*Quality in Primary Care* 2012;20:199–206 

Research paper

# Recruiting children onto research studies by the Scottish Primary Care Research Network: a real team effort

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## ABSTRACT

**Background** Recruiting for research studies is always a challenge, particularly in paediatric studies. Here we report on experiences recruiting children to five studies through primary care.

**Methods** The Scottish Primary Care Research Network (SPCRN) has approval to identify for research studies eligible participants on primary care practice lists. The number of potential participants and the proportion recruited onto five paediatric studies are provided along with factors involved in recruiting practices and patients.

**Results** A total of 4910 individuals were recruited, of whom 367 (7%) participated. Recruitment of practices varied between 7 and 44% for different studies. There was evidence that practices who had participated in previous studies were more likely to participate again. Patient participation was positively related to affluence and there was evidence that adults were more likely to participate than children.

**Discussion** Despite the pressing clinical workload in primary care, many general practices are still able to make accommodation for research activity. What is required is effective communication between colleagues in primary care, researchers, the SPCRN and patients. Given that the majority of medicine is practiced in primary care, there is a desire for evidence-based medicine to be generated from primary care and the SPCRN and other networks can help to provide this.

**Keywords**: children, evidence-based medicine, recruitment, research

**How this fits with quality in primary care**

**What do we know?**
Children commonly present to primary care with acute and chronic respiratory symptoms. Good quality care is based on clinical trials which are only made feasible by recruiting children with respiratory conditions such as asthma. Recruitment from primary care will ensure that results from clinical trials are relevant to primary care.

Children are not small adults and clinical trials in the paediatric age range are necessary. Ethical issues have been addressed and European Union legislation has obliged the pharmaceutical industry to include children in clinical trials.

**What does this paper add?**
Large numbers of eligible children can be identified from primary care databases using a methodology that protects patient confidentiality and causes very little additional work to busy practices. No more than 10% of children (and often less than 5%) invited to take part in studies are ever enrolled. Recruitment can lead to the over-representation of children from more affluent communities.

## Introduction

Children with acute and chronic respiratory illnesses are seen every day in primary care and there is an emerging body of evidence upon which to build guidelines for the management of common conditions such as asthma,[1] bronchiolitis[2] and lower respiratory tract infection.[3] Inevitably, some aspects of management remain based on good practice, rather than evidence, and there is an ongoing interest from patient groups, funding bodies and regulatory bodies for more evaluation of current and new therapies in paediatric respiratory medicine.

In recent decades, the legality and obligation to undertake clinical trials in children has become established. Historically, there were concerns about the ethics of consenting children for research studies[4] but these have now been addressed. Recent legislation from the European Union has obliged the pharmaceutical industry to include children in clinical trials unless the drug in question is not for a childhood condition.[5] The establishment of clinical research networks in the UK[6] and also in Scotland[7] has relieved researchers of some of the regulatory obstacles[8] to moving a research question into a completed clinical trial by providing trial support and access to good clinical practice-trained research nurses. Despite these advances, one of the main obstacles to undertaking clinical trials in children remains identifying and recruiting participants.[9]

Knowing that the majority of paediatric respiratory medicine is delivered in primary care, it makes sense to recruit from there. There are, however, concerns about recruiting children to clinical trials using primary care and these, in our experience, include: (1) an initial reluctance from general practitioners (GPs) to add research activity to the weight of clinical activity already taking place, (2) a lack of enthusiasm for research *per se*, (3) issues of confidentiality in accessing primary care records, and (4) protecting patients from unsolicited invitations to participate in research (for example, patients receiving trial invitations without prior discussion). Our experience is that these issues can be addressed by good interprofessional teamworking. Here, we present our experiences of recruiting to clinical trials from primary care. Although the studies were related to paediatric respiratory medicine, we believe that many of our experiences can be extrapolated generally.

## Methods

### The Scottish Primary Care Research Network (www.sspc.ac.uk/spcrn)

The Scottish Primary Care Research Network (SPCRN) is funded by the Chief Scientist Office (www.cso.scot.nhs.uk) and employs coordinators who, between them, cover all health boards in Scotland. The coordinators liaise between researchers and primary care practices to facilitate recruitment of members of the general population to research studies in a standardised way.

