



UW TASP
tele-antimicrobial stewardship program

echo 

December 19, 2023

Agenda

- *Statistics, applied*
- Case Discussions
- Open Discussion

Why do I have to?



THINGS GOT REALLY INTERESTING WHEN THE STATISTICIAN STARTED DOING WARD ROUNDS.

- Statistics is the math we use to demonstrate relationships: causality, correlations, and lack of relationships
- Statistics may be math, but interpretation is subjective



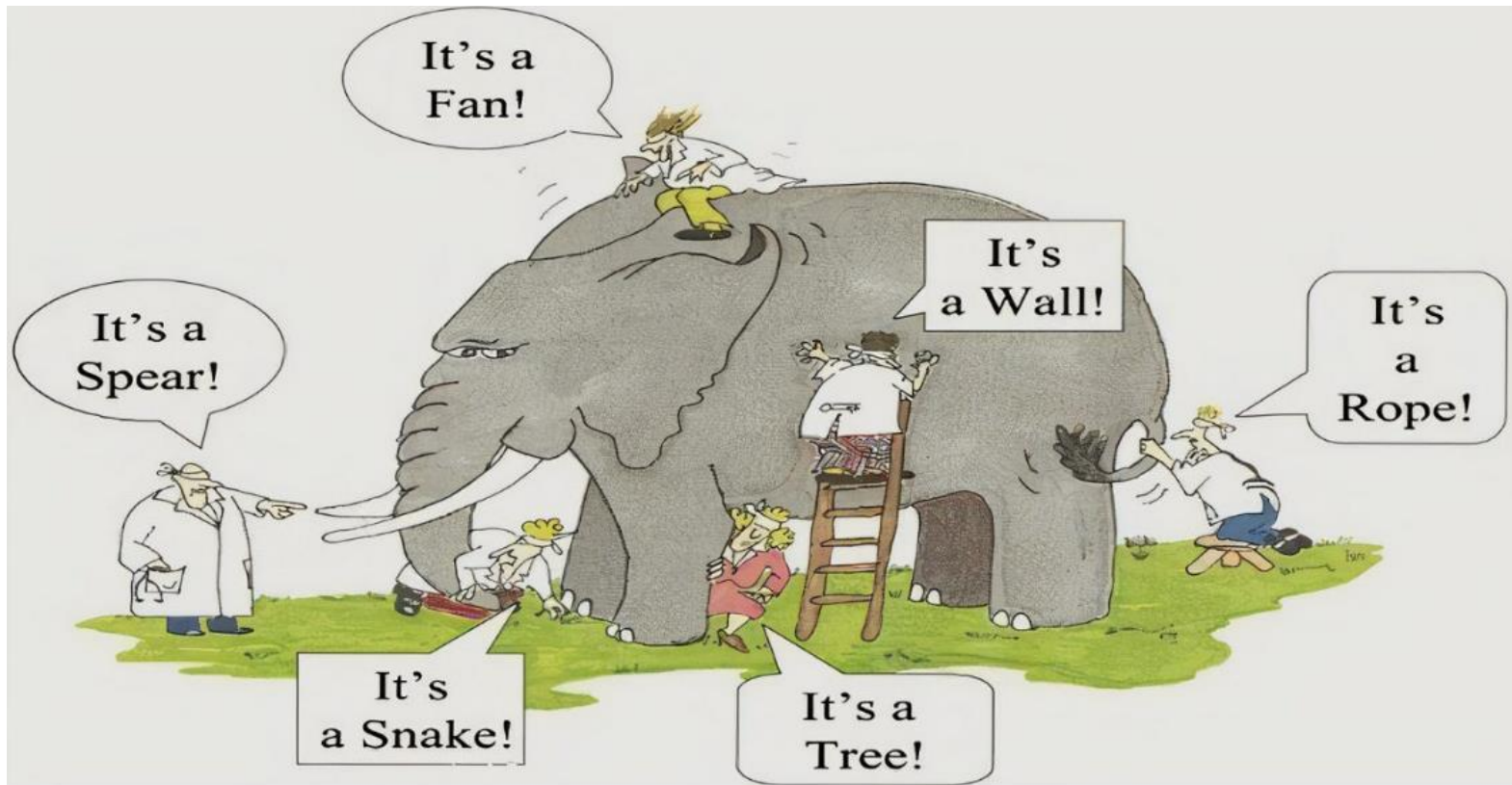
An Observation:

We've been talking a lot about covid-related appendicitis....It's weird how often we have seen it [in the ED] over the last year.

