

Including observational studies in systematic reviews: what, when, how and why

Rigmor C Berg

rigmor.berg@fhi.no

Purpose of research

- **Exploratory:** undertaken to handle new problem areas that haven't been explored in depth; may not offer a conclusion to the perceived issue but lays the foundation for more conclusive research
- **Explanatory:** conducted to understand why something occurs or find what is the impact of a specific change on something else, e.g. by running experiments
- **Descriptive:** focuses on expanding knowledge about something, e.g. describe the behavior of a sample
- Bottom line: we conduct research to *inform* our understanding



Who would prefer *uninformed* decisions about care and treatment?!?

- You can't make an *informed* choice without information

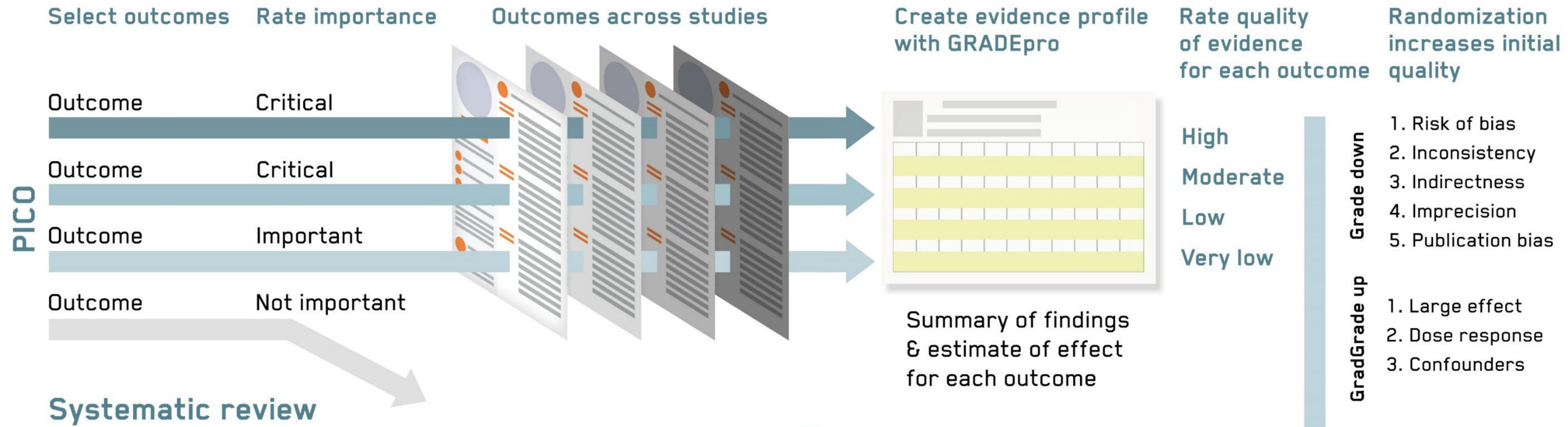


- If a decision is going to be well informed rather than misinformed, you need good information!
- Good information is the best available evidence for the specific decision

Implicit assumptions: Research evidence is insufficiently and/or inappropriately used in practice/policy decision making → Research could and should be more and better used → This would improve systems and services, and in turn, people's lives

