Evaluating **U**se of **M**ethods for **A**dverse **E**vent **U**nder **S**urveillance (EUMAEUS)

Martijn Schuemie, …

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)

EUMAEUS experiment

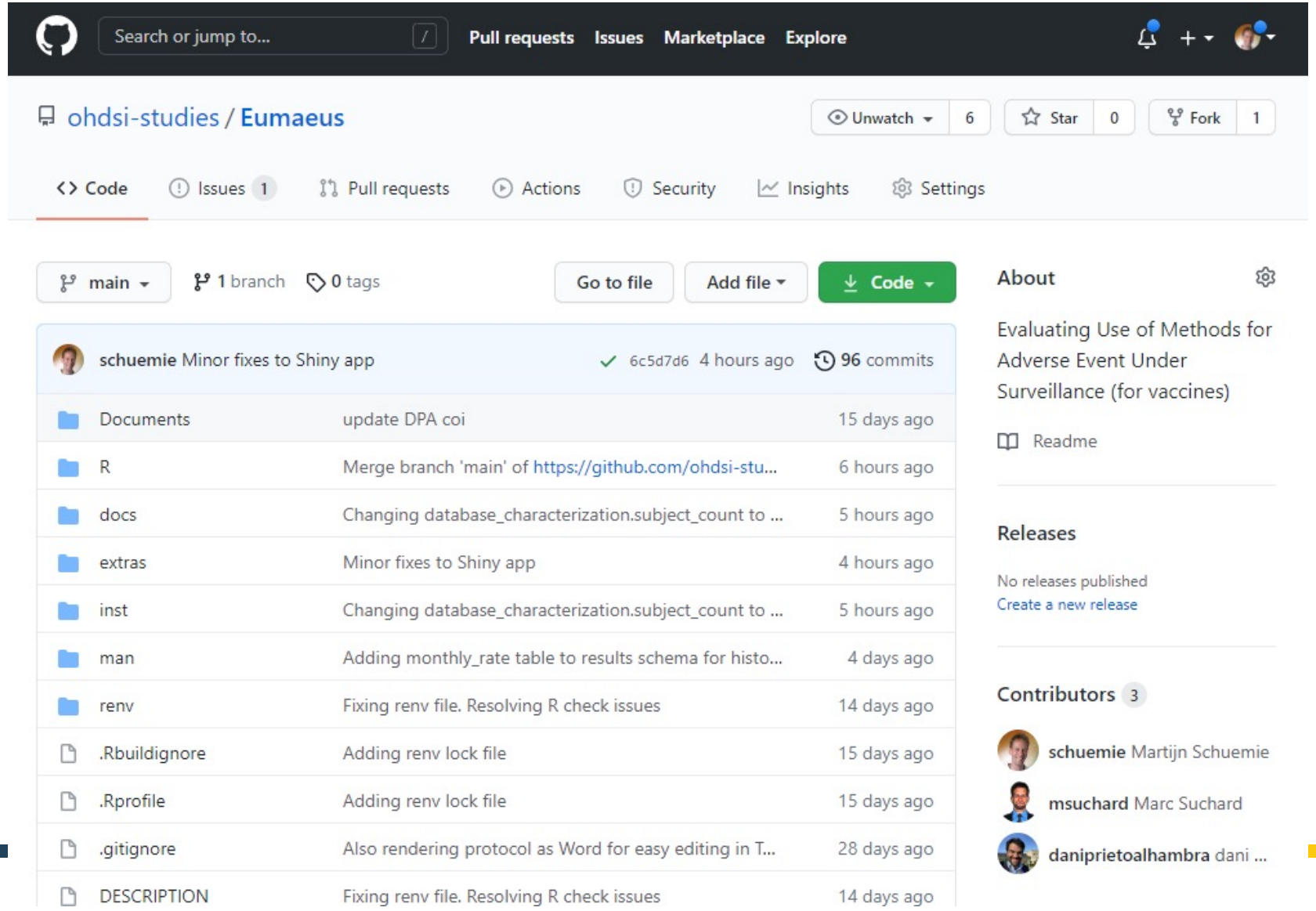
Which method should we use? Which decision rule? Which method works best?

