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Maternal positional therapy for fetal growth and customised birth weight centile benefit in a Bayesian reanalysis of a double-blind, sham-controlled, randomised clinical trial

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ABSTRACT

Objectives To update the Ghana PrenaBelt Trial's (GPT) primary outcome data with the latest fetal growth standard and reanalyse it. To estimate the posterior probability, under various clinically relevant prior probabilities, of maternal nightly positional therapy (PT) throughout the third-trimester having a beneficial effect on customised birth weight centile (CBWC) using Bayesian analyses.

Design A reanalysis of a double-blind, sham-controlled, randomised clinical trial.

Setting A single, tertiary-level centre in Accra, Ghana.

Participants Two-hundred participants entered, 181 completed and 167 were included in the final analysis. Participants were Ghanaian, healthy, aged 18–35 years, with low-risk, singleton pregnancies in their third-trimester, with Body Mass Index<35 kg/m^2 at the first antenatal appointment for the index pregnancy and without known fetal abnormalities, pregnancy complications or medical conditions complicating sleep.

Interventions Participants were randomised to receive treatment with either a PT or sham-PT device.

Primary and secondary outcome measures The primary outcome was the CBWC using the latest Perinatal Institute, Gestation-Related Optimal Weight calculator. Using Bayesian methods, posterior probabilities of achieving a greater than 0%, 5% and 10% benefit in CBWC with PT were estimated. There was no secondary outcome.

Results The median (IQR) CBWC was 42% (15–71) and 28% (9–52) in the PT and sham-PT groups, respectively (difference 8.4%; 95% CI −0.30 to 18.2; p=0.06). For achieving a >0%, >5% and >10% gain in CBWC with PT, the posterior probabilities were highly probable, probable and unlikely, respectively, given a range of prior probabilities reflecting varying degrees of pre-existing enthusiasm and scepticism.

Conclusions Maternal nightly PT throughout the third-trimester did not have a statistically significant effect on CBWC on a frequentist analysis using the latest fetal growth standard. However, from a Bayesian analysis, clinicians can infer that PT is likely to benefit fetal growth but with a modest effect size.

Trial registration number NCT02379728.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A reanalysis of a double-blind, sham-controlled, randomised clinical trial.
⇒ Used the latest Gestation-Related Optimal Weight standard to update the primary outcome using country-of-origin ethnicity coefficients and repeated the original frequentist analysis.
⇒ Completed a Bayesian analysis of the primary outcome, incorporating data from a recent meta-analysis and a range of representative clinical prior beliefs ranging from enthusiasm to scepticism, allowing for more meaningful interpretation of the trial results.
⇒ Results may not be generalisable to pregnancies with medical or pregnancy complications, non-Ghanaian ethnicity or living in other parts of the world.
⇒ All analyses were post hoc, so the results should be interpreted with caution.

INTRODUCTION

Background

The Russo–Williamson thesis states that a causal hypothesis can be established only by using both statistical evidence and evidence of mechanism.[1] In recent years, evidence of mechanism between maternal supine sleeping position after 28 weeks gestation, fetal growth restriction and late stillbirth has been mounting.[2–14] Biological plausibility likely stems from aortocaval compression in the supine position and resultant deleterious changes in maternal and fetal haemodynamics as well as the effect of the supine position on maternal respiratory parameters during pregnancy. Regarding statistical evidence, Owusu *et al* were the first to find an association between supine sleep and low birth weight, and hypothesised that this association may mediate the relationship between

supine sleep and stillbirth.[15] Several other case–control studies have been performed[16–20] culminating in two individual participant data (IPD) meta-analyses that showed the supine going-to-sleep position, when adopted after 28 weeks of pregnancy, is associated with giving birth to a small-for-gestational-age infant and/or having a stillbirth.[21 22] In 2021, the Royal College of Obstetricians and Gynaecologists with the National Institute for Health and Care Excellence analysed this evidence[23] and incorporated sleeping position recommendations into their antenatal care guideline.[24] Clinical standards have also been rewritten in Australia to include advice to settle to sleep on the side in pregnancy starting at 28 weeks.[25]

In 2013, the authors (JC, AK and JW) developed and tested a positional therapy (PT) device to minimise time spent sleeping in the supine position in pregnancy.[26–28] The device does not prevent the user from lying supine during sleep, but it has been shown to cause a significant reduction in the amount of time spent sleeping supine without demonstrable impact on sleep quantity or quality.[26 27] The Ghana PrenaBelt Trial (GPT),[28] was a double-blind, randomised, sham-controlled trial conducted by the authors (JC and AK) to investigate whether nightly use of this PT device by a group of healthy pregnant participants during sleep in the home setting throughout the third-trimester of pregnancy affected birth weight and customised birth weight centile (CBWC) when compared with a similar group who used a sham-PT device. The original publication of the GPT is open access and can be found online.[28]

