Epidemiology, Biostatistics and Evidence-Based Medicine

Curated preclinical study track (not a medical degree, no licensure claim; synthetic datasets, fictional abstracts). Original explanations and practice only, following the reviewed course handout.

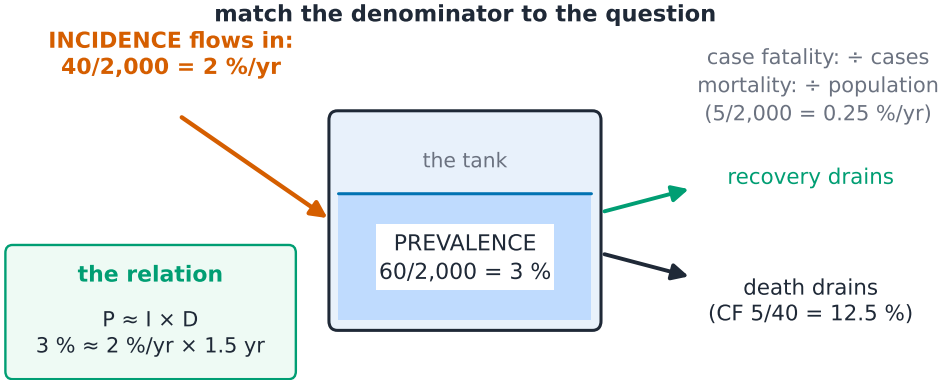
From questions to numbers

- 12.1-12.3 measure and compare; 12.4-12.6 quantify; 12.7 applies.
- Every dataset is synthetic; every abstract fictional.

Measuring disease: incidence and prevalence

1. **Flow Incidence** $40/2{,}000 = 2$ %/yr (new cases, people at risk, time).
2. **Level Prevalence** $60/2{,}000 = 3$ % on survey day; $P \approx I \times$ duration (2 %/yr $\times$ 1.5 yr).
3. **Denominators Case fatality** $5/40 = 12.5$ % (cases); cause-specific $5/2{,}000 = 0.25$ %/yr (population); standardise before comparing crude rates.

The stock-and-flow of cases

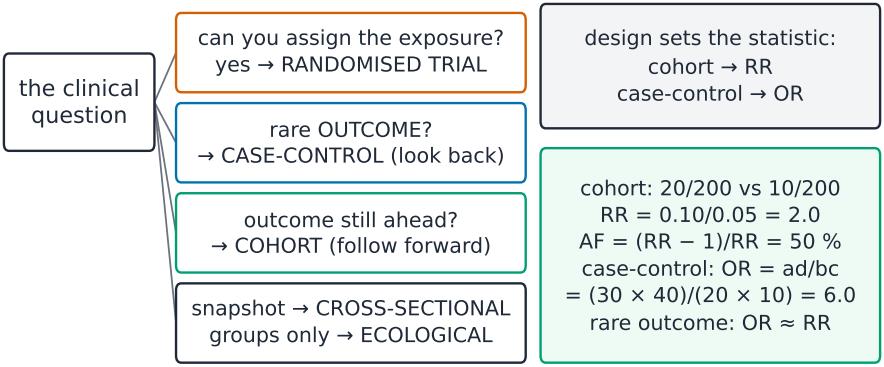


Incidence fills the tank; cure and mortality drain it - **prevalence** is the water level.

Study designs: the ladder and the statistic

1. **Ladder** Trial $\rightarrow$ cohort (by exposure, RR) $\rightarrow$ case-control (by outcome, OR $=$ ad/bc) $\rightarrow$ cross-sectional $\rightarrow$ ecological.
2. **Worked** Cohort 20/200 vs 10/200 $\rightarrow$ 0.10/0.05 $\rightarrow$ RR 2.0, AF 50 %; case-control $30 \cdot 40/10 \cdot 20 =$ OR 6.0.
3. **Why** Sampling by outcome makes arm risks artefacts; rare-disease OR $\approx$ RR.

The design decision tree



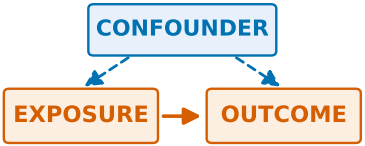
Rare outcome → case-control; exposure ahead → cohort; both at once → trial.

Bias, confounding and causation

1. **Failures Selection bias** (who counts), information/recall **bias** (what is remembered), **confounding** (third variable on both paths).
2. **Proof** Crude RR 2.0 collapsing to 1.0 in both strata = the third variable was the confounder.
3. **Causation** Hill's viewpoints with temporality first: strength, consistency, dose-response, plausibility; randomisation prevents confounding prospectively.

The confounding triangle and its cure

the triangle



crude RR 2.0

a third variable linked to exposure AND outcome

the stratification test

	exposed	unexposed	RR
crude	**20/200**	**10/200**	**2.0**
smokers	18/120	6/40	1.0
non-smokers	2/80	4/160	1.0

RR = 1.0 in each stratum: the exposed held more smokers (120 vs 40)

bias vs confounding: different failures, different cures

SELECTION bias: who gets in
RECALL bias: what is remembered
both are errors of design

confounding: a real third variable
fix: randomise, stratify, adjust
temporality: Hill's must-have

The confounder sits on the back path - stratify and the spurious association collapses.

Diagnostic tests: columns vs rows

1. **Columns** Se = a/(a+c), Sp = d/(b+d) - 90 % each in the worked example.
2. **Rows** 10 % **prevalence**: PPV 90/180 = 50 %, NPV 810/820 = 98.8 %; at 1 %, PPV 9/108 = 8.3 %.
3. **Portable** LR+ = Se/(1−Sp) = 0.9/0.1 = 9 - multiplies pre-test odds anywhere.

