"Top 10" statistical errors

JANUARY 25, 2020

KRISTIN SAINANI, PHD <u>KCOBB@STANFORD.EDU</u>, @KRISTINSAINANI

"Top ten" statistical errors

- 1. Simple math and data errors
- 2. Study design mismatched to statistical question
- 3. Chance findings
- 4. Clinically irrelevant effect sizes
- 5. Exaggerated effect sizes
- 6. Wrong comparisons
- 7. Failure to account for correlated observations
- 8. Misinterpretations of null effects
- 9. Residual/unmeasured confounding
- 10. Spurious correlations/overfitting

1. Simple math and data errors

Simple math errors are surprisingly common!

2+2 = 5

Examples:

-N's don't add up
-Simple calculation errors
-Descriptive statistics don't make sense
-Data in different tables or figures don't match
-Other data errors that may be more hidden

-Meta-analysis of studies of athletes who underwent a short training intervention (8 to 12 weeks)

-Athletes had leg strength (squatting ability) and sprint times measured before and after the intervention.

-Goal was to estimate correlation between improvement in leg strength and improvement in sprinting ability.



Seitz, L.B., Reyes, A., Tran, T.T. *et al.* Increases in Lower-Body Strength Transfer Positively to Sprint Performance: A Systematic Review with Meta-Analysis. *Sports Med* **44**, 1693– 1702 (2014).



Main study conclusion: "The present metaanalysis suggests that there is a transfer of lower-body strength training to sprint performance as indicated by the very large correlation between squat strength ES and sprint ES $(r = -0.77; p \le 0.001)$."

1702 (2014).

How big is a 15-standard deviation improvement in squatting ability?

A. a small effect

B. a medium effect

C. a large effect

D. a very large effect

E. an implausibly large effect

How big is a 15-standard deviation improvement?

For squats, baseline mean and standard deviation were 123 kg +/- 8 kg.

So, a 15-standard deviation improvement would mean that on average athletes increased their squat ability from 123 kg to 243 kg.

What went wrong?

The authors extracted means and *STANDARD ERRORS* from the original paper. They plugged *STANDARD ERRORS* rather than *STANDARD DEVIATIONS* into the effect size formula.

Pre-intervention mean and SEM = 123 kg +/- 1.9 kg Post-intervention mean and SEM = 148 kg +/- 1.5 kg

Pre-intervention mean and SD = 123 kg +/- 8.5 kg Post-intervention mean and SD = 148 kg +/- 6.7 kg \rightarrow +25 kg / 7.6 kg = 3.3

2. Study design mismatched to statistical question



Researchers failed to choose the correct study design for the statistical question of interest, resulting in a study that is unable to answer the question of interest.

Examples:

-power calculation done for the wrong statistical test, resulting in the study being underpowered

-study lacks an appropriate control group to answer the question of interest -superiority study was run when equivalence or non-inferiority was of interest

Example

<u>Aim</u>: The purpose of this study was to identify the clinical effectiveness of **oral versus topical NSAIDs** in the treatment of greater trochanteric pain syndrome.

<u>Methods</u>: A retrospective chart review of **25 patients** diagnosed with greater trochanteric pain syndrome were categorized into two groups: those who received **oral etodolac 400 milligrams** twice daily versus **topical diclofenac 3%** one gram the But lack of a statistically significant

Outcome: Pain scores using the nu difference is not proof of non-inferiority! e, two-week, and six-week follow-up visits.

Results: At **two weeks**, there was a statistically significant improvement in pain in both the oral and topical NSAID groups, with no statistically significant difference between the groups (p=0.77).

Similarly, at **six weeks**, there was a statistically significant improvement in pain in both the oral and topical NSAID groups, with no statistically significant difference between the groups (p=0.59).

Conclusion: Based on this study, the use of topical NSAIDs is non-inferior to oral NSAIDs in the treatment of GTPS.

Study design was mismatched to statistical question...

The goal of the study was to show that topical NSAIDs are "no worse than" oral NSAIDs in the treatment of this pain syndrome. In other words, the goal was to show non-inferiority.

But the study was not designed as a non-inferiority study.

In a non-inferiority study, one must pre-specify a margin of equivalence and calculate sample size needs based on a non-inferiority design.



