# COMPARES-*vaccines*: A **Com**mon **P**rotocol for the **A**nalysis of **R**elative **E**ffectiveness and **S**afety of *Covid-19 vaccine products* using OpenSAFELY

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We present a **common analysis protocol** for **comparing** the **effectiveness and safety** of **Covid-19 vaccine products**, using **routinely-collected English health data** via the **OpenSAFELY** platform.

The protocol will be **re-executed** for each new Covid-19 immunisation campaign in England.

**Covid-19 immunisation campaigns in England** are run in Spring and Autumn each year.

**Two vaccine products are available each campaign** to mitigate unexpected supply or safety issues.

Each campaign is different: vaccine products and eligibility criteria can change, and the background epidemiological context – viral variants, immunity, and behaviours, etc – will vary over time.

Studying these vaccines in **routine healthcare settings** and **more diverse populations** is crucial for campaign surveillance and future planning, complementing evidence from RCTs.

**OpenSAFELY** is an open source software platform for secure, reproducible and transparent research.

It is deployed on top of NHS patient records from **>99% of general practices in England**, with **linked hospital and mortality data**.

- Records remain securely held in the GP data centre;
- Analytic code, which is open for review and re-use, is developed by analysts locally on dummy data;
- Analysts never see real data, only summary outputs.

The full **draft protocol and code are available for inspection** and **we welcome expert review and input** – Please get in touch with your feedback!

We intend for this protocol to be **refined over time** and eventually serve as a **template** for other observational comparisons of one-time exposures, e.g., for RSV or influenza vaccines, and even beyond vaccines.

## Find out more:

GitHub repository containing analytic code

About the OpenSAFELY platform

The protocol describes an **active-comparator new-user design**, comparing recipients of **product A** with recipients of **product B**.

- Vaccine comparisons are made in different eligible populations and subgroups, and across a range of outcomes.
- The analysis incorporates complementary approaches to confounder adjustment and the estimation of the cumulative incidence, to mitigate vulnerabilities to fragile modelling assumptions.
- There are extensive diagnostic checks to detect potential baseline imbalances, for instance by examining standardised differences on confounders and pre-baseline events, and negative outcome controls.

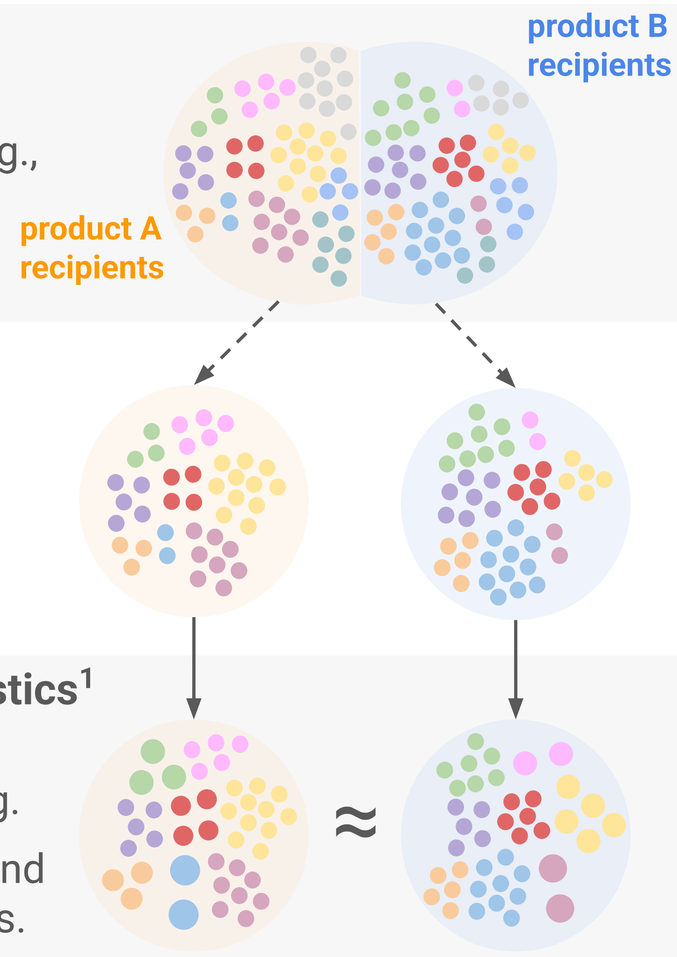
### Select vaccine recipients for a given campaign

and apply exclusion criteria, e.g.,

- registered for <12 weeks,
- missing age or sex.

### Restrict to cohort of interest

- Older adult; *or*
- Clinically vulnerable; *or*
- Immunodeficient; or
- Care home resident.




### Balance baseline characteristics[1]

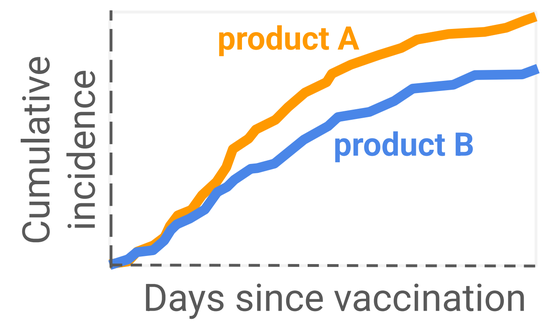
- 1:1 matching; *or*
- Inverse propensity weighting.

Report effective sample size and standardised mean differences.

### Compare on selected outcomes[2]

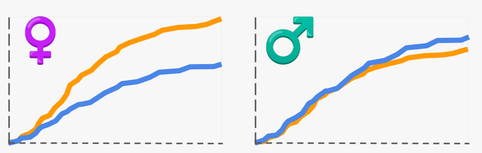
- Kaplan-Meier estimation; *or*
- Pooled logistic regression.

Report risk differences and risk ratios.




### Repeat in subgroups[1]

to identify potential effect heterogeneity.




**1 Confounders (in *italics* if also used subgroup analyses)** date of vaccination; *age*; *sex*; *area of residence*; *area deprivation*; *ethnicity*; *care-home residency*; prior Covid-19 vaccination history (time since previous dose, vaccine product type); *clinical vulnerability*; *immunodeficiency*; other co-morbidities; evidence of recent Covid-19 infection.

**2 Outcomes** Effectiveness: Covid-19 A&E visit; Covid-19 hospital admission; Covid-19 critical care admission; Covid-19 death. Safety: anaphylaxis; Guillain-Barré syndrome; Bell's palsy; venous thrombotic event; arterial thrombotic event; thrombotic thrombocytopenia; myocarditis; pericarditis; menorrhagia; erythema multiforme; All-cause: A&E visit; hospital admission; critical care admission; death. Negative controls: otitis; cellulitis.

This protocol is part of the ECHO study: Evaluating Covid-19 vaccination Histories using OpenSAFELY.
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The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, or the Department of Health.

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