Bayes' Theorem, Psychiatric Diagnosis, and Neuropsychiatry

Joanne Alonso Byars, MD

November 5, 2021

Step 1 in patient care: determine the correct diagnosis

- Everything else follows from this
- How can you treat effectively if you don't know what you're treating?
  - CBT won't improve dementia
  - Donepezil won't treat depression
  - Antibiotics won't treat Alzheimer disease, but will treat neurosyphilis

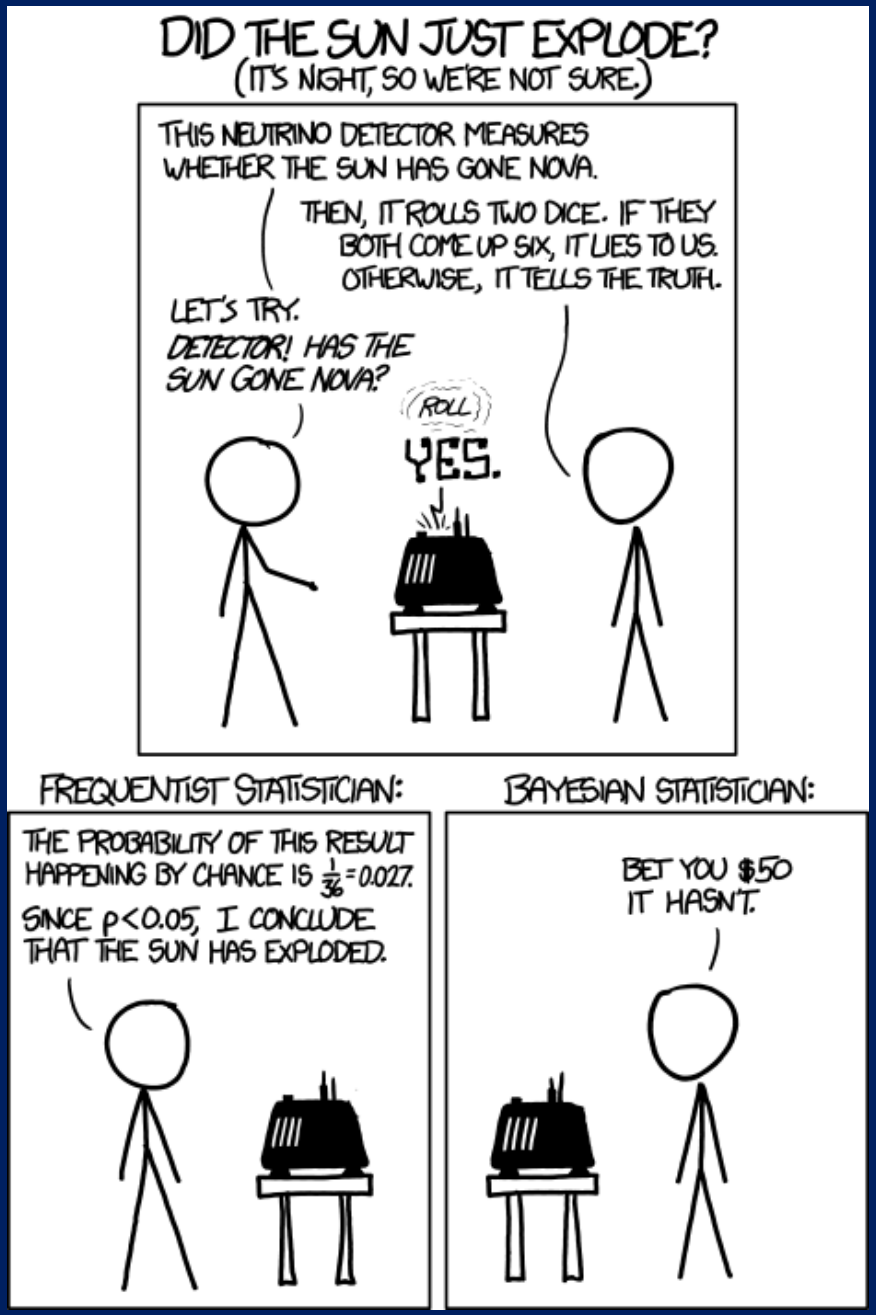
How to determine the correct diagnosis:

- Thorough history
  - Collateral informants if at all possible
- Know the diagnostic criteria AND possible clinical manifestations of different disorders
  - Not every possible clinical feature is in the DSM 5
- Refer for additional testing / imaging / medical workup when needed
- Know what things are common and what things are rare
  - And what's common and rare in the specific population the patient belongs to

Bayesian statistics

- Some condition
- Some observation/test that gives us information about whether the condition is present or absent
- Hypothesis: if the observation is positive, the condition is present
- The probability that this hypothesis is true depends on both:
  - The likelihood that, when this condition is present, the observation is also present
  - The underlying rate of the condition

Frequentists vs. Bayesians



https://xkcd.com/1132/

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- The probability that this hypothesis is true depends on both:
  - The likelihood that, when this condition is present, the observation is also present
  - The underlying rate of the condition
- What if we have two competing hypotheses? How do we decide which one is true?

