Recruitment to trials, a funder's perspective

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Recruitment to trials has improved over the last 20 years. The STEPS study showed that 60% of a cohort of MRC and HTA trials recruited close to their target sample. A more recent, soon to be published cohort of HTA trials is achieving 69% and anecdotal evidence from the HTA monitoring files suggest that this percentage is rising. Some trials recruit very successfully, good example is the CRASH2 study by Ian Roberts and colleagues which recruited 20,000 participants within their target time. Recruitment though was almost exclusively abroad.

Reasons for severe failure

When trials fail it tends to be because of lack of application of the lessons from the previous trials rather than because of lack of new knowledge. Therefore the methods to improve recruitment trials might be investigated by research using methods taken from management or systems researchers rather than by doing trials of new methods.

The reasons for failure include:

- *Unrealistic expectations*. Trialists appear optimistic and many are unrealistic in their recruitment plans. Some plans would be difficult to deliver even in ideal circumstances.
- *Poor planning and project management*. It is vital that a person leading a trial has good management leadership skills rather than merely energy and scientific curiosity. If the chief investigator does not possess these skills it is important that they appoint a very efficient manager and that they delegate authority to that person.
- *Lasagna's law*. Louis Lasagna suggested that the prevalence of any condition went down to 10% of its original value whenever a trial is started. Certainly an inaccurate estimation of the available pool of participants is a not uncommon feature of studies in the NHS. Researchers also fail to put in efficient systems to find and contact potential participants including screening logs and making sure potential recruiters are located in the right part of the NHS.
- *Failure of clinical engagement*. Trialists may have the support of a small number of principle investigators but may fail to win the support of key groups such as junior hospital doctors or nurses who will have to approach participants. This can be fatal to a trial.
- *Site enrolment.* Studies frequently underestimate the burden of getting participating sites up and running and they don't anticipate the support that sites will need in order to navigate the regulatory approvals.
- *Failure to negotiate the regulatory systems promptly*. Some difficulties with obtaining regulatory approval are severe and cannot be anticipated, but many of the difficulties occur in any multicentre trial and can be appropriately dealt with during the set up phase. Some researchers do not put in the necessary resource or expertise to navigate the system.
- *Participant consent*. Unwillingness by potential participants is seldom the cause for major difficulties in recruitment. People are generally open to research and altruistic in their outlook; a more common reason for failure to recruit is unwillingness of doctors to offer randomisation to their patients because they are not in equipoise.

HTA programme response
Teams with experience of running complex trials are well placed to obtain funding. The funding boards carefully examine research proposal for realistic plans and suggest modifications where necessary. Once plans are agreed then researchers are monitored to ensure that trials are delivered according to plan. As public money is less available extensions to project funding are becoming more difficult to obtain.

There is increasing use of internal pilot studies with stop/go rules for viability. External feasibility and pilot studies are commissioned separately from the main trial where there is significant uncertainty about whether a substantive trial will be viable and in some cases a full trial is not funded.

The future
Thanks to the great efforts of clinical trials units and the research networks the performance of trials in undoubtedly improving. The HTA programme will monitor studies more closely by recording accrual data on the web-based forms and by running more frequent face-to-face meetings with researchers where performance is drifting.

There are likely to be a few more closures of trials early and where this is happening it is generally because of lack of available participants or lack of clinician equipoise.

Clinical trials are complex projects delivered in the NHS by research teams. Lessons from management and health service delivery research may help these to be delivered more efficiently in future, further service delivery research rather than trials of methods may be useful.