Challenges in Vaccine effectiveness estimation using observational data

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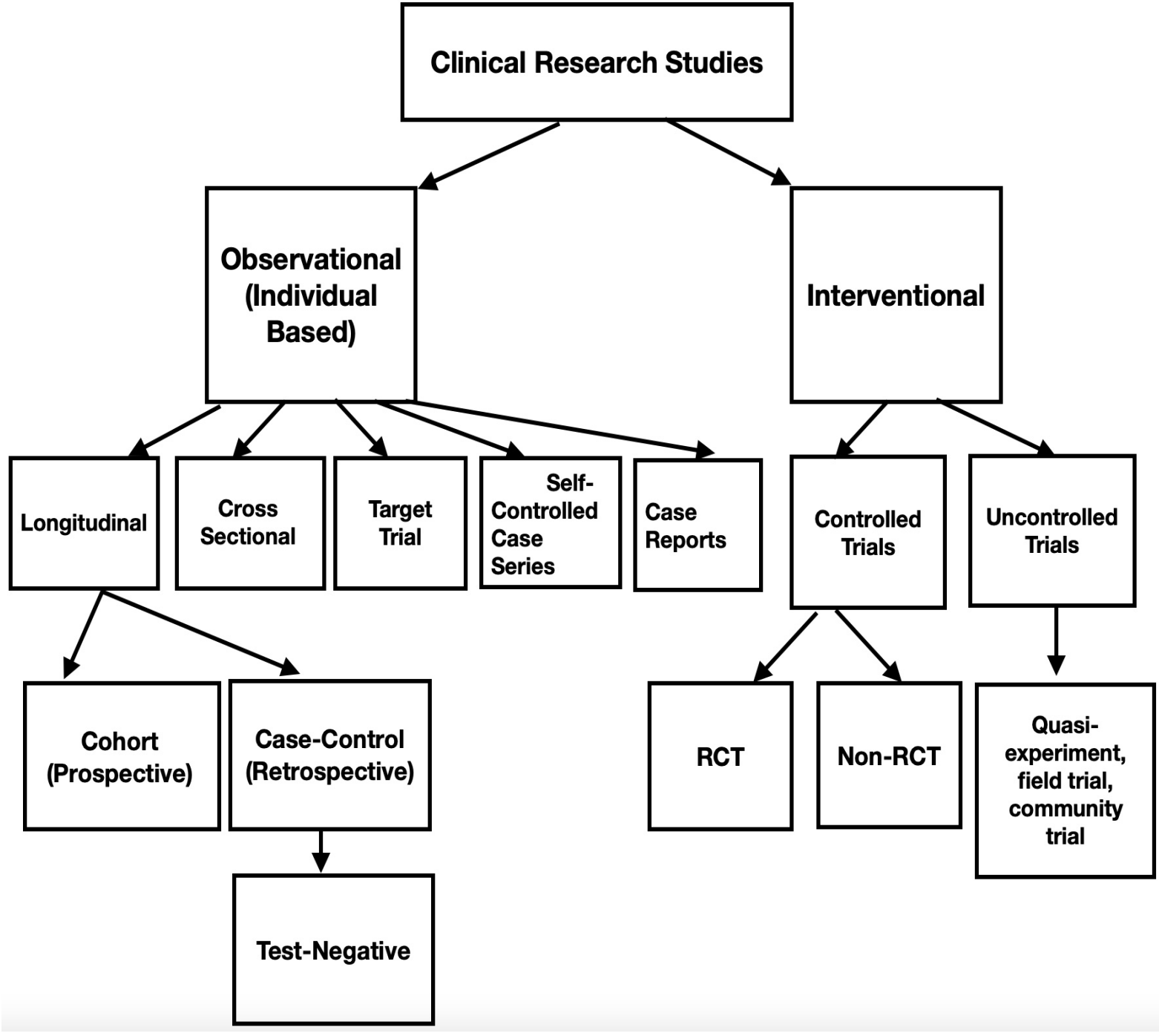
Objective of Effectiveness Studies

- Magnitude and duration of protection
- Effectiveness against new virus variants
- Effectiveness of second vaccination, boosters

Vaccine effectiveness: $\text{VE} = 1 - \text{RR}$.
Metrics:
Incidence Rates: New cases of the disease in vaccinated vs. unvaccinated populations.
Relative Risk (RR) and Odds Ratio (OR): Measures of association between vaccination status and disease occurrence.


