A Bayesian self-controlled method for drug safety surveillance in large-scale longitudinal data

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Longitudinal Healthcare Databases
- Sentinel Initiative - FDA plans to establish an active surveillance system using data from healthcare information holders
- Observational Medical Outcomes Partnership (OMOP) - Researching methods for analyzing healthcare databases to evaluate safety profiles of drugs on the market

Advantages
- Automated
- Better temporal data
- No OTC information

Disadvantages
- Potential analysis techniques: maxSPRT, cohort methods, case control, case-crossover, self-controlled case series

Limitations
- May identify adverse health outcomes associated with drug exposure that were not previously detected
- May not identify adverse health outcomes associated with drug exposure that were not previously detected
- Unreliable temporal information

Self-Controlled Case Series
- Method developed to estimate relative incidence of AEs to assess vaccine safety [Farrington, 1995]
- One drug, one adverse event (AE)

\[ \begin{align*}
\text{Intensity on } (l, d) &= e^{\phi_l + \beta x_{ld}} \\
\phi_l | x_{ld} &\sim \text{Poisson} \left( e^{\phi_l + \beta x_{ld}} \right) \\
L_i &= P(y_1, ..., y_n | x_1, ..., x_n) = P(y_1 | x_1) \prod_{j=2}^{n} P(y_j | x_j)
\end{align*} \]

Bayesian Extension of SSCS
- Longitudinal databases have 100,000s of potential drugs
- High dimensionality with millions of predictors
- Standard ML leads to overfitting; need to regularize

\[ \beta_j \sim \text{Laplace} \left( 0, \frac{1}{X} \right) \]

Data Reduction to Cases Only
- If I has no events (y_i = 0) then \( L^*_i = 1 \), so we only need cases (i.e., \( n_i \geq 1 \) ) in the analysis
- SSCS does within-person comparison of event rate during exposure to event rate while unexposed ("self-controlled")

Multiple Drugs and Interactions
- We extend the model to one AE and multiple drugs

\[ \text{Intensity on } (l, d) = e^{\phi_l + \beta x_{ld}} \]

BSL database (1.5M people)

Results: OMOP Methods Evaluation
- Methods evaluation:
  - Chose 10 drugs, 10 conditions of interest
  - 9 drug-condition pairs with a true association
  - Pairs determined to have no link serve as negative controls
- Evaluation is based on mean average precision (mAP) score

References