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Improving the recruitment activity of clinicians in randomised controlled trials - a systematic review

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ABSTRACT

Background and objectives

Poor recruitment to randomised controlled trials (RCTs) is a widespread problem. Provision of interventions aimed at supporting or incentivising clinicians may improve recruitment to RCTs. The objective of this systematic review was to quantify the effects of strategies aimed at improving the recruitment activity of clinicians in RCTs, complemented with a synthesis of qualitative evidence related to clinicians' attitudes towards recruiting to RCTs.

Methods

Systematic searches were carried out in the electronic databases: The Cochrane Library, Ovid MEDLINE, Ovid EMBASE, Ovid PsycINFO, Ebsco CINAHL, Index to Theses and Open SIGLE from 2001 to March 2011. Additional studies were identified through citation searches of included reports.

Quantitative studies were included if they evaluated interventions aimed at improving the recruitment activity of clinicians, or compared recruitment by different groups of clinicians. Information about study design, participants, interventions, outcomes and host RCT was extracted by one researcher and checked by another. Studies that met the inclusion criteria were assessed for quality using a standardised tool.

Qualitative studies were included if they investigated clinicians' attitudes to recruitment to RCTs. All results/findings were extracted and content analysis was carried out. Overarching themes were abstracted, followed by a metasummary analysis

Results

Eight quantitative reports were indentified describing four interventions and a comparison of recruiting-clinicians. Effective interventions included: the use of qualitative research to identify and overcome barriers to recruitment; reduction of the clinical workload associated with participation in RCTs; and the provision of extra training and protected research time.

Eleven qualitative reports were identified and eight themes were abstracted from the data: understanding of research; communication; perceived patient barriers; patient-clinician relationship; effect on patients; effect on clinical practice; individual benefits for clinicians; and methods associated with successful recruitment. Metasummary analysis identified the most frequently reported sub-themes to be: difficulty communicating trial methods; poor understanding of research; and priority given to patient wellbeing.

Conclusions

Few high quality trials were identified that tested interventions to improve clinicians' recruitment activity in RCTs. The most promising intervention was the use of qualitative methods to identify and overcome barriers to clinician recruitment activity. More good quality studies of interventions are needed to add to the evidence base.

The metasummary of qualitative findings identified understanding and communicating RCT methods as a key target for future interventions to improve recruitment. Reinforcement of the potential benefits, both for clinicians and their patients, could also be a successful factor in improving recruitment. A bias was found toward investigating barriers to recruitment, so future work should also encompass a focus on successfully recruiting trials.

ARTICLE SUMMARY

Article focus

A systematic review to identify and synthesise both evidence of effective interventions aimed at improving clinician recruitment activity in RCTs, and evidence of clinicians perspectives towards recruiting to RCTs.

Key messages

Evidence based recruitment interventions aimed at supporting/incentivising clinicians are necessary for future RCTs to recruit successfully. However, evidence of successful interventions is currently limited, and interventions are being used that have no evidential grounding. The most promising intervention identified by this review was the use of qualitative methods embedded in host RCTs to define appropriate methods, targeted at clinicians, relevant to the context of the individual studies.

The review of qualitative evidence identified a number of themes relating to clinicians' attitudes towards recruitment to RCTs. The metasummary isolated targets for future interventions aimed at improving clinicians' recruitment activity. Of particular interest were: communication; education to remove misunderstanding of trial methods; and reinforcement of the potential benefits of RCTs, both for clinicians and their patients.

Strengths and limitations of this study

Strengths

This review encompasses both quantitative and qualitative evidence regarding clinician involvement in recruiting to RCTs. As such, it highlights the available evidence of successful interventions, and also targets for the design of future interventions.

Qualitative data was managed and synthesised according to a set methodology and is therefore a step beyond simple narrative review. Qualitative metasummary can be the final product of a synthesis project, or used as the initial step in a metasynthesis project. Qualitative metasummary has been defined as "an approach for quantitatively oriented aggregating qualitative findings that are themselves topical or thematic summaries or surveys of data".

Limitations

The quality of evidence varied, and the review includes a wide range of study designs, making comparisons of interventions difficult. However, it is clear that RCTs of trial recruitment interventions are difficult to carry out, so other study designs are commonly used. These designs should not be ignored.

Methodological challenges included: designing a broad search to encompass qualitative and quantitative research; quality assessment of various study designs by one set of criteria; standardising the data extraction and synthesis of qualitative evidence. There are no set guidelines regarding the synthesis of qualitative and quantitative evidence, but it is clear that for many review questions limiting the included study designs would lead to empty reviews.

INTRODUCTION

When evaluating the effectiveness and safety of healthcare interventions, randomised controlled trials (RCTs) are seen as the gold standard research design. It is important that RCTs recruit their target number of participants in order to avoid being underpowered, particularly as a lack of statistical power may lead to the reporting of clinically important effects as statistically non-significant. Statistically non-significant findings can increase the risk that potentially effective interventions may be abandoned before their true value is established, or that there will be a delay in demonstrating their value while more trials are carried out. For example, Collins *et al* calculated that there were as many as 10,000 unnecessary deaths in the USA due to delays in recruitment to a RCT of streptokinase in acute myocardial infarction[1]. Many RCTs are abandoned or do not produce unequivocal evidence due to recruitment difficulties, which also means that the resources spent for setting up the RCT have not been put to their best use.

Studies that fail to recruit their target number of participants also raise ethical problems, particularly when clinicians have exposed participants to interventions with uncertain benefit and, at the end of the trial, are still unable to determine whether the intervention is clinically effective[2]. There are also ethical implications associated with recruiting patients to a trial in which they invest their time, only to be told that the trial will not go ahead. There is the additional financial impact of trials that fail to recruit successfully, or in a timely manner. It has been hypothesised that slow acquisition of trial evidence due to poor recruitment may have reduced investment in the conduct of RCTs by funding agencies, who may prefer to invest in less reliable, but more rapid approaches[3]. Delayed or extended trials cost more, leading to fewer trials being carried out from the limited funds available.

There are a number of published studies that highlight how common recruitment problems are in healthcare RCTs[4-11]. It is likely that 50% of RCTs fail to recruit to target, and that only 50% of those that successfully recruit do so in a timely manner. Table one highlights the problem and the lack of any real improvement over time.

{INSERT TABLE 1 HERE}

The reasons for poor or slow recruitment to RCTs can be found at various levels: the patient, the recruiting clinician, the trial centre, the trial organisation and the trial design[12]. Considerable efforts have been made to understand and incentivise the participation of subjects in trials[2,3,13-16]; but less has been done to investigate interventions that could improve the recruitment activity of clinicians[10,12]. The clinicians' role is clearly important in the recruitment process for RCTs, as patients can only consider taking part when asked to do so. Maintaining recruitment activity over time is also important as it has been shown that enthusiasm for recruiting subjects to RCTs can fade quickly, leading to studies that fail to recruit to target, or which suffer significant loss to follow up due to difficulties in participant retention for the required study period.

The objective of this systematic review was to evaluate interventions aimed at improving the activity of recruiting clinicians in RCTs, and to identify possible targets for future interventions based on clinicians' attitudes to recruitment to RCTs.

METHODS

Search strategy and study identification

Systematic searches were carried out for the period January 2001 to March 2011 in the following databases: the Cochrane Library, Ovid MEDLINE, Ovid EMBASE, Ebsco CINAHL, Ovid PsycINFO, Index to Theses (UK and Ireland), Open SIGLE.

Search terms related to clinicians, recruitment and RCTs were included as keywords to maximise the volume of literature reviewed. An example search strategy is shown in Appendix 1. No methodological filters were used so that both qualitative and quantitative studies would be returned by the searches.

To determine inclusion/exclusion criteria for studies the PICOS framework was used for quantitative studies and the SPICE framework for qualitative studies, as shown in Box 1. Studies were assessed against the pre-specified inclusion and exclusion criteria. Following removal of duplicate reports, a first decision on inclusion/exclusion was made based on study titles and abstracts. For those studies identified in the first stage and for studies where a definite decision could not be made based on title/abstract alone, the full paper was obtained for assessment. In the second stage full papers were assessed against the full inclusion/exclusion criteria. Studies were also identified by performing citation searches of included studies.

Searches and study identification were carried out by one researcher (BF) and checked by a second (AG).

{INSERT FIGURE 1 HERE}

Quality assessment

Quality assessment of quantitative studies was performed using the Effective Public Health Practice Project (EPHPP) quality assessment tool for quantitative studies. This instrument was chosen as it enables different methods to be assessed using the same tool, and was identified as one of only six judged to be suitable for systematic reviews assessing multiple methods[17]. Using the EPHPP tool, studies were assessed against six criteria: selection bias, design, confounders, blinding, data collection methods, withdrawals and dropouts.

Quality assessment of qualitative papers was carried out in accordance with the Critical Appraisal Skills Programme (CASP) qualitative research appraisal tool, which covered rigour, key research methods used, credibility and relevance.

Quality assessment was performed by two researchers independently (BF/AG), and the results were compared for consistency. A consensus decision was made in the case of any disagreement.

No studies were rejected as a result of quality assessment, however quality was taken into account when discussing the results.

Data extraction and analysis

For quantitative studies, data relating to study design, country, setting (i.e. nature of the RCT being recruited to), population, statistical methods, description of intervention and author conclusions were extracted using a piloted data extraction form. Trials were grouped according to intervention and, if binary data was reported (i.e. participants recruited/participants not recruited), then risk ratios were calculated.

For qualitative studies, data extraction was first carried out using the Quality Assessment and Review Instrument (QARI) data extraction tool designed by the Joanna Briggs Institute

(JBI) for Evidence Based Practice. This allowed broad themes to be identified in the included studies. Secondly, all text was extracted from sections labelled as 'results' or 'findings' in the included reports, according to the method suggested by Thomas and Harden [18]. The results were then entered into NVivo software for qualitative content analysis. Line-by-line coding of the extracted data was carried out and codes were organised into related areas in order to construct descriptive themes. Abstracted analytical themes were then created from which effect sizes could be calculated. Effect sizes were calculated by taking the number of studies that contained an abstracted finding and dividing this number by the total number of reports. A criticism of metasummary is that it may not be appropriate to apply numbers to qualitative data. However, quantitative categorisations such as small, medium and large are often used by researchers to "qualitize" data[19]. Effect sizes can be used to extract more meaning from abstracted findings. Qualitative studies "inherently imply a frequency of occurrence of an event sufficient to constitute a pattern or theme", and metasummary can be seen as the next step in this process, as well as helping to verify the presence of themes across studies[20].

Data extraction was carried out by one researcher (BF) and the results checked by a second (AG). Disagreements were resolved by discussion.

RESULTS

Study selection

296 abstracts were screened and 38 full text papers obtained for full assessment against the inclusion/exclusion criteria. Nineteen studies were included in the review (eight quantitative and eleven qualitative).

{INSERT FIGURE 2 HERE}

Study characteristics

{INSERT TABLE 2 HERE}

Of the eight included quantitative studies, three were RCTs[21,22,23], two were observational time series[24,25], two were before and after studies[26,27] and one was a case study with a comparison group[28]. Two studies compared trialists (nurses vs. surgeons; community vs. university medical practices)[21,28]. Two studies assessed the effect of extra involvement of trial coordinators with clinicians (extra communication; on-site initiation visits)[22,23]. One study assessed the effect of change to training and paying for protected research time on recruitment[27]. Two studies from the same authors used embedded qualitative methods to identify targets for improving recruitment[25,26]. One study assessed a complex multifaceted intervention[24]. All but one study investigated recruitment to cancer and chronic disease trials, and the majority took place in the UK (5 of 8).

Three reports all related to the same host RCT of prostate cancer treatment[21,25,26]. Donovan (2002 and 2009) reported the results of using qualitative methods to develop an intervention, in both the feasibility study before the main trial, and the main trial itself. Donovan (2003) compared using nurses and surgeons as recruiters in the same trial. For the purpose of this review these three studies were assessed separately.

{INSERT TABLE 3 HERE}

Of the eleven included qualitative studies nine used interviews (semi-structured; in-depth)[29,31,33-39], two used focus groups[30,32] and one study also analysed trial documents[39]. The methodology used was described as Grounded Theory in three studies[29,31,38], while it was not stated in eight. Thematic analysis (constant comparative; framework analysis) was the most common method of data analysis (nine studies)[29-31,33-34,36-39], with two studies using content analysis [35,39] and one conversation analysis[39]. Data analysis method was unclear in one of the included studies[32].

174 trialists were interviewed or involved in focus groups in total: 62 GPs, 30 community physicians, 16 paediatricians, 11 surgeons, 11 recruiters, 10 clinicians, 10 nurses, 5 trainees, 5 investigators, 4 trial staff, 4 hospital doctors, 2 clinical studies officers, 2 research associates and 2 care coordinators. A broad range of settings were covered by the included studies e.g. primary and secondary care trials; drug trials and pragmatic surgery trials; trials in mental health and cancer - etc.

Quality assessment

No studies were rejected on the basis of quality. Using the EPHPP quality assessment tool for quantitative studies: one study was characterised as strong, one as moderate, with the remaining studies classified as weak. Studies were shown to be particularly weak when reporting controlling for confounders and methods of data collection.

Overall, the qualitative studies assessed using the CASP checklist were found to be of good quality. Methodology and consideration of ethical issues were the two main areas where reporting was unclear.

A summary of the quality of the included studies is Appendix 2 and 3.

Results of quantitative studies

Comparing types of recruiters

Two studies compared the use of different groups of clinicians recruiting to RCTs. Donovan *et al* compared the effect of using nurses or urologic surgeons recruiting to a prostate cancer trial, using a RCT design[21]. The trial showed no difference in recruitment rate between the two groups (RR 0.94, 95% CI 0.76 to 1.17). The study also included an economic assessment that found nurses to be more cost effective recruiters than surgeons.

SSRTG (Submacular Surgery Trials Research Group) compared recruitment at university based and community based medical centres, in recruitment to three RCTs of intraocular surgery[28]. This was a case study with comparison groups. The study found no significant difference between the recruiters (mean number of subjects recruited per centre: university = 38.1, community = 37.3, *t* test p=0.93).

Greater contact between trial coordinator and clinicians/trial sites

Lienard *et al* used a RCT design to assess the impact of on-site monitoring visits on recruitment to a breast cancer RCT[23]. On-site monitoring visits had multiple purposes: to ensure the protection of patients' rights, to verify the accuracy of reported data, and to provide training to site personnel with regard to trial material and protocol. The study found that on-site monitoring visits had no significant effect on patient recruitment, reported as: centres recruiting at least one patient (RR 0.99, 95% CI 0.71 to 1.37); or total numbers of patients recruited (control 271, intervention 301, p>0.05). No differences were found between groups in quality or quantity of reported data, or patient follow up time.

Monaghan (2007) used a RCT to evaluate the effect of extra communication from central trial coordinators on recruitment to a diabetes RCT[22]. The intervention included: frequent e-mails; personalised mail-outs of league tables describing recruitment performance relative to other centres; certificates acknowledging achievement of recruitment milestones; and promotional materials related to the trial. The study found no significant effect of extra communication on median number of patients recruited (control 37.0, intervention 37.5, p=0.68), or median time to half recruitment target (control 4.4 months, intervention 5.8 months, p=0.08).

Use of qualitative research embedded in host RCT

Two studies investigated the use of qualitative methods embedded in a host trial. In both studies, qualitative methods (in depth interviews, audiotape recordings of recruitment appointments, study of trial documents) and analysis (content, thematic and conversation analysis) were used to assess aspects of the trials that were amenable to improvement; followed by the design and implementation of interventions to improve the recruitment activity of clinicians. Donovan *et al* (2002) reports the results of a feasibility study before the main trial (Donovan *et al* 2009)[25,26].

Donovan *et al* (2002) reported the results of an observational time series study investigating recruitment to a prostate cancer RCT[25]. Qualitative methods were used to elicit strategies which had the potential to improve recruitment. Strategies identified by qualitative methods included presentations of the study design and the implementation of a training programme delivered to clinicians. The intervention improved the proportion of eligible patients

consenting to randomisation (after 10 months RR 1.36, 95% CI 1.01 to 1.85), whilst there was no significant change in the proportion of randomised patients accepting allocation (after 10 months RR 0.90, 95% CI 0.70 to 1.15).

Donovan *et al* (2009) reported the results of the main trial[26]. Qualitative methods allowed a complex intervention to be developed which included: regular training for all staff involved in recruitment and initiation for new staff; centre reviews for underperformers; documents providing tips and advice; and personalised individual feedback to recruiters as required. The study reports the results of audits of two centres before and after the intervention (12 and 24 months post intervention). The results of the two centres are not pooled as interventions were tailored to each centre using qualitative research; therefore the intervention that the two centres received was different. The first centre showed a significant improvement in the proportion of eligible patients recruited at 12 months (RR 1.87, 95% CI 1.15 to 3.04) and 24 months (RR 1.79, 95% CI 1.07 to 2.99) post intervention, and no significant change in the proportion of randomised patients accepting allocation (12 months RR 1.22, 95% CI 0.62 to 2.39; 24 months RR 1.43, 95% CI 0.75 to 2.71). The second centre also showed a significant improvement in the proportion of eligible patients recruited at 12 months (RR 1.55, 95% CI 1.11 to 2.16) and no change at 24 months (RR 1.36, 95% CI 0.92 to 2.02) post intervention. No significant change in the proportion of randomised patients accepting allocation was found at 12 months (RR 1.33, 95% CI 0.96 to 1.85) and a slight increase in those accepting allocation at 24 months (RR 1.44, 95% CI 1.05 to 1.99).

Complex intervention

Fletcher *et al* used an observational time series study design to examine whether changes in the conduct of a stroke RCT were associated with changes in recruitment[24]. Over the recruitment period changes included: procedural changes to reduce clinician workload and time to recruitment; enrolment of more sites; and changes to the approach to recruitment and retention of practices. Recruitment rates per 1000 eligible population were calculated and a moving *F* statistic was used to assess changes over time. There was a statistically significant increase in recruitment in the last 6 months of the trial associated with efforts to reduce clinician workload.

Extra training and protected research time

Kenyon *et al* used a before and after study design to measure the effect of increased training, and paying for protected research time for midwives recruiting to a large perinatal multicentre RCT[27]. The intervention involved the employment of lead local midwives to work for three hours per week on the trial. The midwives were provided with intensive training, 6 monthly updates and regular contact visits. Recruitment in all the maternity units improved by an average of 69% (range -89% to 200%) when comparing the six months prior to the intervention with the six months immediately after the intervention.

Content analysis of qualitative findings

Findings relating to clinicians' involvement in, and recruiting to RCTs, were extracted for each study. A line-by-line content analysis isolated a total of 73 findings, which were consolidated into 8 abstracted themes by combining like statements and eliminating redundant statements. There is some overlap between abstracted findings.

Understanding of research (in general; RCTs; in light of specific trials)

RCTs are understood by clinicians to be a valuable tool in healthcare (i.e. description of RCT as 'gold standard'; do RCTs provide the best available evidence), however it is suggested that some clinicians are exposed to 'too much research', leading to a feeling of being overwhelmed with requests for research participation.

It is reported that there is poor understanding among clinicians of RCT methods and concepts (i.e. equipoise, randomisation, allocation, eligibility criteria, informed consent), along with the opinion that RCTs can be too complex.

There is some discussion regarding the funding of research, for example: questioning whether RCTs are the best way to spend money, particularly given the current economic climate; is there enough money available for research.

It is seen to be the responsibility of the whole community (researchers, clinicians and patients) to take part in research. However, some clinicians are suspicious of the motives of researchers, and others have no interest in research whatsoever – leading to resistance to research participation (obstructive/difficult to engage).

Communication (clinician to patient; clinician to trial coordinator)

Clinicians report a difficulty in communicating the aims and concepts of RCTs to patients. The choice of language used is perceived as very important. Communicating research to patients is described as a 'sales pitch'. Language used to describe RCT design is a concern, particularly allocation and randomisation, which has been likened to describing a lottery, with 'winners and losers'.

Clinicians report that they are able to communicate with certain patients and patient groups about RCTs better than others. Social class of patients is discussed, with clinicians finding communication with 'people like themselves' easier.

Poor communication of research by trial coordinators can lead to suspicion of their motives. There is often a perceived divergence between clinical and research goals. Clinicians feel that they should be seen as 'partners in research', with greater involvement in design leading to improved recruitment.

Perceived patient barriers

Barriers to recruitment are often seen by clinicians to be more related to the patients, and therefore out of their control. Perceived patient barriers include: poor community awareness of RCTs; poor understanding of RCTs; low motivation to take part in research; lack of interest; fear and mistrust of being treated as 'guinea pigs'; fear of negative effects of taking part.

Patient-clinician relationship

Clinicians acting as recruiters are particularly concerned with the conflicting roles that taking part in research activities imposed.

Recruiting clinicians may act as 'gatekeepers', only suggesting research to those patients that they deem suitable for research (i.e. not approaching all patients that meet eligibility criteria for a study). This can be perceived to be paternalistic as clinicians make decisions on the patients' behalf, believing they know what is best, without consulting the patients.

Clinicians feel responsible for the patients they put forward for research, particularly as they believe they can influence patients' decision making. Also clinicians put patient needs above those of researchers; patient wellbeing is seen as paramount.

Concern that trust may be affected by asking patients to take part in research is mentioned, as well as the concern for some clinicians that they risk feelings of ineptitude or rejection if they invite patients to take part in RCTs and they refuse.

Effect on patients (harms and benefits)

Clinicians often describe possible patient benefit as motivation for participation in RCTs, and equally concerns are expressed about possible harms. Some clinicians have difficulty reconciling putting individual patients at risk for possible population gain. Clinicians want to avoid being seen to pressurise patients to take part in RCTs.

The stage of patient illness is a concern, as it is suggested that asking terminally ill patients or patients with poor prognosis to take part in an RCT with a placebo can be emotionally detrimental for some patients. Also, side-effects of treatments used in RCTs are seen as possible negatives for patients. It is important to note that these are what the clinicians perceive their patients to be thinking, and the patients themselves may not share these views.