I guess I wondered if patients who have had appendicitis in the last 3-6 months but haven't had an appendectomy yet - should they wait on getting the vaccine?



Observation and Perspective



Though each was partly in the right, all were in the wrong.

Bias

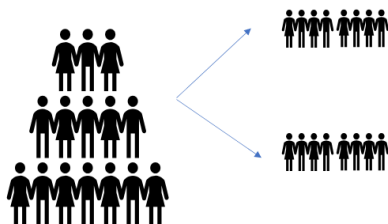
- Remember: Randomized controlled trials are the gold standard in data because they manage bias

The Problem with Observational Studies = BIAS

- Allocation into groups

- Concealed

- Random



Check out the Stats presentation from 3/14/22 for a refresher



Let me get back to you...

The Google logo is centered on the page, rendered in its characteristic multi-colored font.A long, empty search input field with a thin blue border. A small, colorful microphone icon is positioned at the right end of the field.

Google Search

I'm Feeling Lucky



An AE of special interest

VAERS
Vaccine Adverse Event Reporting System



First 6 months of the US COVID-19 vaccination program:

383 cases of appendicitis

= 1.3 reports per million doses administered.



With this information, would you recommend the mRNA vaccine?

- No, Patients at risk for appendectomy (e.g. recent appendicitis, medically managed) should not get the mRNA vaccine
- Yes, This is a rare event, would still recommend the mRNA vaccine
- Observational data is biased, we need an RCT
- I'm not sure



Can I run a randomized controlled trial?

Sample Size Calculator

- Group 1: Incidence of appendicitis in vaccinated) = 2/1,000,000
- Group 2: Incidence of appendicitis in unvaccinated = 1 /1,000,000

Anticipated Incidence

Group 1 [?](#) %

Group 2 [?](#) %

▼

Enrollment ratio [?](#)

Type I/II Error Rate

Alpha [?](#)

Power [?](#)



Can I run a randomized controlled trial?

Sample Size Calculator

- Group 1: Incidence of appendicitis in vaccinated) = $2/1,000,000$
- Group 2: Incidence of appendicitis in unvaccinated = $1/1,000,000$

Sample Size	
Group 1	23546603
Group 2	23546603
Total	47093206



4 Million Danes

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April 25, 2022

Risk of Appendicitis After mRNA COVID-19 Vaccination in a Danish Population

Helene Kildegaard, MD¹; Louise Ladebo, MScPharm, PhD¹; Jacob Harbo Andersen, MSc¹; [et al](#)

