EBM – Biostatistics Review

Pitfalls on Board Exams

Anthony J. Busti, MD, PharmD, MSc, FNLA, FAHA

HIGH-YIELD
MED REVIEWS

Introduction

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Agenda

- Pitfalls on Board Exams
  - Picking the wrong statistical test because you:
    - Failed to identify the number and types of groups
    - Failed to identify the endpoint in question correctly
  - Incorrect interpretation of Power
  - Incorrect interpretation of what a p-value is & is not
  - Incorrect interpretation of 95% Confidence Intervals
  - Incorrect interpretation of relative risk in the context of:
    - Relative Risk Reduction
    - Absolute Risk Reduction → NNT/NNH
- A special coupon code & feedback opportunity
- Live Q&A

HIGH-YIELD MED REVIEWS

Pitfalls on Board Exams

- Picking the Wrong Statistical Test -

Get Oriented!

HIGH-YIELD
MED REVIEWS

Type of Data	Two Independent Samples	Related or Paired Samples	3 or more Independent Samples	3 or more Related Samples	Measures of Correlation
Nominal	1.Chi-square 2.Fisher's Exact	McNemar Test	Chi-square for k independent samples	Cochran Q	Contingency coefficient
Ordinal	1.Mann-Whitney U 2.Wilcoxon Rank Sum	1.Sign test 2.Wilcoxon Signed Rank	Kruskal-Wallis one way ANOVA	Freidman 2 way ANOVA	1.Spearman 2.Kendal rank 3.Kendal Coe
Continuous	1.Student's t-test 2.Mann-Whitney U	Paired t-test	1-way ANOVA	2-way ANOVA	Pearson's Correlation

Pitfalls on Board Exams

- Picking the Wrong Statistical Test -

Identify the Types of Groups Studied

HIGH-YIELD
MED REVIEWS

Type of Groups

Related Groups	Independent Groups
SAME patient in ALL arms	DIFFERENT patients in each arm

• Cross-Over Studies
• Retrospective Study of All Patients Start & End of Study
• Left eye vs right eye on the same patient
• Warning:
  • Patients Randomized to look almost the same
  • Identical Twins
	• RCT
	• Cohort Study
	• Case-Controlled Study

Pitfalls on Board Exams

- Picking the Wrong Statistical Test -

Identify the Endpoint in the Study Question

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Pitfalls on Board Exams

- Correctly identify the endpoint being studied in the study's objective or study question being asked.
  - You must get oriented!
    - This is the killer foil step for most people.
  - How is the endpoint being treated (i.e., type of data)?
    - Nominal
    - Ordinal
    - Continuous

HIGH-YIELD MED REVIEWS

Nominal Data

- Key descriptors:
  - Categorical
  - Dichotomous
  - Binomial distribution
  - No sense of "___________ " or " _____________ "
    - Thus the magnitude of difference between the two does not apply
- Assessment of data:
  - The endpoint is treated at the end as:
    - "yes or no"
    - "either did or didn't ...... "
    - There CANNOT be an average or a mean value

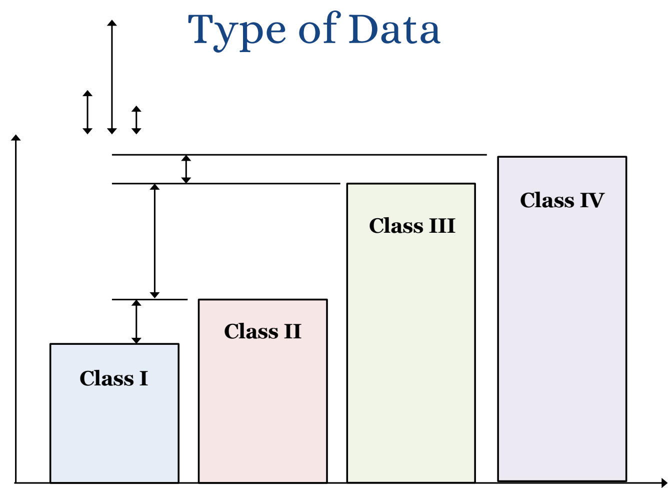
HIGH-YIELD MED REVIEWS

Ordinal Data

- Key descriptors:
  - Data endpoints have a sense of "order" that also has a sense of "ranking" or "scale"
  - Nonparametric (not normally distributed data)
    - Could by continuous data with outliers
- Assessment of data:
  - The "magnitude of difference" between endpoints is ________ the same

