Supplementary File 2: Additional Methodological Details

BAYESIAN PRIORS

Rationale for Choosing a Variety of Priors

In a Bayesian analysis, the prior belief (prior probability) about the treatment effect must be specified. In the absence of existing evidence (e.g., meta-analysis and literature) to inform the priors, the priors must be derived from expert consensus and beliefs, which may be subjective because such beliefs are influenced by and specific to a given investigator and may not be accepted by anyone else.(1) Historically, this was a point of major criticism against Bayesianism, but it no longer needs to be because this can be overcome by choosing a variety of prior probabilities in an attempt to approximate the posterior distribution held by all types of readers. In fact, regulators have accepted this approach, and this is no longer a stumbling block to using Bayesian methods.(1)

Probability of Achieving Various Treatment Effects

To aid in understanding the strength of the enthusiasm or scepticism represented by each of our predefined priors, we computed the probability that a person holding this level of belief (about the treatment effect) would observe positional therapy (PT) achieving an average gain in customised birthweight centile (CBWC) greater than 0%, 5%, and 10% compared to sham-PT on the probability scale.

Furthermore, to aid the interpretation of prior and posterior probabilistic summaries of treatment efficacies, we provided the following probability perception scale: “unlikely” indicates a probability ranging between 0 and 0.5; “probable” indicates a probability

ranging between 0.5 and 0.8; “highly probable” indicates a probability ranging between 0.8 and 0.95; and “almost certain” indicates a probability ranging between 0.95 and 1.00.(2)

Strongly Enthusiastic Prior

For our strongly enthusiastic (SE) prior (μ=9.0; σ=3.9; N(9,3.9)), the probability that a person holding this level of belief (about the treatment effect) would observe PT achieving an average gain in CBWC of greater than 0%, 5%, and 10% compared to sham-PT was almost certain (P(treatment effect>0%) = 0.9894919), highly probable (P(treatment effect>5%) = 0.8474696), and unlikely (P(treatment effect>10%) = 0.398817), respectively, on the probability scale. Assuming the minimum clinically important difference (MCID) was selected as a 5% gain in CBWC, note that other investigators typically use a more enthusiastic prior than we selected and typically aim for a 95% probability of observing a treatment effect as large or larger than the selected MCID,(3) whereas the prior probability of observing PT achieving that MCID with our SE prior is 0.85.

Moderately Enthusiastic Prior

For our moderately enthusiastic (ME) prior (μ=7.0; σ=4.9; N(7,4.9)), the probability that a person holding this level of belief (about the treatment effect) would observe PT achieving an average gain in CBWC of greater than 0%, 5%, and 10% compared to sham-PT was highly probable (P(treatment effect>0%) = 0.9234363), probable (P(treatment effect>5%) = 0.6584231), and unlikely (P(treatment effect>10%) = 0.2701879), respectively, on the probability scale.

45 Non-Informative Prior

46 For our non-informative (NI) prior (μ=0; σ=10; N(0,10)), the probability that a person
47 holding this level of belief (about the treatment effect) would observe PT achieving an
48 average gain in CBWC of greater than 0%, 5%, and 10% compared to sham-PT was
49 unlikely (P(treatment effect>0%) = 0.5), unlikely (P(treatment effect>5%) = 0.3085375),
50 and unlikely (P(treatment effect>10%) = 0.1586553), respectively, on the probability
51 scale.

52 Moderately Sceptical Prior

53 For our moderately sceptical (MS) prior, (μ=0; σ=3.9; N(0,3.9)), the probability that a
54 person holding this level of belief (about the treatment effect) would observe PT
55 achieving an average gain in CBWC of greater than 0%, 5%, and 10% compared to
56 sham-PT was unlikely (P(treatment effect>0%) = 0.5), unlikely (P(treatment effect>5%)
57 = 0.09991233), and unlikely (P(treatment effect>10%) = 0.005172149), respectively, on
58 the probability scale.

59 Strongly Sceptical Prior

60 For our strongly sceptical (SS) prior, (μ=0; σ=2.55; N(0,2.55)), the probability that a
61 person holding this level of belief (about the treatment effect) would observe PT
62 achieving an average gain in CBWC of greater than 0%, 5%, and 10% compared to
63 sham-PT was unlikely (P(treatment effect>0%) = 0.5), unlikely (P(treatment effect>5%)
64 = 0.02495209), and unlikely (P(treatment effect>10%) = 0.00004398719), respectively,
65 on the probability scale. Note that if the MCID was selected as a 5% gain in CBWC, the
66 prior probability of observing a treatment effect as large or larger than this MCID is

0.025 (or 2.5%) on the probability scale, which somewhat matches with the level of confidence utilized in p-value metrics for hypothesis testing. In other words, with our SS prior, there is a 97.5% chance of not observing an MCID of a 5% or greater gain in CBWC. (PT or sham-PT).

BAYESIAN MODEL

We completed a Bayesian simple linear regression using a two-sample model:

$$\mu_i = \beta_0 + \beta_1 x_i$$

Where μ is the mean GROW v.8.0.6.2 calculator CBWC, xi = 0 for the PT group, and xi=1 for the sham-PT group. Therefore, for the PT group, μi = β0 (the intercept), and for the sham-PT group, μi = β0+β1.

The CBWC (GROW v.8.0.6.2 calculator) was regressed on the intervention (PT or sham-PT). Our Bayesian regression model is specified as:

$$y_i \mid \mu_i, \sigma^2, \sim \mathrm{N}(\mu_i, \sigma^2) \text{ where } \mu_i = \beta_0 + \beta_1 x_i.$$

N() is used to denote the normal density function. The prior distributions of these regression parameters, β_0 , β_1 and σ^2, are specified as follows,

$\beta_0 \sim N(\mu = 0, \sigma^2 = 100)$, $\beta_1 \sim N(\mu = 0, \sigma^2 = 10)$, and $\sigma \sim StudentT(\nu = 3, \mu = 0, \sigma = 10)$.

MINIMUM CLINICALLY IMPORTANT DIFFERENCE

We used a range of thresholds for the minimum clinically important difference (MCID) for two reasons. First, we included an MCID of a >0% increase in CBWC with PT compared to sham-PT because this is analogous to the GPT investigators' original frequentist analysis where the null hypothesis was that the mean CBWC of the PT and sham-PT groups were equal and no MCID was specified. Second, we included two additional arbitrary MCID's (>5%, and >10%) because professional societies have not yet agreed upon an MCID in this context as it is difficult to quantify due to the complex interplay between foetal size, growth velocity, and gestational age.

That said, Agarwal, Hugh, and Gardosi have shown that the closer a foetus is to the lower extreme of growth, the more consequential even small changes in CBWC are vis-a-vis stillbirth risk.(4) For example, at 37 weeks' gestation, they demonstrated that a foetus with a CBWC <3rd centile has a two fold risk of stillbirth compared to one with a CBWC in the 3rd to <10th centile range and a five-fold risk of stillbirth compared to one with a CBWC in the normal (10th to 90th centile) range. That said, we acknowledge that arguments could be made to support MCID's in addition to those we chose.

REFERENCES

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