

EPIDEMIOLOGY + DATA MANAGEMENT

Reproducibility and Generalizability in Vaccine Effectiveness Studies

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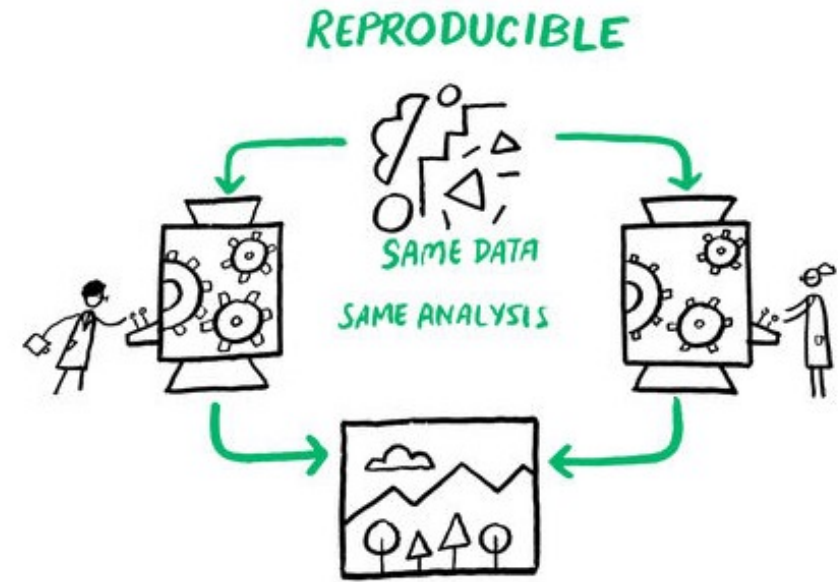
US National Institutes of Health

WHO R&D Blueprint – September 14, 2023

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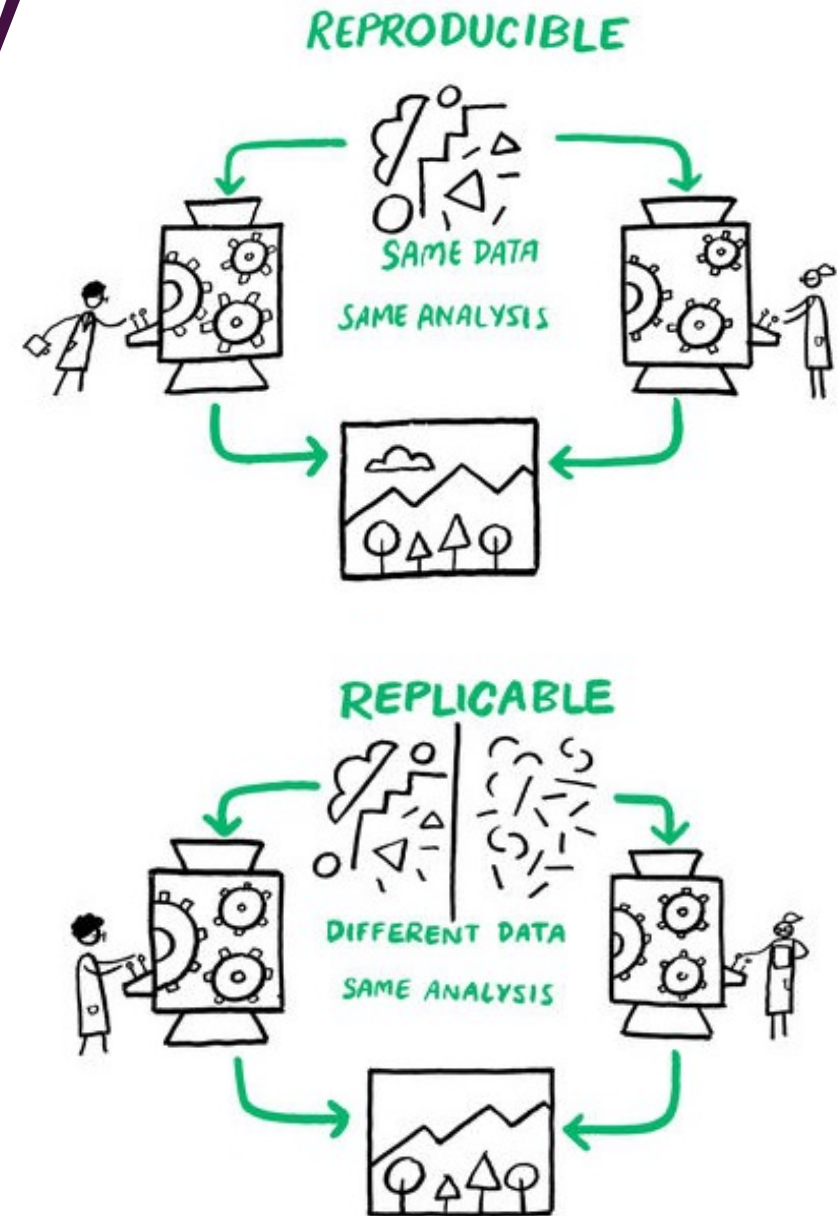
Reproducibility