Evidence

Formulate question



Decision

Guideline development

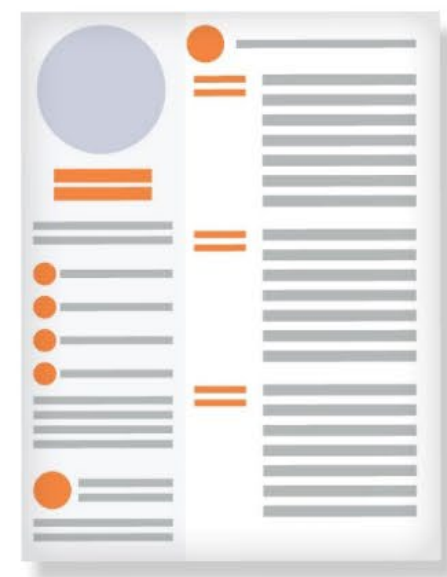
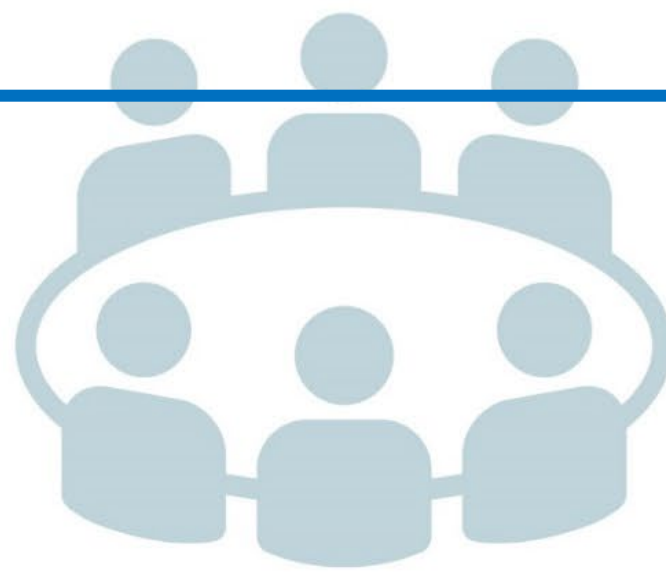
Formulate recommendations:
 For or against (direction)
 Strong or conditional/weak (strength)

By considering:

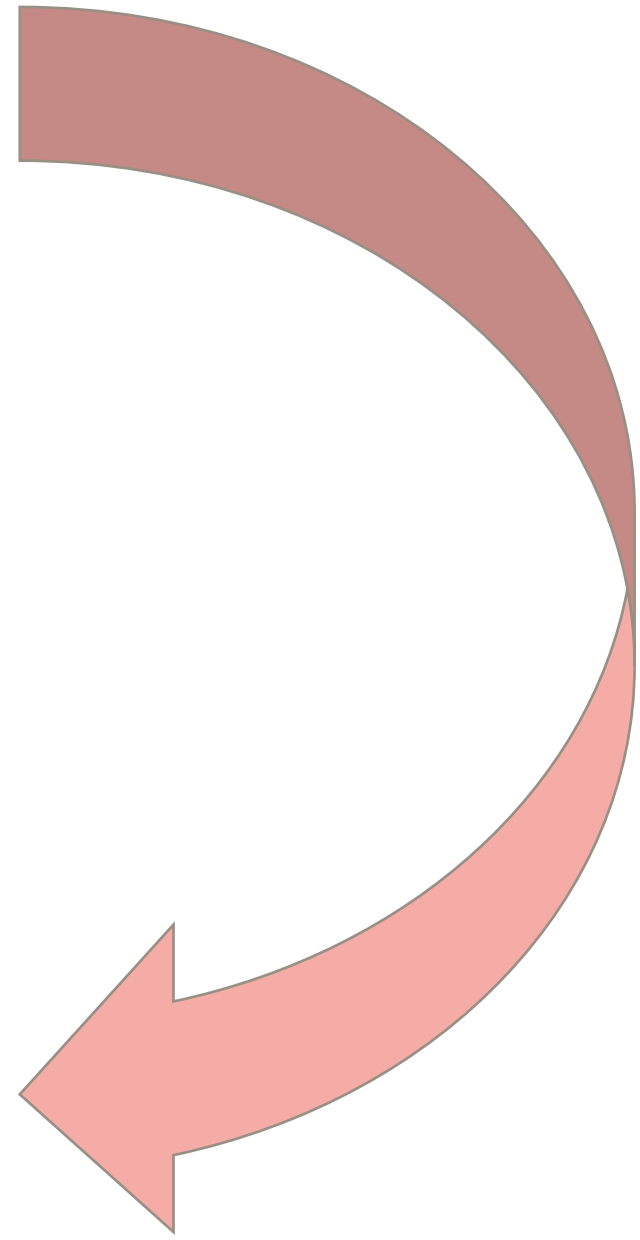
- Quality of evidence
- Balance benefits/harms
- Values and preferences

Revise if necessary by considering:

