Methods: The General Practice Research Database was used to identify cohorts of current antipsychotic users with psychiatric illness, psychiatric diseased nonusers, and matched healthy controls. Outcomes included cardiac mortality, SCD (three separate definitions), coronary heart disease (CHD), ventricular arrhythmias (VA), and overall mortality (excluding suicide). Sensitivity analyses were conducted for age, dose, duration, and psychiatric disease. Poisson regression was used to estimate relative rates (RRs) and 95% confidence intervals (CIs).

Results: Of 183,392 antipsychotic users (including 20,954 olanzapine users), 544,726 healthy controls, and 193,920 psychiatric nonusers were identified. There was no increased risk of all-cause mortality found in patients treated with olanzapine vs. psychiatric nonusers (adjusted relative risk [aRR]: 1.04, CI, 0.93–1.17), vs. an elevated all-cause mortality risk for all antipsychotic users (aRR: 1.75, CI, 1.64–1.87). There was a higher rate of cardiac mortality (aRR: 1.53, CI, 1.12–2.09) in patients treated with olanzapine vs. psychiatric nonusers, consistent with results for both atypical and typical antipsychotics. There was no increased risk of CHD or VA among patients treated with olanzapine vs. psychiatric nonusers, consistent with results for atypical antipsychotics and in contrast to patients treated with typical antipsychotics. Patients aged 30–64 had higher risks of all-cause mortality and cardiac mortality than those aged 65 and greater.

Conclusions: Patients treated with olanzapine were not found to be at increased risk of overall all-cause mortality vs. psychiatric nonusers. However, patients treated with atypical and typical antipsychotics, including olanzapine, had a higher risk of cardiac mortality vs. psychiatric nonusers. Limited SCD cases were available for evaluation.

971. Detection and Magnitude of Methylphenidate Abuse and Misuse Using Vigibase and Correlation with Level of Use in Europe

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Background: Methylphenidate (MPH) is a psycho-stimulant approved for the treatment of attention deficit and hyperactivity disorders. Recently, consistent data suggesting an increase of MPH abuse were identified in France with intravenous administration of crushed tablets. In the same way, a rise in MPH global availability has been identified in France and other European countries.

Objectives: To assess the relationship between the levels of consumption of MPH in European countries and MPH misuse or abuse reported to Vigibase, the WHO global ICSR database

Methods: Data were collected for all Continental European countries for the period 1994–2010. Data on MPH utilization were researched and extracted from national consumption statistics. Using Vigibase, individual case reports of MPH abuse, related with the WHO-ART terms "drug abuse" or "drug dependence" according to Caster's method (Caster 2011), were extracted. Trends in MPH abuse reporting were analysed using a bayesian confidence propagation neural network method, providing a statistical indicator, information component (IC) (Koren et al., 2011).

Results: Despite an extensive variability in the consumption levels, there is a common trend of growing MPH utilization in Europe, with a sharp increase since 2005 (+425% in Denmark (0.8–4.2 DID), + 67% in France (0.18–0.30 DID), +116% in Germany (1.0–2.16 DID) and +122% in Netherlands (2.04–4.53 DID) between 2005 and 2009). Preliminary results from VigiBase showed an increasing relative reporting rate over time for European reports with methylphenidate and drug abuse using the Information Component (IC), which is computed as the logarithm of a shrunk observed-to-expected ratio.

Conclusions: Analysis of the trends in MPH consumption, together with preliminary findings from Vigibase, is consistent with the existence of a positive relationship between the recent MPH increasing availability and the growing frequency of reported dependence-related ADRs. In a way to better understand and characterize this association, a quantitative in-depth analysis of these preliminary results will be undertaken.

972. Changes in Diversion Rates Following the Introduction of a Reformulated Extended Release Oxycodone Product

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Background: In August 2010, Purdue Pharma introduced reformulated extended release (ER) oxycodone (ORF) that is more difficult to crush and that forms a gel when dissolved and is intended to deter abuse.

Objectives: This study examines whether there was a decline in rates of diversion of ER oxycodone manufactured by Purdue following the introduction of ORF using data collected from drug diversion agents participating in the RADARS® System, an established surveillance system

for prescription drug abuse. Other prescription opioids were used as a comparator.