3. Chance findings

Are the authors cherry-picking results or engaging in p-hacking?

Examples:

-running many statistical tests (many endpoints or time points) but only highlighting the few that come out significant

-intentionally or unintentionally manipulating data to get p<.05

Example

Abstract

A field experiment was conducted to assess how diners' taste evaluations change based on how much they paid for an all-you-can-eat (AYCE) buffet. Diners at an AYCE

restaurant of each pic self-percer variance (A less tasty, l tion Study shows customers who pay more at a restaurant buffet perceive the food as tastier than the same food offered at a lower price, shedding new light on the psychology of taste a as ach

of these measures with each additional piece (1 – 0.02). Those who paid so did not experience the same decrement in taste, satisfaction and enjoyment. Paying less for an AYCE experience may face the unintended consequence of food that is both less enjoyable and rapidly declining in taste and enjoyability. In a sense, AYCE customers get what they pay for.

Example

Methods

A field experiment was charged \$4 or \$8 for an dimensions such as phys

Results

Diners who paid \$4 for and had eaten more that buffet (p < 0.05). Diners feelings of guilt and phy they ate the exact same

Conclusion

Paying less for an AYCE paying diners feel thems the higher paying diners

C n si	PUBLIC RELEASE: 17-DEC-2015 Buffet guilt Low prices lead to high regret at all-you-can-eat buffets CORNELL FOOD & BRAND LAB f ♥ @ SHARE	CE restaurant h, participan they overate
t ar s ⁄s	<section-header></section-header>	sically more e diners who higher ratings paid \$8 for
Se Se	IMAGE: BRIAN WANSINK SAYS, "IF YOU DON'T WANT TO EXPERIENCE GUILT OR FEEL STUFFED AFTER A MEAL, EAT FROM A HIGHER PRICED AYCE BUFFET AND FOCUS ON EATING MORE HEALTHY OPTIONS view more > CREDIT: DANIEL MILLER	sing conseque able and gui

t were either its rated e, and guilt.

uncomfortable paid \$8 for the s to overeating, the buffet, even if

ences; lower litier compared to

Blog post: "The grad Student who never said no."

A PhD student from a Turkish university called to interview to be a visiting scholar for 6 months. Her dissertation was on a topic that was only indirectly related to our Lab's mission, but she really wanted to come and we had the room, so I said "Yes."

When she arrived, I gave her a data set of a self-funded, failed study which had null results (it was a one month study in an all-you-can-eat Italian restaurant buffet where we had charged some people ¹/₂ as much as others). I said, "This cost us a lot of time and our own money to collect. There's got to be something here we can salvage because it's a cool (rich & unique) data set." I had three ideas for potential Plan B, C, & D directions (since Plan A had failed). I told her what the analyses should be and what the tables should look like. I then asked her if she wanted to do them.

Every day we would scratch our heads, ask "Why," **and come up with another** way to reanalyze the data with yet another set of plausible hypotheses...

Related email...

I don't think I've ever done an interesting study where the data "came out" the first time I looked at it. The interesting stories come from seeing when things -- like the 1/2 price buffet -- works and when it doesn't.

I would like you to really dig into this to find a number of situations or people for which this relationship does hold -- that is where the 1/2 price buffet did result in a difference.

Here's some things to do.

First, look to see if there are weird outliers (in terms of how much they ate). If there seems to be a reason they are different, pull them out but specially note why you did so, so that this can be described in the method.

Second, think of all the different ways you can cut the data and analyze subsets of it to see when this relationship holds. For instance, if it works on men but not women, we have a moderator. Here are some groups you'll want to break out separately: Females Lunch goers Dinner goers People sitting alone People eating with groups of 2 People eating in groups of 2+ People who order alcohol People who order soft drinks People who sit close to buffet People who sit far away and so on . . .

Third, look at a bunch of different DVs. These might include # pieces of pizza # trips Fill level of plate Did they get dessert Did they order a drink and so on . . .

This is really important to try and find as many things here as possible *before* you come. First, it will make a good impression on people and helps you stand out a bit. Second, it would be the highest likelihood of you getting something publishable out of your visit.

Work hard, squeeze some blood out of this rock, and we'll see you soon.