- Reproducibility = obtaining consistent results using the same input data, computational steps, methods, code, and conditions of analysis.



Reproducibility & Replicability

- Reproducibility = obtaining consistent results using the same input data, computational steps, methods, code, and conditions of analysis.
- Replicability = obtaining consistent results following the same procedures but collecting new data.



What is considered successful replication?

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“It is impossible to identify a single, universal approach to determining [replicability].”

- Royal Netherlands Academy of Arts and Sciences

What is considered successful replication?

- Select and agree upon attribute to be replicated
 - Direction of effect
 - Magnitude of effect
 - Statistical significance
- Decide on allowable variability in attribute

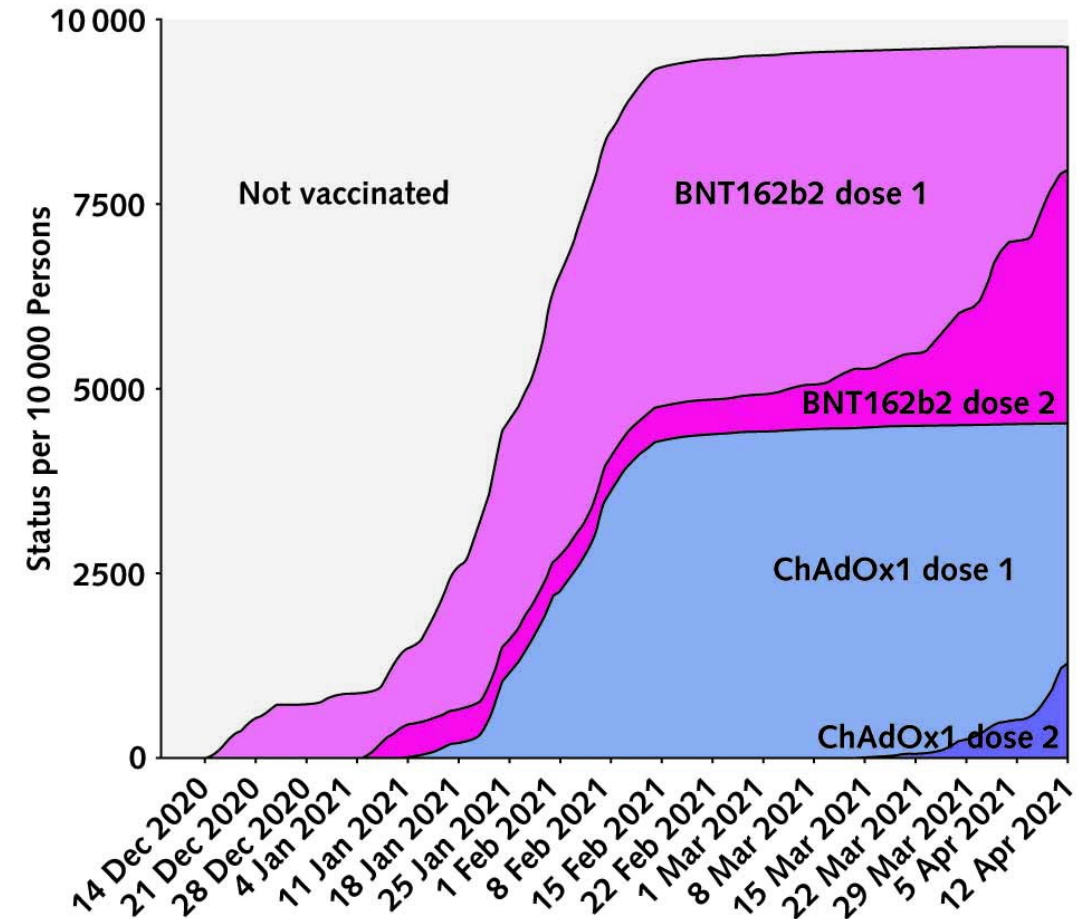
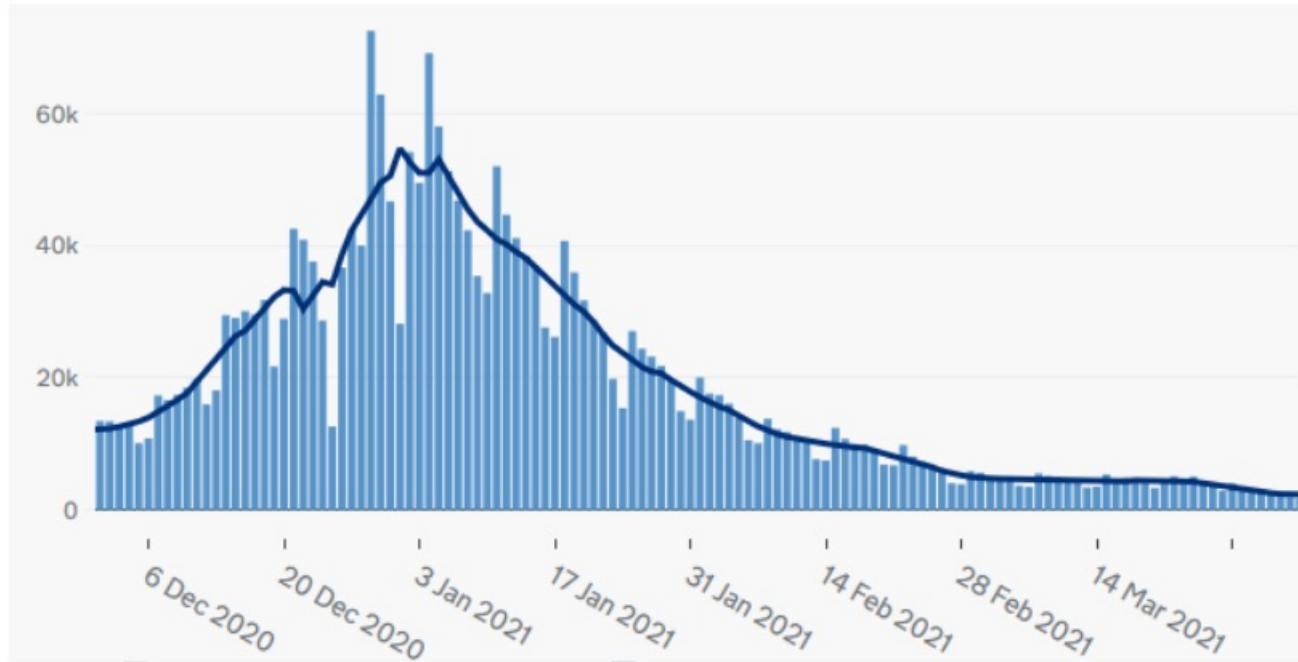
“...regardless of how similar the replication study is, no second event can exactly repeat a previous event.”

Can observational VE studies *be* replicated?

- Study groups may differ in risk of infection for reasons other than their vaccination status
- Estimates and biases vary across populations and times
 - Internal variation in study designs
 - External variation confounders/modifiers
 - Chance



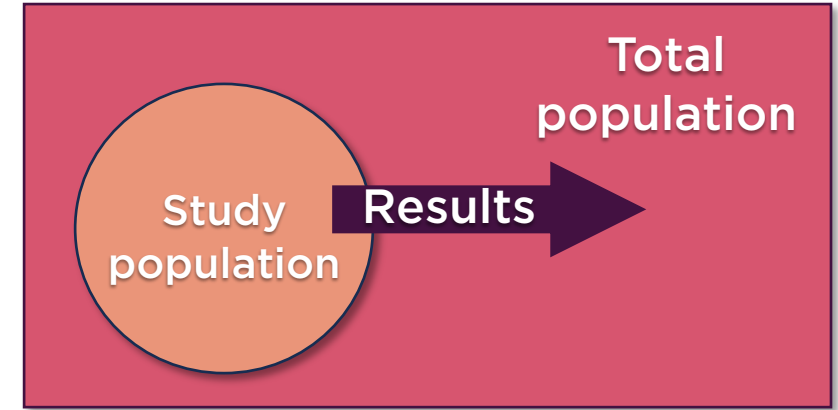
The time at which a VE study is conducted can itself limit replicability



“Rapid changes in incidence require that observational analyses account precisely for calendar time. Emulating a target trial using observational data requires **adequate adjustment** for calendar period and other **potential baseline confounders** through study design or data analysis.”

