Supplementary File 1: Additional Background Information

EVIDENCE OF MECHANISM

In recent years, evidence of mechanism between maternal supine sleeping position after 28 weeks gestation, foetal growth restriction, and late stillbirth has been mounting.(1–13) For example, Couper et al., using advanced magnetic resonance imaging techniques, demonstrated that in healthy pregnancies, the maternal supine position results in a 23.7% reduction in total internal iliac artery blood flow, a 6.2% reduction in oxygen delivery to the foetus, and an 11% reduction in foetal umbilical venous blood flow compared to the lateral position.(3) Based on the first of these three findings, a simple calculation can be performed to demonstrate that, from 28 through 40 weeks' gestation, if two hours per day were spent supine,(14–22) assuming an average of 500 ml/min of maternal blood going to the uterus and 80% of this going to the placenta,(23) the intervillous space (maternal side) of the placenta would experience a cumulative 1,000 litre deficit.

Furthermore, in the supine position, maternal respiratory parameters are affected. Because of increased abdominal pressure when supine, the functional residual capacity of the lungs decreases, the alveolar-arterial oxygen difference increases, and lung compliance decreases.(24–26) Studies have also shown deeper maternal oxygen desaturations, higher apnea-hypopnea index, higher 3% oxygen desaturation index, and higher respiratory disturbance index when sleeping supine in pregnancy.(14,21) Arterial partial pressure of oxygen is lower when supine in pregnancy.(24,27)

Taken together, it is intuitive that maternal supine sleep could affect foetal growth and, consequently, risk of stillbirth via decreased placental blood and oxygen supply.

GESTATION RELATED OPTIMAL WEIGHT STANDARD

The original Ghana PrenaBelt Trial (GPT)(28) selected the Gestation Related Optimal Weight (GROW) standard by Gardosi et al. (Perinatal Institute and Gestation Network, Birmingham, UK) as one of its primary outcomes.(29,30) The reason for using the GROW standard in the original GPT and in this study is because the GROW standard accounts for the main six non-pathological factors affecting birth weight, including gestational age, maternal height, maternal weight at booking, parity, ethnicity and sex of the neonate. As such, the customised birthweight centile (CBWC) computed using the GROW standard enables delineation between constitutional and pathological smallness and more accurate detection of pregnancies at increased risk for adverse outcomes.(31,32)

Changes in the GROW Standard Calculators Between Original and Current Analyses

The GROW standard calculators are continually being updated, according to availability of new databases from different populations from which additional ethnic coefficients can be derived.(33) This enables improvement on predicting normal variation, which reflect on the coefficient of variation of the curve. The extent of the data have enabled derivation of ethnic-specific sets of coefficients.(33) That is, GROW calculators adjust for maternal height and weight, parity, and sex of the neonate for each ethnicity or

country of origin.(33) As such, because we used the ”Ghanaian” ethnicity coefficient with the new (v.8.0.6.2) calculator, all the other coefficients in the model (maternal height and weight, parity, and sex of the neonate) were changed based on new datasets from Ghana because these coefficients are specific to the “Ghanaian” ethnicity. In the original GPT analysis with the old (v6.7.8.1) calculator, the authors used the “West African” ethnicity coefficient (based on West Africans giving birth at Queen’s Medical Centre, Nottingham, UK), which had its own set of coefficients for maternal height and weight, parity, and sex of the neonate.

Role of Maternal Ethnicity in Customised Foetal Growth Standards

We acknowledge that ethnicity can be poorly defined by both patients and clinicians and that assumptions about the impact of ethnicity on health has the potential to result in patient harm. However, several decades of epidemiological research along with several professional organisations (e.g., the Royal College of Obstetricians & Gynaecologists)(34) have established that the benefit outweighs the harm when assessing birth weight against individual growth potential calculated for each baby in each pregnancy (customised standards) rather than against the average of the population (population standards or norms).(35,36) Customised standards, adjusted for the main factors affecting foetal growth (including ethnicity), increase accurate detection of IUGR by improved distinction between physiological and pathological smallness.(35) In contrast, application of population standards fails to identify a significant proportion of pathological smallness (false negative) and erroneously identifies a significant proportion of physiological smallness as IUGR (false positive, risking unnecessary and

potentially harmful intervention).(37–39) In a study of over 130,000 births from 2009-2013, Gardosi et al. have demonstrated that maternal height, maternal weight, maternal ethnicity, parity, and sex of the newborn account for 76% (R-squared 0.759) of the normal variation in birth weight (excluding pathological factors).(36) Regarding the impact of ethnicity alone, it accounts for approximately 24% of the normal variation in birth weight,(36) which highlights the clinical importance of taking maternal ethnicity into account. Finally, there is now a substantial evidence base that supports that differences in foetal growth potential between ethnic groups are physiologic and that customization (which accounts for ethnicity) improves delineation between pathological and physiological smallness.(40–44)

COMPARISON OF FREQUENTIST AND BAYESIAN PARADIGMS

In the frequentist paradigm, the study hypothesis is evaluated indirectly by estimating an objective probability, a relative long-run frequency (also known as the p-value), of observing a treatment effect of the same or larger magnitude than the treatment effect observed in a given study if the same study were repeated indefinitely and assuming the null hypothesis (no effect) is true.(45) According to Royall, the frequentist approach can only guide our decision to either accept or reject the null hypothesis – in light of data, frequentist statistics tells us what to *do*.(46) If we want to know, in light of data, what we should *believe* or how strongly we should believe in different hypotheses, frequentist methods cannot answer that question and, rather, Bayesian methods are required.(46)

In the Bayesian paradigm, the study hypothesis is evaluated directly, that is, Bayesian methods tell us the probability of the study hypothesis being true given the available data.(47,48) Bayes' theorem enables the estimation of a plausible range of values of a treatment effect ("posterior probability") by formally combining data collected in a study with information available prior to the study about the plausible values of a treatment effect ("prior probability").(45) In other words, a unique feature of a Bayesian analysis is that it enables the use of clinically relevant priors probabilities in combination with trial data to provide updated and robust estimates that allow for a more comprehensive interpretation of the existing evidence. As such, one can appreciate the utility of Bayesian methods in clinical practice as clinical decisions can be directly informed by study results and, at the same time, incorporate the influence of clinical judgement and prior beliefs about the treatment effect.(47,49,50)

For readers who may be sceptical of Bayesian methodology, we direct them to a thorough discussion of the rationale, process, and interpretation of Bayesian analyses in a recent, open-access, systematic review in the Lancet, "Clinical trials in critical care: can a Bayesian approach enhance clinical and scientific decision making?" by Yarnell, Abrams, Baldwin, et al.(51)

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