

# RCT

## Playing by the Rules

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for  
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Sponsored by  
Center for Women's Health and Gender Differences

## Levels of Evidence - Design

**Level 1**  
Systematic Reviews  
RCT (≥80% F-up)  
Systematic Reviews - Cohort

**Level 2**  
Individual Cohort  
RCT with <80% F-up  
Outcomes Research

**Level 3**  
Systematic Reviews Case-Control  
Individual Case-Control

## RCT is ...

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Any research project that prospectively assigns human subjects to intervention and comparison groups to study cause and effect relationships between medical interventions and a health outcome.

## Registering your clinical trial

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**Why?**

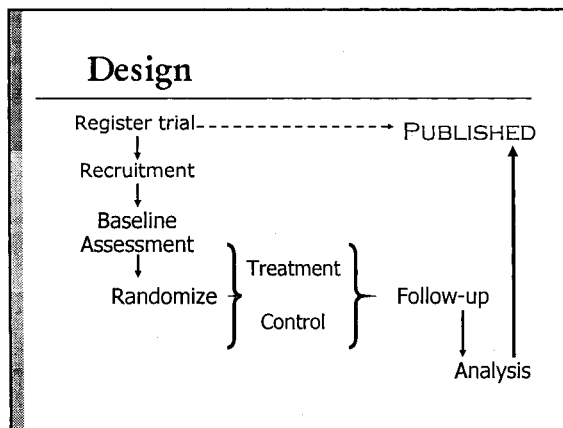
- Because your study may/will not be publishable in top line journals (International Committee of Medical Journal Editors)

**Why really?**

- RCT are critical to EBP
- Many go unreported – knowledge lost or suppressed (e.g., industry, journals, investigator)
- Citizens have a right to know

**How?**

- [Clinicaltrials.gov](http://clinicaltrials.gov)
- Clinical Trials Registration Frequently Asked Questions
- Do it before you recruit a single subject



## CONSORT

### Consolidated Standards of Reporting Trials

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- Best evidence of efficacy or effectiveness if ...
- Diverse approaches to reporting the results
- Many lacking critical elements
- Published in 1995, revised in 2001
- It works! Reporting has significantly improved in BMJ, Lancet, & JAMA (Moher et al 2001)
- Suggestion for other designs are being developed (randomized behavioral, nonrandomized behavioral & public health)

<http://www.consort-statement.org/Downloads/checklist.pdf>

**Which of one of these studies is a RCT?**

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1. Aspirin and secondary mortality after myocardial infarction
2. Antithrombotic therapy in the primary prevention of acute myocardial infarction.
3. Low-dose aspirin for migraine prophylaxis.
4. The effects of heparin versus normal saline for maintenance of peripheral intravenous locks in pregnant women.

**CONSORT Checklist**

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**Title**

- Use the word "randomized" in title or RCT

**Abstract**

- participants were "randomly assigned to ...", "participants were assigned to intervention by using random allocation"
- Structured abstracts

Otherwise your study could be missed in the sea of studies on PubMed

**Methods – eligibility criteria**

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- Explicit eligibility criteria
- Description of sample and setting (location e.g., outpatient clinic, university medical center) for generalizability
- Recruitment approach (e.g., referral, self selection), newspapers (e.g., *Stranger*, flyers, letters, primary care or tertiary setting)

**What is the difference between a ...**

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Primary outcome?

Secondary outcome?

**What is the difference between a ...**

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Primary outcome?

- Most important, bases of power calculations, usually 1-2

Secondary outcome?

- Other outcomes of interest
  - EX: adverse events

**Methods - Details**

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- Describe the interventions in detail
- Describe the control group in detail (active, usual care, placebo)
- Information on who provided the intervention (how many, training, supervision)
- Primary and Secondary outcomes
- Published vs. unpublished instruments

### Methods - More

- Methods to enhance the quality of measurement
  - Strategies – procedures (e.g., BP), training
- Sample size – estimated outcome, alpha level, beta level, SD for continuous variables.
- Explain why you did not meet sample size that was based on power calculations
- Describe interim analysis (specific assessing points and stopping rules)
- If you “looked” at the data report the number of times or don’t do it.

