Researchers' views on ethical challenges in healthcare cluster-randomized trials

Andrew McRae

Joseph L. Rotman Institute of Science and Values; Departments of Epidemiology & Biostatistics and Emergency Medicine.

Introduction

- Cluster-randomized trials (CRTs) commonly used in education, public health, healthcare and social sciences
- Groups of individuals randomly assigned to receive one of 2 (or more) comparator interventions
- Effect of interventions evaluated after collecting data from individual group members
- Ethics guidelines developed for oversight of research enrolling individual subjects
- Little specific guidance for ethical conduct of CRTs
- Lack of guidance may lead to variability in ethics reviews between jurisdictions and over time.

Objectives

- To document researchers' views on the ethical challenges associated with CRTs in practice
- To document researchers' experiences with the ethics review process for CRTs
- To elicit researchers' suggestions for ethics guidelines for CRTs

Methods

- Semi-structured interview with purposive sample of experienced healthcare and public health CRT esearchers
- Sample of 12-20 predicted to achieve data saturation
- Descriptive qualitative analysis of interview transcripts. 2 reviewers working independently
- Responses coded in thematic template that underwent iterative modification using Nvivo 8 software
- Final response thematic coding agreed upon by 2 reviewers.

Results

- 20 experienced CRT researchers (25 approached, 21 agreed, 1 excluded due to poor interview transcript quality)
- Informants from UK (8), Europe (2), US (6) and Canada (4)
- Principal investigator, co-investigator or statistician on 2-20 CRTs

Ethical Challenges in CRTs

1. *Informed Consent*

- Perceived variability in need for informed consent from individual cluster members. Need for consent may be related to the intervention being evaluated, whether it is applied at the group level, or directly to group members.

"The type of intervention that is being trialed is also of crucial importance. So, for example, whether...you are changing the way the entire service is delivered, or whether you are intervening at an individual level and you are just randomizing at a higher level for convenience. So it is about which level...is the intervention being targeted at..." (Primary care researcher, UK)

- Concern over the effect of obtaining informed consent on CRT validity, as obtaining consent may introduce bias on the part of the sample.

"One of the things I am concerned about is bias and if you get really informed consent from people in trials it results in either bias or contamination." (Statistician/Primary care researcher, UK)

2. Role and authority of the cluster gatekeeper or decision-maker

- The gatekeeper is a designated individual who gives permission for a group or cluster to be enrolled in a CRT. Challenges include:
- Identifying an appropriate gatekeeper for a particular group, such as a community, and dealing with groups that may have multiple legitimate gatekeepers.

"In some instances there really is no party to go to for permission when we are doing a community study for example and we are randomly assigning counties or cities. There really isn't anybody that gives permission for that kind of thing. Even in a city where there is a mayor, the mayor can't give permission for a city to participate in something, at least that has always been my view." (Public Health Researcher, US)

"First off you have to have the district agree that you can even work in this district. Then you have to get the principal to agree that they want to participate in the project. And then we had...a parent leader, so it may be a parent teacher organization leader, or in Chicago they used to have these local schools councils made up of parents, it would be the president of the local parent leadership group." (Public Health Researcher, US)

- What, precisely is the scope of the gatekeeper's authority? May they consent on behalf of individual cluster members?

"I think the main issues for me still stem around the issue of consent. Who makes consent? Whether consent needs to be achieved at every level of cluster or whether almost guardian consent is acceptable and that has been where the most discussion has happened really about in the ethical issues of cluster trials for me." (Primary care researcher, UK)

3. Risks and Potential Benefits

- Other than risks to individuals' privacy, informants did not perceive any risks to participation in a CRT.

"Risks were none. I think we came up with some for the ethics committee." (Primary Care Researcher, UK)

"I think the core risk is loss of privacy. That really is the only issue because we weren't studying...a therapeutic intervention...The intervention was to try to get physicians to use what is considered to be best practice." (Hospital Care/QI researcher, Canada)

Experiences with the Ethics Review Process

Variability in review findings over time and between jurisdictions.

"...generally it hasn't been too bad up until the last 5 years. Beforehand we were quite comfortably able to get ethics approval but it very much was a fudge... It was quite comfortable to get through ethics but it is different now" (Statistician/Primary Care Researcher, UK)

"cluster...trials of hospitals randomise independent institutions, each of which has an REB. Each REB, with its slightly different application procedures, forms and timelines has been a separate and trying process." (Primary Care Researcher, Canada)

Suggestions for Ethics Guidelines for CRTs

"There are issues which make cluster trials different to the sort of trials that review boards normally see and it would give me confidence as an investigator if I knew that they fully understood the difference." (Hospital/QI Researcher, UK)

"...Part of the trouble is that most of the thinking about ethics of clinical trials does stem from the very direct surgery or drug intervention on the individual and it's quite difficult for people to understand that you may not be intervening on [patients] the trial." (Primary Care Researcher, UK)

Conclusions

- Researchers vary in their views on their need for informed consent from cluster members. Most feel that the need for consent is related whether the intervention being evaluated is directed at the individual or cluster level.
- There is lack of clarity as to how the appropriate gatekeeper for a community should be identified, and what is the scope of that individual's authority
- Further reflection on the risks of participation in a CRT is required so that appropriate subject protections can be formulated
- Guidelines for the ethical conduct of CRTs may be useful in increasing uniformity of ethic review for CRTs.