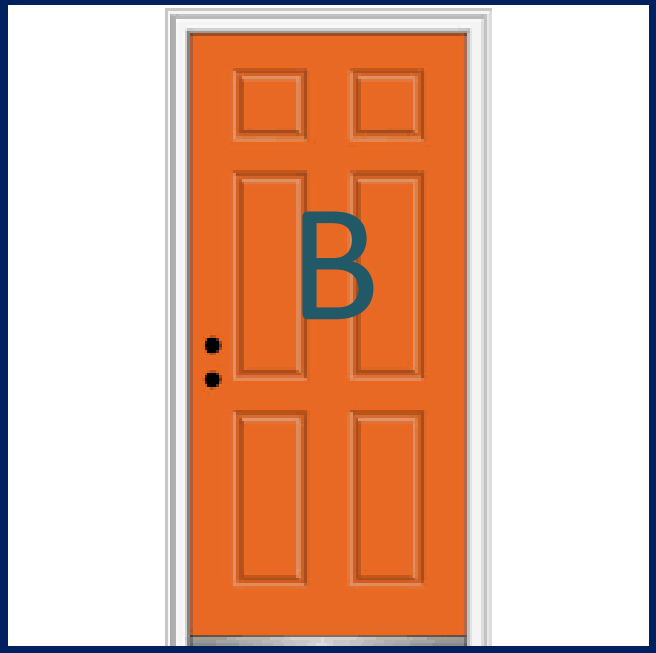
Pretest probability: general

- Pretest probability: knowing nothing but the overall frequency of a particular condition, how likely is it that the condition is present?
  - You haven't done any investigation yet
  - No data specific to the particular case at hand, just overall frequency of the condition

Astronauts and elementary school teachers

- Astronauts: 89% male
- Elementary school teachers: 11% male

There is an astronaut behind this door

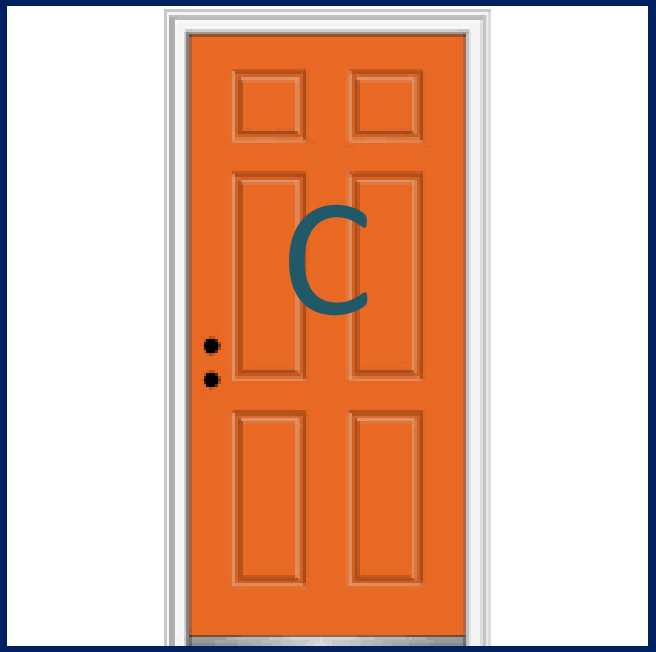


There is an elementary school teacher behind this door

Which door is more likely to have a man behind it: A or B?

