# SYSTEMATIC TECHNIQUES FOR ASSISTING RECRUITMENT TO TRIALS (START)

a study of the feasibility of testing recruitment interventions by nesting across multiple trials in primary care and community settings

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# Contents



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Title

Systematic Techniques for Assisting Recruitment to Trials (START): a study of the feasibility of testing recruitment interventions by nesting across multiple trials in primary care and community settings

## Summary

Our aim is to improve the evidence-base concerning recruitment to trials, enhance recruitment rates and make research more accessible to the public.

Randomised controlled trials (RCTs) are critical to evidence-based practice, but recruitment is often problematic, with little rigorous evidence to assist research teams in recruitment and retention of participants. Without the development of reliable methods, the policy goal of improving health and wealth through research will be hard to realise.

A robust test of the effectiveness of a recruitment method is an RCT comparing one method with an alternative, nested in a host trial. Such nested studies are rare, delivered in an ad hoc way, and almost always tested in the context of a single host trial, limiting their utility.

Our vision is to develop a methodology to develop, deploy and test recruitment interventions nested within ongoing host RCTs, to rapidly and systematically improve the evidence base. To achieve this, we propose a programme of three interrelated work packages:

(a) Methodology – to develop methods for design and analysis of nested recruitment studies

(b) Interventions – to develop effective and useful recruitment interventions

(c) Implementation – to recruit host RCTs and test interventions through nested studies

## Importance

Worldwide, there is a desire to improve health and wealth through research. In the United Kingdom, the National Institute for Health Research (NIHR) vision sees 'more patients and health professionals participating in health research'.[1] Biosciences are now a leading source of UK revenue and making up the UK share of the expanding clinical trials effort is a national priority.

Fundamental to health research is the testing of interventions through randomised controlled trials (RCTs). Achieving high professional and patient participation in RCTs has traditionally been difficult. Published data show that a minority of RCTs recruit successfully in terms of numbers and timeline.[2,3] Recruitment problems reduce the total recruited sample (limiting statistical power and internal validity), and the proportion of eligible participants who are recruited (limiting external validity). The impact of research is reduced if it is delayed or its rigour compromised by recruitment problems.

A recent review outlined three core research areas relating to recruitment: methodological innovation, infrastructure and stakeholder engagement with research.[4] The UK has made major investments in infrastructure to support delivery of research, which has improved the process of recruitment (such as approvals and training for researchers) and outcomes (absolute numbers of patient recruited).[5] However, this infrastructure has not been based on rigorous evidence of the effectiveness of particular models or methods of recruitment, and many recruitment challenges remain. For example, additional resources and support through clinical studies officers means that

RCTs in primary care can now recruit from a large number of individual practices and can therefore increase the *absolute* numbers of patients who are invited. However, the *proportion* of patients taking part often remains low. For example, RCTs in depression in the United Kingdom often report that 10-15% of potentially eligible patients respond to an invitation to 'opt-in' to research. Doubts about the rigour and generalisability of research conducted on such highly selected samples remain.

In previous work we identified four phases usually involved in recruitment to primary care studies.[4] First, clinical teams must agree to participate (stage 1). Many trials of acute conditions require practitioners to recruit patients during consultations (stage 2), but initial enthusiasm for a study often fails to translate into recruitment.[6] Studies involving long-term conditions allow patients identified from clinical records to be approached outside the consultation, but this raises new issues about efficient and ethical ways to approach and motivate patients who are not directly accessing care. Once the patient has been invited, they must then agree to participate (stage 3), and agree to continue in the study over the longer term (stage 4). At each stage there are factors which may facilitate or block recruitment: identifying these provides targets for recruitment interventions.

