What is a confidence interval?

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2. Learning objectives

- In this seminar, you will learn how to:
  - distinguish between statistical significance and clinical significance;
  - interpret confidence intervals;
  - explain the ethical issues associated with inadequate sample sizes.

3. Outline

1. Pop quiz
2. Definitions
3. What is a confidence interval?
4. Practice exercises
5. Repeat of pop quiz

4. Pop quiz

A research paper computes a confidence interval for a relative risk of 0.82 to 3.94. What does this confidence interval tell you.

1. The result is statistically significant and clinically important.
2. The result is not statistically significant, but is clinically important.
3. The result is statistically significant, but not clinically important.
4. The result is not statistically significant, and not clinically important.
5. The result is ambiguous.
6. I do not know the answer.

5. Definitions

- Population: the group you wish to generalize your research results to.
- Usually defined in terms of
  - Demography,
  - Geography,
  - Occupation,
  - Time,
  - Care requirements,
  - Diagnosis,
  - Or some combination of the above.

6. Definitions

- An example of a population would be all infants born in the state of Missouri during the 1995 calendar year who have one or more visits to the Emergency room during their first year of life.

7. Definitions

- Sample: subset of a population.
- Random sample: every item in the population has the same probability of being in the sample.
- Biased sample: some items in the population have a decreased probability of being in the sample.

8. Definitions

- A Type I error is **rejecting the null hypothesis when the null hypothesis is true** (false positive).
- Example involving drug approval: a Type I error is allowing an ineffective drug onto the market.

9. Definitions

- A Type II error is **accepting the null hypothesis when the null hypothesis is false**.
- An example involving drug approval: a Type II error is keeping an effective drug off of the market.

10. **What is a confidence interval?**

- A confidence interval is a range of values that tries to quantify **uncertainty associated with the sampling process**.
- Consider it as a **range of plausible values**.

11. **What is a confidence interval?**

- Wide interval = poor precision
- Narrow interval = good precision
- It is unethical to conduct research if you know that your confidence interval will be so wide as to be uninformative.

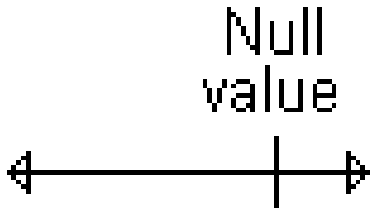
12. **What is a confidence interval?**

- Consider a recent study of **homoeopathic treatment of pain and swelling after oral surgery** (Lokken 1995). When examining swelling 3 days after the operation, they showed that **homoeopathy led to 1 mm less swelling on average**. The **95% confidence interval, however, ranged from -5.5 to 7.5 mm**. This interval implies that **neither a large improvement due to homoeopathy nor a large decrement could be ruled out**.

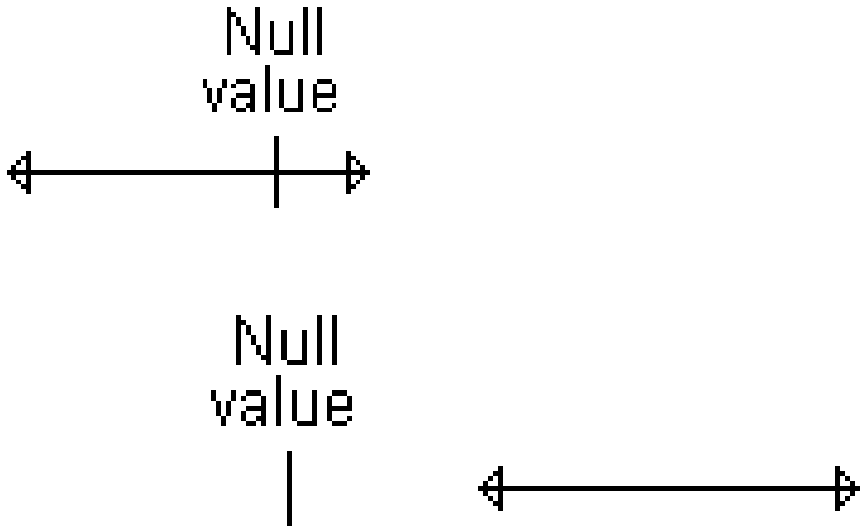
13. **What is a confidence interval?**

- Look for two things:
  1. Does the interval contain a value that implies no change or no effect?

