Stanford Medicine
COVID-19 Journal Club

How to effectively examine a clinical research study

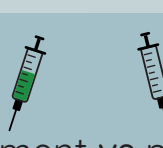
Step 1: Identify the study design

What is being compared?

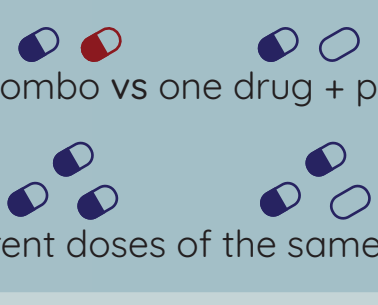
Treatment only, no control group for comparison

No way to tell whether patients would have done better, worse, or the same without the treatment.

Treatment vs placebo



Drug combo vs one drug + placebo



Different doses of the same drug

A control group (placebo, standard of care, or lower drug dose) lets researchers compare how patients did with and without the treatment.

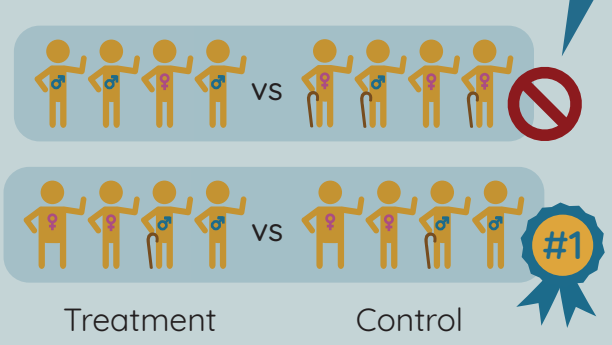
Key

- #1 Optimal design feature
- Ocassionally acceptable, but studies with these features are less likely to be reliable

How similar were the groups of people in each treatment arm?

Ideally the ONLY thing that's different between the groups, on average, is which treatment they're getting. The best way to achieve this is with randomization.

What's wrong here? The controls are mostly elderly and female subjects. Age and sex often affect disease outcomes, so it would be hard to say whether differences between cohorts in this study were due to the treatment, or due to these subjects having different characteristics.

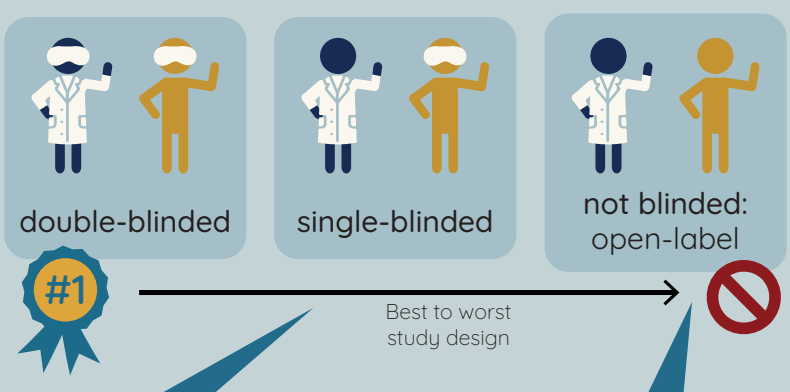


How large was the study?

Larger studies better represent the population and increase the likelihood that differences in outcomes are real. At the start of a study, researchers use statistics to determine how many people they need to achieve the most certain outcome.

Who knew which patients recieved which treatment?

Subjects' and researchers' behavior can influence outcomes if they know who is receiving the treatment. Placebo treatments (i.e. pills or injections that look like the treatment, but contain no active drug) are typically used to keep everyone blinded.



Example: Dr. Smith finds out his patient Ann is in the treatment cohort. He feels hopeful and is less vigilant about her symptoms. Ann gets sicker because of his decreased care, not because of the treatment.

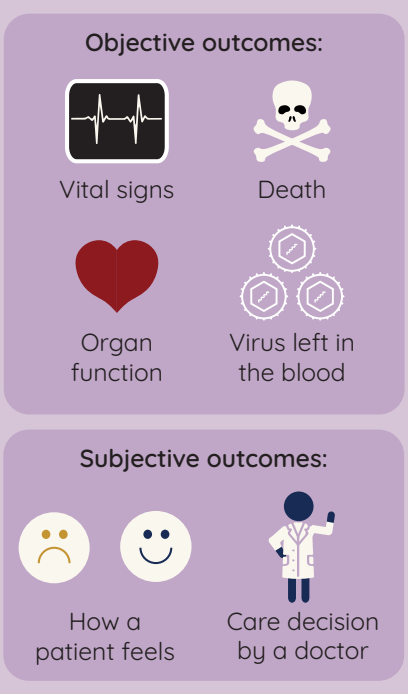
Example: Bob finds out he's in the treatment cohort. This makes him hopeful, so he decides to quit smoking. He becomes healthier because of quitting, not because of the treatment.

Step 2: Assess how well the study was analyzed

What outcomes were measured to determine treatment effectiveness?

