Background: Beta-blockers have been associated with decreased cancer mortality. However, evidence for lung cancer is sparse and reported beneficial effects might be based on biased analyses.

Objectives: In this so far largest study, we investigated the association between beta-blocker use and lung cancer survival.

Methods: Patients with a lung cancer diagnosis between April 1998 and December 2011 were selected from a database linkage of the Netherlands Cancer Registry and the PHARMO Database Network. After matching eligible patients on the propensity score, adjusted hazard ratios (HRs) and corresponding 95% confidence intervals (CI) were calculated using Cox proportional hazards regression to investigate the association between pre-diagnostic and time-dependent beta-blocker use and overall survival. Duration and dose-response analyses and stratified analyses by beta-blocker type, histological subgroups and stage were conducted.

Results: Of 3,340 eligible lung cancer patients, 1437 (43%) took beta-blockers four months prior to diagnosis. Pre-diagnostic beta-blocker use was not associated with overall survival (HR 1.00 (0.92–1.08)) in the adjusted model. Time-dependent post-diagnostic analysis showed similar results with a HR of 1.03 (0.94–1.11). Trend analyses showed no association for cumulative dose (HR 0.99 (0.97–1.02)) and cumulative duration (HR 1.00 (0.96–1.05)).

Conclusions: In this so far largest population-based study addressing the association of beta-blocker use and lung cancer survival, we found no clinically relevant evidence for a survival benefit of pre- or post-diagnostic beta-blocker use among lung cancer patients.

446. Longitudinal analysis of psychotropic medication use in a birth cohort of publicly-insured U.S. children: new users and cumulative exposure

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Background: Over the last two decades, the increased prevalence of psychotropic medication use among very young children has been prominent. Most studies have assessed psychotropic medication use in cross-sectional studies at annual intervals. However, little is known about the longitudinal utilization patterns and cumulative exposure to psychotropic medications in a true 'new-user' approach.

Objectives: We assessed the cumulative incidence of any psychotropic medication use from birth through age 7. In these new users, we further assessed the cumulative psychotropic medication exposure (days) by age 7. Finally, we compared clinical characteristics of preschool initiators (1–4 years old) with early school initiators (5–7 years old) of psychotropic medications.

Methods: Using Medicaid administrative data, we identified a cohort of children born in 2007 ($N = 35{,}244$) and followed them longitudinally from birth to psychotropic medication initiation, loss to follow-up or end of study (2014) using Kaplan–Meier analysis to adjust for censoring. Additionally, we used quantile regression models to assess median psychotropic exposure days and adjust for sociodemographic characteristics.

Results: The cumulative incidence of any psychotropic medication use ranged from 0.3% (age 1) to 2.5% (age 4) to 26.6% by age 7. Stimulants (22.9%) and alpha-agonists (5.9%) were the most commonly used medications by age 7. The cumulative stimulant exposure was 230 median days [Interquartile Range (IQR): 88–464 days], while alpha-agonist exposure was 195 median days (IQR: 74–436 days). Among preschool psychotropic initiators, the leading psychiatric diagnostic groups were behavioral disorders (22.0%), learning disorders (9.3%), adjustment disorders (2.6%) and autism (2.5%). Behavioral disorders (62.9%), adjustment disorders (8.9%), depression (4.9%) and anxiety disorders (3.1%) led among early school initiators.

Conclusions: Compared with previous prevalence studies of psychotropic medication use in very young children, this approach offers a longitudinal perspective on cumulative exposure with implications for long-term safety.

447. The children anticoagulation and pharmacogenetics study (caps): developing a dosing algorithm for acencocoumarol in paediatric patients

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Background: Dosing of vitamin K antagonists (VKA) in paediatric patients is complex. The large variability in VKA dose requirement asks for elucidating the factors associated with this variability and taking these into account when defining the dose for a patient. For warfarin, paediatric dosing algorithms have been developed, but not for acenocoumarol.

Objectives: To develop a dosing algorithm for acenocoumarol in pediatric patients with and without genetic information.

Methods: This multicentre retrospective follow-up study was carried out in Dutch anticoagulation clinics and children's hospitals. Patients were selected when they used acenocoumarol for >1 month between January 1995 and December 2014 and were ≤18 years of age. The primary outcome was the mean daily dose during a stable period. A stable period was defined as ≥3 consecutive international normalized ratio measurements within therapeutic range over a period of ≥3 weeks. Clinical information (including height, weight and indication) and saliva samples for genotyping of CYP2C9 (*2 and *3), VKORC1, CYP4F2, CYP2C18 and CYP3A4 (*1B and *22) were collected. Linear regression was used to analyse their association with the log mean stable dose.

Results: In total, 175 patients were included of whom 86 patients had a stable period and no missing clinical information (clinical algorithm cohort) and of 80 also genetic information was available (genetic algorithm cohort). The mean age at the stable period was 9 years. The most common indications were Fontan circulation, prosthetic heart valve, deep venous thrombosis and dilated cardiomyopathy. The clinical algorithm, containing body surface area and indication, explained 45.0% of the variability in dose requirement of acenocoumarol. By adding the genotypes of VKORC1, CYP2C18, and CYP2C9*2/*3, 61.8% of the variability was explained (genetic algorithm).

Conclusions: Clinical factors had the largest impact on the required dose of acenocoumarol in pediatric patients. Including genetic factors in the algorithm, and especially VKORC1, increased this with 16.8%.

448. Rural and appalachian disparities in neonatal abstinence syndrome prevalence and access to opioid abuse treatment

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Background: Prevalence of Neonatal Abstinence Syndrome (NAS) is increasing due to the rise in prescription and illicit opioid use. Rural states like Kentucky have been disproportionally impacted by opioid abuse, but it is unclear whether NAS burden and access to treatment is also disproportionate.

Objectives: To determine NAS burden nationally and in Kentucky and to examine differences in access to opioid abuse treatment between urban/rural and Appalachian/non counties.

Methods: NAS rates were calculated using national (2013) and Kentucky (2008–2014) National Inpatient Sample (NIS) discharge data, where NAS was identified using International Classification of Disease v9 code 779.5 and live birth codes V30.x-V38.x. Proximity analysis was conducted via mapping from all Kentucky zip code county centroids to nearest opioid treatment facility. Differences in mean distance between nearest type of treatment center in Appalachian and non-Appalachian counties were tested via Mann–Whitney U tests. Differences in mean distance between the nearest type of treatment center by rural classification status were tested via Kruskal–Wallis tests.

Results: NAS cases tripled from 2008 and 2014 in Kentucky counties overall. Rural counties and Appalachian counties experienced a rate of NAS increase per 1,000 births at 2 to 2.5 times higher than urban and non-Appalachian counties between 2008–2014 as well as a greater number of NAS births overall in Appalachian counties. Nationally, NAS rates were nearly 3-times higher in rural areas than in metro areas, and Kentucky's rural NAS rate was nearly 3-times higher than the rural NAS rate nationally. In Kentucky, all opioid treatment facility types were further from rural patients than for urban ($p < 0.001$, all facility types), as well as further for Appalachian compared to non-Appalachian residents ($p < 0.001$, all facility types).

Conclusions: NAS burden disparately affects rural and Appalachian Kentucky counties, while treatment