Jim Thornton's prediction of the CSTICH trial result. (#13267)

Author(s)

Jim Thornton (University of Nottingham) - jim.thornton@nottingham.ac.uk

Created: 08/10/2018 01:03 AM (PT)

Public: 08/16/2018 07:27 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?

C-STICH trial registered here. http://www.isrctn.com/ISRCTN15373349

Trial is testing the hypothesis that monfilament nylon sutures reduce pregnancy loss compared with conventional baided cerclage sutures.

3) Describe the key dependent variable(s) specifying how they will be measured.

Pregnancy loss rate (i.e. miscarriage and perinatal mortality, defined as any stillbirth or neonatal death in the first week of life), collected from the medical records at 7 days after delivery

4) How many and which conditions will participants be assigned to?

1. monofilament suture   2. Braided suture

5) Specify exactly which analyses you will conduct to examine the main question/hypothesis.

A log-binomial regression model to calculate the relative risk and 95% confidence of the primary outcome (pregnancy loss defined as miscarriage or perinatal mortality). Minimisation variables (see section 5.1) will be included in the model as covariates. The statistical significance of the treatment group variable will be determined by an associated chi-squared test. Minimisation variables are:

Indication for the cerclage (history / ultrasound), thus:

▢ A history of three or more previous midterm losses or premature births (≤ 28 weeks), OR

▢ Insertion of cervical sutures in previous pregnancies, OR

▢ A history of mid trimester loss or premature birth with a (current) shortened (≤ 25 mm) cervix, OR

▢ Women whom clinicians deem to be at risk of preterm birth either by history or the results of an ultrasound scan.

▢ Technique planned (with or without bladder dissection)

▢ Intention to commence patient on progesterone (yes / no)

▢ Randomising centre

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

Analysis 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.

Original sample size was 900 total. 450 per group. This was increased to 2,050, 1,025 per group, on advice of independent DMEC, because pooled event rate was lower than expected.

8) Anything else you would like to pre-register? (e.g., secondary analyses, variables collected for exploratory purposes, unusual analyses planned?)

C-STICH data are about half collected. It is also an open trial. However, I'm making this prediction without any knowledge of the interim results. The code has not been broken, and I'm not involved in the trial anyway.

My prediction is that the result will be negative. i.e. that the point estimate for any beneficial effect from monofilament will be smaller that the predefined delta, i.e. any improvement in live birth will be smaller than a relative risk reduction of 41%.

I also predict that the statistical significance level of the primary analysis will be greater than 0.05.

If my prediction above is wrong, I will believe the result and encourage the use of monofilament sutures for this clinical indication.

The reason I predict the result will be negative, is that although I accept the theory that germs can live in the braided suture, I also believe that monofilament sutures are more likely to spontaneously come untied, or cut through the cervix. Hence a net "no effect".