

this disease. **METHODS:** Network Meta Analysis using Winbugs (Bayesian, Markov chain model using dedicated software), which allows to make an informed decision on the clinical effectiveness ranking of some of the healthcare technologies (active substances) used in the treatment of Pulmonary Arterial Hypertension (PAH). The ranking is then compared with the ICER, currently in use by UK NICE and the treatment guidelines set by the UK NHS. **RESULTS:** Using the above methods, the ranking of healthcare technologies (active substances) used in PAH has been established and different scenarios have been identified, with regard to increasing efficiency of public healthcare expenditure on PAH. **CONCLUSIONS:** The various scenarios proposed in this analysis, once confirmed, will contribute to a gain in efficiency of public healthcare expenditure on PAH in the UK.

#### PCV176 DEVELOPMENT OF MEDICAL AND TECHNOLOGICAL DOCUMENTS ON STANDARDIZATION OF MEDICAL CARE IN CARDIOVASCULAR DISEASES IN UKRAINE

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**OBJECTIVES:** Cardiovascular diseases are the leading cause of death and disability in the population of most countries, including Ukraine. Ukraine faces a significant contribution of cardiovascular diseases in the formation of disability-adjusted life year (DALY): men – for 27%, women – for 33% (2013). **METHODS:** At the end of 2014 the multidisciplinary working groups on the development of guidelines and protocols on different areas of cardiovascular diseases were approved. According to the results of a systematic literature review conducted in the databases Medline, PubMed, DynaMed, G-I-N etc. ESC, ACCF/AHA and NICE guidelines were selected for adaptation in Ukraine. **RESULTS:** During the meetings the working groups discussed the opportunities to meet the guidelines' recommendations in real conditions in Ukraine. For example, there were debates concerning mandatory evaluation of highly sensitive troponin on the 99th percentile among patients with NSTEMI, or the appointment of new antiplatelet drugs with high evidence base, which were not registered in Ukraine at this stage (eg. Prasugrel or Argatroban). The adapted guidelines for the treatment of acute and chronic coronary artery disease included separate sections with recommendations for revascularization from 2014 ACCF/AHA guideline, which allows the doctor to stratify patient against the risk of complications and identify high-risk patients who should be enforced urgent percutaneous coronary intervention. As a result of the work there will be prepared adapted clinical guidelines and unified clinical protocols on Acute Coronary Syndromes Without ST Segment Elevation, Stable Coronary Artery Disease, Pulmonary Hypertension, Prevention of Cardiovascular Disease, Dyslipidemia, Heart Failure, and Atrial Fibrillation. **CONCLUSIONS:** Development of medical and technological documents on standardization of medical care in cardiovascular diseases will allow to harmonize Ukrainian practice with international recommendations and timely provide quality medical care for the relevant areas.

#### PCV177 HEART FAILURE MANAGEMENT: A NATIONWIDE POPULATION-BASED COHORT STUDY USING THE FRENCH EGB DATABASE

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**OBJECTIVES:** To describe and analyze heart failure (HF) patients, disease pathway and related healthcare resource use and expenditures in France. **METHODS:** Analysis was based on EGB ("Echantillon Généraliste des Bénéficiaires") database, a permanent random sample (1/97) of the French national healthcare insurance system database (SNIIRAM), linked with the national hospital discharge summary database (PMSI). Patients were selected on the following criteria: HF classified as long-term disease (ALD scheme) in 2012 and/or at least 1 HF hospitalization (ICD-10 codes) on 2008-2012 period and/or at least 3 reimbursements of HF recommended drugs (including beta-blockers (BB), angiotensin-converting-enzyme inhibitors (ACEi), angiotensin-receptor-blockers (ARB), diuretics, digoxin, ivabradine) in 2012. **RESULTS:** 12,981 patients (average age: 74.8 years; 51.6% of men) were included, representing a HF prevalence of 2.2% in the total French population. Most of patients visited a general practitioner (93.1%) on regular basis (9.3 visits/year), but only few of them visited a cardiologist (37.0%) through the year (0.67 visit/year). HF recommended drugs were not prescribed to all patients (BB: 60.3%; ACEi/ARB: 53.3%; diuretics: 46.0%) and the recommended triple therapy (BB+ACEi/ARB+diuretics) was prescribed to only few of them (16.4%). Almost half of patients (47.3%) were hospitalized within the year (1.3 hospitalizations/year), with a quarter of these hospital stays related to HF (27.0%). The annual age-standardized mortality rate was 4.6 higher than in the full EGB database (939.0 versus 71.1 per 10,000 persons). Annual average healthcare costs were 7,956€/patient, mostly driven by hospitalizations (3,683€; 46.3%), drugs (1,287€; 16.2%), paramedical visits (980€; 12.3%) and medical visits (464€; 5.8%). **CONCLUSIONS:** Patients are not optimally managed for their HF, with a limited healthcare resource use. Despite a high rate of hospitalization, cardiologist visits remain at a very low frequency in this HF population. Better referring these patients to cardiologists should improve their management and optimize drugs prescription as recommended in the guidelines.