### Methods - Randomization

- Simple randomization or
- Work with statistician
  - Block – equal number in each group
    - Block in units of 4, 8, 12 ..
  - Stratification on key variables by n units
    - Prognostic characteristics or risk factors
    - Age categories, sex, smoking – only a few
  - Don’t try to manipulate the process
- Beware, if a person is randomized every effort must be made to followed-up (80%)

### Randomization

- Specify the method for generating the randomization sequence (e.g., random number table, computerized random number generator – see statistician.
- Allocation concealment – unable to predict the next assignment to group
  - Block – equal number in each group
    - Block in units of 4, 8, 12 ..
  - Stratification on key variables by n units
    - Prognostic characteristics or risk factors
    - Age categories, sex, smoking – only a few

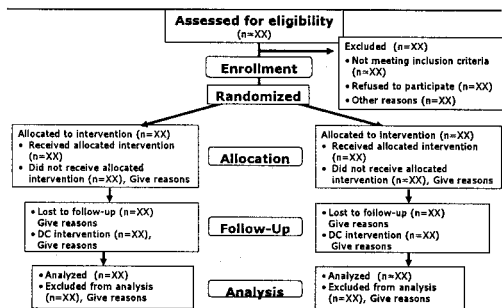
### Intervention - Control

- Blinding (masking)
- Unblinded, single-blind, **double-blind**
  - Assessment of blindness – can the participant determine which group they are in or the provider or the follow-up staff
  - People need protection from “peaking” syndrome
- Follow-up
- Get data on primary outcome data on **EVERYONE**– but honor the participants right to withdrawal (80% rule)

### Statistical Methods

- NOTE: Biostatistician are critical to your success
- State data analysis approach prior to initiating the study (grant)
  - Comparison of Treatment(s) vs control(s) - baseline to follow-up
  - Estimate of treatment effect & 95% CI
  - Use actual P-values not thresholds ( $p < .05$ )
  - Subgroups analysis – stated prior to recruitment, post hoc hypotheses generating
  - Adjusted or covariates planned or “suggested by the data”

### Results - Recommended - Consort Flowchart



## Results – Protocol Deviations

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- Report all departures from the protocol
- Anyone dropped after randomization – not meet eligibility criteria
  - Unplanned changes in protocol, data collection, method of analysis
  - Give the start- stop dates for recruitment and follow-up
  - Early stopping (overestimate the Tx. Effect)

## Results

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- Baseline demographics
- Do not report significant comparisons \*\*
- Test of Treatment
- Analysis of aims – Intent-to-treat or analysis based on initial group assignment
    - What about those with missing data?
      - Analysis of only complete case analysis
      - Missing data - impute
  - All primary and secondary aims are reported
  - Multiple comparisons – across group, across variables - risk of false positive
- Adverse events
- intended, unintended and severity level (e.g., NCI)

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Teach your Team  
how to  
playing by the Rules  
and  
you will all succeed

Questions ?  
Comments?

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Thank You

## CONSORT Checklist of items to include when reporting a randomized trial

<http://www.consort-statement.org/Downloads/checklist.pdf>

PAPER SECTION And topic	Item	Description	Reported on Page #
TITLE & ABSTRACT	1	How participants were allocated to interventions (e.g., "random allocation", "randomized", or "randomly assigned").	
INTRODUCTION Background	2	Scientific background and explanation of rationale.	
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	
Objectives	5	Specific objectives and hypotheses.	
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors).	
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (e.g., blocking, stratification)	
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. When relevant, how the success of blinding was evaluated.	
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	
Recruitment	14	Dates defining the periods of recruitment and follow-up.	
Baseline data	15	Baseline demographic and clinical characteristics of each group.	
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (e.g., 10/20, not 50%).	
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (e.g., 95% confidence interval).	
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	
Adverse events	19	All important adverse events or side effects in each intervention group.	
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	
Generalizability	21	Generalizability (external validity) of the trial findings.	
Overall evidence	22	General interpretation of the results in the context of current evidence.	