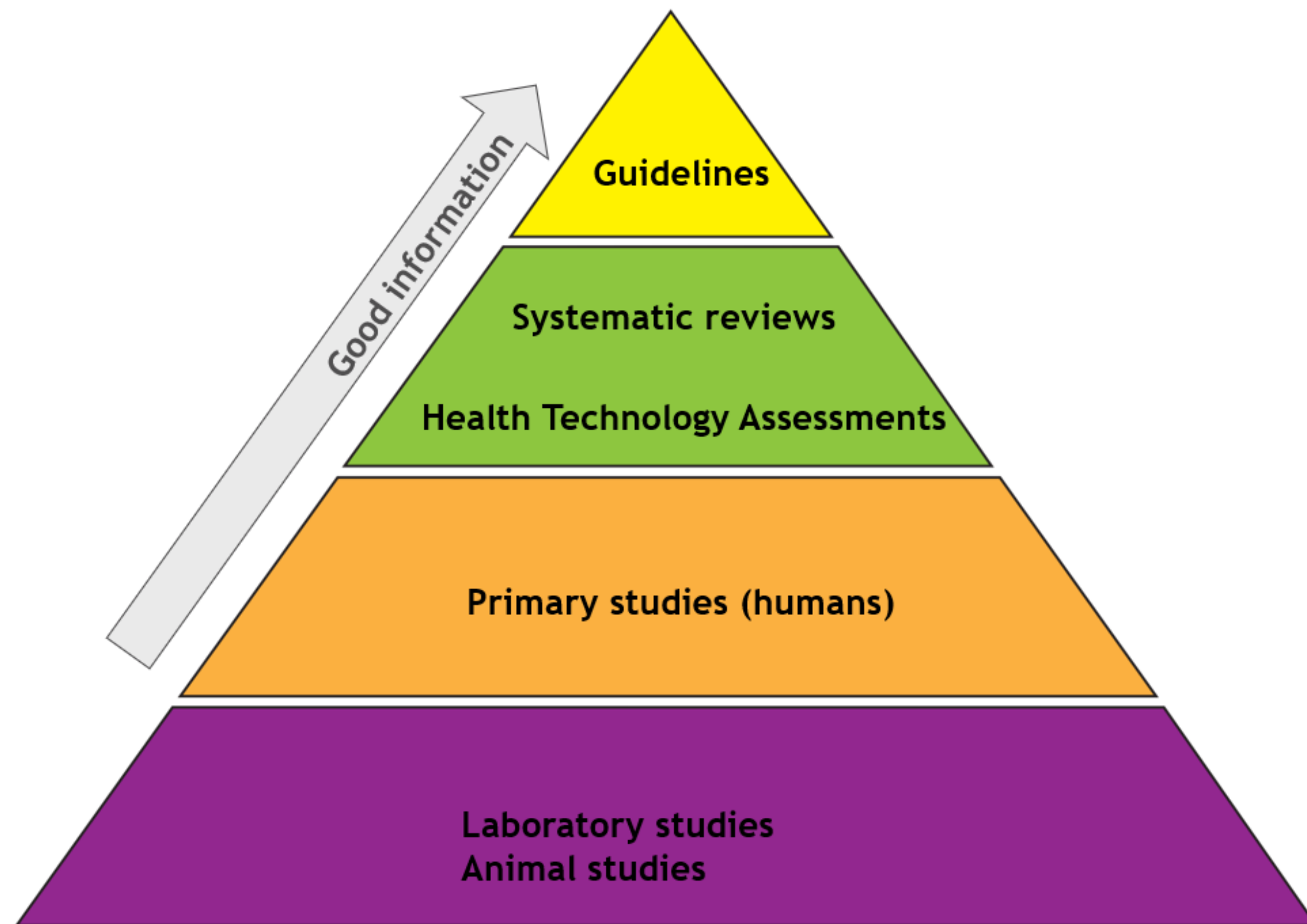
- Resource use (cost)



- "We recommend using..."
- "We suggest using..."
- "We recommend against using..."
- "We suggest against using..."



