Refereed paper

Desktop software to identify patients eligible for recruitment into a clinical trial: using SARMA to recruit to the ROAD feasibility trial

Shaun Treweek BSc (Hons) PhD
Health Services Researcher, Senior Lecturer, Clinical and Population Sciences and Education, University of Dundee, Dundee, UK

Ewan Pearson PhD MA MB BChir MRCP
Senior Clinical Lecturer

Natalie Smith RGN
Research Nurse

Ninewells Hospital and Medical School, Biomedical Research Institute, Dundee, UK

Ron Neville MD FRCP FRCGP DRCOG MBChB
General Practitioner, Westgate Health Centre, Dundee, UK

Paul Sargeant BSc (Hons) MSc PhD
Service Designer, CSO

Brian Boswell Bsc (Hons)
Software Development, Software Engineer

Calico Jack Ltd, Dundee, UK

Frank Sullivan MB ChB (Hons) PhD FRCP FRCGP
NHS Tayside Prof. of Research and Development in General Practice and Primary Care, Clinical and Population Sciences and Education, University of Dundee, Dundee, UK

ABSTRACT

Background Recruitment to trials in primary care is often difficult, particularly when practice staff need to identify study participants with acute conditions during consultations. The Scottish Acute Recruitment Management Application (SARMA) system is linked to general practice electronic medical record (EMR) systems and is designed to provide recruitment support to multi-centre trials by screening patients against trial inclusion criteria and alerting practice staff if the patient appears eligible. For patients willing to learn more about the trial, the software allows practice staff to send the patient’s contact details to the research team by text message.

Aim To evaluate the ability of the software to support trial recruitment.

Design of study Software evaluation embedded in a randomised controlled trial.

Setting Five general practices in Tayside and Fife, Scotland.

Methods SARMA was used to support recruitment to a feasibility trial (the Response to Oral Agents in Diabetes, or ROAD trial) looking at users of oral therapy in diabetes. The technical performance of the software and its utility as a recruitment tool were evaluated.

Results The software was successfully installed at four of the five general practices and recruited 11 of the 29 participants for ROAD (other methods were letter and direct invitation by a practice nurse) and had a recruitment return of 35% (11 of 31 texts sent led to a recruitment). Screen failures were relatively low (7 of 31 referred). Practice staff members were positive about the system.
Introduction

Recruitment to trials is difficult and primary care studies face particular challenges. Reviews of recruitment barriers have highlighted time, memory, consent procedures and difficult research protocols as significant barriers to recruitment trials. Systems that reduce these barriers can be expected to have a positive effect on recruitment although rigorous evidence in favour of particular interventions is sparse.

As a consequence many trials miss their recruitment targets, which often leads to underpowered trials and non-significant results that are nevertheless unable to rule out the possibility that the intervention being evaluated may have an important benefit. The widespread use of EMRs in the UK and elsewhere offers the potential to electronically pre-screen patients based on the content of the medical records. Although patients have not usually provided consent for their records to be used for research purposes, when a patient consults a clinician the doctor or nurse has a legitimate right to view the patient’s details and so can be notified before or during the consultation of patients who may be potentially eligible for studies. This avoids the potential ethical dilemma summarised in Box 1. A US study using this sort of notification system reported a significant increase in doctors’ participation in and recruitment rates to an ongoing trial based in outpatient clinics. In this paper we describe the performance of an SMS-based system, the SARMA system, which is linked to general practice EMR systems and is designed to provide recruitment support to multi-centre trials.

The SARMA system

SARMA is a small piece of software that is installed on the desktop computer of every general practitioner (GP) or other member of practice staff who may see a patient who is potentially eligible for a particular trial. Box 2 gives some brief technical details. Screening

Box 1 Consent for consent

This ethical dilemma may be described as: in order to determine whether a potential study subject consents to their data being accessed to determine whether they are eligible for a study, all potentially eligible subjects would first need to be contacted to provide consent to allow access to their records. In 2009 the Wellcome trust developed a series of overarching principles: Safeguarding patient confidentiality. Use best available technologies to ensure security. Mechanisms for accreditation and accountability, including honorary contracts for research staff when extracting data from practices. Improving public awareness. Transparency: ‘no surprises’. National campaign to raise awareness. Provision of information at local practice level. Opportunity to opt out of use of identifiable information. Role of GP as patient’s advocate. Provide advice and feedback. May need training, support and resources.