In the GPT, the CBWC was calculated using the Gestation-Related Optimal Weight (GROW) standard by Gardosi *et al* (Perinatal Institute and Gestation Network, Birmingham, UK).[29 30] When the original GPT analysis was completed, the ethnicity coefficient used by the GROW calculator (V.6.7.8.1)[31] was a regional coefficient ('West African') because, at that time, country-of-origin specific coefficients for ethnicity were not available; however, since the GPT was published, the GROW calculator was updated (now version 8.0.6.2)[32] and now includes country-of-origin specific coefficients for ethnicity, including 'Ghanaian', which is the ethnicity of the GPT sample. Given the important contribution of maternal ethnicity to fetal growth,[33–35] the authors of this study contacted the GROW team about this update and were advised that the GPT CBWCs should be recomputed with the latest GROW calculator using country-of-origin ethnicity coefficients and reanalysed, which relates to the first objective of this study.

The authors of the GPT used a traditional frequentist analysis and were unable to reject the null hypothesis of no treatment effect of PT (on birth weight or CBWC) because the p-value for each of these outcomes (0.14 and 0.11, respectively) was greater than the commonly accepted cut-off of 0.05.[36] In the biomedical literature, trials analysed under the frequentist paradigm with p-values>0.05 are often labelled as 'negative'.[37 38] While this serves as the function of preventing future and futile investigations of completely ineffective interventions, it could also mean that the trial has low power against an important effect size. This often perpetuates the belief that the treatment under consideration is ineffective or does not work.[39] However, Bayesian analyses have been used on several such 'negative' studies since the early 2000s, which have clarified the results of clinical trials and conveyed more relevant and meaningful information to clinicians.[40 41] Furthermore, even in the frequentist paradigm, it is not uncommon to reanalyse results with updated methodologies (eg, adjusted analyses) and data sets, especially in the context of meta-analyses and for the results of these reanalyses to change clinical practice.[42 43] Here lies the second objective of this study.

See online supplemental file 1 for additional background information.

Objectives

Primarily, to recompute the CBWC values in the GPT using the updated GROW calculator (V.8.0.6.2) and repeat the frequentist analysis employed in the GPT to determine the effect, on CBWC, of use of PT during sleep in the home setting throughout the third-trimester of pregnancy in comparison with sham-PT. Secondarily, to make more clinically relevant use of the GPT data by performing a Bayesian reanalysis of the updated GPT CBWC data. Specifically, to determine the probability of PT benefiting the CBWC by achieving >0%, >5% and >10% improvement in comparison to sham-PT when used during sleep in the home setting throughout the third-trimester of pregnancy. These objectives were previously unplanned for the GPT.

METHODS

Trial design

This study is a reanalysis of the GPT, which was a single-centre, double-blind, randomised (one-to-one), sham-controlled, clinical trial conducted between September 2015 and March 2016.[28]

Patient and public involvement

Patients and the public were not involved in the development of the research question or outcome measures, nor in the design, recruitment, or conduct of the study.

Participants

The GPT recruited participants from antenatal care clinics at the Korle Bu Teaching Hospital (KBTH)—see the original GPT publication (open access) for full details regarding the study setting, eligibility criteria and number of trial participants assessed for eligibility, recruited, randomised and analysed.[28] The GPT was approved and monitored by the Ghana Food and Drugs Authority (Accra, Ghana; Clinical Trial Certificate FDA/CT/152).

Interventions

Each participant was instructed to use their assigned device (PT or sham-PT) every night from approximately

28 weeks' gestation through birth. The PT device was worn at the level of the waist and had two back pockets each containing two rigid, hollow, polyethylene balls held securely in place by a foam insert. The theoretical mechanism of the PT device is based on the tennis-ball technique of PT, which is a common treatment to reduce snoring in sleep medicine.[44] When supine, the balls apply pressure points across the user's lower back, prompting them to reposition themself in a lateral position to maintain comfort. The sham-PT device was identical in appearance, materials and construction to the PT device, but had soft foam balls instead of firm plastic balls and did not have foam inserts. See the original GPT publication for further details regarding the recruitment and follow-up processes.[28]

Outcomes

The primary outcomes for the GPT were birth weight (grams) and CBWC (%). To address the objectives of this study, we recompute and reanalyse only the CBWC in the frequentist paradigm because only the CBWC is affected by the new GROW calculator, and the birth weight values (and analysis) from the GPT are unchanged. In the Bayesian framework, we analyse only the CBWC because the CBWC, owing to its incorporation of the six main non-pathological factors impacting birth weight, is a much more accurate proxy for fetal growth in comparison to birth weight. For a full description of how the measurements composing the CBWC were taken in the GPT, including the study personnel responsible for collecting them, see the original publication.[28]

