

Innovative Proven Clinical-Research Strategies for Participant Recruitment and Retention

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ABSTRACT

The ability to successfully recruit and retain research participants is an important precursor to conducting a successful clinical trial. With respect to participant recruitment, we discuss potential strategies used in well-known and successful research studies to reach out to the targeted populations, including public education on the importance of clinical trials and the use of new media in reaching out to a wider population. The measures used by research studies to engage their participants and their healthcare providers to optimise participant retention are also examined. We conclude by discussing how these strategies may be adapted for use in Singapore.

Keywords: clinical research, recruitment, retention

INTRODUCTION

Clinical research globally is threatened by declining participation rates and misconceptions about clinical research^{1,2,3}. As more clinical trials are being conducted concurrently, the competition for a limited pool of available participants will intensify and the need to recruit and retain participants will become more urgent. In a Thomson CenterWatch survey conducted in the US in 2003 and Europe in 2004, 94% of US clinical trials and 82% of European clinical trials miss their enrolment deadlines¹. The Tufts Center for the Study of Drug Development also reported that the enrolment rates dropped from 75% to 59% from 1999 to 2006, while retention rates declined from 69% to 48%².

Patient participation plays a vital role in conducting successful clinical research. Low participation in clinical research may result in indefinite delays in clinical trials. This is because the study population recruited may be inadequately powered to show a statistically significant effect of the intervention. Participation in clinical research

depends on many factors such as participants' perceptions, attitudes, knowledge and experiences regarding clinical research. Getz reports that while public support for clinical research in the US appears to be high, public mistrust of clinical research professionals is growing. Furthermore, Getz also reports that trial participants are perceived to be "risk takers who are either very ill or greedy" by the public³. These findings are worrying as these negative perceptions may ultimately prevent otherwise willing participants from joining clinical trials.

Singapore's ambitions to be a regional medical research hub are starting to bear fruit; the Health Sciences Authority (HSA) reports that the number of clinical trials conducted in Singapore hit a new high of 286 in 2008, up from 201 in 2004⁴. This number is impressive given the context of Singapore's small population size. That said, the small population size mandates that Singapore be even more tenacious in pursuing trial participants or risk losing relevance in global biomedical research.

While there has been substantial work done internationally elucidating the reasons why patients elect to or withhold participation in clinical research, there is little published data in Singapore on recruiting and retaining of trial participants. Anecdotal accounts from Singapore Principal Investigators (PIs) however suggest that they too face difficulty in recruiting and retaining research participants. To augment Singapore's efforts in clinical trials, we describe here how select leading clinical research centres conduct clinical research studies and distil here some of the best practices of retaining and recruiting participants.

GOOD PRACTICES FOR RECRUITING PARTICIPANTS

Tailoring Recruitment Strategies

The ability to reach out to specific target study populations is a distinguishing trait of successfully conducted studies. Many research studies use innovative recruitment methods such as outreach programmes instead of simply using the conventional methods of advertising and doctor recruitment and referral. One important lesson learnt from studies such as the Trials of Hypertension Prevention (TOHP) and the RENO Diet-Heart Study is that the use of a variety of recruitment strategies tailored to the different communities can yield good results.

In the TOHP study, co-ordinators were able to recruit a total of 2,382 participants over 17 months in 9 different geographical locations, over the targeted 2,250 participants over the same time period. This was achieved using a combination of direct mailing to potential participants, community screening programmes and media advertising, which together accounted for 96% of all participants recruited. Traditional recruitment from healthcare provider referrals only accounted for 4% of the study⁵.

The RENO Diet-Heart Study conducted in the US also demonstrated effective strategies to recruit participants within a short period of time. It used different approaches tailored to recruit different populations of interest including advertisements in local and university newspapers, word-of-mouth personal recruitment, and invited group-recruitment presentations at different organisations and businesses. Flyers, newsletters, special editorials by a local, popular columnist and special recruitment efforts in targeted populations complemented the above⁶. The use of word of

mouth as a recruitment strategy was particularly effective, as it accounted for 47% of the participants in the study. In all, the combined strategies recruited 1,386 potential participants

Public Education into Clinical Research

Public education and outreach is also effective in ensuring that the community's perceptions of trial participants and clinical research organisations are positive. Since trial volunteers come from the community, the perception of trial volunteers making important altruistic contributions to science is likely to increase trial participation in the community. Simmons reports in 2008 that a "Medical Heroes" advertising campaign, which aimed to increase public awareness of research as well as portray the participants in a positive light, increased trial participation in the areas it was shown by 38% as compared to a control group where only traditional trial recruitment advertisements were shown⁷.

Community outreach and involvement can also help bolster recruitment rates⁸. A review on Community-based Participatory Research conducted by Viswanathan indicated that studies that featured community involvement often had improved participation rates. This improvement in recruitment rates is in part attributable to the fact that members of the community are better able to advise on the most effective and culturally sensitive ways to approach their fellow community members. In addition, community participants are also able to provide greater access into the communities being researched, improve the comprehension of the information provided to the patient as well as enhance the reputation of the researchers⁹.

The Internet can also be used effectively to help educate and recruit the public. The Clinical Centre at National Institute of Health (NIH), USA, which has approximately 1,500 active clinical studies at any point in time, imparts useful lessons on how clinical trial information can reach volunteers. The web site, which is easily accessible to all current and potential volunteers, provides comprehensive information about the clinical research study under a single button appropriately titled "participate in clinical studies". It also offers different channels of communication media such as patient information, newsletters and clinical research videos¹⁰. The National Health Services in the UK has also set up an advisory group known as INVOLVE, which

provides the public with a database of all research projects seeking public involvement¹¹. In addition to providing eligibility criteria written in plain English and contact details of trial co-ordinators, the database also helps potential participants better understand how the research is planned and carried out, how to weigh the risks, and how their safety and rights are safeguarded.