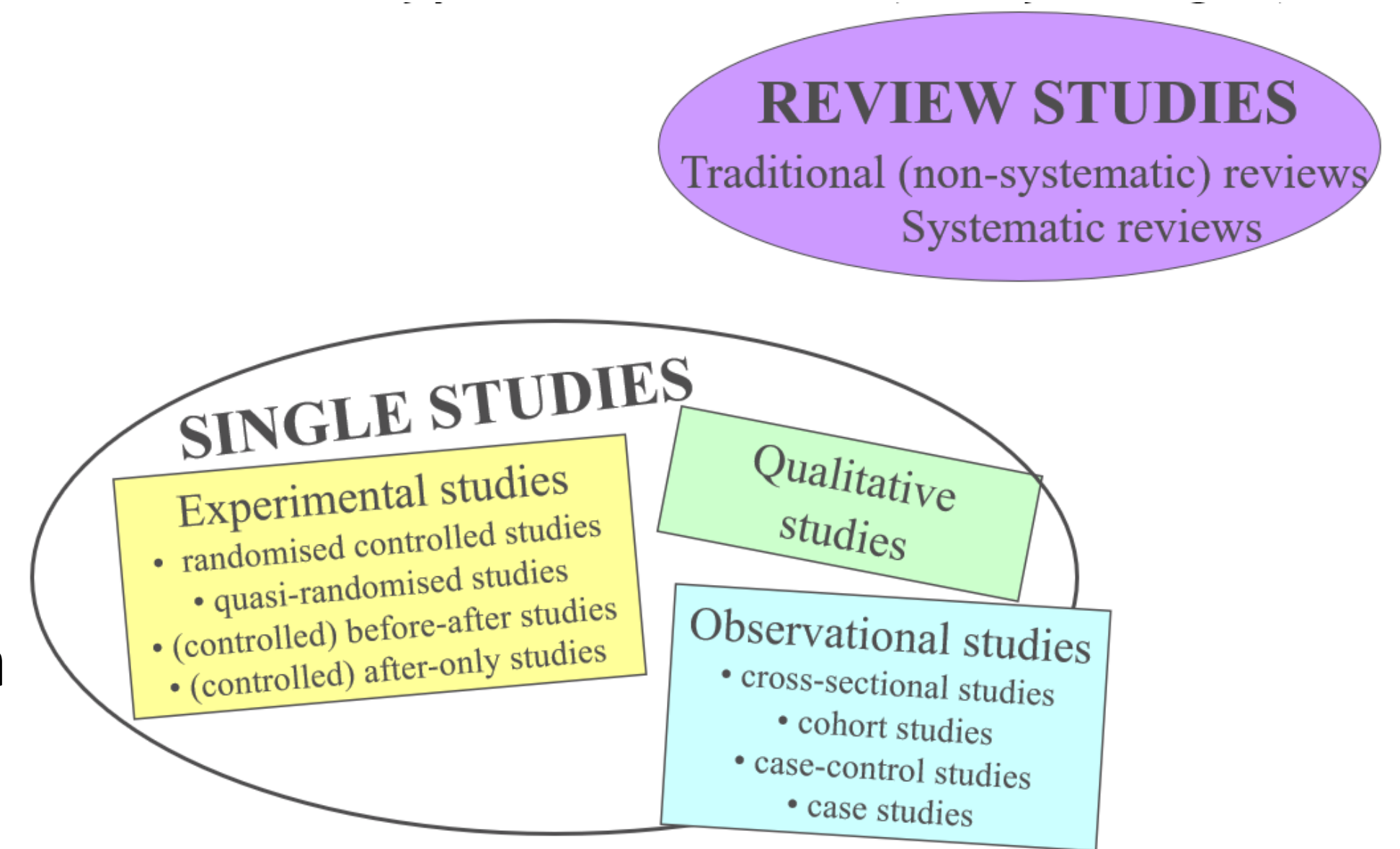
Not all evidence is created equal



- Some evidence is better, stronger or more valid than other pieces of evidence
- In terms of strength of evidence, it is the *validity* of a piece of evidence that is important
- The validity of a study is the extent to which its design and conduct are likely to prevent systematic errors (bias)
- Therefore, the more valid a piece of evidence, the greater its strength and the more secure we can feel making (treatment) decisions based on it

