National Prescription Register. Cox proportional hazard regression models were used to calculate the hazard of miscarriage in women with a partner exposed to methotrexate. The study was approved by the Danish Data Protection Agency (2015-41-4309).

**Results** We identified 1,364,063 registered pregnancies with known paternity, of whom 520 fathers were exposure to methotrexate within the three months before conception to the end of the first trimester. Among these, 46 (8.9%) experienced a miscarriage compared to 122,926 (9.0%) among the unexposed.

There was no increased risk of experiencing a miscarriage in pregnancies to men exposed to methotrexate before pregnancy compared to unexposed (adjusted hazard ratio 0.99 (CI95% 0.67–1.46)). Furthermore, we found no increased risk of experiencing a miscarriage in pregnancies to men exposed to methotrexate during first trimester compared to unexposed (adjusted hazard ratio 0.90 (CI95% 0.61–1.32)).

**Conclusion** We found no association between paternal exposure to methotrexate before pregnancy and miscarriage. Available data suggest that paternal methotrexate exposure should not be of major concern. Multinational recommendations could be changed accordingly.

**Disclosure(s)** Nothing to disclose

**P07**

**ROXITHROMYCIN IN EARLY PREGNANCY AND THE RISK OF MAJOR CONGENITAL MALFORMATION: A REGISTER BASED NATIONWIDE COHORT STUDY**

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**Background** Medicine use during pregnancy often causes concern for fetal harm. Roxithromycin, a macrolide antibiotic, is regarded as inadvisable to use during pregnancy due to lack of safety data. However, alternative macrolides have been associated with adverse outcomes in pregnancy. We conducted a register-based nationwide cohort study testing the hypothesis that use of roxithromycin in the first trimester is associated with major congenital malformations.

**Methods** We included all Danish women giving live birth from 1997 to 2012. Women with at least one redeemed receipt of roxithromycin during first trimester were regarded as exposed. Multivariable logistic regression adjusting for maternal age, multiple birth, parity, year of conception, smoking, educational length, and household income was performed, supplemented by sensitivity analyses comparing unexposed with exposure to increasing accumulated doses of roxithromycin.

**Results** The study included 966,372 pregnancies of which 2,430 children were born to an exposed mother, 78 (3.34%) of the exposed children were diagnosed with a major congenital malformation compared with 33,609 (3.49%) among children born to unexposed mothers. The odds ratio for the occurrence of a major congenital malformation after exposure to roxithromycin was 0.96 (95% CI 0.76–1.20) and multifactorially adjusted 0.94 (0.74–1.18). Sensitivity analyses comparing unexposed with exposure to increasing accumulated doses of roxithromycin showed no dose response relationship. Further, no differences in the type of major malformation according to the EUROCAT subgrouping system were seen.

**Conclusions** We found no association between exposure to roxithromycin in the first trimester of pregnancy and major congenital malformations.

**Disclosure(s)** Nothing to disclose
Background and Purpose Serum neurofilament light chain (sNfL) has recently emerged as a promising biomarker reflecting structural neuro-axonal damage in different neurological diseases. Our study aimed at assessing whether sNfL can predict the functional outcome in preterm infants who suffered from neonatal haemorrhagic brain injury.

Methods In this prospective observational study, we used an ultrasensitive single-molecule array assay to measure serum and cerebrospinal fluid (CSF) concentrations of NfL in preterm infants diagnosed with intraventricular haemorrhage (IVH) in the first few days of life. We determined the temporal profile of serum and CSF NfL levels from first diagnosis of IVH until term equivalent age, their association with cerebral imaging markers, and with clinical and functional outcome until 2 years of age assessed by Bayley Scales of Infant Development. We fitted univariable and multivariable logistic regression models to determine risk factors for lower motor and cognitive development. Longitudinal mixed effects models modelled NfL levels using cubic spline smoothers to track the trajectory over time.

Results The study included 48 infants born with less than 32 weeks of gestation. At the time point of IVH diagnosis, NfL median levels were 271.9 pg/mL (IQR 151.2–389.7), and strongly decreased until term equivalent age to 15.7 pg/mL (IQR 11.1–32.2). CSF values were 113-fold higher (IQR 40–211) than corresponding serum values. Additional cerebral infarction (n=23) but not post-haemorrhagic hydrocephalus with permanent external ventricular drainage (n=29) or other diseases independently determined sNfL levels. In multivariate logistic regression models, the only significant predictor of poor motor outcome at 2 years or death was sNfL level (p=0.02). There was a clear difference between the NfL trajectory for those with poor motor outcome at 1 year.

Conclusions This study shows that early sNfL is an independent prognostic biomarker for motor functional outcome in preterm infants after IVH.

Disclosure(s) Nothing to disclose

Methods Pubmed and Embase (01/01/1997–31/12/2017) were searched for drug trials in pregnant women with diabetes, HIV infection or hypertension. Titles and abstracts were screened, followed by a full text review of eligible articles. Inclusion criteria were interventional clinical trials in pregnant women treated with chronic medication and full text in English. Trial characteristics, maternal and offspring data were extracted. Data was summarised by disease and study. Twelve key items were considered for the offspring. The protocol was registered on PROSPERO (CRD42017057024).

Results Overall, 196 articles reporting 132 clinical trials (diabetes n=55; HIV n=59; hypertension n=18) were included. The number of births were frequently not reported (diabetes 40%; HIV 24%; hypertension 56%). Congenital malformations were infrequently reported with sufficient detail (diabetes 27%; HIV 34%; hypertension 6%). Similar observations were made for other key items (e.g. foetal losses, neonatal deaths, birth weight corrected for gestational age).

Conclusions Underreporting of key data for the offspring was frequent in publications of clinical trials in pregnant women with diabetes, HIV infection or hypertension making the assessment of the benefit-risk ratio of treatment options during pregnancy difficult.

Disclosure(s) Nothing to disclose