

Study Design: an Overview

Dr. med. Pascal M. Frey, MSc

Oberarzt, Inselspital, Universitätsklinik für Allgemeine Innere Medizin



Seminar Series 2021/2022

Why is the study design important?

Before its withdrawal, the paper was viewed more than 150,000 times, cited more than 30 times and included in a number of meta-analyses that collect trial findings into a single, statistically weighted result. In one meta-analysis in the *American Journal of Therapeutics* that found ivermectin greatly reduced COVID-19 deaths⁴, the Elgazzar paper accounted for 15.5% of the effect.

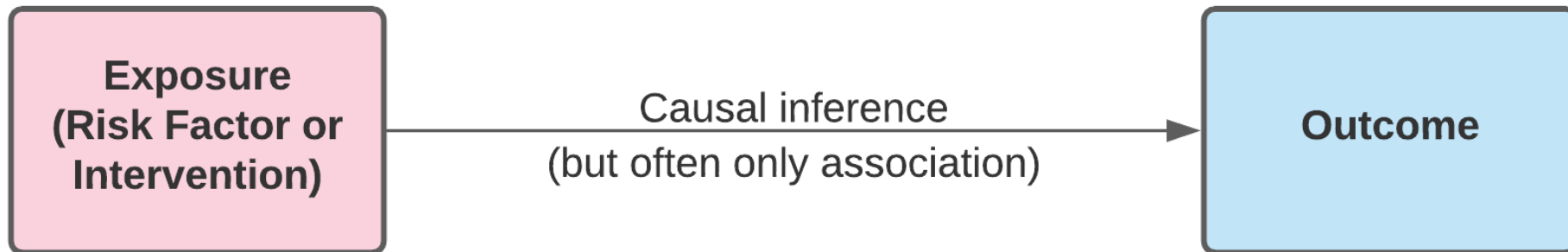


People in Bolivia and elsewhere have been buying ivermectin as protection against COVID-19.

