Design and interpretation of clinical trials

Week 5 reporting results

Johns Hopkins @ coursera

Reporting results from trials

Motivation for reporting guidelines

- Access to literature to help guide practice decisions
- Accurate reporting of clinical trial results is necessary
- Nobody sets out to write a bad paper

Consort

Consolidated standards of reporting trials

25-item checklist

Tool for authors, reviewers, consumers

www.consort-statement.org/home

Purpose: to make experimental process more clear, flawed or not, so that users of the data can more appropriately evaluate its validity for their purposes.

Extensions of consort

- Design
  - Cluster trials
  - Non-inferiority trials and equivalence trials
  - Pragmatic trials
- Intervention
  - Herbal medicinal interventions
  - Non-pharmacological interventions

- Acupuncture interventions

- Data
  - Harms
  - Abstracts
- Under development: quality of life data extension

Consort guidelines

- Title of report
  - Succinct
  - Key design terms: trial and randomized
  - Treatments evaluated
  - Disease or population studied
- Abstract
  - Key to future of the paper: indexing, browsing
  - Separate consort statement for abstracts (conferences and journal articles)
  - Structured: design, methods, results, conclusions
- Introduction
  - Background
  - Rationale
  - Establish equipoise
  - Ideally include a systematic review
  - Objectives/hypothesis
- Methods
  - IRB review and approvals
  - Trial design, allocation ratio
  - Eligibility criteria: explicitly defined

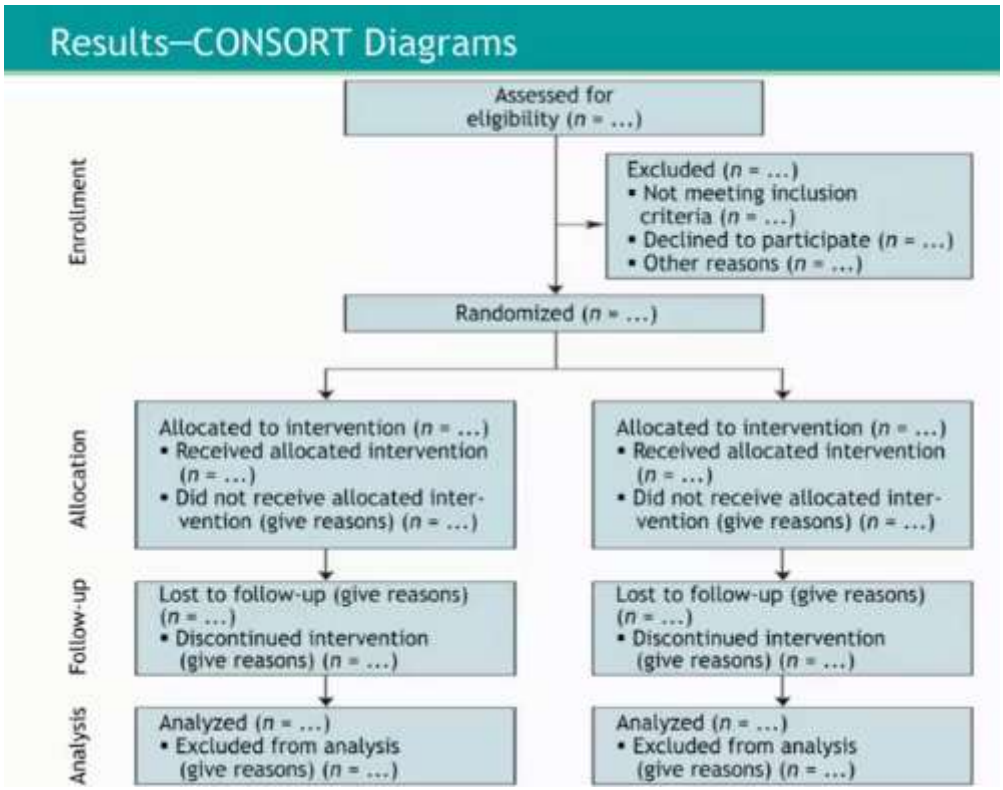
- Setting and location of trial
- Intervention: detailed enough to allow replication
- Outcomes: primary, secondary, how assessed and defined
- Sample size: how determined, interim analysis
- Important changes during the trial
- Randomization: sequence generation-blocking, stratification
- Allocation concealment
- Implementation of randomization
- Masking: who was masked, how masking was achieved
- Statistical methods

