Critical Appraisal Course for Emergency Medicine Trainees

Module 3

Evaluation of a therapy

Evaluating a therapy

- Selection and allocation of trial participants
- Randomisation and allocation concealment
- Blinding
- Outcomes measures
- Follow-up
- Intention to treat analysis
- Measures of effectiveness

Evaluating a therapy

- Nearly always requires comparison of patients receiving the treatment to a control group
- Rare exceptions, e.g. conditions with 100% mortality if untreated
- Use of historical controls (previous untreated patients) over-estimates treatment effect
- Control group should be contemporaneous and receive best alternative treatment

Patient Selection

- Inclusion and exclusion criteria determine patient selection
- This determines whether findings will be generalisable
- Restricted selection may make the trial easier to control, but difficult to generalise

Patient Allocation

- Patients are allocated to treatment or control
- If patients, carers or researchers can control allocation they can preferentially allocate sicker patients to treatment or control
- This will lead to allocation bias
- The more that patients, carers or researchers can influence allocation, the greater the risk of bias

Randomisation

- Random allocation to treatment group
- Patients, carers and researchers cannot decide which treatment to allocate to
- BUT, they can decide whether to enter the trial or not
- This can lead to bias if they know what group they will be allocated to

Allocation concealment

- Allocated group is not revealed until the patient is irreversibly entered into trial
- E.g. telephone randomisation service
- Opaque, sealed envelopes can achieve AC, but may be subverted
- Randomisation by day or alternate allocation do not achieve AC

Blinding

- Outcome measurement may be influenced by awareness of treatment group
- Expectation bias: patients, carers or researchers expect certain outcomes
- Attention bias: patients report positive effect just from receiving attention
- Blinding ensures that patients, carers and/or researchers do not know which treatment has been given

Blinding & allocation concealment

- Allocation concealment occurs BEFORE randomisation
- Blinding occurs AFTER randomisation
- Complete blinding cannot be achieved without allocation concealment
- Allocation concealment without blinding is common (e.g. trials of surgical techniques)

Who should be blind?

- Patients, carers providing treatment, carers providing follow-up, researchers measuring outcomes, & researchers undertaking analysis can all be blinded
- Blinding of researchers measuring outcomes is always ideal
- Blinding of patients and carers depends upon whether the trial is pragmatic or explanatory

How important is blinding?

- Depends upon outcome measured
- Objective outcomes (e.g. mortality) unlikely to be influenced by blinding
- Subjective outcomes (e.g. patient satisfaction) likely to be influenced
- Practicality depends upon treatment: it is easy to blind drugs, but difficult to blind physical or psychological treatments

Intention to treat analysis

- “Analyse as you randomise”
- Patients should be analysed in the group they were randomised to, regardless of the treatment they actually received
- Patients who do not receive the treatment they were allocated to are likely to be systematically different to those who do
- CONSORT diagram

Follow-up

- Ideally all patients should be followed up and have outcomes measured
- Not always practical – depends upon outcome
- In-hospital measures (e.g. mortality) should have nearly 100% follow-up
- Postal questionnaire follow-up may be much lower
- High postal Q follow-up suggests highly selected patient group

Outcomes

- “Hard” outcomes (e.g. mortality): clearly important, but difficult to detect significant differences
- Patient-centred outcomes (e.g quality of life): important, but subject to bias if not measured blind
- Clinical outcomes (e.g. blood pressure): objective, but may not translate into anything meaningful for the patient

Measures of effectiveness

- Hypothesis testing (p-value) tells you whether a treatment is effective, but not how effective it is
- Trials should report a measure of effectiveness with a 95% confidence interval

Relative risk reduction (RRR)

- RRR = difference in outcome rate between treatment and controls divided by outcome rate in controls
- E.g. 15/100 die in treatment group v 20/100 in control
- RRR = ((20/100)-(15/100))/(20/100) = 0.25
- Good measure of “strength” of effect
- Limited use for communicating effectiveness to the individual patient

Absolute risk reduction (ARR)

- Difference in outcome rate between treatment group and controls
- E.g. 15/100 die in treatment group v 20/100 in control
- ARR = (20/100)-(15/100) = 0.05
- ARR takes baseline event rate into account
- More useful for the individual patient

Number need to treat (NNT)

- The number of patients needed to be treated to achieve one additional positive outcome
- NNT = 1/ARR
- E.g. 15/100 die in treatment group v 20/100 in control
- NNT = 1/0.05 = 20
- Good way of communicating treatment effect to the individual patient

Summary

- How were the patients selected?
- How were they allocated to treatment group and was allocation concealed?
- Were patients, carers and researchers blind?
- What outcomes were measured?
- Was analysis intention to treat? (? CONSORT diagram)
- How adequate was follow-up?
- What was the treatment effect?

Any questions or comments?