Clinical Research Studies
Observational (Individual Based)
Interventional
Longitudinal
Cross Sectional
Target Trial
Self-Controlled Case Series
Case Reports
Controlled Trials
Uncontrolled Trials
Cohort (Prospective)
Case-Control (Retrospective)
Test-Negative
RCT
Non-RCT
Quasi-experiment, field trial, community trial

Challenges

Confounders adjustment

Observational studies can be biased because of confounding and because of inadequate design

- Identifying Confounders: Requires comprehensive understanding of the disease and factors influencing vaccination uptake.
- Demographic Factors: Age, sex, race, socioeconomic status.
- Health Status: Pre-existing conditions, comorbidities.
- Behavioral Factors: Health-seeking behavior, adherence to other preventive measures.
  - Vaccination uptake: individuals who actively seek healthcare are more likely to receive vaccinations.
  - Disease detection: those who seek healthcare regularly are more likely to be diagnosed with diseases earlier, affecting disease incidence and severity data.
  - Mask-wearing, social distancing, hand hygiene

Challenges

Confounders adjustment contd.

- Unmeasured Confounding: genetic predispositions and influence to adverse reactions to vaccines, comorbidities not recorded in the study,health literacy, psychosocial factors, lifestyle factors, environmental exposures, cultural beliefs and practices.
  - Sensitivity analysis to assess the potential impact of unmeasured confounding and collecting additional data where possible.

Bias Considerations

- Cohort Studies: Selection bias, and Information bias
  - Selection bias: Differences in baseline characteristics between vaccinated and unvaccinated groups can affect outcomes. (PS matching)
  - Information bias: Misclassification of exposure or outcome status can distort results.
- Case-Control Studies: Recall bias and control selection
  - Recall Bias: Cases may remember their vaccination status differently than controls.
  - Control Selection: Ensuring controls are representative of the population that produced the cases.

Bias Considerations

- Selection/Collider Bias: variable (collider) creates spurious association between the exposure and the outcome, because it is influenced by both the exposure (e.g., vaccination) and the outcome (e.g., disease) and is conditioned upon, either by design or during analysis.
- Collider Bias: Do not restrict the analysis to specific subgroups where the collider is present, such as hospitalized patients only.
  - Use advanced statistical techniques to account for the pathways involving colliders.
  - Conduct sensitivity analyses to estimate the potential impact of collider bias on the results.

Data Quality

- The quality and completeness of data sources like EHRs(CPRD, HES, THIN), linkage to registries, or insurance claims impact the reliability of findings.
- Missing data or inaccuracies, integrating data from different sources can be complex and error-prone.

Ethical and Practical Considerations

- Informed Consent: Often waived for large-scale observational studies using de-identified data.
- Data Privacy: Ensuring confidentiality and security of personal health information.

Effect Modification

- The effect of vaccination might differ across subgroups of the population (e.g., age, comorbidities, ethnicity, deprivation status).

Temporal Factors

- Vaccine effectiveness may change over time due to factors like waning immunity or the emergence of new variants.
- Changes in virus epidemiology and evolving health conditions can affect long and short terms effectiveness estimates.
- Access to healthcare and public health practices can change over time, such as during different waves of the pandemic.
- Time-Varying Confounding: other than baseline there are confounders that change over time, such as social interactions, travel patterns,health status of older adults.

Real-World Context

- Vaccine Uptake and Coverage: Real-world acceptance and logistical challenges.
- Transmission rates (herd immunity), disease severity (reduction in morbidity and mortality), long-term health impacts.