The SPCRN provide an expert service to both researchers and practices. They provide researchers with advice on study design, ensuring that the project is feasible in primary care and minimising any disruption to the normal working of a practice whilst maximising the recruitment of patients. SPCRN provide practices with specialist staff to make their participation in research as easy as possible. SPCRN staff work on behalf of the healthcare team and under practice staff supervision, each having a current NHS

substantive or honorary contract, or research passport, and signing confidentiality agreements with each practice as required. SPCRN staff are familiar with the databases used by GP practices and are expert in designing search templates to match complex eligibility criteria. These templates search practice databases using the 'Read' codes used within the practice database system to code patient information. In this way, they can search for patients that match study requirements without reading through individual patient records. They are also familiar with common research requirements that are generally unfamiliar to practice staff such as random sampling, stratified sampling, assignment of study numbers and extracting anonymised data. Practices receive modest financial reimbursement for facilitating SPCRN studies, typically £300 per study.

## Recruitment of practices

The recruitment strategy adopted by SPCRN is tailored to meet the needs of each project in terms of the number, type and location of the practices invited; a local project requiring a small number of practices within easy reach of secondary care facilities will require a different strategy from that of an international study requiring hundreds of practices or another requiring practices in urban/rural locations or specific socioeconomic indices.

SPCRN start recruiting practices to a study once NHS Research Ethics and Research and Development (R&D) management approvals are in place. The coordinators liaise with the researcher – and with one another if the project is to be run over a wide geographic area – to develop a standardised approach. SPCRN then invite suitable practices to the project, continuing in a step-wise manner until the recruitment target is reached. Practice and patient recruitment may take several months, and continued liaison between the SPCRN team and the researcher is key to a smooth and efficient recruitment process

## Recruitment of patients

Practices that take part in SPCRN-supported studies can either select and invite suitable patients themselves, or invite SPCRN staff to assist them in this process by identifying eligible patients and preparing the ethically approved invitation letters for inclusion in the patient invitation pack (Figure 1). The list of eligible patients is screened by a member of the clinical staff before the letters are sent out. The patient invitation pack usually includes a consent form or reply slip for the patient to complete if they would like to take part in the study, and this is generally returned direct to the research office. Depending on the design of the study, there may be no further involvement for the practice as any future correspondence can take place between the research team and the participant. Practice and patient recruitment may take several months, and continued communication and feedback between the SPCRN team and the researcher is key to a smooth and efficient recruitment process.

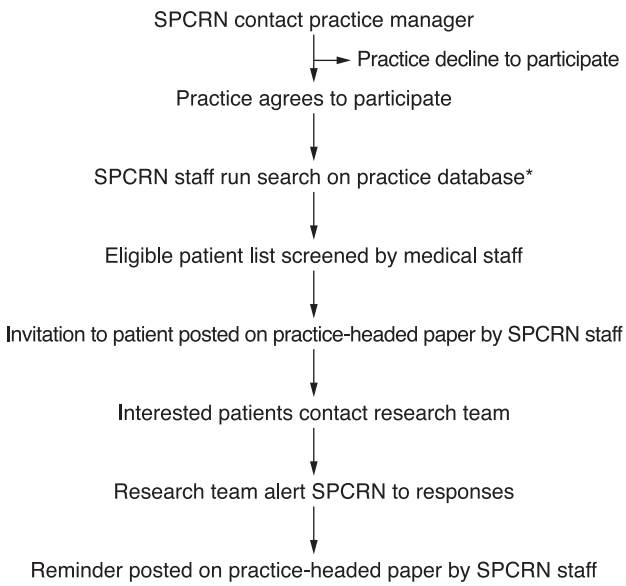


**Figure 1** Flow chart demonstrating the mechanism employed by the SPCRN to recruit individuals for research studies from primary care practices. *Practices can choose to do this themselves

## Clinical trials included as exemplars (see Table 1 for summary)

### *MASCOT*

Management of Asthma in School Age Children On Therapy (www.pcrnnw.nhs.uk/mascot.html). This study was designed to answer the question 'what is the best next treatment step in a child with uncontrolled asthma despite low dose inhaled corticosteroids?'.

### *WAIT*

Wheezing and Intermittent Treatment (www.icms.qmul.ac.uk/chs/pctu/current_projects/wait/25693.html). This study was designed to answer the question 'does treatment with montelukast during acute wheeze reduce the need to seek an unscheduled medical opinion and can better responders be identified by genetic factors?'.