HIGH-YIELD MED REVIEWS

Type of Data



HIGH-YIELD MED REVIEWS

Ordinal Data

- Examples of Ordinal Data:
  - Classification of HF (class I – IV)
  - Severity of pain:
    - Mild, Moderate, or Severe
  - Well's Score for PE (0 – 12.5)
    - Low or PE unlikely (< 4 points)
    - Moderate (4-6 points)
    - High probability (> 6 points)
  - What about:
    - NIH Stroke "Scale"
    - Pain Scale: 0 - 10

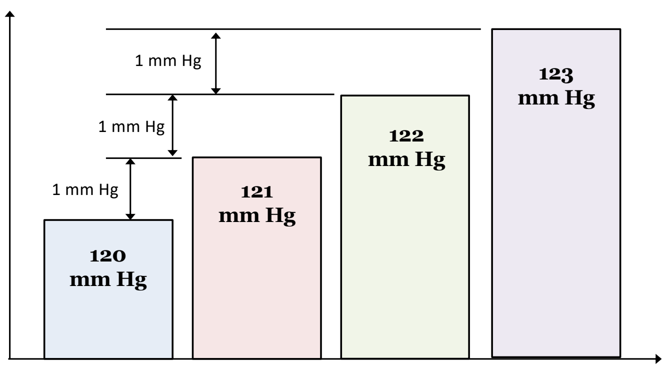
HIGH-YIELD MED REVIEWS

Continuous Data

- Key descriptors:
  - Data endpoints have a sense of "order" that also has a sense of "ranking"
  - Parametrically distributed
    - Assumes no " _______________ "
- Assessment of data:
  - The "magnitude of difference" between endpoints is ________ the same

HIGH-YIELD MED REVIEWS

Type of Data



HIGH-YIELD MED REVIEWS

Continuous Data

- Examples of Continuous Data:
  - Temperature
  - Pulse (heart rate)
  - Blood pressure (without a cutoff or designated goal)
  - Labs (Sodium level)

HIGH-YIELD MED REVIEWS

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Pitfalls on Board Exams

- Picking the Wrong Statistical Test -

Identify the Best Test for Data Obtained

HIGH-YIELD MED REVIEWS

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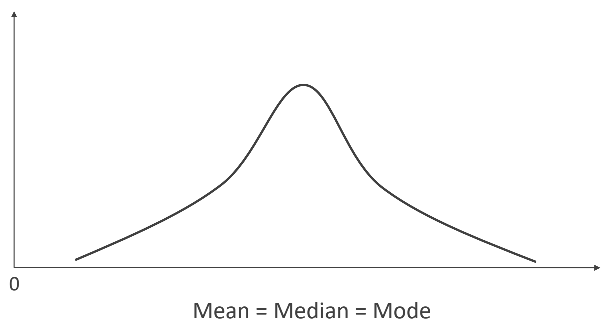
Nonparametric

Parametric

Measures of Variability or Data Dispersion



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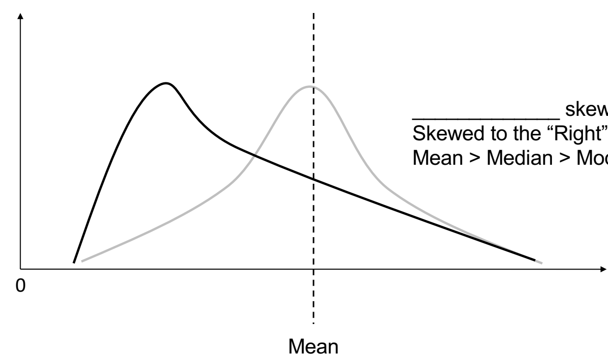

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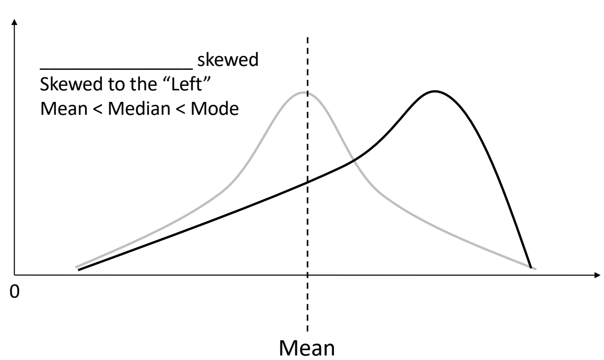
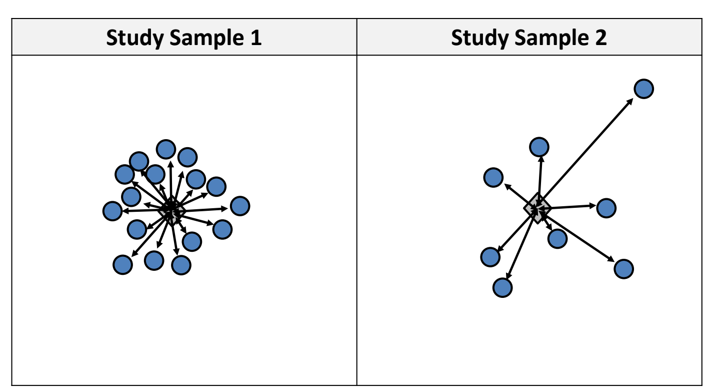


