OBJECTIVES: Compare pregnancy rates post-initiation of 84/7 (84 days levonorgestrel/ethinyl estradiol) to 21/7 or 24/4 (24 days EE/progestin plus 4 days placebo) oral contraceptive regimens over the course of 1 year. METHODS: Data for this study were obtained from the US i3 InVisionTM database from May 2009 through December 2011. Patients enrolled if they received the medication of interest (first use as index date), were age 15-40 on index date, and had continuous insurance coverage from index date through 1 year post index date. The 84/7 EE cohort was matched 2:1 without replacement to the 21/7 placebo cohort based upon age, sex, region, busisness of insurance, insurance product and year of index date. Differences in pregnancy rates in the 1 year post index date were compared using a chi-square statistic.

RESULTS: There were 12,923 individuals in the 84/7 EE cohort and 1,276 individuals in the 21/7 placebo cohort. Matching resulted in a final sample of 3,732 (1:48 in the 84/7 EE cohort and 1,244 in the 84/7 placebo cohort) for a successful match rate of 97.5%. Patients in the matched cohort had a mean age of 26.98 years (SD=7.5), resided predominantly in the South (55.5%) or Midwest (21.14%) and were most commonly insured with point of service insurance (80.47%) or an exclusive provider organization (12.94%). Pregnancy rates in the 1 year post-initiation on an OC were found to be statistically significantly lower for initiators of 84/7 EE compared with 84/7 placebo (3.01% v 4.50%; P<0.0001).

CONCLUSIONS: Pregnancy rates were significantly lower in women using a 84/7 EE regimen compared with a 84/7 placebo regimen.

PIH46

OUTCOMES OF DRUG USE DURING PREGNANCY: A NOVEL DATABASE IN THE NETHERLANDS TO STUDY DRUGS RISK ON THE YET UNBORN
Hoogewielen LMA1, Hukkelhoven CWP2, Schiere AM2, van Wijngaarden RPT2, Herings N1
1Gramophone Institute for Drug Outcomes Research, Utrecht, The Netherlands; 2The Netherlands Perinatal Registry, Utrecht, The Netherlands

OBJECTIVES: Insight into comorbidities and detailed drug exposure before and during pregnancies as well as outcomes in children is pivotal to provide pharmacovigilance and pharmacogenetic pregnancy outcome studies. A database was constructed that captures both detailed drug exposure before and during pregnancy as well as pregnancy related information and outcomes of the neonate (and other relevant clinical information) by linking the Netherlands Perinatal Registry (PNR) with the PHARMO RLS.

METHODS: The PHARMO RLS is a comprehensive nationwide registry, including data from the midwifery, the obstetrics and the neonatology/pediatrics registry. The PHARMO RLS includes data from multiple health care databases such as drug dispensings, hospitalizations, GP data and clinical laboratory measurements and covers approximately 20% of the Dutch population. Both databases were linked using different record linkage techniques. Key variables (e.g. maternal age, gestational duration, parity, singleton birth) were assessed to determine comparability between the PNR and the linked PNR-PHARMO RLS pregnancies.

RESULTS: The linkage is unique. 1,453,504 pregnancies registered between 2000 and 2007 in the PNR with PHARMO RLS resulted in a cohort of 151,250 women with complete drug and clinical data available for 203,972 pregnancies. Linked pregnancies were comparable with all pregnancies. In 67% of all pregnancies at least one prescription drug was used. The most frequently used drugs included anti-anemic preparations (26%), antibacterials (20%) and gynecologic anti-infectives (14%). As dispensing date, duration of use and dose are recorded in the PHARMO RLS, exposure per trimester can be assessed and related to birth outcomes or congenital defects. Comparability between the PNR-PHARMO RLS on pregnancy rates were comparable with all pregnancies.

CONCLUSIONS: The potential for this study to explore detailed drug utilization and comorbidities of mothers before, during and after pregnancy is evident. This enables to study potential adverse effects that might impact pregnancies or child development later on.

