consistent medication use was associated with a lower likelihood of clinical events, whether adherence was measured through trajectory groups or PDC. When evaluating the prediction of future cardiovascular events by including a measure of adherence in the model, the best model reclassification was observed when adherence was measured using three or four trajectory groups (NRI = 0.189 [95% confidence interval: 0.171, 0.210]).

Conclusions: Statin adherence trajectory predicted future cardiovascular events better than measures categorizing PDC. Thus, adherence trajectories may be useful for targeting adherence interventions or adjusting for adherence behavior in comparative effectiveness studies.

355. The Effect of Adherence to Statin Therapy on the Hazard of Cardiovascular Mortality in the Netherlands

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Background: The biological efficacy of statin therapy has been demonstrated in various clinical trials. However, end users may differ from trial participants in relevant ways. Therefore, observational studies are needed to assess clinical effectiveness. Our objective was to assess the clinical effectiveness of adherence to statin therapy in reducing cardiovascular mortality in the Netherlands.

Objectives: The aim of this study was to assess the clinical effectiveness of adherence to statin therapy in reducing cardiovascular mortality in the Netherlands.

Methods: Individual-level mortality information from Statistics Netherlands was linked to pharmacy dispensing data that came from the representative database IADB.nl. We used extended Cox models with adherence to statin therapy as the primary exposure and time to cardiovascular mortality as the primary outcome. We adjusted for age, sex, birth cohort, socio-economic status, diabetic status, and the utilization of various cardiovascular drugs. Covariates were allowed to vary over time. We achieved population-averaged effect estimates through implementation of the parametric G-formula. We also performed a subset analysis by calendar period corresponding to periods of particular cardiovascular prescribing guidelines and a subset analysis by dispensing background to assess the influence of healthy adherer bias.

Results: The conditional estimate was that being fully adherent to statins reduced the hazard of cardiovascular mortality by about 47% (HR: 0.53; 95%CI: 0.46 to 0.61), compared with being fully non-adherent to statins. The population-averaged estimate was of similar magnitude. In addition, we found evidence that estimates of clinical effect approached estimates of trials just after the introduction of statins in the population but became potentially more confounded in later calendar years.

Conclusions: The study provides evidence of the clinical effectiveness of statins, although the final estimates may still be affected by healthy adherer bias.

356. The Risk of Acute Myocardial Infarction after Discontinuation of Antihypertensive Agents

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Background: Sudden discontinuation of some antihypertensive agents such as beta-blockers and centrally acting antihypertensive agents are associated with increased risk of acute coronary events.

Objectives: The aim of this study was to assess the association between discontinuation of different antihypertensive agents and the risk of acute myocardial infarction (AMI).

Methods: A nested case control study was performed in a cohort of antihypertensive drug users from the Utrecht Cardiovascular Pharmacogenetics (UCP) database. Within this cohort, patients who were hospitalized for first AMI were considered cases. Cases were matched (1 up to 4) to controls at the same AMI date (index date). Antihypertensive users were defined as

current users if the index date fell within prescribed duration or as stoppers if this date fell outside the prescribed duration. According to recency of stopping, stoppers were divided into recent stoppers (≤90 days), intermediate-term stoppers (91–180 days), and long-term stoppers (>180 days). The study included only antihypertensive users who were specifically current users or stoppers of one antihypertensive agent. Logistic regression analysis was used to assess the association between the discontinuation of antihypertensive agents and the risk of AMI and to control for confounding.

Results: We included 1245 cases and 4994 controls in our analysis. The risk of AMI was significantly increased with all stoppers of beta-blockers (adjusted OR: 1.54, 95%CI (1.25–1.90)), calcium channel blockers (CCBs) (adjusted OR: 2.25, 95%CI (1.53–3.30)), and diuretics (adjusted OR: 1.76, 95%CI (1.24–2.48)) compared with current users. Moreover, the risk of AMI was significantly increased for long-term stoppers (beta-blockers, CCBs, angiotensin-converting enzyme inhibitors, and diuretics) and intermediate-term stoppers (beta-blockers and CCBs) versus current users. There was no difference in AMI risk between recent stoppers of antihypertensive agents versus current users.

Conclusions: Discontinuation of antihypertensive agents increases the risk of AMI after more than 90 days of stopping. Adherence to antihypertensive agents plays an important role in reducing the risk of AMI in patients with hypertension.

357. Use of Antihypertensive Agents and the Risk of Out-of-hospital Cardiac Arrest: A Case Control Study

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Background: Sudden cardiac arrest (SCA) is a complex multifactorial condition and is commonly caused by ventricular tachycardia/fibrillation (VT/VF). Some antihypertensive agents such as thiazides are associated with increased risk of SCA.

Objectives: The aim of this study was to assess the association between different antihypertensive agents and the occurrence of out-of-hospital cardiac arrest (OHCA), taking into account their potential impact on serum potassium levels.

Methods: Cases were drawn from the Amsterdam Resuscitation Studies (ARREST) registry and controls from the PHARMO database. This study was performed using 1948 cases who had OHCA with electrocardiogram (ECG)-documented VT/VF for the first time. These cases were matched by age, sex, and OHCA date (index date) to 8347 controls. From this dataset, we included only patients who were current users of antihypertensive agents (the index date fell between start date and end date of prescription + 10%). Antihypertensive therapies were classified according to their potential impact on serum potassium levels to therapies with neutral effect, therapies inducing hypokalemia, therapies inducing hyperkalemia, and therapies with unknown effect. Logistic regression analysis was used to study the association between use of antihypertensive agents and occurrence of OHCA and to control for confounding.

Results: We included 1192 cases and 3303 controls who were current users of antihypertensive agents in our analysis. The risk of OHCA was significantly increased with users of antihypertensive therapies inducing hypokalemia (adjusted OR 1.48, 95%CI (1.12–1.94)) and with users of antihypertensive therapies with unknown effect (adjusted OR 1.42, 95%CI (1.13–1.77)) versus users of antihypertensive therapies with neutral effect. There was no difference in OHCA risk between users of antihypertensive therapies inducing hyperkalemia versus users of antihypertensive therapies with neutral effect (adjusted OR 1.13, 95%CI (0.89–1.43)).

Conclusions: The risk of OHCA is significantly increased in patients who were current users of antihypertensive therapies inducing hypokalemia and antihypertensive therapies with unknown effect on serum potassium levels.

358. ABCB1 Gene Variants, Digoxin, and Risk of Sudden Cardiac Death in a General Population

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