Reproducibility and Generalizability in Vaccine Effectiveness Studies

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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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