

Method / Collaborator	Analytic design choices (optimal setting for MDCC-Acute myocardial infarction in italics)
Observational screening (OS) UBC/ProSanos, GlaxoSmithKline [1, 2]	Study design: <i>Self-controlled cohort</i> , Cohort comparison with overall database Exposures to include: <i>All occurrences</i> , First occurrence Outcomes to include: <i>First occurrence</i> , All occurrences Time-at-risk: <i>Length of exposure + 30d</i> , 30d from exposure start, All time post-exposure start Include index date in time-at-risk: <i>No</i> , Yes Control period: <i>Length of exposure + 30d</i> , 30d prior to exposure start, 180d prior to exposure start, 365d prior to exposure start, All time prior to exposure start Include index date in control period: <i>No</i> , Yes Combinations tested: 126
Self-controlled case series (SCCS) OMOP Team [3-8]	Outcomes to include: <i>All occurrences</i> , First occurrence Prior distribution: <i>normal</i> , Laplace Variance of the prior: <i>Determined through cross-validation</i> , Pre-defined at 0.01, Pre-defined at 0.1, Pre-defined at 1, Pre-defined at 10 Time-at-risk: <i>All time post-exposure start</i> , Length of exposure, Length of exposure + 30d, 30d from exposure start Include index date in time-at-risk: Yes, No Apply multivariate adjustment on all drugs: <i>No</i> , Yes Required observation time: <i>None</i> , 180d Combinations tested: 560
Case control (CC) OMOP Team [7-11]	Controls per case: <i>up to 10 controls per case</i> , up to 100 controls per case Required observation time prior to outcome: <i>30d</i> , 180d Time-at-risk: <i>Length of exposure + 30d</i> , Length of exposure, 30d from exposure start, All time post-exposure start Include index date in time-at-risk: <i>No</i> , Yes Case-control matching strategy: <i>Age sex and visit (within 180d)</i> , Age sex and visit (within 30d), Age and sex Nesting within indicated population: <i>No</i> , Yes Exposures to include: <i>First occurrence</i> , All occurrences Metric: <i>Odds ratio with Mantel Haenszel adjustment by age and gender</i> , Unadjusted odds ratio Combinations tested: 384
Temporal pattern discovery (ICTPD) Uppsala Monitoring Centre [12-15]	Control period: <i>-180d to -1d before exposure start</i> , -1080d to -361d before exposure start, -30d to -1d before exposure start, -810d to -361d before exposure start Time-at-risk: <i>360d from exposure start</i> , 30d from exposure start, 60d from exposure start Use control period in expected calculation: Yes, No Use 1mo prior to exposure in expected calculation: <i>No</i> , Yes Use 1d prior to exposure in expected calculation: <i>No</i> , Yes Combinations tested: 42

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New user cohort (CM) OMOP Team [7, 16-21]	<p>Required observation time prior to exposure: <i>180d</i>, None</p> <p>Nesting within indicated population: <i>No</i>, Yes</p> <p>Comparator population: <i>Patients with a diagnosis for the indication of the target drug and at least one exposure to a drug known to be not associated with the outcome,</i> <i>Patients with exposure to most prevalent comparator drug which shares the same indication as the target drug but is not in the same pharmacologic class,</i> <i>Patients with exposure to any comparator drug which shares the same indication as the target drug but is not in the same pharmacologic class</i> <i>Patients with a diagnosis for the indication of the target drug</i></p> <p>Time-at-risk: <i>Length of exposure + 30d</i>, 30d from exposure start, All time post-exposure start</p> <p>Propensity score covariate selection strategy: <i>Bayesian logistic regression using all available covariates,</i> <i>High-dimensional propensity score covariate selection algorithm by Schneeweiss et al,</i> <i>Exposure-specific covariate selection algorithm identified by Brookhart et al,</i> No covariate adjustment</p> <p>Covariate eligibility window: <i>180d prior to exposure</i>, 30d prior to exposure, All time prior to exposure, None</p> <p>Dimensions to include as potential covariates: <i>Drugs conditions and procedures</i>, Drugs only, Drugs and conditions, None</p> <p>Additional covariates include in the propensity score model: <i>Age and sex and index year and Charlson index and number of drugs and number of visits and number of procedures</i>, Age and sex, None</p> <p>Covariate selection algorithm additional parameters: BLR: <i>Normal prior distribution with variance = 1</i>, Laplace prior distribution with variance = 1; HDPS: 100 top confounders from among 200 most prevalent covariates in each dimension that occur in at least 100 persons, 500 top confounders from among 500 most prevalent covariates in each dimension that occur in at least 100 persons</p> <p>Propensity score trimming: <i>None</i>, Trim lower 5% from the comparator group and the upper 5% from the target group</p> <p>Metric: <i>Propensity score adjustment using propensity score as continuous variable in logistic regression outcome model,</i> <i>Propensity score adjustment using 5 strata as indicator variables in logistic regression outcome model,</i> <i>Propensity score adjustment using 20 strata as indicator variables in logistic regression outcome model,</i> <i>Propensity score stratification using Mantel Haenszel adjustment over 5 strata,</i> <i>Propensity score stratification using Mantel Haenszel adjustment over 20 strata,</i> Unadjusted odds ratio from univariate logistic regression predicting outcome from exposure</p> <p>Combinations tested: 126</p>
Disproportionality analysis (DP) OMOP Team [7, 22-25]	<p>Outcomes to include: <i>First occurrence</i>, All occurrences</p> <p>Strategy to stratify data: Classify drug-outcome co-occurrences as exposed/unexposed and with/without outcome</p> <p>Metric: <i>Proportional reporting ratio (PRR)</i>, Information component (BCPNN/IC), Multi-item Gamma Poisson Shrinker</p> <p>Stratify by age: Yes, No</p> <p>Stratify by gender: Yes, No</p> <p>Stratify by year: No, Yes</p> <p>Time-at-risk: <i>Length of exposure + 30d</i>, Length of exposure + 60d, 30d from exposure start, All time post-exposure start</p> <p>Combinations tested: 48</p>
Longitudinal Gamma Poisson Shrinker (LGPS) Erasmus MC [26-28]	<p>Metric: <i>Incidence rate ratio with Mantel-Haenszel adjustment over age-by-gender strata,</i> Longitudinal Gamma Poisson Shrinker</p> <p>Exposures to include: <i>All occurrences</i>, First occurrence</p> <p>Time-at-risk: <i>Length of exposure</i>, Length of exposure + 30d</p> <p>Required observation time prior to exposure: <i>365d</i>, None</p> <p>Apply LEOPARD filtering for protopathic bias: Yes, No</p> <p>Combinations tested: 32</p>