Method name	Contributor	Release date	Description	Parameter settings studied (community optimal setting in bold)
Disproportionality analysis				
Disproportionality analysis (DP)	Columbia / Merck	15-Mar-10	Methods adapted from data mining of spontaneous adverse event reports, where drug–condition pairs are identified if they co-occur disproportionately more frequently than expected if the drug and condition were independent. Metrics include the MGPS, PRR, ROR, and BCPNN.	Condition type (2): first occurrence or **all occurrences of outcome** Metric (3): PRR, **BCPNN/IC**, MGPS/EBGM Stratification (2): with or **without age and sex** Surveillance window (4): 30 d from exposure start, Duration of exposure (drug era start through drug era end) + 30 d, Duration of exposure + 60 d, **All time post-exposure start**
IC Temporal Pattern Discovery (ICTPD)	Uppsala Monitoring Centre	23-May-10	This is a novel method for event history data, focusing explicitly on the detailed temporal relationship between pairs of events. The proposed measure contrasts the observed-toexpected ratio in a period of interest with that in a predefined control period.	Observation period (3): **1d to 30d**; 1d to 60d; or, 1d to 360d Control period (4): -1080d to -361d; -810d to -361d; **-180d to-1d**; or, -30d to -1d Multiple control periods: (4) **100**, 101, 110, or 111 when control period <> -30d (2) 010, 011 when control period = -30d
HSIU cohort method (HSIU)	Regenstrief / Indiana University	8-Jun-10	This method calculates relative risk and incidence rate differences between exposure cohorts relative to population estimates.	Exposure window (2): During exposure or all time post-exposure Stratify on sex? (2): Yes or No Stratify on age? (2): Yes or No Stratify on # of drugs? (2): Yes or No
Case-based methods				
Univariate self-controlled case series (USCCS)	Columbia	2-Apr-10	The method estimates the association between a transient exposure and adverse event using only cases; no separate controls are required because each case acts as its own control.	Condition type (2): **first occurrence** or all occurrences of outcome Defining exposure time-at-risk: Days from exposure start (2): should we include the drug start index date in the period at risk? **No** Surveillance window (4): 30 d from exposure start, **Duration of exposure (drug era start through drug era end),** Duration of exposure + 30 d, Duration of exposure + 60 d Precision of Normal prior (4): **0.5**, 0.8, 1, 2
Multi-set case control estimation (MSCCE)	Columbia / GlaxoSmithKline	16-Apr-10	The program leverages the basic design of a case–control study to enable estimates of drug–condition associations across a large set of drugs and conditions. The algorithm can estimate an odds ratio simultaneously for multiple conditions and allows all exposures to be evaluated for each outcome.	Lead time (4): 30d, 91d, 183d, 400d Controls per case (3): 10, 100, 1000 Exposure window (2): 30d from exposure start, 60d post exposure Analysis (2): Mantel-Haenzsel or Crude OR
Bayesian logistic regression (BLR)	Rutgers / Columbia	21-Apr-10	This is a high-dimensional statistical method that is scalable to a substantial number of covariates, accommodating all drugs and conditions in a single model to predict occurrence of ADEs. The Bayesian approach to logistic regression has several advantages, including avoidance of overfitting, efficiency during model prediction time, and scalability to large numbers of covariates (see also www.bayesianregression.org)	Condition type (2): first occurrence or all occurrences of outcome Include age and sex in model (2): Yes or No Surveillance window (2): 30 d from exposure start Duration of exposure + 30 d Precision of Normal prior (3): 0.5, 1, 2
Case-control surveillance (CCS)	Lilly	2-May-10	The program applies a case–control surveillance design to estimate odds ratios for drug–condition effects, where cases are matched to controls by age, sex, location, and race.	Lead time (3): 30d, **91d**, or 183d Followup time (2): **30d** or 180d Controls per case (2): **4**, 100 Exposure window (2): **30d post exposure**, all time post exposure Match on race and location? (2): Yes or **No**
Case-crossover (CCO)	University of Utah	1-Jun-10	The design uses within-participant comparisons of drug exposures over time to estimate the rate ratio of the outcome associated with the drug under study.	Days enrolled for washout period (2): **91d**, or 180d Days in case window (3): **30d**, 90d, or 180d Days in control window: For 30d: **30d**, 90d, or 180d For 90d: 90d, or 180d For 180d: 180d Control window lag (2): **0d** or 180d Control windows sampled(2): **1** or 2