Sample size

The target sample size of the GPT was 200 participants (100 per group), which accounted for an expected 20%–30% lost-to-follow-up rate and assumed a 300 g difference in birth weight between the PT and sham-PT groups (with pooled SD of 643 g), power (β) 0.80, and type I error probability (α) of 0.05.[28]

Randomisation

Randomisation to either the PT or sham-PT group in the GPT included allocation concealment and followed a one-to-one, simple randomisation scheme.[28]

Blinding

Participants in the GPT remained blinded to the allocation until after study completion. Efforts to ensure that each participant did not know what the alternate device looked or felt like included conducting separate introduction sessions for each group and ensuring no balls or foam inserts were in the device (so it was configured neither as a PT nor sham-PT device) during demonstrations.

Statistical methods

In the GPT, all data were double-entered from scanned PDFs into Microsoft Excel and double-entry checked prior to the final analysis.[28] These data were provided by the principal investigator of the original study (JC). Analyses (below) were performed using the psych, nortest, bmrs, tidyverse and magrittr packages in the R statistical software package (V.4.2.2) and Bayesian inference was conducted using Stan probabilistic programming language via brms in R. The brms uses Stan and employs the Hamiltonian Monte Carlo algorithm to conduct Markov chain Monte Carlo (MCMC) sampling.[45] We used standard, validated, off-the-shelf, open-access MCMC software (ie, Stan) to ensure reproducibility of our study results.

Frequentist methods

We used the same data set and completed the same analysis (difference testing via Wilcoxon rank sum test) as in the original GPT, using the CBCW values from the GROW V.6.7.8.1 calculator, which specified the ethnicity coefficient as West African, and then repeated the same analysis using the GROW V.8.0.6.2 calculator and specifying the ethnicity coefficient as Ghanaian.

Bayesian methods

Bayesian methods focus on providing plausible values for the treatment effect that are compatible with both the observed data and prior knowledge or beliefs.[46] To guide statistical inference, Bayesian analysis enables the use of both non-informative (NI) priors that minimise the influence of priors on the statistical inference, and informative priors that are guided by existing evidence (eg, meta-analysis and literature) or a range of collective expertise from investigators regarding the belief or scepticism regarding treatment efficacy. Under the Bayesian framework, the posterior probabilistic summary of treatment efficacy (also known as an updated belief of treatment efficacy) is obtained by combining the prior beliefs (ie, prior probability distribution of the treatment effect parameter) and the observed data (ie, the likelihood distribution of the data specified with the treatment effect parameter). Thus, a Bayesian analysis of trials can leverage background information allowing the quantification of this information as priors to aid the interpretation of the trial results. Bayesian analyses are particularly appealing and beneficial when the study is underpowered, with a small sample size, through the incorporation of clinically relevant priors to improve estimation precision. See online supplemental file 2 for more details.

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.[47]

Prior probabilities

The prior beliefs about the plausible range of values of the effect of PT on CBCW are represented by a probability density distribution ('prior probability')—see figure 1. The wider (more variance) this distribution, the