Qualitative researchers have explored the recruitment process in depth,[7,8] highlighting the importance of gaining participants' attention, so that they consider devoting time to a study; that research teams are perceived as trustworthy, and that participating should be seen as potentially beneficial, or at least not harmful. Developing rapport and valuing participants' contributions are also important.[9] Some authors advocate a marketing approach to planning recruitment, building 'brand values', 'product and market planning', 'making the sale' and 'maintaining engagement'.[10]

Although insights can be gained into barriers to recruitment through qualitative case studies[11] and research on hypothetical situations,[12] the most robust test of the effectiveness of a recruitment method is an RCT comparing one method with an alternative, nested in a real trial. By nesting, we mean that patients being recruited to an ongoing RCT might be randomised to two different methods of recruitment. For example, Junghans randomly allocated patients to an opt-in (where they were asked to actively signal willingness to participate in research) or opt-out method (where they were contacted repeatedly unless they stated unwillingness to participate).[13] Such studies allow an unbiased and externally valid assessment of the effectiveness of a recruitment intervention.

The acceptance of the RCT as the bedrock of outcomes research has led to a vast number of trials conducted (635167 records on CENTRAL as of October 2010). Given the size of this potential platform for recruitment studies, and the consensus among the research community concerning the challenge of recruitment, it is surprising that nested trials of recruitment interventions remain so rare. Two recent systematic reviews (including a Cochrane review) identified only 14 nested studies in real trials[14] and 27 overall.[15] The Cochrane review concluded that 'it would be better if more researchers included an evaluation of recruitment strategies in real trials'.[15] The failure to grasp this opportunity means that recruitment for science is not underpinned by a science of recruitment.

Although a general increase in the number of nested trials would be welcome, the challenge is to develop a more ambitious approach, to systematically extend the evidence base. The vision is to embed the routine use of nested recruitment trials in the research funding process, so that such trials are an accepted part of RCT delivery, adopted by a significant proportion of RCTs as part of a endeavour across the research community. This would be akin to the way in which patient and public involvement has become routinely embedded in health research. Achieving this would not only rapidly develop the evidence base, it would also have the advantage of allowing recruitment interventions to be tested across multiple trials, increasing generalisability.

Qualitative work conducted by the applicants with key stakeholder groups (principal investigators, research managers, ethical committee chairs and funding representatives) has highlighted key challenges to nested studies.[16] Although respondents recognized the case for nested studies, their enthusiasm was tempered by the challenges of implementation. Perceived challenges for host studies included increased management burden; compatibility between the host and nested study; and the impact of the nested study on trial design and relationships with collaborators. For nested recruitment studies, there were concerns that host investigators might have strong preferences, limiting the nested study investigators' control over their research. Overall, research on recruitment was welcomed in principle, but raised issues over control. To address this concern, it is important to align the interests of all parties. These findings will be invaluable in informing this work.

The START study is designed to develop the conceptual, methodological and logistical framework to improve recruitment through nesting RCTs of recruitment interventions, and to assess feasibility by developing a small number of recruitment interventions and testing them across multiple host RCTs. At the completion of START, we will have rigorously tested 2 potential interventions for adoption into routine practice, and provided the framework to make delivery of nested recruitment RCTs a routine activity. This will assist the rapid development of recruitment to meet policy goals.[17]

If this feasibility study is successful, we would seek further sustainability funding from the NIHR, research networks and other funders to maintain START in the long-term. Although our initial project is focussed on primary care and the community (which is where our expertise lies), the general methods will be relevant across settings. Our aim is to help the UK research community achieve the goals outlined by the NIHR of 'more patients and health professionals participating in health research'.

## Scientific potential

### *People and track record*

The research derives from a programme of development work conducted by the NIHR School for Primary Care Research (www.nspcr.ac.uk/), a partnership between eight primary care research centres in England (Birmingham, Nottingham, Keele, Southampton, Manchester, UCL, Oxford and Bristol). The School has supported a Recruitment and Retention Methods group since its inception. The group has published a series of papers on recruitment issues,[4,18] including a qualitative study of stakeholder views of nested recruitment interventions,[16] and has worked in partnership with the NIHR Primary Care Research Network, which has enabled the programme to draw on the expertise of network staff in developing interventions and applying them in primary care. The current START research team represents members of these groups, together with a range of additional experts who provide the necessary support for this multidisciplinary endeavour.