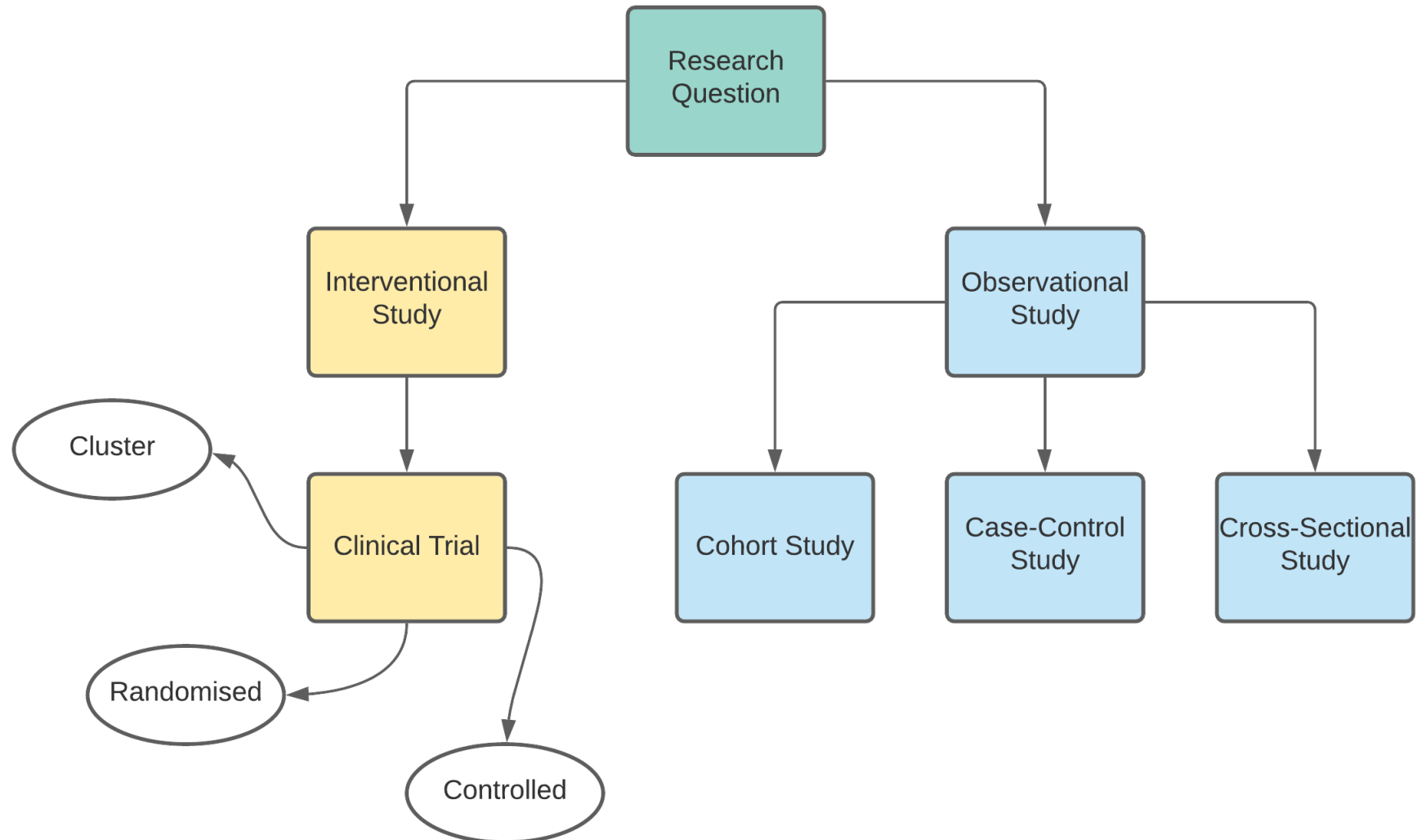
FLAWED PREPRINT HIGHLIGHTS CHALLENGES OF COVID DRUG STUDIES

Readon S, Nature News, 12 August 2021

What is the purpose of a study?



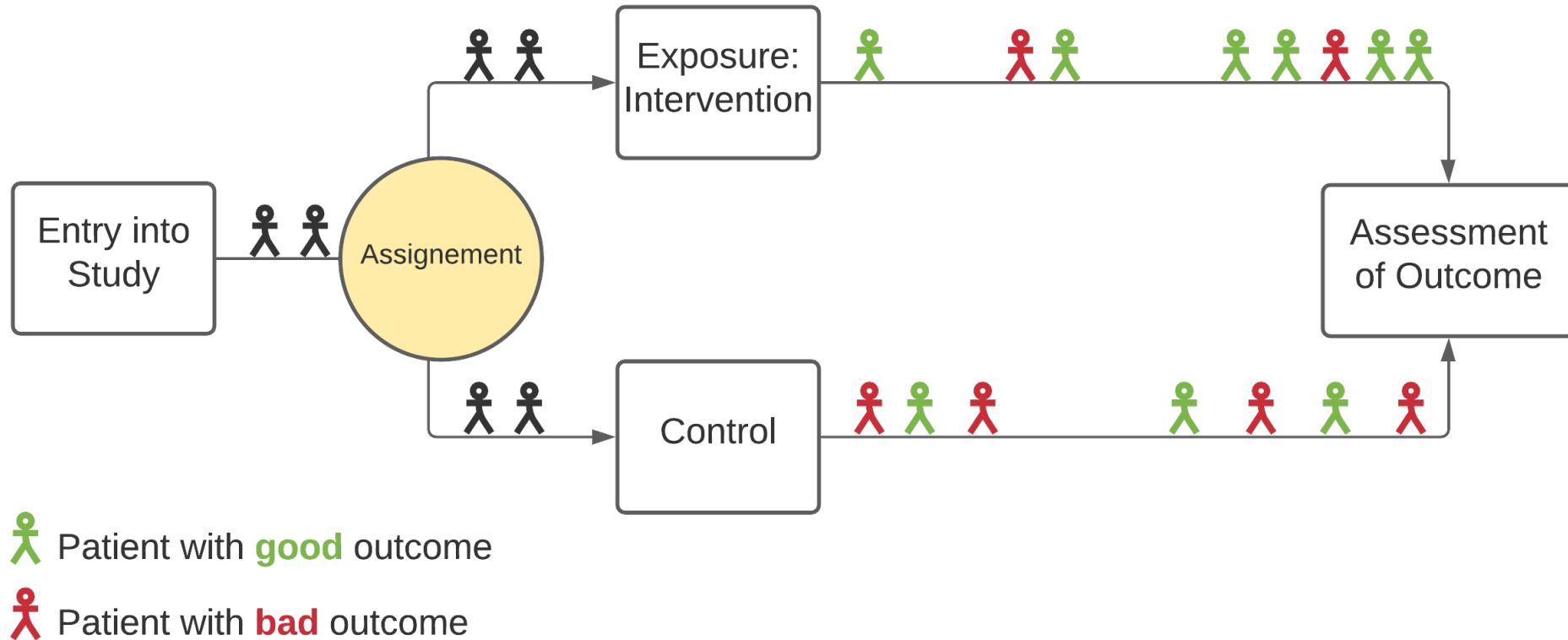
What is the purpose of a study?