Box 2 A summary of the technology

Language
SARMA is developed using Java.

History
SARMA was originally developed as an agent-based system where each patient was represented by a software agent, which performed data extraction and communication on behalf of patients being screened for trial participation.

Current version
As requirements have evolved, the requirement for (and consequent overhead of) an agent-based system has become unnecessary. SARMA no longer has any agent-based functionality.

SARMA is currently implemented as a standard piece of client software, which is installed on each GP workstation. The software is configured with the trial inclusion criteria and queries the underlying database of the practice medical record system to extract the clinical data needed to screen the patient for the trial.

Conclusion
An automated recruitment tool can support primary care trials in Scotland and has the potential to support recruitment in other jurisdictions. It offers a low-cost supplement to other trial recruitment methods and is likely to have a much lower screen failure rate than blanket approaches such as mailshots and newspaper campaigns.

Keywords: computers, computerised medical record systems, medical informatics, patient selection
criteria for the trial are loaded with the software, which then communicates with the practice EMR system. The screening criteria used by the SARMA system therefore have to be available in the medical records system; these criteria may be the same as the trial inclusion criteria if all this information exists in the EMR. The software first screens all patients due to attend a consultation with the GP or nurse at the start of the day and compares the patient’s EMR with the screening criteria. When a patient meeting these criteria enters the consultation, a pop-up window informs the member of practice staff that the patient may be eligible. The staff member then has the opportunity to ask the patient whether he or she would be willing to allow a researcher to contact him or her to discuss taking part in the trial. The GP or nurse may also choose to close the pop-up, or ignore it.

The default implementation would present the member of practice staff with a pop-up window with three buttons: ‘Accept’, ‘Decline’ or ‘Unsuitable’. If the patient says ‘No’ to being contacted, the GP clicks the ‘Decline’ button. If the patient says ‘Yes’, the member of practice staff clicks the ‘Accept’ button, which will first ask the member of practice staff to confirm with the patient that the telephone number held in the EMR is correct, and allow it to be changed if it isn’t. The software will then send an SMS text message to a member of the research team, which will contain the patient’s name and telephone number. An information sheet for the patient can also be printed. If the member of practice staff knows that a patient is not suitable for the trial despite meeting the software’s pre-screen criteria, he or she can click ‘Unsuitable’ and SARMA will record this to ensure that pop-ups do not appear again for this patient. If the member of staff does not have the opportunity to, or does not wish to, raise the trial during the consultation, the pop-up window is automatically cleared when the patient leaves the consultation. The software can be extended to provide additional post-screening logic and interaction along with the necessary pop-ups so that staff may be presented with more than the default, three-button pop-up.

We believe that SARMA addresses the following known barriers to recruitment:

- **Time** Provision of full information on the trial, checking of full eligibility and formal consent is done outside the consultation by the research team. Referring a patient to the research team is a matter of pressing a button.
- **Memory** The member of practice staff no longer needs to remember the inclusion criteria, or indeed that the trial is running. Once installed, the software will remind the member of staff whenever a potentially eligible patient enters the consultation.

- **Difficult study protocol** The bulk of the work for referring a patient to the trial team is done by the software and the research team. The member of practice staff need only raise the trial with the patient and provide basic information, which can either be displayed in the pop-up window for the staff member to refer to or printed for the patient.

Our pilot qualitative work with patients demonstrated that patients had no problems with their names and contact numbers being sent to a research team so long as it was their GP who had raised the trial in the first instance.10

**Method**

The technical performance of SARMA was tested on a test installation and at a single general practice in Dundee over several months. We also did some qualitative work with four general practices in Tayside; two were urban and two were rural. Nine GPs, eight practice nurses, three practice managers, one GP registrar, one medical student and one visiting doctor took part in the these focus groups. Eight patients took part in two focus groups and four patients participated in one-to-one interviews. Seven GPs responded to an email discussion document about recruitment software.