All applicants have extensive experience in the delivery of applied health research, including RCTs, theoretical and empirical analyses of recruitment issues, development of interventions, and implementation of change in health service delivery.

The research group has both academic and practical expertise in health services research in general practice and primary care (PB, JG, PW, SE, DC, AK, CS), systematic review and evidence synthesis (PB, JG, DT, ST, PK), qualitative research (AK, JG), statistics (SE, DT), methodology (SE, DT), translational research (DC) and economics (DT). We also have collaborators from the commercial trials sector (KH) to ensure that the benefits of START are shared with commercial research, as well as collaborative agreements with experts in patient and public involvement research who will assist us with the development of the interventions (LL).

The research team has an extensive publication record. Grants held include core funding such as the NIHR School, together with grants from the NIHR HTA programme, MRC (trials and methodology), NIHR Programme grants and the Department of Health Policy Research Programme.

### *Environment*

The START feasibility study represents a collaboration between multiple academic departments (through the NIHR School for Primary Care Research) and the Primary Care Research Network (www.ukcrn.org.uk/index/networks/primarycare.html). This collaboration will provide the necessary platform for translating research on recruitment methods into routine delivery of research in the NHS. The START team also has links to relevant trials units in the United Kingdom to further support recruitment to the study. The project will be run from the Health Sciences Research Group, School of Community Based Medicine (www.medicine.manchester.ac.uk/research/groups/healthsciences/). Health Sciences has been identified as a strategic priority for the University of Manchester and the group has significant expertise in the design and delivery of primary care and community based trials. The RAE results classified 80% of Primary Care's research in each of the two top international categories with 40% rated 4* (world leading) and 40% 3* internationally excellent.

### *Research plans*

Our long-term aim is to improve the evidence-base concerning recruitment to trials, and thus enhance recruitment rates and make research more accessible to the public.

The aim of the START project is to develop a methodological framework and process of implementation for developing and testing recruitment interventions within ongoing host RCTs in primary care and community settings. To achieve this, we propose three work packages:

1) Methodology – we will develop methods for design and analysis of nested studies
2) Interventions – we will develop recruitment interventions, working closely with patients and professionals
3) Implementation – we will recruit principal investigators of potential host RCTs through UK CRC Registered Clinical Trials Units, NIHR Research Networks, and relevant funding bodies, negotiate the introduction of our recruitment interventions, record the process of implementation and test their effects on recruitment.

## Work package 1: Methodology (months 1-9)

We will develop a methodological and analytic framework for the evaluation of nested recruitment interventions. We will review the design issues and statistical methods specific to studies of nested recruitment interventions (e.g. where the unit of analysis in host and nested studies differ). We will extend the analytic framework to consider issues such as the analysis of the effects of recruitment interventions across different studies, sites and practices. We will also develop a framework for the measurement of the various outcomes of recruitment interventions, including patient satisfaction (e.g. knowledge of the recruitment process, measures of informed consent; and anxiety); numbers of patients recruited; rate of recruitment; rate of retention; sensitivity/specificity of recruitment methods in terms of proportions of eligible/ineligible patients identified; and the costing of recruitment interventions and the recruitment process. The methodological review will be supported by structured searches of the literature, complemented by analysis of the methods used in published trials identified by the earlier reviews. [14,15,19-21]

## Work package 2: Developing Interventions (months 1-12)

We have based our recruitment interventions on our knowledge of the recruitment process and key barriers,[4] gaps in research evidence identified in systematic reviews,[14,15] a qualitiative study of stakeholder perspectives,[18] a researcher workshop conducted at the Society for Academic Primary Care Annual Scientific Meeting, St Andrews (July 2009) and a patient workshop conducted at the Barts & the London Interested Patients Group (September 2009).