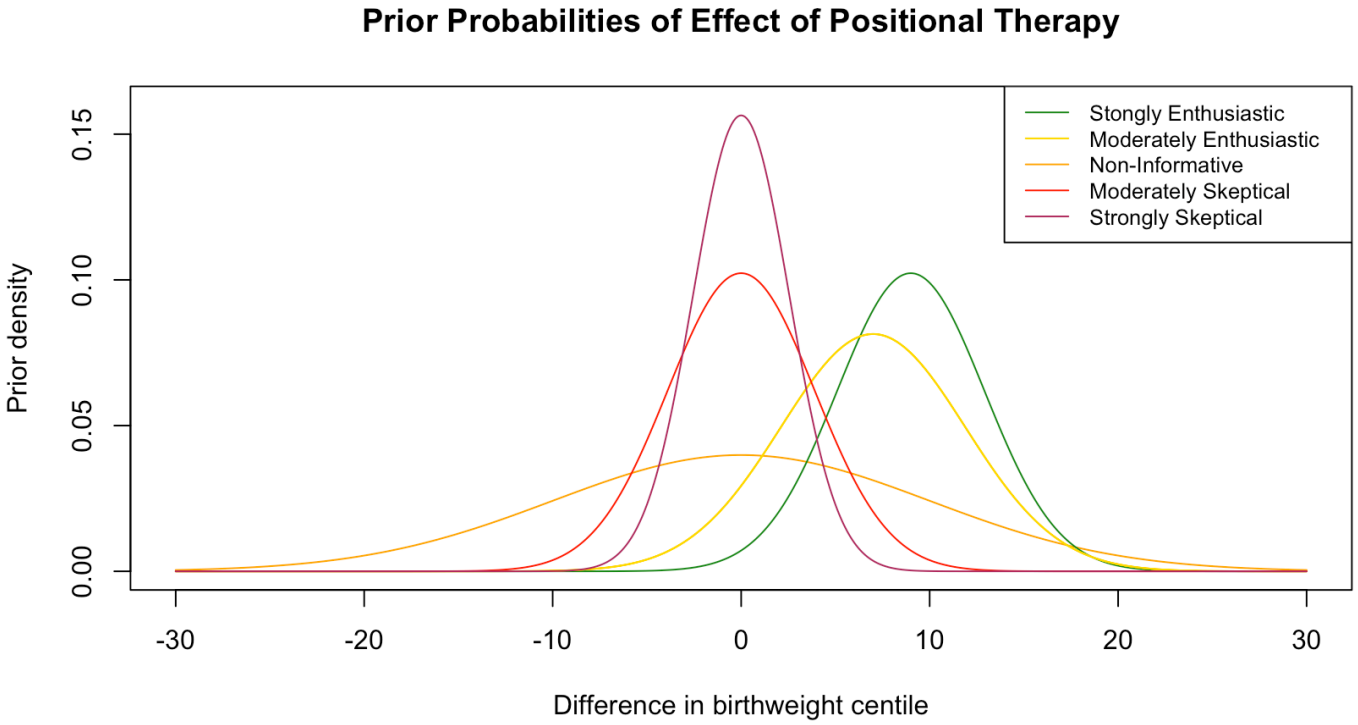

Figure 1 Probability density distributions of a range of priors selected in an effort to match the spectrum of belief in the clinical community about the plausible range of values for the treatment effect of PT on CBWC compared with sham-PT when used nightly across the third-trimester of pregnancy. CBWC, customised birth weight centile; PT, positional therapy.

less certainty about the treatment effect and the narrower (less variance) this distribution, the more certainty about the treatment effect. The area under the distribution and to the right of any given CBWC value is the probability that the treatment effect is greater than that value. To develop each statistical prior for this analysis, we used normal probability distribution defined by two values. The first value was the median gain in CBWC, μ, on which we centred the distribution, which reflects the value for the treatment effect that an enthusiast or a sceptic would assume to have a 50% probability of obtaining. The second value was the width of the distribution defined by a SD, σ, which reflects the magnitude of uncertainty about the plausible range of values for treatment effect.

Five priors were defined to typify varying degrees of enthusiasm and scepticism for the benefit of PT on CBWC consistent with pre-existing controversy in the literature about the association between supine sleeping position and adverse pregnancy outcomes.[23 48–51] These five archetypal beliefs are strongly enthusiastic (SE), moderately enthusiastic (ME), NI, moderately sceptical (MS) and strongly sceptical (SS), are depicted graphically via probability density distributions in figure 1, and were derived as follows.

Strongly enthusiastic prior

For our SE prior, we derived μ and σ from a recent IPD meta-analysis of four case–control studies, which included n=1760 participants.[22] For n=57 participants whose going-to-sleep position in the third-trimester was supine, their infant's mean (SE) CBWC was 40.7% (7.6). For n=1703 participants whose going-to-sleep position in the third-trimester was non-supine, their infant's mean (SE) CBWC was 49.7% (6.7). Comparing these two groups, the adjusted mean difference in CBWC was 9.0 (95% CI: 1.4 to 16.6). Therefore, we set μ=9.0 for our SE prior, and using the 95% CI, we derived σ to be 3.9 assuming a normal distribution. In summary, our SE prior favours a positive treatment effect of a 9% gain in CBWC with PT, and there is some uncertainty in this belief but not enough to make the 95% CI of the treatment effect cross zero.

Finally, to aid in understanding the strength of the enthusiasm or scepticism represented by the SE prior, we computed the probability that a person holding this level of belief (about the treatment effect) would observe PT achieving an average gain in CBWC greater than 0%, 5% and 10% compared with sham-PT on the probability scale. See online supplemental file 2 for these computations for the SE prior and each of the following priors.

Moderately enthusiastic prior

For our ME prior, we derived μ and σ from the original published GPT results in which the mean difference in CBWC between the PT and sham-PT groups was 7.0 (95% CI: −2 to 17). Therefore, we set μ=7.0 for our ME prior, and using the 95% CI, we derived σ to be 4.9 assuming a normal distribution. In summary, our ME prior favours a positive treatment effect of a 7% gain in CBWC with PT, but there is more uncertainty in this belief as this distribution is wider than our SE prior and the 95% CI of the treatment effect crosses zero.