SCIENCE

Here's How Cornell Scientist Brian Wansink Turned Shoddy Data Into Viral Studies About How We Eat

Brian Wansink won fame, funding, and influence for his science-backed advice on healthy eating. Now, emails show how the Cornell professor and his colleagues have hacked and massaged low-quality data into headline-friendly studies to "go virally big time."



Stephanie M. Lee BuzzFeed News Reporter

4. Clinically irrelevant effect sizes

Trivial effects may achieve statistical significance if the sample size is large enou



Example

A prospective cohort study of 34,079 women found that women who exercised >21 MET hours per week (≈60 minutes moderateintensity exercise daily) gained **significantly less** weight than women who exercised <7.5 MET hours (**p**<.001)

Widely covered in the media. Headlines:

- "To Stay Trim, Women Need an Hour of Exercise Daily."
- "New Exercise Goal: 60 Minutes a Day"

How many more pounds do you think the low exercise group gained compared with the high exercise group per year?

A. 5 pounds B. 3 pounds C. 1 pound D. 0.5 pounds E. 0.1 pounds

Mean (SD) Differences in Weight Over Any 3-Year Period by Physical Activity Level, Women's Health Study, 1992-2007a

		Physical Activity, MET Hours per Week				
Group	No. of Women ^b	<7.5	7.5 to <21	≥21	P Value for Trend	P Value for Interactior
All women Analytical model ^c						
Í		0.15 (0.04)	0.12 (0.04)	0 [Reference]	<.001	
2		0.12 (0.04)	0.11 (0.04)	0 [Reference]	<.001	
Age, y						
<55	21 363	0.12 (0.08)	0.02 (0.08)	0 [Reference]	<.001	
55-64	9699	0.24 (0.06)	0.19 (0.06)	0 [Reference]	<.001	<.001
≥65	3017	-0.09 (0.07)	0.07 (0.07)	0 [Reference]	.13	
BMI						
<25.0	17 475	0.21 (0.04)	0.14 (0.04)	0 [Reference]	<.001 T	
25-29.9	10516	-0.04 (0.06)	-0.04 (0.06)	0 [Reference]	.56	<.001
≥30.0	6088	0.16 (0.14)	0.13 (0.16)	0 [Reference]	.50	
Smoking status	17 602	0 18 (0 05)	0 17 (0 05)	0 [Poforonco]	< 001 ¬	
	17.092	0.18 (0.03)	0.17 (0.00)			50
Former	12 169	0.06 (0.06)	0.05 (0.06)	U [Heterence]	.04	.53
Current	4186	0.15 (0.15)	0.12 (0.16)	0 [Reference]	.11 🔟	
Menopausal status Premenopausal	9821	0.19 (0.13)	0.08 (0.13)	0 [Reference]	.03 T	0.4
Postmenopausal	17 762	0.12 (0.04)	0.12 (0.04)	0 [Reference]	<.001	.04

Table 2. Mean (SD) Differences in Weight Over Any 3-Year Period by Physical Activity Level, Women's Health Study, 1992-2007a

Abbreviation: BMI, body mass index, which is calculated as weight in kilograms divided by height in meters squared; MET, metabolic equivalent.

^aThe mean (SD) difference in weight in kilograms is compared with the reference group. The mean (SD) interval during which weight change was assessed was 2.88 (0.41) years. See Table 1 footnote for definition of physical activity levels.

^bNumber of women represents those in the group at baseline.

^C Model 1 was adjusted for age, baseline weight, height, and time interval between weight assessments. Model 2 was additionally adjusted for race; educational attainment; smoking status; menopausal status; hormone replacement therapy use; hypertension; diabetes; alcohol consumption; and quintiles of intakes of total energy, saturated fat, and fruits and vegetables. Analyses according to subgroups of women all used estimates from model 2.

Table 2. Mean (SD) Differences in Weight Over Any 3-Year Period by Physical Activity Level, Women's Health Study, 1992-2007^a



What was the effect size? Those who exercised the least gained 0.15 kg (.33 pounds) more than those who exercised the most over 3 years. 95% confidence interval: 0.09 to 0.44 lbs per 3 years.

Classic example of a statistically significant effect that is not clinically significant.

A picture is worth...



A picture is worth...