### *Intervention 1 - Enhanced information sheets*

Ethics committees rightly want to ensure that participants receive appropriate information and are able to provide fully informed consent. However, long and complex information sheets may impact negatively on recruitment if they are unattractive, confusing or raise inappropriate levels of anxiety. This is especially critical when patients are initially approached by a letter from their health professional, which occurs in a significant proportion of trials in primary care and community settings, especially in patients with long-term conditions. A systematic review has identified evidence that involving consumers in the development of patient information results in higher relevance and readability, without increasing anxiety.[22] To test this approach, a modified version of the study information sheet would be prepared for each host RCT by a small group, including patient and ethical committee representatives, followed by ehancement of the sheet's readability via expertise in writing for patients and its presentation via graphic design.[23] The revision would then be tested using the principles of *user testing*,[24,25] where the ability of patients to locate and understand key pieces of information is evaluated objectively to provide an assessment of the ability of the sheet to inform. Patients in each trial would then be randomised to either the original or modified information sheet.

### *Intervention 2 - Multimedia concerning participation in research*

At present most information about trial participation is presented in written form, but this does not necessarily represent the best way to encourage patients to consider trial participation, to fully

consider the advantages and disadvantages, and to hear the viewpoints of other patients concerning their experience. We therefore propose to develop and test the impact of access to a generic module on trial participation developed in conjunction with *healthtalkonline* (www.healthtalkonline.org/). [26] This is a unique database of patient experiences developed through qualitative research with patients. Most of the content is about living with various conditions, but recent additions have included modules on medical research. We will work with the *healthtalkonline* team to select video materials from their archive for our purposes. The content would be designed to be generic, although we will explore the feasibility of the addition of study-specific content. We would inform the development of the resource by drawing on relevant theoretical and empirical work about patient decision-making generally[27,28] and in trials.[29,30]

*Intervention development process*

We will create a project subgroup for each intervention, including academic members of the START programme team, staff from PCRN involved in set-up and delivery of primary care trials, lay members of the START group (see 6 'Public engagement in science') and subject experts (see collaborators in 3.1 'People and track record'). The project subgroups will develop interventions that are suitable for delivery across multiple 'host' trials. The precise nature of the development process will vary according to the intervention, but will follow current best practice in the development of interventions, drawing on theory and published evidence, and developing interventions with patient and practitioner involvement, to ensure feasibility and acceptability.

## Work package: 3 Implementation and analysis (months 13-33)

We will recruit a cohort of host RCTs for nested studies of our recruitment interventions via research networks and clinical trials units and assess the effects of our interventions on outcomes (in terms of recruitment indices developed in work package 1) across multiple trials.

## Recruitment

Our long-term aim is to embed the concept of nested recruitment studies into the funding and start up process of RCTs in all health care settings, and in public and commerically funded trials, in order to ensure that delivery of nested studies is a routine part of the delivery of RCTs in the United Kingdom. This would require working with major funders (MRC, NIHR HTA, NIHR ETSCC and NIHR Central Commissioning Facility) and Trials Units to identify and recruit host RCTs and deliver nested studies on a rolling basis. However, our immediate aim is to conduct a feasibility study using the recruitment interventions developed in work package 2, tested in host RCTs currently in the set up phase and recruiting from primary care and community settings.

We will recruit 5-6 RCTs for each intervention developed in work package 2 for the feasibility study. To participate, RCTs will have to meet the following criteria:

1) seeking to apply for ethics permission at the beginning of the START trial
2) recruiting from primary care or community settings and involving recruitment procedures amenable to the interventions from work package 2
3) agreement in principle to take part in START, randomise and deliver the interventions according to a protocol and share data on recruitment with the START team as part of an ongoing collaboration.

It is not known exactly how many potentially eligible RCTs will be available at the start of the project. We will seek to recruit from a number of sources, including the trials currently being delivered within the UK CRC Registered Clinical Trials Units, the Primary Care Research Network, and through funders. For example, discussions with UK CRC Registered Clinical Trials Units indicate that most have 4-5 trials at the stage prior to recruitment (where it would be optimal to begin involvement in START), while the Primary Care Research Network is in contact with over 30 trials in the set up phase. We have been in contact with a range of units and have preliminary agreement from York, Dundee, Aberdeen, and Bristol, as well as the Primary Care Research Network.

