Epib 605

A few random thoughts

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Week 5

- Risk of SARS-CoV-2 Infection Among Households With Children in France, 2020-2022
- ClinicalTrials.gov registration NCT04607941

CONCLUSIONS AND RELEVANCE The presence of children, notably very young ones, was associated with an increased risk of SARS-CoV-2 infection in other household members, especially during the Delta and Omicron BA.1 waves. These results should help to guide policies targeting children and immunocompromised members of their household.

Last sentence seems aspirational.

No direct evaluation of any specific policies or interventions, so the policy implications are not strongly supported by the data

Results more useful for generating hypotheses and informing future research rather than guiding immediate policy decisions.

What exactly was the objective

- JAMA paper - “To estimate the risk of SARS-CoV-2 infection among households with children and to evaluate how this risk evolved during the pandemic.”

- Protocol ClinicalTrials.gov - “The objective of the study is to identify socio-demographic factors (age, gender, location of residence, socio-economic level, etc.), behaviors and practices associated with infection with SARS-CoV-2 to help determine where and how patients mostly get infected with SARS-CoV-2.”

Material gap between the two

Where time-period and school-level analyses post-hoc? Would that matter?

Absence of any single primary pre-specified estimand makes interpretation more difficult

Nomenclature

Estimand: A description of the exact treatment effect a study aims to quantify - helps align a study's methods with its aims and ensures clarity in the treatment effect's interpretation, ensure clarity of the research question, and facilitate critical appraisal of the study's methods
Estimator: The statistical method used to compute the estimate of the treatment effect
Estimate: The numerical value computed by the estimator

Reference: The estimands framework: a primer - BMJ 2024;384:e076316 http://dx.doi.org/10.1136/bmj-2023-076316

PICO vs Estimand

PICO frames the research question
Estimand is the exact numerical target that answers the research question
Without it, questions can be interpreted many way
With it, analysis becomes transparent, reproducible, and decision-relevant

Aspect	PICO (good research question)	Estimand (exact numerical target)
Population	Broad description of who	Operational cohort (when/where/how identified; inclusion/exclusion)
Intervention/Exposure & Comparator	Names the arms/conditions	Contrast plus how to handle intercurrent events
Outcome	Names the endpoint	Endpoint definition + timing/window
Measure	Often omitted	Specified (RD, RR, OR, HR, etc.)
Multiplicity	Not addressed	Primary vs secondary estimands declared