The heaviest exercisers weigh less to start, <u>but the weight gain curves between the</u> <u>three baseline groups are almost identical.</u>

5. Exaggerated effect sizes

Presenting relative risks rather than absolute risks can make effects appear more impressive

Odds ratios (from logistic regression) can distort effects when the outcome is common



Example

Researchers studied the beverage purchases of teenagers at 4 stores; each store was measured at baseline and under 3 "caloric conditions" (signs posted outside the store):

- Absolute calories: "Did you know that a bottle of soda or fruit juice has about 250 calories?"
- Relative calories: "Did you know that a bottle of soda or fruit juice has about 10% of your daily calories?"
- Exercise equivalents: "Did you know that working off a bottle of soda or fruit juice takes about 50 minutes of running?"



The Results...

Condition	What percent of drinks purchased wer sugary beverages?		
Pre-intervention (no information)	93.3%		
Absolute calories	87.5%	What	
Relative calories	86.5%	conclusions would you draw?	
Exercise equivalent	86.0%		
Any caloric information (overall)	86.7%	Anticidence Anticidence Anticidence Anticidence	

What do you think is the best conclusion to draw from these data?

A. Exercise equivalents were more effective at reducing sugary beverage purchases than the other two signs.

B. All of the signs were similarly effective at reducing sugary beverage purchases.

C. B. None of the signs were effective at reducing sugary beverage purchases.

What do these data tell us?

Posting a sign did reduce sugary beverage purchase: About 6 out of 100 fewer teenagers purchased a sugary beverage. All three messages were similarly effective.



Headlines...

"'Exercise labels' beat out calorie counts in steering consumers away from junk food"

"Researchers: Exercise labels better at keeping teens away from junk food"

"Exercise labels more effective than calorie counts on soda cans"

"If '250 calorie' label doesn't stop you, '50 minute jog' label might"

The authors explaining their results in a university news video:

"The results are really encouraging. We found that providing any information (via the three signs) relative to none, **reduced the likelihood that they would buy a sugary beverage by 40 per cent**.

"Of those three signs, the one that was most effective was the physical activity equivalent.

"We found that when that sign was posted, the likelihood that they would buy a sugary beverage reduced by around 50 per cent."



Huh?...

What percent of drinks purchased were sugary beverages?

Condition

(overall)

Pre-intervention (no 93.3% information) How is this a 50% Absolute calories 87.5% reduction in risk? **Relative calories** 86.5% 86.0% **Exercise** equivalent Any caloric information



What went wrong? The authors misinterpreted odds ratios.

Condition	Unadjusted Percentage of sugary drinks	Adjusted <mark>Odds rat</mark>	<u>io</u>	
Pre-intervention (no information)	93.3	1.00 (ref)	This does r a "50% di likelihood.	not mean rop in
Absolute calories	87.5	0.62	/	
Relative calories	86.5	0.59	This is not	a "40%
Exercise equivalent	86.0	0.51	drop in lil	elihood."
Any caloric information	86.7	0.56		

Odds ratio vs. risk ratio...

Risk ratio: $\frac{86\%}{93\%} = 0.92$

Corresponding Odds ratio:

$$\frac{\frac{86\%}{14\%}}{\frac{93\%}{7\%}} = 0.46$$

We cannot interpret the odds ratio as indicating a "54% drop in likelihood"! There is a 54% drop in odds, but only an 8% drop in likelihood (risk)!



6. Wrong comparisons

Authors often steal focus from the main comparison by throwing in pvalues from meaningless comparisons.

What do all these statements have in common?

"The effect was significant in the treatment group, but not significant in the control group."

"Intervention 1 caused a significant change but intervention 2 did not."

"The effect was significant in subgroup A but not in subgroup B."

These are all the wrong comparisons!

- "The effect was significant in the treatment group, but not significant in the control group."
- Right comparison: treatment vs. control
- "Intervention 1 caused a significant change from baseline but intervention 2 did not."

• Right comparison: intervention 1 vs. intervention 2

"The effect was significant in subgroup A but not in subgroup B."

• Right comparison: subgroup A vs. subgroup B

The focus should be on betweengroup not within-group comparisons.

Exercise labels study again...