What is a Clinical Trial?

- Design to study the effect of an intervention on a desired outcome
- Usually **controlled** = patients with the intervention are compared to a control group not given the intervention
- Ideally **randomized** = allocation to group (intervention or control) is random and cannot be predicted
- Ideally (double) **blinded** = group allocation is not known to anyone until after data analysis

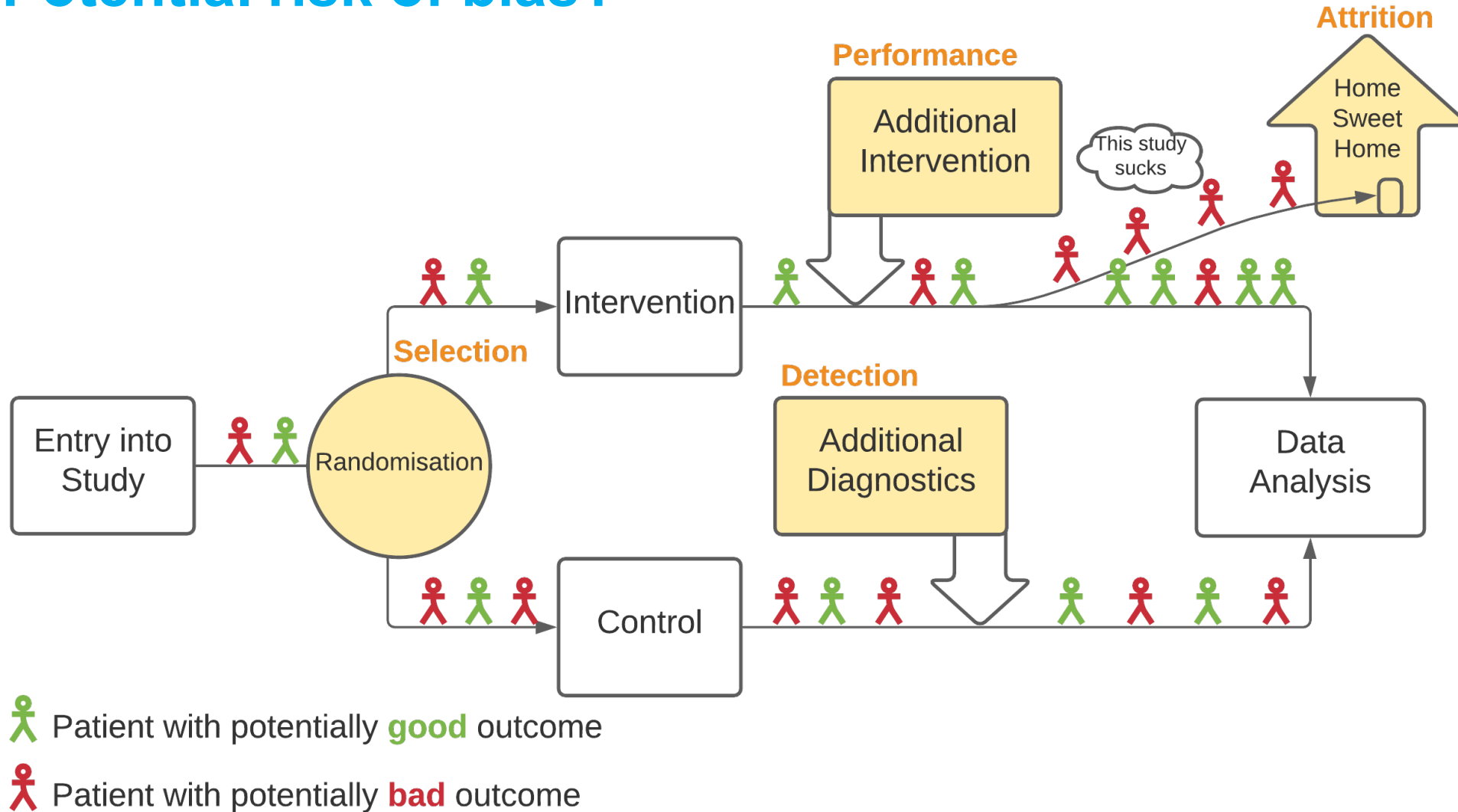
How does it work?



