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► To cite this version:

Elsa Lorthe, Mathilde Quere, Gilles Kayem. Prolonged latency after preterm premature rupture of membranes: an independent risk factor for neonatal sepsis?. *American Journal of Obstetrics and Gynecology*, 2017, 216 (1), pp.84. 10.1016/j.ajog.2016.08.022 . hal-01688574

HAL Id: hal-01688574

<https://hal.sorbonne-universite.fr/hal-01688574>

Submitted on 19 Jan 2018

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Title: Prolonged latency after preterm premature rupture of membranes: an independent risk factor for neonatal sepsis?

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Disclosure statement: The authors report no conflict of interest.

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Word count: 253

Dear editor,

We read with great interest the article by Drassinower et al who investigated the impact of prolonged latency after preterm premature rupture of membranes (PPROM) on neonatal sepsis.(1) The main finding highlights that, for a given gestational age at PPRM, prolonged latency does not increase the risk of neonatal sepsis, except for latencies over 4 weeks associated with reduced risk of sepsis. As rightly underlined by the authors, this result makes sense as the most stable cases of PPRM with the longest latency durations are probably those with the lowest risks of choriomnionitis and neonatal sepsis.

However we would like to raise some key points. First, the primary outcome included both early and late-onset sepsis. This definition seems inappropriate as late-onset sepsis mostly result from pathogens horizontally transmitted after birth,(2) thus do not reflect intra-uterine inflammation. Second, cases of stillbirths and neonatal deaths were not taken into consideration while potentially linked to severe prenatal or postnatal infection. This can lead to underestimate adverse effects of prolonged latency, especially for ruptures at 22 to 24 weeks of gestation that were included in the trial.(3) Third, in the multivariable model, adjustment for both latency and time-dependant covariates (e.g. multiple courses of steroids), may have introduced overadjustment bias.(4) We would also have appreciated to be able to interpret global p-values for each covariate included in the multivariable model.

Such results are likely to greatly impact daily practice, obstetric management and counselling of women with PPRM. Further analyses addressing the previous issues are therefore needed.

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