#### PCV178 INVESTIGATING THE RELATIONSHIP BETWEEN "SEVERITY OF ILLNESS" AND THE "MODIFIED RANKIN SCALE" IN ISCHEMIC STROKE PATIENTS WITH RESPONSE MAPPING

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**OBJECTIVES:** To investigate the relationship between the APR-DRG severity of illness index (SOI) used to determine the reimbursement/payment level for stroke

hospitalisation, and the modified Rankin Scale (mRS), the most frequently used outcome measure in stroke trials. **METHODS:** Data from all ischemic stroke hospitalizations from a teaching hospital in Belgium were collected between 2006 and 2009. Data collection included the SOI, patient characteristics (age, gender), risk factors (hypertension, smoking, hypercholesterolemia, diabetes, CAD, PAD, previous stroke), clinical parameters (aorta-atherosclerosis, cancer, TOAST (large-artery atherosclerosis, cardioembolism, small-vessel occlusion, other), microbleeds, atrial fibrillation, akinesia/hypokinesia, endocarditis, MI), functional scales (NiH, mRS), repeat events. An ordered multinomial regression estimated the relationship between the SOI and these covariates. Using the regression parameters and the mean value of the other covariates, predicted values were generated for each combination of the mRS and the SOI. Monte Carlo simulations generated a set of predicted SOI values per patient (response mapping). Data from 2010 and 2011 were used for validation of the regression model. **RESULTS:** 559 hospitalizations were used for the regression analysis. Factors that were discriminating in predicting the correct SOI category were the mRS ( $p < 0.001$ ), age ( $p = 0.0017$ ), NIH at arrival in hospital ( $p < 0.001$ ), TOAST ( $p = 0.0129$ ), atrial fibrillation (0.0217) and repeat in-hospital event ( $p = 0.0031$ ). Generating Monte Carlo predicted values demonstrated good concordance across SOI levels at the population level (2.3% vs 2.0% categorized in SOI1, 49.8% vs 50.3% in SOI2, 32.9% vs 31.4% in SOI3, 15.4% vs 16.0% in SOI4, for the true and the simulated proportions respectively), and the root mean-squared error was 0.33. Validation of the data with 588 hospitalizations from 2010 and 2011 confirmed the good fit of the model. **CONCLUSIONS:** Factors affecting the reimbursement/payment level of a stroke admission are age, location of the ischemia, atrial fibrillation, scores on stroke functional scales and new in-hospital events.

#### PCV179 IRON DEFICIENCY IN PATIENTS WITH CHRONIC HEART FAILURE: A SYSTEMATIC LITERATURE REVIEW

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**OBJECTIVES:** Iron deficiency (ID) is highly prevalent in chronic heart failure (CHF) patients and imposes a significant disease burden for CHF patients with enormous impact on their outcome. Thus, this study was designed to identify epidemiological data, screening and treatment guidelines, costs as well as outcome of intravenous iron treatment in patients with CHF and iron deficiency. **METHODS:** A comprehensive literature review was undertaken for all publications from 1998 to September 2014 using Medline, EMBASE, Cochrane, Science Direct and Pubmed databases, comprising English and German articles. The review focused on studies based on patients with chronic heart failure and iron deficiency, with or without anemia. Articles were systematically selected if they included data for iron deficiency on at least one of the following criteria: epidemiology, screening and treatment guidelines, costs, clinical outcomes. **RESULTS:** Database search yielded 5,132 articles and 55 additional articles were identified via secondary hand searches. Of the 73 eligible articles; 30 provided information on epidemiological data, 14 on screening and treatment guidelines, 15 on costs and 14 on clinical outcomes. The prevalence of CHF ranges between 0.88-6.4%. Out of these, 8-53% suffer from iron deficiency depending on the disease severity (New York Heart Association classes - NYHA) of heart failure. According to the ESC Guidelines 2012 intravenous iron may be considered to improve symptoms, quality of life and exercise capacity based on the data of FCM (FAIR-HF, CONFIRM-HF-based on 456 patients). Considering the included studies of this review, healthcare expenditure on CHF consumes 1-2% of the total healthcare budget. CHF patients with ID induce higher healthcare costs compared to non-iron deficient patients (+24%). **CONCLUSIONS:** CHF represents a major and growing public health problem and is often associated with ID as co-morbidity. IV iron can be an option to improve outcome (patient status), and reduce health care costs.