Only exercise equivalent labels were significantly different than pre-intervention; odds ratios and 95% confidence intervals:

Absolute calories: OR=0.62 (0.37, 1.04)

```
Relative calories: OR=0.59 (0.34, 1.02)
```

```
Exercise equivalent: OR=0.51 (0.31, 0.85)*
```

Erroneous Implication: exercise equivalents "beat" absolute and relative calories.

No! The three interventions were statistically indistinguishable.

• Relevant comparison: absolute calories vs. relative calories vs. exercise equivalents



7. Failure to account for corrobservations



Correlated observations when pairs or clusters of observations are related and thus are more similar to each other than to other observations in the dataset. Correlated observations require special statistical tests that account for the correlation.

Examples:

The same person measured over time (repeated measures).

Two knees from the same person.

Two hands from the same person.

Related individuals (e.g., twins).

Individuals from the same cluster in a cluster-randomized trial.

Leg strength and sprinting meta-analysis again...

The meta-analysis included 15 studies, but there are 85 datapoints included in the correlation analysis.



Seitz, L.B., Reyes, A., Tran, T.T. *et al.* Increases in Lower-Body Strength Transfer Positively to Sprint Performance: A Systematic Review with Meta-Analysis. *Sports Med* **44**, 1693– 1702 (2014).

By, ignoring the within-study correlation, the authors have...?

A. Underestimated the p-value.

B. Overestimated the p-value.

C. Correctly estimated the p-value.





Seitz, L.B., Reyes, A., Tran, T.T. *et al.* Increases in Lower-Body Strength Transfer Positively to Sprint Performance: A Systematic Review with Meta-Analysis. *Sports Med* **44**, 1693– 1702 (2014).

8. Residual or unmeasured confounding



"We adjusted for confounders" often doesn't cut it.

Higher vitamin D blood levels linked to cardiorespiratory fitness: Study

By Stephen Daniells C 27-Nov-2018 - Last updated on 27-Nov-2018 at 16:57 GMT











High Vitamin D Levels Are Linked to Better Exercise Capacity

The sunshine vitamin is important for bone and brain health, but new research suggests it can also make the lungs and heart more efficient, as well.

By Amanda MacMillan November 01, 2018

Media Coverage

"The study notes that vitamin D could potentially affect cardiorespiratory fitness in several ways. For starters, the nutrient has been shown to boost the production of muscle protein and aid in calcium and phosphorus transport on a cellular level. It may also affect the body's makeup of fasttwitch muscle fibers, 'suggesting that vitamin D may improve aerobic fitness,' the authors wrote."

https://www.health.com/fitness/vitamin-d-improves-fitness-levels

The Study

- •Representative sample of the US population: data from the National Health and Nutrition Survey (NHANES).
- Cross-sectional survey data
- •About 2000 participants between the ages of 20 and 49 years
- •Examined association between vitamin D levels and VO₂ max

Marawan A, Kurbanova N, Qayyum R. Association between serum vitamin D levels and cardiorespiratory fitness in the adult population of the USA. *European Journal of Preventive Cardiology*. 2019;26(7):750-755. doi:10.1177/2047487318807279



"Linear regression models were adjusted for age, sex, race, BMI, hypertension, diabetes mellitus, smoking, Creactive protein, total cholesterol, hemoglobin, and renal function as estimated by the GFR."

Reaching for biological explanations...

"Several lines of evidence support the biological plausibility of a potential role of vitamin D in CRF [cardiorespiratory fitness]. About 3% of all genes are directly or indirectly affected by vitamin D levels and vitamin D receptors are expressed in a large variety of cells, including myocytes.^{5,15} Vitamin D may affect myocytes by increasing muscle protein synthesis and calcium and phosphorus transport in energy production.^{16,17} In addition, vitamin D may increase the relative number of one type of fast-twitch muscle fibers (IIa) and decrease another type of fasttwitch muscle fibers (IIb), suggesting that vitamin D may improve aerobic fitness.¹⁸ In addition to its effect on muscles, animal studies suggest that vitamin D may have a role in heart structure and function.^{5,15,19} Mitochondria from chick cardiomyocytes produced less energy when vitamin D levels were low.¹⁶ In another study, vitamin D deficiency in rodents was associated with decreased myocardial contractility and cardiac output and increased heart rate, changes commonly seen in failing hearts.²⁰ Vitamin D deficiency has been reported to be associated with decreased myofibrillar area and the increased deposition of myocardial collagen in the extracellular space.²¹"





Factors that affect vitamin D levels

- Exposure to sunlight
- •Diet
- Supplements
- •Obesity
- Skin Pigment
- •Age
- Certain diseases
- •Genetics
- Season of measurement

Factors that affect VO₂ max

Physical Activity

Body composition

Sex Age Genetics

They buried the lead...

