PHC

432 Team

12 Critical appraisal skills

Done By: Raghad AL Mutlaq

Reviewed By: Sarah Bin Abdulqader

Objectives

1. Show how to do critical appraisal and check the appropriateness of study design for the research question.
2. Learn how to do careful assessment of the key methodological features of the research design.
3. Learn how to check the potential conflicts of interest.
4. Learn how to examine the suitability of the statistical methods used and their subsequent interpretation.
5. Explain the implications of research findings for individual patients elicit patients' own preferences and develop an appropriate management plan based on the combination of this information.

This lecture will be about appraising RCT studies only

There are primary and secondary resources

1. **Primary:** studies not being critically appraised yet (providing some information but not enough to rely on while practicing in the medical field) e.g.:
   - Cohort studies: best method to measure the associations of risk factors/development of complications
   - Case control studies: best method to know the best-diagnostic investigation
   - RCTs: best method used in a paper/research on therapy (to know which intervention is better)
   - Systematic reviews (SR): collection of the results of different RCTs but without appraising
2. **Secondary:** critically appraised RCTs or SRs, e.g. medical journals

What is RCTs

Clinical Trial studies compare between 2 groups:

Intervention	***Control (placebo)***
Drug (New) Structured exercise program (e.g. osteoporosis) Surgical procedure	Placebo, old drug or old intervention Usual regular advice given (osteoporosis) Another surgical procedure / No surgery

Process of RCT

Your methodology part should include:

- Preparation: Randomization *(when selecting your candidates) could be through:* computer generated list or centralized randomization
- Eligibility assessment (Inclusion/exclusion)
- Consent
- Allocation to study arms (Concealment)
- Baseline assessment
- Initiation of intervention (Blind)

- Follow-up
- Outcome assessment,
  Your outcome can be:
  - Patient's oriented outcome (subjective): e.g. Stroke, mortality, IHD
  - Disease oriented outcome (objective/measurements): e.g. Blood pressure reading, HgA1c
- Data analysis

Appraise the Evidence

- Assess **validity**/correctness (valid studies are more likely to have true results)
- Clinical **importance** (read the results)
- **Applicability** of these results on our patients

A. Validity: *(read the methodology of the study) – first 5 points will be explained in details*

1. Randomization: how the candidates were selected
2. Concealment
3. Blindness (there are different levels of blinding)
4. Follow up complete. How many of them dropped out
5. Intention to treat
6. Similar groups at start: e.g. age education and social backgrounds etc. (in the results table you find it)
7. Both groups treated equally: the groups treated equally, apart from the experimental treatment, means co-intervention should be similar for both e.g. diet physical activity physiotherapy

1. Randomization

- Randomization: similar groups at baseline, equal (50%) chance for each participant to be in the intervention or control group

- Selection bias can be reduced by:
  - Central computerized randomization (best/most valid) entralized randomization, on-site computer system with group assignments in a locked file, sequentially numbered, sealed and opaque envelopes (doubtful)
  - Non-randomized methods: dates of birth, taking patients coming in certain days of the week.

Selection: selecting who will participate in this study

Allocation: distributing participants to either intervention or control

Randomization is in the selection step, concealment in the allocation step.

We want to know how the selection was randomized, and if it was concealed

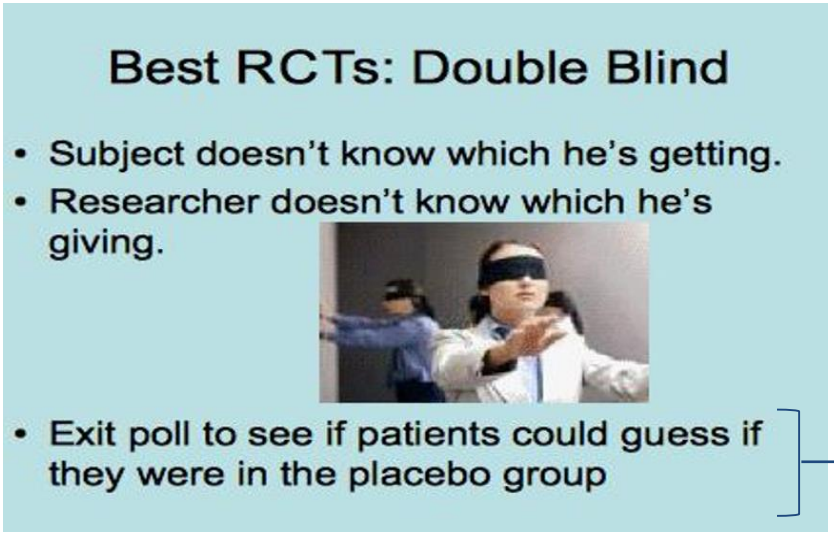
2. Concealed allocation *(you'll find it written clearly in the paper)*

