UE 7.4 - Méthodologie d'analyse d'articles

CM5: Study design, Result checking & Randomised controlled trials

Notions de conception : l'aveugle

- Eviter les biais
  - Du participant
  - Du chercheur

- 3 niveaux
  - Simple participant **ou** chercheur
  - Double participant **et** chercheur
  - Triple participant **et** chercheur**s**

Notions de conception : bras

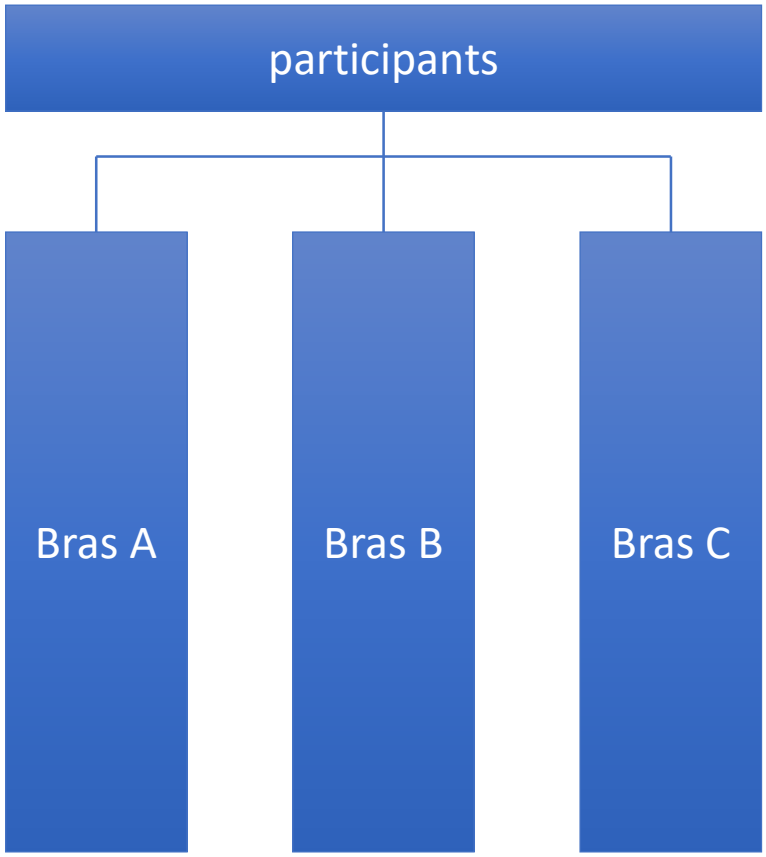
- Séparation selon traitements

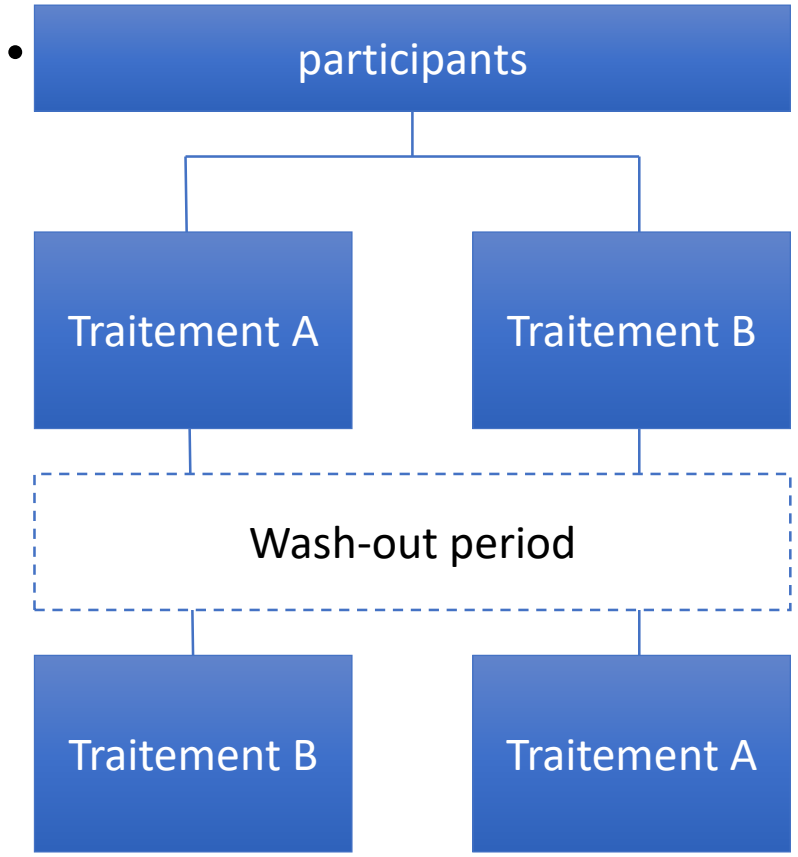
- Types
  - Expérimental
  - Comparaison active
  - Placébo
  - Factice
  - Sans intervention