» Author Affiliations | Article Information

JAMA Intern Med. 2022;182(6):684-686. doi:10.1001/jamainternmed.2022.1222



COVID-19 Resource Center

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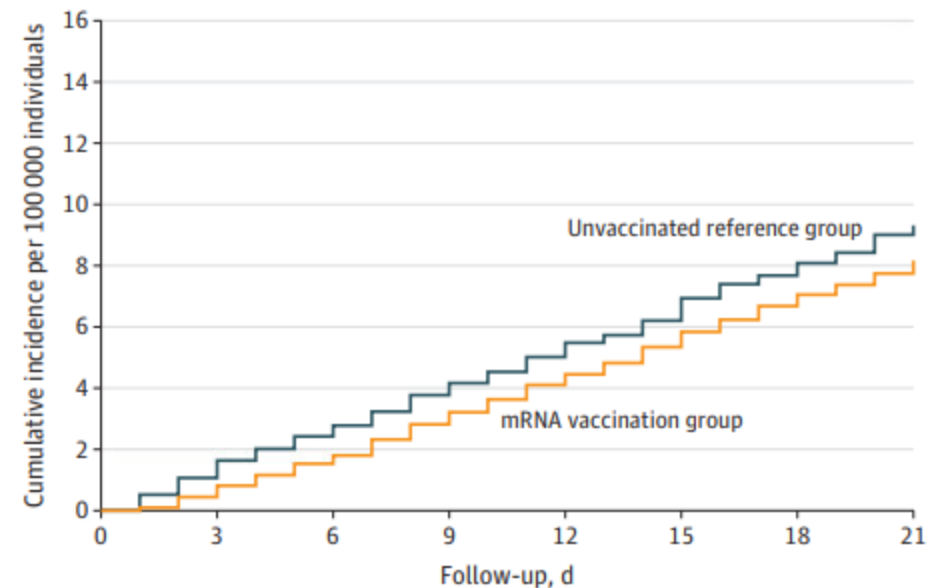


Same or Different?

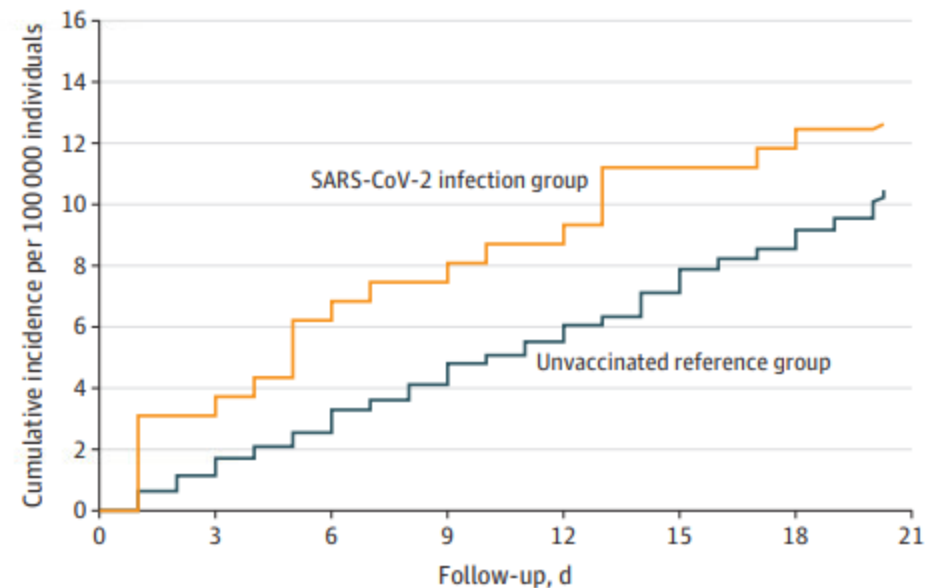
Time for
Statistics!

Figure. The 21-Day Cumulative Incidence of Appendicitis or Appendectomy

A After 1st dose of COVID-19 mRNA vaccine











B After PCR test confirmed SARS-CoV-2 infection



PCR indicates polymerase chain reaction.



Time for Statistics: Determining Differences

	SAME	DIFFERENT
1 minus 1		
0.034 minus 0.034		
1 divided by 1		
14,553 divided by 14,553		



Translating Math into Stats

1 minus 1

0.034 minus 0.034

SUBTRACTION =
"Absolute risk"
"Difference"



Translating Math into Stats

1 minus 1

0.034 minus 0.034

SUBTRACTION =
"Absolute risk"
"Difference"

1 divided by 1

14,553 divided by 14,553

DIVISION =
"Relative risk"
"Risk Ratio"