PIH47

ANALYSIS OF THE FORMULARY PROVISION OF CHILDREN IN UKRAINE
Kacherys Y1, Zaliisky O2, Chavus H2
1State Formulary contains a special section for children
2Danylo Halytsky Lviv National Medical University, Lviv, Ukraine; 3Pharmacy, Lviv, Ukraine

OBJECTIVES: Formulary system of medical provision is created in Ukraine. In the Order of MOH of Ukraine No 529 “About Creation of Formulary System for Health Institutions” was approved in 2009. The Fourth edition of State Formulary approved in 2012. METHODS: We used comparative analysis of drug information for children from all editions of the State Formulary (2009-2012) were conducted. The State Formulary contains a special section for children “Neonatology medicines.”

All medicines in this section are classified into 11 pharmacological groups. RESULTS: In 2009 were included 95 medicines for children, 2010 – 91, 2011 – 81, 2012 – 76 respectively. For the first time in 2011 the State Formulary were included three preparations for replacement surfactant therapy for newborns with respiratory disorders. It’s Ukrainian-made preparation “Neosurf” emulsion, and two imported medicines “Infasurf” suspension, and “Curosurf” suspension. We evaluated the costs of treatment were 203 542 UAH, 404 54 €, 630.6 € respectively. Since 2007 for the state budget were purchased Curosurf, from 2008 – Neosurf, and 2011 – Infasurf. We found regional differences concerning the financing of these medicines. Curosurf funded by 11% of needs in Dnipropetrovsk, Donetsk regions, 10% - in Kyiv, 8% - in Lviv, 5% - in other 37 regions of Ukraine.

CONCLUSIONS: The results showed that in the State Formulary 2009-2012 the number of medicines for children was decreased by 22%. The costs of treatment surfactant is high enough. It is established that the highest compensation surfactants were in the Crimea, Donetsk, Dnipropetrovsk, Lviv regions. Is grounded that it is necessary the creation special Ukrainian Formulary for children, which will include a larger number of children’s medicines.

PIH48

SERVICE USES AND COSTS OF CHILD AND ADOLESCENT PSYCHIATRIC PATIENTS TREATED WITH ANTIPSYCHOTICS IN TAIWAN
Chang HC1, Mccrone P1, Su K2
1China Medical University, Taichung, Taiwan; 2China Medical University, Taichung, Taiwan

OBJECTIVES: With the widespread of second-generation antipsychotics (SGAs) used among children and adolescents, the treatment effectiveness has been of great interest alongside with the efficacy and safety in this population. The study was designed to assess whether SGAs are associated with reduced service uses and service costs in the real world. Factors associated with health service costs were also examined.

METHODS: The claim data (PIMC) of 1996-2008 from the National Insurance Bureau of the National Health Insurance (NHI) of Taiwan was used. The claims were extracted from the National Health Insurance Research Database (NHIRD) and limited to use of antipsychotics and last for over 12 months during this period were included for analysis. Comparisons were made between 8 SGAs and 2 first-generation antipsychotics (FGAs). Changes in service uses and service costs (all-cause, psychiatric service use, non-psychiatric service use, and medication costs) were compared. Mann-Whitney U tests and 95% confidence interval were used to examine differences. Multivariate regressions with propensity scores adjustment were performed to explore factors associated with psychiatric service costs.