Inviting patients to take part in research can have the effect of raising patient awareness of disease, which can be interpreted in both a positive and negative light (i.e. more awareness may lead to increased participation in research but also more health seeking behaviour, stretching current resources).

Research can be thought to be inequitable by clinicians, with some 'special' patient groups seen as receiving more attention than others.

Effects on clinical practice

A positive aspect of taking part in RCTs is the beneficial influence it can have on clinical practice. Being a research active practice enhances services offered by practices, encouraging confidence and loyalty from patients. It is also thought that the discipline needed to adhere to some trial protocols has beneficial effects on clinical practice.

Advancements in clinical practice are dependent on carrying out good quality clinical trials. Taking part in RCTs can improve treatment strategies used in everyday practice, conferring benefits to patients outside the RCT in the medium and long term.

Negatives include the possible disruption caused to normal practice brought about by the extra work involved in assessing patients for eligibility, and approaching those who are eligible for participation (i.e. describing RCT, obtaining informed consent, etc). The extra time associated with recruiting to RCTs in addition to normal duties is often stated as a major barrier to involvement. In the climate of trying to achieve service targets within tight budgets, carrying out extra work to recruit patients to trials may not be seen as a priority.

It is felt by some clinicians that although they are crucial to the successful running of trials by recruiting subjects, they often do not receive the acknowledgment/rewards they feel they deserve. Being asked to recruit for RCTs is seen to be intrusive by some clinicians.

Individual benefits for clinicians

Motivation for involvement in research can be seen to move beyond altruism. Taking part and recruiting patients to RCTs is seen by many to have personal benefits for clinicians. Involvement with colleagues from different fields is seen to be important personally, as well as professionally.

Participation in RCTs is seen by some as crucial for career development, and professional recognition.

Methods associated with successful recruitment

Community awareness of RCTs and research in general is linked to good recruitment. Promotion efforts should be tried to improve awareness which should have the effect of

increasing the number of patients willing to take part in RCTs. Endorsements of research by the patients' own GP or practice can improve recruitment.

The research question addressed by an RCT is of vital importance to clinicians. The question should be both interesting and relevant to practice. Initial contact with clinicians about involvement in a trial should be brief but informative. Trial methods should be easy to understand and then communicate to patients. Inviting recruiters to take part in the design of RCTs could improve recruitment.

Funding of protected research time is an intervention that could improve recruitment performance. This would allow clinicians more time to discuss the trial with patients. More time would also allow clinicians to tailor their approach to each individual, an approach that is desirable for some clinicians. If protected research time is not a possibility then minimisation of workload related to recruitment is then key.

Financial incentives are important for many, with criticism when reimbursement for time is not offered. Clinicians should be reimbursed for time spent on recruitment rather than placing 'a bounty on patients' heads'. Conversely some argue that financial incentives are unethical, and others that being paid would not significantly affect recruitment efforts. It was also noted that all staff should be rewarded for participation in research, not just clinicians.

Organisationally, being part of a research active practice is linked with good recruitment to RCTs. Having a research mentor or a trial coordinator or being involved in a research network are also factors in successful recruitment. Competition with other recruiters is a constructive way to maximise recruitment.

Appropriate training about research methods and recruitment methods is regarded as the key to success by many. Training should focus on addressing many common misconceptions about RCTs, particularly equipoise and informed consent.

Qualitative effect size (metasummary)

By dividing the number of studies containing each theme/sub-theme by the total number of studies, an effect size was calculated. Table 4 shows the findings with effect sizes >20%, as proposed by Sandelowski and Barroso[20]. A full list of findings and effect sizes is given in Appendix 4.

{INSERT TABLE 4 HERE}

DISCUSSION

The aim of this review was to identify, and synthesise, evidence of the effectiveness of interventions aimed at improving the recruitment activity of clinicians in RCTs, and evidence of their attitudes towards recruitment to RCTs.

Methodological challenges

As the aim of the review was to include as much evidence as possible, regardless of method, several methodological issues had to be dealt with. Many systematic reviews of interventions exclude studies that do not use randomised controlled trials. While good quality RCTs of interventions would provide the best evidence, the nature of this research question lends itself to retrospective descriptive studies. This may be due to the logistical, ethical and scientific obstacles of performing randomised trials of recruitment nested within host RCTs[40]. "Evidential nihilism", where narrow exclusion criteria are set regarding trial design would have led to an empty review, which would not help further our understanding of the problem[41]. Qualitative studies were included in this review as it is important not just to understand what works, but also to have an understanding of why. It is hoped that a better understanding of clinicians' attitudes towards recruitment to RCTs may inform the development of interventions aimed to improve the support and training given to those involved in RCTs.

The search was broad and included no methodological filters, but still returned a large number of results. There is always a trade-off between sensitivity and specificity when performing a search for a systematic review, and in this case it was decided to err on the side of over inclusion, so a sensitive search was designed.

No studies were rejected as a result of quality assessment if they met all of the inclusion criteria for this review. Critical appraisal is subjective, and efforts were made to remove some subjectivity by having two researchers assess the studies using predefined checklists. The review of quantitative studies did not find much high quality evidence of interventions aimed at improving clinician activity, and shows the importance of building the evidence base to allow those running RCTs to have access to a range of proven strategies to maximise recruitment. Quality of the included qualitative studies was found to be good; however there was a tendency for the included studies to focus on the barriers to recruitment from the perspective of poorly recruiting trials. Little evidence was found of studies that aimed to assess how and why those clinicians who recruited well did so. It could be argued that facilitators are more illuminating, as barriers can often be seen as excuses, i.e. if the barrier was removed would the clinicians recruit more successfully.

What interventions work?

Evidence based interventions are necessary for RCTs to recruit successfully, however there is currently limited evidence, and interventions are being used that have no evidential grounding. For example, a study of seven primary care-based RCTs found that only 37% of interventions to promote recruitment were judged to be evidence based[7]. Further to this, Graffy *et al* stated that currently, where nested studies of recruitment methods are conducted on the initiative of individual investigators, there is no systematic method of choosing the intervention[40]. The authors go on to suggest the creation of a portfolio of interventions that could be made available to investigators for inclusion within an individual trial, or multiple trials.

This lack of evidence based interventions is particularly salient given that "common sense", interventions that could be assumed to have a positive effect on recruitment often had little or no effect. The most successful intervention identified by this review was in the two trials that used embedded qualitative research to design interventions to improve recruitment.

The qualitative research investigated recruitment appointments, study documents and interviewed clinicians to understand what aspects were amenable to change in order to improve recruitment. In both studies the intervention increased recruitment, but had no effect on proportion of recruited subjects who accepted allocation; i.e. the improvement in quantity was not at the expense of quality. Rather than discuss the strategies used to improve recruitment, the most important factor in studies employing embedded qualitative research is the way that the intervention is developed. The use of qualitative methods allowed tailored interventions to be made that addressed problems with recruitment that were felt by the clinicians and trial subjects (i.e. use of interviews, monitoring of recruitment interviews), as well as problems identified by the trial coordinators. This method is adaptive and allows for continuous monitoring and improvement. Although the interventions themselves are not generalisable, the qualitative methods used to create the interventions, could be transferred to other settings, potentially having the same positive effect on recruitment. Another positive feature of this approach was that improvements were maintained over time. Following intervention at two centres, recruitment was shown to remain significantly higher for at least 24 months.

One possible barrier to the use of this approach may be the extra time, money and personnel needed to carry out the qualitative research. However, the use of qualitative methods in pilot or feasibility trials prior to a full study would provide a cost-effective means of defining suitable interventions that could be fully incorporated into subsequent trials. If these interventions then proved successful in aiding recruitment, the extra efforts and costs involved in the preparatory phases would be offset by the greater potential for a successful full trial that would result, providing greater returns to funders and increasing the scientific validity of the trial overall.

Clinicians' attitudes to recruitment to RCTs

There are three key areas highlighted by the calculation of qualitative effect sizes in this review that may be the best target for improvement in future trials: understanding of RCTs and health research in general (both by the general public and clinicians); communication of trial methods (both trial coordinators to clinicians, and clinicians to patients); and reduction of the workload associated with recruitment.

It should not be assumed by trial coordinators that recruiters have a full understanding of RCT and recruitment methods. Clinicians' understanding of research in general and RCTs in particular could be improved using training specific to the RCT they are involved in as well as education relating to common misconceptions about RCTs.

Conventional wisdom states that those who take part in RCTs face risks they would not face if they received their healthcare in the usual manner; however a systematic review found that the outcomes of patients taking part in RCTs do not differ from those of patients receiving similar treatments who do not participate[42].

Some of the themes identified could be used to emphasise the individual benefits to both trial subjects and clinicians, and the positive effect taking part in research can have on clinical practice. For example a study of centres involved in a multi-centre breast cancer treatment trial, found that both patients and clinicians benefited from participation in the RCT, due to optimised decision making with regards to therapy and patient care[43]. An overall positive effect on the quality of medical care was seen across the centres. As clinicians prioritise patient wellbeing, emphasising the potential patient benefits to them could help remove a barrier to recruitment.

It is clear that reported barriers may often be excuses for why clinicians have not recruited well. Patterson *et al*, for example, found that concerns about taking part in RCTs related to ethics and research approvals, but even when these issues were addressed clinicians

remained less than enthusiastic, and instead shifted the blame to administrative and clinical duties[38]. Removal of the perceived barrier will not necessarily lead to an improvement in recruitment. This again highlights that more investigation is required to illuminate what facilitates trials that easily meet their recruitment targets.

Reducing clinicians' workload associated with recruiting to RCTs was often mentioned. This could be achieved by providing extra staff support, simplification of recruitment protocols, or providing protected research time. However, it remains to be seen whether clinicians saying they do not have enough time is more commonly a barrier or an excuse.

Clinicians place an emphasis on patient wellbeing, and some may feel the need to protect their patients from the risk of taking part in a RCT. A commonly held belief among clinicians is that patients who take part in RCTs face risks that they would not otherwise face if they received their healthcare in the usual manner. However, a systematic review found that the outcomes of patients taking part in RCTs do not differ from those of patients receiving similar treatments who do not participate[43].

Engaging clinicians in RCTs is a crucial step in the recruitment process. It is apparent that clinicians are aware of the impact they have on their patients' decision making regarding involvement in trials, and it has been shown that personal endorsement of trials by clinicians can have a positive effect on recruitment. If clinicians are fully engaged and understand the benefits, to both themselves and patients, of participating in RCTs, recruitment could improve significantly.

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Ethics approval

Ethics approval was not required.

Contributors

BF made substantial contributions to the design of the study, acquisition and interpretation of data, synthesis of qualitative evidence, and wrote the draft of the paper.

AG was involved in checking the searches, and data extraction and quality assessment of included papers.

SW contributed to the design of the study, and was responsible for obtaining funding for the study.

DM contributed to the design of the study, particularly search strategy and quality assessment, and revised drafts of the paper.

SD contributed to the design of the study, advised on qualitative metasummary, revised drafts of the paper, and approved the final draft for submission.

Competing interests

The authors declare no competing interests.

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Table 1 – Reports of difficulties recruiting to RCTs

Authors	Year	Findings
Charleson and Horwitz[4]	1984	A study of 41 trials listed with the National Institutes of Health (USA) showed that a third of trials recruited fewer than 75% of their planned sample.
Easterbrook and Matthews[5]	1992	A review of 720 research projects approved by the Central Oxford Research Ethics Committee 1984-1987 (UK). Report states that the main reason for abandoning a study was due to difficulties recruiting study participants.
Wilson *et al*[6]	2000	A study of recruitment of primary care practices to an endoscopy trial. Of 90 practices contacted, 43 agreed to take part, 31 recruited at least one patient and only 23 recruited more than five patients.
Foy *et al*[7]	2003	A study of seven primary care trials of dyspepsia management in the UK. Only one study reached its recruitment target; five recruited less than 50% of target and three of these closed prematurely.
McDonald *et al*[8]	2006	A study of 114 RCTs funded by two UK funding bodies 1994-2002. 31% of trials achieved their original recruitment target. 53% were extended due to recruitment problems. Early recruitment problems were identified in 63% of the trials.
Bower *et al*[9]	2007	A survey of published primary care trials in the UK. Less than one third of trials recruited to their original timescale.
Raftery *et al*[10]	2008	Data held by the National Coordinating Centre for Health Technology Assessment (UK), shows that two thirds of funded trials fail to pass 80% of their recruitment target.
Toerien *et al*[11]	2009	Review of all reports of RCTs published in July-December 2004 in six major journals. Of 133 trials 21% that reported sample size calculations failed to achieve adequate numbers at randomisation, and 48% at outcome assessment.

Table 2 – summary of included qualitative studies

	Study type	RCT recruiting to	Overview (country, aim)
Donovan (2003) [21]	RCT	ProtecT Trial, prostate cancer treatment	UK. To investigate the comparative effectiveness of nurses and surgeons in recruiting patients
Monaghan (2007) [22]	RCT	ADVANCE trial (diabetes)	Australia. Investigation of the effect of extra communication from central trial coordinators on recruitment.
Lienard (2006) [23]	RCT	Adjuvant treatment of breast cancer	France. To assess the impact of on-site initiation monitoring visits on patient recruitment.
Fletcher (2010) [24]	Observational time series	Primary care based multi-centre RCT, stroke trial	UK. To examine whether changes to the design and conduct of a primary care-based RCT were associated with changes in patient recruitment.
Donovan (2002) [25]	Observational time series	ProtecT trial – treatment for prostate cancer	UK. *Feasibility study for main trial.* Qualitative research used to address barriers to recruitment, and make changes to protocol.
Donovan (2009) [26]	Before and after study	ProtecT trial – treatment for prostate cancer	UK. *Main trial results.* A complex intervention was designed using qualitative methods to improve recruitment (i.e. regular training of recruiting staff, centre reviews if centre not recruiting to target, documents to provide advice, and personal feedback).
Kenyon (2005) [27]	Before and after study	ORACLE trial – double blind RCT antibiotic treatment for women in idiopathic preterm labour	UK. Trial was not recruiting successfully so changes were made (introduction of lead midwife responsible for recruitment with protected time for research).
Submacular Surgery Trials Research Group (2004) [28]	Case study (with comparison group)	SST – submacular surgery trial	USA. Comparison of university and community based practices taking part in three multicentre randomised trials. One outcome measure was patient accrual.

Table 3 – summary of included quantitative studies

	Title	Study method and aims	Recruitment to RCT?
Hales (2001) [29]	The conflicting roles of clinicians versus investigators in HIV randomised clinical trials	**Semi-structured interviews** One theme investigated was recruitment.	**Yes.** Clinical drug trial. Primary care and secondary care
Caldwell (2002) [30]	Paediatricians' attitudes toward randomized controlled trials involving children	**Focus groups** To examine doctors attitudes toward children's participation in RCTs and identify barriers to participation	**Yes.** RCTs involving children. Secondary care (Teaching hospital in Australia)
Jones (2003) [31]	Building research capacity: an exploratory model of GPs' training needs and barriers to research involvement	**Semi-structured interviews** Investigation of GPs research training needs, and barriers to involvement in research.	**Not specified.**
McIntosh (2005) [32]	Recruitment of physician offices for an office based adolescent smoking cessation study.	**Focus groups** To elicit perceptions of facilitators and barriers to initial engagement of physician practices	**Yes.** Adolescent smoking cessation study
Mason (2007) [33]	GPs' experiences of primary care mental health research: a qualitative study of the barriers to recruitment	**Semi-structured interviews** To investigate the perceived barriers among GPs to introducing participation in RCTs to patients with depression.	**Yes.** Primary care mental health research.
Ziebland (2007) [34]	Does it matter if clinicians recruiting for a trial don't understand what the trial is really about? Qualitative study of surgeons' experiences of participation in a pragmatic multi-centre RCT	**In-depth interviews** To explore physicians understanding of the trial purpose and how this understanding had influenced their recruitment.	**Yes.** Multicentre pragmatic RCT. Spinal surgery. UK.
Bill-Axelson (2008) [35]	Experiences of randomization interviews with patients and clinicians in the SPG-IV trial	**Semi-structured interviews.** Investigation of patients' and clinicians' experiences of randomisation with the aim of facilitating future trial participation.	**Yes.** Prostate cancer RCT
Potter (2009) [36]	A qualitative study exploring practice nurses' experience of participating in a primary-care based randomised controlled trial	**Semi-structured interviews** To explore the views of practice nurses' recruiting into a primary care-based RCT, and to investigate factors that influence the success of trial recruitment.	**Yes.** Primary care based RCT to promote adherence to treatment of people with type 2 diabetes.
Howard (2009) [37]	Why is recruitment to trials difficult? An investigation into recruitment difficulties in an RCT of supported employment in patients with severe mental illness	**Interviews** To evaluate reasons for under-recruitment in an RCT. Trial staff and recruiting physicians were interviewed.	**Yes.** RCT of supported employment in patients with severe mental illness.
Patterson (2010) [38]	The great divide: a qualitative investigation of factors influencing researcher access to potential randomised controlled trial participants in mental health settings	**Interviews** Using Grounded Theory process evaluation of a multicentre trial to investigate factors influencing referral to potential RCTs in mental health settings.	**Yes.** Potential RCTs in mental health setting
Paramasivan (2011) [39]	Key issues in recruitment to randomised controlled trials with very different interventions: a qualitative investigation of recruitment to the SPARE trial	**Interviews; content analysis of RCT documents; conversation analysis of recruitment appointments** To explore reasons for low recruitment and attempt to improve recruitment rate by implementing changes suggested by qualitative findings.	**Yes.** Bladder cancer treatment trial – feasibility study.

Table 4 – summary of qualitative findings with effect size >20%

Abstracted finding	Sub-theme	Studies in which sub-theme is present	Effect size (%)
Understanding of research	RCTs provide the best evidence.	[29] [33] [34]	27
	Poor understanding of research	[30] [31] [34] [37] [38] [39]	55
Communication	Difficulty communicating trial methods	[29] [30] [33] [35] [37] [38] [39]	64
Patient-clinician relationship	Conflicting roles of being a recruiting physician	[29] [33] [37] [38]	36
	Clinicians acting as gatekeepers	[36] [37] [38]	27
	Paternalism	[33] [36] [37]	27
	Clinician influence on patient decision making	[30] [33] [35] [37]	36
	Patient wellbeing a priority	[29] [30] [33] [35] [37]	45
Effect on patients	Possible benefits of taking part in RCTs	[29] [30] [32] [36]	36
	Possible harms of taking part in RCTs	[29] [33] [37]	27
Effect on clinical practice	Positive effect of being involved in RCTs	[29] [30] [32] [33] [36]	45
Individual benefit for trialist	Career development	[30] [36] [39]	27
Methods associated with successful recruitment	Importance of research question	[29] [30] [33] [34] [35]	45
	Trial methods easy to understand, communicate and carry out	[30] [32] [35] [36] [39]	45
	Financial incentives	[29] [31] [32]	27
	Appropriate training	[30] [31] [32] [36]	36

PICOS Framework for quantitative studies:

Population

Inclusion
- clinicians recruiting to RCTS

Exclusion
- subjects of RCTs

Intervention

Inclusion
- any intervention aimed at improving the recruitment activity of clinicians
- comparison of clinicians recruiting to trials if the aim was to compare recruitment activity

Exclusion
- interventions aimed at the subjects of RCTs

Comparator

Inclusion
- No intervention, or comparison of two interventions

Exclusion
- Studies comparing recruitment in separate RCTs

Outcomes

Inclusion
- Numbers/proportions of subjects recruited
- Recruitment rates
- Recruiting to target
- Adherence to trial protocol regarding recruitment

Exclusion
- Intention to recruit

Studies

Inclusion
- Any study where a comparison is made between an intervention and a control group, or two or more intervention group.
- RCTS
- Quasi experimental studies
  - Before and after studies
  - Interrupted time-series
- Observational studies
  - Cohort study
  - Case control study
  - Case study (where there is a comparator group)

Exclusion
- Studies with no comparator group
- Qualitative studies
-

SPICE framework for qualitative studies:

Setting
- Randomised controlled trials

Perspective
- Clinicians directly involved in recruiting patients to RCTs

Intervention/phenomena of interest
- Poor recruitment to RCTs

Comparison
- None

Evaluation
- Perceived barriers and facilitators

Figure 1 - Inclusion/exclusion criteria
245x329mm (300 x 300 DPI)

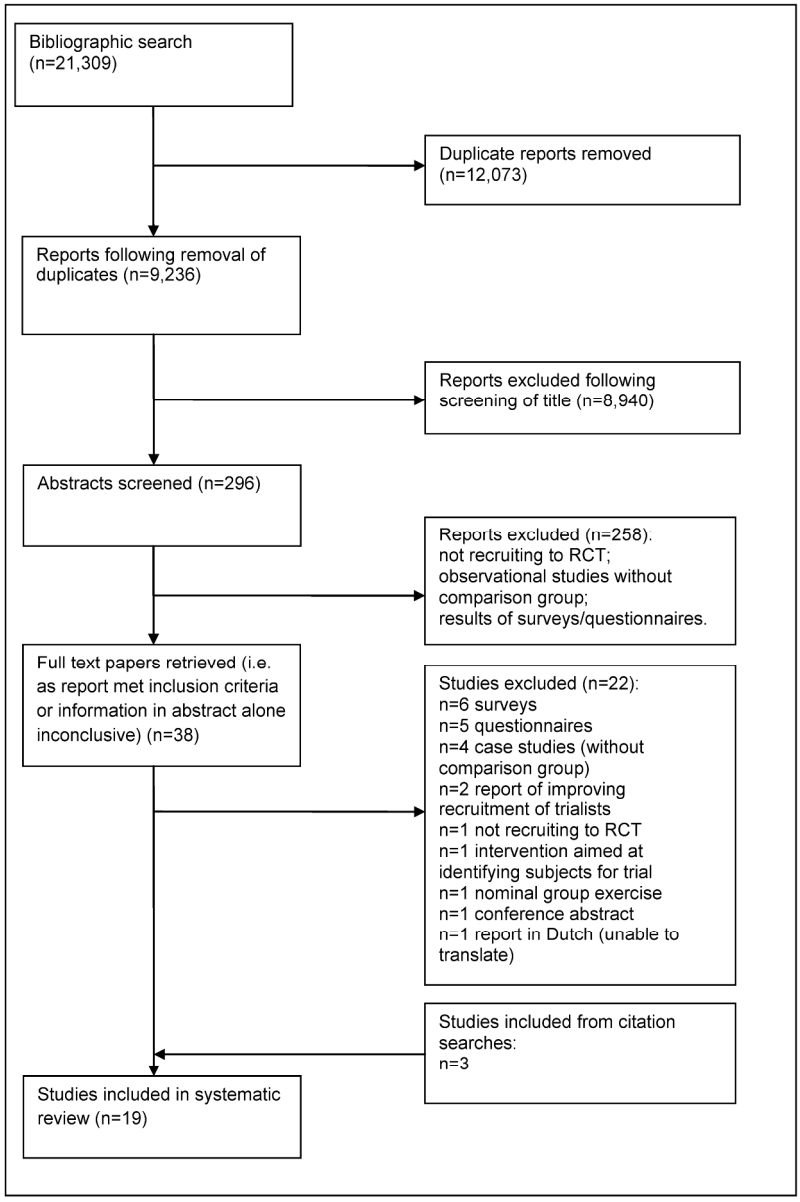

Figure 2 - Study selection
233x348mm (300 x 300 DPI)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1,2
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Figure 1
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	No protocol
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1 In supplementary materials
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5,6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5,6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5,6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5,6

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6 Qualitative metasummary
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Appendix 5,6
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Appendix 2,3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8-12
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	No meta-analyses
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	12 Qualitative metasummary
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13-15
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13-15
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	16

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Improving the recruitment activity of clinicians in randomised controlled trials - a systematic review

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Word count (excluding title page, abstract, references, figures and tables)

6,038

ABSTRACT

Background

Poor recruitment to randomised controlled trials (RCTs) is a widespread problem. Provision of interventions aimed at supporting or incentivising clinicians may improve recruitment to RCTs.

