Pregnancy and Birth

Week 4

Objectives

1. Learn more details about the trial study design
2. Understand the medicalization of pregnancy and birth

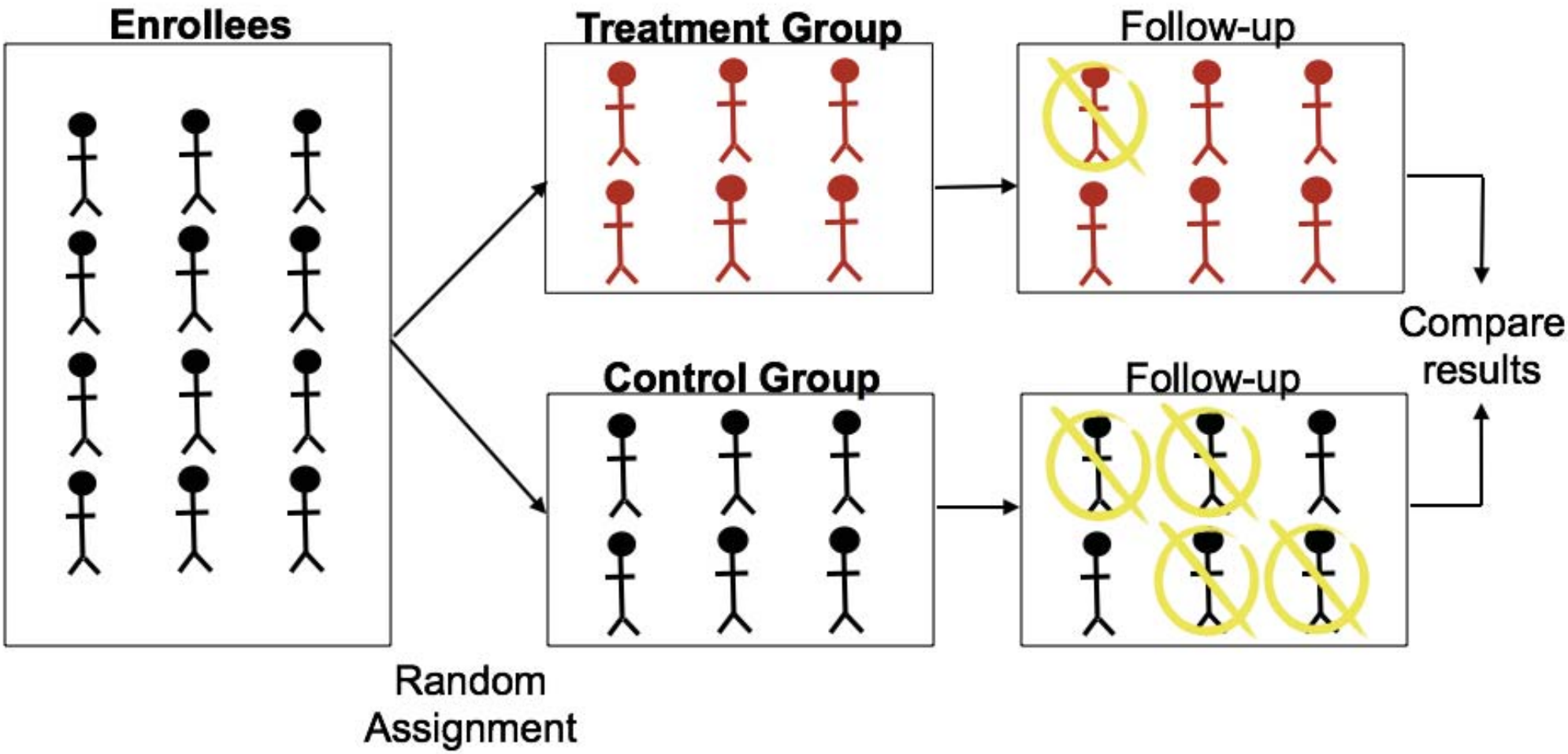
Biases

Misclassification

- Exposure or Outcome
- Non-differential
  - Towards null
- Differential (bias)
  - Over- or underestimate