Method name	Contributor	Release date	Description	Parameter settings studied (community optimal setting in bold)
Exposure-based methods				
Observational screening (OS)	ProSanos / GlaxoSmithKline	8-Apr-10	This is an extension of a traditional cohort epidemiology design where the rate of ADEs can be compared across groups of patients exposed to different medications, allowing comparisons within a cohort population, between treatments, as well as relative to the overall population at large.	Outcome occurrence (3): first occurrence only**, all occurrences,** or first occurrence within exposure period Comparator group (2): **Self-controlled cohort design (post vs. pre-exposure),** or Relative assessment (post vs. overall) Surveillance window (3): 30 d from exposure start, **Duration of exposure (drug era start through drug era end) + 30 d,** All time post-exposure start Include index date in post-exposure time-at-risk (2): **Yes** or No For self-controlled design: Surveillance window length pre-exposure: Length of exposure + 30d, 30d, **180d**, 365d, All time pre-exposure (used for all time post-exposure comparison) Include index date in pre-exposure time-at-risk (2)**:** Yes or **No**
High-dimensional propensity score (HDPS)	Harvard Medical School / Columbia	6-Aug-10	This is a multistep algorithm to implement high-dimensional proxy adjustment in observational data. Used in conjunction with a new-user cohort design, it offers a novel approach to minimizing confounding when assessing the relative association between patient exposed to alternative medications and the occurrence of a health outcome of interest.	Washout period (1): **180d** Surveillance window (3): **30 days from exposure start**; exposure + 30d ; all time from exposure start Covariate eligibility window (3): **30 days prior to exposure**, 180, 9999 # of confounders (2): **100**, 500 covariates used to estimate propensity score Propensity strata (2): 5, **20 strata** Analysis strategy (3): Mantel-Haenszel stratification (MH), propensity score adjusted (PS), **propensity strata adjusted (PS2)** Comparator cohort (2): **drugs with same indication, not in same class**; most prevalent drug with same indication, not in same class
Incident user design (IUD-HOI)	University of North Carolina	26-Oct-10	This implementation of the inception cohort design applies various approaches for propensity score adjustment to balance baseline covariates and uses a Cox proportional hazards model to estimate drug-related effects	**Intent-to-treat** or on-treatment analysis? (2) Propensity score covariates? (2): **Parsimonious (gender, age)** or High-dimensional Propensity score trimming (2): No trim or **5% of both tails** Comparator cohort (2): **drugs with same indication, not in same class**; most prevalent drug with same indication, not in same class
Sequential testing methods				
Maximized Sequential Probability Ratio Test (MSPRT)	Harvard Pilgrim / Group Health	25-Jul-10	MaxSPRT is a sequential analysis method designed for continuous or frequent (e.g., weekly) monitoring of a potential elevated risk for an adverse event after introduction of a drug or vaccine of interest.	Washout period (3): 91d, 183d, 400d Alpha spending (3): 0.001, 0.01, 0.05 Analysis strategy (2): Stratification or regression Covariates in regression (3): age gender age*gender prior drugs, + inpatient visits, +outpatient visits Comparator cohort (4): drugs with same indication; drugs in same class; drugs with same indication, not in same class; most prevalent drug with same indication, not in same class
Conditional sequential sampling procedure (CSSP)	Harvard Pilgrim / Group Health	30-Aug-10	CSSP is a practical group sequential method with a finite number of interim tests to determine whether the drug of interest leads to an elevated risk compared with a comparator drug. It is designed for settings in which information for both the drug of interest and the comparator drug accumulates over time.	Washout period (3): 91d, 183d, 400d Alpha spending (3): 0.001, 0.01, 0.05 Analysis strategy (2): Stratification or regression Covariates in regression (3): age gender age*gender prior drugs, + inpatient visits, +outpatient visits Comparator cohort (4): drugs with same indication; drugs in same class; drugs with same indication, not in same class; most prevalent drug with same indication, not in same class