12.6 Clinical trials and systematic reviews

Name: _____ Class: _____ Date: _____ **Total: 24 marks**

KEY WORDS number needed to treat • forest plot

Objective

Run the trial spine; read the forest; recompute the NNT.

1 Key knowledge and worked examples

■ **The spine**

Randomise (concealed) → blind → intention to treat (as randomised; dilutes toward the null) ✓. Forest: squares weighted, diamond pooled, I^2 the disagreement gauge.

■ **Worked example: NNT arithmetic**

Control 20 % vs treated 12 % → ARR 8 % → NNT 12.5 → 13 ✓. Baseline 5 %, same RR: ARR 2 % → NNT 50.

2 Practice

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]

3 Exam-style questions

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 ($1/0.06 = 16.7 \to 17$) ✓. 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]

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]

Solutions

2.1

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

2.2

- ARR = 10 %; NNT = 1/0.10 = 10 ✓.

2.3

- The trials disagree – pooling may be dishonest ✓.

3.1

- ARR = 20 % − 14 % = 6 %; NNT = 16.7 → 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 ✓.

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 → 13; at baseline 5 % ARR 2 % → NNT 50 ✓.

exercises.lol exercises.com.cn