dystonia, akathisia, parkinsonism and tardive dyskinesia). Outcome-specific incidences were stratified by short-term (1 year or less) and long-term (more than 1 year) antipsychotic use. We used multivariate modified Poisson regressions to determine factors associated with these outcomes among preschoolers.

Results: The overall crude incidence during PA-approved antipsychotic use was highest for EPS and obesity (57 and 19 cases per 1000 children-years, respectively). The rate of these two outcomes significantly differed by duration of antipsychotic use. We observed a higher obesity (23.8 vs. 9.6, p value less than 0.05) and dystonia incidence (7.2 vs. 2.5, p value less than 0.05) but lower akathisia incidence (44.4 vs. 60.6, p value less than 0.05) among long-term antipsychotic users compared to short-term users. Five outcomes—ventricular arrhythmia, other cardiovascular side effects, hyperprolactinemia, parkinsonism and tardive dyskinesia—occurred rarely (less than 2.0 per 1000 children-years). Preschoolers who were younger at baseline (0–2 vs. 4–5 years old) and Black (vs. White) were at a higher risk of EPS. Antipsychotic users with baseline anticonvulsants (vs. without) had a higher risk of EPS, while users with anxiolytics/hypnotics/sedatives had a higher risk for obesity.

Conclusions: Risk for EPS and obesity deserves clinical attention during antipsychotic treatment among preschoolers. Controlled studies that allow interpretation of these incidence rates in the context of background risk and that formally quantify the incremental risk associated with antipsychotic initiation during early childhood are needed.

451. Early life antibiotic use and the risk of asthma and asthma exacerbations in children

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Background: The use of antibiotic therapy early in life might influence the risk of developing asthma. Studies assessing the influence of early life antibiotic use on the risk of asthma exacerbations are limited and the results are inconsistent.

Objectives: To study the association between use of antibiotics during the first three years of life and the risk of developing childhood asthma and the occurrence of asthma exacerbations.

Methods: Data from four large childhood cohorts were used; two population-based cohorts to study the risk of developing asthma (physician-diagnosed asthma) at age of 10 years: Generation R ($n=7{,}393$, the Netherlands) and SEATON ($n=924$, Scotland, UK), and two asthma cohorts to assess the risk of asthma exacerbations (defined as asthma-related visits to an emergency department and/or the use of oral corticosteroids): PACMAN ($n=674$, the Netherlands) and BREATHE ($n=806$, Scotland, UK). Odds ratios (ORs) were derived from multivariate logistic regression analysis (adjusted for age, gender, and family history of asthma/allergy) within each database followed by pooling the results using a fixed- or random-effect model.

Results: Exposed vs. never exposed to antibiotic use during the 1st year of life was associated with an increased risk of asthma in a meta-analysis of the Generation R and SEATON data (OR: 2.18, 95% CI: 1.04–4.60; I^2: 76.3%). There was no association between antibiotic use during the first three years of life and risk of asthma exacerbations later in life in a meta-analysis of the PACMAN and BREATHE data (OR: 0.93, 95% CI: 0.65–1.32; I^2: 0.0%).

Conclusions: Early life exposure to antibiotics is associated with an increased risk of developing asthma, but there is no evidence that the exposure to antibiotic is associated with an increased risk of asthma exacerbations.

452. Incidence of bleeding and thrombotic events in non-institutionalized paediatric patients using warfarin in the United Kingdom

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Background: Dosing of vitamin K antagonists (VKA) is complex with large inter- and intra-individual variability in patients' required VKA dose. Over- and underdosing can result in bleeding and thrombotic events. The incidence of these events in paediatric patients on warfarin therapy in a European population is unknown.

Objectives: To estimate the incidence of bleeding and thrombotic events in warfarin using paediatric patients in the UK and to characterise patients who do or do not experience a bleeding or thrombotic event.