Types of bias

- Lump or split
  - Information
  - Recall
  - Selection
  - Etc



Randomized Controlled Trial

Advantages

- If well done, provide most assurance about finding
- Minimize alternative explanations of chance, bias, and confounding
- Optimal for detecting small to moderate-sized effects
- Greater degree of control over exposure
- If randomized, minimizes confounding by known and unknown factors
- Through placebo, blinding or objective outcome definition, minimizes observation bias

Disadvantages

- Logistically difficult (compliance, losses to follow-up)
- Expensive (cost and feasibility)
- Ethical considerations
- Remember: trade-off of internal validity with external validity (generalizability)

Exposure Allocation

All confounders (known and unknown) distributed equally among groups

- Minimizes confounding

- Remember: Difference between randomization (exposure) and random selection of participants

  - Randomization only in a trial, to minimize confounding

  - Random selection in any study, to have representative individuals

Different types of allocation

- Crossover randomized controlled trial

  - Individuals serve as own historical control after washout period

Comparison Group

Cannot give less than standard of care

- Usual care
- Other doses of same treatment
- Other treatments
- Placebo
    - Inert agent that looks indistinguishable from active agent
    - Minimizes observation bias
    - Depends on subjectivity of outcome
    - Placebo or blinding may not be practicable

Minimize bias

- Blind (participant) and double-blind (investigator) techniques (aka “masked, double-masked”)

Compliance

Crucial to demonstrate a true effect

Noncompliance will bias relative risk towards the null value

Need to ascertain compliance (e.g., spot blood/urine checks)

Methods to maintain high compliance critical

- Allocating regimen = taking regimen (e.g., using calendar packs – double blinded, costs)

Data and Safety Monitoring Board

Expert, independent (scientific and financial) group

Goal: safeguard trial participants

- Communicate unexpected harm/benefit (change in equipoise)
- Ensure trial integrity
- Review (unblinded) progress of trial
    - Consider early stopping rules (benefit or harm)

Analysis

Basic analysis, similar to cohort study

- Compare risk of outcome in treated (“exposed”) versus placebo (“unexposed”)
- First table will be to ascertain if randomization "worked"
- Treatment groups comparable at baseline with respect to baseline characteristics (i.e., potential confounders)
- Standardization of reporting: first figure, consort diagram
- Register on www.clinicaltrials.gov.

Effective Sample Size

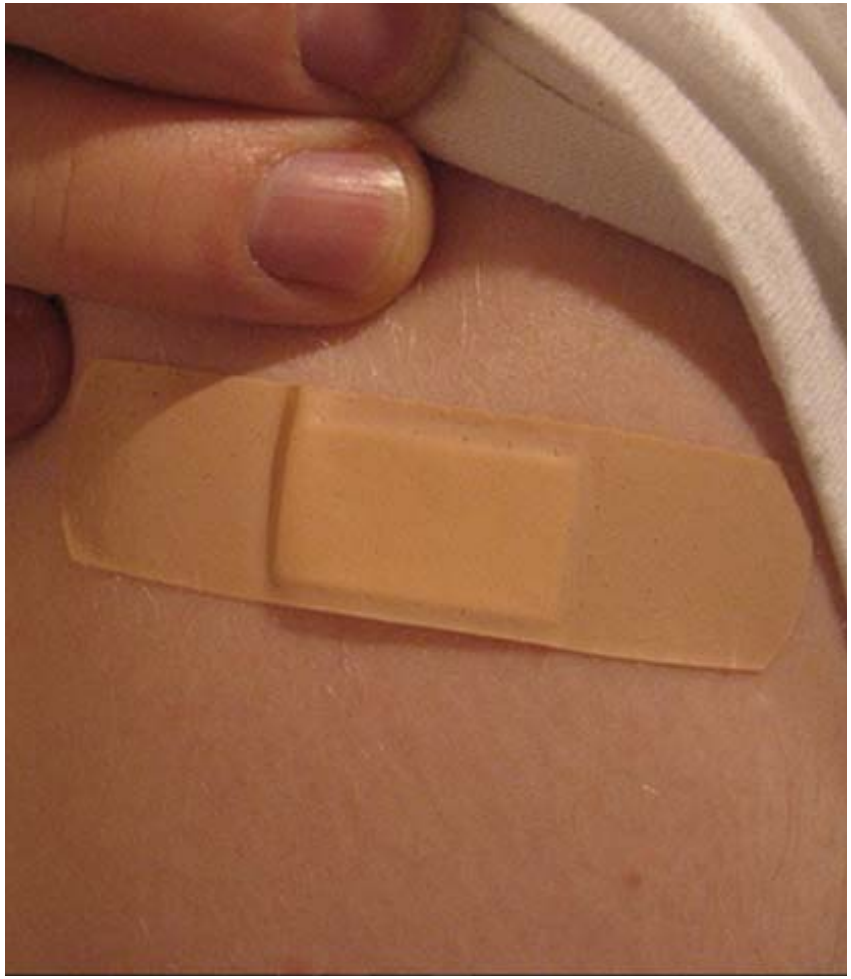
- Not number of participants, but number of ENDPOINTS

