Jim Thornton's prediction of the PHOENIX trial results. (#18336)

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Created: 01/05/2019 03:09 AM (PT)
Public: 01/05/2019 03:13 AM (PT)

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?
The PHOENIX trial is testing the hypothesis that for women with pre-eclampsia between 34+0 and 36+6 weeks, expectant management reduces adverse outcomes compared with delivery within 48 hours.

3) Describe the key dependent variable(s) specifying how they will be measured.
Primary short term maternal outcome: Composite of maternal morbidity of fullPIERS outcomes with the addition of recorded systolic blood pressure ≥160 mmHg (with or without medication) post randomisation.

Primary short term perinatal outcome: Composite of perinatal deaths (antenatal/intrapartum stillbirths and deaths
within 7 days of delivery but not deaths due to congenital anomalies) or NNU admissions (physical separation of baby from the mother) prior to infant hospital discharge.

Primary long term infant outcome: PARCA-R Parent Report Composite score for neurodevelopment at two years of age corrected for prematurity

4) How many and which conditions will participants be assigned to?
Planned immediate delivery (typically by induction with prostaglandins, or by Caesarean section if induction contra-indicated) undertaken as soon as feasible (up to 48 hours) after randomisation
Expectant management of pregnancy, as indicated by the NICE guidelines and delivery at 37 weeks of gestation or sooner as clinical needs dictate.

5) Specify exactly which analyses you will conduct to examine the main question/hypothesis.
There is an analysis plan and I'm happy to trust the trial statistician to follow it.

6) Describe exactly how outliers will be defined and handled, and your precise rule(s) for excluding observations.
Analysis will be by intention to treat.

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.
900 women. 450 per group.

8) Anything else you would like to pre-register? (e.g., secondary analyses, variables collected for exploratory purposes, unusual analyses planned?)
Trial recruitment is complete and final outcome data entry is ongoing. The database has not yet been locked. I am a clinician in one of the participating centres and have recruited a small number of participants. However, I do not, and have never had, any access to trial outcomes by group, so these predictions are data independent.

My predictions are as follows:
1. The primary maternal outcome will favour immediate delivery. This will be statistically significant at the P<0.05 level. However after exclusion of the component "recorded systolic blood pressure ≥160 mmHg" from the primary maternal composite outcome the difference will no longer be nominally significant. I appreciate that this could be judged a data driven analysis, which is why I am registering my prediction here.
2. The primary short term baby outcome will favour expectant management. This will be statistically significant at the P<0.05 level.
3. The primary long term baby outcome (PARCA-R at 2 years) will not show any statistically significant difference (at the 5% level) between the groups. However I predict that the point estimates for those measures which had been predefined in the analysis plan e.g. mean or median scores, or rates of scores below various cut offs, will all favour expectant management.

There is one final issue I wish to register prior to seeing the data.
Three of the of the secondary baby outcomes are:
1. Customised/population birth weight centile. 2. Birth weight <10th customised/population centile 3. Birth weight <3rd customised/population centile
I can see no justification for customised/population centiles. If the authors, or others, seek to favour early delivery on the grounds that fewer baby's birth weights are below specified centiles I will request further analyses using a birth weight centile standard. e.g. the Intergrowth-21 or WHO standards.