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 low 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

P10 REPORTING OF OFFSPRING DATA IN DIABETES, HIV INFECTION AND HYPERTENSION TRIALS DURING PREGNANCY: A SYSTEMATIC REVIEW

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Background According to international guidelines clinical trials are conducted during pregnancy to evaluate benefits and risks of medicines for both the mother and her offspring. Consolidated Standards of Reporting Trials (CONSORT) reporting criteria apply to these trials and should include safety data on the offspring. The safety of maternal treatments is a key issue for health care professionals and parents. Diabetes, human immunodeficiency virus (HIV) infection and hypertension are among the most frequent chronic diseases worldwide in women of child bearing potential. The objective of this systematic review was to analyse offspring data reported in clinical trials conducted in pregnant women receiving chronic drug treatment for one of these conditions.
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

P11 NEONATAL AND PAEDIATRIC PROTOCOL DEVELOPMENT AND DRUG SAFETY: POINTS TO CONSIDER FOR RISK MANAGEMENT AND SAFETY DATA COLLECTION

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Background Protocol development for neonatal or paediatric clinical trials needs to take into account the age group specifics of the study population (e.g. pharmacokinetics, reference values for laboratory data and vital signs). Drug safety and risk management for neonatal/paediatric trials require an understanding of how these change throughout childhood. We were interested in reviewing and summarising the literature to identify publications which provide researchers with practical information of how the neonatal/paediatric drug safety profile informs age group specific safety data collection and risk management in the protocol.
Methods Pubmed, Embase and regulatory authority (RA) websites were searched for publications up to 31/12/2018 for children (0–18 years). In addition, the bibliography of included publications was reviewed to identify additional publications.
Results RA websites provided general and disease specific guidance on neonatal/paediatric clinical trials with sections relating to drug safety. No publication was identified describing the practicalities of how the neonatal/paediatric drug safety profile can be included throughout the various sections of a clinical trial protocol. The existing literature was summarised providing an overview of how the neonatal/paediatric drug safety profile supports the development of the various protocol sections. For example laboratory values in the exclusion criteria and safety monitoring sections need to be adjusted for age. Vital sign and psychomotor assessment should be done at least at baseline, trial completion and follow-up. Monitoring of

adverse events of interest requires consideration of how these may present in neonatal/paediatric patients.
Conclusions In order to support the protocol development with regards to neonatal/paediatric drug safety a dual competence in both paediatrics and drug safety is required. This review provides an overview of the practical aspects related to neonatal/paediatric drug safety during protocol development.
Disclosure(s) Nothing to disclose

P12 PUBLIC ANTIBIOTIC AWARENESS CAMPAIGN ORGANISED BY GOVERNMENT SIGNIFICANTLY REDUCED INAPPROPRIATE ANTIBIOTIC USE IN PAEDIATRIC PRIMARY CARE SETTINGS

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Serbia, like most other countries in southern Europe, has struggled with high rate of antibiotic consumption. Previous results showed that most of antibiotics were prescribed inappropriately, mainly for influence - like illness[1]. The first short term media antibiotic awareness campaign (AAC) was held in 2011. and 2014. respectively. Shortly after, Ministry of Health, Republic of Serbia in November 2015 has started with public AAC simultaneously across all regions of Republic of Serbia.

Apart from media, the campaign included education, producing national guidelines, as well as regulations. The education goals for public (preschool and school children, parents, pregnant women, students) and healthcare professionals (paediatricians, nurses, pharmacists, etc.) was based on results of analysis of antibiotic consumption in children from 2007.to 2014. which methodology was published previously.[1] Media campaign included public relations activities, press conferences, billboards, printed materials, etc.

In 2017. prescribing rates of antibiotics per 1000 children in primary care settings were decreased by 18% comparing to 2011., after first and by 12% comparing to 2014. when second short term media campaign was performed. After the third, government organised public AAC, prescribing rates of antibiotics per 1000 children in primary care settings were decreased by 6% for only one year (2017 vs. 2016) in all age groups from 2 months up to 17 years. Significant decrease of prescribed rate of antibiotics per 1000 children during 2017. was recorded for indication with policy of delayed or no antibiotic prescription recommended by guidelines. Seasonal oscillations showed that highest prescribing rate during the winter months (I and the IV quarter) of 2017. is in line with the lowest prescribing rate during the summer months (II and the III quarter) from 2007. up to 2013.

We can conclude that continuous antibiotic awareness campaign supported by state government is the best way to achieve successful results.

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P13 SERIOUS ADVERSE REACTIONS AND OFF LABEL AND UNLICENSED DRUG USE IN CHILDREN – DECADE OF PHARMACOVIGILANCE STUDY IN SERBIA

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Background Off label (OL) and unlicensed (UL) drug use in children is a widespread global problem. Previous study showed that only 66% of all available drugs for children is with licence in Serbia.[1] Data on safety of medicines in children remain lacking, so the key intervention for the effective use of medicine is safety monitoring. Therefore, the aim of this study is to evaluate safety implication of OL and UL drug use in children up to 12 years old.
Method We conducted a retrospective study based on reports of suspected adverse reactions (ADRs) collected from 2008. to 2018. by Medicines and Medical Devices Agency of Serbia, using the Medical Dictionary for Regulatory Activities and organized by System Organ Class. Sources of information about medicines including vaccines (license, drug formulation, etc.) are the Summary of Product Characteristics and Serbia´s official drug registry.
Results Within 10 years, we observed 1595 ADRs. Vaccines, antineoplastic and antimicrobial drugs were the most frequently pharmacotherapeutic subgroups involved. Out of total number of observed ADRs, 433 (28%) were serious; 189 of them led to hospitalization, 31 to life threatening conditions and 7 were fatal. More than a half (63%) of serious ADRs were detected in children for the age group of 28 days - 23 months, followed by the age group of 2 to 11 years (34%) and finally by age group of 0 to 27 days (3%). Serious ADRs were detected in boys (55%) as well as in girls (45%). Out of total number of registered only 3% (46) of ADRs were associated with off-label use; 18 of them were serious, 7 led to life threatening conditions and 3 were fatal.
Conclusion This research provided new insight on the factors such as OL and UL use, that might increase the risk of serious ADRs in children.

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P14 PHARMACOVIGILANCE IN PEDIATRIC PATIENTS: THE CHALLENGE OF IDENTIFYING NEW SIGNAL

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Introduction The importance of reporting adverse drug reactions (ADRs) is well known. However, the reporting rate is very low, and therefore, identifying new signal is challenging.
Objective To create an interventional program in order to improve reporting rate and trying to identify new signal.