Objectives

To quantify the effects of strategies aimed at improving the recruitment activity of clinicians in RCTs, complemented with a synthesis of qualitative evidence related to clinicians' attitudes towards recruiting to RCTs.

Data sources

A systematic review of English and non-English articles identified from: The Cochrane Library, Ovid MEDLINE, Ovid EMBASE, Ovid PsycINFO, Ebsco CINAHL, Index to Theses and Open SIGLE from 2001 to March 2011. Additional reports were identified through citation searches of included articles.

Study eligibility criteria

Quantitative studies were included if they evaluated interventions aimed at improving the recruitment activity of clinicians, or compared recruitment by different groups of clinicians. Information about host trial, study design, participants, interventions, outcomes and host RCT was extracted by one researcher and checked by another. Studies that met the inclusion criteria were assessed for quality using a standardised tool; the Effective Public Health Practice Project (EPHPP) tool.

Qualitative studies were included if they investigated clinicians' attitudes to recruiting patients to RCTs. All results/findings were extracted and content analysis was carried out. Overarching themes were abstracted, followed by a metasummary analysis. Studies that met the inclusion criteria were assessed for quality using the Critical Appraisal Skills Programme (CASP) qualitative checklist.

Data extraction

Data extraction was carried out by one researcher using predefined data fields, including study quality indicators, and verified by another.

Results

Eight quantitative studies were included describing four interventions and a comparison of recruiting-clinicians. One study was rated as strong, one as moderate and the remaining six as weak when assessed for quality using the EPHPP tool. Effective interventions included: the use of qualitative research to identify and overcome barriers to recruitment; reduction of the clinical workload associated with participation in RCTs; and the provision of extra training and protected research time.

Eleven qualitative studies were identified and eight themes were abstracted from the data: understanding of research; communication; perceived patient barriers; patient-clinician relationship; effect on patients; effect on clinical practice; individual benefits for clinicians; and methods associated with successful recruitment. Metasummary analysis identified the most frequently reported sub-themes to be: difficulty communicating trial methods; poor understanding of research; and priority given to patient wellbeing. Overall, the qualitative studies were found to be of good quality when assessed using the CASP checklist.

Conclusions

There were few high quality trials that tested interventions to improve clinicians' recruitment activity in RCTs. The most promising intervention was the use of qualitative methods to identify and overcome barriers to clinician recruitment activity. More good quality studies of interventions are needed to add to the evidence base.

The metasummary of qualitative findings identified understanding and communicating RCT methods as a key target for future interventions to improve recruitment. Reinforcement of the potential benefits, both for clinicians and their patients, could also be a successful factor in improving recruitment. A bias was found toward investigating barriers to recruitment, so future work should also encompass a focus on successfully recruiting trials.

ARTICLE SUMMARY

Article focus

A systematic review to identify and synthesise evidence of evaluations of interventions aimed at improving clinician recruitment activity in RCTs, and evidence of clinicians' attitudes towards recruiting to RCTs.

Key messages

Evidence based recruitment interventions aimed at supporting/incentivising clinicians are necessary for future RCTs to recruit successfully. However, evidence of successful interventions is currently limited, and interventions are being used that have limited evidential grounding. The most promising intervention identified by this review was the use of qualitative methods embedded in host RCTs to define appropriate methods, targeted at clinicians, relevant to the context of the individual studies.

The review of qualitative evidence identified a number of themes relating to clinicians' attitudes towards recruitment to RCTs. The metasummary isolated targets for future interventions aimed at improving clinicians' recruitment activity. Of particular interest were: communication of trial methods; education to remove misunderstanding of trial methods; and reinforcement of the potential benefits of RCTs, both for clinicians and their patients.

Strengths and limitations of this study

Strengths

This review encompasses both quantitative and qualitative evidence regarding clinician involvement in recruiting to RCTs. As such, it highlights the available evidence, successful and unsuccessful interventions, areas of uncertainty, and also targets for the design of future interventions.

Qualitative data was managed and synthesised according to a set methodology and is therefore a step beyond simple narrative review. Qualitative metasummary can be the final product of a synthesis project, or used as the initial step in a metasynthesis project. The purpose of qualitative metasummary was to determine how frequently each abstracted thematic finding occurred in the included studies. Qualitative metasummary is appropriate for synthesising studies that are thematic summaries or surveys of data.

Limitations

The quality of evidence varied, and the review includes a wide range of study designs, making comparisons of interventions difficult. It is clear that RCTs of trial recruitment interventions are perceived to be difficult to carry out, so other study designs are commonly used. RCTs of recruitment interventions should be encouraged in order to increase the quality of currently available evidence.

Methodological challenges included: designing a broad search to encompass qualitative and quantitative research; quality assessment of various quantitative study designs by one set of criteria; standardising the data extraction and synthesis of qualitative evidence. There are no set guidelines regarding the synthesis of qualitative and quantitative evidence, but it is clear that for many review questions limiting the included study designs would lead to empty reviews.

INTRODUCTION

When evaluating the effectiveness of healthcare interventions, randomised controlled trials (RCTs) are seen as the gold standard research design. It is important that RCTs recruit their target number of participants in order to avoid being underpowered, particularly as a lack of statistical power may lead to the reporting of clinically important effects as statistically non-significant. Statistically non-significant findings can increase the risk that potentially effective interventions may be abandoned before their true value is established, or that there will be a delay in demonstrating their value while more trials are carried out. For example, Collins *et al* calculated that there were as many as 10,000 unnecessary deaths in the USA due to delays in recruitment to a RCT of streptokinase in acute myocardial infarction[1]. Many RCTs are abandoned or do not produce unequivocal evidence due to recruitment difficulties, which also means that the resources spent for setting up and running the RCT have not been put to their best use.

Studies that fail to recruit their target number of participants also raise ethical problems, particularly when clinicians have exposed participants to interventions with uncertain benefit and, at the end of the trial, are still unable to determine whether the intervention is clinically effective[2]. There are also ethical implications associated with recruiting patients to a trial in which they invest their time, only to be told that the trial will not go ahead. There is the additional financial impact of trials that fail to recruit successfully, or in a timely manner. It has been hypothesised that slow acquisition of trial evidence due to poor recruitment may have reduced investment in the conduct of RCTs by some funding agencies, who may prefer to invest in less reliable, but more rapid approaches[3]. Delayed or extended trials may cost more, leading to fewer trials being carried out from the limited funds available.

There are a number of published studies that highlight how common recruitment problems are in healthcare RCTs[4-11]. It is likely that 50% of RCTs fail to recruit to target, and that only 50% of those that successfully recruit do so in a timely manner as shown in Table 1. The table also demonstrates the lack of any real improvement over time.

{INSERT TABLE 1 HERE}

The reasons for poor or slow recruitment to RCTs can be found at various levels: the patient, the recruiting clinician, the trial centre, the trial organisation and the trial design[12]. Considerable efforts have been made to understand and incentivise the participation of subjects in trials[2,3,13-16]; but less has been done to investigate interventions that could improve the recruitment activity of clinicians[10,12]. The clinicians' role is clearly important as patients can only consider taking part in trials when asked to do so. Maintaining recruitment activity over time is also important as it has been shown that enthusiasm for recruiting subjects to RCTs can fade quickly, leading to studies that fail to recruit to target, or which suffer significant loss to follow up due to difficulties in participant retention for the required study period[6].

The objective of this systematic review was to evaluate interventions aimed at improving the activity of recruiting clinicians in RCTs, and to identify possible targets for future interventions based on clinicians' attitudes to recruitment to RCTs.

METHODS

Search strategy and study identification

Systematic searches were carried out for the period January 2001 to March 2011 in the following databases: the Cochrane Library, Ovid MEDLINE, Ovid EMBASE, Ebsco CINAHL, Ovid PsycINFO, Index to Theses (UK and Ireland), Open SIGLE.

Search terms related to clinicians, recruitment and RCTs were combined to identify studies. An example search strategy is shown in Appendix 1. No methodological filters were used so that both qualitative and quantitative studies would be returned by the searches. Furthermore, filters were avoided due to the complexity of searching for trails within trials.

To determine inclusion/exclusion criteria for studies the PICOS framework was used for quantitative studies and the SPICE framework for qualitative studies, as shown in Figure 1. Studies were assessed against the pre-specified inclusion and exclusion criteria. Following removal of duplicate reports, a first decision on inclusion/exclusion was made based on study titles and abstracts. For those studies identified in the first stage and for studies where a definite decision could not be made based on title/abstract alone, the full paper was obtained for assessment. In the second stage full papers were assessed against the full inclusion/exclusion criteria. Studies were also identified by performing citation searches of included studies.

Searches were carried out by one researcher (BF), and study identification by two researchers (BF, AG), and any disagreements reconciled by discussion.

{INSERT FIGURE 1 HERE} Title “Study selection criteria”

Quality assessment

Quality assessment of quantitative studies was performed using the Effective Public Health Practice Project (EPHPP) quality assessment tool for quantitative studies[17]. This instrument was chosen as it enables different study designs to be assessed using the same tool, and was identified as one of only six judged to be suitable for systematic reviews assessing multiple study designs[19]. Using the EPHPP tool, studies were assessed against six criteria: selection bias, design, confounders, blinding, data collection methods, and withdrawals and dropouts.

Quality assessment of qualitative papers was carried out in accordance with the Critical Appraisal Skills Programme (CASP) qualitative research appraisal tool, which covered rigour, key research methods used, credibility and relevance[18].

Quality assessment was performed by two researchers independently (BF/AG), and the results were compared for consistency. Following discussion, a consensus decision was made in the case of any disagreement.

Data extraction and analysis

For quantitative studies, data relating to study design, country, setting (i.e. nature of the RCT being recruited to), population, statistical methods, description of intervention and author conclusions were extracted using a piloted data extraction form. Trials were grouped according to intervention and, if binary data was reported (i.e. participants recruited/participants not recruited), then risk ratios were calculated. Relative risks with 95% confidence intervals were calculated using RevMan software, where appropriate, to describe the effect of interventions.

For qualitative reports, data extraction was first carried out using the Quality Assessment and Review Instrument (QARI) data extraction tool designed by the Joanna Briggs Institute (JBI) for Evidence Based Practice. This allowed broad themes to be identified in the included reports. Secondly, all text was extracted from sections labelled as 'results' or 'findings' in the included reports, according to the method suggested by Thomas and Harden [20]. The results were then entered into NVivo software for qualitative content analysis. Line-by-line coding of the extracted data was carried out and codes were organised into related areas in order to construct descriptive themes. Abstracted analytical themes were then created by combining similar descriptive themes, from which effect sizes could be calculated. Effect sizes were calculated by taking the number of reports that contained an abstracted finding and dividing this number by the total number of reports. A criticism of metasummary is that it may not be appropriate to apply numbers to qualitative data. However, quantitative categorisations such as small, medium and large are often used by researchers to "qualitize" data[21]. Effect sizes can be used to extract more meaning from abstracted findings. Qualitative studies "inherently imply a frequency of occurrence of an event sufficient to constitute a pattern or theme", and metasummary can be seen as the next step in this process, as well as helping to verify the presence of themes across studies[22].

Data extraction was carried out by one researcher (BF) and the results checked by a second (AG). Disagreements were resolved by discussion.

RESULTS

Study selection

The search identified 9,236 abstracts of which 296 were screened, and 38 full text papers obtained for full assessment against the inclusion/exclusion criteria. Nineteen studies were included in the review (eight quantitative and eleven qualitative).

{INSERT FIGURE 2 HERE} Title “Study selection flow diagram”

Study characteristics

{INSERT TABLE 2 HERE}

Of the eight included quantitative studies, three were RCTs[23,24,25], two were observational time series[26,27], two were before and after studies[28,29] and one was a case study with a comparison group[30]. Two studies compared clinicians (nurses vs. surgeons; community vs. university medical practices)[23,30]. Two studies assessed the effect of extra involvement of trial coordinators with clinicians (extra communication; on-site initiation visits)[24,25]. One study assessed the effect of change to training and paying for protected research time on recruitment[29]. Two studies from the same authors used embedded qualitative methods to identify targets for improving recruitment[27,28]. One study assessed a complex multifaceted intervention[26]. All but one study investigated recruitment to cancer or chronic disease trials, and the majority took place in the UK (5 of 8).

Three reports all related to the same host RCT of prostate cancer treatment[23,27,28]. Donovan (2002 and 2009) reported the results of using qualitative methods to develop an intervention, in both the feasibility study before the main trial, and the main trial itself. Donovan (2003) compared using nurses and surgeons as recruiters in the same trial. For the purpose of this review these three studies were assessed separately.

{INSERT TABLE 3 HERE}

Of the eleven included qualitative studies nine used interviews (semi-structured; in-depth)[31,33,35-41], two used focus groups[32,34] and one study also analysed trial documents[41]. The methodology used was described as Grounded Theory in three studies[31,33,40], while it was not stated in eight. Thematic analysis (constant comparative; framework analysis) was the most common method of data analysis (nine studies)[31-33,35-36,38-41], with two studies using content analysis[37,41] and one conversation analysis[41]. Data analysis method was unclear in one of the included studies[34].

174 trialists were interviewed or involved in focus groups in total: 62 GPs, 30 community physicians, 16 paediatricians, 11 surgeons, 11 recruiters, 10 clinicians, 10 nurses, 5 trainees, 5 investigators, 4 trial staff, 4 hospital doctors, 2 clinical studies officers, 2 research associates and 2 care coordinators. A broad range of settings were covered by the included studies e.g. primary and secondary care trials; drug trials and pragmatic surgery trials; trials in mental health and cancer - etc.

Quality assessment

Using the EPHPP quality assessment tool for quantitative studies: one study was characterised as strong[24], one as moderate[25], with the remaining studies classified as weak[23, 26-30]. Studies were shown to be particularly weak when reporting controlling for confounders and methods of data collection.

Overall, the qualitative studies assessed using the CASP checklist were found to be of good quality. Methodology and consideration of ethical issues were the two main areas where reporting was unclear.

A summary of the quality of the included studies is Appendix 2 and 3.

Results of review of quantitative studies

Comparing types of recruiters

Two studies compared the use of different groups of clinicians recruiting to RCTs. Donovan *et al* compared the effect of using nurses or urologic surgeons recruiting to a prostate cancer trial, using a RCT design[23]. The trial showed no significant difference in recruitment rate between the two groups (RR 0.94, 95% CI 0.76 to 1.17). The study also included an economic assessment that found nurses to be more cost effective recruiters than surgeons.

Submacular Surgery Trials Research Group (SSRTG) compared recruitment at university based and community based medical centres, in recruitment to three RCTs of intraocular surgery[30]. This was a case study with comparison groups. The study found no significant difference between the settings (mean number of subjects recruited per centre: university = 38.1, community = 37.3, *t* test p=0.93).

Greater contact between trial coordinator and clinicians/trial sites

Two studies examined the extent of contact on recruitment. Lienard *et al* used a RCT design to assess the impact of on-site monitoring visits on recruitment to a breast cancer RCT[25]. On-site monitoring visits had multiple purposes: to ensure the protection of patients' rights, to verify the accuracy of reported data, and to provide training to site personnel with regard to trial material and protocol. The study found that on-site monitoring visits had no significant effect on patient recruitment, reported as: centres recruiting at least one patient (control 34 of 67, intervention 35 of 68, p>0.05); or total numbers of patients recruited (control 271, intervention 302, p>0.05). No significant differences were found between groups in quality or quantity of reported data, or patient follow up time.

Monaghan (2007) used a RCT to evaluate the effect of extra communication from central trial coordinators on recruitment to a diabetes RCT[24]. The intervention included: frequent e-mails; personalised mail-outs of league tables describing recruitment performance relative to other centres; certificates acknowledging achievement of recruitment milestones; and promotional materials related to the trial. The study found no significant effect of extra communication on median number of patients recruited (control 37.0, intervention 37.5, p=0.68), or median time to half recruitment target (control 4.4 months, intervention 5.8 months, p=0.08).

Use of qualitative research embedded in host RCT

Two studies investigated the use of qualitative methods embedded in a host trial. In both studies, qualitative methods (in depth interviews, audiotape recordings of recruitment appointments, study of trial documents) and analysis (content, thematic and conversation analysis) were used to assess aspects of the trials that were amenable to improvement; followed by the design and implementation of interventions to improve the recruitment activity of clinicians. Donovan *et al* (2002) reports the results of a feasibility study before the main trial (Donovan *et al* 2009)[27,28].

Donovan *et al* (2002) reported the results of an observational time series study investigating recruitment to a prostate cancer RCT[27]. Qualitative methods were used to elicit strategies which had the potential to improve recruitment. Strategies identified by qualitative methods included presentations of the study design and the implementation of a training programme

delivered to clinicians. The intervention improved the proportion of eligible patients consenting to randomisation (after 10 months RR 1.36, 95% CI 1.01 to 1.85), whilst there was no significant change in the proportion of randomised patients accepting allocation (after 10 months RR 0.90, 95% CI 0.70 to 1.15).

Donovan *et al* (2009) reported the results of the main trial[28]. Qualitative methods allowed a complex intervention to be developed which included: regular training for all staff involved in recruitment and initiation for new staff; centre reviews for underperformers; documents providing tips and advice; and personalised individual feedback to recruiters as required. The study reports the results of audits of two centres before and after the intervention (12 and 24 months post intervention). The results of the two centres are not pooled in this review as interventions were tailored to each centre using qualitative research; therefore the intervention that the two centres received was different. The first centre showed a significant improvement in the proportion of eligible patients recruited at 12 months (RR 1.87, 95% CI 1.15 to 3.04) and 24 months (RR 1.79, 95% CI 1.07 to 2.99) post intervention, and no significant change in the proportion of randomised patients accepting allocation (12 months RR 1.22, 95% CI 0.62 to 2.39; 24 months RR 1.43, 95% CI 0.75 to 2.71). The second centre also showed a significant improvement in the proportion of eligible patients recruited at 12 months (RR 1.55, 95% CI 1.11 to 2.16) and no significant change at 24 months (RR 1.36, 95% CI 0.92 to 2.02) post intervention. No significant change in the proportion of randomised patients accepting allocation was found at 12 months (RR 1.33, 95% CI 0.96 to 1.85) and a slight increase in those accepting allocation at 24 months (RR 1.44, 95% CI 1.05 to 1.99).

Complex intervention

Fletcher *et al* used an observational time series study design to examine whether changes in the conduct of a stroke RCT were associated with changes in recruitment[26]. Over the recruitment period changes included: procedural changes to reduce clinician workload and time to recruitment; enrolment of more sites; and changes to the approach to recruitment and retention of practices. Recruitment rates per 1000 eligible population were calculated and a moving *F* statistic was used to assess changes over time. There was a statistically significant increase in recruitment in the last 6 months of the trial associated with efforts to reduce clinician workload.

Extra training and protected research time

Kenyon *et al* used a before and after study design to measure the effect of increased training, and paying for protected research time for midwives recruiting to a large perinatal multicentre RCT[29]. The intervention involved the employment of lead local midwives to work for three hours per week on the trial. The midwives were provided with intensive training, 6 monthly updates and regular contact visits. Recruitment in all the maternity units improved by an average of 69% (range -89% to 200%) when comparing the six months prior to the intervention with the six months immediately after the intervention.

Results of review of qualitative studies

Findings relating to clinicians' involvement in, and recruiting to RCTs, were extracted for each of the eleven included studies. A line-by-line content analysis isolated a total of 73 findings, which were consolidated into 8 abstracted themes by combining like statements and eliminating redundant statements. There is some overlap between abstracted findings. The abstracted themes are described below.

Understanding of research (in general; RCTs; in light of specific trials)

RCTs are understood by clinicians to be a valuable tool in healthcare (i.e. description of RCT as gold standard; RCTs provide the best available evidence), however it is suggested that some clinicians are exposed to too much research, leading to a feeling of being overwhelmed with requests for research participation.