Methods: Diversion cases were obtained on a quarterly basis from law enforcement agencies. The Diversion Program surveyed 300 reporters in 50 states, covering 61% of the US population in the 3rd quarter of 2011. Diversion rates per 100,000 population and per 1,000 unique recipients of dispensed drug (URDD) were calculated for each quarter. October 1, 2008 through September 30, 2010 was considered the period before, and October 1, 2010 to September 30, 2011 the period after, introduction of ORF. The mean rate of drug diversion was compared before and after the introduction of ORF for ER oxycodone and other prescription opioids using negative binomial regression.

Results: There was a 47% decline (95% CI: 34–57%) in the ER oxycodone diversion population rate from 0.35 per 100,000 before to 0.18 per 100,000 after the introduction of ORF. There was a 45% decline (95% CI: 32–57%) in the ER oxycodone diversion URDD rate from 1.45 to 0.79 per 1,000 URDD before vs. after introduction of ORF. There was no significant change in diversion rates for other opioids.

Conclusions: These findings indicate that the introduction of the new formulation was followed by a decline in diversion of ER oxycodone manufactured by Purdue that did not occur for other prescription opioids. The decreased diversion of ER oxycodone to illegal channels suggests a decline in demand for the new formulation vs. the original formulation.

973. Risk Factors of Medication Non-Adherence in Depression and Anxiety, Preliminary Results

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Background: Depression has been shown a risk-factor for non-adherence to medication regimens. Non-adherence undermines optimal treatment of depression, anxiety and co-morbid conditions. Because non-adherence is difficult to identify in clinical practice, insight into risk factors of non-adherence is important to reveal non-adherence and optimise therapy.

Objectives: The aim of this study was to assess the rate of non-adherence, and risk factors for non-adherence in the Netherlands Study on Depression and Anxiety (NESDA), a large cohort study sample in a naturalistic setting.

Methods: All participants who used medication (n = 1899) at the 4 years follow-up of the NESDA cohort of 2,402 participants (age 22–69 years) were selected. The effects of patient-, disease-, and treatment-related factors on non-adherence, were analysed by means of univariate and multivariate regression. Adherence was assessed using the Medication Adherence Rating Scale (MARS).

Results: In univariate analysis, risk factors for non-adherence were lower age (OR = 1.16; $p < 0.001$), low social support (OR = 1.23; $p = 0.03$), higher IDS score (OR = 1.12; $p = 0.003$), higher neuroticism scores (OR = 1.11; $p = 0.023$), being employed (OR = 1.25; $p = 0.03$) and having a depression diagnosis (OR = 1.25; $p = 0.03$). In multivariate analysis, risk factors for non-adherence were lower age (OR = 1.19; $p < 0.001$), low social support (OR = 1.11; $p = 0.01$), higher IDS score (OR = 1.18; $p = 0.005$) and male gender (OR = 1.24; $p = 0.049$).

Conclusions: In this large study sample in a naturalistic setting, lower age, less social support, higher depression severity and male gender, are all risk factors for non-adherence. Clinicians should recognise these risk factors and apply adherence-improving strategies to improve patient outcome.

974. Antiepileptic Drugs and the Risk of Acute Hypothyroidism

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Background: Disturbance in thyroid function hemostasis associated with the use of antiepileptic drugs (AED) has been reported. However, AEDs related hypothyroidism remained controversial.

Objectives: To investigate the association between exposure of AEDs and hypothyroidism.

Methods: Electronic data sets containing 2 million individuals, which were randomly sampled from the National Health Insurance Research Database (NHIRD) in Taiwan, were used for this study. We selected thyroxine as an indicator of hyperthyroidism and performed a prescription sequence symmetry analysis (PSSA) from 2001 to 2009. The ratio of the patients initiating each AED after vs. before initiating thyroxine was described as the crude sequence ratio (SR). The adjusted SR and 95% confidence intervals (CI) were derived from dividing the crude SR by the null-effect SR. Two indicators, amiodarone and methimazole were selected to be internal and external standards respectively to test the sensitivity and specificity of PSSA. Besides, case–control (1:20) design were also conducted to test the robustness of the results of PSSA.

Results: In older AEDs, phenytoin (adjusted SR, 1.92; 1.55–2.39), carbamazepine (1.20; 1.01–1.46) and valproate