Jim Thornton's prediction of the EPPPIC study's result (#13413)

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1) Have any data been collected for this study already?
It's complicated. We have already collected some data but explain in Question 8 why readers may consider this a valid pre-registration nevertheless.

2) What's the main question being asked or hypothesis being tested in this study?
Does progestagen treatment reduce adverse fetal outcomes in premature labour?
Protocol registered here. http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017068299
EPPPIC website here. https://www.york.ac.uk/crd/research/epppic/

3) Describe the key dependent variable(s) specifying how they will be measured.
Fetal/infant death (fetal death occurring at any point after trial entry, stillbirth or death of live born infant before hospital discharge following birth, or to 28 days, whichever is longer) Preterm birth or fetal death (<37, < 34, <28 weeks)

4) How many and which conditions will participants be assigned to?
Progestagen. Placebo or no treatment

5) Specify exactly which analyses you will conduct to examine the main question/hypothesis.
Analyses will evaluate overall effectiveness of main and additional outcomes on an intention to treat basis, that is, participants will be analysed according to allocated treatment, irrespective of whether the treatment was received.
Parallel but separate analyses focusing on singleton, twin and triplet pregnancies will be undertaken.

Dichotomous outcomes will be analysed by calculating the risk ratio for the effect of progestogen compared to the control treatment (placebo or usual care). Odds ratios may be used where risk ratios cannot be computed. For continuous outcomes, mean differences between treatment arms will be reported. Hazard ratios will be calculated for time-to-event outcomes. The IPD will be synthesised across trials using meta-analysis. Both 'two-stage' models (where effect estimates are calculated for each trial, and subsequently pooled in a meta-analysis) and 'one-stage' models (where all IPD from all trials are analyzed in one step, taking account of clustering within trials) will be used.

6) Describe exactly how outliers will be defined and handled, and your precise rule(s) for excluding observations.
No exclusions

7) How many observations will be collected or what will determine sample size? No need to justify decision, but be precise about exactly how the number will be determined.
65% of trials, including 80% of trial participants have been collected.

8) Anything else you would like to pre-register? (e.g., secondary analyses, variables collected for exploratory purposes, unusual analyses planned?)
I have no involvement in EPPPIC. In fact I was specifically asked to remove myself from the study group because of my previously expressed strong opinion that progestagens were ineffective for this indication. Although I have of course seen the published versions of the various trials, I have seen no individual trial data and no analyses from EPPPIC.

I predict that progestagens will not reduce fetal mortality. .

If however, they turn out to be effective in one or more subgroups I will believe this result. I would not advocate their use on the basis of such evidence, but would support further trials to test such EPPPIC generated hypotheses.