The aim will be to recruit a sample of RCTs (see 'Sample Size' below) which recruit patients using comparable procedures (e.g. approaching patients from the disease register) but do so in relation to different clinical and health service areas and in different contexts. We will negotiate with the principal investigator in each host RCT, to test the acceptability of nesting a recruitment study. We do not expect or require all eligible RCTs to participate. We will record the process of negotiation and reasons for participation or non-participation.

## Outcomes

The study is designed to provide two estimates relating to recruitment interventions:

1) the effectiveness of recruitment interventions in the context of a single host RCT
2) a measure of the variability in effectiveness across multiple host RCTs.

A large number of RCTs in primary care and community settings recruit patients with existing health conditions from registers in primary care. For the purposes of the power analysis, we assume that the primary outcome is the proportion of potentially eligible patients who agree to participate following an invitation. Therefore, the denominator will be the number of patients who are initially invited following screening. It should be noted that this is a larger number than that required for power for an analysis of clinical outcomes within individual trials. For example, a trial which is seeking to recruit 300 patients will need to approach approximately 600-1500 depending on the overall uptake rate. It is the latter, higher figure which is of relevance for the power analysis of START in these contexts. It is likely that if studies are properly powered for primary outcomes in recruited patients, they will have necessary power to assess outcomes comparing proportions of recruited and non-recruited patients in the wider sample who are approached to take part.

To provide a conservative sample size estimation, we assume a base response rate of 50% to invitations (although rates in many studies will be significantly lower). We define a significant improvement in recruitment rate as an increase in response of 10%. If individual patients are

randomized (for example, to a conventional or modified information sheet), 400 patients per arm would be required to provide 80% power to detect a 10% difference (alpha 0.05). We will thus restrict START to RCTs that involve at least this level of recruitment, although we will not exclude studies where interventions can be introduced after recruitment has begun, or where recruitment continues beyond the end of the START study.

In terms of variability across host trials, we will explore this in a meta-analytic framework. The proportions of invited patients recruited into each trial will be entered into a meta-analysis, and the heterogeneity of the intervention effect across trials will be assessed using the $I^2$ statistic. If significant heterogeneity is demonstrated, we will explore differences between trials that might explain that variation. The power of any such analyses will be limited because of the small number of trials, but we will explore this issue qualitatively using data collected on the trial, the patient population and the context of the study.

Where possible, we will work with trials to include additional outcome measures, such as satisfaction with information, understanding of the trial and anxiety.

## Timetable

We will undertake the review work for workpackage one in the first 9 months, simultaneously seeking relevant permissions and identifying and recruiting relevant trials. We will complete our intervention development in the 3 months after trials have been recruited, so we can ensure that host trial principal investigators can contribute to intervention design where possible. We will aim deploy our interventions in host trials during months 13-33. This is likely to encompass the entire recruitment period for some trials, although it is possible that the interventions will be deployed after the start of the trial in some cases, and that our project will finish before the end of the trial in others. We will be unable to collect extensive data on retention as many trials will collect follow up data after START has ended, although we expect that such data can be made available through other sources such as the Cochrane review on recruitment interventions[15] (applicant ST is the lead author on that review). We have 3 months for final analysis and report writing.

## Ethics and research governance

The use of nested trials does raise a number of ethical issues, including the issue of whether patients should be informed about their inclusion in a nested trial, and the potential for inequitable treatment if patients are approached and consented differently. Many of these issues were raised in our earlier qualitative work.[16] The procedures to be used in our nested trials would have to be agreed with relevant research ethics committees in line with current regulatory procedures in the United Kingdom, either as part of the first ethics application or as an amendment after the initial application made by the host trial. There is the possibility that individual committees will reject applications to 'nest' trials of recruitment procedures, although our study suggests that the risk is relatively low.[16]