Notions de conception : attribution

- Distribution aléatoire ou non aléatoire
- Randomisation
  - *A priori*
    - Par blocs permutés
    - Par strates - en fonction des caractéristiques des patients
  - *A posteriori*
    - Adaptive – tient compte des attributions qui précèdent
    - Minimisée – adaptive par strates
    - Gagnant renforcé – efficacité précédente prise en compte

Notions de conception : croisement



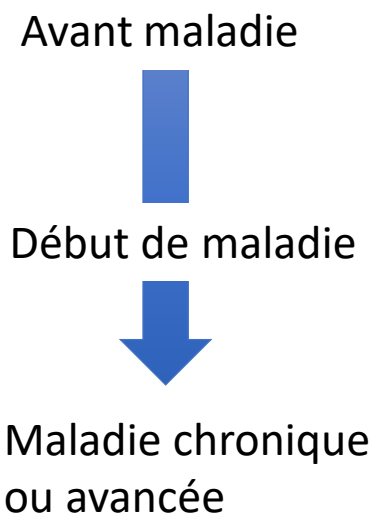


A+B = B+A ?

Autres approches de classification des études

- Par méthodologie
  - Observation
  - Intervention

- Par objectif (réf. NIH)
  - Prévention
  - Dépistage
  - Diagnostic
  - Traitement
  - Qualité de vie
  - Accès étendu – tt non-approuvé