Non-informative prior

A NI prior, tantamount to keeping an 'open mind', has little influence on the posterior distribution because it regards all possible treatment effect values to be equally likely. With an NI prior, minimal information is added to the study data in the Bayesian analysis, and the resulting posterior distribution is essentially dependent on the study data alone.[52] For our NI prior, we set μ=0 and σ=10, reflecting ignorance about the treatment effect of PT and sham-PT. As such, the 95% CI of our NI prior spanned −19.6 to +19.6. At this width, the level of uncertainty of our NI prior was more than double the uncertainty of our next most uncertain prior (ME prior, σ=4.9). In summary, being centred at 0%, our NI prior does not favour any treatment effect and there is much uncertainty in this belief as this distribution is very wide relative to our other priors.

Moderately sceptical prior

For our MS prior, we set μ=0, which does not favour a treatment effect, and σ=3.9, which just happens to be the same uncertainty level as our SE prior. The choice of σ was based on the notion that for a person who is MS, the width of the MS prior distribution should be set such that there is an approximate 10% probability of achieving a treatment effect as large or larger than the minimum clinically important difference (MCID), which we chose as a 5% gain in CBWC for the purposes of defining our priors—see online supplemental file 2. In summary, being centred at 0%, our MS prior does not favour any treatment effect and there is some uncertainty in this belief (the same level of uncertainty as in our SE prior).

Strongly sceptical prior

For our SS prior, we also set μ=0, which does not favour a treatment effect, but we reduced the width (uncertainty) of the distribution by setting σ=2.55. This time, the choice of σ was based on the notion that for a person who is strongly sceptical, the width of the SS prior distribution should be set such that there is very small probability (2.5% or less) of achieving a treatment effect as large or larger than the MCID. In summary, being centred at 0%, our SS prior does not favour any treatment effect and there is little uncertainty in this belief (this is our narrowest prior), reflecting that the sceptic is very confident that his/her belief that PT has no treatment effect is correct.

Posterior probabilities

MCMC modelling (with four chains, 5000 iterations burn-in and 5000 saved iterations per chain; see the Stan Reference Manual[45] for full details of the implementation and configuration of the MCMC algorithm) was used to fit Bayesian generalised linear models to derive estimates of the treatment effect and 95% credible intervals (CrI's) from the median 2.5th and 97.5th percentiles of each posterior distribution. Note that the 95% CrI is the interval that has a 95% probability of containing the true treatment effect.[53] Each of the prior distributions was updated by the study data (CBWC values from the GROW V.8.0.6.2 calculator) to estimate the posterior probabilities that the treatment effect of PT, in comparison to sham-PT, exceeds a range of thresholds for the MCID, namely, a >0%, >5% and >10% centile increase in the CBWC. In the Bayesian regression analysis, NI priors (ie, N(0,100) and Student-t(0,10, df=3)), were used for nuisance parameters including the regression intercept term and the variance term as these parameters do not quantify treatment effectiveness. Convergence of the Bayesian estimation is examined using trace plots and the R-hat convergence index (a cut-off of 1.01).[54]

RESULTS

Of two-hundred and seventy-six participants assessed for eligibility, 200 were recruited, and 167 (n=83 in the PT group, and n=84 in the sham-PT group) were included in the final analysis of the CBWC. See the original GPT publication for full details on excluded participants and sample characteristics.[28]

Frequentist analysis of customised birth weight centile

For the frequentist analysis of difference in CBWC between the PT and sham-PT groups with the GROW V.6.7.8.1 calculator and specifying the ethnicity coefficient as West African, we arrived at the same results presented in the GPT (see table 1). Repeating the same analysis with values from the GROW V.8.0.6.2 calculator and specifying the ethnicity as Ghanaian gave a similar result and the p-value (0.06) associated with the difference was close to what many frequentists would consider statistically significant. Note that while table 1 presents the unadjusted difference, the GROW centile is already

Table 1 Frequentist analysis of customised birth weight centile in the GPT

	Positional therapy (n=83)	Sham positional therapy (n=84)	Treatment—Sham difference (95% CI)	P value
GROW v6.7.8.1 centile (%)	43 (18 to 67)	31 (14 to 58)	6.8* (−1.7 to 16.6)	0.11
GROW v8.0.6.2 centile (%)	42 (15 to 71)	28 (9 to 52)	8.4* (−0.3 to 18.2)	0.06

Variables are non-normally distributed and presented as median (IQR).
*Wilcoxon rank sum test.
GPT, Ghana PrenaBelt Trial; GROW, Gestation-Related Optimal Weight.