This work confirmed that the software was technically able to work and that general practice staff and patients were positive about the system so long as it did not intrude into the consultation. Further testing of the software required it to be used in a real trial. For this we used the ROAD feasibility trial (www.nres.npsa.nhs.uk/researchsummaries/?entryid29=24000 and p=2). Details of the ROAD feasibility trial are given in Box 3.

Our evaluation had four components:

1. a review of technical challenges encountered during the ROAD feasibility trial
2. a comparison of the software with ROAD’s other recruitment methods
3. a comparison of the list of potential participants identified by the software with clinic lists to see if SARMA had identified all potentially eligible participants
4. collating any feedback from general practice staff and patients on the software.

Five general practices took part in the ROAD trial: all of them used the Vision (INPS, UK) EMR system.
**Box 3 The ROAD trial**

The ROAD trial aims to establish a prospective study of incident users of oral therapy to investigate phenotypic and pharmacogenetic determinants of response to oral hypoglycaemic agents in patients with type 2 diabetes, and to compare time to treatment failure in patients randomised to second-line oral agents. The aims of the feasibility trial were to assess recruitment methods, numbers of eligible patients and the trial process and to further develop and evaluate the SARMA system. Diabetes drug naïve patients with an HbA1c $\geq 7\%$ were eligible to receive metformin (Cohort 1). Those receiving metformin or who were previously intolerant of metformin were randomised at drug initiation to one of gliclazide, pioglitazone or sitagliptin (Cohort 2).

Participants were recruited from hospital clinics and general practice by range of methods, one of which was SARMA:

1. Patients having an HbA1c $>7\%$ were selected from practice records and invited by their GP to participate in the study.
2. Incident cases were identified using SARMA.
3. Practices not using the software could manually refer interested and suitable participants during a consultation.
4. Suitable patients attending for a routine hospital diabetic clinic appointment were approached by a research nurse and asked if they would consider taking part.

The SARMA component identified patients by screening the following information from the electronic medical record system:

**Cohort 1:**
- Age 35–80, HbA1c $>7\%$ and $<10\%$, no prescription for any diabetes therapy in previous six months, latest eGFR (in preceding six months) $>60$ ml/min.

**Cohort 2:**
- Age $\geq 35$ and $<80$, HbA1c $>7\%$ and $\leq 9\%$, recent prescription for metformin (within the last six months), latest eGFR $\geq 50$ ml/min, no recent prescription of potential interacting medication (gemfibrozil, rifampicin, miconazole, phenylbutaxone), no prescription of a loop diuretic (surrogate measure of heart failure), latest ALT (if measured) $\leq 2.5$ (upper limit of normal) and no history of osteoporosis.

In addition to these screened criteria, the GP or nurse was asked a few questions (simply requiring yes/no responses) once the pop-up window occurred. For Cohort 1, this was to check that the patient had had at least six weeks of diet and lifestyle intervention. For Cohort 2, this was to check if the patient was staying on metformin (metformin tolerant) or changing to second line treatment (metformin intolerant); and given the potential for randomisation to a thiazolidinedione the GP or nurse was asked to say if the patient had a history of cardiac failure.

**Results**

**Technical challenges**

The software was successfully installed at four of the five general practices. At the four practices using the software, both GPs and practice nurses used the system. An initial difficulty was that practice staff forgot to run the software so the system was modified to start automatically when the desktop machine was switched on.