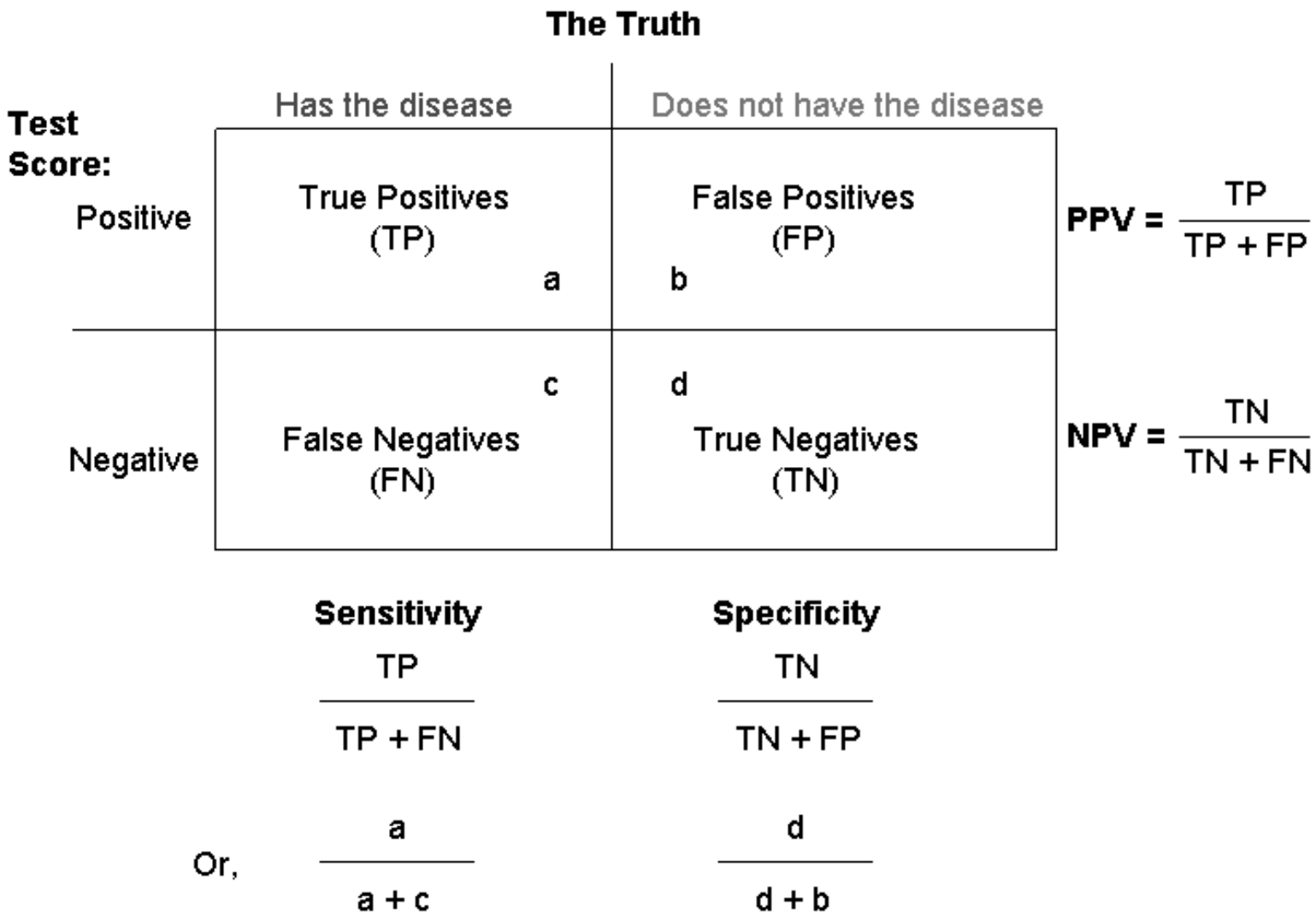
Méthodes itératives

- Adaptive design
  - Stratégie d'optimisation
  - Evaluations régulières
  - Modifications
    - Dosage
    - Taille d'échantillon
    - Traitement
    - Critères d'inclusion
    - Traitements associés
- Translational research

Vérification de résultats

- Test-retest
  - Comparaison des résultats d'un même test après un laps de temps
- Inter-rater reliability
  - Comparaison des résultats à un même test de deux évaluateurs différents

- Spécificité
  - Bonne identification des vrais négatifs, peu de faux positifs
- Sensibilité
  - Bonne Identification des vrais positifs, peu de faux négatifs


The Truth
Has the disease
Does not have the disease
Test Score:
Positive
True Positives (TP)
a
False Positives (FP)
b
PPV = TP / (TP + FP)
Negative
c
False Negatives (FN)
d
True Negatives (TN)
NPV = TN / (TN + FN)
Sensitivity
TP / (TP + FN)
Specificity
TN / (TN + FP)
Or,
a / (a + c)
d / (d + b)

Tests post-hoc

- Réduction ou élimination des erreurs, notamment de type I
- Nombreuses méthodes statistiques
  - Scheffé, Tukey, Bonferroni, Dunn, Fischer's LSD, Newman-Keuls, Dunnett's…
  - Choix dépendra de la nature des données et du test initial

L’essai (ou étude) randomisé contrôlé

- Une référence (gold standard)
  - Méthode rigoureuse pour identifier une relation cause-effet entre un traitement et un résultat
- Méthode de randomisation choisie au besoin
- Aveugle utilisé lorsque c’est possible

L’étude randomisée contrôlée

+

- Niveau de preuve le plus élevé pour évaluer un traitement
- Meilleure démonstration de lien cause à effet
- La randomisation limite l’influence des facteurs de confusion potentiels
- Pas de doute sur la chronologie
- Permet les études en aveugle et ainsi limite certains biais
- Peut mesurer incidence et résultats multiples

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- Problèmes éthiques pour l’attribution.
- Coûteux et long.
- Peu efficace lorsque la pathologie est rare ou lorsque l’effet est retardé.
- Generalisabilité – les participants peuvent être plus enclins à adhérer au traitement que la population plus large.

PMC full text: Can J Hosp Pharm. 2014 Sep-Oct; 67(5): 366–372.

Table 1.

Limitations of Randomized Clinical Trials (RCTs) Potentially Addressed by Cohort and Case–Control Studies

Limitation of RCT*	Complementary Aspect of Cohort and Case–Control Studies
Use of a strict study protocol that is often not representative of typical care	Usually representative of settings of routine medical care
Exclusion of key patient populations, such as children, pregnant women, and elderly people	May focus on vulnerable and under-represented populations
Limited sample size	May include large number of patients, especially if secondary data sources are used, thereby allowing rare events to be detected
Short duration	May follow patients for long periods of time (e.g., years)
Evaluation of irrelevant treatment comparisons	May compare several relevant therapies
Outcomes measured may not be important to the patient (e.g., surrogate end points)	May include any outcome that is measurable within the data source
High cost	Relatively low cost

*These limitations apply to typical RCTs. Designing more pragmatic RCTs would also overcome many these limitations.

Can J Hosp Pharm

Analyse de la méthodologie d'une étude contrôlée randomisée : SURE 2016

1. Does the study address a clearly focused question/hypothesis ?

   Population/Problem?

   Intervention?

   Comparator/control?

   Outcomes?

   Can you identify the primary outcome?

2. Was the population randomised?

   If YES, were appropriate methods used?

   E.g. : random number tables, opaque envelopes

   Note: The following methods are not appropriate: alternating participants coin toss, birth dates, record numbers, days of the week

3. Was allocation to intervention or comparator groups concealed?

   Is it possible for those allocating to know which group they are allocating people to?

   As above, methods such as alternating participants coin toss, birth dates, record numbers, days of the week will not allow appropriate allocation concealment.

4. Were participants/investigators blinded to group allocation?

   If NO, was assessment of outcomes blinded?