RESULTS: A total of 943 encounters were included and results showed reduced psychiatric service uses in SGAs group, but not psychiatric services costs in the SGAs group. Antipsychotics service costs were nearly 6-fold higher in the SGAs group, but the antipsykinmedian-
OBJECTIVES: In developed countries, rotavirus disease causes significant burden, both on health care systems and society. Two effective and well-tolerated rotavirus vaccines were marketed in Europe & USA in 2006. Since then, there have been significant discrepancies in policy decisions and health technology assessments (HTAs) relating to the inclusion of universal rotavirus vaccination in developed countries. METHODS: A comprehensive literature search and critical appraisal of rotavirus HTAs, statements and policy decisions was performed in 20 developed countries (17 Western European countries, USA, Canada & Australia). RESULTS: Rotavirus HTAs/statements have been issued in 15 out of 20 countries included in this study. In mid-June 2012, 8 countries have implemented rotavirus vaccination programmes; 2 countries have not recommended vaccination; 2 countries have recommended and funding processes are ongoing. In all other countries, the rotavirus decision-making process has not started or is underway. Despite significant differences in HTA criteria, methods and processes across countries, there is consistency in the key parameters impacting policy decisions: burden of disease, economic evaluation, vaccine efficacy and safety. Positive or negative outcomes largely depend on varying interpretations of similar evidence. For example, several National Immunisation Technical Advisory Groups and policy makers considered evidence pertaining to rotavirus disease burden (morbidity) as significant enough to justify its inclusion in the national immunisation programme, whereas others considered it as insufficient since rotavirus mortality is low.

CONCLUSIONS: This study highlights the need for a common decision analytic framework to foster structured and transparent HTAs and improved decision-making processes, with the ultimate aim of enhancing future European population access to rotavirus vaccination.

TRENDS IN POST-MARKETING COMMITMENTS RELATED TO PREGNANCY AND LACTATION

Albanzo JD, Roberts SS, Benter U, Whitehouse J

OBJECTIVES: Five years ago the United States government passed the Food and Drug Administration Amendments Act of 2007 (FDAAA) expanding the FDA’s authority to require post-marketing studies. Prior to this, pregnancy registries, a valuable tool for studying the teratogenicity of newly marketed drugs, were primarily voluntary and of limited scope. Both the FDA (2002) and EMA (2005) issued guidance on post-marketing studies during pregnancy. The objectives of this research were to evaluate the impact of FDAAA on childbearing populations and trends in post-market commitments/requirements (PMCs/RS). METHODS: Publicly available FDA databases were analyzed to identify all new molecular entities approved between January 2008 and May 2012 and associated PMC/RS and REMS related to pregnancy/lactation in humans. Data was augmented from the FDA’s list of pregnancy registries and assigned pregnancy drug category. RESULTS: Over the 4.5 year period, the FDA approved 125 new compounds (100 drugs, 25 biologics). Overall 78% had at least one PMC/RS (79% of drugs, 84% of biologics). The proportion of new drugs with a pregnancy related PMC/RS was 9% overall and increased over time from 5% in 2008 to a peak of 19% in 2010 before declining to 4% in 2011. Pregnancy categories were B8 (26), C4 (17), D7 (9), X1 (4); of the 57 pregnancy categories listed on the FDA’s website, 13 are associated with drugs approved during the time period under study however only 6 of these were PMC/RS and all were for category C compounds. A single category X drug had a pregnancy/lactation related PMC/RS. CONCLUSIONS: The majority of pregnancy categories for medicines with FDA assigned pregnancy classification X are not more likely to have REMS or PMC/RS despite their known potential for reproductive harm. Population characteristics such as gender, age and indication for the prescription are powerful indicators of when PMC/RS are necessary.

REVIEW OF ALL PRODUCTS AUTHORIZED BY THE EUROPEAN MEDICINES AGENCY FROM 1995 TO 2011 IN REGARD TO PEDIATRIC INVESTIGATION PLAN APPLICATIONS

