Background: Clopidogrel is a pro-drug that requires activation by the cytochrome P450 (CYP) enzyme system. Patients receiving clopidogrel are often treated with selective serotonin reuptake inhibitors (SSRIs) for co-existing depression. SSRIs that inhibit the CYP2C19 enzyme have the potential to reduce the effectiveness of clopidogrel; however the clinical outcomes of this interaction have not been examined.

Objectives: To assess clinical outcomes following initiation of clopidogrel among patients treated with an SSRI that inhibits CYP2C19.

Methods: Using five US databases (1998-2013), we conducted a population-based cohort study of adults who initiated treatment with clopidogrel while treated with an SSRI. Patients were variable ratio matched by propensity score (PS) and followed for as long as they were exposed to both clopidogrel and the index SSRI group (CYP2C19- inhibiting SSRIs (fluoxetine and fluvoxamine) vs non-inhibiting SSRIs) in the primary analysis and for 180 days (intention to treat approach) following clopidogrel initiation in a sensitivity analysis. Primary outcomes included a composite ischemic event (myocardial infarction, ischemic stroke, or a revascularization procedure) and a composite major bleeding event (gastrointestinal bleed or hemorrhagic stroke).

Results: The PS-matched cohort comprised 9,281 clopidogrel initiators on CYP2C19-inhibiting SSRIs and 44,278 patients treated with non-inhibiting SSRIs. As compared to those treated with a non-inhibiting SSRI, patients on a CYP2C19-inhibiting SSRI had an increased risk of ischemic events (hazard ratio [HR], 1.12; 95% confidence interval [CI], 1.01-1.24) following clopidogrel initiation. The increase in risk was more pronounced in patients 65 years of age and older (HR, 1.22; 95% CI, 1.00-1.48). The HR for major bleeding was 0.76 (95% CI, 0.50-1.17).

Conclusions: Initiation of clopidogrel while treated with a CYP2C19-inhibiting SSRI may be associated with decreased effectiveness of clopidogrel. Treatment with an SSRI that does not interact with clopidogrel should be considered.

441. Effectiveness of Recommended Drug Classes in Secondary Prevention of Acute Coronary Syndrome in France

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Background: Guidelines for cardiovascular secondary prevention are based on evidence from relatively old clinical trials and need to be evaluated in daily clinical practice.

Objectives: To evaluate effectiveness of the recommended drug classes after an acute coronary syndrome (ACS) for secondary prevention of cardiovascular diseases and all-cause mortality.

Methods: This cohort study used data from a representative sample of the French national healthcare insurance system database (EGB). Patients hospitalised for an incident ACS between 2006 and 2011, and aged $\geq$ 20 years at time of ACS were included in the study. Patients non-exposed to any of the four recommended drug classes (beta-blockers, antiplatelet agents, statins, and angiotensin-converting-enzyme inhibitors, ACEI, or angiotensin II receptor blockers, ARB) in the first 3 months following ACS or who died during this period were not included in the cohort. Exposure status was determined daily during follow-up. Effectiveness of the four therapeutic classes in preventing the composite outcome ACS, transient ischemic attack, ischemic stroke, or all-cause-death was estimated using a time-dependent Cox proportional hazards model, which was adjusted for time-fixed confounders measured at baseline (general characteristics and characteristics of the initial ACS) and time-dependent confounders during follow-up (co-morbidities and co-medications).

Results: Of the 2874 patients included in the study, 33.9% were women and the median age was 67 years (interquartile range, IQR: 56-77). The median time of

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follow-up was 3.6 years (IQR: 2.2-5.3). The risk of the composite outcome decreased with use of antiplatelet agents (adjusted hazard ratio (aHR) 0.76, 95% confidence interval (CI) 0.63; 0.91), use of statins (aHR 0.71, 95%CI 0.57; 0.87), and use of ACEI/ARB (aHR 0.67, 95%CI 0.57; 0.80). Use of beta-blockers was not associated with a lower risk of the composite outcome (aHR, 0.90, 95%CI 0.74; 1.09]).

Conclusions: Use of antiplatelet agents, statins, and ACEI/ARB after an ACS, but not beta-blockers, was associated with a lower risk of cardiovascular morbidity and all-cause mortality.

442. Treatment with Carvedilol, Bisoprolol or Metoprolol Tartrate and the Risk of Mortality and Hospital Readmission Among Older Adults with Heart Failure

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Background: The long-term use of ß-blockers has been shown to improve the outcomes of patients with heart failure (HF). However, it is still disputed whether this is a class effect, and whether carvedilol or bisoprolol are superior to metoprolol tartrate.

Objectives: To compare the effectiveness of ß-blockers for older patients following a primary hospital admission for HF.

Methods: We conducted a cohort study using Quebec administrative databases to identify patients who were prescribed the ß-blockers, carvedilol, bisoprolol or metoprolol tartrate after the diagnosis of HF. We characterize the patients by the type of ß-blocker prescribed at discharge of their first HF hospitalization. To control for differences among patient characteristics, a multivariate Cox proportional hazards model was used to compare the primary endpoint of all-cause mortality and the secondary endpoint of HF readmission. We conducted analyses by matching for a propensity score for initiation of β-blocker therapy.

Results: Of the 3197 patients with HF with a median follow-up of 2.8 years, the crude annual mortality (per 100 person-years) was 16, 14.9 and 17.7 for metoprolol tartrate, carvedilol, and bisoprolol, respectively. After controlling for covariates, we found that carvedilol (HR 0.92; 0.78-1.09) and bisoprolol (HR 1.04; 0.93-1.16) were not superior to metoprolol tartrate in improving survival. After matching for propensity score, carvedilol and bisoprolol shown no additional benefit on all-cause mortality and HF readmission compared to metoprolol tartrate.

Conclusions: We suggest that there is no evidence of a differential effect of β-blockers on all-cause mortality and HF readmission in older patients with HF.

443. Real-Life Statin Use and LDL-Cholesterol Reduction in a General Population: A Retrospective Study of Primary Care Electronic Medical Records

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Background: Guidelines on management of dyslipidemia recommend statins based on their capacity to lower LDL-C levels. However, these recommendations are mainly based on clinical trials. Observational studies of the general population describing real-life statin use, in terms of potency and adherence, are scarce.

Objectives: To describe the effect of statin potency and adherence on LDL-C reduction in a general population from a primary care electronic medical record database.

Methods: Retrospective cohort study of 322,283 statin new users (53.37% women), aged 35 to 74y. Inclusion criteria: one LDL-C measurement without statin treatment in the previous 6 months and a second LDL-C measurement after statin initiation. Exposure: statin potency and MPR (≤50, 50-70, >70). Outcome: relative LDL-C reduction. Total LDL-C measurements: 1,461,936. Study period: 2006-2014.

Results: Regimes of potency use were 3.08% (low), 68.72% (moderate), 25.6% (high) and 2.52% (very high);6-month mean MPR: 60.89%, 65.16%, 66.20%

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