Evaluating Use of Methods for Adverse Event Under Surveillance (EUMAEUS)

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Vaccine safety

How do we know whether a vaccine is safe?

- **Randomized trial**
  - ‘Limited’ sample size (tens of thousands), so not powered for rare AEs
  - May not be representative of actual users

- **Spontaneous reports**
  - Underreporting
  - Denominator?
  - How many reports would you expect?

- **Observational data (claims and/or electronic health records)**
  - Periodically evaluate safety (e.g. every month)
How do we use observational data?

- **Historic comparator**: compute incidence rate (IR) in the past, see if rate after vaccination is higher
- **Cohort method**: compare those vaccinated to those not vaccinated (perhaps adjusting using propensity scores)
- **Self-Controlled Case Series / Self-Controlled Risk Interval**: is the outcome more likely right after vaccination, compared to other times (of the same patients)?
- **Case-Control**: Are cases more likely to be recently vaccinated than controls?
When to declare a ‘signal’?

• When $p < 0.05$?
  – What about multiple testing?
• Maximum Sequential Probability Ratio Test (MaxSPRT)
Which method should we use? Which decision rule? Which method works best?

Evaluation:
- Look at real historical data of vaccines (e.g. H1N1 vaccines)
- Define outcomes that are unlikely to be caused by those vaccines (negative controls)
- Create synthetic outcomes ‘caused’ by vaccines (positive controls)
- How well can a method flag positive controls, while not signaling negative controls?
Protocol + package finalized

Protocol registered with ENCEPP
Writing papers!

Results are collected in a database, can be explored via a Shiny app

• Paper 1: Eumaeus study design and rationale (including literature review) – Led by Lana Lai
• Paper 2: Performance of the historical comparator design – Led by Dani Prieto-Alhambra
• Paper 6: Overview of performance across all methods – Led by me
• Paper 7: Performance for multi-dose vaccines – Led by Nicole Pratt