## Data preservation for sharing

Data on recruitment from individual trials will remain the property of the trial team or other organisation depending on existing contractual arrangements. Access to the data from individual studies for the purposes of START will be gained via signed data-sharing agreements in line with the 'Principles for access to, and use of, MRC funded research Data' report, negotiated at the outset. All data provided to the START team for analysis will be anonymised by removal of personal identifiers. All analyses conducted for START and publications arising from the study will be shared among the contributing teams, with agreements about authorship and dissemination of results from the individual studies and the combined dataset. Ongoing access to the data would depend on agreement with the individual trial teams but it is likely that summary data on recruitment rates and other outcomes would be made available through open access sources such as the Cochrane review on recruitment interventions,[15] since all studies successfully completed through START are likely to meet the criteria for the review. Subject to the consent of the providers of the other datasets, the corresponding primary data and relevant metadata will be made available in a fully anonymised format suitable for release in the public domain.

## Public engagement in science

Patient and public involvement is a fundamental part of the drive to improve recruitment to trials and has been an important part of the development work preceding this bid. Members of the Recruitment and Retention Methods Group met with 10 members of the NIHR Biomedical Research Unit Interested Patients Group at Barts & The London on 18th September 2009. Patients advised on the advantages and disadvantages of particular recruitment interventions, which shaped the ideas for the interventions in this proposal. To ensure ongoing and substantive patient and public involvement in START, we will draw on the following sources:

(a) the PRIMER group at the NIHR School for Primary Care Research (www.nspcr.ac.uk)

(b) lay members of the PCRN East of England Management Group

(c) The NIHR BRU Interested Patients Group at Barts & The London.

Two patient representatives will be involved in the START project management group, and we will also seek to ensure that at least 1 representative is attached to each intervention development group. To ensure that patient and public involvement is achieved at all stages of the research programme (with a special focus on the development of patient-oriented interventions as part of work package 2), we will include funds for travel and reimbursement of time (in line with INVOLVE recommendations - http://www.invo.org.uk/pdfs/PaymentGuideWEB240510.pdf).

## Exploitation and dissemination

We will publish results in peer-reviewed health services research and methodological journals, and disseminate our work through attendance at conferences including those conducted by NIHR Networks. Through our previous work in the National Primary Care Research and Development Centre (www.npcrdc.ac.uk), we have extensive experience of providing useful and practical guidance in the form of accessible handbooks, and we will explore the development of web based dissemination of guidance on our interventions should they prove successful. If the project proves feasible, we will also seek further funding from and collaboration with funding bodies to continue the START initiative in the longer term. We have already begun discussions with the NIHR HTA programme use around of their trials portfolio for host study recruitment (personal correspondence Andrew Cook, NIHR Evaluations Trials and Studies Co-ordinating Centre Wessex Institute).

# Reference list


1 Department of Health. *Best Research for Best Health - a new national health research strategy.* London. Department of Health, 2006.

2 McDonald A, Knight R, Campbell M, et al. What influences recruitment to randomised controlled trials? A review of trials funded by two UK funding agencies. *Trials* 2006;**7**:9

3 Bower P, Wilson S, Mathers N. How often do UK primary care trials face recruitment delays? *Fam Pract* 2007;**24**:601-603.

4 Bower P, Wallace P, Ward E, et al. Improving recruitment to health research in primary care. *Fam Pract* 2009;**26**:391-397.

5 Department of Health. *Embedding Health Research (National Institute for Health Research Annual Report 2009/10).* London. Department of Health, 2010.

6 Wilson S, Delaney B, Roalfe A, et al. Randomised controlled trials in primary care: case study. *BMJ* 2000;**321**:24-7.

7 Hummers-Pradier E, Scheidt-Naveb C, Martin H et al. Simply no time? Barriers to GPs' participation in primary health care research. *Fam Pract* 2008;**25**:105-112.

8 Salmon P, Peters S, Rogers A, et al. Peering through the barriers in GPs' explanations for declining to participate in research: the role of professional autonomy and the economy of time. *Fam Pract* 2007;**24**:269-275.

9 Feldman M, Bell J, Berger M. *Gaining Access*. Walnut Creek, CA: AltaMira Press, 2003.

10 Campbell M, Snowdon C, Francis C, et al. Recruitment to randomised trials: strategies for trial enrolment and participation study. *Health Technol Assess* 2007;**11 (48)**:

11 Bell-Syer S, Klaber-Moffett J. Recruiting patients to randomized trials in primary care: principles and case study. *Fam Pract* 2000;**17**:187-191.