### *REFRESH*

Reducing Families' Exposure to Second-Hand Smoke in the Home (www.ashscotland.org.uk/projects/refresh). This study was designed to answer the question 'in the homes of young children whose mothers smoke, does the addition of indoor air quality measurements to standard motivational interview (MI) reduce the child's exposure to second-hand smoke more than standard MI alone?'.

### *PAGES*

Paediatric Asthma Gene Environment Study (www.asthma-pages.com). This mechanistic study was designed to answer the question 'are interactions between genetic and environmental factors associated with asthma severity?'. Ethical permission was obtained to collect gender, age and socio-economic status (Scottish Index of Multiple Deprivations, SIMD) for all children identified.

### *MSD*

This mechanistic study, funded by Merck Sharp and Dohme, was designed to ask the question 'How does montelukast affect airway epithelial cell release of mediators in adults and children with asthma and is this influenced by hayfever?'. Nasal cells were samples using a small interdental brush and cultured and exposed to montelukast *in vitro*.

**Table 1** Summary of the characteristics of the studies in which patients were recruited by the SPCRN

| | Study design | Trial design | Inclusion criteria | Age range | Follow up |
|---|---|---|---|---|---|
| MASCOT | Multicentre randomised controlled trial | Low dose ICS vs low dose ICS + LABA vs low dose ICS + LTRA | Doctor-diagnosed asthma, on low dose ICS, poor asthma control | 6–14 years | 12 months |
| WAIT | Multicentre randomised controlled trial | Intermittent LTRA vs placebo (stratified by genotype) | Two or more episodes of wheeze (at least one confirmed by doctor) | 10–60 months | 12 months |
| REFRESH | Feasibility study | Standard smoking education vs enhanced smoking intervention | Mother active smoker, child aged 1–5 years, less affluent communities | 10–60 months | 1 month |
| PAGES | Epidemiology study | | Doctor-diagnosed asthma | 6–16 years | |
| MSD | Mechanistic study | | Diagnosed asthma, non-smoker, treatment with LTRA | 8–60 years | |

ICS, inhaled corticosteroid; LABA, long-acting beta agonist; LTRA, leukotriene receptor antagonist. Study acronyms are defined in the text.

### *Recruitment from secondary care*

Initially, recruitment was solely from secondary care for MASCOT, MSD and PAGES, but participants from primary care were sought after experiencing difficulties in recruitment for the former two studies and a desire to compare results between primary and secondary care for PAGES. Recruitment for REFRESH was only through primary care and for WAIT was through both primary care (including the out-of-hours service) and secondary care.

### *Ethics*

Each study was approved by an ethics committee, including the method for recruiting from primary care.

## Results

### Recruitment of practices

Prior to the first study (MASCOT), no children had been recruited to clinical trials in Grampian using the SPCRN. Figure 2 demonstrates how the number of practices approached varied between 17 and 133 and the percentage of practices recruited varied between 44% (PAGES) and 75% (MASCOT, REFRESH).

### *MASCOT*

Recruitment started in secondary care in May 2009 and in primary care in November 2009 and ended in May 2010. There were 546 children identified from 18 practices and of these, nine attended for initial assessment of whom two (0.3%) were randomised, both were followed up for 12 months.

### *WAIT*

Recruitment began in January 2011 for secondary care and May 2011 for primary care and is expected to continue until December 2012. At the time of writing, 521 children had been identified from 14 practices and of these, 44 (8%) attended for initial assessment and all were randomised.

### *REFRESH*

There were 1693 children identified from 23 practices. Recruitment took between June 2010 and February 2011. There were 279 mothers who responded to the invitation of whom 68 were interested in participation and 59 were eligible. There were 22 replies returned due to the wrong address. There were 48 households who completed the study, 3% of those initially identified.

### *PAGES*

There were 1955 children identified from 41 practices in Grampian and Highland between May and November 2011 and 228 children were recruited (11%). Among the 52 Grampian practices who were approached by SPCRN for the first time for any study, 39% (9/23) agreed to take part whilst 58% (15/29) of those previously approached agreed to participate ($\chi^2$ [df = 1] = 0.82, $P = 0.366$). Those children who did participate were of a similar age to those who were invited (mean age 11.4 years [SD 2.6] for participants compared with 11.6 [SD 2.7] for all identified) and no more likely to be boys (55% compared with 60% for all identified). Participation did differ across socioeconomic groups (Figure 3) and was 6% among the two least affluent quintiles rising to 15% for the most affluent quintile ($\chi^2$ [df = 4] = 19.7, $P = 0.001$).