Measure of Variability



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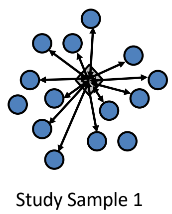

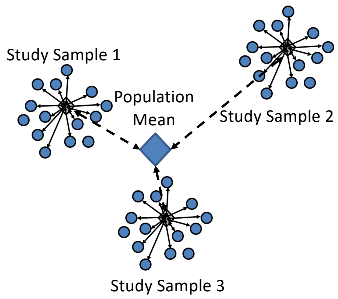

Standard Deviation	Standard ______________
Measure of amount of variability within a sample from population	Measure of how close the population mean estimates to each sample mean

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Chi-squared vs. Fisher's exact

Variable	Chi-square test	Fisher's exact test
Sample Size	Large	Small
Desired Accuracy	Approximate	"Exact"
Considerations	▪ Becomes more accurate with larger sample sizes	▪ More exact regardless of number but harder to calculate by hand using computer. ▪ Note: is it really "exact"? ▪ Typically used when > 20% of the cells have a frequency of < 5 because an approximation at this level is inadequate.

HIGH-YIELD MED REVIEWS

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Nonparametric

Parametric

Pitfalls on Board Exams

- Incorrect Interpretation of Power -

HIGH-YIELD MED REVIEWS

Hypothesis Testing – Power Analysis

- Power = 1 - β
  - Indicates the probability that a statistical test can detect a significant difference when in fact, it truly exists.
  - Since Beta (β) indicates the probability of making a type __________ , the power calculation tells you the probability that you will NOT make a ________________.

Beta (β)	Zβ	Sample Size (n)
0.01 or 1%	2.32	36
0.05 or 5%	1.64	26
0.1 or 10%	1.28	21
0.2 or 20%	0.85	16

HIGH-YIELD MED REVIEWS

Pitfalls on Board Exams

- Incorrect Interpretation of P-values -

HIGH-YIELD MED REVIEWS

P-Values

- Example Scenario:
  - Which of the following results has the greater clinical significance?
    - Study Endpoint 1 → p = 0.0003
    - Study Endpoint 2 → p = 0.001

HIGH-YIELD MED REVIEWS

P-Values

- Interpretation:
  - Helps assess if the results are from chance or random error
  - HAS NOTHING TO DO WITH CLINICAL SIGNIFICANCE
  - Interpret the p-value:
    - P = 0.003
      - ________ chance the results are due to random error or are by chance alone
    - P = 0.01
      - ________ chance the results are due to random error or are by chance alone
    - A p-value < 0.05 suggests the null hypothesis should be rejected or is "less true"

HIGH-YIELD MED REVIEWS

Pitfalls on Board Exams

- Incorrect Interpretation of 95% CI -

HIGH-YIELD MED REVIEWS

95% Confidence Intervals

- Example Scenario:
  - Which of the following results reflects the true population result?
    - Study Endpoint 1 → RR 0.65 (0.45 – 0.76)
    - Study Endpoint 2 → RR 0.78 (0.71 – 0.82)
  - Which one is statistically significant
    - BOTH
  - Interpret endpoint 1
    - ___________________________
    - ________ of the risk of the outcome was removed by being exposed to the intervention

HIGH-YIELD MED REVIEWS

95% Confidence Intervals

- Basics:
  - Get oriented!
  - If 95% CI is for HR, OR, RR, or Risk Ratio then:
    - If the 95% CI crosses through and includes ______ it CANNOT be statistically significant
  - If the 95% CI for a "mean or average" then:
    - If the 95% CI crosses through and includes ______ it CANNOT be statistically significant

HIGH-YIELD MED REVIEWS

Pitfalls on Board Exams

- Incorrect Interpretation of Relative Risk -

HIGH-YIELD MED REVIEWS

Relative Risk

- RR = $\dfrac{\text{incidence rate in exposed patients}}{\text{incidence rate in non-exposed patients}}$

- RR = 1 (incidence is the same for both groups)
- RR = >1 (incidence in exposed group is higher)
- RR = <1 (incidence in exposed group is less)

HIGH-YIELD MED REVIEWS

Relative Risk

- Relative Risk Reduction (RRR)
  - Remember it is = 1 – RR

- Absolute Risk Reduction (ARR)
  - It is the difference between the incidence of the exposed group and the unexposed group
  - Used to calculate NNT or NNH
    - NNT = ___________
    - It must then be put into the context of the clinical trial duration/method of treatment