Why use it?

- Randomisation makes effect attributable to intervention
- **Conclusions on causality possible!**
- Low risk of bias if designed well

Potential risk of bias?



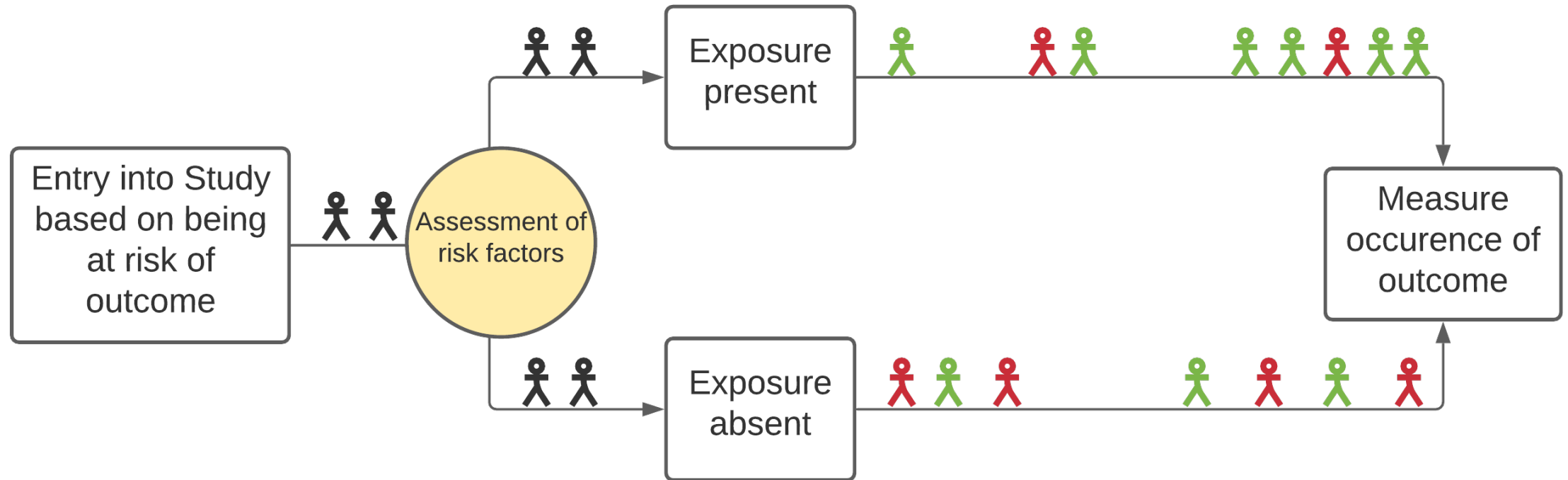
Weaknesses

- Cost: RCT is the most expensive study design
- Not always feasible because of ethics
- Generalisability sometimes difficult (often narrowly defined study population)
- Loss to follow-up (biased results)

What is a Cohort Study?