Two other problems required more work. Firstly, the time taken by SARMA to interrogate the patient’s medical record was excessive (several minutes) and required a significant rewriting of the system’s code. This issue was, however, completely resolved and the software’s interrogation of the medical record is now essentially instantaneous. The second problem was that the software occasionally scrambled the on-screen display of the medical record system’s appointments book. The contents of the appointments book were not affected and refresh of the screen corrected the display of the appointments. The problem was nevertheless an unacceptable side effect. A software modification solved this problem at three of the four practices; the problem persisted at the fourth practice but only occurred very intermittently (i.e. once or twice a week) and was not felt by the practice staff to be a significant problem. It remains unclear why this problem persisted, or why SARMA could not be installed at the fifth practice.
Comparing SARMA with ROAD’s other recruitment methods

Table 1 compares the alternative recruitment methods used by the five general practices in the ROAD feasibility trial. In summary, SARMA recruited 11 of the 29 participants recruited to ROAD, most of them to the cohort of patients starting second line treatment. There were 31 potential participants picked up by the software and forwarded to the ROAD research nurse, one of whom could not then be contacted (see Figure 1).

Table 1 Comparison of the recruitment methods used in the ROAD trial

<table>
<thead>
<tr>
<th>Cohort 1 – metformin (n = 11)</th>
<th>Cohort 2 – gliclazide, pioglitazone or sitagliptin (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Via initial letter = 2 recruited</td>
<td>Via initial letter = 7 recruited</td>
</tr>
<tr>
<td>10 letters sent</td>
<td>20 letters sent</td>
</tr>
<tr>
<td>5 no response</td>
<td>8 yes (1 failed before screening due to recent &lt;HbA1c)</td>
</tr>
<tr>
<td>3 said no</td>
<td>4 said no</td>
</tr>
<tr>
<td></td>
<td>8 no response</td>
</tr>
<tr>
<td>Via SARMA = 2 recruited</td>
<td>Via SARMA = 9 recruited</td>
</tr>
<tr>
<td>9 texts sent</td>
<td>22 texts sent</td>
</tr>
<tr>
<td>4 not eligible (one due to mistake in the initial coding of screening criteria, two because HbA1c changed, 1 commenced on metformin by GP prior to visit 1)</td>
<td>1 uncontactable</td>
</tr>
<tr>
<td>1 declined</td>
<td>3 not eligible (one due to mistake in the initial coding of screening criteria, 2 because HbA1c changed)</td>
</tr>
<tr>
<td>2 changed their minds</td>
<td>3 changed their minds</td>
</tr>
<tr>
<td>Via clinic = 2 recruited</td>
<td>Via clinic = 2 recruited</td>
</tr>
<tr>
<td>4 identified</td>
<td>4 identified</td>
</tr>
<tr>
<td>2 did not attend</td>
<td>2 changed their minds</td>
</tr>
<tr>
<td>Via practice nurse = 5 recruited</td>
<td>Via practice nurse = 0 recruited</td>
</tr>
</tbody>
</table>

Figure 1 Overview of the text messages sent by the recruitment system
Of particular importance is that 23 of the 30 (77%) potential participants were confirmed by the ROAD research nurse (NS) as being eligible for the trial. The reasons for exclusion of the remaining seven patients were: one patient had osteoporosis (this was not part of the software's screening process but was part of the full list of exclusion criteria for Cohort 2); one patient had too low an eGFR (this was an error in the coding of the screening criteria); four patients had an HbA1c that had subsequently fallen above or below the inclusion criteria (this could be avoided in future by setting the screening criteria just within the inclusion criteria limits) and one patient had been started on metformin by their GP prior to the visit. In other words, the number of screen failures is low; with modification to the recruitment criteria such as the HbA1c limits, screen failures in this study could have been reduced to almost zero. We see this as a considerable advantage of the SARMA system, where both the GP and research team are only involved when there is a high likelihood of patient eligibility. Of the 31 eligible patients, 14 said no when asked by GP if they would be willing to be contacted by the ROAD research team. Reasons for saying no included ‘prefers tried and tested meds’, ‘wants to improve diet’ and ‘work commitments’. Five patients subsequently said no after speaking to the study’s research nurse (NS). Adverse events listed on the patient information sheet were cited as one reason for saying no at this stage of recruitment.