Table 2 Bayesian analysis of customised birth weight centile in the GPT

	Probability of gain in CBCW						
	>0%		>5%		>10%		
Prior belief	Prior	Posterior	Prior	Posterior	Prior	Posterior	95% CrI of treatment effect
SE	0.99	1.00	0.85	0.91	0.40	0.37	3.0–15.0
ME	0.92	0.99	0.66	0.82	0.27	0.29	1.3–14.8
NI	0.50	0.96	0.31	0.70	0.16	0.27	7.4–15.7
MS	0.50	0.88	0.10	0.33	0.01	0.02	−2.4–9.5
SS	0.50	0.81	0.025	0.09	0.00	0.00	−2.4–6.4

Cells are colour-coded according to the previously defined probability perception scale. Red indicates unlikely. Orange indicates probable. Yellow indicates highly probable. Green indicates almost certain.
CBWC, customised birth weight centile; CrI, credible interval; ME, moderately enthusiastic; MS, moderately skeptical;; NI, non-informative; SE, strongly enthusiastic; SS, strongly skeptical.

adjusted for the six main non-pathological affecting birth weight.

Bayesian reanalysis of customised birth weight centile

For the Bayesian reanalysis of the GPT data, the effect of PT (in comparison to sham-PT) on CBWC per the GROW standard (V.8.0.6.2) was computed under varying levels of enthusiasm and scepticism (see table 2). In table 2, for three levels of gain in CBWC (>0%, >5% and>10%), each prior probability for each predefined level of prior belief (SE, ME, NI, MS and SS) from online supplemental file 2 can be compared with its corresponding posterior probability so one can appreciate how the prior belief and GPT data influence the posterior probability. For example, considering the SE prior, when its prior probabilities of achieving a >0%, >5% and >10% gain in CBWC (0.99 (almost certain), 0.85 (highly probable) and 0.40 (unlikely), respectively, see online supplemental file 2) are combined with the GPT data, the posterior probabilities are 1.00 (almost certain), 0.91 (almost certain) and 0.37 (unlikely), respectively. The estimated 95% credible interval of the treatment effect of PT on CBWC under the posterior probability resulting from combining the GPT data with the SE prior was a gain of 3%–15% in CBWC. In summary, with maternal nightly PT from 28 weeks' gestation to birth, there is a highly probable (from the sceptics) to almost certain (from the NI and enthusiasts) benefit of >0% gain in CBCW; an unlikely (from the sceptics) to highly probable (from the enthusiasts) benefit of >5% gain in CBWC and an unlikely (from everyone) benefit of >10% in CBWC. That is, maternal nightly PT from 28 weeks' gestation to birth is likely to benefit CBWC, but the effect size is considered to be reasonably modest.

The results in table 2 are represented graphically in figure 2. While table 2 presents the posterior probabilities at three discrete thresholds of gain in CBCW with PT (>0%, >5% and >10%), figure 2 shows the distributions of the prior probabilities (darker shade) and posterior probabilities (lighter shade) for all thresholds. For ease of reference, the 0%, 5% and 10% thresholds are indicated by blue, purple and pink vertical dashed lines, respectively. The probability of PT conferring a gain in CBWC more than a given threshold is the area to the right of the threshold and under the posterior probability distribution curve. Furthermore, basic probability rules can be used to work out the probability of PT not attaining any given threshold for gain in CBWC, which is also just the area to the left of the threshold and under the posterior probability distribution curve. Note that after combining the prior probabilities with the GPT data, regardless of the level of enthusiasm or scepticism regarding the plausible range of the treatment effect of PT, all the posterior probability distributions became taller, narrower and moved to the right in comparison with their corresponding prior probability distribution. For all of the resulting posterior probability distributions, the bulk of the areas under the curve lie to the right of the zero percentile line, which indicates that PT, when used during sleep nightly from 28 weeks gestation through birth, benefits (results in a gain) the CBWC in comparison to sham-PT under the levels of enthusiasm and scepticism that we specified. Even with the SS prior, PT is more likely to result in a gain in CBWC (probability=0.81; see table 2) than a loss (probability=1.0–0.81 = 0.19). For an SE, ME and NI prior, it can also be stated that the probability of PT resulting in more than a five percentile gain in CBWC (probability 0.91, 0.82 and 0.70, respectively; see table 2) is greater than the probability of it not doing so (0.09, 0.18 and 0.30, respectively) since the majority of the areas under the curve for these posterior probability distributions lie to the right of the fifth percentile line.