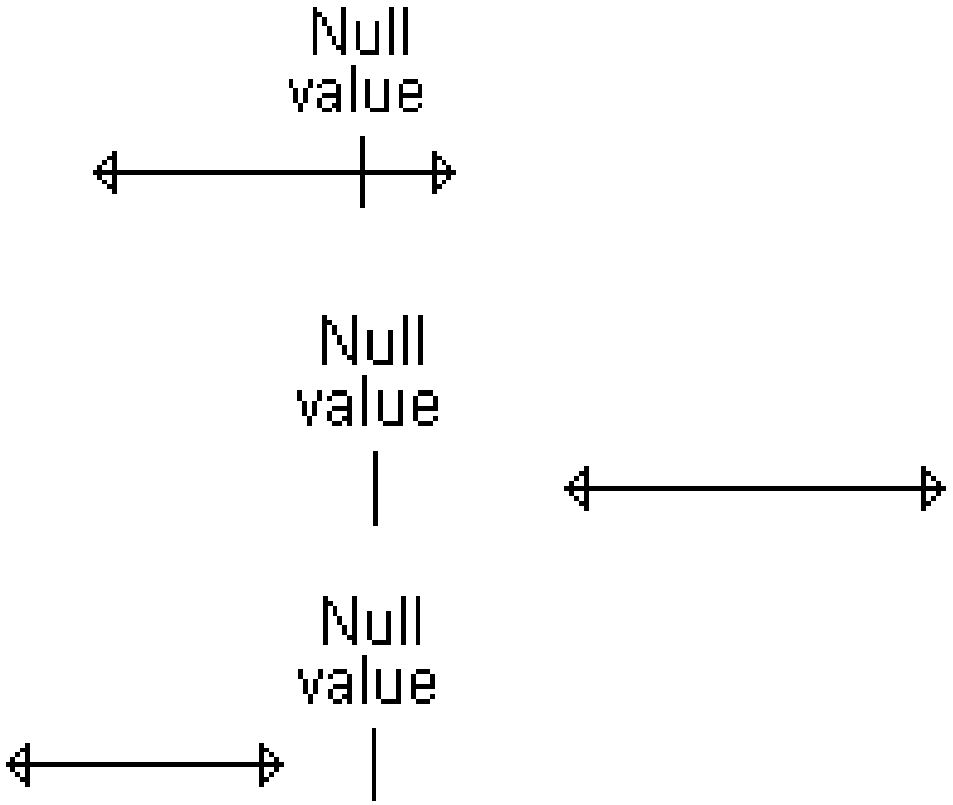
14. **No change,…**



15. **No change, a positive change,…**



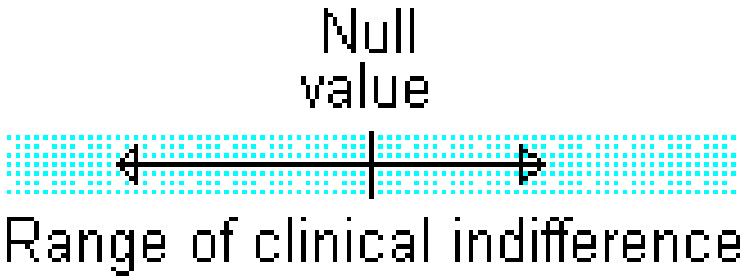
16. **No change, a positive change, and a negative change**



