

Exercise walk-through

12.6

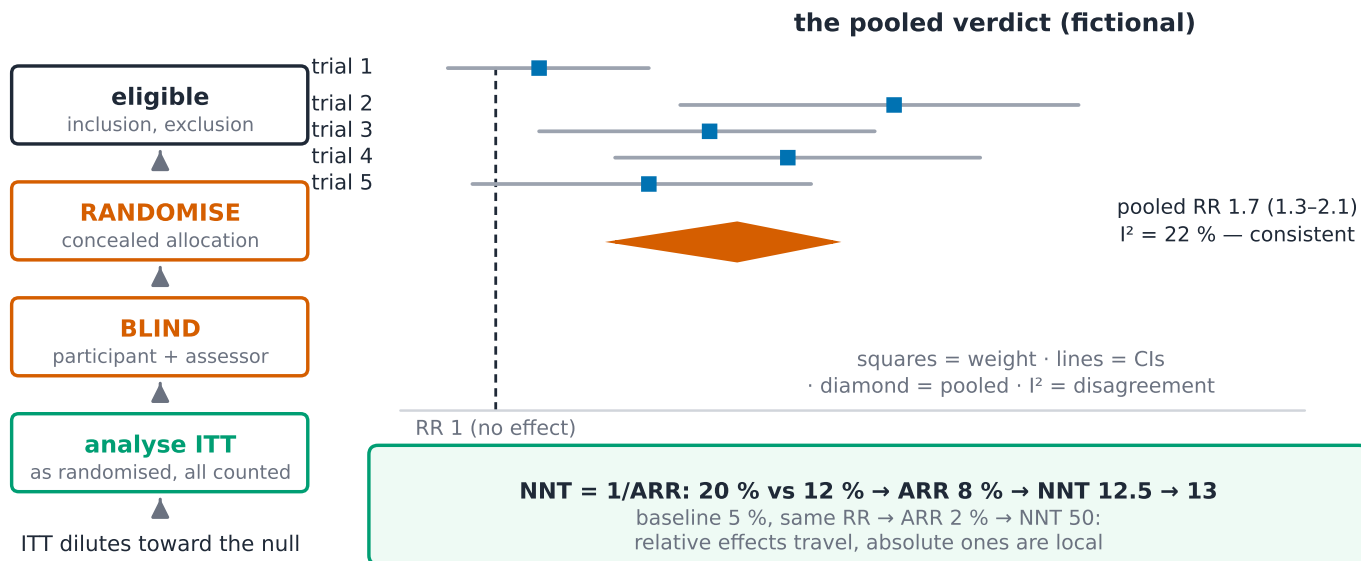
Clinical trials and systematic reviews

University Medicine

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 risk 5 percent with the same RR gives ARR 2 percent → 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



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

Exercises 2.1-2.3

2.1 What does ITT do with dropouts?

[3]

2.2 Control 30 %, treated 20 % – ARR and NNT?

[3]

2.3 What does a high I^2 warn about?

[3]

Exercises 2.1-2.3

2.1 What does ITT do with dropouts? [3]

2.1

- Analysed as randomised – counted in their assigned arm ✓.
-

2.2 Control 30 %, treated 20 % – ARR and NNT? [3]

2.2

- $ARR = 10\%$; $NNT = 1/0.10 = 10$ ✓.
-

2.3 What does a high I^2 warn about? [3]

2.3

- The trials disagree – pooling may be dishonest ✓.

Exercise 3.1

3.1 A fictional trial: 500 randomised per arm; control event rate 20 %, treated 14 %, with 15 % of the treated arm stopping early.

Compute ARR (6 %) and NNT ($1/0.06 = 16.7 \rightarrow 17$) ✓. Explain how ITT handles the 15 % stoppers (counted as randomised; effect diluted toward the null) and why per-protocol analysis would overstate the effect (adherence correlates with prognosis) ✓. State the design features that protected the result (concealed randomisation, blinding, ITT) ✓. [8]

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3.1

- $ARR = 20 \% - 14 \% = 6 \%$; $NNT = 16.7 \rightarrow 17$ ✓.
- ITT: the 15 % stay in their randomised arm – dilution toward the null ✓.
- Per-protocol overstates: adherent patients differ prognostically ✓.
- Protecting features: concealed randomisation, blinding, ITT ✓.

Exercise 3.2

3.2 A fictional forest: four trials with RRs 1.2, 1.9, 2.2, 1.6 and wide CIs; pooled diamond 1.7 (1.4–2.1); $I^2 = 30\%$.

Read the plot: individual trials wide (small), diamond excludes 1, heterogeneity modest ✓. Explain what would change with $I^2 = 80\%$ (investigate why the trials disagree before trusting the pool) ✓. Compute the NNT if the pooled result implies ARR 8 % (NNT 13) and at baseline 5 % (ARR 2 %, NNT 50) ✓. [7]

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3.2

- Individual squares wide (small trials); diamond 1.7 (1.4–2.1) excludes 1; $I^2 = 30\%$ modest ✓.
- With $I^2 = 80\%$: investigate disagreement (populations, interventions, outcome definitions) before pooling ✓.
- NNT at ARR 8% = $1/0.08 = 12.5 \rightarrow 13$; at baseline 5% ARR 2% $\rightarrow$ NNT 50 ✓.