Randomized Trial of Bandaid Removal

Exercise

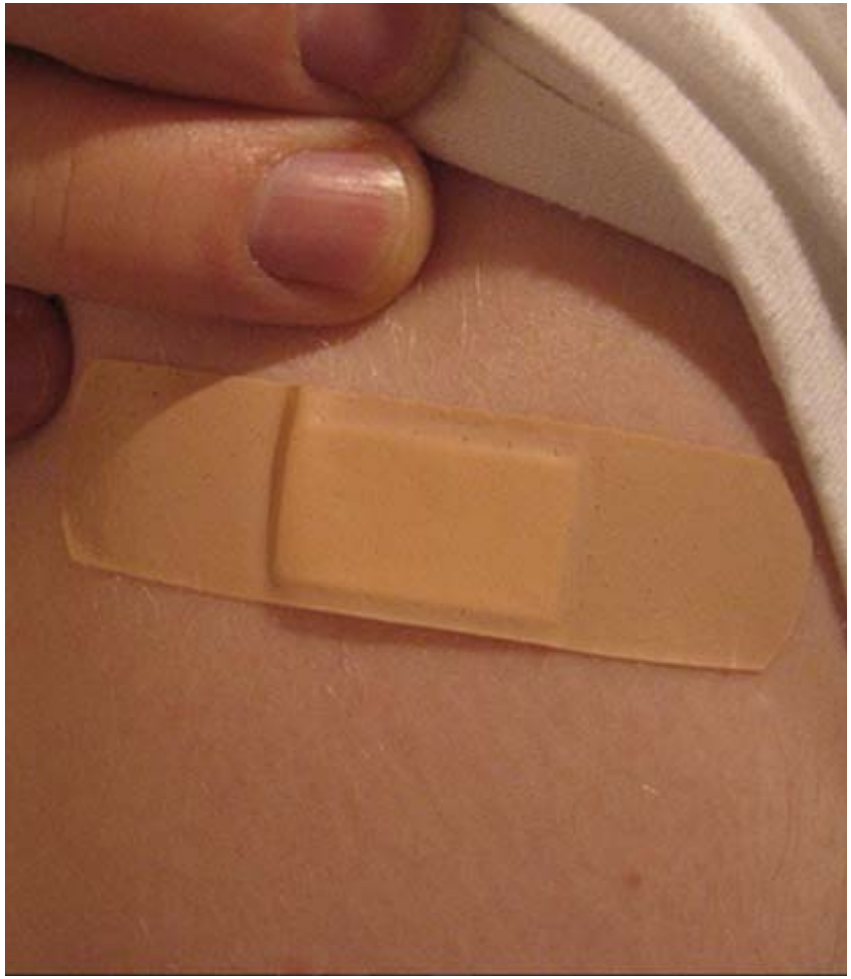
Study Summary

- Applying bandaids to wounds is common practice, although removal of the bandaids can be painful
- While pain reduction research has focused on new products, it has not evaluated different speeds of removal
- The investigators designed a prospective randomized crossover trial comparing fast bandaid removal (FBAR - single rapid movement) with slow bandaid removal (SBAR - removal over the course of 2 seconds)



