



Evaluating **U**se of **M**ethods for **A**dverse Event **U**nder **S**urveillance (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)



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

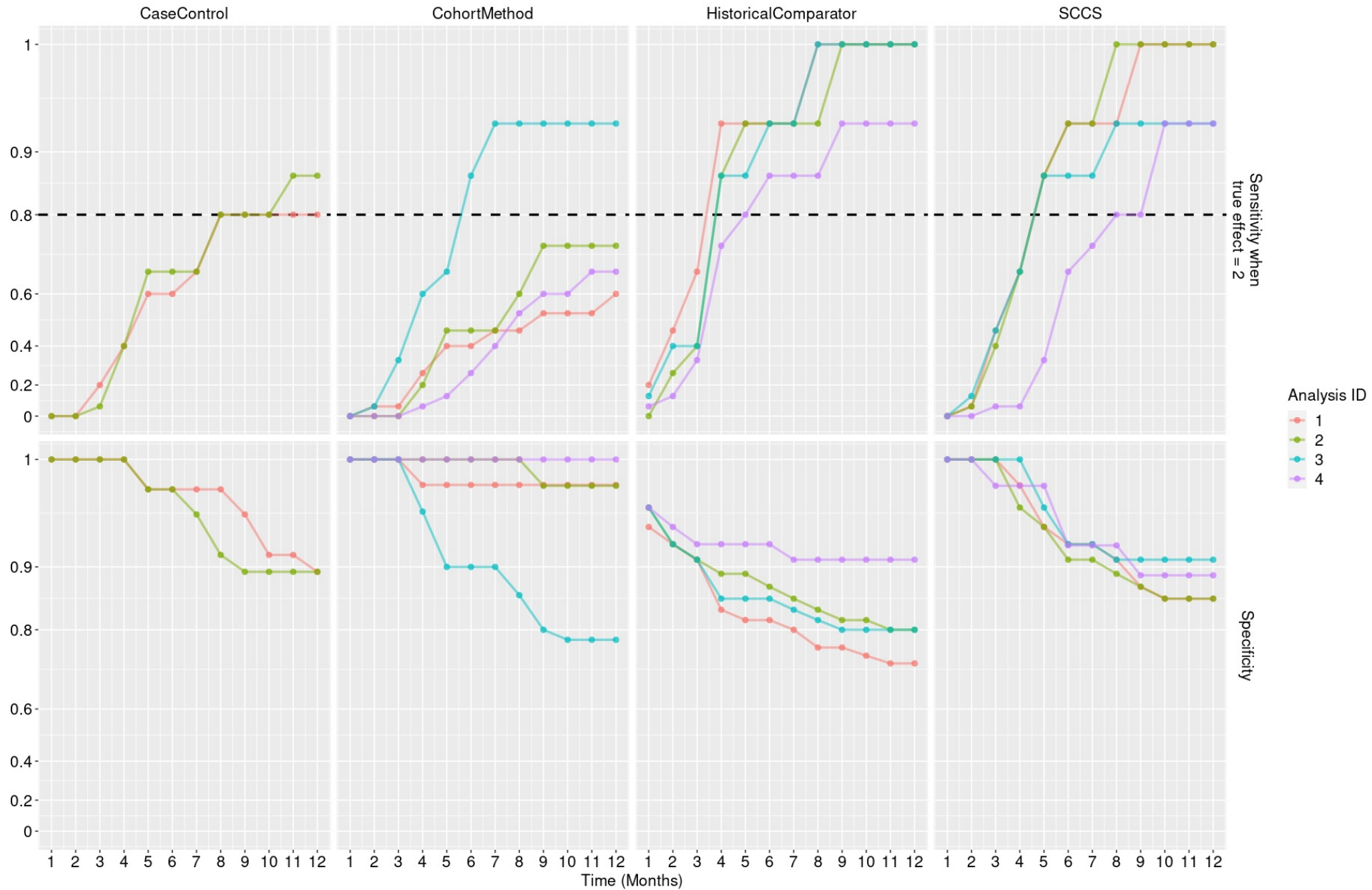
Protocol registered
with ENCEPP

The screenshot shows the GitHub interface for the repository 'ohdsi-studies / Eumaeus'. The repository is currently on the 'main' branch, which has 1 branch and 0 tags. The repository has 6 pull requests, 1 issue, and 0 stars. The repository description is 'Evaluating Use of Methods for Adverse Event Under Surveillance (for vaccines)'. The repository has 3 contributors: schuemie, msuchard, and daniprietoalhambra. The repository contains several folders and files, including 'Documents', 'R', 'docs', 'extras', 'inst', 'man', 'renv', and various configuration files like '.Rbuildignore', '.Rprofile', '.gitignore', and 'DESCRIPTION'.

File/Folder	Commit Message	Time Ago
Documents	update DPA coi	15 days ago
R	Merge branch 'main' of https://github.com/ohdsi-stu...	6 hours ago
docs	Changing database_characterization.subject_count to ...	5 hours ago
extras	Minor fixes to Shiny app	4 hours ago
inst	Changing database_characterization.subject_count to ...	5 hours ago
man	Adding monthly_rate table to results schema for histo...	4 days ago
renv	Fixing renv file. Resolving R check issues	14 days ago
.Rbuildignore	Adding renv lock file	15 days ago
.Rprofile	Adding renv lock file	15 days ago
.gitignore	Also rendering protocol as Word for easy editing in T...	28 days ago
DESCRIPTION	Fixing renv file. Resolving R check issues	14 days ago



Preliminary results





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