Towards
4+5
Research
Programme
Consortium

Ethical challenges in cluster randomised controlled trials

Experiences from public health interventions in Africa and Asia

Interventions that lead to improvements in public health affect groups of people, and one way to evaluate them is with cluster - or group - randomised controlled trials (RCT). Cluster RCTs are quantitative experiments in which groups, such as schools, villages, or districts are randomly assigned to receive an intervention. This contrasts with RCTs that were originally developed for testing the effectiveness of drugs or targeted interventions on specific individuals. The use of cluster RCTs to evaluate public health interventions is increasing, a predictable development given their importance as a source of evidence for health care.

RCTs present a number of ethical challenges for researchers. Members from the Towards 4+5 Research Programme Consortium have drawn on their experiences of conducting large-scale maternal and newborn health trials in South Asia and Africa to reflect on these issues. In particular, ethical challenges include: the need to reconcile individual autonomy with the common good, the problem of gaining consent on behalf of groups as well as individuals, the debates about benefits to control groups and standard of care, and the question of what happens when a trial ends. This briefing paper explores these challenges in more detail and describes some approaches that have been used to overcome them.

The ethics of public health research in low-income countries

Much of the emphasis in current research guidelines is on the protection of the individual: the Hippocratic obligation is to benefit the individual patient and the hallmarks of research ethics are consent to participation and the right to non-interference. This emphasis has arisen primarily as a result of historical tragedies in which investigators took advantage of vulnerable people. Topics of recent international controversy include the use of placebo control groups, testing interventions that were likely to be less effective than current 'best practice' and ensuring continued access to therapy when a trial ends.

Whilst this important debate has led to improvements in the way trials are managed and in procedures to make sure that participants understand their involvement clearly, it does focus on the individual, and this does not necessarily resonate with our experience of social life, the connectivity between people, and the need for public health to benefit the many. It is easy to see that trials of public health interventions involve a tension between the individual and 'the greater good'. The work of Towards4+5, for instance, aims to improve the experience and outcomes of maternity, and much of it involves testing the effects of community women's groups on health, care-seeking and survival. This requires testing strategies, through cluster RCTs, to improve quality and uptake of health care in contexts where best practice is far from a reality.

Ensuring both group and individual consent

Who should agree for a group of people to participate in a trial? Commonly, local guardians and representatives are chosen to give consent. To do so, they have to decide that participation is in the best interests of their community. In a complex and contested society, it is more difficult to identify individuals who speak for the many. For example, Nepal's Makwanpur women's group trial took place during a Maoist insurgency. When the legitimacy of both an existing government and an insurgent group are contested, deciding who can speak for local people is difficult. Likewise, in rural Malawi, the coexistence of traditional community structures and government representatives has to be taken into account. The best option seems to be

to cover as many bases as possible. For example, in Bangladesh researchers held meetings and took consent from community leaders, religious leaders, local chairmen, and elected administrative union heads.

Group consent is not a substitute for individual agreement. Community members need to be made aware of a trial and asked if they would like to participate. This is relatively straightforward if the intervention is 'opt-in'. It is not so simple if members of a community will receive an intervention whether they like it or not, for instance smoking bans and fluoridation of the water supply.

Timing of consent

Because of the scale of work, it is often easier to allocate clusters to the intervention and control groups before seeking consent. There are many precedents for this, but if possible agreement should be taken before allocation. This is also a way of making sure that community guardians understand the nature of the trial. People find it easy to understand the principles of randomisation if they are presented in everyday ways. For example, in the recent allocation process for a trial in rural Nepal, community leaders and government representatives were invited to a meeting for which a lottery machine had been hired. After a briefing and question-and-answer session about the trial, representatives were invited to spin the cage and select numbered balls representing the clusters.

Ethical approval

Two particular challenges to ethical approval are that it may not be easy to find an ethical committee that has a sufficient mandate for, or experience in, public health interventions, and that there is a blurred line between public health interventions and trials. Most ethical boards are used for trials conducted in hospitals. When a trial takes place in a sector with few precedents for ethical review, individuals within the system may not see it as necessary to apply for ethical approval, or to seek group or individual consent. For example, public sector health systems are used to introducing new procedures, but not necessarily to comparing their effects with control areas.

Benefits to control groups

What should be the standard of care for control groups in a public health intervention trial? If we genuinely do not know if a change in health services or community action will lead to better outcomes than the status quo, it seems reasonable for individuals in control groups to experience existing health care norms. However, the team believes in the maxim 'no survey without service', and control groups should receive reasonable benefits in terms of health system strengthening. In Bangladesh, for example, the implementors undertook training in maternal and newborn care for heath service providers and traditional birth attendants. Pregnant women were encouraged to use health facilities. And in Malawi, they undertook training in newborn care for health service providers and strengthening of the programme for prevention of mother-to-child transmission of HIV, through multiplier funding. There should also be a duty of care for participants in control clusters when data collection teams identify risks to their health.

Post-trial adoption

We consider cluster RCTs to be a first step in the roll-out of interventions that may benefit public health. An intervention is introduced in a limited number of groups, its effectiveness is evaluated and, if the trial suggests that it is effective, it is rolled out to the control groups, with modifications based on experience. If the trial shows no benefit, members of the public are protected from interventions that are unlikely to work. Participants should have the opportunity to access superior care if the trial shows that an intervention is effective, and communities involved in studies should benefit in the medium term.

Conclusions

Cluster RCTs of public health interventions in low-income countries have the potential to strengthen the evidence of effect before large-scale changes are made in health systems.

It is increasingly agreed that public health research has not delivered credible evidence as often as it could have. We should also consider the ethics of not doing research: good research tells us if things work – or if they do not – and ethics may be served equally by protecting people from exposure to costly but ineffective interventions. From the point of view of research, the RPC's multi-site exposure to ethical challenges and debate has led to a comprehensive understanding of the issues involved. Member teams are more fully aware of the pitfalls, and are often able to prevent problems before they arise.

This briefing paper is based on the following publication

- Osrin D, Azad K, Fernandez A, Manandhar D, Mwansambo C, Tripathy P, Costello A: Ethical challenges in cluster randomized controlled trials: experiences from public health interventions in Asia and Africa. Bull WHO 2009, 87:772-779.

About Towards 4+5

Towards 4+5 is a five year Research Programme Consortium on maternal and newborn health, funded by the Department for International Development (DFID), UK. The goal is to support evidence based policy and practice for maternal and newborn health to facilitate the achievement of the Millennium Development Goals 4 and 5. Research is concentrated in five developing countries. These are Bangladesh, Burkina Faso, Ghana, Malawi and Nepal. It focuses on ways to improve mother and infant care at both the facility and community levels.

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