Table 1- PPH-related outcomes and adverse events in the modified intention-to-treat population, TRAAP trial

Outcome or event	Tranexamic Acid Group (N=1945)	Placebo Group (N=1946)	Risk Ratio (95% CI)	Mean difference (95% CI)	P value
Primary outcome: PPH, defined by blood loss ≥ 500 mL, measured with a graduated collector bag – no./total no. (%)	156/1921 (8.1)	188/1918 (9.8)	0.83 (0.68-1.01)	/	0.07
PPH, defined by blood loss > 500 mL, measured with a graduated collector bag – no./total no. (%)	127/1921 (6.6)	169/1918 (8.8)	0.75 (0.60-0.94)	/	0.01
Clinically significant PPH according to caregivers – no./total no. (%)	151/1945 (7.8)	203/1945 (10.4)	0.74 (0.61-0.91)	/	0.004
Severe PPH, defined by blood loss ≥ 1000 mL – no./total no. (%)	47/1921 (2.5)	57/1918 (3.0)	0.82 (0.56-1.21)	/	0.3
Additional uterotonics – no./total no. (%)	141/1945 (7.3)	189/1945 (9.7)	0.75 (0.61-0.92)	/	0.006
Arterial embolisation or surgery for postpartum hemorrhage –no./total no. (%)	3/1945 (0.2)	5/1945 (0.3)	0.60 (0.14-2.51)	/	0.8
Blood transfusion – no./total no. (%)	17/1945 (0.9)	18/1945 (0.9)	0.94 (0.49-1.83)	/	0.9
Mean (SD) peripartum change in hemoglobin (g/dL)	0.76 (1.23) (n=1837)	0.78 (1.26) (n=1800)	/	-0.02 (-0.10-0.06)	0.6
Mean (SD) peripartum change in hematocrit (%)	1.97 (3.72) (n=1746)	1.94 (3.84) (n=1721)	/	0.03 (-0.22-0.28)	0.8
Nausea or/and vomiting in labor ward - no./total no. (%)	136/1945 (7.0)	63/1945 (3.2)	2.16 (1.61-2.89)	/	<0.0001
Mean (SD) postpartum uremia (mmol/l)	3.43 (0.93) (n=1605)	3.43 (0.95) (n=1593)	/	-0.00 (-0.07-0.06)	0.9
Mean (SD) postpartum creatininemia (micromole/l)	54.67 (9.79) (n=1648)	54.66 (9.85) (n=1633)	/	0.01 (-0.69-0.66)	1.0
Thrombotic event*– no./total no. (%)	1/1945 (0.05)	4/1945 (0.2)	0.25 (0.03-2.23)	/	0.2

*TXA group: 1 woman with superficial venous thrombosis; Placebo group : 1 woman with superficial venous thrombosis, 1 woman with deep vein thrombosis and 2 women with ovarian vein thrombosis

2 DNA methylation of genes in the maternal HPA axis during pregnancy is linked with birth outcomes

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OBJECTIVE: Exposure to psychosocial stress has been shown to be related to a variety of epigenetic changes including DNA methylation. The aim of this study was to examine exposure to psychosocial stress and DNA methylation during pregnancy on birth outcomes.

STUDY DESIGN: A multi-site longitudinal study was conducted in a total of 744 pregnant women. Exposure to stress was assessed using a battery of self-reports to derive a latent stress factor as well as the interviewer-based Stressful Life Events Schedule (SLES). Pyrosequencing of bisulfite converted DNA was performed covering two regulatory regions in each of the Corticotropin Releasing Hormone (CRH), CRH Receptor 1 (CRHR1) and Nuclear Receptor Subfamily 3, Group C, Member 1 (Glucocorticoid Receptor) (NR3C1) genes measured during the 2nd and 3rd trimesters. Birth outcomes included small for gestational age (below 10th percentile), spontaneous pre-term birth (<37 weeks' gestation) gestational age at delivery, and birth weight. Analyses controlled for age, body mass index, smoking, race, and newborn's sex as well as cell-types based on the mRNA levels of CD4, CD19, CD3E, CD8A, and CD19 assessed in peripheral blood.

RESULTS: Latent class trajectory analyses identified three SLES stress trajectories across pregnancy - low stable, moderate-decreasing, and high-increasing. Increased levels of SLES stress during pregnancy (high-increasing) had a significant association with spontaneous preterm birth ($p < 0.03$). In addition, increased SLES stress was associated with a reduction in methylation in a highly-methylated region of CRH, which in turn was associated with earlier gestational age at delivery. Self-report stress was significantly and positively associated with the extent of DNA methylation of the CRHR1 gene ($p < 0.03$) during the third trimester and was significantly associated with an increase in methylation in CRHR1 gene from 2nd to 3rd trimester ($p < 0.05$) among women with preterm birth. Finally, increased methylation of NR3C1 at the 2nd trimester as associated with decreased birthweight ($p < 0.04$).

CONCLUSION: Maternal stress is associated with preterm birth and a reduction in birthweight that appears to be in part moderated by changes in DNA methylation in genes central to the stress response during pregnancy.

3 Timing of Serial Ultrasound In At Risk Pregnancies: A Randomized Controlled Trial (SUN Trial)

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OBJECTIVE: Pregnancies with several complications are at risk for abnormalities of fetal growth or of amniotic fluid (AF) and are at risk of adverse neonatal outcomes. To detect these abnormalities, serial 3rd trimester ultrasound examinations (USE) are recommend every 2 to 4 weeks (ACOG Practice Bulletin Ultrasound in Pregnancy 2016). We hypothesized that among at risk pregnancies, USE every 2 weeks will have higher detection rates of abnormal growth or of AF abnormalities than USE every 4 weeks.

STUDY DESIGN: Women with singleton pregnancies complicated by various medical comorbidities at 24-28 weeks were randomized (NCT02719886) to USE every 2 versus every 4 weeks. The primary outcome was findings of fetal growth restriction (FGR), large for gestational age (LGA), oligo- or poly-hydramnios. A total of 228 participants were needed to detect a 30% difference in detection of fetal growth or AF abnormalities between groups (baseline 58%; alpha = 0.05, power=0.8).

RESULTS: All randomized women (N=112 to every 2 weeks; N=116 to every 4 weeks) were included in the intent to treat analysis. The primary outcome was similar amongst USE groups every 2 vs 4 weeks (41% vs 38%; RR 1.11; 95% CI 0.78 - 1.58). The following also occurred with similar frequency between groups: admission and/or delivery related to abnormal USE findings (12% vs 18%; P=0.53); cesarean delivery (41% vs 39%; P=0.78) and pre-specified composite maternal and neonatal morbidity (Table 1). The predictive accuracy of detecting small for gestational age was similar with USE every 2 vs 4 weeks (positive likelihood ratio of 7.3 and 8.3, respectively). Detection of large for gestational age was also similar with the two schema: LR (+) of 5.6 with USE every 2 weeks and 9.2 with every 4 weeks (Table 2).

CONCLUSION: In at risk pregnancies, serial ultrasound examinations every 2 weeks as compared to every 4 weeks did not improve the detection of abnormal fetal growth or of amniotic fluid.