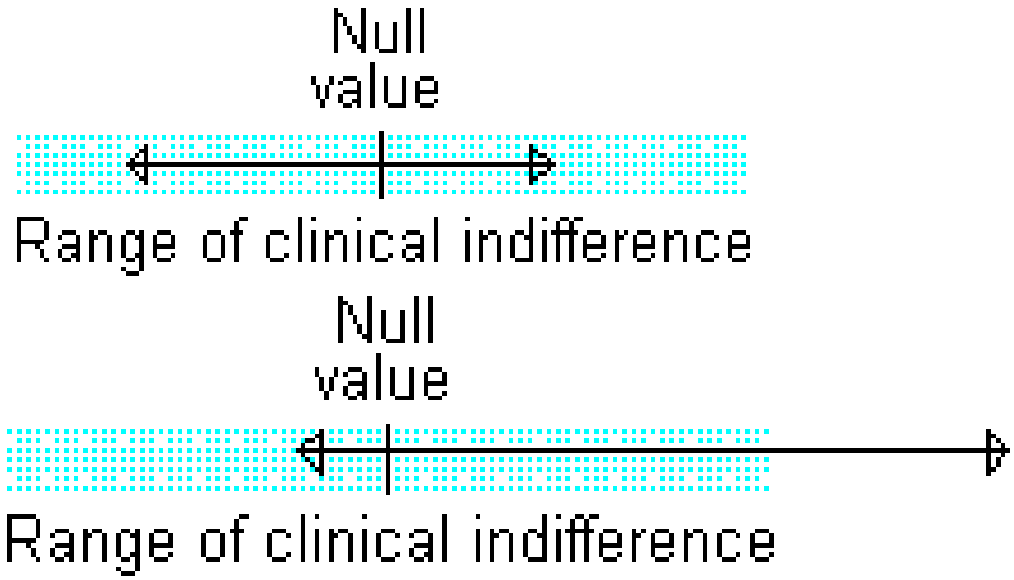
17. **What is a confidence interval?**

- Look for two things:
  1. Does the interval contain a value that implies no change or no effect?
  2. Does the interval lie entirely inside the range of clinical indifference?

