Results The analysis included 3117 twin pregnancies (605 MC and 2512 DC). The total risk of early pregnancy loss (miscarriage and neonatal death) before 24 weeks in MC twins (60.3 per 1000 fetuses) was significantly higher than in DC twins (6.5 per 1000 fetuses), with a hazard ratio (HR) of 9.18 (95% CI, 6.0–13.9). Survival analysis showed a significant difference in overall and early mortality between MC and DC twins (Log-rank test, $p < 0.0001$), while no difference was noted after 24 weeks of gestation (Log-rank test, $p = 0.08$).

Conclusions Early pregnancy loss is significantly more common in MC than in DC twins, but the trend in prospective risk of mortality in MC twins is not evident after 24 weeks' gestation. This rate has almost halved compared to those in the published literature. Early detection and prompt treatment of complications in MC twins is likely to have contributed to this improvement in outcomes.

PP.08 MANCHESTER ADVANCED MATERNAL AGE STUDY (MAMAS) – DOES AN AGEING MATERNAL ENVIRONMENT AND ALTERED PLACENTAL FUNCTION EXPLAIN HIGHER RISK OF POOR PREGNANCY OUT COME IN ADVANCED MATERNAL AGE?

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Background Women of advanced maternal age (AMA; ≥35 years) have increased risk of fetal growth restriction and stillbirth. The aetiology is unknown; however both conditions are linked with placental dysfunction, including reduced nutrient transport and altered placental morphology. Ageing is associated with increased systemic inflammation; whether this contributes to poor pregnancy outcome is unknown. We hypothesise an ageing maternal environment adversely affects placental function, resulting in poor pregnancy outcome.

Methods Women (20–30, 35–39 and ≥40 years) with singleton pregnancies are being recruited to MAMAS. Maternal serum samples are collected at 28 and 36 weeks gestation for measurement of inflammatory markers by ELISA. Placental function is assessed by amino acid uptake by placental villous tissue. Placental morphology was quantified by density of Syncytial Nuclear Aggregates (SNA's), fetal capillaries and quantification of proliferation.

Results Preliminary ELISA analysis of 40 samples revealed lower anti-inflammatory cytokine interleukin-10 (IL-10) in maternal serum of women ≥35 ($p = 0.016$, Kruskal-Wallis test). Other cytokines were unchanged. Preliminary data suggests higher placental uptake of taurine in women ≥35, but system A activity appears unaltered. SNA's were increased, but vascularity and proliferation were unchanged in placentas from women ≥35 ($p < 0.05$ Kruskal-Wallis test).

Conclusion MAMAS is the only prospective observational study investigating AMA and placental function. Preliminary data indicate accelerated placental ageing with increased SNA and an altered maternal environment with reduced anti-inflammatory cytokines. Understanding the mechanisms underlying AMA and pregnancy complications may help improve outcome for these women. Measuring circulating biomarkers of ageing prenatally may enable detection of high risk pregnancies.

PP.09 FOLIC ACID SUPPLEMENTATION AND RISK OF INTRAUTERINE GROWTH RESTRICTION (IUGR)

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Objective To determine whether there is a reduction in the risk of IUGR with folic acid supplementation.

Design A retrospective cohort study using the West Midlands Perinatal Institute population based database.

Setting West Midlands, UK.

Participants Births to West Midlands residents (July 2009-June 2012). Multiple pregnancies and congenital anomalies were excluded.

Main Outcome Measures Prevalence and relative risk of IUGR, defined as birth weight <10th customised centile with 95% confidence intervals.

Results There were n = 117260 births with data for folic acid supplementation antenatally, of which 85% of women reported taking folic acid. Nullips constituted 42.6% of the cohort overall and 44% of those that took folic acid antenatally. For those women where the dose of folic acid was recorded (n = 42537), 95% took a dose of 400 mcg, 4% at 5 mg and 1% at other dose. For timing of folic acid supplementation, 26% commenced pre-conception, 34% at <5 weeks, 35% at 5–10 weeks and 5% at a later gestation. There were n = 60077 cases with complete pregnancy and demographic data allowing a logistic regression analysis adjusted for maternal age, smoking, hypertension, deprivation, ethnicity, employment status, diabetes (including gestational), BMI, single/partner, drug use, father blood relation, time of booking and parity. The risk of IUGR for women with no folic acid supplementation was prevalence13%, RR 1.09 (1.03–1.16), $p < 0.01$. For women that took folic acid, only the 400 mcg dose taken pre-conception showed a significant reduction, prevalence 9.7%, RR 0.90 (0.83–0.98) $p = 0.01$.

