Title: Improving recruitment in clinical trials: the human touch

Infoline: Person to person contact is still a crucial element of clinical trial recruitment

Starting recruitment in a randomized clinical trial is an important milestone in the life cycle of the trial. It often marks the end of months, or even years, of planning and is an exciting time for the investigators. However, despite the best planning, recruitment into clinical trials is never easy. Recruitment can be difficult for a multitude of reasons. These may relate to the trial; the inclusion and exclusion criteria, although intellectually robust, may prevent any patients from ever being eligible. Recruitment may be difficult due to issues with investigators. There may be trouble accessing the correct type of patients, the trial may be underfunded leaving investigators unwilling to recruit participants and the investigator may be inexperienced with regards to the intervention or population under study. Of course there are also patient factors that also determine participation rates. Do the patients understand the research and protocol, is it onerous, what is the perceived risk? All of these factors work in a complex interplay to determine the success of trial recruitment strategies [1,2,3].

In this issue of the Journal, a report from the investigators of the Evaluating recruitment strategies in the Australian Study for the Prevention through Immunisation of Cardiovascular Events (AUSPICE) trial [4] report their experience in recruiting patients for a large pragmatic trial of pneumococcal vaccine against placebo. They found that participation rates in response to a mailing was only 3%, far short of the expected 10%. Through use of social media, television and further reminders they managed to improve this rate but it remained low. So why were rates so low? There was a sufficient patient population to target which was identified through electronic health records. There was a simple study design that would be relatively easy to understand. The risk to participants was low. The burden of study visits was low. All of these factors have been described as barriers to patient participation in randomized trials [1,2,3]. Large pragmatic trials such as AUSPICE have been felt to be

a good solution to the issue of complexity in clinical trials, patient burden as well as cost [5]. So if these design issues did not seem to be a barrier, perhaps it was a patient factor? Could it be the method of patient contact?

Multiple studies have reported that face to face contact is an important factor that drives recruitment [1,2]. In an analysis of 87 protocols in paediatric trials and studies, of which 2/3rds reached a target enrolment of >=80%, one of the biggest determinants of whether a protocol successfully recruited its target number was if an in person, face to face approach was made by the investigators to the participants [6]. Of the trials that did successfully reach their target, 86% had used in person approaches, in the studies that failed, 70% used in person approaches. Study complexity and long duration of study along with complex inclusion and exclusion criteria were the only significant predictors of missing the recruitment target. Patients rate that their experience of research is higher when they have a chance to engage with and discuss the research with investigators [7]. It is therefore perhaps not surprising that in AUSPICE patients did not respond as well as expected to a letter or advertising. While these methods are attractive ways to find patients, they are relatively cheap and can be used to target a large population, investigators need to be aware that response rates will be very low, although reminders help [1], as was shown in AUSPICE. If in person contact is better are there any specific aspects of in person contact that patients respond to more? It seems that recruiter flexibility and building rapport are two key qualities [8]. Patients may also be more responsive is there is already a relationship with the study team or if the study team is introduced by a member of the patient's clinical team [2,9]. This personal contact therefore appears to be crucial in successful recruitment strategies. In contrast to non-selective methods such as postal approaches, it must be remembered that in-person recruitment may be subject to bias (both conscious and unconscious) which may also influence recruitment and representativeness of participants.

If we are to improve the rates of recruitment into clinical trials we must not forget that at the centre of this effort is a patient who is going to entrust their health, and potentially life, to an investigator and their team often for no direct benefit to them. This requires trust and confidence which is often hard to convey from a distance. While large scale electronic datasets, traditional and social media have transformed many aspects of clinical trials, it may be that successful recruitment still requires that human touch.

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