  Methods for comparison of primary and secondary

  Subgroup analyses/adjusted analyses

- Results: consort diagrams
  - Using flow chart

    Example:



- Dates conducted, why trial ended
- Baseline data
- Number analyzed
- Outcomes, treatment effect and uncertainty
- Ancillary analyses

  Subgroups

  Adjusted

  Pre-specified vs. exploratory
- Harms: adverse events

- Tables and figures
  - Should convey essence of results without having to read text
  - Legends should be succinct
  - Provide numerator and denominator data
  - Columns are the treatments comparison
  - For aesthetics and easier reading, decimal align table
- Discussion
  - Interpretation
    - Study hypothesis conclusion, key results
    - Limitations

      Potential sources of bias

      Imprecision
  - Generalizability
  - Interpretation:

    Other relevant evidence

    Best achieved by including a formal systematic review
  - Appropriate balance of benefit and harms

- Other information
    - Registration
    - Protocol – where can it be accessed
    - Funding, role of funders

Evaluation of literatures

- Legitimate stat of equipoise? – is it a fair comparison?
- Investigators trustworthy?

  ~ conflicts of interest
- Adequate protections against bias?

  ~ randomization

  ~ masking

  ~ follow-up design and execution
- ITT (intention-to-treat) analysis?

  ~ have all events (outcomes) observed been counted in the treatment group assigned?

  ~ variations in denominator explained (and consistent with good practice)?
- Appropriate subgroup analysis interpretation?

  ~ ad hoc or post hoc status
- Have the authors done an adequate analysis to support their results?
- Do the authors recognize and discuss potential weaknesses of their design and execution?

Marks of a good trial

- Relevant question
- Randomized
- Adequate sample size

- Meaningful outcome measure
- Adequate period of follow-up
- Analysis by original treatment assignment
- Adequate bias control procedures
- Adequate performance
- Comprehensive reporting
- Timely reporting

Quiz

1. CONSORT guidelines were developed because the reporting of clinical trial results has always been excellent, and scientists felt a need to document how researchers have been reporting their findings.

   - ○ True
   - ● False

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2. The title of a clinical trial report should be as creative as possible in order to allow room for different interpretations.

   - ● False
   - ○ True

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3. The introduction of a clinical trial report should reference a systematic review if possible.

   - ● True
   - ○ False

4. A clinical trial report should include a description of the trial design (e.g. parallel, factorial, crossover, group allocation, superiority, equivalence, non-inferiority).

- ○ False
- ● True

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5. If authors have described a trial as 'randomized' in the title or abstract, it is not necessary for them to also describe how the random allocation sequence was generated in a clinical trial report.

- ○ True
- ● False

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6. Authors should describe how the primary and secondary outcomes of a study were measured in their clinical trial report.

- ○ False
- ● True

7. The methods section of a clinical trial report should include a description of the statistical methods utilized to analyze the data.

- ● True
- ○ False

8. It is not necessary to report adverse events observed during a trial if authors are struggling with the word count limit.

- ○ False
- ● True

Correct answer: false

9. The discussion section of a clinical trial report should emphasize the strengths of the study and understate the limitations.

- (●) False
- ( ) True

10. A well-written clinical trial report contains sufficient information for the reader to replicate the study procedures.

- (●) True
- ( ) False

1. CONSORT guidelines were developed because physicians need access to accurate and detailed literature on clinical trial results to help guide their clinical decisions.

- ( ) False
- (●) True

3. Since the abstract of a clinical trial report often states the study's primary objective, it is not necessary to describe this again in the introduction of the report.

- (●) False
- ( ) True

6. In a clinical trial report, authors should indicate whether masking was implemented, and if so, which parties were masked.

- ( ) False
- (●) True

7. Investigators should only report details about the final protocol and do not need to discuss important changes that were made to the study protocol (e.g. eligibility criteria, outcome measures) while the trial was in progress.

- (●) False
- ( ) True

8. A clinical trial report should include a table showing baseline demographic and clinical characteristics of each treatment group.

- (●) True
- ( ) False

10. A well-conducted clinical trial usually has a follow-up period that is too short to observe a clinically meaningful effect if one exists.

- (●) False
- ( ) True