Methods: Data were obtained from the UK CPRD in the period between January 1998 and November 2016. Using a cohort design, we identified all patients with ≥1 prescription for warfarin and who were ≤18 years. The date of the first prescription marked the start of the follow-up. Follow-up was classified into periods of warfarin use and non-use. Patients were followed until 19 years of age, death or departure from the practice. The incidence of non-fatal bleeding and thrombotic events was assessed using both information from CPRD and the linked Hospital Episode Statistics (HES). Fatal events were identified usings the linked mortality data from the Office for National Statistics (ONS). For calculating the incidence of thrombotic events only patients without a history of thrombosis were included.

Results: In total, 685 patients were identified (median age 15 years, 45.4% female) of whom 372 could be linked to the HES and ONS databases. The incidence of bleeding and thrombotic events during warfarin use was 4.08 and 1.27/100 patient years, respectively. The incidence of bleeding events during non-use was 2.65/100 patient years (relative risk 1.58, 95% confidence interval [0.89–2.80]). Only 2 fatal events occurred, one bleeding and one thrombotic event. Patients with a bleeding event tended to have a higher percentage of INR measurements with a value above 4 (9.4 vs 3.9%) and a lower fraction below 2 (18.4 vs 39.1%) compared to patients without a bleeding event during the whole follow-up. Patients with a thrombotic event showed the opposite trend, a higher percentage of INRs below 2 (45.8 vs 29.5%) and a lower percentage of INRs above 4 (2.7 vs 5.3%). All differences were not statistically significant which maybe due to the small sample size.

Conclusions: The incidence of bleeding events was higher than of thrombotic events. The trends in percentages of INRs under and above therapeutic range suggest that keeping the INR within range could decrease the occurence of these events.

453. Preliminary results of cardiometabolic risk factors in newly diagnosed individuals with autism spectrum disorder (ASD)

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Background: Children with ASD have been found to be at risk of cardiometabolic complications (CMC). Little is known about the factors that may precipitate these complications in ASD youths.

Objectives: To identify the predictors of CMC in a cohort of newly diagnosed ASD subjects in the province of Quebec (Canada).

Methods: A nested cases–control study was conducted using RAMQ databases. Newly diagnosed subjects with ASD aged lower than 26 years old (≥2 diagnoses ICD-9 codes: 299.X, excluding 299.2) were identified, between January 1998 and December 2010. ASD subjects were free of CMC and known risk factors (neuro-psychiatric diagnosis, psychoactive drugs and corticosteroid use.) in the 5 years prior to cohort entry. Cases were defined as subjects presenting CMC (using ICD-9 codes) or using specific therapies (for hypertension, diabetes, dyslipidemia or obesity) during the follow-up. CMC cases were matched to 10 controls. Univariate conditional logistic regression analyses were performed to identify CMC predictors (measured in the year prior to the CMC date).

Results: A cohort of 1,343 newly diagnosed ASD subjects with a median age of 6 years was constituted. The mean duration of follow-up was 4.3 years. The incidence rate of CMC was of 10.8 per 1,000 person-year. We identified 63 CMC cases that were matched to 630 controls. The type of CMC were as follows: 66.7% obesity, 12.7% hypertension, 11.1% dyslipidemia and 9.5% diabetes. Males had a lower risk of CMC (Rate Ratio (RR): 0.47; 95% CI: 0.26–0.84), whereas welfare status (RR: 1.74; 1.04–2.94) and other neuro-psychiatric disorders (RR: 1.95;1.14–3.33) were associated with a higher risk of CMC. Among the other neuro-psychiatric disorders, schizophrenia (RR: 9.36; 2.27–38.63) and anxiety disorders (RR: 3.26; 1.57–6.81) had the highest impact. Among the psychoactive drugs, antipsychotics (RR: 2.21; 1.22–4.03) presented the strongest association.

Conclusions: Preliminary results suggest that socioeconomic status, neuro-psychiatric diseases and psychoactive drugs seem to increase the risk of CMC. Further analyses are under progress (e.g. adjustment, effect per specific CMC and drug exposure).