Thursday June 9, 14:00-15:15

Parallel session 4

Pharmacoepidemiology

Chairs: Charlotte Bekker & Marleen van Gelder

14:00 Antibiotic exposure during pregnancy and risk of wheezing in the offspring: a prospective cohort study (O16)
Michelle Clevis

14:15 The utilisation of low-dose rivaroxaban in patients with atherosclerotic cardiovascular disease in the United Kingdom and The Netherlands (O17)
Nicolas Hunt

14:30 Sex differences in the primary prevention of cardiovascular diseases in a Dutch primary care setting (O18)
Pauline Kiss

14:45 Representativeness of the PHARMO Electronic Health Records (EHRs) from primary care (O19)
Jetty Overbeek

15:00 Sex differences in treatment patterns for non-metastatic muscle-invasive bladder cancer – an analysis of 3,484 patients of the Netherlands Cancer Registry (O20)
Anke Richters

O16. Antibiotic exposure during pregnancy and risk of wheezing in the offspring: a prospective cohort study.

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Background: Both antibiotic use during pregnancy and asthma prevalence have been rising the past decades. Several studies have reported an increased risk of wheezing in children of mothers who used antibiotics during pregnancy. However, these studies did not address the complex patterns of antibiotic use and trajectories of wheezing in childhood. Therefore, we determined whether prenatal antibiotic exposure is associated with infant wheezing in the first two years of life, with special attention for timing of exposure and outcome.

Methods: We included 5,864 pregnancies with deliveries between 2012 and 2019 from the PRIDE Study, a prospective cohort study among pregnant women in the Netherlands. Information was collected using web-based questionnaires and pharmacy records. Group-based trajectory modeling was used to identify clusters of children following similar wheezing patterns. Crude and adjusted risk ratios (RR) and 95% confidence intervals (CI) were estimated for the association between prenatal exposure to antibiotics and trajectories of wheezing using inverse probability of censoring weights. Secondary analyses were conducted to account for timing, dosage, and indication of antibiotic use, as well as mode of delivery.

Results: We identified 5 distinct trajectories of wheezing in the first 2 years of life. Although any use of antibiotics during pregnancy was not associated with ever-wheezing (RR 1.01, 95% CI 0.87-1.18), an association with wheezing in the first two months of life was observed (RR 1.28, 95% CI 1.03-1.60). Third trimester antibiotic use was associated with any infant wheezing (RR 1.25, 95% CI 1.01-1.55). We found no evidence for a dose-response relationship or effect modification by delivery mode.

Conclusion: Prenatal antibiotic use is associated with wheezing in the first two months of life, but this association diminishes for wheezing later in life. Third trimester antibiotic use is associated with a slightly increased risk of any offspring wheezing.

O17. The utilisation of low-dose rivaroxaban in patients with atherosclerotic cardiovascular disease in the United Kingdom and the Netherlands.

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Low-dose rivaroxaban has been indicated for the management of atherosclerotic cardiovascular disease (ASCVD), since recent (2019-20) updates to European and national prescribing guidelines. We aim to describe the trends of low-dose rivaroxaban utilisation between 2015-2020, in two European countries, and to determine the characteristics of users vs non-users. In patients with a prior ASCVD diagnosis, utilisation of low-dose rivaroxaban was measured in CPRD Aurum (UK) and the PHARMO database network (Netherlands, NL). Using monthly cross-sections, incidence rates (IR) were calculated and incidence rate ratios (IRR) compared utilisation in 2019 and 2020 to 2015-2018, prior to the guideline changes. Users were compared to non-users using mean differences (MD) in demographic covariates and chi-squared tests. We included 708,390 (UK) and 415,380 (NL) ASCVD patients. In the UK, the IR of low-dose rivaroxaban use in the period 2015-2018 was 13.24 per 100,000 person-years, in 2019 the IR was 41.89 (IRR 3.16, 95%CI [2.55;3.91]) and in 2020, 117.16 (IRR 8.85, 95%CI [7.46;10.50]). In the Netherlands, the IR in 2015-2018 was 2.04, in 2019 the IR was 37.30 (IRR 18.26, 95%CI [12.10;27.55]) and in 2020, 20.91 (IRR 10.24, 95%CI [6.41;16.36]). Users were younger at the start of follow-up (UK MD 6.50 years; NL MD 2.31 years, both $p<0.05$) and more likely male (UK 74.3% vs 62.9%; NL 76.8% vs 58.6%, both $p<0.001$). European and national prescribing guideline changes were associated with a vast increase in use of low-dose rivaroxaban among patients with ASCVD in the UK and in the Netherlands.

O18. Sex differences in the primary prevention of cardiovascular diseases in a Dutch primary care setting.

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Background: Increasing evidence has shown sex differences in the primary prevention of cardiovascular diseases (CVD). The purpose of this study was to assess these sex differences in primary care in the Netherlands.