- Did investigators know to which group the potential subject would be assigned before enrolling them?
- Trials with unconcealed allocation consistently overestimate benefit by ≃ 40%

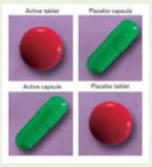
3. Blindness

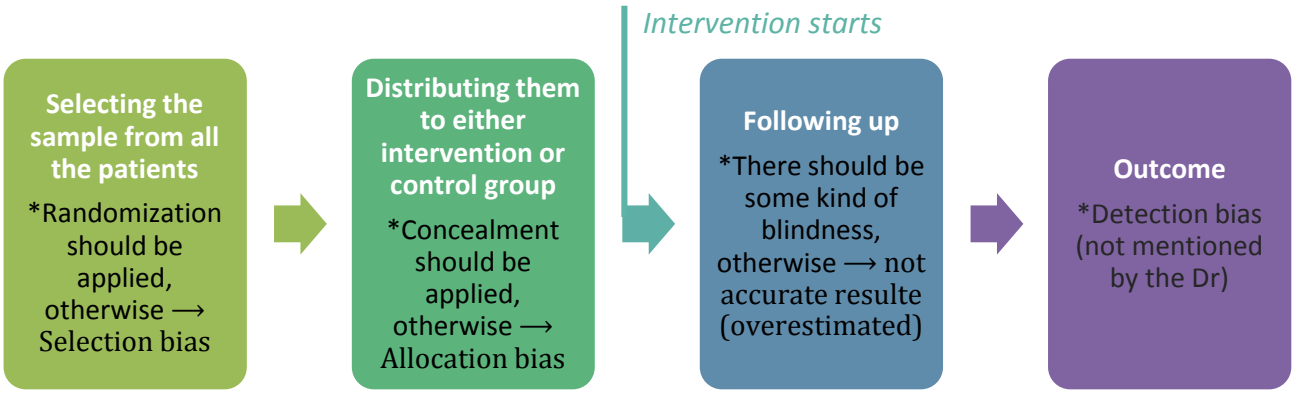
- It means not knowing who is in the intervention or in the control group in the process of gathering data
- Who can be Blind:
  - Physicians, patients, nurses, data gathering staff, outcome assessors, data analyzers (not necessarily all of them, but the larger the portion of blind people the more accurate results)
- Levels of blindness
  - Single (only physician are blind)
  - Double (physicians and patients) – you can consider this the lowest blinding level that is acceptable when appraising a RCT
  - Etc.

- How not being blind can affect the results?
  - If patient knows: Placebo effect those who are on effective treatment perform better than those who receive Placebo
  - If physician knows: Overestimate Treatment effect (More care, Co-intervention)
- Most important to use "blinded" outcome assessors when outcome is not objective
- Papers should report ***who*** was blinded and ***how*** it was done



e.g. patients are gathered in the waiting area, knowing they're participating in the study, asking each other about the look, taste, and smell of the drugs they're using, if the drugs are not similar they might figure out (affecting the blindness) or worse, exchange the drugs.





4. Follow up

- Duration of study: should be complete and sufficiently long enough for the action of the drug/side effects to appear (e.g. HTN drug for 6 months only

and prevention of stroke? Too short. You have to judge from your own medical knowledge)

- Drop out must be < 20% (should be mentioned and calculated) – drop out means the percentage of those who didn't come for the follow up
- "5 & 20 rule of thumb":
  - 5% probably leads to little bias
  - >20% poses serious threats to validity

5. Intention to treat - ITT *(in the paper they'll tell you it's been used, and you can find it calculated in the table)*

- All patients *analyzed* in the groups to which they *were allocated*
- Check this example: *(see the chart below)*

At the beginning: The whole sample= 200, where the intervention= 100, and control= 100

After following up: 50 patients of the intervention group and 30 patients of control group dropped out.