- Participants (the cohort) is selected based on being at risk of an outcome
- Exposure and risk factors ideally assessed before outcome occurs (prospectively)

How does it work?



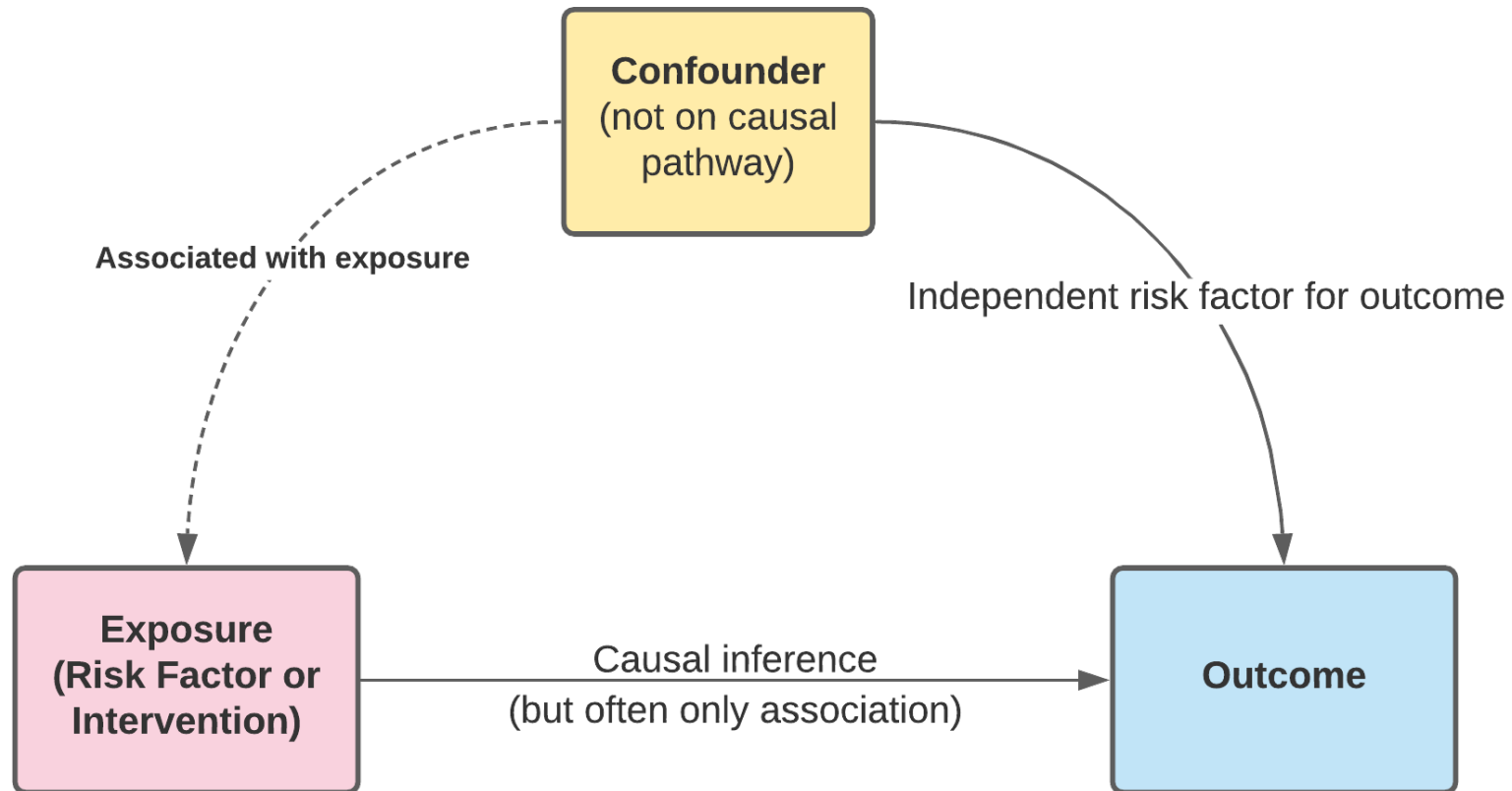
 Patient with **good** outcome

 Patient with **bad** outcome

Why use it?