### *MSD*

Recruitment in secondary care began in March 2011 and in primary care in November 2011. There were 16

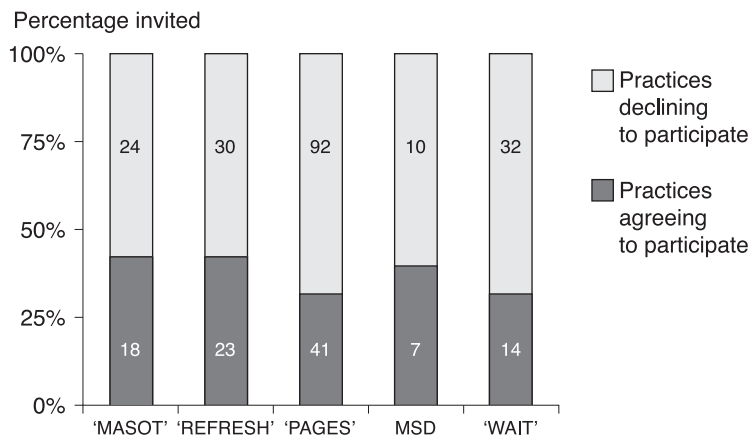


**Figure 2** Proportion of practices that agreed and declined to take part in recruitment for the five studies. The numbers within the bars correspond to actual numbers of practices

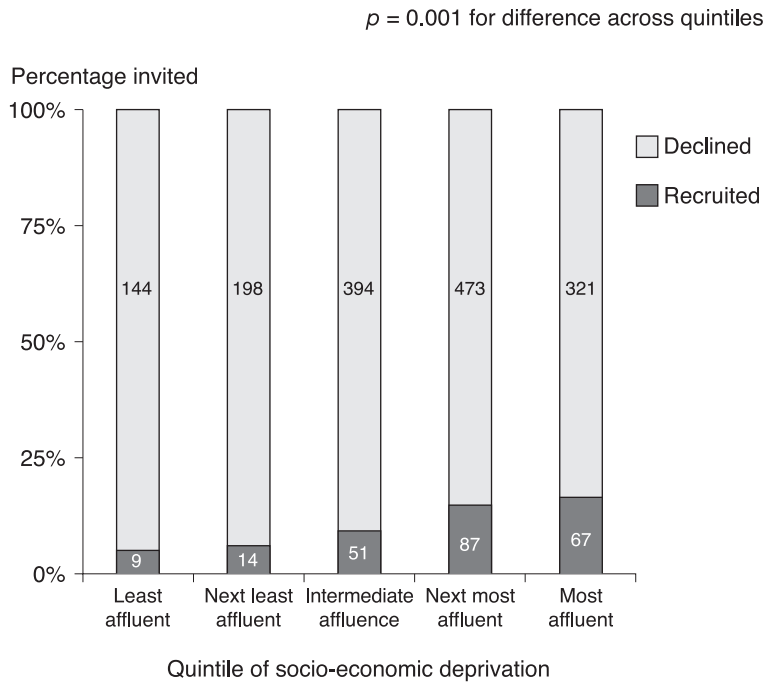


**Figure 3** Proportion of children invited to take part in the PAGES study across quintiles of socio-economic deprivation

children (i.e. aged 16 years or younger) identified from seven practices and of these, none attended the assessment. Additionally, 179 adults were identified from these practices of whom 34 (19%) were recruited ($\chi^2$ [df = 1] = 3.79, $P = 0.051$).

## Discussion

The aim of this study was to demonstrate how teamworking between practice managers, GPs, SPCRN staff, researchers based in secondary care and also patients, can successfully recruit children to research studies. Additionally we have provided evidence that patient recruitment may be less successful in children compared with adults (MSD study) and among children of less affluent families (PAGES). Despite the low proportion of children recruited through primary care, the absolute numbers recruited are impressive. We anticipate that, as recruitment for research studies becomes part of usual activity in primary care, both practice and patient participation rates will increase.

General practices are places busy with clinical activity and research can appear to be an unwanted additional burden on staff, however, as the majority of health care is delivered in primary care, it is important that research is also given accommodation there. Our experience is that the desirability for research is acknowledged by practices, additional duties are seen to be minimal and small payments are made to cover practice costs, and most practices can accommodate SPCRN. Specific comments from practices included 'SPCRN do all the hard work' and 'it feels good to be a small cog in the research network wheel'. Increasingly, 'real world' observations from primary care databases such as General Practice Research database are recognised as a valuable[10] supplement, if not a replacement, for clinical trials and with goodwill from practices and funding from government and funding bodies, then primary care can be expected to have an ever higher research profile.

