**DISCUSSI0N**

## Research on public health interventions in poor countries

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In countries like India the researcher's responsibilities to research participants may sometimes come into conflict with the search for affordable drugs and therapies for problems of the poor. An on-going trial in Mumbai illustrates this situation, and is being presented here for discussion.

The trial evaluates the use of clinical breast examination (CBE) by trained health workers for breast cancer and visual screening of the cervix for cervical cancer. The control arm receives only health education messages - effectively a placebo. Both the Helsinki Declaration and the Indian Council of Medical Research's ethical guidelines state that placebos cannot be used when an effective intervention is available.

Dr Indraneel Mittra, surgeon at the Tata Memorial Hospital, Mumbai, is overseeing this trial. In October 2000, he was kind enough to describe the purpose of this study and its details. As the subject may deserve public discussion the following note has been prepared based primarily on notes from the interview with Dr Mittra. Detailed references supporting Dr Mittra's statements are not given here. The note is followed by some questions, and readers are invited to comment.

### Screening

The purpose of screening - going out into the community and inviting people to come in for testing - is to detect the problem early and thus to reduce mortality from the condition. A screening technique's value is based not only on whether it catches the problem early, or finds more cases through screening; it should also result in a reduction in the mortality rate from that condition.

However, mammogram screening for breast cancer has various problems. Because of false positives, false negatives (true for all screening techniques), over-diagnosis and unnecessary treatment of more relatively benign tumours identified by screening, many women would be subjected to psychological trauma and unnecessary treatment.

There is also the question of whether mammograms are cost-effective. It is believed that mammogram screening would be cost-effective only if it resulted in a 20 per cent drop in mortality from breast cancer. However, Dr Mittra stated, the results of various studies suggest that it can contribute to not more than a 10 per cent drop.

Even with this limited value, mammography cannot be considered for use as a screening tool in India. In addition to the problems posed by an anticipated increase in false positives given the lower estimated incidence of breast cancer here, mammogram screening would entail training radiologists, quality control, and a learning curve of 10 years before it could possibly become an effective tool.

Dr Mittra also implied that unlike in the West, mammograms are too expensive to be offered as part of a public health intervention. In India, he said, we need simpler screening methods. Elsewhere he has been quoted as saying about his trial of a cheaper screening method: "The studies are investigating appropriate diagnostic technologies that can be used on a mass scale in India… We're trying to show that low cost does not mean bad science." (1)

He also referred to a recent randomised clinical trial in Canada, comparing clinical breast examination (CBE) by nurses, with CBE plus mammograms. Researchers found no difference in death rate in the two groups. In other words, mammograms provided no additional benefit. (2)

### The trial

An ongoing trial conducted by Dr Mittra and funded by the US National Institutes of Health is evaluating the value of CBE as a screening tool. It is described in the press as one of 'the world's largest randomised control studies on early detection of common cancers among women.' (1) The participants are 150,000 women in 10 slum areas of Mumbai. Every 18 months over a period of six years, 75,000 women in the experimental group undergo CBE by trained health workers. They also receive health messages on the value of early detection, and dangers of tobacco. To make the trial more cost-effective, another component has been added: visual examination of the cervix with 4% acetic acid for early detection of changes in the form of white patches. The 75,000 women in the control group get only the health awareness messages.

One assumption behind this study design is that comparing CBE with mammograms would not permit effective evaluation of the cheaper and affordable screening techniques. It would not provide information on whether the cheaper screening technique would bring down the mortality rate due to the disease in question. Dr Mittra has stated, "We wish to validate low-cost, low-technology and simple preventive and diagnostic techniques for women's cancers in the most scientifically stringent way." (1)

### Ethical guidelines

International and national ethical guidelines on medical research do not permit the use of placebos in trials if an effective treatment exists. The earlier Helsinki Declaration already stated this. Following the controversy on placebo control trials to prevent the vertical transmission of HIV (3), revisions in October 2000 were even more explicit: experimental interventions were to be compared with the 'best proven' prophylactic, diagnostic

or therapeutic interventions. (4) The Indian Council of Medical Research recently finalised ethical guidelines on biomedical research. These guidelines do not address trials of such public health interventions. However, the section on drug trials does state that placebos cannot be used when an effective treatment is available. (5)

**Some questions**

It is true that 75,000 poor Indian women get some form of care. The other 75,000 are no worse off than they would have been otherwise. Perhaps they are better off, since they are educated on the dangers of tobacco and the importance of early detection. Does the fact that the participants would not otherwise have access to care justify such a study? The control group will be part of a research project but will be offered no diagnosis or treatment, though they are not prevented from seeking such services on their own. Is this justified? Mammography is accepted as the current standard of care, despite its many limitations. Even if it cannot be implemented as a screening technique in India, it can be provided to the control group. On the other hand, the results of the Indian trial could enable the medical community in India to decide whether CBE is an effective, affordable intervention. Providing mammogram screening to the control group will lower the quality of information from the study. Does the researcher's belief that the question is best answered only if one group receives no care justify the trial?

This study could not have been done in the West. Researchers in the Canadian study state that it was 'deemed unethical to have an unscreened control group'. (6) In the BMJ, Dr Mittra and his colleagues suggest that a trial in the West compare the two screening techniques against each other. "Proper information on which to base decisions, either about participating in a trial comparing CBE and mammography or for informing the development of a trial protocol, is essential for both the public and the profession. This could be achieved through a national questionnaire survey involving the eligible women." (7) Is it justified to conduct a study that could not have been conducted in the funding country (or others like it)?

It is unlikely that the cheaper technique will be implemented in a country where the public health system already deprives people of the most basic life-saving care. On the other hand, information gathered in India will certainly benefit screening programmes in the West. Should the fact that the results will not be implemented in the local community stop the researcher from undertaking what could be a very useful study?

If the intention is to provide services to the local community, once evidence emerged that the cheaper technique would work, could the researchers have focused on training health workers to do the screening well? Could they do this knowing that they cannot quantify the gains of such a technique?

A study of such complexity only underlines the need for voluntary informed consent, and this doesn't mean just signed forms. The participants are poor, already deprived of their right to accessible, affordable care, and any contact with a health worker is welcomed as providing some form of care. In such circumstances, how voluntary can their consent be? Second, how well could the concept of screening be explained to this particular group of women? Did they understand that some of them would get screening and others would get just health messages? Dr Mittra mentioned that about 20 per cent of the women approached refused to participate. However, it is possible that their refusal has nothing to do with their understanding of the trial. It would be interesting to learn whether and how the NIH ethics committee and the TMC ethics committee addressed such questions. Institutions conducting research would do well to make the deliberations of their ethics committees public.

**Why ask these questions?**

An earlier version of this note was circulated to the IME editorial group. The responses indicated that some of the questions raised were worth discussing. However, there was also some debate on the value of raising such questions. There may be more pressing concerns for groups such as ours than dissecting a study in which women are not actively harmed; they are only not offered care as part of the study. Does such questioning divert our energies from addressing blatant malpractice and corruption in the medical profession?

However, it was also felt that surely we must call upon medical researchers to reflect on the aspects of their work which go beyond its scientific elements, to explain it to the public, and to take active part in the debates on ethics.

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