#### PCV180 TOTAL CHOLESTEROL (TC), LOW-DENSITY LIPOPROTEIN CHOLESTEROL (LDL-C) AND HIGH-DENSITY LIPOPROTEIN CHOLESTEROL (HDL-C) LEVELS IN PATIENTS WITH HYPERTENSION (HT), DIABETES (DM), BOTH (HT AND DM) AND CHRONIC KIDNEY DISEASE (CKD)

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**OBJECTIVES:** One of the main modifiable risk factors is the blood lipid levels, due to changes in lifestyle and treatment. The aim of this study is to characterize total cholesterol, low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) levels in adults with hypertension, diabetes, HT and DM, and CKD, reported to Cuenta de Alto Costo, 2014. **METHODS:** Descriptive and retrospective study. The information was obtained from the medical records of approx. 53 health insurance companies in Colombia. Data from 2,995,061 patients was used. Stata 13 was used for data analysis. Qualitative variables were described by its frequency distribution. **RESULTS:** 73% of patients had diagnosis of HT, 6.7% of DM, 19.6% of HT and DM, and 30% had CKD. In the population with HT, 30.6% had TC levels in upper limits and 16.4% in a high level. In patients with DM, 54.3% had desirable levels. In patients with both diseases, 25.5% had TC levels in upper limits and 14.1% in a high level. In CKD patients, 15% had high level of TC. Regarding HDL levels, 56.2% HT patients had HDL levels between 40-60mg/dl. Near 36.1% of DM patients had low HDL levels (<40mg/dl), patients with both diseases had similar levels (33.5%). Optimum LDL levels were identified in 42.8% of patients with both diseases (HT and DM), in contrast with 32.8% and 35% HTA and DM patients respectively. Around 9% of both diseases had high LDL levels and 4% had very high LDL levels. 54% of CKD patients had HDL levels between 40-60mg/dl and 27.8% had HDL levels under 40mg/dl. In CKD patients we found that 8.3% had high LDL-C levels. **CONCLUSIONS:** patients with both diseases (HT and DM) had better LDL and TC levels than patients with other diseases, however HDL-C levels under 40mg/dl were higher in this patients group.

## PCV181

## PILOT ASSESSMENT OF PHARMACEUTICALS BASED ON THE EUNETHTA CORE MODEL FOR RAPID RELATIVE EFFECTIVENESS ASSESSMENT

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**OBJECTIVES:** The objective of EUNETHTA is to strengthen the practical application of tools and approaches to cross-border HTA collaboration. Rapid relative effectiveness assessments (REAs) are jointly produced, aiming for efficiency gains and application in a national context. The 5th REA concerned the assessment of Vorapaxar, indicated in the reduction of thrombotic cardiovascular events in patients with a history of myocardial infarction. **METHODS:** Assessment was done using the HTA Core Model for Rapid REA, developed by EUNETHTA. The project duration was 10 months and consisted of a scoping phase of 4 months, followed by an assessment phase of 6 months after the positive CHMP opinion. The project was coordinated by The Dutch Healthcare Institute. The main author of the report was French national authority for health, with the Ministry of Health of Slovakia as co-author. Six other European agencies were involved as reviewers in the different assessment steps. The marketing authorization holder (MAH) was provided the opportunity to review the report. **RESULTS:** Assessment report included 4 domains: health problem, description of the technology, clinical effectiveness and safety, and has been published on 19/06/2015. Vorapaxar is a selective antagonist of PAR-1 (thrombin receptor platelets). The MAH provided TRA 2°P-TIMI 50 trial to evaluate safety and efficacy of vorapaxar as an add-on therapy: vorapaxar + ASA ± clopidogrel versus ASA ± clopidogrel in subjects with a history of myocardial infarction. The results and experiences of the joint assessment will be provided during the ISPOR congress. Also we will discuss the extent to which national adaptation of the report takes place. **CONCLUSIONS:** HTA agencies have shown that they are able to provide a common assessment, using common guidelines, even within the different processes and reimbursement systems they are using. The joint assessment process is evaluated regularly by the agencies involved. This improves the core model and the procedures.