The 2×2 table and its natural-frequency tree

the 2×2 table

	diseased	healthy
test +	**a = 90** TP	**b = 90** FP
test −	**c = 10** FN	**d = 810** TN

Se = 90/100 = 90 % · Sp = 810/900 = 90 %
columns: test properties

natural-frequency tree: 1,000 people, 10 % prevalence



rows: population properties

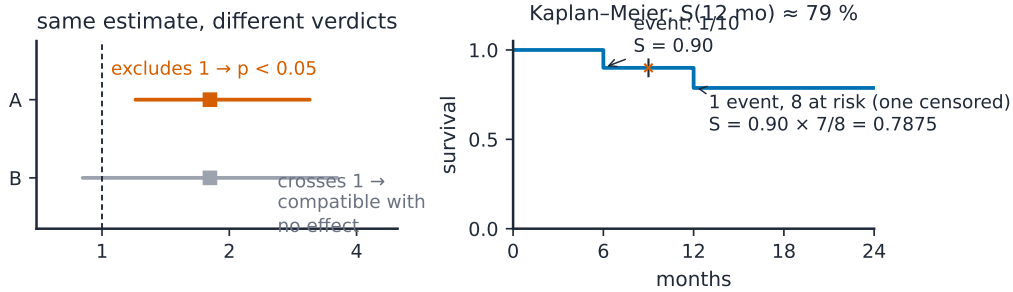
PPV 90/180 = 50 % · NPV 810/820 = 98.8 %
at 1 % prevalence: PPV 9/108 = 8.3 %
LR+ = Se/(1−Sp) = 0.9/0.1 = 9 — travels with you

Sensitivity and **specificity** live in the columns; **predictive values** live in the rows.

Statistical inference for clinical data: intervals and steps

1. **Interval** RR 1.8 (1.2–3.1) excludes 1; RR 1.8 (0.9–3.6) is compatible with no effect - same estimate, different verdicts.
2. **Tests** Counts χ^2 · two means t (paired if twice-measured) · several means ANOVA · skewed rank · correlation.
3. **Survival** Kaplan–Meier multiplies (1 − events/at-risk): S = 0.90 then $0.90 \times 7/8 = 0.7875$; median = the 50 % crossing.

CI forest and Kaplan–Meier plots



p-value: P(data this extreme | null) — surprise, not size · CI carries both · tests: χ^2 · t · ANOVA · rank · correlation

The interval carries size and precision; the survival curve steps down at events.

Clinical trials and systematic reviews: spine and pool

1. **Spine** Eligible → randomise (concealed) → blind → **intention to treat** (as randomised; dilutes toward null).
2. **NNT** Control 20 % vs treated 12 % → ARR 8 % → **NNT** 12.5 → 13; baseline 5 %, same RR → ARR 2 % → NNT 50.
3. **Pool** Forest: squares weighted by precision, diamond pooled, I^2 the disagreement gauge (22 % fine, 78 % investigate).

Trial flow into the forest plot

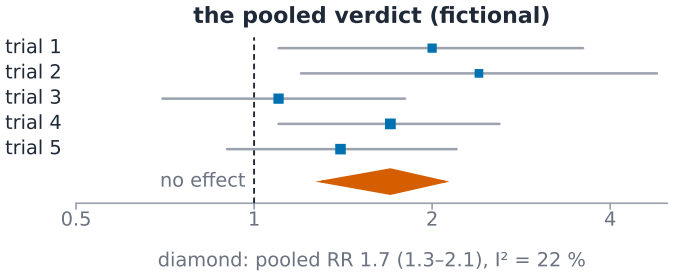
eligible
inclusion criteria

RANDOMISE
concealed allocation

BLIND
patient + assessor

analyse ITT
as randomised

ITT pulls toward no effect



NNT = 1/ARR = 1/(20 % − 12 %) = 12.5 → 13

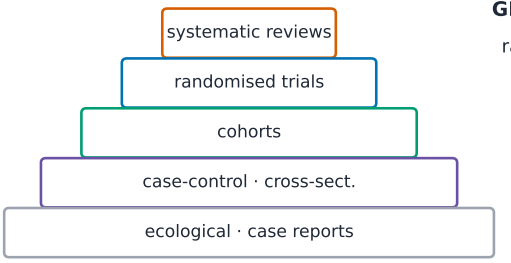
same RR at a 5 % baseline: ARR 2 %, NNT 50

Randomise, blind, analyse as randomised - then pool into the **forest plot**.

Critical appraisal and applying evidence

1. **Spine** PICO frame; validity (**bias**?); size (RR 0.75, 0.60–0.94 in the fictional abstract); applicability (was my patient enrolled?).
2. **GRADE** Trials start high, observational low; downgrade for bias, inconsistency, indirectness, imprecision; upgrade for large effects or a dose-response gradient.
3. **Apply** Recompute absolutes: baseline 5 % with the same RR turns ARR 8 % into 2 % and **NNT** 13 into 50.

The evidence hierarchy with caveats



ranks AVERAGE susceptibility
to bias, not each truth

GRADE: the pyramid is only the starting point

randomised evidence starts HIGH, observational LOW

DOWNGRADE for

risk of bias · inconsistency · indirectness
imprecision · publication bias

UPGRADE for

large effect · dose-response gradient

certainty: high · moderate · low · very low
appraise: PICO → validity → size → applicability

The pyramid ranks average susceptibility to **bias**, not the truth of each study.

Check yourself

- 40 new cases in 2,000 people-year…? (2 % per year.)
- Se = Sp = 90 % at 1 % **prevalence**: PPV…? (8.3 %.)
- ARR 8 % → **NNT**…? (12.5 → 13.)
- The Kaplan–Meier rule after 1/8 at risk…? ($\times$ 7/8.)