Web 2.0 — Use of New Media in Clinical Trials Recruitment

Pharmaceutical companies are beginning to use patient support group social networking sites such as Inspire.com and patientslikeme.com to advertise and recruit patients for clinical trials and other forms of clinical research. This strategy allows them to reach out to disease-specific communities who would otherwise be difficult to find in the general population. Other examples of the use of new media in clinical research recruitment are armyofwomen.org, a web site dedicated to recruiting 1 million women for a cohort study looking at breast cancer and prevention and trialx.com, a web site which matches patients to trials based on their clinical information. Both these web sites have applications in Facebook and twitter to advertise events and activities. In addition, trialx.com is also able to use online medical records such as Microsoft's Healthvault and Google Health to match potential research subjects with clinical trials. While there may still be issues related with subject confidentiality and the ability of researchers to effectively blind their studies, the potential of new media cannot be ignored¹².

IMPROVING PARTICIPANT RETENTION

The ability to retain participants in studies is as important as recruiting them. Loss of follow-up of participants represents a significant loss in information and data. The RENO Diet-Heart Study exemplifies best practices in patient retention with 90% of participants still participating in the study at its 5th year. The factors that appear to contribute to higher retention of participants are thorough explanation of study expectations at the beginning, regular education programmes and feedback on their results, annual participant incentives and an all-out effort in maintaining rapport with participants. Some examples of the latter point included personal notes written by the principal investigator on each letter sent for the rescheduling of their annual appointment and a Valentine's Day newsletter sent each year to keep

the participants informed about some of the study accomplishments and important study findings that they have contributed to. We believe that a high level of engagement activities which serve to inform and show appreciation to the participants allow volunteer retention to be high.

The Framingham Heart Study (FHS) is another study that further illustrates the importance of community engagement. It has been ongoing for 60 years, spans 3 generations of volunteers and has produced 1,973 publications along the way¹³. Recognising the dedication and loyalty of the research participants in the FHS studies, the FHS organising committee routinely shows appreciation to the participants, maintaining the goodwill that has been generated by the study. The level of altruism and loyalty shown by the participants is also matched by the dedication of those conducting the research by organising anniversary celebrations and providing regular updates to the participants on the findings of the study. In addition, the FHS participants and other members of the community are also involved in the research ethics committee of the FHS¹⁴, enabling the community to maintain a high level of trust with the investigators involved.

Engaging providers who are otherwise more focused in providing clinical services to help in the research will also yield significant improvements in participant retention and recruitment. This is done by ensuring that there is sufficient support given to the healthcare providers, including ensuring timely responses to all of the provider's queries and moving some research staff to sites to assist the physician in collecting samples. Both Leathem¹⁵ and McKinstry¹⁶ report that efforts to engage providers yielded higher retention rates of patients.

Table 1 (overleaf) summarises the strategies that can be used to recruit and retain participants.

IMPLICATIONS FOR SINGAPORE

Conventional methods of recruitment should be done in concert with a variety of other recruiting strategies specifically focused at target population as seen in the RENO Diet-Heart study. The example of the NIH Centre also emphasises the importance of transparency and accessibility of clinical trial information. A clinical trials registry/database, modelled after INVOLVE in the UK to make it patient and public friendly, can be set up. The HSA, being the regulatory body which governs clinical trials,

Table 1. Summary table for strategies used to recruit and retain participants

Strategies to increase recruitment	<ul style="list-style-type: none"> • Use a variety of outreach methods targeted at desired patient population rather than just relying on patient referrals from other providers • Educate the public on the importance of clinical research in developing new cures and portray current or former trial participants in a positive light • Involve members of the community when planning the clinical trial protocols • Create a website which shares clinical trial information in a centralised database to help interested participants contact study PI's • Use social networking and disease specific support group sites to reach out to otherwise difficult to access populations • Match potential clinical trial participants to PI's using electronic medical records systems
Strategies to increase retention	<ul style="list-style-type: none"> • Engage the community by informing them of trial results and celebrating achievements with them • Ensure that partnering physicians are kept actively engaged on the progress of the trial • Make the trial participant process be as convenient as possible for participants and physicians by creating satellite or mobile research units or providing research assistants to clinics

would have information on all clinical trials which are conducted in Singapore, making it the ideal agency for housing the clinical trial registry. Given also the high broadband and Internet penetration in Singapore, more sophisticated use of new media in addition to conventional methods need to be enhanced.

In terms of patient retention, no effort should be spared in attempts to ensure participant satisfaction. A high level of engagement by the staff to address concerns and queries will be important. Strategies that would either move the research sites closer (such as mobile research units) to the target populations or engage providers who are more focused in providing clinical services to help in the research would be possible strategies that can be adopted. In the Singapore context, this might mean working more closely with the polyclinics and general practitioners (GPs) and perhaps using the same mobile or satellite testing centres in strategic locations throughout the island. The FHS is a good example that maintaining a high level of enthusiasm and dedication among research participants, without compensation, through continuous engagement by staff is possible.

As Singapore embarks on becoming a regional biomedical research hub including emphasis on clinical trials, it is vital that it pays special attention

to trial participant recruitment and retention. Given Singapore's small population as compared to many of the countries where clinical research is carried out, and the complexity of issues surrounding participant recruitment and retention, the adoption of successful participant recruitment and retention strategies will be important to prevent Singapore's ambitions as a clinical research hub from derailing.

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