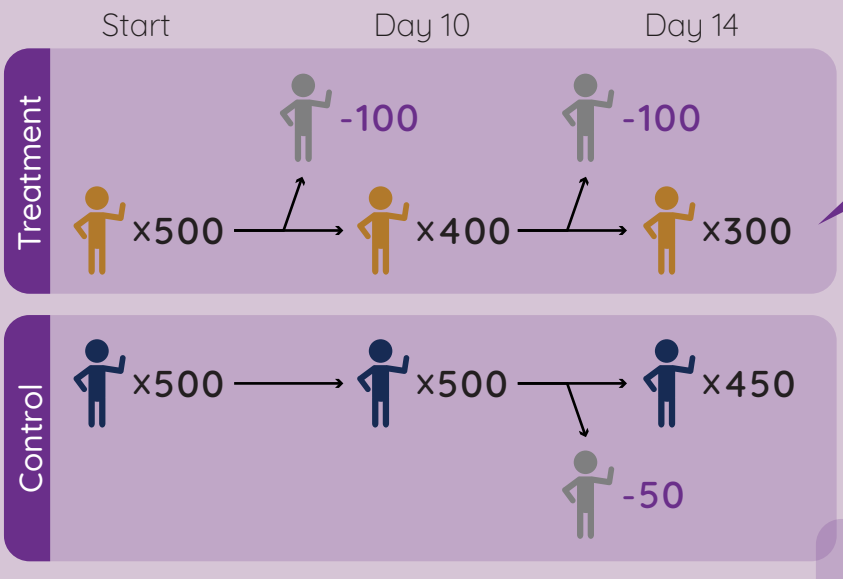
Outcomes to be measured are determined before a study begins and should not change during the study. Objective outcomes are more reliable to measure, but subjective outcomes can be equally as important.

As an example of when subjective outcomes are important: if patients feel a drug gives them unacceptable side effects they may not take the drug even if it is proven to improve objective outcomes.



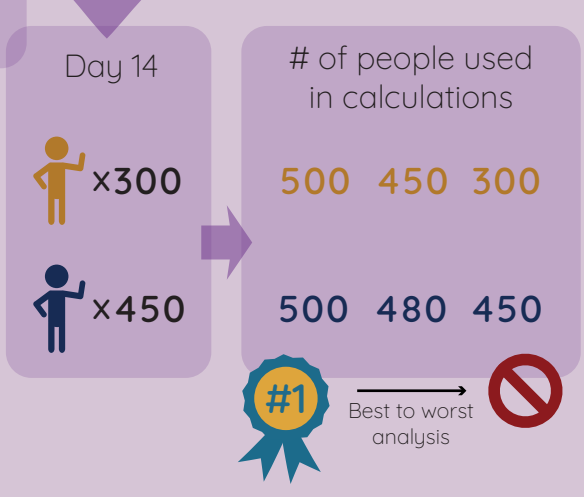
How many patients remained in the study? Was that number different between control and treated groups?

When more people drop out of a particular group of the study, this indicates something was uneven between the groups.



Uneven dropout can happen when, for example:

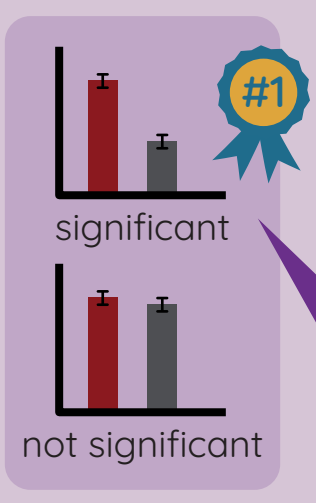
- the study population was not effectively randomized
- one of the groups experiences more severe side effects or death that causes them to leave the study

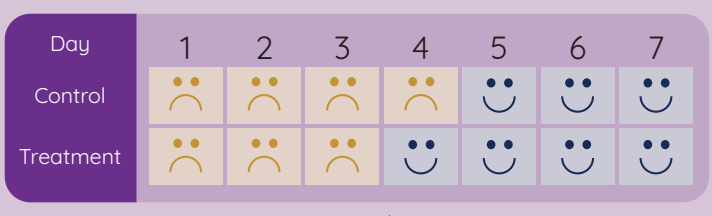


Were all the people who entered the study included in the final analysis?

Ideally, the entire cohort of people the researchers intended to treat should be included, and not just the number left at the end of the study.

Were the findings "significant", statistically or clinically?





If the study followed #1 practices up to this point, this finding is likely meaningful and can be evaluated for FDA approval!

Even if the results are statistically significant, we have to ask whether they would make a practical difference to patients. Sometimes a drug only slightly shortens an illness, or only helps a small fraction of patients.

What happens next?

Studies that showed a treatment results in significantly improved outcomes:	If no differences were seen between treatment vs. control groups, or the treatment group was significantly worse:
☐ FDA evaluates for approval	☐ The new treatment is not used
☐ If approved, "Phase 4" Clinical Trial starts to assess long-term outcomes and side effects	☐ The "standard of care" remains the treatment of choice for the disease being assessed.
Even if approved, sometimes a treatment may not work in the real world because the population is more diverse than the study group, or because there is no clinician present to make sure a patient takes a treatment correctly.	☐ Researchers may design a repeat clinical trial to study interesting outcomes that were observed in the original study (but not directly tested), or change the sample size, or population.

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