## PCV182

## REVEALED OPPORTUNISM: HOW PHYSICIANS GAME PRIOR AUTHORIZATION PROTOCOLS UNTIL THEY ARE RESCINDED

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**OBJECTIVES:** Prior authorization (PA) is a managerial technique frequently implemented to curtail use of expensive drugs and to improve drug-prescribing quality. PA requirements may incentivize physicians to document adverse effects (AEs) to drugs, sometimes falsely, to meet eligibility requirements for approval. The objective of this study was to evaluate the effect of a PA requirement on documentation rates of AEs of drugs necessary for approval of more expensive drugs. **METHODS:** We conducted a retrospective analysis of physician electronic-reporting behavior of AEs to angiotensin converting enzyme inhibitors (ACE-Is) before and after revocation of a PA requirement for angiotensin receptor blockers (ARBs) during the years 2004-2013 in an Israeli HMO. Data were stratified by newly treated and patients who had been treated for at least one year. The annual rate of AEs to ACE-Is in treated patients (number of reported cases of AEs per 1000 ACE-I treated patients) was calculated for the five years before and after revocation of the PA constraint. **RESULTS:** 151,845 patients met inclusion criteria of the study. AE rates amongst newly treated patients peaked to 10.0 cases per 1000 patients during 2007 gradually falling to 4.6 after the PA requirement was rescinded ( $P < 0.001$ ). Amongst previously treated patients a fall from 5.4/1000 to 1.8/1000 patients was observed. **CONCLUSIONS:** The PA requirement under investigation was observed to be significantly associated with physician propensity for reporting drug side-effects, possibly erroneously. The decline in incidence of reported of side-effects in both subpopulations upon revocation of the PA requirement confirm our suspicion that physicians were incentivized to document side effects to ACE-Is to meet eligibility requirements for approval of ARBs. The risk of gaming behavior in documentation of drug side effects may increase when side effects cannot be substantiated with laboratory tests or diagnostic imaging.

## PCV183

## LIPID MODIFYING THERAPY TREATMENT PATTERNS AND CHOLESTEROL CONTROL AFTER CARDIOVASCULAR EVENTS IN THE UNITED KINGDOM

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**OBJECTIVES:** To estimate real-world utilisation of lipid modifying therapy (LMT) and low-density lipoprotein cholesterol (LDL-C) goal attainment in the United Kingdom. **METHODS:** Individuals with their first and, if present, repeated cardiovascular (CV) related hospitalisations were identified from 2006-2012 Clinical Practice Research Datalink and Hospital Episode Statistics data. Patients >18 years receiving LMT within 180 days before the CV (index) event were followed for 12 months. Patient cohorts were classified as CV Low/Moderate Risk, CV High Risk, and CV Event History. Adherence (medication possession ratio), persistence, switching, and therapy augmentation were calculated for statins, ezetimibe and fibrates during the follow-up period. Attainment of the recommended LDL-C target of <1.8 mmol/L was assessed for risk groups at the index and 12 months afterward. **RESULTS:** Across cohorts, 97% were receiving statins before or at index. Moderate intensity statins were used the most. Medication possession ratio ranged from 0.76-0.79 for statins, 0.72-0.79 for ezetimibe, and 0.58-0.73 for fibrates users. Persistence at 12 months was 51%-52% for statin, 40%-50% for ezetimibe, and 36%-45% for fibrate users. Approximately 2% of statin users switched to new medications, compared

to 11%-16% of ezetimibe users, and 11%-19% of fibrate users. Nearly 4% of statin users augmented their regimen during the year, compared with 56%-61% of ezetimibe and 38%-51% of fibrate users. The proportion of patients not meeting the LDL-C target was 71% and 69% in the CV High Risk and CV Event History cohorts at index, respectively, and 65% for both at 12 months. Approximately 60% of diabetic patients of CV High Risk cohort did not meet LDL-C target at both index and 12 months. **CONCLUSIONS:** Adherence to LMT after CV events was best for statins. Patients receiving fibrates or ezetimibe had higher rates of switching or augmentation. LDL-C goal attainment is low, representing a substantial unmet medical need.