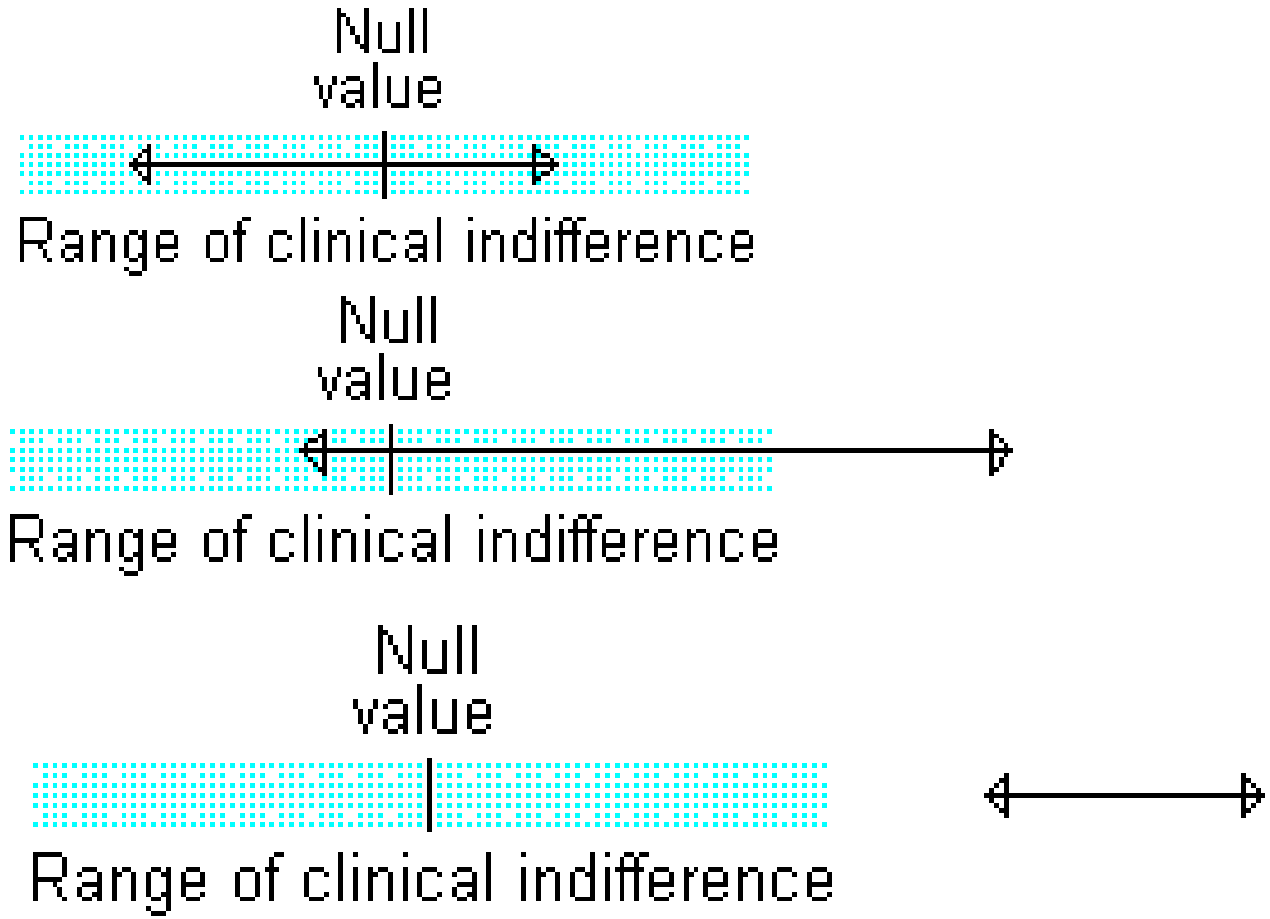
18. **A true null finding,...**



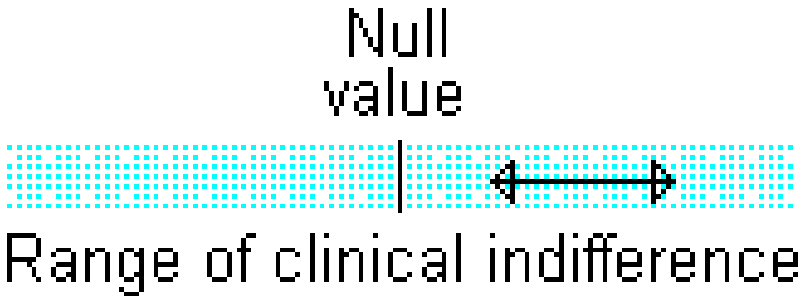
19. **A true null and an ambiguous finding, …**



20. **A true null, an ambiguous, and a true positive finding.**



21. **Statistical significance without practical significance**



22. Practice exercise: interpret the confidence intervals shown below.

1. **The Outcome of Extubation Failure in a Community Hospital Intensive Care Unit: A Cohort Study**. Seymour CW, Martinez A, Christie JD, Fuchs BD. *Critical Care 2004*, 8:R322-R327 (20 July 2004) **Introduction:** Extubation failure has been associated with poor intensive care unit (ICU) and hospital outcomes in tertiary care medical centers. Given the large proportion of critical care delivered in the community setting, our purpose was to determine the impact of extubation failure on patient outcomes in a community hospital ICU. **Methods:** A retrospective cohort study was performed using data gathered in a 16-bed medical/surgical ICU in a community hospital. During 30 months, all patients with acute respiratory failure admitted to the ICU were included in the source population if they were mechanically ventilated by endotracheal tube for more than 12 hours. Extubation failure was defined as reinstitution of mechanical ventilation within 72 hours (n = 60), and the control cohort included patients who were successfully extubated at 72 hours (n = 93). **Results:** The primary outcome was total ICU length of stay after the initial extubation. Secondary outcomes were total hospital length of stay after the initial extubation, ICU mortality, hospital mortality, and total hospital cost. Patient groups were similar in terms of age, sex, and severity of illness, as assessed using admission Acute Physiology and Chronic Health Evaluation II score ($P > 0.05$). Both ICU (1.0 versus 10 days; $P < 0.01$) and hospital length of stay (6.0 versus 17 days; $P < 0.01$) after initial extubation were significantly longer in reintubated patients. ICU mortality was significantly higher in patients who failed extubation (odds ratio = 12.2, 95% confidence interval [CI] = 1.5–101; $P < 0.05$), but there was no significant difference in hospital mortality (odds ratio = 2.1, 95% CI = 0.8–5.4; $P < 0.15$). Total hospital costs (estimated from direct and indirect charges) were significantly increased by a mean of US$33,926 (95% CI = US$22,573–45,280; $P < 0.01$). **Conclusion:** Extubation failure in a community hospital is univariately associated with prolonged inpatient care and significantly increased cost. Corroborating data from tertiary care centers, these adverse outcomes highlight the importance of accurate predictors of extubation outcome.