5. Were interventions (and comparisons) well described and appropriate?

   Aside from the intervention, were the groups treated equally?

   Was exposure to intervention and comparison adequate?

   Was contamination acceptably low?

6. Was ethical approval sought and received?
    - Do the authors report this?
7. Was a trial protocol published?
    - Was a protocol published in a journal or clinical trial registry before participants were recruited?
    - If a protocol is available, are the outcomes reported in the paper listed in the protocol?
8. Were the groups similar at the start of the trial?
    - Are baseline characteristics provided and discussed (eg age, sex, social class, life style etc.)?
    - Are any differences >10%?
9. Was the sample size sufficient?
    - Were there enough participants?
    - Was there a power calculation? If YES, for which outcome?
    - Were there sufficient participants?
10. Were participants properly accounted for?
    - Was follow-up ≥ 80%?
    - Were patients analysed in the groups to which they were randomised?
    - Was an Intention to Treat analysis conducted?
    - Was the follow-up period long enough?

Specialist Unit for Review Evidence (SURE) 2016.
Questions to assist with the critical appraisal of randomised controlled trials and other experimental studies
available at: http://www.cardiff.ac.uk/specialist-unit-for-review-evidence/resources/critical-appraisal-checklists

11. Data analysis

Are the statistical methods well described?

Consider: How missing data was handled; were potential sources of bias (confounding factors) controlled for; How loss to follow-up was addressed.

12. Results

Were outcome measures reliable (eg objective or subjective measures)?

Were all outcome measurements complete?

Were all important outcomes assessed?

Are the authors' conclusions adequately supported by the results?

13. Is any sponsorship/conflict of interest reported?

14. Finally…consider:

Did the authors identify any limitations?

Are the conclusions the same in the abstract and the full text?

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Un modèle d'analyse : Coughlan *et al.* (2007)

Section one – elements influencing the believability of the research

Writing style

Is the report well written – concise, grammatically correct, avoid the use of jargon? Is it well laid out and organised?

Author

Do the researcher(s) qualifications/positions indicate a degree of knowledge in this particular field?

Report title

Is the title clear, accurate and unambiguous?

Abstract

Does the abstract offer a clear overview of the study, including the research problem, sample, methodology, findings and recommendations?

Cited by : Fothergill, A., and A. Lipp. "A guide to critiquing a research paper on clinical supervision: enhancing skills for practice." Journal of psychiatric and mental health nursing (2014)

Section two – elements influencing the robustness of the research

Purpose/research problem

Is the purpose of the study/research problem clearly identified?

Logical consistency

Does the research report follow the steps of the research process in a logical manner? Do these steps naturally flow and are the links clear?

Literature review

Is the review logically organised? Does it offer a balanced critical analysis of the literature? Is the majority of the literature of recent origin? Is it mainly from primary sources and of an empirical nature?

Theoretical framework

Has a conceptual or theoretical framework been identified? Is the framework adequately described? Is the framework appropriate?

Cited by : Fothergill, A., and A. Lipp. "A guide to critiquing a research paper on clinical supervision: enhancing skills for practice." Journal of psychiatric and mental health nursing (2014)

Aims/objectives/research question/hypotheses

Have aims and objectives, a research question or hypothesis been identified? If so are they clearly stated? Do they reflect the information presented in the literature review?

Sample

Has the target population been clearly identified? How was the sample selected? Was it a probability or non-probability sample? Is it of adequate size? Are the inclusion/exclusion criteria clearly identified?

Ethical considerations

Were the participants fully informed about the nature of the research? Was the autonomy/confidentiality of the participants guaranteed? Were the participants protected from harm? Was ethical permission granted for the study?

Operational definitions

Are all the terms, theories and concepts mentioned in the study clearly defined?

Cited by : Fothergill, A., and A. Lipp. "A guide to critiquing a research paper on clinical supervision: enhancing skills for practice." Journal of psychiatric and mental health nursing (2014)

Methodology

Is the research design clearly identified? Has the data gathering instrument been described? Is the instrument appropriate? How was it developed? Were reliability and validity testing undertaken and the results discussed? Was a pilot study undertaken?

Data analysis/results

What type of data and statistical analysis was undertaken? Was it appropriate? How many of the sample participated? Significance of the findings?

Discussion

Are the findings linked back to the literature review? If a hypothesis was identified was it supported? Were the strengths and limitations of the study including generalizability discussed? Was a recommendation for further research made?

References

Were all the books, journals and other media alluded to in the study accurately referenced?

Application

Article 3 – RCT

Thomeer, Marcus L., et al. "Randomized Controlled Trial of *Mind Reading* and In Vivo Rehearsal for High-functioning Children with ASD." *Journal of autism and developmental disorders* 45.7 (2015): 2115-2127.