DISCUSSION

On a frequentist analysis, using the latest GROW calculator (V.8.0.6.2) to calculate the CBWC in the GPT, we failed to reject the null hypothesis (p-value 0.06) that nightly maternal PT to minimise supine sleeping time from 28 weeks through birth does not have an effect on CBWC compared with sham-PT. See online supplemental

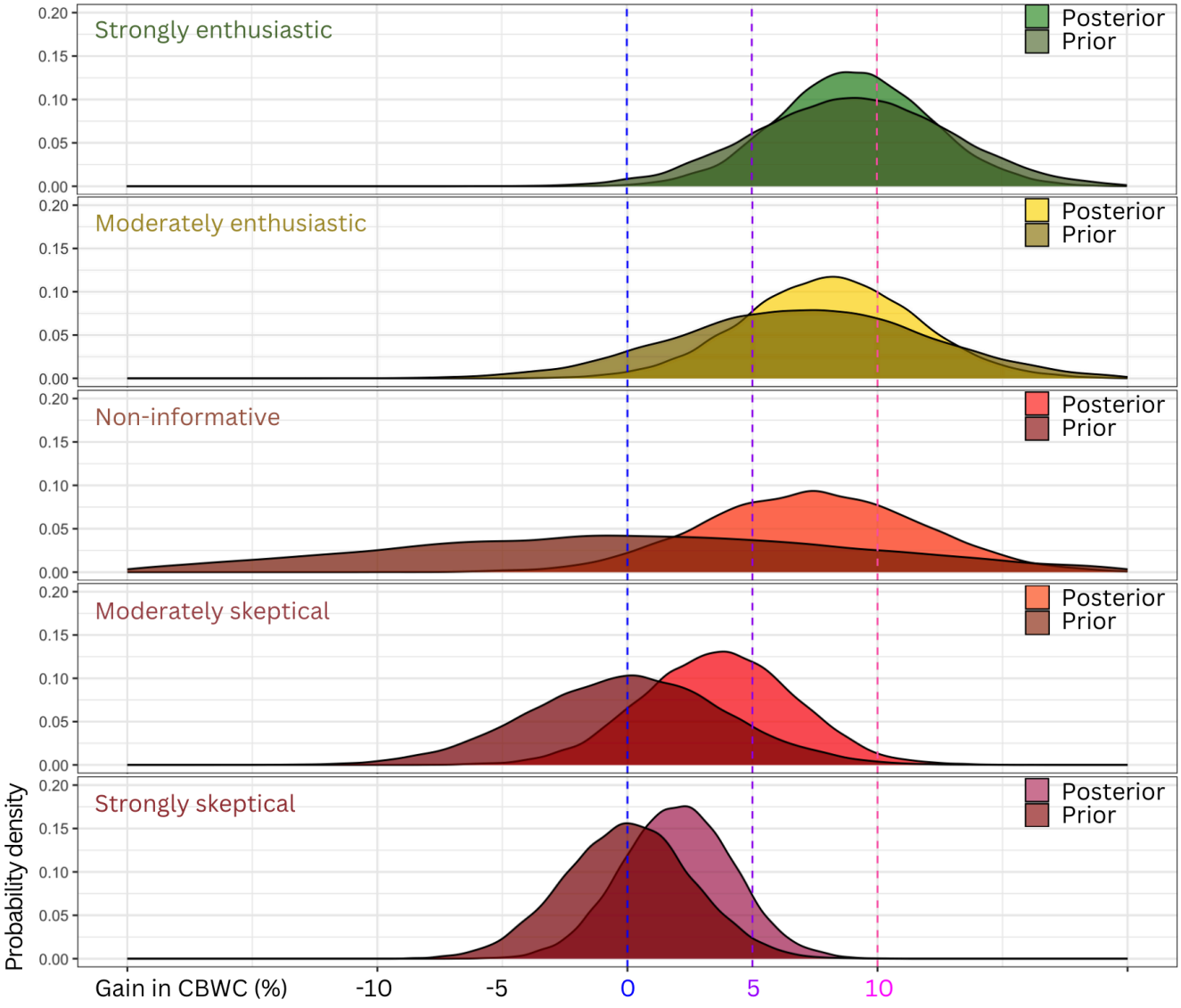

Figure 2 Probability density curves for prior and posterior probabilities for five levels of enthusiasm and scepticism regarding the plausible range of values for the treatment effect of positional therapy on customised birth weight centile compared with sham-positional therapy when used nightly across the third-trimester of pregnancy. Blue, purple and pink vertical dashed lines show the 0%, 5% and 10% thresholds for gain in customised birth weight centile.

file 3 for additional discussion. In summary, within the frequentist framework, we are unable to draw definitive conclusions, including disproving our null hypothesis, about the treatment effect of PT on CBWC based on the GPT results because the 95% CI of the mean difference in treatment effect includes clinically important values, which implies a lack of sensitivity (underpowered).

