Authors' reply re: Antenatal magnesium sulphate for the prevention of cerebral palsy in infants born preterm: a double-blind, randomised, placebo-controlled, multi-centre trial. (Response to BJOG-20-0534)

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Letter to the Editor, BJOG Exchange

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[Authors' title] Time range for treatment with magnesium sulphate

We thank Larsen et al.[1] for their interest in our newly published randomised controlled trial on the use of magnesium sulphate ($MgSO_4$) for neuroprotection in preterm birth.[2] Larsen et al. argue that $MgSO_4$should only be offered to women in imminent preterm birth at gestational age (GA) below 32 weeks. Larsen et al. present the expected number needed to treat. These numbers are based on Danish data and may not be extrapolated to other countries.

Unlike the Cochrane review cited by Larsen et al.,[3] an updated meta-analysis, which included the results from our randomised controlled trial, demonstrated a significantly decreased risk of cerebral palsy (CP) in children exposed to antenatal $MgSO_4$ not only given before GA 28, but also before GA 32 weeks.[4] It seems likely that the lack of statistically significance at higher GAs is due to lack of power. Accordingly, the main reason for recommending treatment prior to GA 32 is the increasing number needed to treat with higher GA. This, together with the potential and known adverse effects of $MgSO_4$, must be weighed against the consequences of CP for the child, family and society.

Based on the current evidence, we agree that $MgSO_4$should be reserved for women in imminent preterm birth before GA 32 weeks due to the lower frequency of CP with higher GA. This recommendation may, however, be revised when results of future studies are ready, in particular from the ongoing randomised controlled trial in women at imminent risk for preterm delivery at GA 30 to 34 weeks.[5]

With regard to the lower limit for GA, the studies in our meta-analysis only contain few, if any, infants born before GA 24 weeks. If the foetus is considered viable and the woman is offered antenatal steroids for fetal lung-maturation, it could be argued that $MgSO_4$should also be an option despite the lack of scientific evidence. Due to the expected higher rate of CP in infants born prior to GA 24 weeks and anticipation of

a similar effect of $MgSO_4$ as that seen at higher GA, the number needed to treat will most likely be lower than for infants born at a higher GA.

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1. Larsen M, Krebs L, Rackauskaite G, Hoei-Hansen C, Greisen G. Re: Antenatal magnesium sulphate for the prevention of cerebral palsy in infants born preterm: a double-blind, randomised, placebo-controlled, multi-centre trial. (First comment letter, reference to be added).

2. Wolf HT, Brok J, Henriksen TB, Greisen G, Salvig JD, Pryds O, et al. Antenatal magnesium sulphate for the prevention of cerebral palsy in infants born preterm: a double-blind, randomised, placebo-controlled, multi-centre trial. BJOG. 2020 Apr 1. doi: 10.1111/1471-0528.16239. [Epub ahead of print]

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4. Wolf HT, Huusom LD, Henriksen TB, Hegaard HK, Brok J, Pinborg A. Magnesium sulphate for foetal neuroprotection at imminent risk for preterm delivery: a systematic review with meta-analysis and trial sequential analysis. BJOG. 2020 Mar 31. doi: 10.1111/1471-0528.16238. [Epub ahead of print]

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