Outcomes: improved patients in both groups = 40, still need calculations

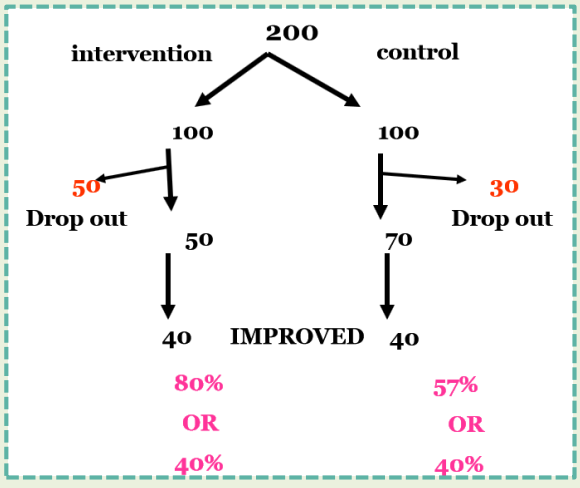
- Ignoring the drop out:
  - Intervention: 40 out of the remaining 50 got improved (which means 80%!)
  - Control: 40 out of the remaining 70 got improved (which means 57%!)

Notice the difference? This is the wrong way of calculating (which are sometimes used intentionally to overestimate the results). Now let's calculate them in the right way:

- Considering the drop out:
  - Intervention: 40 out of the whole 100 patients= 40%
  - Control: 40 out of the whole 100 patients= 40%

At the end, there is no difference between the 2 groups

** remember drop out more than 20% is already one tick to doubt the validity of the study, like in this case.*



- ITT Principle *(Maintaining the Randomization)*: Once a patient is randomized, s/he should be analyzed in the group randomized to, even if they discontinue, never receive treatment, or crossover.
    - *Exception: If patient is found on a blind reassessment to be ineligible based on pre-randomization criteria.*

How RCTs differ from other designs

Two balanced groups:

- *Start Balanced: All prognostic factors are equally distributed at the start (Concealed Randomization)*
- *Run Balanced: All prognostic factors are maintained balanced throughout the study (Blindness)*
- *End Balanced: All prognostic factors are maintained balanced at the end of the study (Intention to treat)*

B. Importance:

Measure the association:

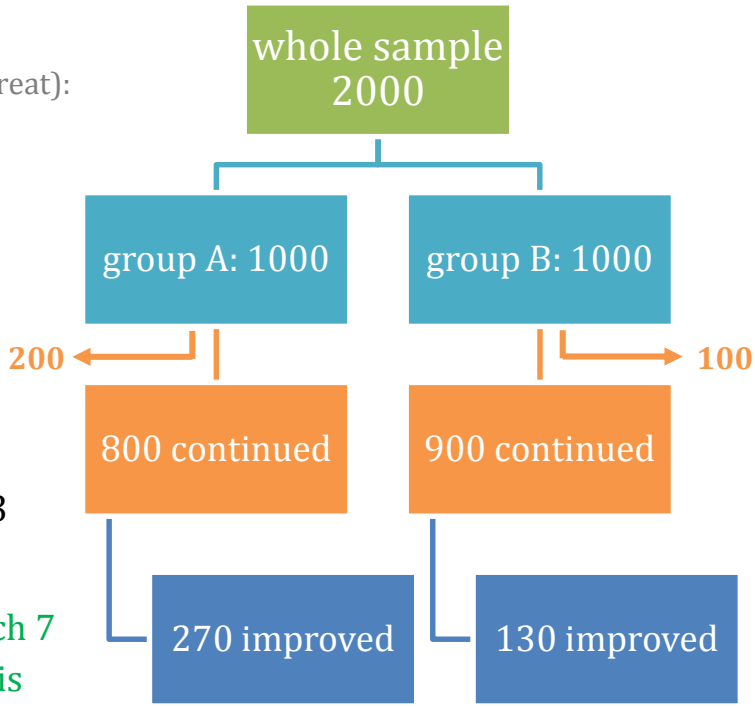
- Experimental event rate – EER: Risk (or chance) of outcome event in experimental group
- Control event rate – CER/CEER Risk (or chance) of outcome event in control group.
- Relative Risk (RR) – *not explained*: A measure of the chance of the event occurring in the experimental group relative to it occurring in the control group.
    - RR = EER / CER
- Relative Risk Reduction (RRR) – *not explained*:
    - RRR=CER-EER/CER
    - A RRR of 25% means that the new treatment reduced the risk of death by 25% relative to that occurring among control patients; the greater the relative risk reduction, the more effective the therapy.