Approaching the data from a different analytical paradigm (Bayesian), however, indicates that there is a high probability that nightly maternal PT, compared with sham-PT, during sleep throughout the third-trimester confers a significant benefit to fetal growth, even for the sceptic. Bayesian analyses make more efficient use of the available data and present results in more clinically relevant format, telling clinicians the information that they want to know when making clinical decisions, namely, the direct probability of clinically important benefits. A clinician who is strongly sceptical about PT may be interested to know that PT is more likely to result in a gain in CBWC than to result in a loss—a probability of 0.81 (highly probable) to be exact. A more enthusiastic clinician, such as one with knowledge of Anderson *et al*'s IPD meta-analysis of sleeping position and fetal growth (the only such study to date),[22] may wish to update their knowledge with new information from the GPT via our Bayesian analysis. Combination of Anderson *et al*'s data with data from the GPT did not attenuate the treatment effect but, rather, confirmed a beneficial effect with less uncertainty (see taller and narrower posterior probability curve in figure 2). Such a clinician may be interested to know that there is a 95% probability that PT will benefit CBWC between 3% and 15% (95% credible interval).

They may also be interested in knowing that the probability of PT effecting at least a 5% and 10% gain in CBWC is 0.91 (highly probable) and 0.37 (unlikely), respectively. Similarly, a clinician without any prior knowledge in this domain (NI) may be interested to know that the probability of PT effecting any gain and at least a 5% gain in CBWC is 0.96 (almost certain) and 0.70 (probable), respectively. Given the relatively low probability of harm from PT, evidence of benefit for the CBWC may justify its use in clinical practice.

Limitations

First, it must be stated that limitations of this analysis include those inherent in the original GPT.[28] This includes lack of video-confirmation of sleeping position; lack of objective measurements of sleep architecture; reliance on participants' self-reported adherence to device (PT or sham-PT) use; informing participants' of the link between supine sleeping position, stillbirth and low birth weight as part of the informed consent process; the possibility that some participants may have become unblinded if they came into contact with a participant in the alternative and sought to compare their devices and limited generalisability to healthy pregnancies in Ghana. Furthermore, the average self-reported nightly adherence to device use, 56%, was lower than expected, which may have diluted the treatment effect.

Given that the present analysis was unplanned and post-hoc, the results must be interpreted with caution.[55] The original GPT publication had two primary outcomes: birth weight and CBWC. One factor that provides some protection against erroneous conclusions is that the present analysis tested the same hypothesis and the same primary endpoint (CBWC) as the original trial; however, we did not analyse the raw birth weight, so conclusions regarding the effect of PT on raw birth weight cannot be made. The reason the CBWC was chosen for reanalysis is two-fold. First, CBWC is more reflective of fetal growth than birth weight alone because it accounts for the six main non-pathological factors affecting growth,[29] which raw birth weight alone does not account for. For example, a 2500 g infant born at 35 weeks gestation may be normally grown, whereas a 2500 g infant born at 39 weeks gestation would be severely underweight. Second, the original analysis of birth weight from the GPT under the frequentist paradigm is unchanged because raw birth weight is not affected by the updated ethnicity coefficients in the GROW CBWC calculator.

To demonstrate how inferences from a Bayesian analysis of a trial can combine information from the trial with information external to the trial, we reanalysed the GPT data using a prior probability distribution of the estimated treatment effect of PT on CBWC derived from an earlier IPD meta-analysis of sleeping position by Anderson *et al* (see 'SE prior' in 'Methods' section).[22] One limitation is that the data composing the meta-analysis are from case–control studies, not interventional trials of PT. Another limitation is that the participant samples of the four studies included in the meta-analysis are different from the participant sample in the GPT. See online supplemental file 3 for more details.

CONCLUSIONS

A frequentist analysis of CBWCs (updated per the latest version of the GROW calculator) from the GPT does not show a statistically significant treatment effect (p=0.06) of nightly PT compared with sham-PT from 28 weeks gestation through birth. A Bayesian reanalysis of the GPT data enabled a more flexible and clinically relevant interpretation of the trial data. Using the data at hand, including a previous meta-analysis and the GPT data, we were able to report the probabilities of a range of beneficial treatment effects of PT on CBWC across a menu of prior beliefs, from enthusiasm to scepticism, reflecting the current range of controversy around the importance of sleeping position in pregnancy. Using Bayesian inference, we showed that nightly PT from 28 weeks gestation through birth is highly probable or almost certain to benefit CBWC compared with sham-PT.

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Contributors JC, AJK and JW conceived the Bayesian reanalysis of the GPT. AJK and SG recomputed the customised birth weight centiles using the GROW V.8.0.6.2 calculator with updated ethnicity coefficients. AJK wrote the R code to analyse the study data under the frequentist and Bayesian paradigms under the supervision of KL. AJK drafted and revised this manuscript and is guarantor. JC, SG, JW, SRH and KL made intellectual contributions to this manuscript.

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