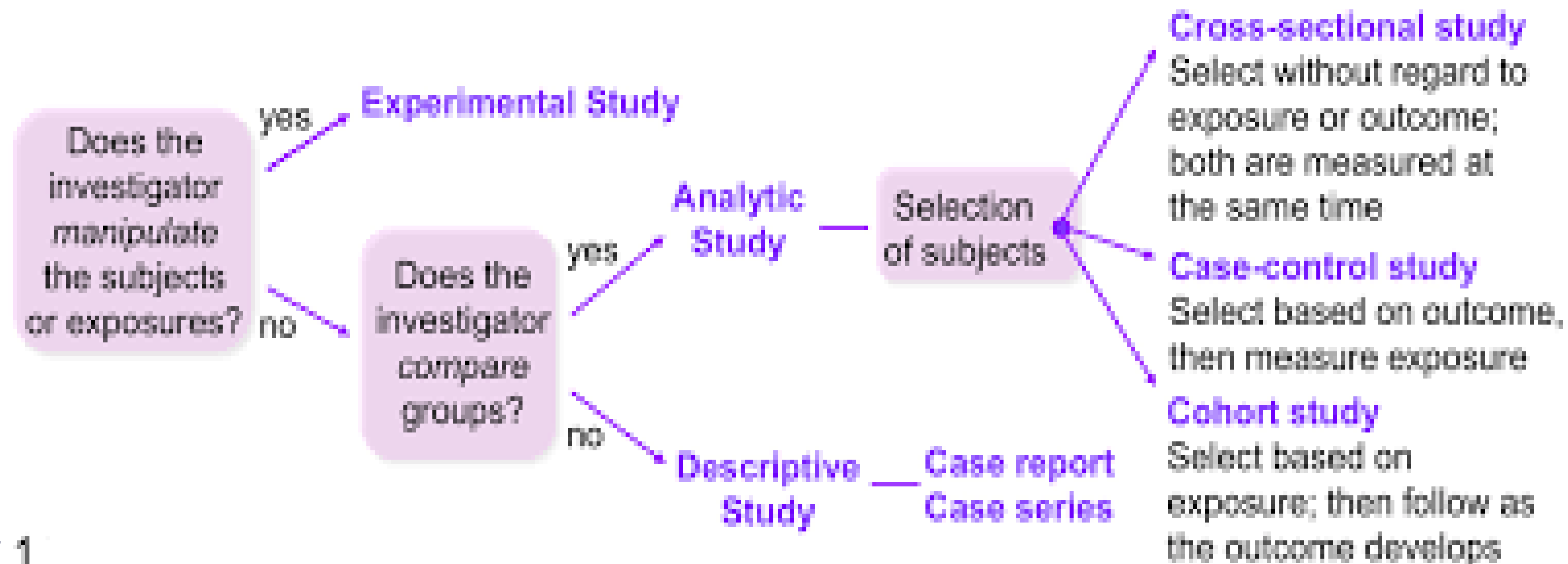
Why use an observational study

- To ensure *best available evidence* is used to answer a question
- Recall:
 - Different research designs address different types of questions
 - Research design provides the blueprint for conducting a research study and shapes what kind of knowledge is generated by the study
 - The aim of research is/should be to establish the ‘truth’ and research design aims to minimise or exclude the threats to the internal validity of the study (that is, that the conclusions are warranted by the observations)



What is an observational study

- Observational: we *observe* certain variables and try to determine what is occurring (no forced change to people's circumstances)
- Experimental: we *control* certain variables and try to determine if there is any causality



When is an observational study appropriate

- Different research designs address different types of questions:

CORE QUESTION (FOCUS)		PRIMARY RESEARCH DESIGN
How many suffer from this illness / disease / problem?	Prevalence & incidence	Cross-sectional studies
Why do some people develop ...?	Etiology (cause)	Cohort studies Case-control studies Qualitative studies
How do we know if a person suffers from...?	Measurement, tests, diagnosis	Cross-sectional studies with gold standard
How do we help ...? What is the effect of ...?	Effect of prevention, treatment, rehabilitation	Randomized controlled trials
What is the development of ...?	Prognosis	Cohort studies
How does it feel ?	Experiences, attitudes	Qualitative studies

When is an observational study appropriate

For a question about *causality*

- RCT is usually the best design for studying causal relationships (obtain estimates of average treatment effects, ATE) because it is likely to provide *balance* in covariates when the sample size is large
- Main advantage of RCT is that it can, if well-conducted, give an unbiased estimate of an ATE in a study (trial) sample and thus provide evidence that the treatment caused the outcome in some individuals in that sample
- Sometimes RCT is not feasible: e.g. small population
- Sometimes RCT is unethical: e.g. unnecessarily exposes (many) people to possible harm

 **HHS Public Access**
Author manuscript
Soc Sci Med. Author manuscript; available in PMC 2018 August 01.

Published in final edited form as:
Soc Sci Med. 2018 August ; 210: 2–21. doi:10.1016/j.socscimed.2017.12.005.

