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Three meetings and fewer funerals—misoprostol in postpartum haemorrhage

These traditional birth attendants (figure) are involved in a study investigating use of misoprostol to treat postpartum haemorrhage—poignantly, one of their daughters died because of postpartum haemorrhage a couple of years ago. WHO estimates that there are 14 million obstetric haemorrhages a year, and postpartum haemorrhage is the single most common cause of maternal death worldwide.[1] Over the past year, three important meetings have begun to confront this global problem.

In September, 2003, at its triennial meeting in Santiago, Chile, the International Federation of Obstetrics and Gynecology (FIGO) made postpartum haemorrhage its top priority. FIGO and the International Confederation of Midwives recommend active management during the third stage of labour, with uterotonics, cord traction, and fundal massage as the optimum ways to reduce postpartum haemorrhage. Most maternal deaths, however, occur in remote areas during home delivery when there is no trained birth attendant to implement active management of the third stage.[2]

Misoprostol is an E1 prostaglandin that stimulates uterine contractions, rapidly and powerfully. It has an excellent safety profile, is heat-stable, low-cost, and has been identified as an important technology for reducing maternal mortality in home births.[3] In Tanzania, traditional midwives are using 1000 μg misoprostol rectally to treat postpartum haemorrhage; in the Gambia, women are given 600 μg to prevent haemorrhage; and in an innovative study in Indonesia, parturient women self-administered misoprostol as soon as the baby was delivered.

Traditional birth attendants in western Tanzania

Experienced gynaecologists, trained midwives, traditional birth attendants, and illiterate village women are all enormously impressed by the rapid and consistent way in which misoprostol controls bleeding. One Tanzanian woman travelled 75 km because she learned that a traditional birth attendant had a drug to control bleeding, and another stole misoprostol tablets in an effort to protect herself at the next delivery.

Building on the FIGO leadership and ongoing research, the imperative to control postpartum haemorrhage has stimulated two more meetings, this time at a government level in east Africa. In Uganda, Jotham Musinguzi, Director of the Population Secretariat in the Ministry of Finance, Planning and Development, organised a meeting in Kampala, on the challenge of the prevention of maternal deaths in Uganda (May 18–19, 2004). In Kenya, Richard Muga, Director of the National Council for Population and Development, held a similar meeting in Nairobi (July 28, 2004). Uganda's regional meeting called for misoprostol to be made widely available in private pharmacies and the public sector, along with appropriate instructions: in the words of a resolution from the meeting, to "ensure that misoprostol is available to all pregnant women whose lives could be saved by using it". Kenya's meeting called for specific studies to guide policy on the use and availability of this drug.

The priority FIGO has given to postpartum haemorrhage, and the two governmental meetings in Africa highlighting the potential of misoprostol for women's health, are important partly because of the political nature of this drug. Misoprostol was originally marketed by Searle in 1987 for the treatment of gastric ulcers, but it is also the drug recommended by the US Food and Drug Administration for use with mifepristone for

medical abortion. Pfizer, who now owns the drug, has not endorsed obstetric and gynaecological uses, despite over 200 publications in peer-reviewed journals.[4] Even more difficult from the perspective of reducing maternal mortality is the fact that misoprostol is not even on the market in those parts of Africa where the largest number of deaths from postpartum haemorrhage occur. Fortunately, generic misoprostol is now manufactured in China, Taiwan, India, Egypt, Colombia, and Brazil, and efforts are now being made to facilitate a south-south trade in this life-saving drug.

African governments are painfully aware that it will be impossible to get anywhere near the Millennium Development Goal of reducing maternal mortality by 75% between 1990 and 2015 unless deaths from postpartum haemorrhage can be greatly reduced. Maternal deaths are highest where transport is most difficult, poverty most pervasive, and the status of women lowest. This is exactly where misoprostol can save the most lives. Had misoprostol been available a few years ago, the daughter of the midwife in the picture would probably still be alive and there would have been one less funeral in Africa.