It is reported that there is poor understanding among clinicians of RCT methods and concepts (i.e. equipoise, randomisation, allocation, eligibility criteria, informed consent), along with the opinion that RCTs can be too complex.

There is some discussion regarding the funding of research, for example: questioning whether RCTs are the best way to spend money, particularly given the current economic climate; is there enough money available for research.

It is seen to be the responsibility of the whole community (researchers, clinicians and patients) to take part in research. However, some clinicians are suspicious of the motives of researchers, and others have no interest in research whatsoever – leading to resistance to research participation (obstructive/difficult to engage).

Communication (clinician to patient; clinician to trial coordinator)

Clinicians report a difficulty in communicating the aims and concepts of RCTs to patients. The choice of language used is perceived as very important. Communicating research to patients is described as a sales pitch. Language used to describe RCT design is a concern, particularly allocation and randomisation, which has been likened to describing a lottery, with 'winners and losers'.

Clinicians report that they are able to communicate with certain patients and patient groups about RCTs better than others. Social class of patients is discussed, with clinicians finding communication with 'people like themselves' easier.

Poor communication of research by trial coordinators can lead to suspicion of their motives. There is often a perceived divergence between clinical and research goals. Clinicians feel that they should be seen as 'partners in research', with greater involvement in design leading to improved recruitment.

Perceived patient barriers

Barriers to recruitment are often seen by clinicians to be more related to the patients, and therefore out of their control. Perceived patient barriers include: poor community awareness and understanding of RCTs; low motivation to take part in research; lack of interest; fear and mistrust of being treated as guinea pigs; fear of negative effects of taking part.

Patient-clinician relationship

Clinicians acting as recruiters are particularly concerned with the conflicting roles that taking part in research activities imposed.

Recruiting clinicians may act as gatekeepers, only suggesting research to those patients that they deem suitable for research (i.e. not approaching all patients that meet eligibility criteria for a study). This can be perceived to be paternalistic as clinicians make decisions on the patients' behalf, believing they know what is best, without consulting the patients.

Clinicians feel responsible for the patients they put forward for research, particularly as they believe they can influence patients' decision making. Also clinicians put patient needs above those of researchers; patient wellbeing is seen as paramount.

Concern that trust may be affected by asking patients to take part in research is mentioned, as well as the concern for some clinicians that they risk feelings of ineptitude or rejection if they invite patients to take part in RCTs and they refuse.

Effect on patients (harms and benefits)

Clinicians often describe possible patient benefit as motivation for participation in RCTs, and equally concerns are expressed about possible harms. Some clinicians have difficulty reconciling potentially putting individual patients at risk for possible population gain. Clinicians want to avoid being seen to pressurise patients to take part in RCTs.

The stage of patient illness is a concern, as it is suggested that asking terminally ill patients or patients with poor prognosis to take part in an RCT with a placebo can be emotionally detrimental for some patients. Also, side-effects of treatments used in RCTs are seen as possible negatives for patients. It is important to note that these are what the clinicians perceive their patients to be thinking, and the patients themselves may not share these views.

Inviting patients to take part in research can have the effect of raising patient awareness of disease, which can be interpreted in both a positive and negative light (i.e. more awareness may lead to increased participation in research but also more health seeking behaviour, stretching current resources).

Research can be thought to be inequitable by clinicians, with some special patient groups seen as receiving more attention than others.

Effects on clinical practice

A positive aspect of taking part in RCTs is the beneficial influence it can have on clinical practice. Being a research active practice enhances services offered by practices, encouraging confidence and loyalty from patients. It is also thought that the discipline needed to adhere to some trial protocols has beneficial effects on clinical practice.

Advancements in clinical practice are dependent on carrying out good quality clinical trials. Taking part in RCTs can improve treatment strategies used in everyday practice, conferring benefits to patients outside the RCT in the medium and long term.

Negatives include the possible disruption caused to normal practice brought about by the extra work involved in assessing patients for eligibility, and approaching those who are eligible for participation (i.e. describing RCT, obtaining informed consent, etc). The extra time associated with recruiting to RCTs in addition to normal duties is often stated as a major barrier to involvement. In the climate of trying to achieve service targets within tight budgets, carrying out extra work to recruit patients to trials may not be seen as a priority.

It is felt by some clinicians that although they are crucial to the successful running of trials by recruiting subjects, they often do not receive the acknowledgment/rewards they feel they deserve. Being asked to recruit for RCTs is seen to be intrusive by some clinicians.

Individual benefits for clinicians

Motivation for involvement in research can be seen to move beyond altruism. Taking part and recruiting patients to RCTs is seen by many to have personal benefits for clinicians. Involvement with colleagues from different fields is seen to be important personally, as well as professionally.

Participation in RCTs is seen by some as crucial for career development, and professional recognition.

Methods associated with successful recruitment

Community awareness of RCTs and research in general is linked to good recruitment. Promotion efforts should be tried to improve awareness which should have the effect of increasing the number of patients willing to take part in RCTs. Endorsements of research by the patients' own GP or practice can improve recruitment.

The research question addressed by an RCT is of vital importance to clinicians. The question should be both interesting and relevant to practice. Initial contact with clinicians about involvement in a trial should be brief but informative. Trial methods should be easy to understand and then communicate to patients. Inviting recruiters to take part in the design of RCTs could improve recruitment.

The funding of protected research time is an intervention that could improve recruitment performance. This would allow clinicians more time to discuss the trial with patients. More time would also allow clinicians to tailor their approach to each individual, an approach that is desirable for some clinicians. If protected research time is not a possibility then minimisation of workload related to recruitment is then key.

Financial incentives are important for many, with criticism when reimbursement for time is not offered. Clinicians should be reimbursed for time spent on recruitment rather than placing a bounty on patients heads'. Conversely some argue that financial incentives are unethical, and others that being paid would not significantly affect recruitment efforts. It was also noted that all staff should be rewarded for participation in research, not just clinicians.

Organisationally, being part of a research active practice is linked with good recruitment to RCTs. Having a research mentor or a trial coordinator or being involved in a research network are also factors in successful recruitment. Competition with other recruiters is a constructive way to maximise recruitment.

Appropriate training about research methods and recruitment methods is regarded as the key to success by many. Training should focus on addressing many common misconceptions about RCTs, particularly equipoise and informed consent.

Qualitative effect size (metasummary)

By dividing the number of studies containing each theme/abstracted finding by the total number of studies, an effect size was calculated. Table 4 shows the findings with effect sizes >20%, as proposed by Sandelowski and Barroso[22]. A full list of findings and effect sizes is given in Appendix 4.

{INSERT TABLE 4 HERE}

Difficulty communicating trial methods (randomisation, equipoise, etc) was the most common sub theme (64%), and was linked to a poor understanding of research methods by clinicians, and research in general by the public (55%). Ease of understanding and carrying out RCT

methods was also commonly described as associated with successfully recruiting trials (45%).

Clinicians found it difficult reconciling the roles of clinician and recruiter (36%). Clinicians were often described to only put forward patients who they deemed appropriate (gatekeeping)(27%), which links to paternalism (27%) and prioritising patient wellbeing (45%).

The positive and negative aspects of taking part in RCTs was frequently mentioned, with a balance between possible negative (36%) and positive effects on patients (27%), and the effect on clinical practice (45%).

The most frequently found abstracted finding was methods associated with successful recruitment to RCTs, with four sub-themes with a frequency effect greater than 20%. It was thought that the research question should be interesting and relevant to practice (45%). Financial incentives were seen by most as important for participation (27%). Training relevant to running trials should improve recruitment by targeting poor understanding of RCT methodology, as well as teaching recruitment methods (45%).

DISCUSSION

The aim of this review was to identify, and synthesise, evidence of the effectiveness of interventions aimed at improving the recruitment activity of clinicians in RCTs, and evidence of their attitudes towards recruitment to RCTs.

Methodological challenges

As the volume of evidence was perceived to be small an aim of the review was to include as much evidence as possible, regardless of method, several methodological issues had to be dealt with. Many systematic reviews of interventions exclude studies that do not use randomised controlled trials. While good quality RCTs of interventions would provide the best evidence, the nature of this research question lends itself to retrospective descriptive studies. This may be due to the logistical, ethical and scientific obstacles of performing randomised trials of recruitment nested within host RCTs[42]. Challenges for host trials include: increasing complexity and management burden; compatibility between host and nested study; and the impact of the nested study on host trial design. Challenges for nested studies include: investigators' concerns that host study investigators might have strong preferences, limiting the nested study investigators control over their research; and concerns about sample size which might limit statistical power. "Evidential nihilism", where narrow inclusion criteria are set regarding trial design would have led to an emptier review, which would not help further our understanding of the problem as much[43]. Qualitative studies were included in this review as it is important not just to understand what works, but also to have an understanding of why. It is hoped that a better understanding of clinicians' attitudes towards recruitment to RCTs may inform the development of interventions aimed to improve the support and training given to those involved in RCTs.

The search was broad and included no methodological filters, but still returned a large number of results. There is often a trade-off between sensitivity and specificity when performing a search for a systematic review, and in this case it was decided to err on the side of over inclusion, so a sensitive search was designed.

The review of quantitative studies found limited high quality evidence of interventions aimed at improving clinician activity, and shows the importance of building the evidence base to allow those running RCTs to have access to a range of proven strategies to maximise recruitment. Quality of the included qualitative studies was found to be good; however there was a tendency for the included studies to focus on the barriers to recruitment from the perspective of poorly recruiting trials. Little evidence was found of studies that aimed to assess how and why those clinicians who recruited well did so. It could be argued that facilitators are more illuminating, as barriers can often be seen as excuses, i.e. if the barrier was removed would the clinicians recruit more successfully?

What interventions work?

Evidence based interventions are necessary for RCTs to recruit successfully, however there is currently limited evidence, and interventions are being used that have no evidential grounding. For example, a study of seven primary care-based RCTs found that only 37% of interventions to promote recruitment were judged to be evidence based[7]. Further to this, Graffy *et al* stated that currently, where nested studies of recruitment methods are conducted on the initiative of individual investigators, there is no systematic method of choosing the intervention[42]. The authors go on to suggest the creation of a portfolio of interventions that could be made available to investigators for inclusion within an individual trial, or multiple trials.

This lack of evidence based interventions is particularly salient given that "common sense", interventions that could be assumed to have a positive effect on recruitment often had little

or no effect. The most successful intervention identified by this review was in the two trials that used embedded qualitative research to design interventions to improve recruitment. The qualitative research investigated recruitment appointments, study documents and interviewed clinicians to understand what aspects were amenable to change in order to improve recruitment. In both studies the intervention increased recruitment: i.e. the proportion of eligible subjects who consented to be randomised in the study. Rather than discuss the strategies used to improve recruitment, the most important factor in studies employing embedded qualitative research is the way that the intervention is developed. The use of qualitative methods allowed tailored interventions to be made that attempted to address problems with recruitment that were experienced by the clinicians and trial subjects (i.e. use of interviews, monitoring of recruitment interviews), as well as problems identified by the trial coordinators. This method is adaptive and allows for continuous monitoring and improvement. Although the interventions themselves may not be generalisable, the qualitative methods used to create the interventions, could be transferred to other settings, potentially having a positive effect on recruitment. Another positive feature of this approach was that improvements were maintained over time. Following intervention at two centres, recruitment was shown to remain significantly higher for at least 24 months.

One possible barrier to the use of this approach may be the extra time, money and personnel needed to carry out the qualitative research. However, the use of qualitative methods in pilot or feasibility trials prior to a full study would provide a cost-effective means of defining suitable interventions that could be fully incorporated into subsequent trials. If these interventions then proved successful in aiding recruitment, the extra efforts and costs involved in the preparatory phases would be offset by the greater potential for a successful full trial that would result, providing greater returns to funders and increasing the scientific validity of the trial overall.

Clinicians' attitudes to recruitment to RCTs

Setting aside the debate regarding the utility of metasummary effect sizes, in this review there are three key areas highlighted by the calculation of qualitative effect sizes that may be the best target for improvement in future trials: understanding of RCTs and health research in general (both by the general public and clinicians); communication of trial methods (both trial coordinators to clinicians, and clinicians to patients); and reduction of the workload associated with recruitment.

It should not be assumed by trial coordinators that recruiters have a full understanding of RCT and recruitment methods. Clinicians' understanding of research in general and RCTs in particular could be improved using training specific to the RCT they are involved in as well as education relating to common misconceptions about RCTs.

Some of the themes identified could be used to emphasise the individual benefits to both trial subjects and clinicians, and the positive effect taking part in research can have on clinical practice[44]. For example a study of centres involved in a multi-centre breast cancer treatment trial, found that both patients and clinicians benefited from participation in the RCT, due to optimised decision making with regards to therapy and patient care[45]. An overall positive effect on the quality of medical care was seen across the centres. As clinicians prioritise patient wellbeing, emphasising the potential patient benefits to them could help remove a barrier to recruitment.

It is clear that reported barriers may often be excuses for why clinicians have not recruited well. Patterson *et al*, for example, found that concerns about taking part in RCTs related to ethics and research approvals, but even when these issues were addressed clinicians remained less than enthusiastic, and instead shifted the blame to administrative and clinical duties[40]. Removal of the perceived barrier will not necessarily lead to an improvement in

recruitment. This again highlights that more investigation is required to illuminate what facilitates trials that easily meet their recruitment targets.

Reducing clinicians' workload associated with recruiting to RCTs was often mentioned. This could be achieved by providing extra staff support, simplification of recruitment protocols, or providing protected research time. However, it remains to be seen whether clinicians saying they do not have enough time is more commonly a barrier or an excuse.

Clinicians place an emphasis on patient wellbeing, and some may feel the need to protect their patients from the risk of taking part in a RCT. A commonly held belief among clinicians is that patients who take part in RCTs face risks that they would not otherwise face if they received their healthcare in the usual manner. However, a systematic review found that the outcomes of patients taking part in RCTs do not differ from those of patients receiving similar treatments who do not participate[45].

Engaging clinicians in RCTs is a crucial step in the recruitment process. It is apparent that clinicians are aware of the impact they have on their patients' decision making regarding involvement in trials, and it has been shown that personal endorsement of trials by clinicians can have a positive effect on recruitment. If clinicians are fully engaged and understand the benefits, to both themselves and patients, of participating in RCTs, recruitment could improve significantly.

CONCLUSION

Few high quality trials were identified that tested interventions to improve clinicians' recruitment activity in RCTs. The most promising intervention was the use of qualitative methods to identify and overcome barriers to clinician recruitment activity. It is clear that the barriers to nested trials of recruitment interventions in host RCTs must be overcome in future in order to add to the evidence base.

The metasummary of qualitative findings identified understanding and communicating RCT methods (clinician to patient and trial coordinator to clinician) as a key target for future interventions to improve recruitment. Reinforcement of the potential benefits, both for clinicians and their patients, could also be a successful factor in improving recruitment. A bias was found toward investigating barriers to recruitment, so future work should also encompass a focus on successfully recruiting trials.

Few reviews attempt to synthesise qualitative evidence using the methods demonstrated here, and it is hoped that this review demonstrates the utility of methods for synthesising diverse evidence. Hopefully by bringing together a review of qualitative and quantitative studies, we have created a report that is more informative than carrying out two reviews in isolation.

It is hoped that this work will inform the development of future studies investigating clinicians' attitudes to recruitment, as well as the design of possible future recruitment interventions to be tested using a robust trial design.

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Contributors

BF made substantial contributions to the design of the study, acquisition and interpretation of data, synthesis of qualitative evidence, and wrote the final draft of the article.

AG was involved in acquisition, analysis and interpretation of data.

SW contributed substantially to the conception and design of the study, and was responsible for obtaining funding for the study..

DM contributed substantially to the design of the study, particularly search strategy, data analysis and quality assessment of quantitative papers.

SD contributed substantially to the design of the study, advised on qualitative quality assessment, data extraction and metasummary,.

All authors contributed to drafting the manuscript and revising it critically for intellectual content, and all authors have seen and approved the final version of the manuscript.

Competing interests

The authors declare no competing interests.

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Table 1 – Reports of difficulties recruiting to RCTs

Authors	Year	Findings
Charleson and Horwitz[4]	1984	A study of 41 trials listed with the National Institutes of Health (USA) showed that a third of trials recruited fewer than 75% of their planned sample.
Easterbrook and Matthews[5]	1992	A review of 720 research projects approved by the Central Oxford Research Ethics Committee 1984-1987 (UK). Report states that the main reason for abandoning a study was due to difficulties recruiting study participants.
Wilson *et al*[6]	2000	A study of recruitment of primary care practices to an endoscopy trial. Of 90 practices contacted, 43 agreed to take part, 31 recruited at least one patient and only 23 recruited more than five patients.
Foy *et al*[7]	2003	A study of seven primary care trials of dyspepsia management in the UK. Only one study reached its recruitment target; five recruited less than 50% of target and three of these closed prematurely.
McDonald *et al*[8]	2006	A study of 114 RCTs funded by two UK funding bodies 1994-2002. 31% of trials achieved their original recruitment target. 53% were extended due to recruitment problems. Early recruitment problems were identified in 63% of the trials.
Bower *et al*[9]	2007	A survey of published primary care trials in the UK. Less than one third of trials recruited to their original timescale.
Raftery *et al*[10]	2008	Data held by the National Coordinating Centre for Health Technology Assessment (UK), shows that two thirds of funded trials fail to pass 80% of their recruitment target.
Toerien *et al*[11]	2009	Review of all reports of RCTs published in July-December 2004 in six major journals. Of 133 trials 21% that reported sample size calculations failed to achieve adequate numbers at randomisation, and 48% at outcome assessment.

Table 2 – Summary of included quantitative studies

	Study type	RCT recruiting to	Overview (country, aim)
Donovan (2003) [23]	RCT	ProtecT Trial, prostate cancer treatment	UK. To investigate the comparative effectiveness of nurses and surgeons in recruiting patients
Monaghan (2007) [24]	RCT	ADVANCE trial (diabetes)	Australia. Investigation of the effect of extra communication from central trial coordinators on recruitment.
Lienard (2006) [25]	RCT	Adjuvant treatment of breast cancer	France. To assess the impact of on-site initiation monitoring visits on patient recruitment.
Fletcher (2010) [26]	Observational time series	Primary care based multi-centre RCT, stroke trial	UK. To examine whether changes to the design and conduct of a primary care-based RCT were associated with changes in patient recruitment.
Donovan (2002) [27]	Observational time series	ProtecT trial – treatment for prostate cancer	UK. *Feasibility study for main trial.* Qualitative research used to address barriers to recruitment, and make changes to protocol.
Donovan (2009) [28]	Before and after study	ProtecT trial – treatment for prostate cancer	UK. *Main trial results.* A complex intervention was designed using qualitative methods to improve recruitment (i.e. regular training of recruiting staff, centre reviews if centre not recruiting to target, documents to provide advice, and personal feedback).
Kenyon (2005) [29]	Before and after study	ORACLE trial – double blind RCT antibiotic treatment for women in idiopathic preterm labour	UK. Trial was not recruiting successfully so changes were made (introduction of lead midwife responsible for recruitment with protected time for research).
Submacular Surgery Trials Research Group (2004) [30]	Case study (with comparison group)	SST – submacular surgery trial	USA. Comparison of university and community based practices taking part in three multicentre randomised trials. One outcome measure was patient accrual.

Table 3 – Summary of included qualitative studies

	Title	Study method and aims	Recruitment to RCT?
Hales (2001) [31]	The conflicting roles of clinicians versus investigators in HIV randomised clinical trials	**Semi-structured interviews** One theme investigated was recruitment.	**Yes.** Clinical drug trial. Primary care and secondary care
Caldwell (2002) [32]	Paediatricians' attitudes toward randomized controlled trials involving children	**Focus groups** To examine doctors attitudes toward children's participation in RCTs and identify barriers to participation	**Yes.** RCTs involving children. Secondary care (Teaching hospital in Australia)
Jones (2003) [33]	Building research capacity: an exploratory model of GPs' training needs and barriers to research involvement	**Semi-structured interviews** Investigation of GPs research training needs, and barriers to involvement in research.	**Not specified.**
McIntosh (2005) [34]	Recruitment of physician offices for an office based adolescent smoking cessation study.	**Focus groups** To elicit perceptions of facilitators and barriers to initial engagement of physician practices	**Yes.** Adolescent smoking cessation study
Mason (2007) [35]	GPs' experiences of primary care mental health research: a qualitative study of the barriers to recruitment	**Semi-structured interviews** To investigate the perceived barriers among GPs to introducing participation in RCTs to patients with depression.	**Yes.** Primary care mental health research.
Ziebland (2007) [36]	Does it matter if clinicians recruiting for a trial don't understand what the trial is really about? Qualitative study of surgeons' experiences of participation in a pragmatic multi-centre RCT	**In-depth interviews** To explore physicians understanding of the trial purpose and how this understanding had influenced their recruitment.	**Yes.** Multicentre pragmatic RCT. Spinal surgery. UK.
Bill-Axelson (2008) [37]	Experiences of randomization interviews with patients and clinicians in the SPG-IV trial	**Semi-structured interviews.** Investigation of patients' and clinicians' experiences of randomisation with the aim of facilitating future trial participation.	**Yes.** Prostate cancer RCT
Potter (2009) [38]	A qualitative study exploring practice nurses' experience of participating in a primary-care based randomised controlled trial	**Semi-structured interviews** To explore the views of practice nurses' recruiting into a primary care-based RCT, and to investigate factors that influence the success of trial recruitment.	**Yes.** Primary care based RCT to promote adherence to treatment of people with type 2 diabetes.
Howard (2009) [39]	Why is recruitment to trials difficult? An investigation into recruitment difficulties in an RCT of supported employment in patients with severe mental illness	**Interviews** To evaluate reasons for under-recruitment in an RCT. Trial staff and recruiting physicians were interviewed.	**Yes.** RCT of supported employment in patients with severe mental illness.
Patterson (2010) [40]	The great divide: a qualitative investigation of factors influencing researcher access to potential randomised controlled trial participants in mental health settings	**Interviews** Using Grounded Theory process evaluation of a multicentre trial to investigate factors influencing referral to potential RCTs in mental health settings.	**Yes.** Potential RCTs in mental health setting
Paramasivan (2011) [41]	Key issues in recruitment to randomised controlled trials with very different interventions: a qualitative investigation of recruitment to the SPARE trial	**Interviews; content analysis of RCT documents; conversation analysis of recruitment appointments** To explore reasons for low recruitment and attempt to improve recruitment rate by implementing changes suggested by qualitative findings.	**Yes.** Bladder cancer treatment trial – feasibility study.