23. Practice exercise: interpret the confidence intervals shown below.

2. Elevated White Cell Count in Acute Coronary Syndromes: Relationship to Variants in Inflammatory and Thrombotic Genes. Byrne CE, Fitzgerald A, Cannon CP, Fitzgerald DJ, Shields DC. *BMC Medical Genetics 2004*, 5:13 (1 June 2004)
Background: Elevated white blood cell counts (WBC) in acute coronary syndromes (ACS) increase the risk of recurrent events, but it is not known if this is exacerbated by pro-inflammatory factors. We sought to identify whether pro-inflammatory genetic variants contributed to alterations in WBC and C-reactive protein (CRP) in an ACS population. **Methods:** WBC and genotype of interleukin 6 (IL-6 G-174C) and of interleukin-1 receptor antagonist (IL1RN intronic repeat polymorphism) were investigated in 732 Caucasian patients with ACS in the OPUS-TIMI-16 trial. Samples for measurement of WBC and inflammatory factors were taken at baseline, i.e. Within 72 hours of an acute myocardial infarction or an unstable angina event. **Results:** An increased white blood cell count (WBC) was associated with an increased C-reactive protein ($r = 0.23$, $p < 0.001$) and there was also a positive correlation between levels of β-fibrinogen and C-reactive protein ($r = 0.42$, $p < 0.0001$). IL1RN and IL6 genotypes had no significant impact upon WBC. The difference in median WBC between the two homozygote IL6 genotypes was 0.21/mm3 (95% CI = -0.41, 0.77), and -0.03/mm3 (95% CI = -0.55, 0.86) for IL1RN. Moreover, the composite endpoint was not significantly affected by an interaction between WBC and the IL1 ($p = 0.61$) or IL6 ($p = 0.48$) genotype. **Conclusions:** Cytokine pro-inflammatory genetic variants do not influence the increased inflammatory profile of ACS patients.

24. Practice exercise: interpret the confidence intervals shown below.

3. Is There a Clinically Significant Gender Bias in Post-Myocardial Infarction Pharmacological Management in the Older (>60) Population of a Primary Care Practice? Di Cecco R, Patel U, Upshur REG. *BMC Family Practice 2002*, 3:8 (3 May 2002) **Background:** Differences in the management of coronary artery disease between men and women have been reported in the literature. There are few studies of potential inequalities of treatment that arise from a primary care context. This study investigated the existence of such inequalities in the medical management of post myocardial infarction in older patients. **Methods:** A comprehensive chart audit was conducted of 142 men and 81 women in an academic primary care practice. Variables were extracted on demographic variables, cardiovascular risk factors, medical and non-medical management of myocardial infarction. **Results:** Women were older than men. The groups were comparable in terms of cardiac risk factors. A statistically significant difference (14.6%: 95% CI 0.048–28.7 p = 0.047) was found between men and women for the prescription of lipid lowering medications. 25.3% (p = 0.0005, CI 11.45, 39.65) more men than women had undergone angiography, and 14.4 % (p = 0.029, CI 2.2, 26.6) more men than women had undergone coronary artery bypass graft surgery. **Conclusion:** Women are less likely than men to receive lipid-lowering medication which may indicate less aggressive secondary prevention in the primary care setting.

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