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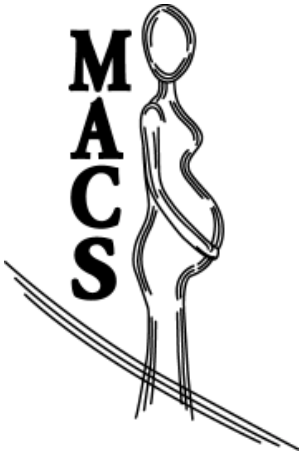

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Dear colleagues,

I want to take this opportunity to say hello and to talk about the recent randomized controlled trial of single vs. multiple courses of antenatal corticosteroids (ACS) published in JAMA.
(Guinn, Debra A., Atkinson, M. Wendy et al. Single vs weekly courses of antenatal corticosteroids for women at risk of preterm delivery: A randomized controlled trial. JAMA.2001;13:1581-1587.)

The authors of this paper stopped their study early before reaching its intended sample size and thus the study lacks power for finding clinically important reductions in adverse perinatal outcomes.

Despite the small number of women recruited in the Guinn study, we were very encouraged by the promising evidence suggesting benefit. The risk of the primary outcome, a composite measure of death or neonatal morbidity was significantly reduced in the weekly course group in the subgroup of infants most likely to benefit, that is those delivering between 24 and 27 weeks (RR [95%CI]: 0.80 [0.65, 0.98]), and there was a statistically significant reduction overall in the incidence of severe respiratory distress syndrome in the weekly course group (RR [95%CI]: 0.63 [0.44, 0.91]). We were also very reassured by the fact that the weekly course group did not result in a reduction in either birth weight, head circumference or gestational age at delivery, a concern that has come out of the animal research and the retrospective clinical studies.

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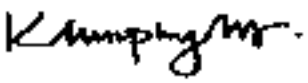
The authors have drawn heavily on their finding of a trend towards a higher risk of severe intraventricular hemorrhage in the weekly course group (RR [95%CI]: 3.80 [0.85, 17.45]) to suggest the possibility of harm. We believe that the likelihood that this difference is due to chance is high given the number of statistical tests undertaken. The authors also stress the evidence for harm found in the retrospective clinical studies but these are all seriously affected by selection bias which was the reason for needing an adequately sized randomized controlled trial in the first place.

It is thus with concern that we read the authors' interpretation of their study findings. Rather than declare that their study is too small to answer the question, they use their data to dismiss the potential for benefit and emphasize the possibility of harm, none of which is well supported by the study findings. If physicians and pregnant women were to accept the authors' interpretation of their findings, ethical concerns would stop the conduct of further randomised controlled trials of repeated courses of antenatal corticosteroids. This would be unfortunate as we might then miss the opportunity of finding that the results of the Guinn study were actually true – that is, that repeated courses of antenatal corticosteroids might reduce the risk of adverse perinatal outcome and death from 28.0% and 3.8% to 22.5% and 2.0% respectively. A potential benefit of this magnitude demands further study.

My hope is that you will find this letter to be helpful and that you find the JAMA article inspiring as it brings home the reason for why we are all working so hard to complete MACS. The true risks and benefits of multiple courses of ACS are not known, and will not be known until the results from MACS and the other large international trials are completed.

Thanks again for your support.



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