Table 4 – Summary of qualitative findings with effect size >20%

Abstracted finding	**Sub-theme**	**Studies in which sub-theme is present**	**Effect size (%)**
Understanding of research	RCTs provide the best evidence.	[31] [35] [36]	27
	Poor understanding of research	[32] [33] [36] [39] [40] [41]	55
Communication	Difficulty communicating trial methods	[31] [32] [35] [37] [39] [40] [41]	64
Patient-clinician relationship	Conflicting roles of being a recruiting physician	[31] [35] [39] [40]	36
	Clinicians acting as gatekeepers	[38] [39] [40]	27
	Paternalism	[35] [38] [39]	27
	Clinician influence on patient decision making	[32] [35] [37] [39]	36
	Patient wellbeing a priority	[31] [32] [35] [37] [39]	45
Effect on patients	Possible benefits of taking part in RCTs	[31] [32] [34] [38]	36
	Possible harms of taking part in RCTs	[31] [36] [39]	27
Effect on clinical practice	Positive effect of being involved in RCTs	[31] [32] [34] [35] [38]	45
Individual benefit for clinician	Career development	[32] [38] [41]	27
Methods associated with successful recruitment	Importance of research question	[31] [32] [35] [36] [37]	45
	Trial methods easy to understand, communicate and carry out	[32] [34] [37] [38] [41]	45
	Financial incentives	[31] [33] [34]	27
	Appropriate training	[32] [33] [34] [38]	36

BMJ open

Improving the recruitment activity of clinicians in randomised controlled trials - a systematic review

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2011-000496.R1
Article Type:	Research
Date Submitted by the Author:	18-Nov-2011
Complete List of Authors:	Fletcher, Benjamin; University Of Birmingham, Health and Population Sciences Gheorghe, Adrian; University of Birmingham, Health and Population Sciences Moore, David; University of Birmingham, Health and Population Sciences Wilson, Sue; University of Birmingham, Health and Population Sciences Damery, Sarah; University of Birmingham, Health and Population Sciences
Primary Subject Heading:	Evidence-based practice
Secondary Subject Heading:	Epidemiology, Research methods
Keywords:	randomised controlled trial, recruitment, clinicians, systematic review, qualitative metasummary

PICOS Framework for quantitative studies:

Population
- Inclusion
  - clinicians recruiting to RCTS
- Exclusion
  - subjects of RCTs

Intervention
- Inclusion
  - any intervention aimed at improving the recruitment activity of clinicians
  - comparison of clinicians recruiting to trials if the aim was to compare recruitment activity
- Exclusion
  - interventions aimed at the subjects of RCTs

Comparator
- Inclusion
  - No intervention, or comparison of two interventions
- Exclusion
  - Studies comparing recruitment in separate RCTs

Outcomes
- Inclusion
  - Numbers/proportions of subjects recruited
  - Recruitment rates
  - Recruiting to target
  - Adherence to trial protocol regarding recruitment
- Exclusion
  - Intention to recruit

Studies
- Inclusion
  - Any study where a comparison is made between an intervention and a control group, or two or more intervention group.
  - Randomised controlled trials
  - Quasi experimental studies
    - Before and after studies
    - Interrupted time-series
  - Observational studies
    - Cohort study
    - Case control study
    - Case study (where there is a comparator group)
- Exclusion
  - Studies with no comparator group
  - Qualitative studies

SPICE framework for qualitative studies:

Setting
- Randomised controlled trials

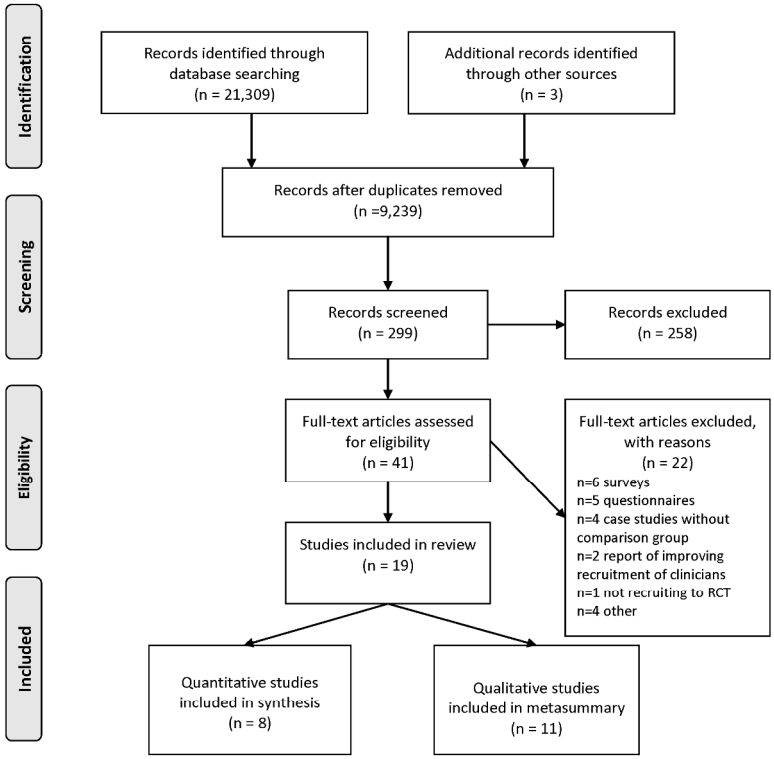
Perspective
- Clinicians directly involved in recruiting patients to RCTs

Intervention/phenomena of interest
- Poor recruitment to RCTs

Comparison
- None

Evaluation
- Perceived barriers and facilitators

210x297mm (300 x 300 DPI)



215x279mm (300 x 300 DPI)

SUPPLEMENTARY MATERIAL

Appendix 1 – example search strategy

OVID MEDLINE search

1. researcher*.ti,ab.
2. investigator*.ti,ab.
3. experimenter*.ti,ab.
4. trialist*.ti,ab.
5. recruiter*.ti,ab.
6. clinician*.ti,ab.
7. physician*.ti,ab.
8. doctor*.ti,ab.
9. nurse*.ti,ab.
10. healthcare professional*.ti,ab.
11. healthcare practitioner*.ti,ab.
12. trial coordinator*.ti,ab.
13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14. recruit*.ti,ab.
15. select*.ti,ab.
16. allocat*.ti,ab.
17. participat*.ti,ab.
18. enlist*.ti,ab.
19. enrol*.ti,ab.
20. accru*.ti.ab.
21. involve*.ti,ab.
22. Invit*.ti,ab.
23. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24. randomised controlled trial*.ti,ab.
25. randomized controlled trial*.ti,ab.
26. randomised clinical trial*.ti.ab.
27. randomized clinical trial*.ti,ab.
28. controlled trial*.ti,ab.
29. RCT*.ti,ab.
30. 24 or 25 or 26 or 27 or 28 or 29
31. 13 and 23 and 30

Appendix 2 – quality of included quantitative studies

Study	SELECTION	DESIGN	CONFOUNDERS	BLINDING	DATA COLLECTION METHODS	WITHDRAWALS AND DROP-OUTS	GENERAL RATING
Donovan (2003) [23]	Moderate	Strong	Weak	Moderate	Weak	Strong	Weak
Monaghan (2007) [24]	Moderate	Strong	Strong	Moderate	Moderate	Strong	Strong
Lienard (2006) [25]	Moderate	Strong	Moderate	Moderate	Weak	Strong	Moderate
Fletcher (2010) [26]	Moderate	Moderate	Weak	Weak	Weak	NA	Weak
Donovan (2002) [27]	Moderate	Moderate	Weak	Weak	Weak	NA	Weak
Donovan (2009) [28]	Moderate	Moderate	Weak	Weak	Weak	NA	Weak
Kenyon (2005) [29]	Moderate	Moderate	Weak	Weak	Weak	NA	Weak
SSRTG (2004) [30]	Moderate	Weak	Weak	Moderate	Strong	NA	Weak

Appendix 3 – Summary of methodology and quality of studies included in qualitative metasummary

Study	**Hales (2001) [31]**	**Caldwell (2002) [32]**	**Jones (2003) [33]**	**McIntosh (2005) [34]**	**Mason (2007) [35]**	**Ziebland (2007) [36]**	**Bill-Axelson (2008) [37]**	**Potter (2009) [38]**	**Howard (2009) [39]**	**Patterson (2010) [40]**	**Paramasivan (2011) [41]**
Methodology	Grounded Theory	Unclear	Grounded Theory	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Grounded Theory	Unclear
Data analysis	Thematic	Thematic constant comparative	Thematic	Unclear	Thematic framework	Thematic constant comparative	Content analysis	Thematic framework	Thematic constant comparative	Thematic constant comparative	Thematic, content, conversation
Was there a clear statement of the aims of research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Is qualitative methodology appropriate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the research design appropriate to address the aims of the project?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the recruitment strategy appropriate to the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the data collected in a way that addressed the research issue?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Has the relationship between researcher and participants been adequately considered?	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear
Have ethical issues been taken into consideration?	Unclear	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Yes	Unclear	Yes	Unclear
Was the data analysis sufficiently rigorous?	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Is there a clear statement of findings?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Is the research valuable?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Appendix 4 – full list of qualitative findings

Abstracted finding	Theme
Understanding of research	RCTs provide the best evidence
	Too much research
	Poor understanding of research
	Community responsibility to take part
	Suspicious of researchers' motives
Communication	Difficulty communicating trial methods
	Choice of language important
	Social class of patient a factor
	Poor communication from trial coordinators
Perceived patient barriers	Poor community awareness
	Lack of motivation/ interest
	Mistrust of being asked to participate
	Fear of negative effects
Patient-clinician relationship	Conflicting roles of being a recruiting clinician
	Clinicians act as gatekeepers
	Paternalism
	Responsibility for patients
	Clinician influence on patient decision making
	Patient wellbeing a priority
	Effect on patient trust in clinician
	Clinician feeling of rejection if patient refuses to participate
Effect on patients	Possible potential benefits of taking part in RCTs
	Possible harm associated with taking part in RCTs
Effect on practice	Positive effect on practice of being involved in RCTs
	Negative effect on practice of being involved in RCTs
Individual benefit for clinician	Career development
	Involvement with other clinicians
Methods associated with successful recruitment	Importance of research question
	Personal endorsement of RCT
	Trial methods easy to understand, communicate and carry out
	Protected research time
	Financial incentives
	Minimisation of workload
	Research active practice
	Competition with other recruiters
	Appropriate training
	Trial coordinator/trial nurse
	Increasing community awareness of RCTs

Appendix 5 – Data extraction tables for included quantitative studies

Study details	Author	Donovan J
	Year	2003
	Country	UK
	Authors' objective	A comparison of the effectiveness/cost effectiveness of nurses and surgeons as recruiters
	Outcomes measured	Proportion of subjects recruited
	Setting	RCT of treatment for prostate cancer (ProtecT trial)
Inclusion/Exclusion	Population	Nurses and urologic surgeons
	Inclusion criteria	Already involved in ProtecT trial
	Exclusion criteria	Not reported
Baseline characteristics		Not reported
Methods	Study design	Randomised trial
	Methods of randomisation	Randomisation to nurse or urologist was conducted by telephone to central trial office, employing random permuted blocks of size six, computer generated by someone not involved in recruitment.
	Method of data collection	Not reported
	Statistical analysis	Intention to treat Chi-square test Power calculation
Intervention details	Intervention	Nurse recruiting
	Comparator	Urologic surgeon recruiting
Results	Number recruited	Number of nurses and surgeons involved – not reported. 150 patients agreed to be randomised to nurse or surgeon for recruitment appointment.
	Description of outcome measure 1	Recruitment rate (proportion recruited of those eligible)
	Intervention follow-up data	67% (50/75)
	Comparator follow up data	71% (53/75) p=0.60
Additional comments	Authors comments, study limitations, biases not reported, validity of authors conclusions, generalisability	Cost minimisation analysis showed that using nurses instead of surgeons was more cost effective.

Study details	Author	Monaghan H
	Year	2007
	Country	19 countries in Asia, Australasia, Europe and North America
	Authors' objective	To evaluate the effect of additional communication from central trial coordinators on recruitment.
	Outcomes measured	Median time to half recruitment target Median number of participants recruited
	Setting	Diabetes blood pressure monitoring trial (ADVANCE trial)
Inclusion/Exclusion	Population	Clinical sites were unit of randomisation
	Inclusion criteria	Sites already involved in the ADVANCE trial
	Exclusion criteria	Sites were excluded if they were unable to communicate in English
Baseline characteristics		Groups compared for: Location of centres; mean recruitment target; range of recruitment target. Control and intervention were similar at baseline.
Methods	Study design	Single blind randomised controlled trial
	Methods of randomisation	Computer generated algorithm stratified by country and recruitment target
	Method of data collection	Bespoke internet-based trial management system
	Statistical analysis	Power calculation Intention to treat Wilcoxon rank tests to compare medians and distributions as the data was skewed
Intervention details	Intervention	As comparator plus additional communication including: Frequent e-mails Personalised mail-outs of league tables and graphs describing recruitment performance relative to other centres Individualised certificates acknowledging achievement of recruitment milestones Items relating to study (i.e. ADVANCE trial mouse mat)
	Comparator	Usual communication from trial coordinators: Generic newsletters, e-mails, faxes
Results	Number recruited	167 centres 7,847 patients
	Description of outcome measure 1	Median number of participants randomised (median/IQR)
	Intervention follow-up data	37.5 (27.0 - 51.5)
	Comparator follow up data	37.0 (21.0 - 54.5) p=0.68
	Description of outcome measure 2	Median time to half recruitment target (median/IQR)
	Intervention follow-up data	4.4 months (1.8 - 7.1)
	Comparator follow up data	5.8 months (2.7 – 8.2) p=0.08
Additional comments	Authors comments, study limitations, biases not reported, validity of authors conclusions, generalisability	"This study suggests that an additional communication strategy targeted at the clinical sites participating in a large scale multi-centre clinical trial may increase the speed with which participants are recruited. Failure of this improvement to reach conventional levels of statistical significance is likely to reflect inadequate power."

Study details	Author	Lienard JL
	Year	2006
	Country	France
	Authors' objective	To assess the impact of on-site monitoring visits on recruitment
	Outcomes measured	1. Patient recruitment 2. Quantity of reported data 3. Quality of reported data 4. Patient follow-up time
	Setting	RCT of breast cancer treatment (AERO-B2000 trial)
Inclusion/Exclusion	Population	Oncology centres
	Inclusion criteria	Centres involved in the AERO-B2000 trial
	Exclusion criteria	Centres located outside France
Baseline characteristics		Intervention and control groups compared using: region (Paris, province), centre type (public, private) Groups were similar at baseline.
Methods	Study design	Randomised controlled trial
	Methods of randomisation	Centres were randomly allocated by "a minimisation technique to ensure balance between groups"
	Method of data collection	Investigators used case report forms. Consisted of 9 pages for patients with full follow up.
	Statistical analysis	Intention to treat Statistical tests adjusted for intra-centre correlation.
Intervention details	Intervention	On-site monitoring visits (initiation, on-going and closeout visits). On site monitoring has several purposes: to ensure that the rights of patients are protected; to verify the accuracy of reported data; and to provide training to site personnel with regard to protocol and trial material
	Comparator	No on-site monitoring visits
Results	Number recruited	135 centres 573 patients
	Description of outcome measure 1	Patient recruitment (centres recruiting at least one patient)
	Intervention follow-up data	51.5% (35/68)
	Comparator follow up data	50.7% (34/67) [no sig. diff.]
	Description of outcome measure 2	Patient recruitment (total number of patients)
	Intervention follow-up data	302
	Comparator follow up data	271 [no sig. diff.]
Additional comments	Authors comments, study limitations, biases not reported, validity of authors conclusions, generalisability	Of centres that entered at least one patient: 91% were visited in the intervention group – should be 100% 6% were visited in the no-visit group – should be 0% Other: No difference detected between visited and non-visited groups for data quality, data quantity and patient follow-up time

Study details	Author	Fletcher K
	Year	2010
	Country	UK
	Authors' objective	"To examine whether changes to the design and conduct of a primary care based RCT were associated with changes in patient recruitment."
	Outcomes measured	Number of subjects recruited
	Setting	A primary care bases multicentre RCT of aspirin versus warfarin for stroke prevention (BAFTA)
Inclusion/Exclusion	Population	Recruiting clinicians
	Inclusion criteria	Clinicians involved in BAFTA trial
	Exclusion criteria	NA
Baseline characteristics		NA
Methods	Study design	Observational time series
	Methods of randomisation	NA
	Method of data collection	Not reported
	Statistical analysis	Recruitment rate per 1000 population calculated (patients aged >75). In order to determine whether there was a significant change in recruitment rate, change point analysis was carried out with a moving *F* statistic using the first seven quarters as the baseline sample and a moving average of three quarters.
Intervention details	Intervention	"Over the recruitment period, inclusion criteria were revised; procedural changes were introduced to reduce primary care workload and time to recruitment; more sites were enrolled and our approach to the recruitment and retention of practices changed."
	Comparator	Before change
Results	Number recruited	330 practices 973 subjects
	Description of outcome measure 1	Recruitment
	Intervention follow-up data	There was a significant increase in recruitment rate in the last six months of the study ($p<0.05$).
	Comparator follow up data	NA
Additional comments	Authors comments, study limitations, biases not reported, validity of authors conclusions, generalisability	"Following protocol changes aimed to reduce clinical workload, there was a significant increase in recruitment during the final six months of the study, during a period when there was not a similarly large increase in the total population available." "The lessons learnt, for example, with regard to workload minimisation and simplification of study protocol, could be considered by investigators designing trials."

Study details	Author	Donovan J
	Year	2002
	Country	UK
	Authors' objective	Use of qualitative methods to investigate and improve the process of recruitment to a RCT.
	Outcomes measured	Proportion of eligible patients consenting to randomisation. Proportion of eligible patients who accept allocation following randomisation.
	Setting	ProtecT trial (prostate testing for cancer and treatment) feasibility study.
Inclusion/Exclusion	Population	Recruiting clinicians
	Inclusion criteria	Already involved in ProtecT trial
	Exclusion criteria	NA
Baseline characteristics		NA
Methods	Study design	Observational time series
	Methods of randomisation	NA
	Method of data collection	Not reported
	Statistical analysis	Exact binomial method
Intervention details	Intervention	"We used qualitative findings to devise presentation strategies, which were implemented initially in one centre. We reproduced the finding and recommendations for changes to the content and presentation of information in three documents, and we developed a training programme and delivered it to recruiters."
	Comparator	Before intervention
Results	Description of outcome measure 1	Proportion eligible patients consenting to randomisation
	Intervention follow-up data	After 10 months 70% (108/155)
	Comparator follow up data	51% (23/45) **p<0.05**
	Description of outcome measure 2	Proportion of randomised subjects accepting allocation
	Intervention follow-up data	After 10 months 70% (76/108)
	Comparator follow up data	78% (18/23) p>0.05
Additional comments	Authors comments, study limitations, biases not reported, validity of authors conclusions, generalisability	"Changes to information and presentation resulted in efficient recruitment acceptable to patients and clinicians. Such methods probably have wider applicability and may enable even the most difficult evaluative questions to be tackled."

Study details	Author	Donovan J
	Year	2009
	Country	UK
	Authors' objective	"We developed and evaluated a complex intervention to increase levels of randomisation and informed consent."
	Outcomes measured	Eligible subjects accepting randomisation and allocation
	Setting	ProtecT trial. An RCT of prostate cancer treatment
Inclusion/Exclusion	Population	Nurse recruiters
	Inclusion criteria	Involved at 2 centres in the main trial
	Exclusion criteria	NA
Baseline characteristics		NA
Methods	Study design	Before and after study
	Methods of randomisation	NA
	Method of data collection	Not reported
	Statistical analysis	Differences before and after centre reviews were investigated using two-tailed Fisher's Exact Test for each centre separately.
Intervention details	Intervention	"A complex intervention was developed based on the findings from the feasibility study (Donovan 2002): regular training for all staff and initiation for new staff; centre reviews if study targets were not maintained; documents to provide tips and advice; individual feedback as required."
	Comparator	Before intervention
Results	Description of outcome measure 1	Proportion eligible patients consenting to randomisation
	Intervention follow-up data	Centre A 12 months 86% (12/14) p=0.020 24 months 83% (9/11) Centre B 12 months 78% (31/40) p=0.013 24 months 68% (17/25)
	Comparator follow up data	Centre A 45% (11/24) Centre B 50% (23/46)
	Description of outcome measure 2	Proportion of those randomised who accepted allocation
	Intervention follow-up data	Centre A 12 months 67% (8/12) p=0.68 24 months 78% (7/9) Centre B 12 months 65% (12/31) p=0.096 24 months 94% (16/17)
	Comparator follow up data	Centre A 55% (6/11) Centre B 65% (15/23)
Additional comments	Authors comments, study limitations, biases not reported, validity of authors conclusions, generalisability	"This complex intervention resulted in high levels of randomisation and informed consent in a difficult trial. The generic aspects of the intervention could be applied to other trials to maximise randomisation and informed consent, and allow the mounting of trials previously considered too difficult

Study details	Author	Kenyon S
	Year	2005
	Country	UK
	Authors' objective	"This paper outlines a strategy employed by a large perinatal multicentre randomised controlled trial that overcame poor recruitment rates to result in recruitment targets being achieved within the given time frame."
	Outcomes measured	Number of eligible patients recruited per month
	Setting	ORACLE trial – overview role of antibiotics for curtailment of labour and early delivery.
Inclusion/Exclusion	Population	Recruiting lead midwives
	Inclusion criteria	Involved in ORACLE trial
	Exclusion criteria	NA
Baseline characteristics		NA
Methods	Study design	Before and after study
	Methods of randomisation	NA
	Method of data collection	Monitoring by trial coordinator
	Statistical analysis	Unclear, but limited
Intervention details	Intervention	The strategy involved the employment of lead local midwives to work three hours a week. The midwives were provided with an initial intense two day induction programme supported by six monthly updates, monthly phone contacts and regular contact visits from regional midwives.
	Comparator	No protected time for research or extra training/support. Before intervention,
Results	Description of outcome measure 1	Change in recruitment. Comparison of six month period before intervention (01-06/1997) and after intervention (06/1999-11/1999)
	Intervention follow-up data	Mean 69% (range -89 to 200%) increase in average recruitment
	Comparator follow up data	NA
Additional comments	Authors comments, study limitations, biases not reported, validity of authors conclusions, generalisability	"Any number of issues could have improved recruitment including: the midwives having protected paid time; the initial training and knowledge; the support structure with regular contact with regional midwives, etc."