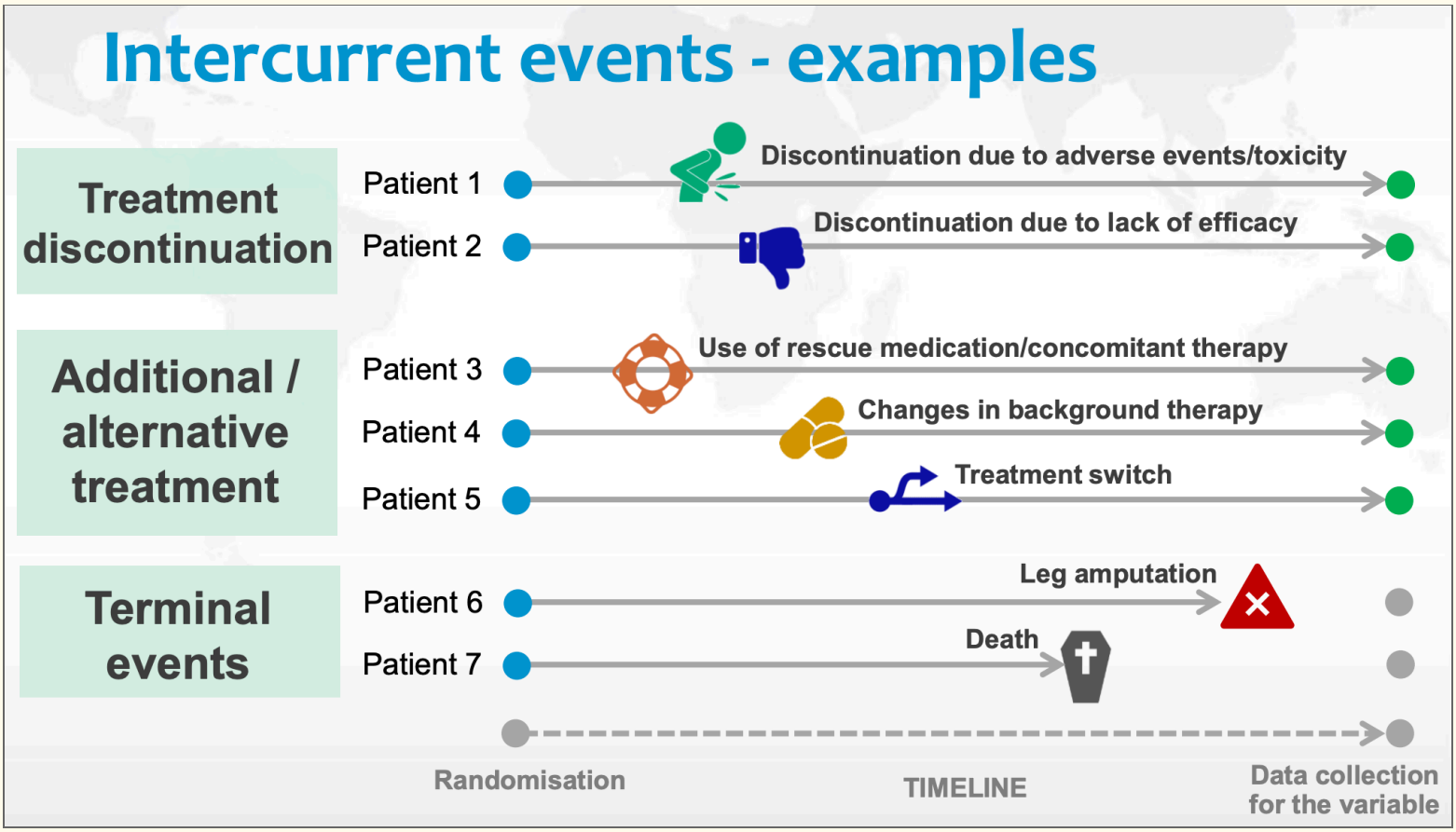
Aspect	PICO (good research question)	Estimand (exact numerical target)
Reproducibility	Moderate	High—two analysts compute the same target

Reference: The estimands framework: a primer - BMJ 2024;384:e076316 http://dx.doi.org/10.1136/bmj-2023-076316

From PICO → Estimand (add T-I-M-E)

T — Time window: When is the outcome assessed? Over what horizon?
I — Intercurrent events: How will you handle events that occur after treatment/exposure assignment and affect interpretation? (Choose a strategy and state it.)
M — Measure: Which effect measure summarizes the contrast (RD, RR, OR, HR, etc.)?
E — Eligible population (operational): The practical definition of who is actually included (sampling frame, time, data source).

Intercurrent events



Intercurrent events - common strategies

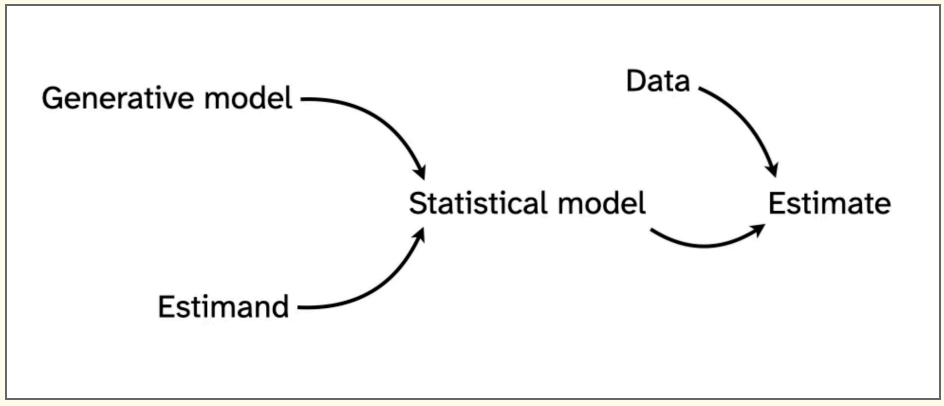
Treatment policy: Analyze as randomized/assigned, regardless of intercurrent events.
While-on-treatment: Count outcomes only up to discontinuation/switch.
Hypothetical: Model the outcome had the intercurrent event not occurred.
Composite: Make the intercurrent event part of the endpoint (e.g., death or hospitalization or infection).
Principal stratum: Restrict to the subgroup in which the intercurrent event would not occur.