## MENTAL HEALTH – Clinical Outcomes Studies

## PMH1

## DOES USE OF ANTIPSYCHOTICS INCREASE THE RISK OF DEATH: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

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**BACKGROUND:** Use of antipsychotic medications has been associated with increased risk of mortality; however, this association remains questionable given conflicting evidence in the literature. **OBJECTIVES:** We conducted a systematic review and meta-analysis of observational studies to determine whether mortality was higher among antipsychotic (AP) users than AP nonusers. **METHODS:** All articles published from 1970 to March 2015 were identified by comprehensively searching PubMed, MEDLINE, and EMBASE without language restrictions. Three reviewers independently extracted study characteristics and indicators of study quality. Random or fixed effects models were used to calculate pooled odds ratios (ORs) and evaluate heterogeneity (I<sup>2</sup>). **RESULTS:** We identified 17 (13 cohort and 4 case-control) eligible studies with 123,116 deaths. Use of APs was associated with increased risk of all-cause mortality [OR 1.38, 95% confidence interval (CI) 1.12-1.69, I<sup>2</sup> = 91.0%] and significantly higher risk of sudden cardiac death [OR 2.24, 95% CI 1.71-2.92, I<sup>2</sup> = 22.8%]. Compared to AP nonusers, the pooled OR for risk of death was 1.49 [95% CI 1.20-1.85, I<sup>2</sup> = 84.3%] with first-generation antipsychotics (FGAs) exposure and 1.50 [95% CI 1.24-1.81, I<sup>2</sup> = 89.3%] with second-generation antipsychotics (SGAs) exposure. Subgroup analysis reported that current users of FGAs were at a higher risk of mortality [OR 1.78, 95% CI 1.67-1.90, I<sup>2</sup> = 0%]. The pooled OR from current use of SGAs was 1.81 [95% CI 1.44-2.28, I<sup>2</sup> = 85.3%]. Use of FGAs and SGAs among elderly patients was associated with a lower risk of death with a pooled OR of 1.13 [95% CI 0.69-1.85, I<sup>2</sup> = 87.1%] and 1.36 [95% CI 0.90-2.05, I<sup>2</sup> = 91.7%], respectively. **CONCLUSIONS:** APs use, especially current users of SGAs, was associated with an increased risk of all-cause mortality. Exposure to APs was associated with a greater increase in sudden cardiac death. We did not observe a significant difference between subgroup analyses of FGAs and SGAs.

## PMH2

## RISK FACTORS FOR DEMENTIA DIAGNOSIS IN GERMAN PRIMARY CARE PRACTICES

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**OBJECTIVES:** There are several factors that affect the risk of developing dementia. Various studies have shown that defined diagnoses and medications increase or decrease dementia risk. But the relatively small numbers of dementia patients in some of these studies make the interpretation of their results difficult. The aim of this work was to estimate risk factors for dementia in German primary care patients. **METHODS:** The case-control study included 11,956 primary care patients in the age group 70-90 years with first dementia diagnosis during the index period (01/2010-12/2014) (Disease Analyser, Germany). Furthermore, 11,956 controls without any dementia diagnosis were included after individual matching (1:1) to dementia cases on age, sex, type of health insurance and physician. The practice visit records were used to determine 10-year prior index continuous follow-up. Multivariate logistic regression models were fitted with dementia as dependent variable and the potential predictors. **RESULTS:** Mean age of patients and controls was 80.4 (SD: 5.3) years. 39.0% of them were male and 1.9% had a private health insurance. In multivariate regression model, the following variables were significantly related to an increased risk for dementia: diabetes (OR: 1.17; 95% CI: 1.10-1.24), lipid metabolism (OR: 1.07; 1.00-1.14), stroke incl. TIA (OR: 1.68; 1.57-1.80), Parkinson disease (OR: 1.89; 1.64-2.19), intracranial injury (OR: 1.30; 1.00-1.70), coronary heart disease (OR: 1.06; 1.00-1.13), mild cognitive impairment (OR: 2.12; 1.82-2.48), mental and behavioural disorders due to use of alcohol (OR: 1.96; 1.50-2.57). Use of statin (OR: 0.94; 0.90-0.99) and proton-pump inhibitors (PPI) (OR: 0.93; 0.90-0.97) were protective for the incidence of dementia. **CONCLUSIONS:** Risk factors for dementia found in this study were in line with the literature. There is also evidence for a protective effect of statin use with respect to the incidence dementia. Further studies are required to investigate the association between PPIs and a decreased risk of dementia.

## PMH3

## COGNITIVE SYMPTOMS IN MAJOR DEPRESSIVE DISORDER AND THEIR ITALIAN PSYCHIATRISTS' PERCEPTION

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