Study details	Author	SSRTG
	Year	2004
	Country	USA
	Authors' objective	To compare the performance of community versus university based clinical centres in 3 multicentre randomised clinical trials of intraocular surgery.
	Outcomes measured	Patient accrual
	Setting	Three submacular surgery trials
Inclusion/Exclusion	Population	Unit of measurement is centre
	Inclusion criteria	Centres involved in one of three trials
	Exclusion criteria	NA
Baseline characteristics		NA
Methods	Study design	Case study
	Methods of randomisation	NA
	Method of data collection	Site visits by trial coordinators
	Statistical analysis	Because of the small number of centres in each category, no formal statistical tests were used to compare the two groups
Intervention details	Intervention	University based centre
	Comparator	Community based centre
Results	Number recruited	17 community based centres (381 subjects) 10 university based centres (634 subjects)
	Description of outcome measure 1	Patient accrual/centre (mean/median)
	Intervention follow-up data	37, 38.1
	Comparator follow up data	41, 37.3 Difference in means = 0.8 (95% CI -19.32 to 20.92) p=0.93
Additional comments	Authors comments, study limitations, biases not reported, validity of authors conclusions, generalisability	"Almost all centres performed at a very high level, although there was a trend for some community based centres to be at the lower end of most distributions."

Appendix 6 – Data extraction and quality assessment forms for studies included in qualitative review

Study ID:	Hales (2001)	12988
	Yes/No/Unclear	**Comments**
Was there a clear statement of the aims of the research?	Yes	
Is a qualitative methodology appropriate?	Yes	
Was the research design appropriate to address the aims of the research?	Yes	
Was the recruitment strategy appropriate to the aims of the research?	Yes	Sample includes almost all of the doctors involved in the trial.
Was the data collected in a way that addressed the research issue?	Yes	
Has the relationship between researcher and participants been adequately considered?	Unclear	
Have ethical issues been taken into consideration?	Unclear	
Was the data analysis sufficiently rigorous?	Yes	
Is there a clear statement of findings?	Yes	
Is the research valuable?	Yes	

Study ID: Hales (2001) 12988	
Method Semi-structured interviews	
Methodology Grounded theory	
Data analysis Thematic analysis	
Setting and context Clinician investigators were interviewed during the course of an intensive phase II clinical trial. Australia.	
Participants (number/description) 7 GP researchers and 4 participating hospital doctors. Additionally 3 GPs provided a written account.	
Interventions/phenomena of interest Exploring the conflicting roles of clinician investigators.	
Findings	**Narrative description**
Ethics	Doctors concerned with trial ethics: question, equipoise, financial inducements
Positive aspects of involvement	Scientific advancement, providing hope for patients, offering new treatments, enhancement of practice
Negative aspects of involvement	Work overload, lack of involvement in trial design, disruption of patient doctor relationship, conflicting roles
Authors' conclusions "Difficulties encountered in engaging in clinical trials were described as problems with the time involved in clinical trial work, and ethical dilemmas in recruitment and retention. Further tensions were associated with the often conflicting demands of patients' interests and research goals."	
Comments Good study, however, a lot of emphasis placed on how doctors perceived how trial subjects felt and acted the way they did rather than the doctors motives for involvement and recruitment to RCTs.	

Study ID:	Caldwell (2002)	4525
	Yes/No/Unclear	**Comments**
Was there a clear statement of the aims of the research?	Yes	
Is a qualitative methodology appropriate?	Yes	
Was the research design appropriate to address the aims of the research?	Yes	
Was the recruitment strategy appropriate to the aims of the research?	Yes	Convenience sample.
Was the data collected in a way that addressed the research issue?	Yes	Focus groups ensured "free discussion and interaction".
Has the relationship between researcher and participants been adequately considered?	Yes	"A professional facilitator unknown to the participants conducted the discussions, with one observer taking field notes."
Have ethical issues been taken into consideration?	Unclear	
Was the data analysis sufficiently rigorous?	Yes	
Is there a clear statement of findings?	Yes	
Is the research valuable?	Yes	

Study ID: Caldwell (2002) 4525	
Method Focus groups	
Methodology Unclear	
Data analysis Thematic analysis (constant comparative)	
Setting and context To examine paediatricians' attitudes towards children's participation in RCTs and indentify possible barriers to participation.	
Participants (number/description) 16 paediatricians and 5 trainees from a teaching hospital in Australia.	
Interventions/phenomena of interest Attitudes and barriers to recruitment	
Findings	**Narrative description**
Perceived gains	Professional benefits for paediatricians, improved patient care, scientific advancement
Perceived risks	Inconvenience, inadequate resources, potential harm to doctor-patient relationship
Authors' conclusions "This study suggests that children's participation in trials will be enhanced by increasing paediatricians' awareness of RCTs through education and involvement in trials and by improving risk-gains balance."	
Comments Good overall study.	

Study ID:	Jones (2003)	Citation
	Yes/No/Unclear	**Comments**
Was there a clear statement of the aims of the research?	Yes	
Is a qualitative methodology appropriate?	Yes	
Was the research design appropriate to address the aims of the research?	Yes	
Was the recruitment strategy appropriate to the aims of the research?	Yes	A convenience sample was used. Cross section of rural and urban GPs
Was the data collected in a way that addressed the research issue?	Yes	
Has the relationship between researcher and participants been adequately considered?	Unclear	
Have ethical issues been taken into consideration?	Unclear	
Was the data analysis sufficiently rigorous?	Yes	
Is there a clear statement of findings?	Yes	
Is the research valuable?	Yes	

Study ID: Jones (2003) citation	
Method Semi structured interviews	
Methodology Grounded Theory	
Data analysis Thematic analysis	
Setting and context GPs in rural and metropolitan South Australia. To determine GPs research training needs and barriers to involvement in research.	
Participants (number/description) 11 GPs "selection ensured a cross section of rural and urban GPs".	
Interventions/phenomena of interest Research involvement	
Findings	**Narrative description**
Individual issues	Lack of research training/experience; concepts and attitudes to research; research interest
Systems issues	Funding arrangements for general practice; access to resources; opportunity for publication; role of GP association
Authors' conclusions "GPs perceived both individual and systems solutions to building research capacity, including multifaceted interventions."	
Comments Citation from Mason (2007) 2162	

Study ID:	McIntosh (2005)	3398
	Yes/No/Unclear	**Comments**
Was there a clear statement of the aims of the research?	Yes	
Is a qualitative methodology appropriate?	Yes	
Was the research design appropriate to address the aims of the research?	Yes	
Was the recruitment strategy appropriate to the aims of the research?	Yes	Convenience sample: 17 paediatricians and 13 family practitioners
Was the data collected in a way that addressed the research issue?	Yes	
Has the relationship between researcher and participants been adequately considered?	Yes	"focus groups were conducted by a nationally recognised research company, and moderated by a single experienced facilitator" – not involved in RCT
Have ethical issues been taken into consideration?	Unclear	
Was the data analysis sufficiently rigorous?	Unclear	Not clear how the data was analysed, although probably thematic analysis
Is there a clear statement of findings?	Yes	
Is the research valuable?	Yes	

Study ID: McIntosh (2005) 3398	
Method Focus groups	
Methodology Unclear	
Data analysis Unclear	
Setting and context Tobacco cessation trial in adolescents. Physician offices (Primary care) USA	
Participants (number/description) 30 community physicians	
Interventions/phenomena of interest Perceptions of facilitators and barriers to enrolment of physician offices to a RCT.	
Findings	**Narrative description**
Facilitators	Office staff involvement On-site presentation of study aims
Barriers	Time commitments Lack of incentives
Authors' conclusions "recruitment is a multicomponent process; the process of communication, engagement, and enrolment must be carefully planned and implemented to achieve maximal results."	
Comments Good study. Investigates facilitators, which is a rarity.	

Study ID:	Mason (2007)	2162
	Yes/No/Unclear	**Comments**
Was there a clear statement of the aims of the research?	Yes	
Is a qualitative methodology appropriate?	Yes	
Was the research design appropriate to address the aims of the research?	Yes	
Was the recruitment strategy appropriate to the aims of the research?	Yes	Purposive sampling. Range of practices. GPs with a range of experience. Sample structured by whether GP was full/part time and the number of patients they identified for the RCT.
Was the data collected in a way that addressed the research issue?	Yes	Topic guide was developed, drawing on literature and issues of interest from initial recruitment to depression trial.
Has the relationship between researcher and participants been adequately considered?	Yes	Interviewer was previously involved in the running of the RCT so "may have influenced openness of GPs".
Have ethical issues been taken into consideration?	Yes	Ethical approval received.
Was the data analysis sufficiently rigorous?	Yes	
Is there a clear statement of findings?	Yes	Three main themes
Is the research valuable?	Yes	Little previous work in understanding recruitment to mental health trials.

Study ID: Mason (2007) 2162	
Method Semi structured interviews	
Methodology Unclear	
Data analysis Framework approach	
Setting and context Interviews with GPs regarding barriers to recruiting to RCTs in mental health. Primary care trusts in SW England who were collaborating with University of Bristol in an RCT recruiting patients with depression.	
Participants (number/description) 41 GPs from 5 primary care trusts	
Interventions/phenomena of interest To investigate the perceived barriers among GPs towards introducing participation in RCTs to patients presenting with depression.	
Findings	**Narrative description**
Concern about protecting vulnerable patients and impact on doctor-patient relationship	
Perceived lack of skill and confidence of GPs to introduce a request for research participation during sensitive consultation	
Priority given to clinical and administrative issues over health research participation.	
Authors' conclusions "Depressed patients were often viewed as vulnerable and in need of protection and it was seen as difficult and intrusive to introduce research."	
Comments Well reported study. However, as authors state that the study recruited well, would it not also have been interesting to ask GPs what enabled them to recruit well.	

Study ID:	Ziebland (2007)	329
	Yes/No/Unclear	**Comments**
Was there a clear statement of the aims of the research?	Yes	
Is a qualitative methodology appropriate?	Yes	
Was the research design appropriate to address the aims of the research?	Yes	
Was the recruitment strategy appropriate to the aims of the research?	Yes	The purposive sample for this study was selected to represent different rates of institutional involvement with the trial and geographical spread.
Was the data collected in a way that addressed the research issue?	Yes	
Has the relationship between researcher and participants been adequately considered?	Yes	Qualitative researcher with social science background and experience of interviewing surgeons.
Have ethical issues been taken into consideration?	Yes	Approved by Eastern MREC. Confidentiality of surgeons a priority.
Was the data analysis sufficiently rigorous?	Yes	
Is there a clear statement of findings?	Yes	
Is the research valuable?	Yes	

Study ID: Ziebland (2007) 329	
Method In depth interviews	
Methodology Unclear	
Data analysis Thematic analysis (constant comparative)	
Setting and context Interviews with surgeons who took part in SST a pragmatic multicentre surgery RCT. To explore understanding of trial purpose and how this influenced recruitment.	
Participants (number/description) 11 participating surgeons	
Interventions/phenomena of interest Recruitment Understanding of trial design	
Findings	**Narrative description**
Use of RCT methods	
(mis)understanding of trial design	
Patient eligibility criteria	
Authors' conclusions "We conclude that it does matter if clinicians do not understand the rationale for the trial if, as we have shown here, their perception of the trial aims and methods adversely effects who they recruit; if their views affect what the patients are told; and if they mistakenly view the results as unscientific, unreliable and ultimately irrelevant to their practice."	
Comments Paper mainly concentrates on clinicians' understanding of a particular trial, but as the title says, this may have an effect on recruitment.	

Study ID:	Bill-Axelson (2008)	Hand search
	Yes/No/Unclear	**Comments**
Was there a clear statement of the aims of the research?	Yes	
Is a qualitative methodology appropriate?	Yes	
Was the research design appropriate to address the aims of the research?	Yes	
Was the recruitment strategy appropriate to the aims of the research?	Yes	
Was the data collected in a way that addressed the research issue?	Yes	
Has the relationship between researcher and participants been adequately considered?	Yes	Researcher used for interviews was not involved in RCT, so was impartial.
Have ethical issues been taken into consideration?	Unclear	
Was the data analysis sufficiently rigorous?	Yes	Discussed ranges of opinions and possible reasons for them.
Is there a clear statement of findings?	Yes	
Is the research valuable?	Yes	

Study ID: Bill-Axelson (2008) hand search	
Method Semi-structured interviews	
Methodology Unclear	
Data analysis Content analysis	
Setting and context Clinicians and patients involved in SPCG-IV trial (prostate cancer RCT). Sweden	
Participants (number/description) 5 randomising clinicians	
Interventions/phenomena of interest "to understand attitudes to the randomisation process among patients and clinicians in the hope of rendering the process more acceptable in future."	
Findings	**Narrative description**
Decision making	Patients should be left to make up their own mind, however clinicians always have input into decision making.
Strategies	Tailor strategy to individual. Find out what patient needs from consultation about randomisation
Attitudes to research	Relevance of research question. Principal issue is patient wellbeing.
Equipoise	Difficulty in maintaining equipoise over long period in rapidly changing field.
Authors' conclusions "To establish a good platform for randomisation the clinician needs to know about the patients' treatment preferences and the patients' attitudes concerning the role of the clinician to facilitate the decision making."	
Comments Good report, however small sample.	

Study ID:	Potter (2009)	17833
	Yes/No/Unclear	**Comments**
Was there a clear statement of the aims of the research?	Yes	
Is a qualitative methodology appropriate?	Yes	
Was the research design appropriate to address the aims of the research?	Yes	
Was the recruitment strategy appropriate to the aims of the research?	Yes	Purposive sample of 10 nurses decided by number of participants recruited, location of surgery (rural/urban), and whether nurse had dedicated time for research.
Was the data collected in a way that addressed the research issue?	Yes	
Has the relationship between researcher and participants been adequately considered?	Unclear	
Have ethical issues been taken into consideration?	Yes	States that study received ethical approval
Was the data analysis sufficiently rigorous?	Yes	Familiarisation-thematic framework-index applied to all interviews-data rearranged according to themes
Is there a clear statement of findings?	Yes	
Is the research valuable?	Yes	

Study ID: Potter (2009) 17833	
Method Semi-structured telephone interviews	
Methodology Unclear	
Data analysis Thematic framework	
Setting and context Primary care RCT promoting adherence to treatment in patients with Type 2 diabetes.	
Participants (number/description) 10 practice nurses: good and bad recruiters; rural and urban practice; with/without set aside research time	
Interventions/phenomena of interest Nurses' experience of participation in RCTs and influence on recruitment.	
Findings	**Narrative description**
How nurses became involved in the study	
Reasons for need to take part in the study	Patient benefit. Advantages for practice.
Recruitment	Nurses recruited better if had protected research time.
Gatekeeper role	Nurses were selective about those they invited to take part in RCT.
Reasons for poor recruitment	Lack of time during patient consultation. Perceived lack of patient interest in trial.
Incentives to recruit	Financial incentive not important. Regular newsletters from research team.
Authors' conclusions "Overall, nurses were positive about recruiting into the trial, particularly if the research area could benefit patients and if directly asked to take part."	
Comments Link with nurse v urologists trial.	

Study ID:	Howard (2009)	1550
	Yes/No/Unclear	**Comments**
Was there a clear statement of the aims of the research?	Yes	
Is a qualitative methodology appropriate?	Yes	Similar to ProtecT trial methods – i.e. using qualitative methods to try and improve recruitment
Was the research design appropriate to address the aims of the research?	Yes	
Was the recruitment strategy appropriate to the aims of the research?	Yes	Purposive sample. Tried to get a broad range of recruiters
Was the data collected in a way that addressed the research issue?	Yes	
Has the relationship between researcher and participants been adequately considered?	Unclear	
Have ethical issues been taken into consideration?	Unclear	
Was the data analysis sufficiently rigorous?	Unclear	
Is there a clear statement of findings?	Yes	
Is the research valuable?	Yes	

Study ID: Howard (2009) 1550	
Method Interviews	
Methodology Unclear	
Data analysis Thematic analysis (constant comparative)	
Setting and context Qualitative study during recruitment phase of an RCT of supported employment for patients with mental illness.	
Participants (number/description) Initially 4 trial staff: chief investigator, principal investigator, trial coordinator and research nurse. Followed up with two care coordinators.	
Interventions/phenomena of interest Why recruitment to trials is difficult.	
Findings	**Narrative description**
Misconceptions about RCTs	Failure to understand randomisation
Equipoise	Maintain equipoise a problem
Misunderstanding of trial arms	Trialists did not understand usual care control arm.
Eligibility	Misunderstanding of eligibility criteria. Also protection of vulnerable patients (non entry of some even though they may meet criteria)
Paternalism	Investigator-clinician conflict – making decisions of behalf of patient.
Authors' conclusions "Reasons for recruitment difficulties in trials involving patients with severe mental illness include issues that occur in trials in general, but others are more specific to these patients."	
Comments Clinician and patient involvement in trial design may improve recruitment to similar trials	

Study ID:	Patterson (2010)	189
	Yes/No/Unclear	**Comments**
Was there a clear statement of the aims of the research?	Yes	
Is a qualitative methodology appropriate?	Yes	
Was the research design appropriate to address the aims of the research?	Yes	Multiple viewpoints
Was the recruitment strategy appropriate to the aims of the research?	Yes	Theoretical sampling
Was the data collected in a way that addressed the research issue?	Yes	Interviews, focus group and observational data
Has the relationship between researcher and participants been adequately considered?	Yes	"All of the authors had ongoing involvement in the RCT"
Have ethical issues been taken into consideration?	Yes	"favourable opinion from a National Research Ethics Committee"
Was the data analysis sufficiently rigorous?	Yes	
Is there a clear statement of findings?	Yes	
Is the research valuable?	Yes	

Study ID: Patterson (2010) 189	
Method Interviews, focus group, observation	
Methodology Grounded theory	
Data analysis Thematic analysis (constant comparative)	
Setting and context Process evaluation during MATISSE trial, a three arm parallel controlled trial designed to test the effectiveness of art therapy in improving global functioning of people with schizophrenia."	
Participants (number/description) Interviews: 2 clinical studies officers, 2 research associates, 5 investigators, 5 clinicians. Focus group: all research associates and 3 clinical studies officers.	
Interventions/phenomena of interest Factors influencing referral to a RCT.	
Findings	**Narrative description**
Conflicting roles	"we found evidence of a fundamental disjunction between research and clinical practice."
Organisational + Personal	"Organisational culture and the knowledge and attitudes of service providers regarding research generally resulted in exclusion of many potentially eligible participants."
Authors' conclusions "These findings highlight the need for development of genuinely collaborative partnerships between the research and clinical communities."	
Comments	

Study ID:	Paramasivan (2011)	Citation
	Yes/No/Unclear	**Comments**
Was there a clear statement of the aims of the research?	Yes	Use of qualitative methods to improve recruitment to a RCT
Is a qualitative methodology appropriate?	Yes	
Was the research design appropriate to address the aims of the research?	Yes	Multiple view points. Interviews, conversation analysis of recruitment appointments, content analysis of RCT documents.
Was the recruitment strategy appropriate to the aims of the research?	Yes	
Was the data collected in a way that addressed the research issue?	Yes	
Has the relationship between researcher and participants been adequately considered?	Unclear	Lead author carried out the interviews
Have ethical issues been taken into consideration?	Unclear	
Was the data analysis sufficiently rigorous?	Yes	
Is there a clear statement of findings?	Yes	
Is the research valuable?	Yes	

Study ID: Paramasivan 2011 citation	
Method Interviews, observation, analysis of trial documents	
Methodology Unclear	
Data analysis Content analysis of trial documents Thematic analysis of interviews Conversation analysis of recordings of recruitment appointments	
Setting and context Qualitative recruitment investigation in the SPARE (bladder cancer) trial	
Participants (number/description) 9 recruiters and 2 non-recruiters from 4 centres	
Interventions/phenomena of interest Reasons for low recruitment	
Findings	**Narrative description**
Explaining trial	Investigators and recruiters had considerable difficulty articulating the trial design in simple terms.
Communication between trialists	Recruitment pathway was complicated, involving staff across different specialties/centres, and communication often broke down.
Loaded terminology	Recruiters inadvertently used 'loaded terminology' leading to unbalanced presentation.
Treatment preferences	Strong treatment preferences were expressed by potential participants and trial staff.
Authors' conclusions "There were two key issues comprising five challenges that hindered recruitment to the SPARE trial: the first had origins in detailed aspects of the trial design and conduct; the second involved the difficulties recruiters experienced because of their perception that patients had clear treatment preferences."	
Comments Link to Protect and Quartet trials (Donovan)	

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1,2
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Figure 1
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	No protocol
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1 In supplementary materials
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6,7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6,7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6,7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6,7

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7 Qualitative metasummary
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Appendix 5,6
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Appendix 2,3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9-13
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	No meta-analyses
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	13,14 Qualitative metasummary
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-17
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15-17
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Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

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Improving the recruitment activity of clinicians in randomised controlled trials - a systematic review

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ABSTRACT

Background

Poor recruitment to randomised controlled trials (RCTs) is a widespread problem. Provision of interventions aimed at supporting or incentivising clinicians may improve recruitment to RCTs.

