**Evaluating Risk Antenatally in Twins**

*Statistical Analysis Plan*

Version 1.0 – 01/11/2021

This statistical analysis plan describes in more detail the analysis outlined in sections 4.4.4 – 4.4.6 of the Study Protocol, Version 1.2.

**Primary Outcome**

The primary outcome measure is the frequency of adverse pregnancy outcome defined as one of the following occurring in one of more babies: late fetal death (before 24 weeks’ gestation), perinatal death (stillbirth after 24 weeks’ gestation or neonatal death), hypoxic ischaemic encephalopathy, iatrogenic preterm delivery due to fetal compromise and unexpected admission to the neonatal intensive care unit. Hypoxic ischaemic encephalopathy (HIE) will be defined as a diagnosis of HIE recorded in the neonatal period. Any grade of HIE will be included. Unexpected admission to the neonatal unit is an admission occurring to an infant born ≥37 weeks’ gestation with no fetal anomalies (NB the presence of fetal anomaly is an exclusion criteria for recruitment).

The frequency of adverse outcome will be reported for all pregnancies and will also be broken down by chorionicity of twins (dichorionic and monochorionic twins).

We will also report gestation at birth grouped into four different groups, ≤28 weeks’ gestation, 28-32 weeks’ gestation, 32-36 weeks’ gestation and ≥37 weeks’ gestation. This will be reported for all pregnancies and broken down by chorionicity of twins.

**Secondary outcome measures**

*Pilot Study outcomes*

The proportion of women approached to participate who agreed to do so and the proportion of women who consented to participate who completed the study will be calculated and reported. Study completion is defined as information available on the primary outcome and the appropriate number of questionnaires were completed for the gestation at birth.

*Exposures*

We will report the frequency of different characteristics or exposures in participants. We will report this for all pregnancies and split by chorionicity.

We initially plan to report the frequency of: maternal age, parity, ethnicity, depriviation, cigarette smoking, body mass index (BMI), use of assisted conception (including supraovulation, IVF and ICSI), maternal going to sleep position, maternal perception of fetal movements, presence of hyperemesis in early pregnancy, gestational diabetes, presence of selective fetal growth restriction or fetal growth restriction in both twins. Where possible e.g. age, BMI will be reported as continuous variables.

Selective fetal growth restriction (FGR) will be defined as two out of three of the following criteria: a difference of 25% in estimated fetal weight where one twin has an estimated fetal weight <10th centile and umbilical artery pulsatility index of the smaller twin > 95th centile.[[1]](#footnote-1) FGR of both twins will be defined where both twins are <10th centile.

We will assess whether the use of different growth percentiles (Intergrowth21ST, GROW and Twin Centiles[[2]](#footnote-2)) alters the frequency of diagnosis of FGR or selective FGR. If estimated fetal weight cannot be calculated then an abdominal circumference <10th centile will be used.

We will compare the frequency of exposures with the MiNESS dataset for singleton non-anomalous stillbirths and livebirths.[[3]](#footnote-3)

For monochorionic twins we will also report the frequency of signs of specific complications e.g. Twin to Twin Transfusion Syndrome, Twin Anaemia Polycythaemia Sequence.

We will determine whether exposures are associated with or predictive of the frequency of composite adverse pregnancy outcome using Chi-squared test, Mantel-Haenszel Odds Ratios and Nagelkerke R-squared. No variables will be excluded based upon the frequency of exposure.

1. Khalil A et al. Consensus definition and essential reporting parameters of selective fetal growth restriction in twin pregnancy: a Delphi procedure Ultrasound Obstet Gynecol 2019;53(1):47-54. [↑](#footnote-ref-1)
2. Stirrup O et al. Fetal growth reference ranges in twin pregnancy: analysis of the Southwest Thames Obstetric Research Collaborative (STORK) multiple pregnancy cohort Ultrasound Obstet Gynecol . 2015 Mar;45(3):301-7. [↑](#footnote-ref-2)
3. Platts J et al. The Midland and North of England Stillbirth Study (MiNESS) BMC Pregnancy Childbirth 2014 May 21;14:171. [↑](#footnote-ref-3)