Methods: Data was obtained from individuals registered at one of the general practices participating in the Julius General Practitioner's Network (JGPN). Linear and Poisson regressions were used to investigate sex differences in four aspects of cardiovascular risk management: risk factor assessment, risk factors levels, the proportion of individuals with pharmacological treatment and the proportion of individuals achieving adequate levels in the risk factors according to Dutch guidelines.

Results: The 2018 JGPN database included 90 147 individuals (50% women; mean age 53 years). Most of the risk factors studied were more commonly assessed in women than in men, with the highest Risk Ratio (RR) for Estimated Glomerular Filtration Rate (eGFR; RR 1.22, 95% Confidence Interval (CI): 1.18 – 1.26). Total Cholesterol (TC), Low Density Lipoprotein Cholesterol (LDL-c), High Density Cholesterol (HDL-c), and Body Mass Index (BMI) levels were higher in women as compared to men, while blood pressure, eGFR and Glycated Hemoglobin (HbA1c) levels were higher in men. Among individuals with a treatment indication, women were more likely to receive antihypertensive medication (RR 1.03, 95% CI: 1.01 – 1.04) and less likely to receive lipid lowering medication (RR 0.78, 95% CI: 0.75 – 0.80), compared to men. Among treated individuals, women were more likely to achieve adequate levels of blood pressure (RR 1.19, 95% CI: 1.13 – 1.26) and less likely to achieve adequate levels of LDL-c (RR 0.74, 95% CI: 0.69 – 0.79), as compared to men.

Conclusion: Sex differences in the care of CVD in a primary care setting have been observed. When compared to men, women were more likely to achieve blood pressure control but less likely to achieve LDL-c control.

O19. Representativeness of the PHARMO Electronic Health Records (EHRs) from primary care.

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Real world evidence obtained from observational data plays an increasing role in healthcare decision making. Representativeness of this data is pivotal to provide valid and generalisable study results and conclusions. Representativeness of electronic health records (EHRs) from primary care of the PHARMO Data Network of the general Dutch population was assessed in this study. A cross-sectional study, using data from 2018, was performed comparing demographic characteristics, medication use, diagnoses and deaths. PHARMO's general practitioner (GP) Data comprises data from EHRs on diagnoses, laboratory test results, referrals to specialists and healthcare product/drug prescriptions. Data on the Dutch population was obtained from Statistics Netherlands (CBS). CBS obtains demographic data from the population register of all Dutch municipalities, statistics on reimbursed medication from the National Health Care Institute of the Netherlands, and diagnosis data from the Nivel Primary Care Database. Standardised mean difference (SMD) was used to compare proportions between the Dutch population and PHARMO's GP population. An SMD >0.2 was considered a difference. On January 1st, 2018, 3,466,321 persons were included in PHARMO's GP population (mean age: 41.6 years, 49.7% males). Sex and age distribution was similar to the Dutch population. Regarding medication use, only 'viral vaccines' and 'hormonal contraceptives for systemic use' differed (SMD >0.2); use in PHARMO's GP population was higher compared to the Dutch population. These differences can be explained as these pharmacological subgroups are not completely reimbursed via basic health insurance. No differences were observed regarding diagnoses. Mortality was lower in PHARMO's GP population than in the Dutch population, which is in line with expectations. Persons who die are more often older and no longer under the care of a GP (i.e. institutionalised). EHRs from primary care of the PHARMO Data Network are representative of the Dutch population regarding demographic characteristics and provided primary care in terms of medication use and diagnoses. Medication use was more difficult to compare as EHRs in the PHARMO Data Network includes non-reimbursed medication, whereas national data does not.

O20. Sex differences in treatment patterns for non-metastatic muscle-invasive bladder cancer – an analysis of 3,484 patients of the Netherlands Cancer Registry.

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Background: Bladder cancer (BC) is a common malignancy with well-established differences in incidence, clinical manifestation and outcomes between men and women with BC. Despite a lower incidence, women have in general poorer outcomes than men. It is not known to what extent differences in treatment approaches contribute to disparities in outcomes. This paper describes treatment patterns among men and women with muscle-invasive BC with a focus on radical cystectomy.

Methods: A retrospective population-based cohort study was performed with data from the Netherlands Cancer Registry. All patients with an initial diagnosis of muscle-invasive, non-metastatic BC (MIBC, cT2-4a, N0/X, M0/X) in the years 2018, 2019 and 2020 were identified. Initial treatment was compared between men and women with descriptive statistics and multivariable logistic regression analyses.

Results: A total of 3,471 patients were diagnosed with MIBC in 2018-2020 in the Netherlands, of whom 28% were women. Women had higher T-stage and more often non-urothelial histology. Among all strata of clinical T-stage, women less often received treatment with curative intent and less often underwent a radical cystectomy. Among radical cystectomy-treated patients, women more often received neoadjuvant treatment (except for cT4 disease). When adjusted for other pre-treatment factors, sex was not independently associated with undergoing curative treatment, radical cystectomy or neoadjuvant treatment.

Conclusion: Improved understanding of the factors contributing to the sex differences in treatment patterns could help reducing differences in treatment patterns and subsequent disparities in outcomes between men and women with MIBC.