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We are both involved in a trial of misoprostol in Tanzania. MC is founder of the not-for-profit Venture Strategies for Health and Development, which is supporting the trial. Our fee for writing this Comment will be donated to traditional birth attendants in Tanzania for aprons, delivery sheets, lanterns, and umbrellas.

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What should the burden of proof be for acceptance of a new breast-cancer screening technique?

Les Irwig and colleagues[1] recently did a systematic review of the literature assessing the accuracy of imaging modalities that might be used to replace or complement film mammography in population screening for breast cancer. They looked at four techniques: gadolinium-enhanced MRI, ultrasound, full-field digital mammography, and computer-assisted detection. Irwig and colleagues conclude that there is insufficient evidence to lend support to the adoption of any of these techniques for general screening. I agree; but given that there are trials underway to compare the accuracy of digital versus film mammography and to assess the value of screening ultrasound for women at high risk,[2] this conclusion could be premature. Irwig also advocates that after a cross-sectional comparison of a new technique with the standard screening test has shown benefit, further large randomised controlled trials should be done. Although this goal is laudable, it is neither practical nor realistic. The review stimulates examination of what is a reasonable burden of proof for implementing a new screening modality and whether we need to follow a "one size fits all" philosophy for screening.

Mammography screening has received unprecedented scrutiny. Subjected to extensive testing in randomised controlled trials, it has been assessed for survival and mortality as endpoints. To date, mammography is the only imaging screening technique shown to contribute to a reduction in mortality due to breast cancer.[3,4] Mammography has been validated in the research and clinical setting.[5] But today's mammography is far from perfect, both in its sensitivity and specificity, because of technological limitations and variability of skill in image interpretation. Moreover, some tumours are simply not visible on mammography. To improve breast-cancer detection we need information based on properties other than differences in X-ray absorption, such as tumour angiogenesis or physiological changes. Breast MRI, for example, can detect cancers that are occult on mammography (figure).

Are randomised controlled trials necessary to validate a new screening modality? These trials are very expensive, require tens of thousands of participants, and take many years to complete,

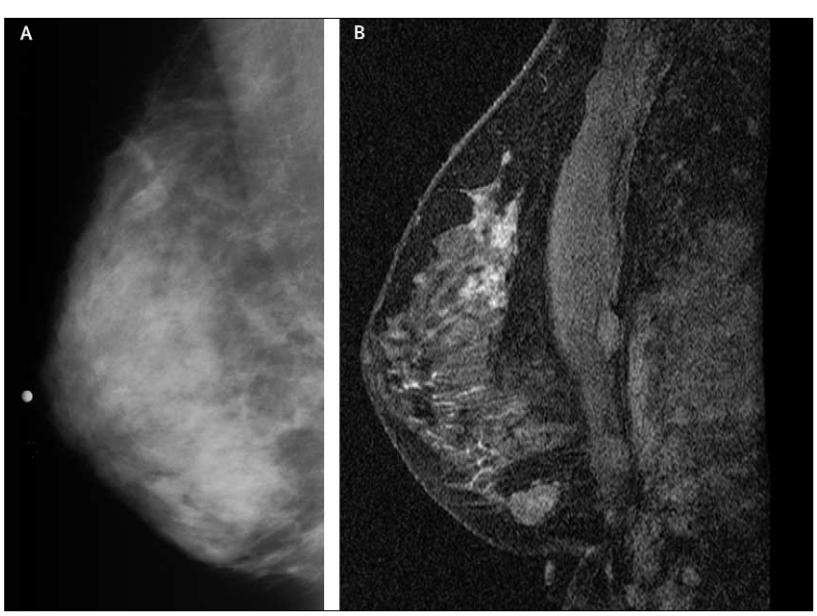

Figure: **Normal mammogram (A) with only a few scattered calcifications—inadequate evidence to initiate further investigation. On breast MRI (B), strong enhancement occurs due to angiogenesis from invasive ductal carcinoma**