Understanding and misunderstanding randomized controlled trials

Angus Deaton and
Princeton University, NBER, and University of Southern California

Nancy Cartwright
Durham University and UC San Diego

Abstract

Randomized Controlled Trials (RCTs) are increasingly popular in the social sciences, not only in medicine. We argue that the lay public, and sometimes researchers, put too much trust in RCTs over other methods of investigation. Contrary to frequent claims in the applied literature, randomization does *not* equalize everything other than the treatment in the treatment and control groups, it does not automatically deliver a precise estimate of the average treatment effect (ATE), and it does not relieve us of the need to think about (observed or unobserved) covariates. Finding out whether an estimate was generated by chance is more difficult than commonly believed. At best, an RCT yields an unbiased estimate, but this property is of limited practical value. Even then, estimates apply only to the sample selected for the trial, often no more than a convenience sample, and justification is required to extend the results to other groups, including any population to which the trial sample belongs, or to any individual, including an individual in the trial. Demanding 'external validity' is unhelpful because it expects too much of an RCT while undervaluing its potential contribution. RCTs do indeed require minimal assumptions and can operate with little prior knowledge. This is an advantage when persuading distrustful audiences, but it is a disadvantage for cumulative scientific progress, where prior knowledge should be built upon, not discarded. RCTs can play a role in building scientific knowledge and useful predictions but they can only do so as part of a cumulative program, combining with other methods, including conceptual and theoretical development, to discover not 'what works', but 'why things work'.

Evidence for Health Decision Making — Beyond Randomized, Controlled Trials

Thomas R. Frieden, M.D., M.P.H.

Article Figures/Media Metrics August 3, 2017
N Engl J Med 2017; 377:465-475
DOI: 10.1056/NEJMra1614394
Chinese Translation 中文翻译

98 References 443 Citing Articles 11 Comments

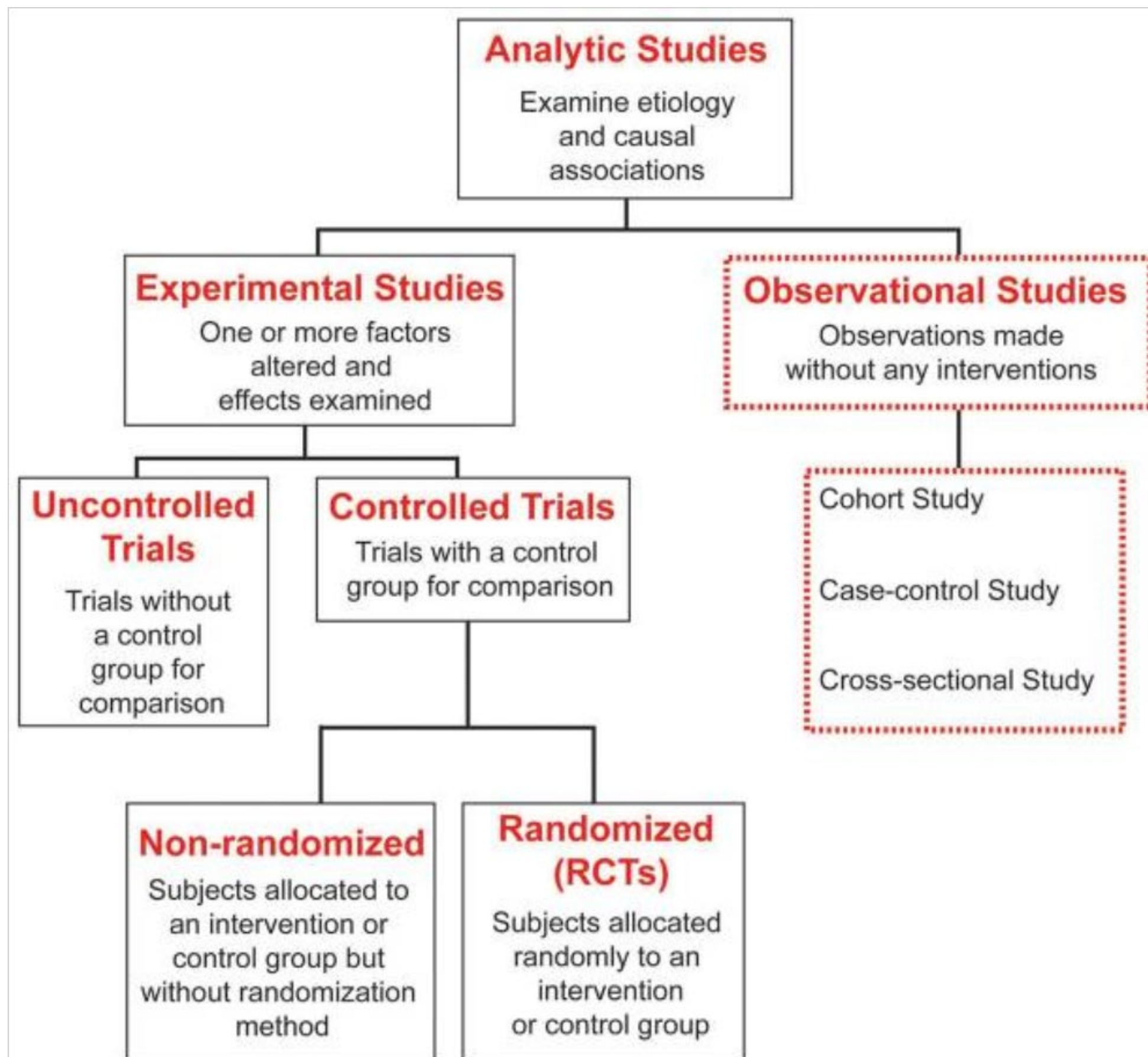
When is an observational study appropriate

