or complications, time to start ambulation and time to start lactation.

**RESULTS:** The maternal characteristics at randomization between the groups were no different including: gestational age, blood pressure, laboratory parameters, and the use of antihypertensives. No maternal deaths occurred in either group. There were no differences in the rate of eclampsia or maternal complications such as hemorrhage, respiratory depression and severe hypertension between the groups. Time to ambulation and time to lactation were significantly shorter in the no Mag group. (Table)

**CONCLUSION:** In this large randomized study the use of Mag for 24 hours post partum in patients with severe preeclampsia that had received at least 8 gm of Mag prior to delivery, was not associated with a reduction in eclampsia or other maternal complications post partum.

| | Mag N=555 | No Mag N=558 | p value |
|---|---|---|---|
| Eclampsia N(%) | 1(0.18) | 2(0.35) | 0.99 |
| Hemorrhage N(%) | 11(2.0) | 13(2.3) | 0.76 |
| Resp. Depression N(%) | 5(0.9) | 4(0.7) | 0.67 |
| Severe HTN N(%) | 53(9.5) | 50(9.0) | 0.60 |
| Time to amb. (hours) | 18.1 ± 10.6 | 11.8 ± 10.8 | 0.0001 |
| Time to lact. (hours) | 24.1 ± 17.1 | 17.1 ± 16.8 | 0.0001 |

## 5 Enoxaparin for the prevention of preeclampsia and intrauterine growth restriction in women with a prior history (the eppi trial): an open-label international multicentre randomized controlled trial

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**OBJECTIVE:** To determine whether daily enoxaparin commenced prior to 16+0 weeks' gestation, in addition to standard high risk care (SHRC), reduces the recurrence of pre-eclampsia and/or fetal growth restriction in women deemed to be at high risk of these conditions based on their past obstetric history.

**STUDY DESIGN:** An open-label randomised controlled trial in five obstetric units in New Zealand, Australia and the Netherlands. Inclusion criteria were: $\geq 6^{+0}$ and $\leq 15^{5+6}$ weeks' gestation with fetal viability and singleton pregnancy confirmed, and most recent pregnancy complicated by (i) pre-eclampsia delivered $\leq 35^{+6}$ weeks, (ii) small for gestational age (SGA) $<10^{th}$ customised birthweight centile (CBWC) delivered $\leq 35^{+6}$ weeks, or (iii) SGA$\leq 3^{rd}$ CBWC delivered at any gestation. Women were randomly assigned to SHRC plus enoxaparin 40mg subcutaneously daily or SHRC only. SHRC included prescription of daily low dose aspirin and calcium. Randomisation was stratified according to inherited thrombophilia status. Uterine and umbilical artery Doppler waveform studies were performed at 20 and 24 weeks' gestation and serum samples were taken for assessment of placental and angiogenic markers at recruitment, 20 and 30 weeks' gestation. The primary outcome was the incidence of pre-eclampsia and/or SGA $<5^{th}$ CBWC. Based on the available literature the sample size was calculated to assess a reduction in the primary outcome from 25% to 7% (160 women required with 5% drop-out rate provides 80% power at a 2-sided significance level 0.05). This was an intention to treat analysis. ACTRN12609000699268.

**RESULTS:** Data were analysed for 156 women, 8 women delivered <20 weeks and were not included in further analysis. Preeclampsia and/or SGA $<5^{th}$ CBWC occurred in 35 women (23.5%). Enoxaparin in addition to SHRC did not reduce the rate of preeclampsia and/or SGA $<5^{th}$ CBWC (OR 1.17, 95%CI 0.5-2.6) or of any secondary outcomes (table).

**CONCLUSION:** In women with a prior pregnancy complicated by preeclampsia and/or fetal growth restriction, the addition of enoxaparin to high risk obstetric care did not reduce the risk of recurrence.