Study Summary

- They enrolled 65 healthy volunteers from an undergraduate medical school program
- Medium sized bandaids were applied bilaterally in three standard body locations (arm, hand, ankle) and removed using slow and fast techniques
- Participants were randomly assigned sequentially numbered data collection sheets in sealed opaque envelopes to determine which removal technique would be tested first (FBAR or SBAR) and which side of the body (right or left) would be tested first.
- The primary outcome was a validated pain score from a 11-point verbal numeric pain scale, from no pain (0) to worst pain imaginable (10). This was assessed immediately after dressing removal.



Crossover Design

Generally, in a crossover randomized trial, participants receive both exposures and are observed during two or more periods

In this design, each participant serves as their own control

- A strength of this design is that it controls for between-person confounding, effectively controlling for both measured and unmeasured inter-individual confounding

Assumptions:

- Exposure effect duration is short
- Exposure has no carry-over effect
- Outcome is an abrupt, reversible event
- All prognostic factors other than treatment remain constant

In this study, participants were assigned and received either SBAR or FBAR and had their pain score assessed

Participants then received the other exposure and the pain score was assessed

Randomized Trial of Bandaid Removal

1. What impact does this design have on confounding (bias)?

Since the **same people** receive both exposures, we are not concerned about confounding.

To use this design, the outcome must be **acute** and **reversible**.

It assumes that subjects at the beginning of the second exposure period **are in the same state** that they were at the beginning of the first exposure period.

Randomized Trial of Bandaid Removal

2. Two investigators attended a 1-hour training session on dressing removal and the lead investigators observed all dressing removals to ensure consistency of technique.

   Why did they train the investigators and have the lead investigator observe all dressing removals (i.e. what bias were they attempting to minimize)?

To minimize **operator bias** (a type of **observational bias**)

Randomized Trial of Bandaid Removal

3. The authors did not adjust their analysis for sex. However, the authors did find that women reported lower average pain scores after bandaid removal than men. Are you concerned that their results could be confounded (biased) by sex?

No—this was a r**andomized crossover trial** so there should be no confounding by sex

Although **sex is related to average pain score**, it will **not differ by exposure status** due to the design of the study

Randomized Trial of Bandaid Removal

4. To whom can the results of this study be generalized? And to whom can they not be generalized?

The study sample was **young healthy adults**, with **no wounds**

May not be applicable to **other age groups** (children & elderly)

For example, children and older people may have more **delicate skin** and may have different pain scores than adults

Not applicable to patients with wounds, like chronic wounds and ulcers, that may adhere to the dressings

They chose to use human rather than **mechanical operators** to increase their ability to generalize results, since mechanical operators are not likely available in clinical settings

Randomized Trial of Bandaid Removal

5. Are there any next steps that should be pursued to further address this question?

Performing the study among subjects with **wounds**

The effect of speed of removal on pain when using **larger or smaller** bandaids

Performing a study among **children** or the **elderly**

Business of Being Born Assessment

1. Approximately what percent of births in the US end in Cesarean Section?

   b. 33%

2. What percent of births does the World Health Organization (WHO) estimate should end in Cesarean Section?

   c. 15%

3. The percent of births by Cesarean Section in the US over the last decade has:

   b. Increased by 60%

4. When Cesarean Section rates increase in a country, it is usually because

   b. Doctors are more comfortable doing cesareans

5. The number of births taking place at home in the US over the last 5 years has:

   a. Increased

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