- Investigate rare exposures
- Multiple outcomes (in participants at risk)
- Can measure incidence of a disease
- Intermediate cost

Risk of Confounding



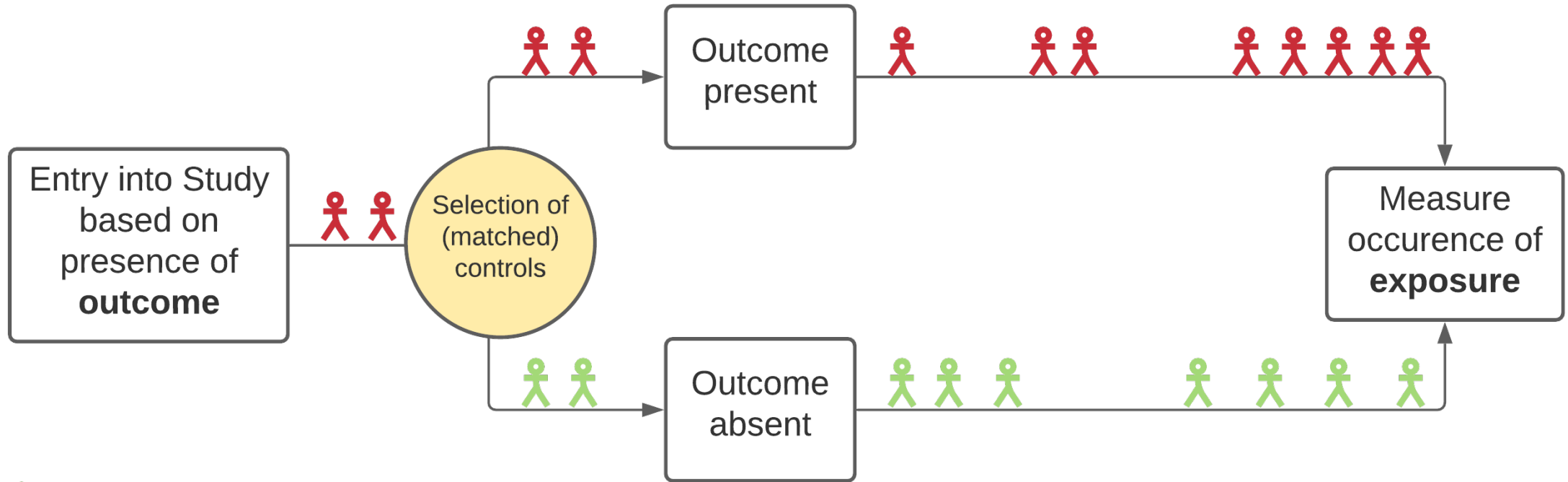
Weaknesses

- Cost: less expensive than RCT, but still expensive
- Time to completion (usually months to years [to decades])
- Loss to follow-up may bias results

What is a Case-Control Study?

- Participants (the cases) are selected based on **outcome**
- Exposure often assessed after occurrence of outcome

How does it work?



 Patient **without** outcome

 Patient **with** outcome

Why use it?

- Investigate rare outcomes or multiple exposures (for rare outcomes)
- Quicker and cheaper than a cohort

