

Friday June 10, 9:00-10:15

Parallel session 4

Reproductive Epidemiology

Chairs: Nel Roeleveld & Nhung Trinh

- 9:00 Maternal phthalate and bisphenol urine concentrations during pregnancy and early markers of vascular health in children (O46)
Sophie Blaauwendraad
- 9:15 Kidney injury rates among children with solitary functioning kidney in a Dutch long-term follow-up study (O47)
Sander Groen in 't Woud
- 9:30 Registration of congenital anomalies in the Netherlands: Agreement between a national perinatal registry (Perined) and EUROCAT, the Dutch branch of population-based registries of congenital anomalies (O48)
Audrey Meulendijks
- 9:45 Spontaneous clearance of asymptomatic anogenital and pharyngeal *Neisseria gonorrhoeae*: Results from the NABOGO trial (O49)
Buhari Teker
- 10:00 Trajectories of maternal depressive symptoms during pregnancy and infant wheezing up to two years of age: a prospective cohort study (O50)
Marleen van Gelder

O46. Maternal phthalate and bisphenol urine concentrations during pregnancy and early markers of vascular health in children.

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Background: Exposure to the endocrine-disrupting chemicals bisphenols and phthalates is increasing due to their extensive use in common consumer products. Fetal exposure to phthalates and bisphenols might lead to fetal cardiovascular developmental adaptations and predispose individuals to cardiovascular disease in later life. Carotid intima-media thickness and distensibility are well-known markers of vascular health and independently related with cardiovascular events.

Objectives: We examined the associations of maternal urinary bisphenol and phthalate concentrations in pregnancy with offspring carotid intima-media thickness and distensibility at the age of 10 years

Methods: In a population-based, prospective cohort study among 935 mother-child pairs, we measured maternal urinary phthalate and bisphenol concentrations in each trimester. At age 10, we measured child carotid intima-media thickness and distensibility using ultrasound.

Results: Maternal urinary average or trimester-specific phthalate concentrations were not associated with child carotid intima-media thickness at age 10 years. Higher maternal average concentration of total bisphenol, especially bisphenol A, were associated with a lower carotid intima-media thickness (differences -0.16 standard deviation score (95% confidence interval -0.24, -0.09) and -0.15 (-0.23, -0.07) per interquartile range increase in maternal urinary bisphenol concentration). Trimester specific analysis showed that higher maternal third trimester total bisphenol and bisphenol A concentrations were associated with lower child carotid intima-media thickness (all p-values <0.05). Maternal urinary bisphenol or phthalate concentrations were not associated with child carotid distensibility.

Conclusion: In this large prospective cohort, higher maternal urinary bisphenols concentrations were associated with smaller childhood carotid intima media thickness. This implies that fetal exposure to those chemicals might cause structural developmental adaptations of the vascular endothelium. Further studies are needed to replicate this association and to identify potential underlying mechanisms.

O47. Kidney injury rates among children with solitary functioning kidney in a Dutch long-term follow-up study.

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Introduction: A solitary functioning kidney (SFK) in children is a condition leading to increased risks of kidney injury, although it is unclear to which magnitude. Our objective was to investigate the risks and risk factors for kidney injury in children with SFK.

Methods: Children with SFK were recruited in 36 hospitals throughout The Netherlands. Information was collected from electronic health records and parental questionnaires. We used Kaplan-Meier curves to estimate survival without signs of kidney injury and Cox regression to evaluate risk factors. Multivariable analyses were performed on imputed datasets to account for missing data and sensitivity analyses informed us about selective missingness.

Results: Detailed clinical information was available for 944 patients with an SFK. After a median follow-up of 12.8 years, proteinuria was present in 68 patients (7%), a reduced kidney function in 290 (31%), and high blood pressure in 323 (34%), while antihypertensive medication was used by 84 patients (9%). Cumulative proportions of children with at least one sign of kidney injury were 23% at 5 years, 43% at 10 years, 63% at 15 years, and 76% at 18 years of age.

Conclusions: Kidney agenesis, additional congenital anomalies of the kidney and urinary tract (CAKUT), and being overweight at last follow-up were associated with an increased risk of kidney injury in patients with a congenital SFK. Kidney agenesis and overweight were mainly associated with proteinuria and hypertension, whereas additional CAKUT was more strongly associated with reduced kidney function. Data from this large SFK cohort indicates that over 75% of patients with an SFK will have at least 1 sign of kidney injury at 18 years of age, which stresses the need for long term follow-up. Differences in risk factors for different outcomes indicate that multiple pathophysiological mechanisms may play a role.

O48. Registration of congenital anomalies in the Netherlands: Agreement between a national perinatal registry (Perined) and EUROCAT, the Dutch branch of population-based registries of congenital anomalies..

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Background: Registration of congenital anomalies (CAs) can vary in terms of definition and timing of diagnosis, impacting the quality and completeness of the registrations. In the Netherlands, data on CAs is available from two registries (neither a gold standard): a national registry for perinatal care (Perined) and the Dutch branch of an European epidemiological surveillance program for CA (EUROCAT) in three North provinces. The aim of this study was to investigate the level of agreement in coding CAs between Perined and EUROCAT.

