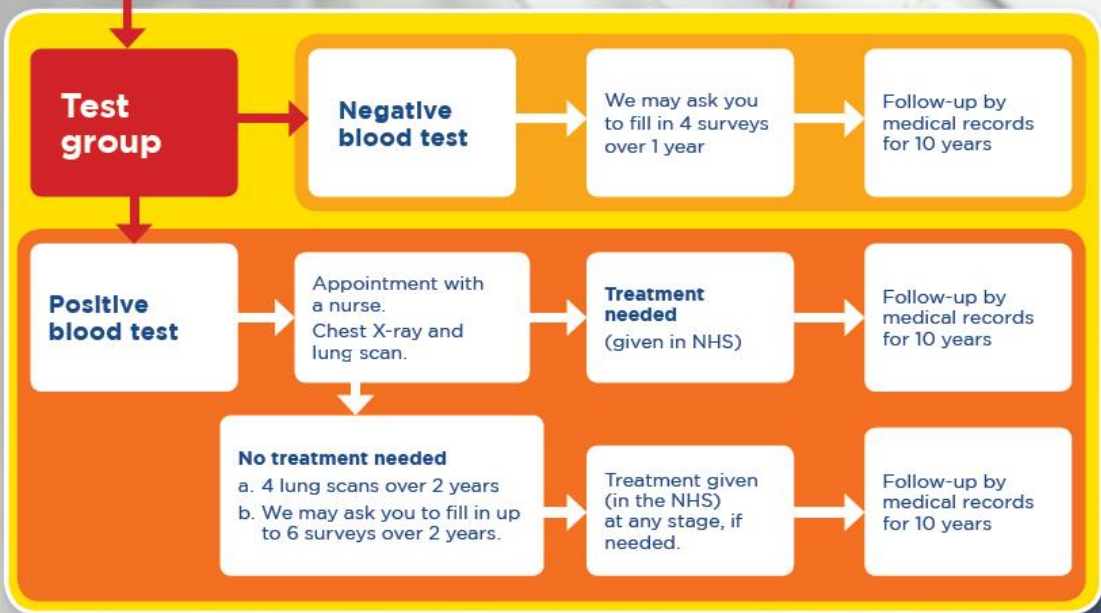
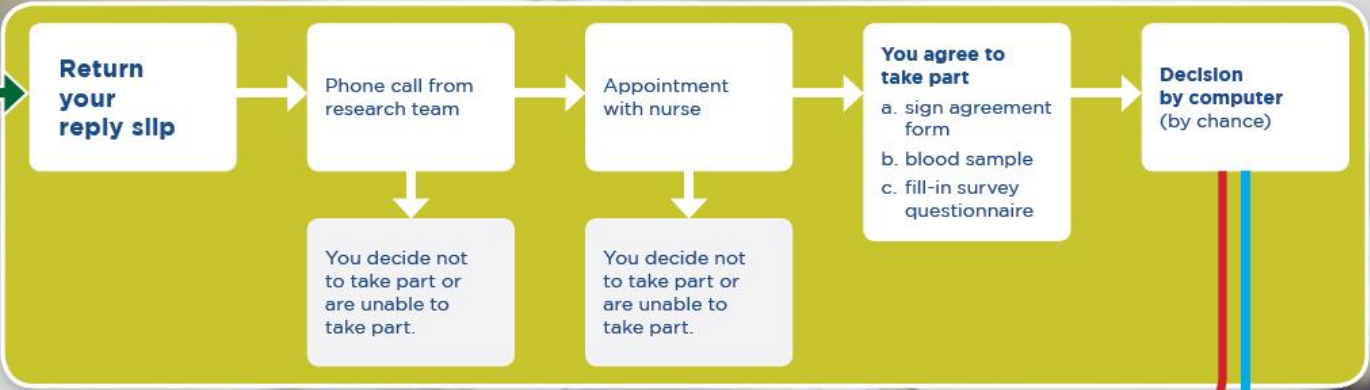
If you have any any questions, or have mislaid the GP letter, please phone or email the study researchers:

Tayside: 01382 383060

Glasgow: 0141 232 9525


Email: info@eclsstudy.org

Start here



Appendix 4: optimised GP cover letter

Send on GP headed note paper



[insert date]

Dear [insert name]

Important new Scottish study to find lung cancer sooner - can you help?

Our practice is one of many across Glasgow and Tayside that are helping with an important study aimed at finding lung cancer much sooner. To be a success, the study needs 10,000 people. You may benefit if you take part, and you will also help future generations.

We are not asking you because we think you have lung cancer. We are writing to all patients aged 50 to 75 who smoke or who smoked in the past – this puts you at higher risk.

Sadly lung cancer is often found too late - finding it sooner can save lives. A new blood test may pick up very small, early lung cancer, even before people feel unwell. The ECLS study will see if the new blood test saves lives and also ask people what they think of it. Your taking part will help us to find this out.

Please read the summary over the page and the enclosed booklet. If you want to take part (or would prefer not to take part), **please fill in the reply slip below and post it in the FREEPOST envelope.** Or you can find out more by contacting the researchers (see pages 2 or 27 of the booklet) - they will not pass on your details to anyone.

Posting the reply slip does not mean you have to get involved but it allows you to find out more. Thank you for taking the time to read about the study.

Yours sincerely

[insert GP signature]

General Practitioner

**Please
turn
over**

ECLS Ref No: [insert number] Name: [insert name]

Yes, I am interested in taking part.

My contact details (please give any that apply): Daytime number:

Mobile number: Email address:

No, I would prefer not to take part, please don't contact me again.

A quick 10 point summary of the ECLS study

1. Lung cancer is often found too late to help – we want to be able to find it much sooner. When lung cancer is found late, only 1% (1 in 100) patients are ~~alive~~ 5 years later. But when it is found early, 60% (60 in 100) patients are alive after 5 years.
2. A new blood test (called the ~~Early CDT~~ Lung Test) may help. This important study is looking at whether the blood test can find lung cancer even before people feel unwell.
3. The study is funded by the Scottish Government and ~~Oncoimmune~~, the company that developed the blood test. The study is led by the University of Dundee.
4. For the study to succeed, we need 10,000 people in Scotland to take part. By taking part you may benefit yourself - and you would be helping future generations.
5. We are inviting people in Tayside, Glasgow and surrounding areas - where lung cancer is more common. You are being invited because your age (50-75) or smoking (now or in the past) puts you at higher risk. We may also include people with a close relative who has had lung cancer.
6. Being invited does not mean that your GP thinks you have lung cancer, only that you may be at higher risk.
7. If you want to take part, you will first have a short appointment with a study nurse. Then, after joining the study half of those taking part will be put into the 'Test Group' and half into the 'Non-Test Group'. This is done by chance (like tossing a coin). The study has these two groups to find out how well the blood test detects lung cancer.
8. People in the 'Test Group' will have their blood tested. If your blood test is positive, you are at higher risk of getting lung cancer. You would have an X-ray and lung scans over the next 2 years and may be asked to fill in some short surveys. If needed, you would be referred for treatment. If your blood test is negative, you are at lower risk. These people may be asked to fill in some short surveys over a year.
9. People in the 'Non-Test Group' may be asked to fill in some short surveys over a year.
10. All those taking part will contribute to the study's success, whether in the 'Non-Test Group' or 'Test Group'. They will all be followed up by their medical records for 10 years.

The enclosed booklet contains full details of the ECLS study.



Please fill in the reply slip (over) and post it in the FREEPOST envelope.