HIGH-YIELD MED REVIEWS

Main Results

Outcome	Dexamethasone	Placebo	RR (95% CI)	P-value
Unfavorable Outcome				
All patients	23/157	36/144	< 1	
S. pneumoniae	15/58	26/50	< 1	
N. meningitidis	4/5	5/47	< 1	
Other bacteria	2/12	1/17	> 1	
Death				
All patients	11/157	21/144	< 1	
S. pneumoniae	8/58	11/50	< 1	
N. meningitidis	2/50	1/47	> 1	
Other bacteria	1/12	1/17	> 1	

NEJM 2002;347(20):1549-56.

HIGH-YIELD MED REVIEWS

Main Results

RR = $\dfrac{\text{incidence rate in exposed patients}}{\text{incidence rate in non-exposed patients}}$

1. Calculate the incidence in each group

HIGH-YIELD MED REVIEWS

Main Results

Outcome	Dexamethasone	Placebo	RR (95% CI)	P-value
Unfavorable Outcome				
All patients	23/157	36/144		
S. pneumoniae	15/58 **(0.26)**	26/50 **(0.52)**		
N. meningitidis	4/5	5/47		
Other bacteria	2/12	1/17		
Death				
All patients	11/157	21/144		
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HIGH-YIELD MED REVIEWS

Main Results

RR = incidence rate in exposed patients / incidence rate in non-exposed patients

1. Calculate the incidence in each group
2. RR = 0.26 / 0.52 = 0.5

HIGH-YIELD MED REVIEWS

Main Results

Outcome	Dexamethasone	Placebo	RR (95% CI)	P-value
Unfavorable Outcome				
All patients	23/157	36/144		
S. pneumoniae	15/58 **(0.26)**	26/50 **(0.52)**	0.50 (0.30 – 0.83)	
N. meningitidis	4/5	5/47		
Other bacteria	2/12	1/17		
Death				
All patients	11/157	21/144		
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HIGH-YIELD MED REVIEWS

Main Results

Outcome	Dexamethasone	Placebo	RR (95% CI)	P-value
Unfavorable Outcome				
All patients	23/157	36/144	0.59 (0.37 – 0.94)	
S. pneumoniae	15/58 **(0.26)**	26/50 **(0.52)**	0.50 (0.30 – 0.83)	
N. meningitidis	4/5	5/47	0.75 (0.21 – 2.63)	
Other bacteria	2/12	1/17	2.83 (0.29 – 27.8)	
Death				
All patients	11/157	21/144	0.48 (0.24 – 0.96)	
S. pneumoniae	8/58	11/50	0.41 (0.19 – 0.86)	
N. meningitidis	2/50	1/47	1.88 (0.76 – 20.1)	
Other bacteria	1/12	1/17	1.42 (0.10 – 20.5)	

Which results are significant?

NEJM 2002;347(20):1549-56.

HIGH-YIELD MED REVIEWS

NNT

RR = incidence rate in exposed patients / incidence rate in non-exposed patients

1. Calculate the incidence in each group
2. RR = 0.26 / 0.52 = 0.5
3. ARR = 0.26 – 0.52 = 0.26
4. NNT = 1/0.26

   = 3.8 or ~ 4

   - You would have to treat about 4 patients with dexamethasone 10 mg IV x 6 hrs x 4 days with *S. pneumonia* meningitis for 1 patient to have a favorable outcome.
   - Versus …… 10 patients if considering "all patients"

HIGH-YIELD MED REVIEWS

NNH Calculation

- Example:
  - The CURE Study showed the following for risk of major bleeding:
    - Group A (Treated with Aspirin) = 2.7%
    - Group B (Aspirin + clopidogrel) = 3.7%
  - NNH –1/Attributable Risk (or Absolute Increase in Risk)
    - Attributable Risk = 0.037 – 0.027 = 0.01
    - NNH = 1/0.01 = 100
    - For every 100 patients treated with aspirin + clopidogrel, 1 patient would develop a major bleed

HIGH-YIELD MED REVIEWS

Closing

- Avoiding common pitfalls on board exams:
  - Getting oriented on study design and question being asked/studied to pick the right statistical test
  - Using P-values in their proper context
  - Understanding what the Power of a study means
  - Getting oriented to data variable for the 95% CI
  - Keeping the relative risk numbers right

HIGH-YIELD MED REVIEWS

Coupon

- Limited time coupon
  - Coupon = ______________________
    - *10% OFF ENTIRE ORDER*
  - Expires = **February 28, 2023**
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Live Q&A

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