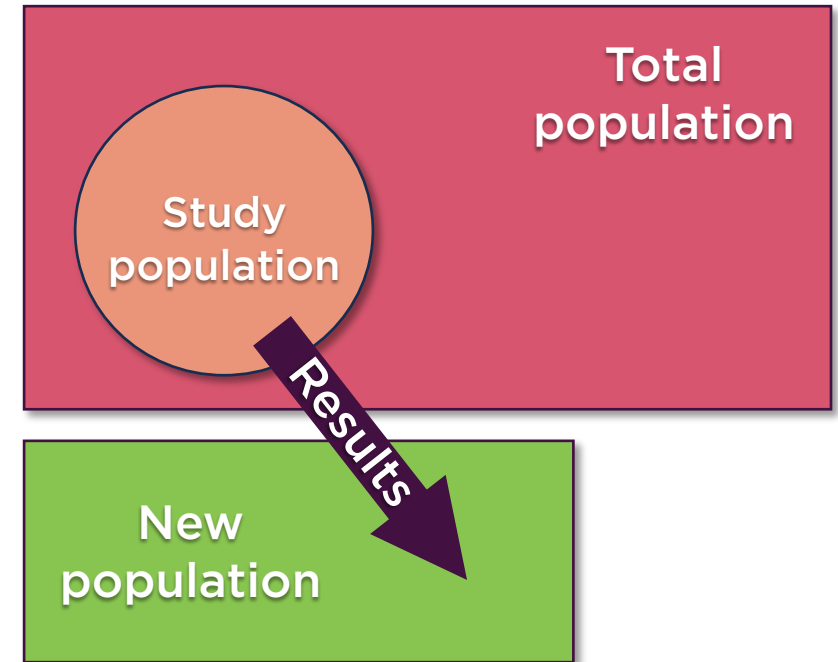
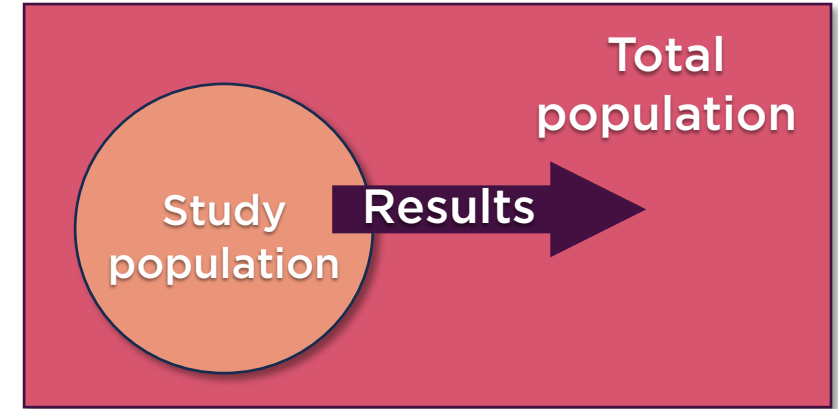
Generalizability

- Generalizability = study results can be applied to the whole population **from** which the sample was drawn.