Mouchet J, Acquaro C, Emsley M, Maier W

OBJECTIVES: Pediatric Investigation Plans (PIPs) were introduced by the European Commission in January 2007 to help ensure that medicines for children are included in the mainstream drug development process in Europe. The objective of this study was to review all authorized products by the European Medicines Agency (EMA) from 1995 to 2011 to identify products with a pediatric indication, and (2) products with a PIP application. METHODS: On the EMA website, the European Public Assessment Reports (EPARs) were searched manually. For each product, the Summary of Product Characteristics (SmPC) was reviewed to explore quotes relative to any potential pediatric indication. The products were categorized in four categories: C1=adult indication only; C2=safety/efficacy not studied in children; C3=adult and pediatric indication; and C4=pediatric indication only. For each product, the EMA pediatric database was searched for PIP applications. RESULTS: A total of 633 products authorized by the EMA (286 and 352 in 2001-2007). From 1995 to 2006, 33.53% of the authorized products presented a lack of evidence in the pediatric population as did 57% in the period of 2007-2011. In total, 746 PIP applications were identified (products authorized and under development; 21% was requested at the time of the product authorization for the regulation (1995-2006) and for 19% of the products authorized after the EU pediatric regulation. CONCLUSIONS: The categorization of authorized products according to the SmPC quotes showed that many products had potential pediatric indications being the recognition of a need for a common decision disability progression and an increase in caregiver burden. METHODS: THE EVOCOST study is a prospective 12-month multicentre cohort study recruiting community-dwelling moderate AD patients in Spain, Visits were scheduled at baseline, 3 and 12 months according to routine clinical practice. Data on socio-demographic characteristics, disease history and comorbidities were collected at baseline. Clinical evolution and caregiver burden were measured using the following assessment tools: Global Deterioration Scale (GDS) for severity, Mini-Mental State Examination (MMSE) for cognition, Clinical Global Impression (CGI) for global status, Basic and Instrumental Activities of Daily Living (BADL and IADL) for functional disability, brief Neuropsychiatric Inventory (NPI-Q) for behaviour, Zanit Burden Interview (ZBI) and time spent on care for caregiver burden. Changes from baseline, 3 and 12 months were assessed using Wilcoxon signed rank tests. RESULTS: A total of 209 patients were included at baseline, 76.1% of them were women, with a mean age of 78.4 years and a mean MMSE of 15.2. At the 12-month visit, data were available on 144 patients (69% of patients lost to follow-up rate 16.8%). Clinical symptoms worsened significantly during the 12-month study follow-up in terms of severity (GDS0=0.5, p<0.001), cognition (AMMSE=−2.9, p<0.001), global status (ACG=−0.3, p<0.001), and function (ΔBADL=−1.7, p<0.001; ΔIADL=−1.2, p<0.001). No significant change was observed for NPI/Q-15 (ΔNPI=-0.325; ΔNPI-distress =0, p=0.375). Caregiver burden also worsened significantly (ΔZBI=−2.5, p=0.002; Δtime spent on care =+66h per month, p<0.001). CONCLUSIONS: The EVOCOST study illustrates the well patient clinical worsening and the increase in caregiver’s burden associated with management of moderate AD.

EFFECT OF COGNITIVE BEHAVIOURAL THERAPY IN MULTIPLE SCLEROSIS

Frank-Garcia A, Salva A, Leonc C, Gimeno V, Milesa D, Bineau S

OBJECTIVES: To assess the clinical effectiveness of cognitive behavioural therapy (CBT) in patients with multiple sclerosis (MS) fatigue. METHODS: Embase® and Cochrane databases were searched up to June 2012 to identify randomised controlled trials published in English evaluating effect of CBT (disseminated by any method) in patients with MS fatigue. Eligibility of trials was assessed by two reviewers with any discrepancy reconciled by a third, independent reviewer. To compare CBT with other therapies, random-effect meta-analysis was conducted using standardised mean difference change from baseline to end of follow-up in fatigue score. RESULTS: Four studies of 107 retrieved citations met pre-defined inclusion criteria. Two studies compared CBT to no therapy and one study each compared CBT to relaxation therapy (RT) and supportive-expressive group therapy (SEG). All studies were well conducted and no significant heterogeneity was observed between studies for demographic characteristics. Weighted mean difference (WMD) demonstrated statistically significant reduction for change in fatigue score at 2 months from baseline with CBT versus no therapy (-7.04; p<0.001). When CBT was compared to RT, WMD was -4.29 (p=0.001) at 2 months, -2.74 (p=0.013) at 5 months, and -2.74 (p=0.027) at 8 months indicating that CBT group improved significantly more than RT group and this improvement was sustained over a period of time. Further,