Example where RCT unethical

- ECMO (Extracorporeal Membrane Oxygenation): treatment for newborns with persistent pulmonary hypertension; developed in 1970s through directed trial and error, guided by understanding of disease and how the oxygenator worked
- In early experimentation: mortality down from 80% to 20%
- Adaptive RCT: each success in an arm increased the probability of the next baby being assigned to that arm. Result: One baby received conventional therapy and died, 11 received ECMO and lived
- Standard RCT: with a stopping rule of four deaths, 4 more babies (out of 10) died in the control group and 0 of the 9 who received ECMO



How are observational studies used



- All research study designs have inherent strengths and flaws
- The study design used to answer a particular research question depends on the *nature of the question* and usually the availability of resources
- Cross-sectional studies, case-control studies, cohort studies, case reports, case series, ecological studies, qualitative studies
- Data linkage, registries, propensity score matching, etc.
- All evidence is context sensitive – all observations are context specific
- Global evidence – the best evidence from around the world – the best starting point for judgements about the impacts of policies
- Local evidence is necessary to inform most other judgements about what to do

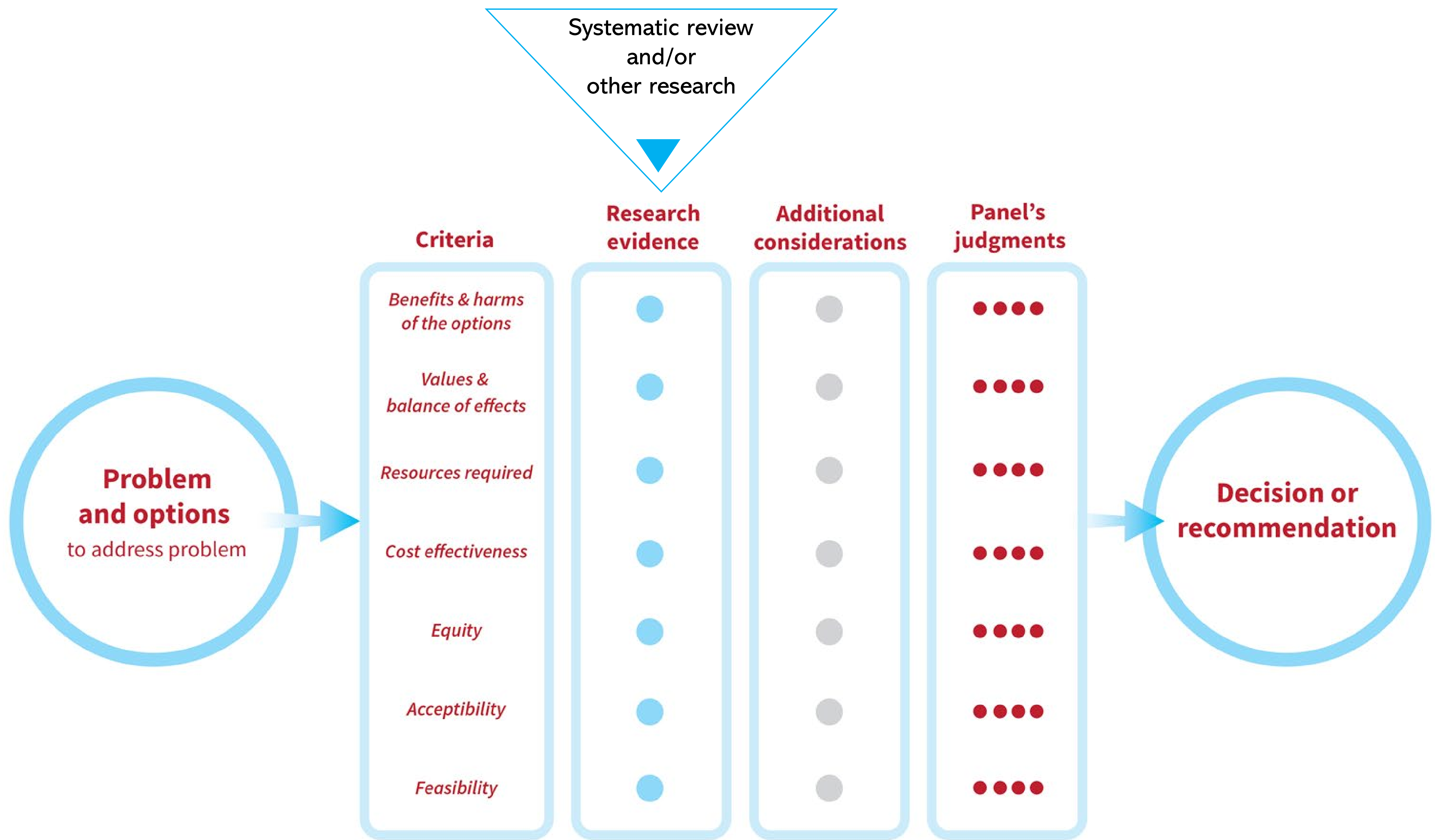
How are observational studies used



Framework for going from evidence to decisions



A structured and transparent way to inform decisions in the context of (clinical) recommendations, coverage decisions, and health system or public health recommendations and decisions



Example of case where evidence is from observational studies

- **Question:** What is the effect of shared physical custody for children?