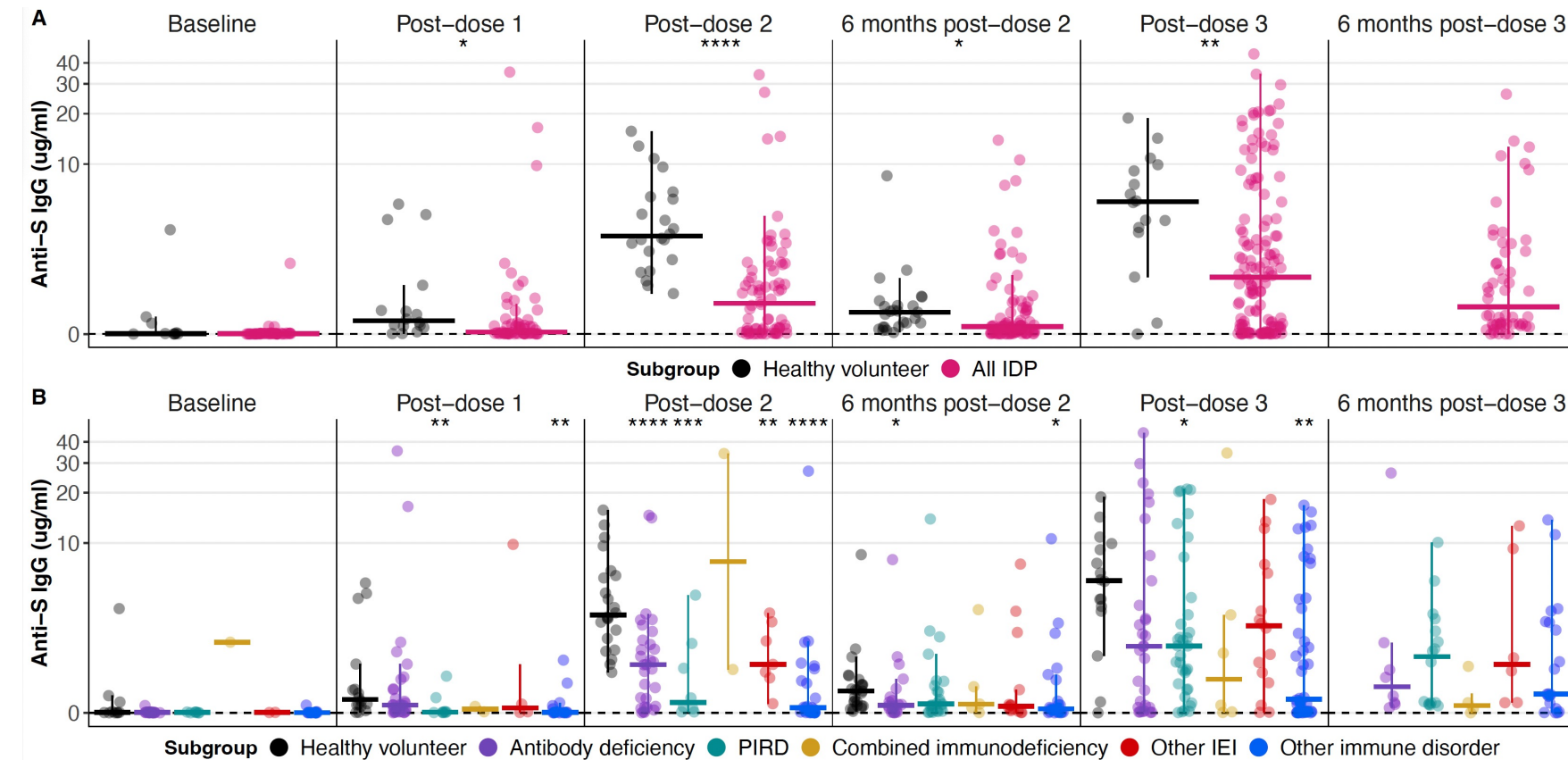


Generalizability & Transportability

- Generalizability = study results can be applied to the whole population from which the sample was drawn.
- Transportability = study results can be applied to a different population than was sampled for the study.



Generalizability requires assumptions about study and target populations and is not always achievable



In a prospective cohort of 195 IDP and 35 healthy volunteers, anti-spike IgG was detected in 88% of IDP post-dose 2, increasing to 93% by six months post-dose 3.

Despite high seroconversion, median IgG levels for IDP never surpassed 1/3 that of healthy volunteers.

Closing thoughts

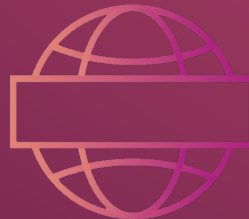
- Observational studies, despite inherent flaws, are important for assessing VE, especially in settings and populations not conducive to RCTs.
- Study results may still have utility in the target population even if the estimate is not perfectly generalizable.
- Policymakers should be clear about assumptions regarding generalizability of study results, but not paralyzed by them.

Questions?

Contact me!



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<https://tinyurl.com/EDMUnit>