Outcomes according to treatment group

| Outcome | SHRC plus enoxaparin (n=71) | SHRC (n=77) | Odds ratio (95%CI) or p value |
|---|---|---|---|
| Pre-eclampsia and/or SGA <5th CBWC | 18 (25%0 | 17 (22.1%) | 1.17 (0.5-2.6) |
| Pre-eclampsia | 6 (8.5%) | 5 (6.5%) | 1.28 (0.4-4.6) |
| SGA<5th CBWC | 15 (20.8%) | 13 (16.9%) | 1.35 (0.6-3.2) |
| SGA<10th CBWC | 23 (31.9%) | 22 (28.6%) | 1.16 (0.6-2.4) |
| Pre-eclampsia del <34+0 weeks | 2 (2.8%) | 1 (1.3%) | 2.02 (0.1-28.4) |
| Stillbirth/neonatal death | 1 (1.4%) | 3 (3.9%) | 0.45 (0.04-5.7) |
| Mean gestational age at delivery (weeks + days) | 37+5 | 37+1 | p=0.45 |
| Delivery <37 weeks | 15 (21.1%) | 19 (25.0%) | p=0.70 |
| Mean birthweight | 2999g | 2907g | p=0.50 |
| Mean CBWC | 32.0 | 31.3 | p=0.87 |

## 6 Prevention of preterm birth with pessary in singletons (PoPPS): a randomized controlled trial

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**OBJECTIVE:** To determine if pessary use prevents preterm birth (PTB) in singleton gestations with a short transvaginal ultrasound (TVU) cervical length (CL) and without a prior spontaneous PTB.

**STUDY DESIGN:** Multicenter randomized controlled trial of asymptomatic women with singleton gestations with a TVU CL $\leq$ 25 mm at $18^0$ - $23^6$ weeks and no prior spontaneous PTB. Subjects were randomized to receive the Bioteque cup pessary or no pessary. Pessaries were inserted by MFM staff centrally trained in proper placement. Randomization was stratified by study site and CL($\leq$ 20 mm or >20-25mm). Treatment with vaginal progesterone was recommended to all women with a TVU CL $\leq$ 20 mm. Primary outcome was PTB<37 weeks. Composite adverse neonatal outcome included necrotizing enterocolitis, intraventricular hemorrhage (grade 3 or 4), respiratory distress syndrome, bronchopulmonary dysplasia, retinopathy, sepsis and neonatal death. Analysis was by intention-to-treat. Our required total sample size was 242. The trial was stopped prematurely by the DSMB due to the start of a competing NICHD MFMU pessary trial.

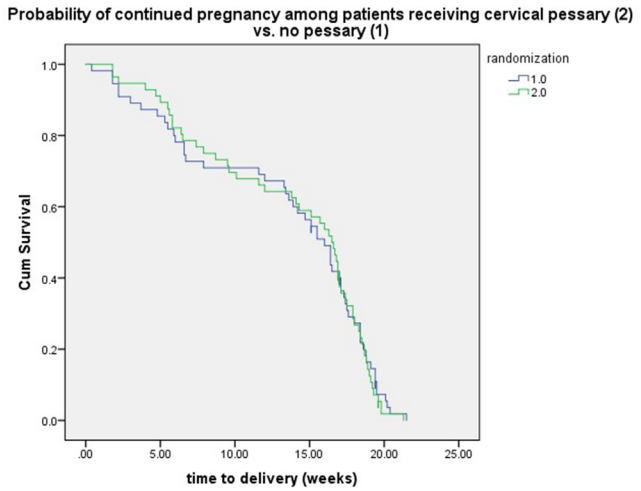
**RESULTS:** A total of 17,388 women were screened with TVU CL; 446 (2.6%) had a TVU CL $\leq$ 25 mm. Of the 394 (88.3%) who met eligibility criteria, 122 (31.0%) consented to randomization. As of the time of submission, 111 women have delivered, 56 (92%) in the pessary and 55 (90%) in the no pessary groups. Demographic characteristics, mean gestational age (21 $\pm$ 1 week) and mean CL (16 $\pm$ 7 mm) at enrollment were similar in both groups. There were no significant differences between the pessary and no pessary groups in rates of PTB<37 weeks, PTB<34 weeks, PTB<28 weeks, gestational

age at delivery, birth weight and composite neonatal outcome (Table).

**CONCLUSION:** Our study showed that treatment with a cervical pessary did not prevent PTB in women with singleton gestations with a TVU CL $\leq$ 25 mm at $18^0$ - $23^6$ weeks and without a prior spontaneous PTB. Though study recruitment was stopped before we reached our enrollment goal, our findings are consistent with the recent studies that failed to show efficacy of pessaries in similar clinical settings.