Buried in the discussion: "The results were not adjusted for vitamin D intake or physical activity, both of which may have an effect on the observed association."



9. Misinterpretations of null effects

Lack of statistical significance is not proof of no effect.

NSAIDs study again...

<u>Aim</u>: The purpose of this study was to identify the clinical effectiveness of **oral versus topical NSAIDs** in the treatment of greater trochanteric pain syndrome.

<u>Methods</u>: A retrospective chart review of **25 patients** diagnosed with greater trochanteric pain syndrome were categorized into two groups: those who received **oral etodolac 400 milligrams** twice daily versus **topical diclofenac 3%** one gram two to three times daily for two weeks.

Outcome: Pain scores using the Lack of a statistically significant difference is not proof of no effect!

<u>Results</u>: At **two weeks**, there was a statistically significant improvement in pain in both the oral and topical NSAID groups, with no statistically significant difference between the groups (p=0.77).

Similarly, at **six weeks**, there was a statistically significant improvement in pain in both the oral and topical NSAID groups, with no statistically significant difference between the groups (p=0.59).

Conclusion: Based on this study, the <mark>use of topical NSAIDs is non-inferior to oral NSAIDs in the treatment of GTPS.</mark>

10. Spurious correlations/ov

When sample size is small, a single data point (or a few datapoints) can have undue influence on a correlation coefficient or model.

o

0



Systematic Review with Meta-Analysis. *Sports Med* **44**, 1693–1702 (2014).

Plot showing the correlation between DNA methylation of the glucocorticoid receptor gene (*NR3C1*) and cortisol reactivity, r = 0.41; P < .05



Barry M. Lester, Elisabeth Conradt, Linda L. LaGasse, Edward Z. Tronick, James F. Padbury, Carmen J. Marsit. Epigenetic Programming by Maternal Behavior in the Human Infant. *Pediatrics*, 2018; e20171890 DOI: <u>10.1542/peds.2017-1890</u>



Further resources

How to be a Statistical Detective webinar:

https://www.youtube.com/watch?v=JG_gCIGFaQI

Medical Statistics Certificate Program: <u>https://online.stanford.edu/programs/stanford-medical-</u> <u>statistics-certificate</u>

Statistically Speaking column: https://onlinelibrary.wiley.com/doi/toc/10.1016/(ISSN)1934-1563.statistics

Relevant PM&R columns:

1. Simple math and data errors

Avoid Careless Errors: Know your data How to be a Statistical Detective Ten Common Statistical Errors from All Phases of Research, and Their Fixes

2. Study design mismatched to statistical question

Ten Common Statistical Errors from All Phases of Research, and Their Fixes

3. Chance findings

The Problem of Multiple Testing

- 4. Clinically irrelevant effect sizes Clinical Versus Statistical Significance
- 5. Exaggerated effect sizes

Understanding Odds Ratios Communicating Risks Clearly: Absolute Risk and Number Needed to Treat

Relevant PM&R columns:

6. Wrong comparisons

Misleading Comparisons: The Fallacy of Comparing Statistical Significance Ten Common Statistical Errors from All Phases of Research, and Their Fixes

7. Failure to account for correlated observations

The Importance of Accounting for Correlated Observations Ten Common Statistical Errors from All Phases of Research, and Their Fixes

- 8. Misinterpretations of null effects Interpreting "Null" Results
- 9. Residual/unmeasured confounding The Limitations of Statistical Adjustment
- 10. Spurious correlations/overfitting The Value of Scatter Plots How to be a Statistical Detective

Further resources

How to be a Statistical Detective webinar:

https://www.youtube.com/watch?v=JG_gCIGFaQI

Medical Statistics Certificate Program: <u>https://online.stanford.edu/programs/stanford-medical-</u> <u>statistics-certificate</u>

Statistically Speaking column: https://onlinelibrary.wiley.com/doi/toc/10.1016/(ISSN)1934-1563.statistics