Randomized Controlled *Trials* & Observational *Studies*

Medical studies are used to explore whether an exposure or intervention **causes** a certain outcome[1]

A better **understanding of causation** helps **support** decision making[1,2]

Both **randomized controlled trials** and **observational studies** can be used to generate medical evidence[2]

Well-designed randomized controlled clinical trials are considered **the "gold standard"** for medical evidence[1]

Observational studies are a source of data for **real-world evidence (RWE)**, providing evidence in situations **outside** of carefully controlled clinical environments[3]

Confounders[4]

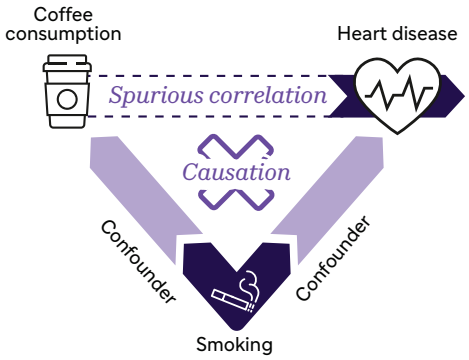
Observational studies can have the issue of *confounders*

Confounders are factors associated with the outcome of interest and the other factors studied

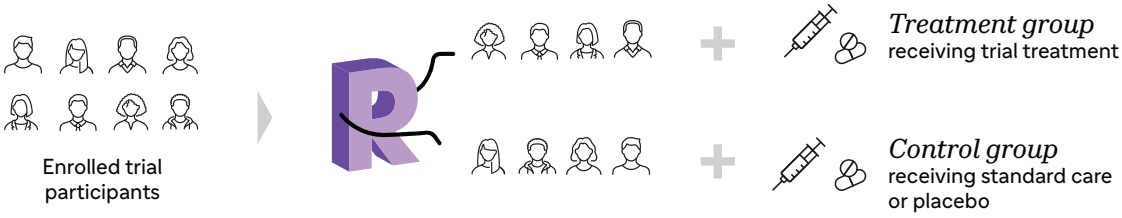
Can lead to *non-comparable* groups and *incorrect conclusions*

A *well-designed* trial can help reduce confounders

Example of a confounder



A well-designed randomized controlled trial helps balance confounders[1,4]



Adapted from Brody (2016).[5]

Randomization can provide a **similar distribution of confounders** across groups[4]

Groups should be **comparable** except for treatment[1]

A **treatment–outcome relationship** can often be determined[4]

References:
1. Friedman LM, Furberg CD, DeMets DL, Reboussin CBG. Fundamentals of clinical trials. 5th ed. Switzerland: Springer; 2015. **2.** International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use. Generation considerations for clinical studies (R1). Available at: https://database.ich.org/sites/default/files/E8-R1_Guideline_Step4_2021_1006.pdf. Accessed December 6, 2022. **3.** Faries D, Zhang X, Kadziola Z, Siebert U, Kuehne F, Obenchain RL, Haro JM. Real world health care data analysis: causal methods and implementation using SAS®. Cary, NC: SAS Institute Inc.; 2020. **4.** Hackshaw AK. A concise guide to observational studies in healthcare. London: Wiley; 2015. **5.** Brody T. Clinical trials: study design, endpoints and biomarkers, drug safety and FDA and ICH guidelines. 2nd ed. London: Academic Press; 2016.

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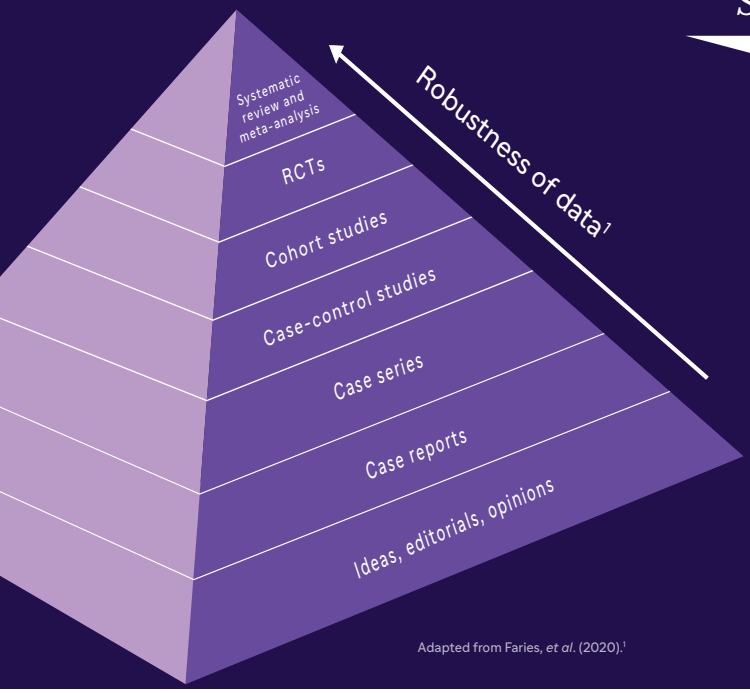
Characteristics of RCTs and Observational Studies[1-3]

RCTs		Observational studies
Predefined inclusion and exclusion criteria	Participant selection and enrolment	Data from **real-world** populations
Rigorous, with an aim towards **reproducibility**	Data collection	Uses available data, **no control over the exposure, may be more difficult to reproduce, improved generalizability**
Random assignment	Treatment assignment	Assignment is **observed**, not at random
High quality when designed and conducted correctly	Data quality and validity	**Dependent** on the **research method** used
Can assess causal effects	Intervention–outcome relation	**Association**

Summary



Adapted from Faries, *et al.* (2020).[1]

RCTs are considered the *gold standard* for clinical research and can be used to assess efficacy of an intervention[2]

Observational studies *add to evidence* from RCTs – providing additional data from a *broad patient population* or subgroups of patients typically excluded from, or not represented in, RCTs[1]

References:
1. Faries D, Zhang X, Kadziola Z, Siebert U, Kuehne F, Obenchain RL, Haro JM. Real world health care data analysis: causal methods and implementation using SAS®. Cary, NC: SAS Institute Inc.; 2020. **2.** Friedman LM, Furberg CD, DeMets DL, Reboussin CBG. Fundamentals of clinical trials. 5th ed. Switzerland: Springer; 2015. **3.** Hackshaw AK. A concise guide to observational studies in healthcare. London: Wiley; 2015.

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Do not use this piece after September 30, 2025, as some of the information may be outdated.

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