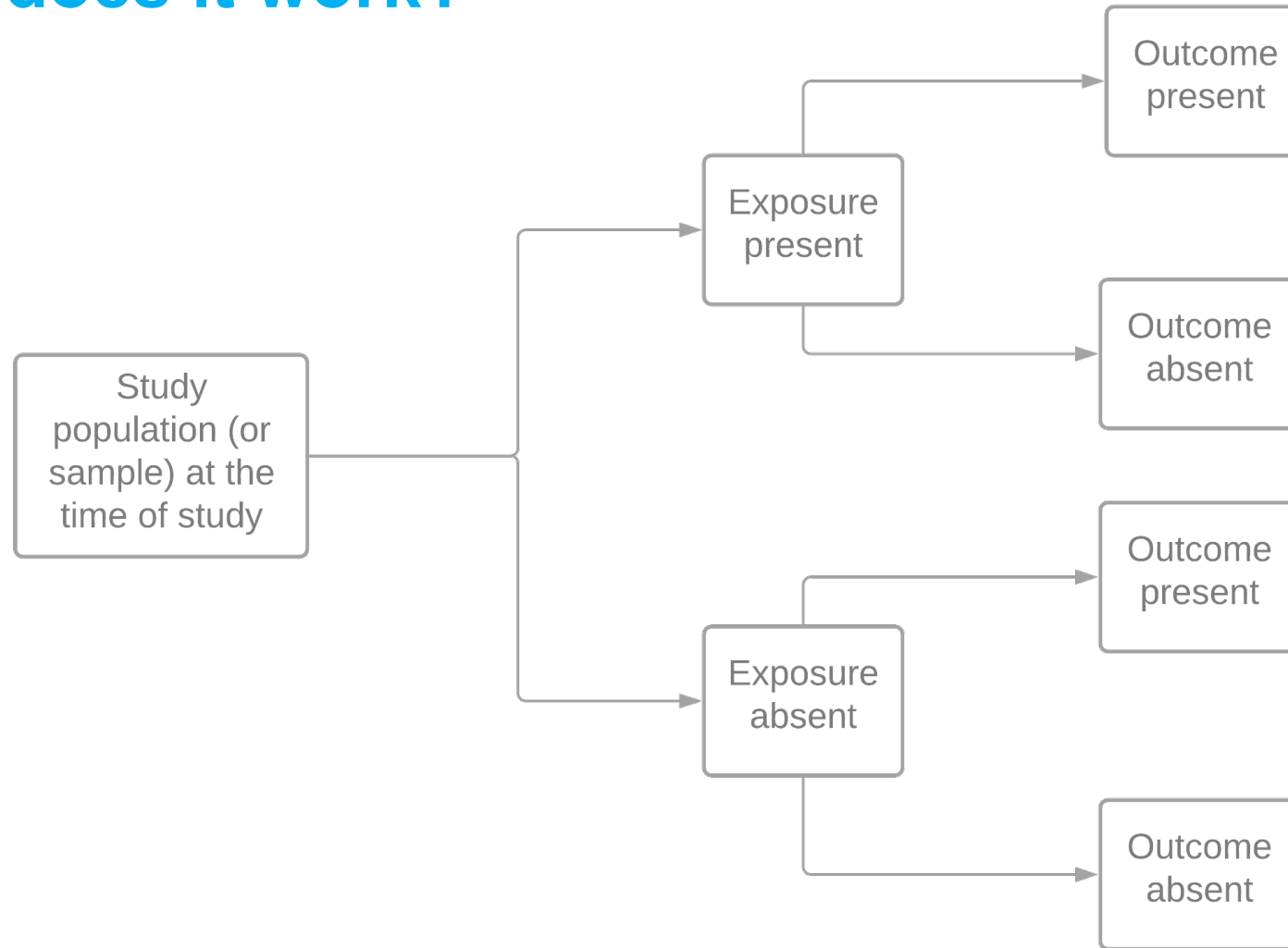
Weaknesses

- Not useful for multiple outcomes
- Difficult for rare exposures
- High risk of bias (especially selection bias) and confounding
- Temporal sequence of exposure and outcome can be unclear

What is a Cross-Sectional Study?

- Exposure and outcome assessed at the same time

How does it work?



Why use it?

- Faster and cheaper than a cohort
- Can measure prevalence of diseases

Weaknesses

- High risk of bias and confounding
- Temporal sequence of exposure and outcome are sometimes unclear

Take Home Message

Randomised Controlled Trial

- Only way to make inferences about causality
- Expensive and sometimes not feasible

Cohort Study

- Participants selected based on being at risk of outcome
- Investigate rare exposures or multiple outcomes
- Take time and cost, risk of confounding

Case-Control Study

- Participants selected based on outcome
- Useful for rare outcomes

Cross-Sectional Study

- Exposure and outcome assessed at the same time
- Faster and cheaper than cohorts, high risk of bias and confounding