12 Llewellyn-Thomas H, McGreal M, Thiel E. Cancer patients decision making and trial-entry preferences: the effects of framing information about short-term toxicity and long-term survival. *Med Decis Making* 2010;**15**:4-12.

13 Junghans C, Feder G, Hemingway H, et al. Recruiting patients to medical research: double blind randomised trial of "opt-in" versus "opt-out" strategies. *BMJ* 2005;**331**:940

14 Watson J, Torgerson D. Increasing recruitment to randomised trials: a review of randomised controlled trials. *BMC Med Res Methodol* 2006;**6**:

15 Treweek S, Mitchell E, PitKethly M, et al. Strategies to improve recruitment to randomised controlled trials. *Cochrane Database of Systematic Reviews* 2010;**Issue 1 Art. No.:MR000013. DOI: 10.1002/14651858.MR000013.pub4**:

16 Graffy J, Bower P, Ward E, 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* 2010;**10**:

17 Department of Health. *Equity and excellence: liberating the NHS.* London. The Stationary Office, 2010.

18 Graffy J, Grant J, Boase S, et al. UK research staff perspectives on improving recruitment and retention to primary care research; nominal group exercise. *Fam Pract* 2009;**26**:48-55.

19 Rendell J, Merritt R, Geddes J. Incentives and disincentives to participation by clinicians in randomised controlled trials. *Cochrane Database of Systematic Reviews* 2007;**Issue 2. Art. No.: MR000021. DOI: 10.1002/14651858.MR000021.pub3.**:

20 Raftery J, Bryant J, Powell J, Kerr C, Hawker S. Payment to healthcare professionals for patient recruitment to trials: systematic review and qualitative study. *Health Technol Assess* 2008;**12 (10)**:

21 Bryant J, Powell J. Payment to healthcare professionals for patient recruitment to trials: systematic review. *BMJ* 2005;**331**:1377-1378.

22 Nilsen E, Myrhaug H, Johansen M et al. Methods of consumer involvement in developing healthcare policy and research, clinical practice guidelines and patient information material. *Cochrane Database of Systematic Reviews* 2006;Art. No.: CD004563. DOI: 10.1002/14651858.CD004563.pub2.

23 Raynor T, Dickinson D. Key principles to guide development of consumer medicine information - content analysis of information design texts. *Annals of Pharmacotherapy* 2010;**45**:DOI 10.1345/aph.1L522

24 Knapp P, Raynor D, Silcock J, Parkinson B. Performance-based readability testing of participant information for a Phase 3 IVF trial. *Trials* 2009;**10**:

25 Knapp P, Raynor D, Silcock J, Parkinson B. Performance-based readability testing of participant materials for a phase I trial: TGN1412. *Journal of Medical Ethics* 2009;**35**:573-578.

26 Ziebland S, McPherson A. Making sense of qualitative data analysis: an introduction with illustrations from DIPEx (personal experiences of health and illness). *Med Educ* 2006;**40**:405-414.

27 Conner M, Norman P. Predicting health behaviour: a social cognition approach. In: M Conner, P Norman, eds. *Predicting Health Behaviour: Research and Practice with Social Cognition Models*. Maidenhead: Open University Press, 2005;1-27.

28 Michie S, Johnston M, Abraham C, et al. Making psychological theory useful for implementing evidence-based practice: a consensus approach. *Qual Saf Health Care* 2005;**14**:26-33.

29 Llewellyn-Thomas H, McGreal M, Thiel E et al. Patients' willingness to enter clinical trials: measuring the association with perceived benefit and preference for decision participation. *Soc Sci Med* 1991;**32**:35-42.

30 Bower P, King M, Nazareth I et al. Patient preferences in randomised controlled trials: conceptual framework and implications for research. *Soc Sci Med* 2005;**61**:685-695.