CASE STUDY RESPONSES

Research ethics involves continuous learning

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The study poses two issues: How do we evaluate the ethical approaches of a study conducted many years ago when ethical guidelines were less clearly defined? Could the same study be conducted today?

I believe that it's important to examine the ethics of a study by examining the accepted practices that were in place when the study was conducted. Were the investigators acting in a manner consistent with the practices of the mid 1960s to the early 1970s? This was a time of an increasing awareness that research ethics needed to be more clearly defined, especially the rights of the study participants. Beecher had come out with his classic article (1); the Tuskegee study (2) had been recently uncovered; and the Helsinki Declaration (3) was being more widely circulated. Though the Nuremberg Code (4) had clearly spoken of the necessity of informed consent, this principle had not been put in place in most developing countries, especially where illiteracy was common and the study subjects were rural populations.

Most investigators felt that it was their duty to protect the subjects and it was almost an insult to suggest that they would do otherwise. They saw themselves as parents ("*in loco parentis*") to people who didn't have any real understanding of the scientific method and what was necessary to conduct a modern trial. That is not to say that they would take advantage of participants, but that they thought they knew what was best for them and others who might benefit from the results.

The actual study (5) began in Punjab in the mid-1960s and ended prematurely in the early 1970s, supposedly due to security reasons in the militarily sensitive area near the Pakistan border. Initiated at the request of the government of India's health and family planning officials, all policy was set in consultation with government authorities. The various studies involved multiple Indian institutions and one foreign institution. Communities made the final decisions about what could be implemented. In reviewing the study report, it is clear that the investigators were very concerned with the welfare of the communities in which they worked.

The overall goal of the project was the development of cost-effective affordable packages of integrated services for rural areas. New patterns of services had to be developed which would require different relationships within the health team; training objectives had to change with the added role of village level auxiliaries; and the community was called on to help develop solutions for their own problems.

Villagers were not necessarily required to participate but village leaders were supposed to encourage everyone to be part of the study. There is no evidence in the report that individual informed consent was taken. The report also does not discuss the reasoning behind the use of controls or the ethical dilemmas involved in having 10 villages act as controls. If you wanted to prove to the government and the world (especially the academic community) that an intervention worked, you had to try it against the current practice, which, in this case, was the government programme (the control group). The studies were conducted in Punjab, which at this time was undergoing profound changes in development and rapidly becoming a wealthy state by India's standards. The investigators felt that this rapid change alone might account for any improvements in the villages. This is another argument that might be given for using control villages.

Within this environment, what should have been expected of the investigators in terms of research ethics? Should they have told the control villages about the planned interventions (dietary supplements, infectious disease treatments, or a combination of the two) and then let them do whatever they wanted? If they really did not know that the supplement or knowledge of how to prepare and use it might improve the nutritional status of children, then it was reasonable to compare nutritional intervention with standard care. On the other hand, if earlier studies had clearly demonstrated that the same nutritional intervention or knowledge would significantly benefit children, then the investigators were obligated to inform the control villages. If that were done then the study would have focused their attention on the effect of health workers (one of the study objectives) rather than the intervention itself.

What did the investigators do in the control villages? They clearly state that if health workers found a child dying, going blind, or suffering from other illnesses that would leave permanent damages, the worker was instructed to call the doctor to start intensive care. Is this doing enough and if not what else could have been done? And what if the investigators did find significant difference between the groups before the study was completed? Were they prepared to measure this? Were they prepared to intervene in the control communities

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during or after the study was completed if the results showed significant improvement?

By the standards commonly used in its day, the study was conducted in an ethical and scientifically appropriate manner. In hindsight the investigators probably should have done more to protect the control communities by giving them greater access to relevant information during and after the study. It is now 40 years since this study was initiated and there have been changes in the world of research ethics. As research has become increasingly globalised, knowledge and awareness of ethical guidelines for research have become more widespread. At the same time differences remain in their interpretation and application. The golden rule of development and by extension research support still applies ("he who has the gold makes the rules"), but there is an increasing sensitivity to the importance of the context in which the research is being conducted.

Over the years, more attention has been paid to the process of informed consent with particular concern that it be appropriate to the population involved in the research. Informing without ensuring that participants understand the study is not the purpose of the process. Individual informed consent is required unless the investigator makes a very good case for why it could be deferred in a study.

The use of controls (persons or communities), where appropriate, is usually seen as the gold standard of study design. Results are clearer because bias is minimised. It may hasten the processes by which data are collected and analysed, which can be very important in evaluating life-saving interventions. The control community, however, should not be put at risk and the benefits of the intervention, if any, must be made accessible to them or there should be a plan to do so. But should we be examining other study designs which give us results that might not be quite as robust but which avoid some of the ethical conundrums that often plague community-based research? How often could the community act as its own control? How might historical data be better utilised? What level of difference are we looking for in two groups? Are we seeking a level that is statistically significant or one that is programmatically significant? They may be quite different.

The history of research ethics is one of continuous learning and growing. We should never feel satisfied that we now have all the answers. New challenges and new problems keep coming up. Forty years ago few would have predicted stem cells, cloning, or the development of the human genome. All these issues have raised new and challenging questions in research ethics. We must also be humble in our interpretation of the guidelines that now exist and realise that there are different and legitimate interpretations of some of the guidelines that are based on context, culture, and history. We need to avoid the tyranny of moral righteousness, which often creeps into our assessment of others. Our goal is both to protect the subject and community while allowing scientific study to move forward to answer the many questions that will help everyone attain better health.

References

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