Conclusion Folic acid supplementation pre-conception significantly reduces the risk of IUGR.

PP.10 CRL DISCORDANCE AND ADVERSE PERINATAL OUTCOME IN TWINS THE STORK MULTIPLE PREGNANCY COHORT

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Background The role of first trimester ultrasound in predicting the outcome in twin pregnancies is conflicting. The aim of this study is to determine the association between crown-rump length (CRL) discordance and adverse perinatal outcome in twin pregnancies.

Methodology CRL discordance was related to early fetal loss <20, <24 weeks, perinatal mortality, birth weight (BW) and ultrasound estimated fetal weight (USS EFW) discordance ≥25%, intrauterine growth restriction (IUGR) and preterm birth <34 weeks of gestation. ROC and logistic regression analysis was performed to evaluate the importance CRL discordance in determining adverse perinatal outcome.

Results A total of 2,155 twin pregnancies [420 monochorionic (MC) and 1,735 dichorionic (DC)] were included in the study. CRL discordance had very poor prediction for fetal loss <20 (AUC of 0.61), < 24 weeks (AUC: 0.54), perinatal mortality (AUC of 0.52), BW discordance (AUC of 0.61), BW < 5th centile (AUC of 0.56), USS EFW discordance (AUC of 0.55) and preterm birth (AUC of 0.50). Overall mortality was significantly higher ($p = 0.016$) in MC (21/420) compared to DC (45/1735) twins. Logistic regression analysis demonstrated that chorionicity ($p = 0.033$ OR: 2.09, 95% C.I. from 1.06 to 4.010) independently contribute in determining mortality while CRL discordance ($p = 0.201$) did not. After adjusting for chorionicity, CRL discrepancy did not improve the detection of adverse outcome in either MC or DC twin pregnancies.

Conclusion CRL discordance is of poor predictive value for adverse perinatal outcomeafter 14 weeks of gestation in either MC or DC twin pregnancies.

PP.11 ONE THIRD OF NON-ANOMALOUS TERM STILLBIRTHS ARE ASSOCIATED WITH ABNORMAL FETAL GROWTH

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Background Approximately one third of all stillbirths occur at term. These losses are potentially preventable by early delivery at 37 weeks. One means of screening to detect babies at risk of term stillbirth would be to use ultrasound to assess abnormalities of fetal growth. However, there is limited information on the importance of fetal growth in determining the risk of stillbirth at term.
Methods/Results We studied registries of Scottish maternity and stillbirth data and identified 668,887 eligible records of term births since 1992. Birth weight was classified on the basis of sex and gestational age specific percentiles. The relationship between birth weight percentile and the risk of stillbirth (all causes except congenital anomaly) was assessed referent to birth weight percentiles in the range 20–80th. The risk (odds ratio [95% CI] P) of stillbirth was increased with birth weight between the 1st–3rd percentile (OR = 8.2 [CI:6.8–9.9] P < 0.001), 4th–10th percentile (OR = 3.5 [CI:2.8–4.0] P < 0.001) and the 11th–20th percentile (OR = 1. 8 [CI:1.4–2.2] P < 0.001). The risk of stillbirth was also increasing among the largest infants: 98th–100th percentile (OR = 2.3 [CI:1.7–3.1] P < 0.001). The attributable fraction for stillbirth associated with these birth weight categories was 33% (95% CI: 28 to 37%). The associations were minimally affected by adjusting for maternal characteristics, including smoking.
Conclusion Approximately one third of all term stillbirths are associated with growth abnormality. These data indicate that population screening for growth abnormality could identify babies at increased risk of term stillbirth.