Objectives

To quantify the effects of strategies aimed at improving the recruitment activity of clinicians in RCTs, complemented with a synthesis of qualitative evidence related to clinicians' attitudes towards recruiting to RCTs.

Data sources

A systematic review of English and non-English articles identified from: The Cochrane Library, Ovid MEDLINE, Ovid EMBASE, Ovid PsycINFO, Ebsco CINAHL, Index to Theses and Open SIGLE from 2001 to March 2011. Additional reports were identified through citation searches of included articles.

Study eligibility criteria

Quantitative studies were included if they evaluated interventions aimed at improving the recruitment activity of clinicians, or compared recruitment by different groups of clinicians. Information about host trial, study design, participants, interventions, outcomes and host RCT was extracted by one researcher and checked by another. Studies that met the inclusion criteria were assessed for quality using a standardised tool; the Effective Public Health Practice Project (EPHPP) tool.

Qualitative studies were included if they investigated clinicians' attitudes to recruiting patients to RCTs. All results/findings were extracted and content analysis was carried out. Overarching themes were abstracted, followed by a metasummary analysis. Studies that met the inclusion criteria were assessed for quality using the Critical Appraisal Skills Programme (CASP) qualitative checklist.

Data extraction

Data extraction was carried out by one researcher using predefined data fields, including study quality indicators, and verified by another.

Results

Eight quantitative studies were included describing four interventions and a comparison of recruiting-clinicians. One study was rated as strong, one as moderate and the remaining six as weak when assessed for quality using the EPHPP tool. Effective interventions included: the use of qualitative research to identify and overcome barriers to recruitment; reduction of the clinical workload associated with participation in RCTs; and the provision of extra training and protected research time.

Eleven qualitative studies were identified and eight themes were abstracted from the data: understanding of research; communication; perceived patient barriers; patient-clinician relationship; effect on patients; effect on clinical practice; individual benefits for clinicians; and methods associated with successful recruitment. Metasummary analysis identified the most frequently reported sub-themes to be: difficulty communicating trial methods; poor understanding of research; and priority given to patient wellbeing. Overall, the qualitative studies were found to be of good quality when assessed using the CASP checklist.

Conclusions

There were few high quality trials that tested interventions to improve clinicians' recruitment activity in RCTs. The most promising intervention was the use of qualitative methods to identify and overcome barriers to clinician recruitment activity. More good quality studies of interventions are needed to add to the evidence base.

The metasummary of qualitative findings identified understanding and communicating RCT methods as a key target for future interventions to improve recruitment. Reinforcement of the potential benefits, both for clinicians and their patients, could also be a successful factor in improving recruitment. A bias was found toward investigating barriers to recruitment, so future work should also encompass a focus on successfully recruiting trials.

ARTICLE SUMMARY

Article focus

A systematic review to identify and synthesise evidence of evaluations of interventions aimed at improving clinician recruitment activity in RCTs, and evidence of clinicians' attitudes towards recruiting to RCTs.

Key messages

Evidence based recruitment interventions aimed at supporting/incentivising clinicians are necessary for future RCTs to recruit successfully. However, evidence of successful interventions is currently limited, and interventions are being used that have limited evidential grounding. The most promising intervention identified by this review was the use of qualitative methods embedded in host RCTs to define appropriate methods, targeted at clinicians, relevant to the context of the individual studies.

The review of qualitative evidence identified a number of themes relating to clinicians' attitudes towards recruitment to RCTs. The metasummary isolated targets for future interventions aimed at improving clinicians' recruitment activity. Of particular interest were: communication of trial methods; education to remove misunderstanding of trial methods; and reinforcement of the potential benefits of RCTs, both for clinicians and their patients.

Strengths and limitations of this study

Strengths

This review encompasses both quantitative and qualitative evidence regarding clinician involvement in recruiting to RCTs. As such, it highlights the available evidence, successful and unsuccessful interventions, areas of uncertainty, and also targets for the design of future interventions.

Qualitative data was managed and synthesised according to a set methodology and is therefore a step beyond simple narrative review. Qualitative metasummary can be the final product of a synthesis project, or used as the initial step in a metasynthesis project. The purpose of qualitative metasummary was to determine how frequently each abstracted thematic finding occurred in the included studies. Qualitative metasummary is appropriate for synthesising studies that are thematic summaries or surveys of data.

Limitations

The quality of evidence varied, and the review includes a wide range of study designs, making comparisons of interventions difficult. It is clear that RCTs of trial recruitment interventions are perceived to be difficult to carry out, so other study designs are commonly used. RCTs of recruitment interventions should be encouraged in order to increase the quality of currently available evidence.

Methodological challenges included: designing a broad search to encompass qualitative and quantitative research; quality assessment of various quantitative study designs by one set of criteria; standardising the data extraction and synthesis of qualitative evidence. There are no set guidelines regarding the synthesis of qualitative and quantitative evidence, but it is clear that for many review questions limiting the included study designs would lead to empty reviews.

INTRODUCTION

When evaluating the effectiveness of healthcare interventions, randomised controlled trials (RCTs) are seen as the gold standard research design. It is important that RCTs recruit their target number of participants in order to avoid being underpowered, particularly as a lack of statistical power may lead to the reporting of clinically important effects as statistically non-significant. Statistically non-significant findings can increase the risk that potentially effective interventions may be abandoned before their true value is established, or that there will be a delay in demonstrating their value while more trials are carried out. For example, Collins *et al* calculated that there were as many as 10,000 unnecessary deaths in the USA due to delays in recruitment to a RCT of streptokinase in acute myocardial infarction[1]. Many RCTs are abandoned or do not produce unequivocal evidence due to recruitment difficulties, which also means that the resources spent for setting up and running the RCT have not been put to their best use.

Studies that fail to recruit their target number of participants also raise ethical problems, particularly when clinicians have exposed participants to interventions with uncertain benefit and, at the end of the trial, are still unable to determine whether the intervention is clinically effective[2]. There are also ethical implications associated with recruiting patients to a trial in which they invest their time, only to be told that the trial will not go ahead. There is the additional financial impact of trials that fail to recruit successfully, or in a timely manner. It has been hypothesised that slow acquisition of trial evidence due to poor recruitment may have reduced investment in the conduct of RCTs by some funding agencies, who may prefer to invest in less reliable, but more rapid approaches[3]. Delayed or extended trials may cost more, leading to fewer trials being carried out from the limited funds available.

There are a number of published studies that highlight how common recruitment problems are in healthcare RCTs[4-11]. It is likely that 50% of RCTs fail to recruit to target, and that only 50% of those that successfully recruit do so in a timely manner as shown in Table 1. The table also demonstrates the lack of any real improvement over time.

{INSERT TABLE 1 HERE}

The reasons for poor or slow recruitment to RCTs can be found at various levels: the patient, the recruiting clinician, the trial centre, the trial organisation and the trial design[12]. Considerable efforts have been made to understand and incentivise the participation of subjects in trials[2,3,13-16]; but less has been done to investigate interventions that could improve the recruitment activity of clinicians[10,12]. The clinicians' role is clearly important as patients can only consider taking part in trials when asked to do so. Maintaining recruitment activity over time is also important as it has been shown that enthusiasm for recruiting subjects to RCTs can fade quickly, leading to studies that fail to recruit to target, or which suffer significant loss to follow up due to difficulties in participant retention for the required study period[6].

The objective of this systematic review was to evaluate interventions aimed at improving the activity of recruiting clinicians in RCTs, and to identify possible targets for future interventions based on clinicians' attitudes to recruitment to RCTs.

METHODS

Search strategy and study identification

Systematic searches were carried out for the period January 2001 to March 2011 in the following databases: the Cochrane Library, Ovid MEDLINE, Ovid EMBASE, Ebsco CINAHL, Ovid PsycINFO, Index to Theses (UK and Ireland), Open SIGLE.

Search terms related to clinicians, recruitment and RCTs were combined to identify studies. An example search strategy is shown in Appendix 1. No methodological filters were used so that both qualitative and quantitative studies would be returned by the searches. Furthermore, filters were avoided due to the complexity of searching for trails within trials.

To determine inclusion/exclusion criteria for studies the PICOS framework was used for quantitative studies and the SPICE framework for qualitative studies, as shown in Figure 1. Studies were assessed against the pre-specified inclusion and exclusion criteria. Following removal of duplicate reports, a first decision on inclusion/exclusion was made based on study titles and abstracts. For those studies identified in the first stage and for studies where a definite decision could not be made based on title/abstract alone, the full paper was obtained for assessment. In the second stage full papers were assessed against the full inclusion/exclusion criteria. Studies were also identified by performing citation searches of included studies.

Searches were carried out by one researcher (BF), and study identification by two researchers (BF, AG), and any disagreements reconciled by discussion.

{INSERT FIGURE 1 HERE} Title “Study selection criteria”

Quality assessment

Quality assessment of quantitative studies was performed using the Effective Public Health Practice Project (EPHPP) quality assessment tool for quantitative studies[17]. This instrument was chosen as it enables different study designs to be assessed using the same tool, and was identified as one of only six judged to be suitable for systematic reviews assessing multiple study designs[19]. Using the EPHPP tool, studies were assessed against six criteria: selection bias, design, confounders, blinding, data collection methods, and withdrawals and dropouts.

Quality assessment of qualitative papers was carried out in accordance with the Critical Appraisal Skills Programme (CASP) qualitative research appraisal tool, which covered rigour, key research methods used, credibility and relevance[18].

Quality assessment was performed by two researchers independently (BF/AG), and the results were compared for consistency. Following discussion, a consensus decision was made in the case of any disagreement.

Data extraction and analysis

For quantitative studies, data relating to study design, country, setting (i.e. nature of the RCT being recruited to), population, statistical methods, description of intervention and author conclusions were extracted using a piloted data extraction form. Trials were grouped according to intervention and, if binary data was reported (i.e. participants recruited/participants not recruited), then risk ratios were calculated. Relative risks with 95% confidence intervals were calculated using RevMan software, where appropriate, to describe the effect of interventions.

For qualitative reports, data extraction was first carried out using the Quality Assessment and Review Instrument (QARI) data extraction tool designed by the Joanna Briggs Institute (JBI) for Evidence Based Practice. This allowed broad themes to be identified in the included reports. Secondly, all text was extracted from sections labelled as 'results' or 'findings' in the included reports, according to the method suggested by Thomas and Harden [20]. The results were then entered into NVivo software for qualitative content analysis. Line-by-line coding of the extracted data was carried out and codes were organised into related areas in order to construct descriptive themes. Abstracted analytical themes were then created by combining similar descriptive themes, from which frequency effect sizes could be calculated. Frequency sizes were calculated by taking the number of reports that contained an abstracted finding and dividing this number by the total number of reports. A criticism of metasummary is that it may not be appropriate to apply numbers to qualitative data. However, quantitative categorisations such as small, medium and large are often used by researchers to "qualitize" data[21]. Frequency effect sizes can be used to extract more meaning from abstracted findings. Qualitative studies "inherently imply a frequency of occurrence of an event sufficient to constitute a pattern or theme", and metasummary can be seen as the next step in this process, as well as helping to verify the presence of themes across studies[22].

Data extraction was carried out by one researcher (BF) and the results checked by a second (AG). Disagreements were resolved by discussion.

RESULTS

Study selection

The search identified 9,236 abstracts of which 296 were screened, and 38 full text papers obtained for full assessment against the inclusion/exclusion criteria. Nineteen studies were included in the review (eight quantitative and eleven qualitative).

{INSERT FIGURE 2 HERE} Title "Study selection flow diagram"

Study characteristics

{INSERT TABLE 2 HERE}

Of the eight included quantitative studies, three were RCTs[23,24,25], two were observational time series[26,27], two were before and after studies[28,29] and one was a case study with a comparison group[30]. Two studies compared clinicians (nurses vs. surgeons; community vs. university medical practices)[23,30]. Two studies assessed the effect of extra involvement of trial coordinators with clinicians (extra communication; on-site initiation visits)[24,25]. One study assessed the effect of change to training and paying for protected research time on recruitment[29]. Two studies from the same authors used embedded qualitative methods to identify targets for improving recruitment[27,28]. One study assessed a complex multifaceted intervention[26]. All but one study investigated recruitment to cancer or chronic disease trials, and the majority took place in the UK (5 of 8).

Three reports all related to the same host RCT of prostate cancer treatment[23,27,28]. Donovan (2002 and 2009) reported the results of using qualitative methods to develop an intervention, in both the feasibility study before the main trial, and the main trial itself. Donovan (2003) compared using nurses and surgeons as recruiters in the same trial. For the purpose of this review these three studies were assessed separately.

{INSERT TABLE 3 HERE}

Of the eleven included qualitative studies nine used interviews (semi-structured; in-depth)[31,33,35-41], two used focus groups[32,34] and one study also analysed trial documents[41]. The methodology used was described as Grounded Theory in three studies[31,33,40], while it was not stated in eight. Thematic analysis (constant comparative; framework analysis) was the most common method of data analysis (nine studies)[31-33,35-36,38-41], with two studies using content analysis[37,41] and one conversation analysis[41]. Data analysis method was unclear in one of the included studies[34].

174 trialists were interviewed or involved in focus groups in total: 62 GPs, 30 community physicians, 16 paediatricians, 11 surgeons, 11 recruiters, 10 clinicians, 10 nurses, 5 trainees, 5 investigators, 4 trial staff, 4 hospital doctors, 2 clinical studies officers, 2 research associates and 2 care coordinators. A broad range of settings were covered by the included studies e.g. primary and secondary care trials; drug trials and pragmatic surgery trials; trials in mental health and cancer - etc.

Quality assessment

Using the EPHPP quality assessment tool for quantitative studies: one study was characterised as strong[24], one as moderate[25], with the remaining studies classified as weak[23, 26-30]. Studies were shown to be particularly weak when reporting controlling for confounders and methods of data collection.

Overall, the qualitative studies assessed using the CASP checklist were found to be of good quality. Methodology and consideration of ethical issues were the two main areas where reporting was unclear.

A summary of the quality of the included studies is Appendix 2 and 3.

Results of review of quantitative studies

Comparing types of recruiters

Two studies compared the use of different groups of clinicians recruiting to RCTs. Donovan *et al* compared the effect of using nurses or urologic surgeons recruiting to a prostate cancer trial, using a RCT design[23]. The trial showed no significant difference in recruitment rate between the two groups (RR 0.94, 95% CI 0.76 to 1.17). The study also included an economic assessment that found nurses to be more cost effective recruiters than surgeons.

Submacular Surgery Trials Research Group (SSRTG) compared recruitment at university based and community based medical centres, in recruitment to three RCTs of intraocular surgery[30]. This was a case study with comparison groups. The study found no significant difference between the settings (mean number of subjects recruited per centre: university = 38.1, community = 37.3, *t* test p=0.93).

Greater contact between trial coordinator and clinicians/trial sites

Two studies examined the extent of contact on recruitment. Lienard *et al* used a RCT design to assess the impact of on-site monitoring visits on recruitment to a breast cancer RCT[25]. On-site monitoring visits had multiple purposes: to ensure the protection of patients' rights, to verify the accuracy of reported data, and to provide training to site personnel with regard to trial material and protocol. The study found that on-site monitoring visits had no significant effect on patient recruitment, reported as: centres recruiting at least one patient (control 34 of 67, intervention 35 of 68, p>0.05); or total numbers of patients recruited (control 271, intervention 302, p>0.05). No significant differences were found between groups in quality or quantity of reported data, or patient follow up time.

Monaghan (2007) used a RCT to evaluate the effect of extra communication from central trial coordinators on recruitment to a diabetes RCT[24]. The intervention included: frequent e-mails; personalised mail-outs of league tables describing recruitment performance relative to other centres; certificates acknowledging achievement of recruitment milestones; and promotional materials related to the trial. The study found no significant effect of extra communication on median number of patients recruited (control 37.0, intervention 37.5, p=0.68), or median time to half recruitment target (control 4.4 months, intervention 5.8 months, p=0.08).

Use of qualitative research embedded in host RCT

Two studies investigated the use of qualitative methods embedded in a host trial. In both studies, qualitative methods (in depth interviews, audiotape recordings of recruitment appointments, study of trial documents) and analysis (content, thematic and conversation analysis) were used to assess aspects of the trials that were amenable to improvement; followed by the design and implementation of interventions to improve the recruitment activity of clinicians. Donovan *et al* (2002) reports the results of a feasibility study before the main trial (Donovan *et al* 2009)[27,28].

Donovan *et al* (2002) reported the results of an observational time series study investigating recruitment to a prostate cancer RCT[27]. Qualitative methods were used to elicit strategies which had the potential to improve recruitment. Strategies identified by qualitative methods included presentations of the study design and the implementation of a training programme

delivered to clinicians. The intervention improved the proportion of eligible patients consenting to randomisation (after 10 months RR 1.36, 95% CI 1.01 to 1.85), whilst there was no significant change in the proportion of randomised patients accepting allocation (after 10 months RR 0.90, 95% CI 0.70 to 1.15).

Donovan *et al* (2009) reported the results of the main trial[28]. Qualitative methods allowed a complex intervention to be developed which included: regular training for all staff involved in recruitment and initiation for new staff; centre reviews for underperformers; documents providing tips and advice; and personalised individual feedback to recruiters as required. The study reports the results of audits of two centres before and after the intervention (12 and 24 months post intervention). The results of the two centres are not pooled in this review as interventions were tailored to each centre using qualitative research; therefore the intervention that the two centres received was different. The first centre showed a significant improvement in the proportion of eligible patients recruited at 12 months (RR 1.87, 95% CI 1.15 to 3.04) and 24 months (RR 1.79, 95% CI 1.07 to 2.99) post intervention, and no significant change in the proportion of randomised patients accepting allocation (12 months RR 1.22, 95% CI 0.62 to 2.39; 24 months RR 1.43, 95% CI 0.75 to 2.71). The second centre also showed a significant improvement in the proportion of eligible patients recruited at 12 months (RR 1.55, 95% CI 1.11 to 2.16) and no significant change at 24 months (RR 1.36, 95% CI 0.92 to 2.02) post intervention. No significant change in the proportion of randomised patients accepting allocation was found at 12 months (RR 1.33, 95% CI 0.96 to 1.85) and a slight increase in those accepting allocation at 24 months (RR 1.44, 95% CI 1.05 to 1.99).

Complex intervention

Fletcher *et al* used an observational time series study design to examine whether changes in the conduct of a stroke RCT were associated with changes in recruitment[26]. Over the recruitment period changes included: procedural changes to reduce clinician workload and time to recruitment; enrolment of more sites; and changes to the approach to recruitment and retention of practices. Recruitment rates per 1000 eligible population were calculated and a moving *F* statistic was used to assess changes over time. There was a statistically significant increase in recruitment in the last 6 months of the trial associated with efforts to reduce clinician workload.

Extra training and protected research time

Kenyon *et al* used a before and after study design to measure the effect of increased training, and paying for protected research time for midwives recruiting to a large perinatal multicentre RCT[29]. The intervention involved the employment of lead local midwives to work for three hours per week on the trial. The midwives were provided with intensive training, 6 monthly updates and regular contact visits. Recruitment in all the maternity units improved by an average of 69% (range -89% to 200%) when comparing the six months prior to the intervention with the six months immediately after the intervention.

Results of review of qualitative studies

Findings relating to clinicians' involvement in, and recruiting to RCTs, were extracted for each of the eleven included studies. A line-by-line content analysis isolated a total of 73 findings, which were consolidated into 8 abstracted themes by combining like statements and eliminating redundant statements. There is some overlap between abstracted findings. The abstracted themes are described below.

Understanding of research (in general; RCTs; in light of specific trials)

RCTs are understood by clinicians to be a valuable tool in healthcare (i.e. description of RCT as gold standard; RCTs provide the best available evidence), however it is suggested that some clinicians are exposed to too much research, leading to a feeling of being overwhelmed with requests for research participation.

It is reported that there is poor understanding among clinicians of RCT methods and concepts (i.e. equipoise, randomisation, allocation, eligibility criteria, informed consent), along with the opinion that RCTs can be too complex.

There is some discussion regarding the funding of research, for example: questioning whether RCTs are the best way to spend money, particularly given the current economic climate; is there enough money available for research.

It is seen to be the responsibility of the whole community (researchers, clinicians and patients) to take part in research. However, some clinicians are suspicious of the motives of researchers, and others have no interest in research whatsoever – leading to resistance to research participation (obstructive/difficult to engage).

Communication (clinician to patient; clinician to trial coordinator)

Clinicians report a difficulty in communicating the aims and concepts of RCTs to patients. The choice of language used is perceived as very important. Communicating research to patients is described as a sales pitch. Language used to describe RCT design is a concern, particularly allocation and randomisation, which has been likened to describing a lottery, with 'winners and losers'.

Clinicians report that they are able to communicate with certain patients and patient groups about RCTs better than others. Social class of patients is discussed, with clinicians finding communication with 'people like themselves' easier.

Poor communication of research by trial coordinators can lead to suspicion of their motives. There is often a perceived divergence between clinical and research goals. Clinicians feel that they should be seen as 'partners in research', with greater involvement in design leading to improved recruitment.

Perceived patient barriers

Barriers to recruitment are often seen by clinicians to be more related to the patients, and therefore out of their control. Perceived patient barriers include: poor community awareness and understanding of RCTs; low motivation to take part in research; lack of interest; fear and mistrust of being treated as guinea pigs; fear of negative effects of taking part.

Patient-clinician relationship

Clinicians acting as recruiters are particularly concerned with the conflicting roles that taking part in research activities imposed.

Recruiting clinicians may act as gatekeepers, only suggesting research to those patients that they deem suitable for research (i.e. not approaching all patients that meet eligibility criteria for a study). This can be perceived to be paternalistic as clinicians make decisions on the patients' behalf, believing they know what is best, without consulting the patients.

