Clinical trials: can technology solve the problem of low recruitment?

Getting people to take part in clinical trials is often difficult. **Toby Reynolds** looks at new strategies to increase participation

All doctors depend on people who volunteer to participate in research. So do all patients. Without the volunteers, there could be almost no research, and without the research, how could anyone know which treatments are safe, let alone effective?

But researchers often struggle to recruit volunteers. As anyone who has tried to recruit patients to a clinical trial will know, you approach 100 and randomise perhaps 10, if you are lucky. This difficulty is prompting thought on what can be done to increase participation, and whether the public should be encouraged to see clinical research differently.

"Recruitment is probably the biggest challenge that clinical trialists face," said Shaun Treweek, senior lecturer at the University of Dundee and assistant director of the Tayside Clinical Trials Unit.

"Difficulties with recruitment are very, very common, and some trials are just kicked into touch because they cannot recruit," he added. "If you feel that there are areas where we should be doing more trials—and I do—then that needs even more people, and trialists are already struggling."

A 2007 study of 114 multicentre trials funded by the UK's Medical Research Council and Health Technology Assessment programme found that only a third kept up with their planned recruitment schedule.[1]

Recruitment problems don't only mean more work and greater costs. Studies that don't get enough volunteers might not record enough events to show a benefit, or detriment, while studies that miss "hard to recruit" patient groups generate results that are difficult to apply in real life.

Ethnic minorities are often poorly represented in published clinical trials.[2] But Tom MacDonald, professor of clinical pharmacology and head of the University of Dundee's Medicines Monitoring Unit, is keen to note other imbalances.

Increasing awareness

"People interested in their health do trials, and therefore they have good health," he said. "One of the problems we have in trials is that we power the study for a 2% event rate, from the general population, and then we find a 0.5% event rate because all the healthy people were the ones who took part. We can't get the people who are unhealthy to take part, and we can't get elderly people to take part. But they are the ones who need all the drugs."

Numerous recruitment hurdles have been identified. It can be hard to contact people, for example. Ethics committees generally prefer researchers not to contact patients independently (the opt-out approach) but to wait until the patient has discussed the project with his or her clinical team (opt-in). Clinicians are busy, and trying to interest patients in research is usually not their top priority.

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But the greatest barrier may simply be public engagement, starting with a lack of awareness. Professor MacDonald, frustrated by recruitment rates to studies run by his team, ran a project to see what effect a media campaign exhorting patients to "get randomised" would have on public perceptions of research in Scotland.[3]

Before the three month campaign, only 29% of those surveyed had heard of a randomised clinical trial, and less than 3% of respondents agreed that "we all need treatment at some point and trials tell us about the best treatments."

The advertisements, on television, radio, and in newspapers, had some effect: the proportion of respondents who had heard of a randomised clinical trial rose to 38%, for example. But it didn't change their responses when asked if they would take part in one.

"Engaging the public in research is extremely hard. It is not going to change any time soon unless we can work out better strategies for continuously trying to explain to people what research is about and what the benefits are," said Professor MacDonald.

"It is like exercise, smoking, and low salt diet campaigns. They need to be continuous, high profile, on all the time in different places so people can't avoid them," he added.

In the United States, a longer running public service advertising campaign celebrating the "everyday medical heroes" of clinical research has been developed and is being screened by the Centre for Information and Study on Clinical Research Participation (CISCRP), a non-profit organisation.

Tufts University researcher Ken Getz, who set up CISCRP in 2003, believes that the public has a poor and often negative understanding of clinical research. "There is an incredibly low proportion of people who even know what a clinical trial is," he said.

According to CISCRP, close to 60% of the American public recalled having seen an advertisement for clinical trial volunteers. "Not a single person could remember what the trial was for because there is no context for people," he added.

"Unless they are right in the heart of needing to be in a trial themselves or for a loved one, it is all just purely passing curiosity."

Technological solutions

So what can recruiters do to get their numbers up?

A few strategies have been shown to be effective.[4] Most, however, are either not very adventurous—telephone reminders, for example—or are methodologically or ethically problematic, such as open label trials without blinding or opt-in approaches allowing researchers to contact patients directly. The evidence for other interventions, such as providing trial information as a video or modifying recruiter training, is equivocal.