- **Assessment:** Best available research evidence on the effect of shared physical custody for children
→ conducted a systematic review
 - Familiarized ourselves with the topic and debates in the field
 - Had close dialogue with the commissioner, experts on the topic, specialists, parents' groups, family therapists
 - Wrote report that explained the topic, the debate, the existing research and our evaluation of it
 - Presented, explained, discussed, debated findings of report to different interest groups, in different ways, using full report and tailored products



Example of case where evidence is from observational studies

How can we know if a child has been the victim of abuse? How can we elicit truthful disclosure or recall of events from children?

- Question: What is the effect of open-ended prompts in conversations with children in eliciting truthful disclosure of abuse?
- Assessment: Best available research evidence on the 'effects' of open-ended prompts → conduct a systematic review
 - Familiarized ourselves with the topic and debates in the field
 - Had close dialogue with the commissioner, experts on the topic, specialists, parents' groups, family therapists
 - Wrote a report that explained the topic, the debate, the existing research and our evaluation of it
 - Presented, explained, discussed, debated findings of report to different interest groups, in different ways, using full report and tailored products



Summary

- Observational study: we merely *observe* and there's no forced change to people's circumstances
- Different designs for different questions
- The validity of a piece of evidence must be considered
- Cumulative scientific progress is difficult, and prior knowledge should be built upon, to *inform*
- When go from evidence to decision, most evidence is observational



Thank you for your kind attention 

Mange tak! *Merci bien!*

Tack! **Takk!**