Even though we report on a small number of studies, there was a striking difference between the proportions of practices recruited for different trials. One explanation for this might be that practices perceive some trials as more 'important' than others and anecdotally, the intervention to reduce second-hand exposure to smoke in preschool children (REFRESH) was perceived to be important. Another factor for practices agreeing to take part is previous participation. In the PAGES study, many practices (often in more rural areas) who had not previously worked with SPCRN were approached to increase the coverage; although the difference in participation rates (39 and 58%) failed to achieve significance, this is most likely due to an underpowered analysis. Other relevant factors may include a desire to be involved in research, a sense of being part of the team if the practice has previously taken part in a study through SPCRN and having knowledge or professional contacts with local researchers and hence a sense of obligation not to let

them down. A combination of more than one factor is likely to be important when practices decide whether to agree to participate.

We have previously reported how almost 50% of children identified through secondary care were recruited to PAGES,[11] whereas the proportion recruited through primary care was considerably smaller (11%). By contrast, the MASCOT study, where recruitment was also from both primary and secondary care, overall recruitment was 10%;[9] it is possible that 50% recruitment is the exception and 10% is more usual. Severity of illness is likely to be one important factor influencing participation rates and secondary care can be expected to include children with more severe symptoms, hence recruitment might be higher in the hospital setting. A second factor important to recruitment in primary and secondary care is affluence; children from less affluent families in both primary and secondary care were less likely to participate in PAGES. The reasons for failing to recruit in less affluent communities are beyond the remit of this study, but literacy may be important. We have also reported how children recruited from secondary care are slightly younger and more likely to be female[11] but we did not see this in secondary care, suggesting that different factors may drive recruitment in primary and secondary care.

There are a number of strengths and limitations in recruiting children through SPCRN. As we have demonstrated, the SPCRN is able to identify a large number of potentially eligible patients for studies in a relatively short time (e.g. 1955 identified in six months for PAGES). An additional strength is that the SPCRN team can identify practices that are better suited to recruiting for individual trials, e.g. population demographics, previous participation. There are also some limitations to recruiting through SPCRN. First, the proportion of participants who agree to take part is $\sim$ 10% and, in the MSD study, we observed evidence that adults are more likely to be recruited compared with children. Second, we have demonstrated that although non-participation did not influence the age or proportion of boys recruited for PAGES, there was a clear gradient where recruitment increased from a low in the least affluent communities to a high in the most affluent communities; individuals recruited are therefore not likely to be representative of the general population but this has been observed previously.[12] Third, some participants may be wrongly identified due to out-of-date information held on practice records although only 1% (22/1693) of REFRESH invitations were sent to the wrong address. Finally, diagnosis in primary care is not always objective and this may result in heterogeneous diagnostic phenotypes being recruited although this limitation is equally applicable to secondary care recruitment.

There is more than one level of research activity in primary care and our experience is that with inter-professional negotiation, the majority of primary care practices can accommodate research at a level where study subjects can be identified. Given the huge challenge in recruiting to research studies, the activity of networks such as SPCRN in primary care provides an invaluable solution to an age-old problem. Whilst there have been rallying calls for an increased research profile in primary care,[13] there are barriers to delivering research in this setting; in addition to the points mentioned in the introduction, there are issues of training in academic primary care, repeated organisations of primary care[14] which often do not consider how this might affect research activity advantage and changes in evaluation of research output. Whatever the barriers, we believe that we have demonstrated that teamwork between partners shown in Figure 1 can facilitate research activity in primary care through the SPCRN and this is likely to benefit patients, clinicians and researchers at the cost of minimal disruption. The SPCRN feeds back the results of trials to practices where patients have been recruited, ideally this is within six months but more than a year can lapse, and what remains to be seen is whether this inspires some individuals to become more research active in primary care.

## ACKNOWLEDGEMENTS

The authors are grateful to Alison Hinds for her comments on the methodology section of this manuscript.

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## FUNDING

The SPCRN is funded by the Chief Scientist Office in partnership with the Scottish National Health Service (NHS).

## PEER REVIEW

Commissioned, internally peer reviewed.

## CONFLICTS OF INTEREST

None.

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*Received 1 February 2012*
*Accepted 18 March 2012*