Clinicians feel responsible for the patients they put forward for research, particularly as they believe they can influence patients' decision making. Also clinicians put patient needs above those of researchers; patient wellbeing is seen as paramount.

Concern that trust may be affected by asking patients to take part in research is mentioned, as well as the concern for some clinicians that they risk feelings of ineptitude or rejection if they invite patients to take part in RCTs and they refuse.

Effect on patients (harms and benefits)

Clinicians often describe possible patient benefit as motivation for participation in RCTs, and equally concerns are expressed about possible harms. Some clinicians have difficulty reconciling potentially putting individual patients at risk for possible population gain. Clinicians want to avoid being seen to pressurise patients to take part in RCTs.

The stage of patient illness is a concern, as it is suggested that asking terminally ill patients or patients with poor prognosis to take part in an RCT with a placebo can be emotionally detrimental for some patients. Also, side-effects of treatments used in RCTs are seen as possible negatives for patients. It is important to note that these are what the clinicians perceive their patients to be thinking, and the patients themselves may not share these views.

Inviting patients to take part in research can have the effect of raising patient awareness of disease, which can be interpreted in both a positive and negative light (i.e. more awareness may lead to increased participation in research but also more health seeking behaviour, stretching current resources).

Research can be thought to be inequitable by clinicians, with some special patient groups seen as receiving more attention than others.

Effects on clinical practice

A positive aspect of taking part in RCTs is the beneficial influence it can have on clinical practice. Being a research active practice enhances services offered by practices, encouraging confidence and loyalty from patients. It is also thought that the discipline needed to adhere to some trial protocols has beneficial effects on clinical practice.

Advancements in clinical practice are dependent on carrying out good quality clinical trials. Taking part in RCTs can improve treatment strategies used in everyday practice, conferring benefits to patients outside the RCT in the medium and long term.

Negatives include the possible disruption caused to normal practice brought about by the extra work involved in assessing patients for eligibility, and approaching those who are eligible for participation (i.e. describing RCT, obtaining informed consent, etc). The extra time associated with recruiting to RCTs in addition to normal duties is often stated as a major barrier to involvement. In the climate of trying to achieve service targets within tight budgets, carrying out extra work to recruit patients to trials may not be seen as a priority.

It is felt by some clinicians that although they are crucial to the successful running of trials by recruiting subjects, they often do not receive the acknowledgment/rewards they feel they deserve. Being asked to recruit for RCTs is seen to be intrusive by some clinicians.

Individual benefits for clinicians

Motivation for involvement in research can be seen to move beyond altruism. Taking part and recruiting patients to RCTs is seen by many to have personal benefits for clinicians. Involvement with colleagues from different fields is seen to be important personally, as well as professionally.

Participation in RCTs is seen by some as crucial for career development, and professional recognition.

Methods associated with successful recruitment

Community awareness of RCTs and research in general is linked to good recruitment. Promotion efforts should be tried to improve awareness which should have the effect of increasing the number of patients willing to take part in RCTs. Endorsements of research by the patients' own GP or practice can improve recruitment.

The research question addressed by an RCT is of vital importance to clinicians. The question should be both interesting and relevant to practice. Initial contact with clinicians about involvement in a trial should be brief but informative. Trial methods should be easy to understand and then communicate to patients. Inviting recruiters to take part in the design of RCTs could improve recruitment.

The funding of protected research time is an intervention that could improve recruitment performance. This would allow clinicians more time to discuss the trial with patients. More time would also allow clinicians to tailor their approach to each individual, an approach that is desirable for some clinicians. If protected research time is not a possibility then minimisation of workload related to recruitment is then key.

Financial incentives are important for many, with criticism when reimbursement for time is not offered. Clinicians should be reimbursed for time spent on recruitment rather than placing a bounty on patients heads'. Conversely some argue that financial incentives are unethical, and others that being paid would not significantly affect recruitment efforts. It was also noted that all staff should be rewarded for participation in research, not just clinicians.

Organisationally, being part of a research active practice is linked with good recruitment to RCTs. Having a research mentor or a trial coordinator or being involved in a research network are also factors in successful recruitment. Competition with other recruiters is a constructive way to maximise recruitment.

Appropriate training about research methods and recruitment methods is regarded as the key to success by many. Training should focus on addressing many common misconceptions about RCTs, particularly equipoise and informed consent.

Qualitative frequency effect size (metasummary)

By dividing the number of studies containing each theme/abstracted finding by the total number of studies, a frequency effect size was calculated. Table 4 shows the findings with frequency effect sizes >20%, as proposed by Sandelowski and Barroso[22]. A full list of findings and frequency effect sizes is given in Appendix 4.

{INSERT TABLE 4 HERE}

Difficulty communicating trial methods (randomisation, equipoise, etc) was the most common sub theme (64%), and was linked to a poor understanding of research methods by clinicians, and research in general by the public (55%). Ease of understanding and carrying out RCT

methods was also commonly described as associated with successfully recruiting trials (45%).

Clinicians found it difficult reconciling the roles of clinician and recruiter (36%). Clinicians were often described to only put forward patients who they deemed appropriate (gatekeeping)(27%), which links to paternalism (27%) and prioritising patient wellbeing (45%).

The positive and negative aspects of taking part in RCTs was frequently mentioned, with a balance between possible negative (36%) and positive effects on patients (27%), and the effect on clinical practice (45%).

The most frequently found abstracted finding was methods associated with successful recruitment to RCTs, with four sub-themes with a frequency effect greater than 20%. It was thought that the research question should be interesting and relevant to practice (45%). Financial incentives were seen by most as important for participation (27%). Training relevant to running trials should improve recruitment by targeting poor understanding of RCT methodology, as well as teaching recruitment methods (45%).

DISCUSSION

The aim of this review was to identify, and synthesise, evidence of the effectiveness of interventions aimed at improving the recruitment activity of clinicians in RCTs, and evidence of their attitudes towards recruitment to RCTs.

Methodological challenges

As the volume of evidence was perceived to be small an aim of the review was to include as much evidence as possible, regardless of method, several methodological issues had to be dealt with. Many systematic reviews of interventions exclude studies that do not use randomised controlled trials. While good quality RCTs of interventions would provide the best evidence, the nature of this research question lends itself to retrospective descriptive studies. This may be due to the logistical, ethical and scientific obstacles of performing randomised trials of recruitment nested within host RCTs[42]. Challenges for host trials include: increasing complexity and management burden; compatibility between host and nested study; and the impact of the nested study on host trial design. Challenges for nested studies include: investigators' concerns that host study investigators might have strong preferences, limiting the nested study investigators control over their research; and concerns about sample size which might limit statistical power. "Evidential nihilism", where narrow inclusion criteria are set regarding trial design would have led to an emptier review, which would not help further our understanding of the problem as much[43]. Qualitative studies were included in this review as it is important not just to understand what works, but also to have an understanding of why. It is hoped that a better understanding of clinicians' attitudes towards recruitment to RCTs may inform the development of interventions aimed to improve the support and training given to those involved in RCTs.

The search was broad and included no methodological filters, but still returned a large number of results. There is often a trade-off between sensitivity and specificity when performing a search for a systematic review, and in this case it was decided to err on the side of over inclusion, so a sensitive search was designed.

The review of quantitative studies found limited high quality evidence of interventions aimed at improving clinician activity, and shows the importance of building the evidence base to allow those running RCTs to have access to a range of proven strategies to maximise recruitment. Quality of the included qualitative studies was found to be good; however there was a tendency for the included studies to focus on the barriers to recruitment from the perspective of poorly recruiting trials. Little evidence was found of studies that aimed to assess how and why those clinicians who recruited well did so. It could be argued that facilitators are more illuminating, as barriers can often be seen as excuses, i.e. if the barrier was removed would the clinicians recruit more successfully?

What interventions work?

Evidence based interventions are necessary for RCTs to recruit successfully, however there is currently limited evidence, and interventions are being used that have no evidential grounding. For example, a study of seven primary care-based RCTs found that only 37% of interventions to promote recruitment were judged to be evidence based[7]. Further to this, Graffy *et al* stated that currently, where nested studies of recruitment methods are conducted on the initiative of individual investigators, there is no systematic method of choosing the intervention[42]. The authors go on to suggest the creation of a portfolio of interventions that could be made available to investigators for inclusion within an individual trial, or multiple trials.

This lack of evidence based interventions is particularly salient given that "common sense", interventions that could be assumed to have a positive effect on recruitment often had little

or no effect. The most successful intervention identified by this review was in the two trials that used embedded qualitative research to design interventions to improve recruitment. The qualitative research investigated recruitment appointments, study documents and interviewed clinicians to understand what aspects were amenable to change in order to improve recruitment. In both studies the intervention increased recruitment: i.e. the proportion of eligible subjects who consented to be randomised in the study. Rather than discuss the strategies used to improve recruitment, the most important factor in studies employing embedded qualitative research is the way that the intervention is developed. The use of qualitative methods allowed tailored interventions to be made that attempted to address problems with recruitment that were experienced by the clinicians and trial subjects (i.e. use of interviews, monitoring of recruitment interviews), as well as problems identified by the trial coordinators. This method is adaptive and allows for continuous monitoring and improvement. Although the interventions themselves may not be generalisable, the qualitative methods used to create the interventions, could be transferred to other settings, potentially having a positive effect on recruitment. Another positive feature of this approach was that improvements were maintained over time. Following intervention at two centres, recruitment was shown to remain significantly higher for at least 24 months.

One possible barrier to the use of this approach may be the extra time, money and personnel needed to carry out the qualitative research. However, the use of qualitative methods in pilot or feasibility trials prior to a full study would provide a cost-effective means of defining suitable interventions that could be fully incorporated into subsequent trials. If these interventions then proved successful in aiding recruitment, the extra efforts and costs involved in the preparatory phases would be offset by the greater potential for a successful full trial that would result, providing greater returns to funders and increasing the scientific validity of the trial overall.

Clinicians' attitudes to recruitment to RCTs

Setting aside the debate regarding the utility of metasummary frequency effect sizes, in this review there are three key areas highlighted by the calculation of qualitative effect sizes that may be the best target for improvement in future trials: understanding of RCTs and health research in general (both by the general public and clinicians); communication of trial methods (both trial coordinators to clinicians, and clinicians to patients); and reduction of the workload associated with recruitment.

It should not be assumed by trial coordinators that recruiters have a full understanding of RCT and recruitment methods. Clinicians' understanding of research in general and RCTs in particular could be improved using training specific to the RCT they are involved in as well as education relating to common misconceptions about RCTs.

Some of the themes identified could be used to emphasise the individual benefits to both trial subjects and clinicians, and the positive effect taking part in research can have on clinical practice[44]. For example a study of centres involved in a multi-centre breast cancer treatment trial, found that both patients and clinicians benefited from participation in the RCT, due to optimised decision making with regards to therapy and patient care[45]. An overall positive effect on the quality of medical care was seen across the centres. As clinicians prioritise patient wellbeing, emphasising the potential patient benefits to them could help remove a barrier to recruitment.

It is clear that reported barriers may often be excuses for why clinicians have not recruited well. Patterson *et al*, for example, found that concerns about taking part in RCTs related to ethics and research approvals, but even when these issues were addressed clinicians remained less than enthusiastic, and instead shifted the blame to administrative and clinical duties[40]. Removal of the perceived barrier will not necessarily lead to an improvement in

recruitment. This again highlights that more investigation is required to illuminate what facilitates trials that easily meet their recruitment targets.

Reducing clinicians' workload associated with recruiting to RCTs was often mentioned. This could be achieved by providing extra staff support, simplification of recruitment protocols, or providing protected research time. However, it remains to be seen whether clinicians saying they do not have enough time is more commonly a barrier or an excuse.

Clinicians place an emphasis on patient wellbeing, and some may feel the need to protect their patients from the risk of taking part in a RCT. A commonly held belief among clinicians is that patients who take part in RCTs face risks that they would not otherwise face if they received their healthcare in the usual manner. However, a systematic review found that the outcomes of patients taking part in RCTs do not differ from those of patients receiving similar treatments who do not participate[45].

Engaging clinicians in RCTs is a crucial step in the recruitment process. It is apparent that clinicians are aware of the impact they have on their patients' decision making regarding involvement in trials, and it has been shown that personal endorsement of trials by clinicians can have a positive effect on recruitment. If clinicians are fully engaged and understand the benefits, to both themselves and patients, of participating in RCTs, recruitment could improve significantly.

CONCLUSION

Few high quality trials were identified that tested interventions to improve clinicians' recruitment activity in RCTs. The most promising intervention was the use of qualitative methods to identify and overcome barriers to clinician recruitment activity. It is clear that the barriers to nested trials of recruitment interventions in host RCTs must be overcome in future in order to add to the evidence base.

The metasummary of qualitative findings identified understanding and communicating RCT methods (clinician to patient and trial coordinator to clinician) as a key target for future interventions to improve recruitment. Reinforcement of the potential benefits, both for clinicians and their patients, could also be a successful factor in improving recruitment. A bias was found toward investigating barriers to recruitment, so future work should also encompass a focus on successfully recruiting trials.

Few reviews attempt to synthesise qualitative evidence using the methods demonstrated here, and it is hoped that this review demonstrates the utility of methods for synthesising diverse evidence. Hopefully by bringing together a review of qualitative and quantitative studies, we have created a report that is more informative than carrying out two reviews in isolation.

It is hoped that this work will inform the development of future studies investigating clinicians' attitudes to recruitment, as well as the design of possible future recruitment interventions to be tested using a robust trial design.

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Contributors

BF made substantial contributions to the design of the study, acquisition and interpretation of data, synthesis of qualitative evidence, and wrote the final draft of the article.

AG was involved in acquisition, analysis and interpretation of data.

SW contributed substantially to the conception and design of the study, and was responsible for obtaining funding for the study..

DM contributed substantially to the design of the study, particularly search strategy, data analysis and quality assessment of quantitative papers.

SD contributed substantially to the design of the study, advised on qualitative quality assessment, data extraction and metasummary,.

All authors contributed to drafting the manuscript and revising it critically for intellectual content, and all authors have seen and approved the final version of the manuscript.

Competing interests

The authors declare no competing interests.

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Table 1 – Reports of difficulties recruiting to RCTs

Authors	Year	Findings
Charleson and Horwitz[4]	1984	A study of 41 trials listed with the National Institutes of Health (USA) showed that a third of trials recruited fewer than 75% of their planned sample.
Easterbrook and Matthews[5]	1992	A review of 720 research projects approved by the Central Oxford Research Ethics Committee 1984-1987 (UK). Report states that the main reason for abandoning a study was due to difficulties recruiting study participants.
Wilson *et al*[6]	2000	A study of recruitment of primary care practices to an endoscopy trial. Of 90 practices contacted, 43 agreed to take part, 31 recruited at least one patient and only 23 recruited more than five patients.
Foy *et al*[7]	2003	A study of seven primary care trials of dyspepsia management in the UK. Only one study reached its recruitment target; five recruited less than 50% of target and three of these closed prematurely.
McDonald *et al*[8]	2006	A study of 114 RCTs funded by two UK funding bodies 1994-2002. 31% of trials achieved their original recruitment target. 53% were extended due to recruitment problems. Early recruitment problems were identified in 63% of the trials.
Bower *et al*[9]	2007	A survey of published primary care trials in the UK. Less than one third of trials recruited to their original timescale.
Raftery *et al*[10]	2008	Data held by the National Coordinating Centre for Health Technology Assessment (UK), shows that two thirds of funded trials fail to pass 80% of their recruitment target.
Toerien *et al*[11]	2009	Review of all reports of RCTs published in July-December 2004 in six major journals. Of 133 trials 21% that reported sample size calculations failed to achieve adequate numbers at randomisation, and 48% at outcome assessment.

Table 2 – Summary of included quantitative studies

	Study type	RCT recruiting to	Overview (country, aim)
Donovan (2003) [23]	RCT	ProtecT Trial, prostate cancer treatment	UK. To investigate the comparative effectiveness of nurses and surgeons in recruiting patients
Monaghan (2007) [24]	RCT	ADVANCE trial (diabetes)	Australia. Investigation of the effect of extra communication from central trial coordinators on recruitment.
Lienard (2006) [25]	RCT	Adjuvant treatment of breast cancer	France. To assess the impact of on-site initiation monitoring visits on patient recruitment.
Fletcher (2010) [26]	Observational time series	Primary care based multi-centre RCT, stroke trial	UK. To examine whether changes to the design and conduct of a primary care-based RCT were associated with changes in patient recruitment.
Donovan (2002) [27]	Observational time series	ProtecT trial – treatment for prostate cancer	UK. *Feasibility study for main trial.* Qualitative research used to address barriers to recruitment, and make changes to protocol.
Donovan (2009) [28]	Before and after study	ProtecT trial – treatment for prostate cancer	UK. *Main trial results.* A complex intervention was designed using qualitative methods to improve recruitment (i.e. regular training of recruiting staff, centre reviews if centre not recruiting to target, documents to provide advice, and personal feedback).
Kenyon (2005) [29]	Before and after study	ORACLE trial – double blind RCT antibiotic treatment for women in idiopathic preterm labour	UK. Trial was not recruiting successfully so changes were made (introduction of lead midwife responsible for recruitment with protected time for research).
Submacular Surgery Trials Research Group (2004) [30]	Case study (with comparison group)	SST – submacular surgery trial	USA. Comparison of university and community based practices taking part in three multicentre randomised trials. One outcome measure was patient accrual.

Table 3 – Summary of included qualitative studies

	Title	Study method and aims	Recruitment to RCT?
Hales (2001) [31]	The conflicting roles of clinicians versus investigators in HIV randomised clinical trials	**Semi-structured interviews** One theme investigated was recruitment.	**Yes.** Clinical drug trial. Primary care and secondary care
Caldwell (2002) [32]	Paediatricians' attitudes toward randomized controlled trials involving children	**Focus groups** To examine doctors attitudes toward children's participation in RCTs and identify barriers to participation	**Yes.** RCTs involving children. Secondary care (Teaching hospital in Australia)
Jones (2003) [33]	Building research capacity: an exploratory model of GPs' training needs and barriers to research involvement	**Semi-structured interviews** Investigation of GPs research training needs, and barriers to involvement in research.	**Not specified.**
McIntosh (2005) [34]	Recruitment of physician offices for an office based adolescent smoking cessation study.	**Focus groups** To elicit perceptions of facilitators and barriers to initial engagement of physician practices	**Yes.** Adolescent smoking cessation study
Mason (2007) [35]	GPs' experiences of primary care mental health research: a qualitative study of the barriers to recruitment	**Semi-structured interviews** To investigate the perceived barriers among GPs to introducing participation in RCTs to patients with depression.	**Yes.** Primary care mental health research.
Ziebland (2007) [36]	Does it matter if clinicians recruiting for a trial don't understand what the trial is really about? Qualitative study of surgeons' experiences of participation in a pragmatic multi-centre RCT	**In-depth interviews** To explore physicians understanding of the trial purpose and how this understanding had influenced their recruitment.	**Yes.** Multicentre pragmatic RCT. Spinal surgery. UK.
Bill-Axelson (2008) [37]	Experiences of randomization interviews with patients and clinicians in the SPG-IV trial	**Semi-structured interviews.** Investigation of patients' and clinicians' experiences of randomisation with the aim of facilitating future trial participation.	**Yes.** Prostate cancer RCT
Potter (2009) [38]	A qualitative study exploring practice nurses' experience of participating in a primary-care based randomised controlled trial	**Semi-structured interviews** To explore the views of practice nurses' recruiting into a primary care-based RCT, and to investigate factors that influence the success of trial recruitment.	**Yes.** Primary care based RCT to promote adherence to treatment of people with type 2 diabetes.
Howard (2009) [39]	Why is recruitment to trials difficult? An investigation into recruitment difficulties in an RCT of supported employment in patients with severe mental illness	**Interviews** To evaluate reasons for under-recruitment in an RCT. Trial staff and recruiting physicians were interviewed.	**Yes.** RCT of supported employment in patients with severe mental illness.
Patterson (2010) [40]	The great divide: a qualitative investigation of factors influencing researcher access to potential randomised controlled trial participants in mental health settings	**Interviews** Using Grounded Theory process evaluation of a multicentre trial to investigate factors influencing referral to potential RCTs in mental health settings.	**Yes.** Potential RCTs in mental health setting
Paramasivan (2011) [41]	Key issues in recruitment to randomised controlled trials with very different interventions: a qualitative investigation of recruitment to the SPARE trial	**Interviews; content analysis of RCT documents; conversation analysis of recruitment appointments** To explore reasons for low recruitment and attempt to improve recruitment rate by implementing changes suggested by qualitative findings.	**Yes.** Bladder cancer treatment trial – feasibility study.

Table 4 – Summary of qualitative findings with frequency effect size >20%

Abstracted finding	Sub-theme	Studies in which sub-theme is present	Frequency effect size (%)
Understanding of research	RCTs provide the best evidence.	[31] [35] [36]	27
	Poor understanding of research	[32] [33] [36] [39] [40] [41]	55
Communication	Difficulty communicating trial methods	[31] [32] [35] [37] [39] [40] [41]	64
Patient-clinician relationship	Conflicting roles of being a recruiting physician	[31] [35] [39] [40]	36
	Clinicians acting as gatekeepers	[38] [39] [40]	27
	Paternalism	[35] [38] [39]	27
	Clinician influence on patient decision making	[32] [35] [37] [39]	36
	Patient wellbeing a priority	[31] [32] [35] [37] [39]	45
Effect on patients	Possible benefits of taking part in RCTs	[31] [32] [34] [38]	36
	Possible harms of taking part in RCTs	[31] [36] [39]	27
Effect on clinical practice	Positive effect of being involved in RCTs	[31] [32] [34] [35] [38]	45
Individual benefit for clinician	Career development	[32] [38] [41]	27
Methods associated with successful recruitment	Importance of research question	[31] [32] [35] [36] [37]	45
	Trial methods easy to understand, communicate and carry out	[32] [34] [37] [38] [41]	45
	Financial incentives	[31] [33] [34]	27
	Appropriate training	[32] [33] [34] [38]	36