Evaluation:

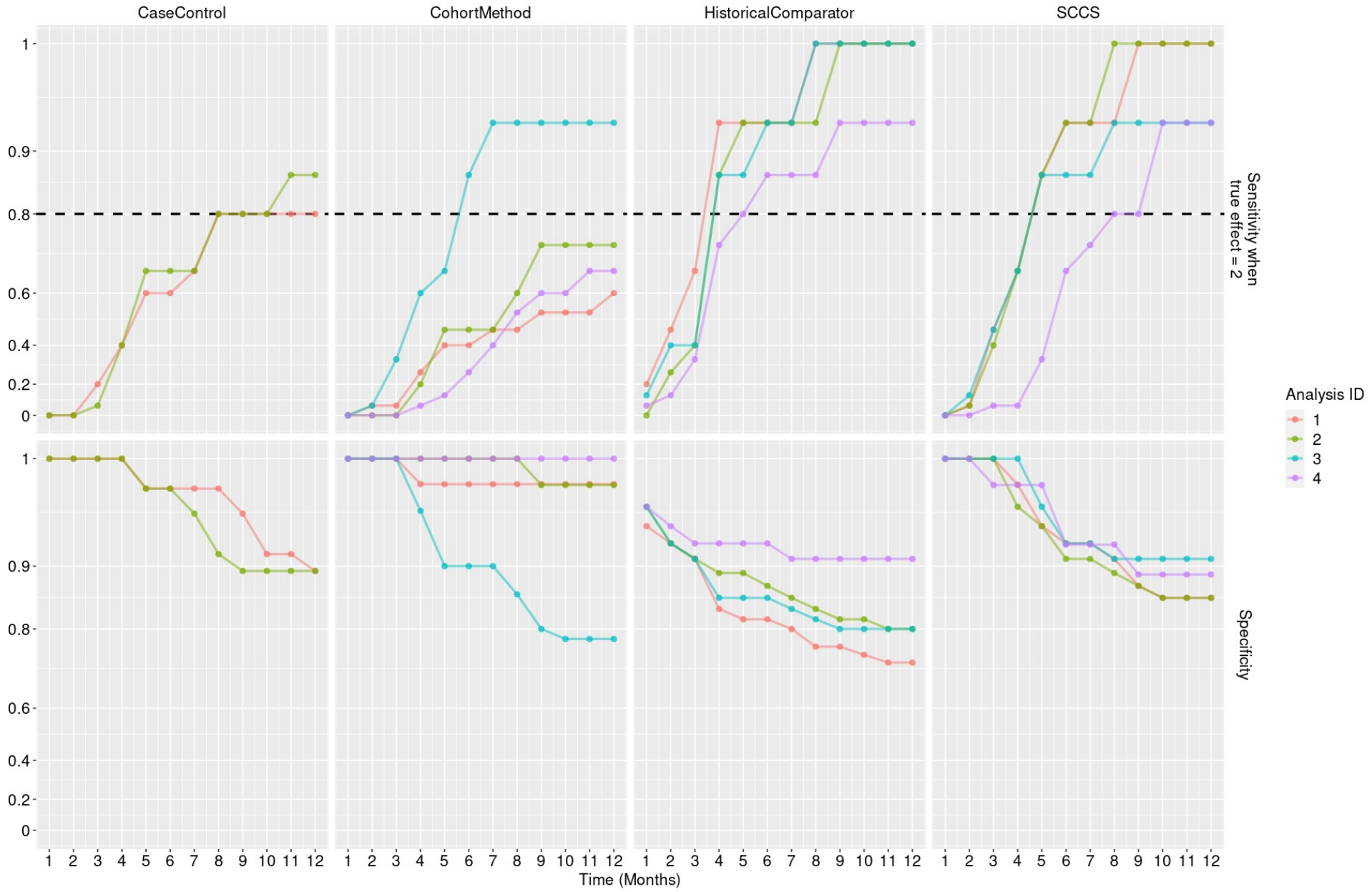
- Look at real historical data of **vaccines** (e.g. H1N1 vaccines)
- Define outcomes that are unlikely to be caused by those vaccines (**negative controls**)
- Create synthetic outcomes ‘caused’ by vaccines (**positive controls**)
- How well can a method flag positive controls, while not signaling negative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

Protocol + package finalized

Protocol registered with ENCEPP



Preliminary results



IBM CCAE
Zoster vaccine

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