- Absolute relative risk (ARR): The absolute difference between the risk of the event in the control and experimental groups.
  - ARR = EER - CER
- Number need to treat or number need to harm – NNT or NNH: Measure of clinical significance, it represents the number of persons who would have to receive an intervention for **one** of them to benefit/harms. (NNH is incase of nfavorable outcomes e.g. death, weight gain)
  - NNT=1/ARR

Take this example:

Wrong calculation (not using intention to treat):

- EER=270/800 = 33%= 0.33
- CER= 130/900 =14 %= 0.14
- ARR= 0.33-0.14 = 0.19
- NNT=1/0.19 = 5.2= 6



Right calculation:

- EER= 270/1000 = 27% = 0.27
- CEER= 130/1000 = 13% = 0.13
- ARR= 0.27-0.13 = 0.14
- NNT= 1/0.14 = 7 (means in each 7 patients you will treat using this medication, one of them at least will get benefit, you can always use as long as **NNT is less than 10**) the opposite for number need to harm: if less than 10 don't give it to reduce the risk.

Magnitude (treatment effect):

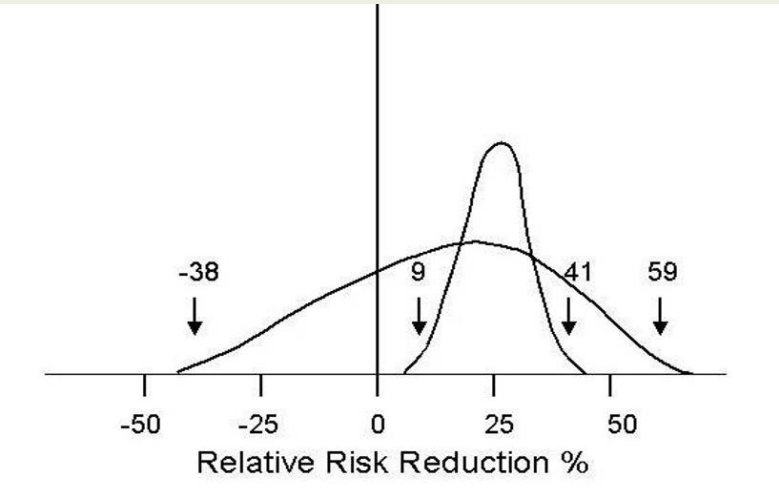
- Absolute effects (ARR & NNT)
- Relative effects (RR, RRR)

Precision:

- P value *(the probability of obtaining a result equal to or "more extreme" than what was actually observed)*
- Confidence interval: The range within which the likelihood of a true value is expected to be within a given degree of certainty, usually evaluated at 95% CI

Confidence Intervals estimation in DVT study:

- Incidence of DVT
  - Stocking group = 0
  - No Stocking group = 0.12
- Risk difference = 0.12 - 0 = 0.12
- (95% CI, 0.058 - 0.20) The true value could be as low as 0.058 or as high as 0.20 - but is probably closer to 0.12
- Since the CI does not include the no effect value of '0' the result is statistically significant (means the range is either above 0 or below it, not including it)



Result Tabulation:

	Event + Ve	Event - Ve	Total
Experimental	a	b	a+b
Control	c	d	c+d

- EER = Experimental Event Rate (a/a+b)
- CER = Control Event Rate (c/c+d)

	Bleeding present	Bleeding Absent	Total
Drug A	20	80	100
Drug B	40	60	100

- EER -A (Risk A) = 20/100 = 20% (0.2)
- CER -B (Risk B) = 40/100 = 40% (0.4)
- ARR = CER - EER = 0.4 – 0.2 = 0.2 (20%)
- NNT = 1 / ARR = 1/0.2 = 5
- RR = EER/CER (Risk A/Risk B) = 0.2/0.4 = 0.5
- RRR = 1 – RR = 1 – 0.5 = 0.5 (50%)

C. Applicability

- Can I apply these valid, important results to my patient?
- Do these results apply to my patient?
- Is our patient so different?
- Is the treatment feasible?
- Potential benefits and harms?
- Are my patient's values and preferences satisfied by the intervention offered?

Summary

Steps of appraising RCT

- Validity

Both groups treated equally
Randomization
Concealment
Blindness
Follow up
Intention to treat
Both groups are similar at the beginning

- Importance

EER	CER
ARR = EER- CER	NNT/NNH = 1/ARR

Questions

1) Which of the following studies is the best to identify diagnostic investigations?

a. Cohort Study
b. Case Control Study
c. Randomized Clinical Trial
d. Cross Sectional Study

2) What is the best and most valid method to reduce selection bias in randomized control trials?

- Central computerized randomization

3) All of the following measures of association are applicable for randomized control trails except?

a. Odd ratio
b. Relative Risk
c. Control event rate
d. Absolut relative risk

432 PHC Team Leader

Yazeed A. Alhusainy
phcteams@gmail.com
Raghad Al Mutlaq
Phc432teams@gmail.com

Answers:

1st Question: B

2nd Question: -

3rd Question: A