Risk Ratio of Appendicitis

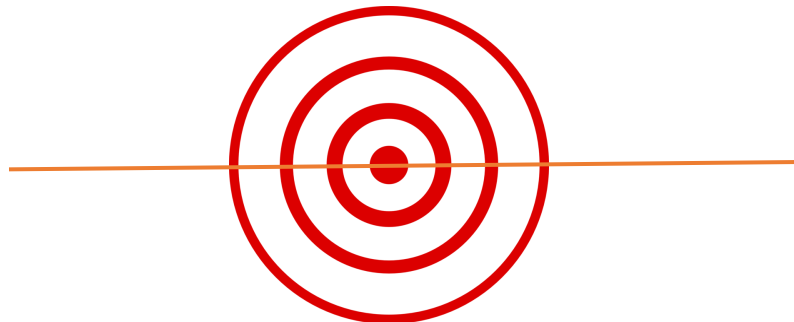
$$\text{Risk Ratio} = \frac{\text{\# with appendicitis} / \text{\# in vaccine group}}{\text{\# with appendicitis} / \text{\# in non-vaccinated group}}$$

If one number divided by another = 1, then they are not different



After Vaccination

- 0.93
The risk is a little lower with vaccination!
- 95% CI, 0.84, 1.18
Actually, no it is not different



DIFFERENCE = NOT THE SAME



Interpreting Outcomes: Why Confidence intervals?



The confidence interval is the precision of your estimate

- A smaller interval is more precise and reliable
- A wider interval indicates more variation

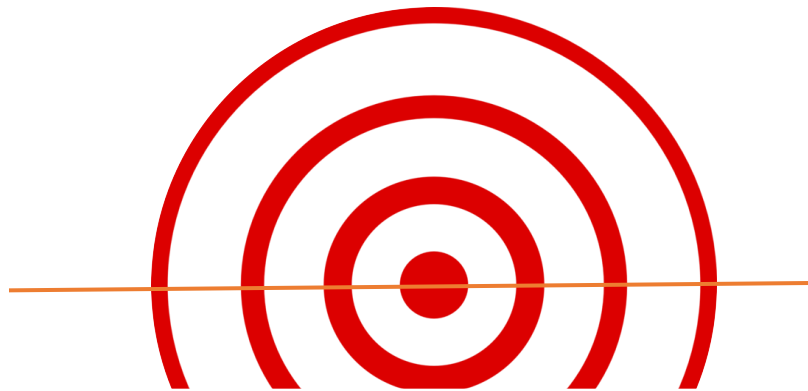
Bullseye range (AKA Confidence interval) doesn't include 1



Risk Ratio of Appendicitis

If one number divided by another = 1, then they are not different

$$\text{Risk Ratio} = \frac{\# \text{ with appendicitis} / \# \text{ in SARS-CoV-2 infection group}}{\# \text{ with appendicitis} / \# \text{ in non-infected group}}$$



After SARS-CoV-2 infection

- 1.25

The risk is a little higher with infection

- 95% CI, 0.79-1.99

Actually, no it is not different



Context



Original Investigation

January 25, 2022

Myocarditis Cases Reported After mRNA-Based COVID-19 Vaccination in the US From December 2020 to August 2021

Matthew E. Oster, MD, MPH^{1,2,3}; David K. Shay, MD, MPH¹; John R. Su, MD, PhD, MPH¹; [et al](#)

» [Author Affiliations](#) | [Article Information](#)

JAMA. 2022;327(4):331-340. doi:10.1001/jama.2021.24110

- 50-100 cases of myocarditis per 1 million doses of COVID vaccine
- 1.3 cases of appendicitis per 1,000,000 vaccine



With this information, would you recommend the mRNA vaccine?

- No, Patients at risk for appendectomy (e.g. recent appendicitis, medically managed) should not get the mRNA vaccine
- Yes, This is a rare event, would still recommend the mRNA vaccine
- Observational data are biased, we need an RCT
- I'm not sure



Conclusion:

Humbly I share the information and validate the question

I'm not sure these numbers support a recommendation to wait to get the vaccine.

I think you're right though that there's probably a number of unknown nuances with the vaccine