Some recent developments, however, indicate that technology might have a role. Since busy clinicians don't have time to recruit, Scottish and US academics have separately investigated computer programs that can scan electronic health records and then show a prompt that a patient is eligible for a specific trial.[5 6]

PUBLIC SERVICE CAMPAIGN FROM CISCRP

Everyday medical heroes: this glossy public service advertising campaign from the US celebrates ordinary people who take part in clinical research

A group of US researchers even ran a double blind, randomised controlled trial of glucosamine versus placebo almost entirely over the internet, using online self assessments of arthritic pain from participants.[7] The approach has yet to take on, but it has been explored by a few other groups.[8]

Public enthusiasm for data sharing and social networks has led some researchers to think about recruiting through these portals. In March this year, biopharmaceutical services company Quintiles, which carries out contract research for drug companies, announced that more than 2.5 million patients had joined its MediGuard website. The site offers members information on drug interactions and side effects but can also put them in contact with researchers.

After research suggested off-label use of lithium might slow progression of amyotrophic lateral sclerosis (ALS), members of commercial patient data sharing site PatientsLikeMe suggested reporting their experiences of experimentation with the drug. The site itself proposed more rigorous data gathering, leading to a study published earlier this year.[9]

Such approaches can make it easier for patients to be involved, said Jonathan Sheffield, chief executive of the National Institute for Health Research Clinical Research Network in England.

"We are very nervous about using social networking, but we have to think radically about how we deliver trials and make them convenient for patients, and also get them to be sharing in the whole process, so they become far less of a passive recipient of research and more of an active participant."

Researchers in Dundee and Edinburgh are beginning to set up a national register of people resident in Scotland who would be happy to be contacted about research studies, Dr Treweek said.

This would get around the thorny question of whether researchers should be able to look through patient records to find those who might be suitable for a trial, because individuals on the register would have already given their consent for this.

It might also help normalise the idea of research participation. After all, working on public knowledge and perceptions may be more important than adding a new recruitment technique.

"The challenge of patient recruitment has been around for 40 years. And every year there is some new flavour, some new technology, some new approach that everybody is heralding as the answer," said Mr Getz. "Now it is social media that is going to get all these new patients in our studies, or the use of demographic and psychographic databases. That all of these things are not really improving recruitment rates really tells us something."

Integration with clinical care

Mr Getz says CISCRP's aim is not to recruit more people to clinical trials. He says some of the people who see the advertisements, hear talks, or visit exhibitions put on by the organisation will decide not to take part in research they otherwise might have signed up for.

"We want people to self-advocate, we want them to be educated, we want them to engage their healthcare providers in helping them think through this profound decision."

But he adds, "Ultimately we do believe that a more informed and aware patient and public community is going to volunteer more frequently."

Dr Sheffield looks forward to a point when patients look to clinicians to tell them about research opportunities.

"The place where we need to be in the National Health Service is where patients ask their doctors what research they can be involved in," he said. "The way we get healthcare professionals involved in research is to get patients to ask them what research is available to them. Once we get patients thinking about how important research is to their condition, we can then achieve a really major culture change."

He also thinks research needs to be more integrated into the clinical pathway, and points to participation in cancer trials. The proportion of cancer patients in the UK joining clinical studies has risen in the past decade to around 1 in 6 of those diagnosed, from 1 in 26, according to the National Cancer Research Network. Dr Sheffield adds that this is a result of funding to make research part of a common process for people with cancer.

There is already movement towards this in the UK. This year, a government commissioned report by the Academy of Medical Sciences recommended cultural change to embed research as a core NHS function and easier access to patient data for researchers.[10]

Professor MacDonald argues that invitations to participate in research should be the rule, not the exception.

"I think there is a disconnect between the evidence for the drugs that we prescribe and their effectiveness in the real world, and the only way we are going to improve that process is by people accepting that part of the normal care in the NHS is to be part of the evaluation," he says.

He adds that getting research embedded into normal care may be the only way to cut costs enough to carry out more than just headline studies.

"People should allow their medical data to be anonymously analysed, and they should expect to be asked to be randomly allocated to a drug. If the ethics committees were not in equipoise they wouldn't let us do the trials," he adds.

"If some new drug comes out at £1000 (€1100; $1600) a month versus £30 a month or 25p a month, is it worth paying for? It might be, but we can't find out by any simple, reliable method in the setting of normal healthcare unless we can engage the public in these processes. It is probably something that the NHS at the highest level needs to embrace."

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