The flow of the 38 potential participants identified by SARMA through to recruitment of 11 participants is shown in Figure 1. For the ROAD trial, each participating GP received about one pop-up window a month, with the rate of recruitment being around 0.3 participants per month.

### Comparing the list of potential participants identified by SARMA with clinic lists

Patient lists for diabetic clinics held at two general practices were compared to the SARMA log file to confirm that all potentially eligible patients had been identified by the software. Diabetic clinics held on two separate days were checked; a summary is given in Table 2. All potentially eligible patients were correctly identified by the software.

### Feedback from general practice staff

Feedback from practice staff was positive and often focused on the lack of work required to use the software. Two example quotes are given below.

Comment from a practice nurse:

‘I haven’t found the system any problem at all, being a small practice, it didn’t flag up often and it was easy to sign into in the morning when the computer was switching on.’

---

**Table 2 A comparison of diabetic clinic patient lists with the SARMA log files**

<table>
<thead>
<tr>
<th>Practice 1 (nurse-led clinic)</th>
<th>Practice 2 (GP-led clinic)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinic 1 (28 April 2009)</td>
<td>Clinic 1 (15 July 2009)</td>
</tr>
<tr>
<td>• 23 patients booked in</td>
<td>• 14 patients booked in (4 by telephone)</td>
</tr>
<tr>
<td>• 16 patients attended</td>
<td>• 10 patients attended</td>
</tr>
<tr>
<td>• 15 patients not eligible for ROAD because outside trial age or HbA1c ranges</td>
<td>• 9 patients not eligible for ROAD because outside trial age range or no recorded HbA1c</td>
</tr>
<tr>
<td>SARMA identified the 1 eligible patient (Cohort 1) and a text message was sent.</td>
<td>SARMA identified the 1 eligible patient (Cohort 2) but text message was not sent (pop-up was closed or ignored by GP).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinic 2 (20 May 2009)</th>
<th>Clinic 2 (20 August 2009)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 12 patients booked in</td>
<td>• 21 patients booked in (3 by telephone)</td>
</tr>
<tr>
<td>• 12 patients attended</td>
<td>• 18 patients attended</td>
</tr>
<tr>
<td>• 10 patients not eligible for ROAD because outside trial HbA1c range</td>
<td>• 16 patients not eligible for ROAD because outside trial age range or no recorded HbA1c</td>
</tr>
<tr>
<td>SARMA identified the 2 eligible patients (Cohort 2) but text messages were not sent (pop-up was closed or ignored by clinic nurse).</td>
<td>SARMA identified the 2 eligible patients (Cohort 2). A text message was sent for 1 patient but pop-up was closed or ignored by GP for other patient.</td>
</tr>
</tbody>
</table>

* The software is currently not configured to work with telephone consultations.
Comment from a GP:

‘I found SARMA really rather good and user friendly. The only weakness was that I frequently forgot to log onto it. It would be good if it would log in automatically when starting up Vision and let you have the option to opt out.’

Only one patient made a comment when completing the feedback questionnaire:

‘On the whole this was well coordinated. I felt that the survey being offered by your GP at consultation worked well since they can clarify any concerns immediately and then the wheels were in motion. I think a request letter is too easy to ignore or forget. I also felt the study highly motivational.’

Discussion

This work with SARMA has demonstrated that recruitment to primary care trials can be supported by software that screens patient data held in EMR systems and alerts the GP or other member of practice staff to potentially eligible patients. Practice staff need no longer remember either the trial or its inclusion criteria when a potentially eligible patient presents. The software could support trials in other ways. It could independently record the number of eligible patients presented and recruited, which would provide important information about case mix in trials, for example, whether patients in the trial had a different disease severity compared to those not taking part. The software could also be used to run through practice records while planning a trial to get better estimates of the likely number of eligible participants and could, therefore, enable trialists to make more informed decisions about the number of practices needed for a given trial.