Methods: Perined (N=139,041, all pregnancies ≥ 16 weeks) and EUROCAT (n=3,094, only pregnancies with Ca's) registrations of CAs for the period 2010-2018 in Groningen, Drenthe and Friesland were pseudoanonymised and linked at individual child level in the remote microdata environment of the Statistics Netherlands. Analyses were limited to 42 diagnostic codes used in both registries and included a) the overall and per diagnosis agreement at group level assessed with Cohen's Kappa; b) agreement on case level for subsamples using a qualitative assessment by content experts and Cohen's Kappa.

Results: Analyses of any diagnosis (yes/no CA) revealed a moderate level of agreement between Perined and EUROCAT (Cohen's Kappa (CK): 0.42 CI:0.41-0.45), however the agreement varied strongly at diagnosis level (Cohen's Kappa range 0.08-0.75). Agreement on case level occurred mostly in cases with an isolated CA. For multiple CA's, Perined tended to register the most severe CA/syndrome while EUROCAT also registered the corresponding CA's. Perined included a large proportion (8%-52% per organ system) of unspecified categories ('other') with 0%-57% of CAs having specific diagnosis in EUROCAT. Qualitative case by case assessment revealed a number of patterns for inconsistencies between the registries.

Conclusion: Overall agreement between the registries was moderate, however it varied strongly between diagnoses. A substantial proportion of unspecified diagnoses reduces the value of Perined for epidemiological research into specific CA's.

O49. Spontaneous clearance of asymptomatic anogenital and pharyngeal Neisseria gonorrhoeae: Results from the NABOGO trial.

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Background: Spontaneous clearance of asymptomatic Neisseria gonorrhoeae (Ng) does occur, but data are scarce. We aimed to assess spontaneous clearance among patients with asymptomatic anal, pharyngeal, vaginal, and urethral Ng infections who participated in the NABOGO trial. In addition, we assessed determinants associated with spontaneous clearance.

Methods: The NABOGO trial was a randomized controlled, double-blind, single-center, non-inferiority trial assessing non-inferiority of ertapenem, gentamicin, and fosfomycin to ceftriaxone for the treatment of uncomplicated gonorrhoea. For a subset of asymptomatic NABOGO participants, we collected pre-enrolment and enrolment visit samples before trial medication was given. Spontaneous clearance was defined as a positive pre-enrolment nucleic acid amplification testing (NAAT) result, followed by a negative NAAT at enrolment. We compared the median time between pre-enrolment and enrolment visits for patients who cleared spontaneously and for those who did not. Determinants for spontaneous clearance were assessed using logistic regression.

Results: Thirty-two of 221 (14.5%) anal Ng infections cleared spontaneously, and 17/91 (18.7%) pharyngeal, 3/13 (23.1%) vaginal, and 9/28 (32.1%) urethral Ng infections. Median time between the pre-enrolment and enrolment visit was only longer for patients who cleared their pharyngeal infection spontaneously compared to those who did not (median 8 [interquartile range (IQR)=7-11] vs. 6 days [IQR=4-8]; $p=0.012$). Overall, patients with more days between pre-enrolment and enrolment visit were more likely to clear spontaneously (adjusted OR (aOR)=1.06 per additional day (95% confidence interval (95%CI)=1.01-1.12).

Conclusion: A significant proportion of asymptomatic patients cleared their Ng infections spontaneously. Given these results, treatment of all Ng infections after a one-time NAAT may be excessive unnecessary and additional confirmatory testing of asymptomatic patients before treatment may help reduce antibiotic use.

O50. Trajectories of maternal depressive symptoms during pregnancy and infant wheezing up to two years of age: a prospective cohort study.

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Background: Maternal depressive symptoms during pregnancy have been associated with infant wheezing. Previous studies, however, did not take timing of exposure and trajectories of wheezing in childhood into account. We aimed to determine whether patterns of maternal depressive symptoms are associated with trajectories of wheezing up to 2 years of age.

Methods: This study was embedded in the PRenancy and Infant DEvelopment (PRIDE) Study, a prospective cohort study among pregnant women and their offspring. Women with a delivery in 2012-2019 completed web-based questionnaires throughout pregnancy and during childhood. Maternal depressive symptoms were assessed using the Hospital Anxiety and Depression Scale and the Edinburgh Depression Scale at enrollment and in gestational weeks 17 and 34. Group-based trajectory modelling was used to identify women with similar patterns of depressive symptoms and children with similar patterns of wheezing. Risk ratios (RRs) with 95% confidence intervals (CIs) were estimated for the associations between trajectory groups of depressive symptoms and wheezing. We adjusted for a sufficient set of confounders and weighted using inverse probability of censoring weights.

Results: Among the 5833 women included, four distinct trajectories of depressive symptoms during pregnancy were identified, as well as 5 trajectories of wheezing in the first 2 years of life. We observed an association between maternal depressive symptoms in mid-pregnancy (RR 1.30, 95% CI 1.05-1.63) and late pregnancy (RR 1.35, 95% CI 1.07-1.70) and infant wheezing up to 6 months. The trajectory of a steady increase of depressive symptoms throughout pregnancy was associated with infant wheezing between 12 and 18 months (RR 1.45, 95% CI 1.05-2.00). We did not identify associations for other exposure-outcome combinations.

Conclusion: Maternal depressive symptoms in mid- and late pregnancy may be a risk factor for the development of infant wheezing. Monitoring of depressive symptoms throughout pregnancy by healthcare providers is recommended.