PP.12 WEIGHT DISCORDANCE AND PERINATAL MORTALITY IN TWINS: THE STORK MULTIPLE PREGNANCY COHORT

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Objectives The main aim of this study was to ascertain the performance of BW and ultrasound EFW discordance in the prediction of perinatal loss in twin pregnancies.
Methods A retrospective study of all twin pregnancy births from a large regional cohort of 9 hospitals over a ten year period. Intertwin BW and ultrasound EFW discordance were related to stillbirth and neonatal death of one or both twins obtained from a mandatory national register. Receiver operating characteristic (ROC), survival and logistic regression analyses were performed to evaluate the contribution of weight discordance in determining perinatal loss.
Results A total of 2,161 twin pregnancies were included in the analysis. A BW discordance of ≥25% was associated with the highest AUC for the prediction of stillbirth and neonatal death (BW AUC = 0.72; 95% CI: 0.65–0.80). The perinatal loss in twins with a BW discordance of ≥25% was significantly greater (60.9 per 1,000 fetuses) than that in twins with an EFW discordance <25% (8.6 per 1,000 fetuses) (p < 0.0001); the predictive accuracy was similar using either BW or ultrasound EFW discordance (EFW AUC = 0.69; 95% CI: 0.62–0.77, p = 0.62). Logistic regression analysis demonstrated that BW discordance and gestational age, but not chorionicity or individual fetal size percentile, were independently associated with perinatal mortality.
Conclusions An EFW discordance of ≥25% represents the optimal cut-off for the prediction of stillbirth and neonatal mortality irrespective of chorionicity or individual fetal size. A policy of increased fetal surveillance commencing from 26 weeks' gestation and elective delivery by 38 weeks might be reasonable.

PP.13 PREVIOUS CAESAREAN DELIVERY AND THE RISK OF UNEXPLAINED STILLBIRTH: ANALYSIS OF 128,585 SECOND PREGNANCIES IN SCOTLAND, 1999–2008

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Background A previous study (Lancet 2003; 362:1779–84) reported an increased risk of unexplained stillbirth in women with previous caesarean delivery among women having second births in Scotland, 1992–1998. Subsequent studies have yielded heterogeneous results but have employed data, analytic approaches and interpretation of variable quality.
Methods/Results We replicated our previous methods and analysed 128,585 eligible singleton second births between 1999 and 2008. There were 88 stillbirths among 23,688 women with a previous caesarean (2.33 per 10,000 women per week) and 288 stillbirths in 104,897 women who previously delivered vaginally (1.67 per 10,000 women per week, P = 0.002). When analysed by cause, women with a previous caesarean had an increased risk (hazard ratio [95%CI] P) of unexplained stillbirth (1.47 [1.12–1.94] P = 0.006) and the excess risk was apparent from 34 weeks onwards (1.75 [1.23–2.49] P = 0.002). When the analysis was confined to 96,988 women with linked records from the first and second pregnancy (confirming exact mode of previous delivery) the association was stronger (2.12 [1.55–2.88] P < 0.001). Adjustment for maternal characteristics and first pregnancy complications had a minimal effect (1.97 [1.43–2.72] P < 0.001). The association was similar weather the previous caesarean was performed prior to labour (2.1[1.24–3.80] p = 0.007) or during labour (2.50 [1.53–4.08] p < 0.001) and when the analysis was confined to previous term births (2.35 [1.50–3.53] p < 0.001).
Conclusion We confirm that previous finding that previous caesarean delivery is a risk factor for unexplained stillbirth. The association is independent of maternal characteristics, obstetric outcome or the indication for the caesarean delivery.

PP.14 PROGESTERONE MODULATES CERVICAL ANTIMICROBIAL IMMUNITY

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Introduction Human beta defensins (HBD1, 2.3) have antimicrobial and immunomodulatory properties and are components of the cervical mucus plug. Vaginal progesterone delays delivery in women with cervical shortening, but the mechanism(s) underlying this effect remain undetermined. This study describes the expression of HBDs by cervical epithelia in response to stimulation with classical infective and inflammatory agonists and progesterone.
Methods The human endo-cervical cell-line End1/E6E7 and ecto-cervical cell-line Ect1/E6E7 were stimulated with bacterial (Lipopolysaccharide, LPS; Peptidoglycan, PGN) and inflammatory (Interleukin 1 beta, IL-1β; Interferon gamma, IFNγ) agonists and progesterone for up to 24 hours. HBD secretion was assessed by ELISA.