The use of text messaging makes it easy for practice staff to refer patients to the research team. However, it would be possible to generate emails instead, which may be preferable in some trials. A particular advantage for a trial like ROAD is that the number of screen failures was low (23%), and with minor code corrections and adjustment to the screening criteria could be reduced to close to zero. This compares favourably with a similar study described by Embi and colleagues, although referrals in that study increased by a factor of ten, recruitment increased by a factor of only two because of screen failures. This is, of course, dependent on the quality of data held in the medical record system. If crucial inclusion criteria were not available to SARMA then screen failures could be expected to be higher. For four of the five practices involved in ROAD, using SARMA was unobtrusive and trial participants were recruited with little effort required from practice staff. Practice staff involved in the ROAD trial were very positive about the software.

Some challenges remain. It is still not clear why the fifth practice was unable to use SARMA, although we continue to work on this. The software is currently only able to operate with the Vision medical record system. Modification to enable it to work with other medical record systems is not expected to be onerous (especially for the Scottish GPASS system) but needs to be undertaken before this recruitment tool can be widely used in Scotland-wide trials. It will also operate throughout the UK as the clinical computing systems used in Scottish practices are subject to the same requirements for accreditation as those in England, Wales and Northern Ireland. Increasing interoperability of electronic records in Europe should allow recruitment systems to be used more widely in the near future. In the USA such tools could avoid the difficulties experienced by researchers as a result of the 1996 Health Insurance Portability and Accountability Act.

More discussion with practice staff may be required to discover why the pop-up window is closed or ignored so often (see Table 2), although there may be legitimate reasons (e.g. lack of time in the consultation) for ignoring a pop-up. Indeed, the fact that practice staff can ignore the pop-up may make it easier for them to agree to having the software installed. Like other trial software and procedures, training will be necessary to support practice staff in their use of automated recruitment software such as SARMA. The software is mostly invisible so any training will be linked to the pop-up screens and will almost certainly be less time-consuming and costly than the training required for more traditional recruitment methods that require practice staff to remember and apply inclusion criteria, or obtain informed consent. That about one-third of participants in the ROAD trial were recruited via the software suggests that the system is likely to complement other recruitment strategies rather than be a trial’s sole recruitment strategy. However, given that SARMA needs no attention once installed, it is a low-cost way of delivering an additional stream of trial participants.

Conclusions

SARMA can support recruitment to primary care trials in Scotland and has the potential to support recruitment in other jurisdictions. It is specifically designed to make it easy for practice staff to refer patients to the research team, transferring most of the work of recruiting a participant away from the practice. Finally, it offers a low-cost supplement to other trial recruitment methods and is likely to have a much
lower screen failure rate than blanket approaches such as mailshots and newspaper campaigns.

ACKNOWLEDGEMENTS
We thank the Chief Scientist Office, Scotland, for supporting work on agent technology medical communications, which underpins the concepts behind SARMA. The Scottish Funding Council supported Shaun Treweek for part of the work described in this paper through project funding for the Scottish Collaboration of Trialists. We would also like to acknowledge the contribution made by Suraj Ajit while at Calico Jack.

REFERENCES
3 McDonald AM, Knight RC, Campbell MK et al. What influences recruitment to randomised controlled trials? A review of trials funded by two UK funding agencies. Trials 2006;7:9.
6 Watson JM and Torgerson DJ. Increasing recruitment to randomised trials: a review of randomised controlled trials. BMC Medical Research Methodology 2006;6:34.

ETICAL APPROVAL
This study was approved by the Tayside Committee on Medical Research Ethics B, reference 08/S1402/47.

INTELLECTUAL PROPERTY
Excluding copyright in the written work, all rights in the content and subject matter of this paper are reserved to the authors and/or their respective employers.

CONFLICTS OF INTEREST
ST and FS (on behalf of the University of Dundee) and RN hold intellectual property rights on the SARMA software. PS and BB are employed by Calico Jack Ltd, which may in the future market SARMA as a recruitment tool.

ADDRESS FOR CORRESPONDENCE
Shaun Treweek
Clinical and Population Sciences and Education
University of Dundee
Kirsty Semple Way
Dundee DD2 4BF
UK
Email: s.treweek@cpse.dundee.ac.uk

Accepted February 2010