Criticism of misguided Chu *et al.* article

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J R Soc Med 2012 105: 454
DOI: 10.1258/jrsm.2012.12k080

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Chu, Brhlikova and Pollock's article suggests the WHO rethink its decision to include misoprostol on the Essential Medicines List. Their paper is a sad example of workers in an elite setting advocating policies with the potential to endanger the lives of thousands of vulnerable women in low-resource settings.

The self-administration of misoprostol, or use by traditional birth attendants, is the most immediate and practical solution to help the least developed countries move towards achieving Millennium Development Goal 5.[1] It is true that in some studies oxytocin performs marginally better than misoprostol,[2] but as mentioned by Chu *et al.*, oxytocin administration is not currently feasible in most low-resource settings. Misoprostol presents an opportunity to achieve some semblance of health equity.[3]

The paper is also methodologically and ethically flawed. It reviews the 172 published papers on the use of misoprostol to control postpartum haemorrhage (PPH) in the framework of high-quality obstetric services and it explicitly omits studies that are not randomized controlled trials (RCTs). However, RCTs are often impossible to conduct in most low-resource settings where maternal death rates are highest. The paper by Prata *et al*[4]. included in the review, in fact, was not an RCT. In the case of misoprostol, an undisputed powerful uterotonic, the most practical RCT would compare misoprostol to a placebo, since the reality in low-resource settings leaves only these two options. Consequently, a RCT would randomly allocate the risk of death to women in the control arm when we know that misoprostol might have the potential to save their lives.

Since Chu *et al.* conducted their review; a RCT in Belgaum India found 400 μg sublingual misoprostol to be more effective than 10 IU intramuscular oxytocin, as measured by blood loss (mean blood loss 192 ± 124 mL with misoprostol and 366 ± 136 mL blood loss with oxytocin).[5] These data, together with compelling literature from non-RCTs in low-resource settings, strongly endorse the WHO's decision, which weighed all of the evidence, with considerations of the larger context and implications. A reversal of their decision would only hurt the very women that Chu *et al.* purport to be helping.

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Competing interests
None declared

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DOI: 10.1258/jrsm.2012.12k080

Rethinking WHO Guidance

I write due to concern that persons who wish to restrict misoprostol use, because of personal biases against termination of pregnancy, might attempt to use the article by Chu, Brhlikova, and Pollock to influence policy. The safety and efficacy of misoprostol has been demonstrated in hospital settings, and does not merit debate.

The authors review only four studies of misoprostol use in community and home births. Studies of community and home births are difficult, comparison with placebo is deemed unethical by many, and blinding of misoprostol use is essentially impossible due to the shivering. The one study, by Hoj, which utilized a placebo found a significant difference in severe blood loss, the outcome (other than death) which is most critical. The authors attempt to discredit studies due to exclusion of high risk patients. The exclusion criteria listed for the Mobeen study include planning not to deliver at the birth center, previous Cesarean section, and 'unlikely to deliver vaginally', conditions which would appropriately and ethically mandate referral for hospital delivery. The excluded women would be at increased risk of uterine rupture, which is not primarily treated with uterotonics. They note that Mobeen's study shows that PPH rates in both groups decreased as the study progressed, and hypothesized this was due to later-recruited midwives being more skilled. This supports the use of misoprostol by less-skilled birth attendants, rather than not using it at all, if one wants to decrease PPH.

Oxytocin alone does not always work, whether for induction of labor or prevention or treatment of hemorrhage. Those of us who attend births in the developed world often use misoprostol in addition to oxytocin. I would hate to have misoprostol withdrawn from my pharmacopeia in the USA. The issue is not whether WHO should keep misoprostol on the essential drug list, but rather who should be allowed access to misoprostol, which is an issue that each nation should decide, depending on its own national needs and priorities.

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Competing interests
None declared

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