Outcomes according to study group

| | PessaryN=56 | No pessaryN=55 | RR (95% CI) | P-value |
|---|---|---|---|---|
| PTB<37 weeks | 24 (43%) | 23 (42%) | 1.02 (0.70,1.48) | |
| PTB<34 weeks | 20 (36%) | 17 (31%) | 1.11 (0.76,1.62) | |
| PTB<28 weeks | 11 (20%) | 14 (25%) | 0.84 (0.52,1.37) | |
| PTB<24 weeks | 2 (4%) | 5 (9%) | - | |
| Mean GA at delivery (weeks) | 34.7 ±5.7 | 34.4 ±6.5 | | P=0.83 |
| Birth weight(g) | 2359 ±1073 | 2404 ±1143 | | P=0.83 |
| Composite neonatal outcome | 14 (25%) | 16 (30%) | 0.90 (0.58, 1.39) | |




## 7 Potential mechanisms of contemporary strain Zika virus replication in human placental trophoblasts

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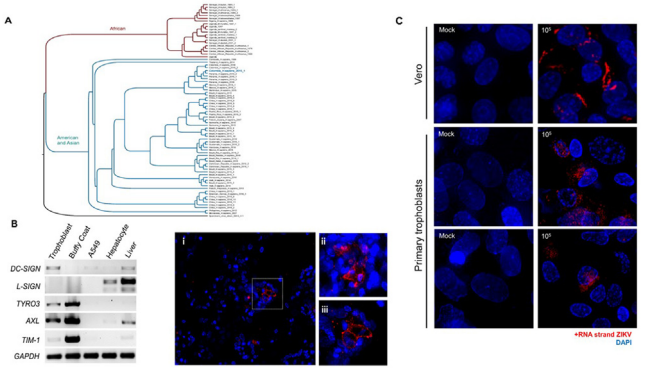
**OBJECTIVE:** Zika virus (ZIKV) is an emerging mosquito-borne flavivirus. A causal link explaining the delay between maternal symptoms and fetal infection is missing, and why prior African outbreaks were not associated with fetal malformations is unknown. In this study, we sought to answer these questions using state-of-the-science approaches with a single passage contemporary ZIKV strain and infection of high purity trophoblasts from uninfected donors.

**STUDY DESIGN:** ZIKV-FLR was isolated by inoculating *A. albopictus* C6/36 mosquito cells with serum from a non-pregnant subject infected in Barranquilla, Colombia. Subsequent deep sequencing on the Illumina platform was performed, and alignments to all 77 sequenced genomic strains was made. We isolated $n$=20 uninfected human primary trophoblasts, and examined expression of putative ZIKV cell entry receptors. We documented intracellular infection in trophoblasts using single molecule RNA FISH to both negative and positive viral strands. Finally, we examined the potential role of miRNAs in modulating trophoblast infection.

**RESULTS:** Phylogenetic trees were generated from all currently available complete ZIKV sequences ($n$ of 77; **Fig 1A**). The resultant phylogenetic tree demonstrates phylogenetic delineation noted between African strains (non known to cause microcephaly) and the current Americas and recent Asian strains. Moreover, primary human trophoblasts express putative cell entry receptors for ZIKV (**Fig 1B**) prior to infection with ZIKV. Upon co-culturing with a current strain of ZIKV, we observe intracellular localization of ZIKV as evidenced by single molecule FISH (**Fig 1C**). Finally, ZIKV infection is associated with a significant diminution of the ssRNA-ligand sensing miRNA, mir21 (0.7 fold lower, $p<0.01$) but not the C19 cluster miRNA species.

**CONCLUSION:** Contemporary ZIKV strains are genomically distinct from historic epidemic strains, mirroring their association with microcephaly and fetal malformations. Placental trophoblasts express putative ZIKV entry receptors, and cytoplasmic replication can visualized by single molecular RNA FISH. Select placental miRNAs (mir-21) are significantly and specifically down-modulated following ZIKV infection. We speculate that these findings are of potential mechanistic interest to ZIKV perinatal pathogenesis.




## 8 Whole exome sequencing in the evaluation of fetal structural anomalies: A prospective study of sequential patients

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**OBJECTIVE:** Small studies have reported the use of whole exome sequencing (WES) in the prenatal evaluation of fetal structural anomalies and have reported pathogenic variant rates of 10-30%. These studies however have all used selected patients that were felt to have a high likelihood of having a genetic etiology. We sought to evaluate the incremental value of WES in routine prenatal diagnosis including all structural anomalies.

**STUDY DESIGN:** Under an IRB protocol, all sequential patients with a fetal structural anomaly were offered WES as part of the fetal genetic evaluation. Those having diagnostic prenatal testing had WES, karyotype, and chromosomal microarray done on amniotic fluid or CVS and those not having PND had cord blood obtained at birth for testing. All results were returned to the patients.