Study withdrawal, loss-to-follow-up and other reasons for missing data (such as administrative censoring in survival studies) are not generally regarded as intercurrent events, but rather as missing data problems.

Estimands and workflow

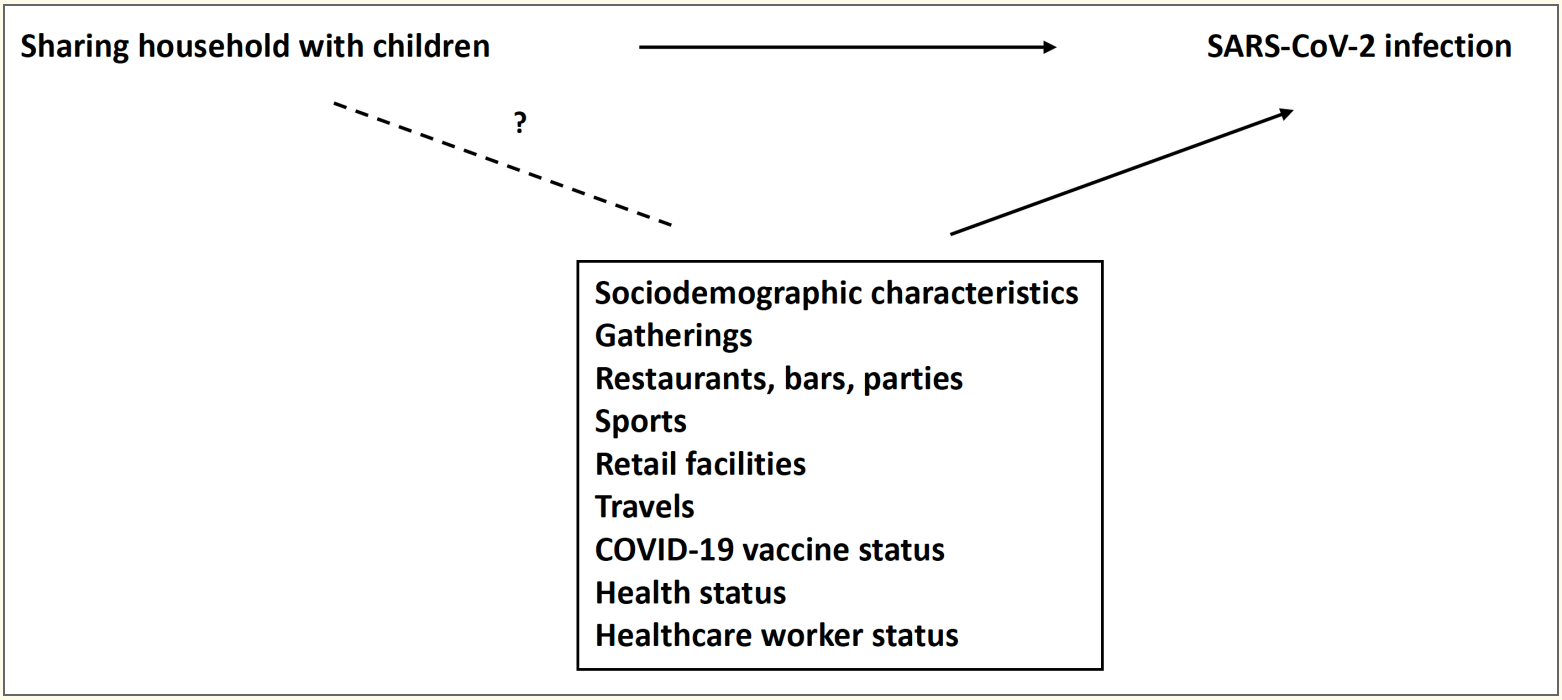
Estimand = the precise quantity a study intends to estimate for a specific population, tying the scientific question to a statistical summary

Sample potential estimand: Among French adults from Oct-2020 to Oct-2022, the adjusted odds ratio (AOR) for different waves of SARS-CoV-2 infection comparing adults who live with ≥1 child vs those who do not, adjusting for covariates per the DAG



Generative model includes DAG + their functional relationships

Residual confounding?



Possible other confounders not included in the DAG:

- Household crowding & dwelling ventilation
- Baseline immunity status
- School-level mitigation strategies (mask mandates, class size, ventilation, hybrid/closures, etc)
- Adult occupation exposure beyond healthcare worker status (teachers, retail, transport, hospitality)

A few slides

Speaker notes