Astronauts and elementary school teachers

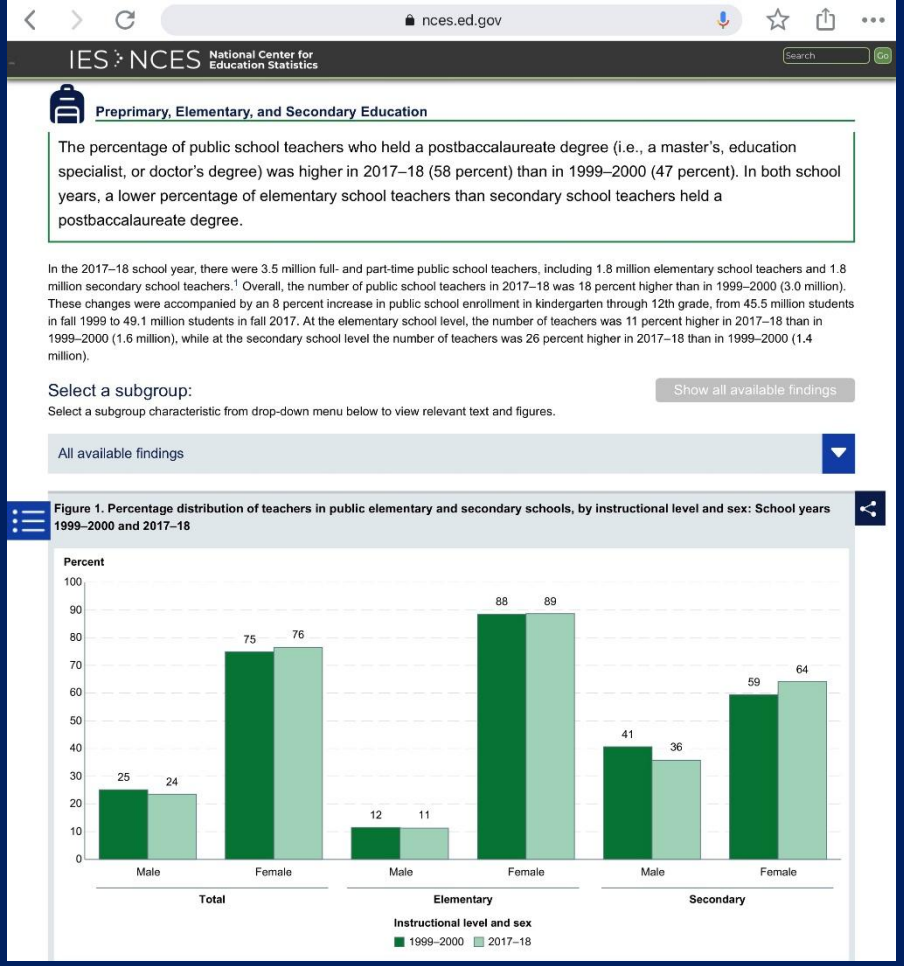
- Astronauts: 89% male
- Elementary school teachers: 11% male



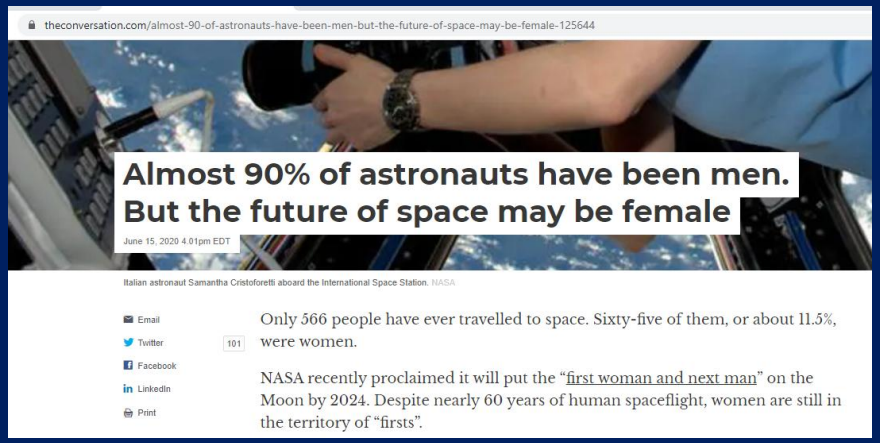
There is a man behind this door

Who is more likely to be behind this door:
an astronaut or an elementary school teacher?

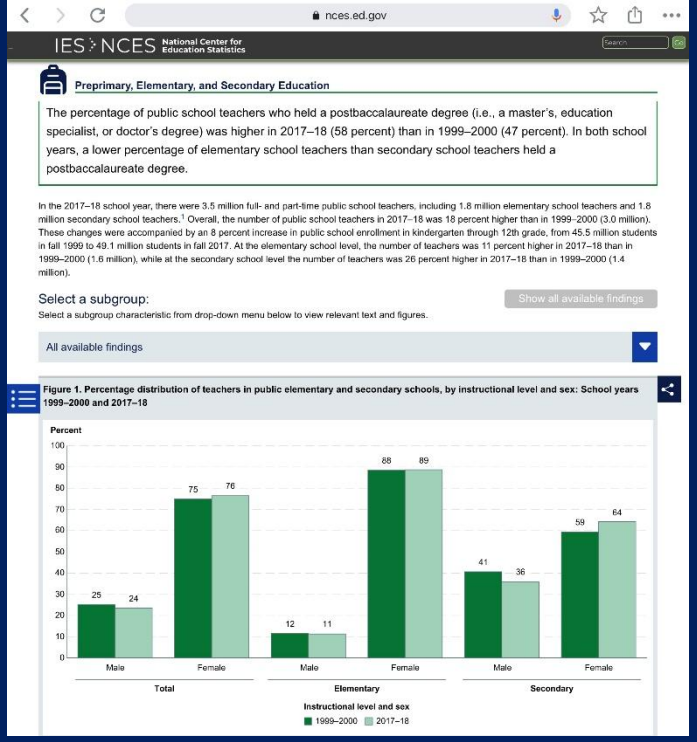
- What else do we need to know?



- 1.8 million elementary school teachers
- 11% of these are men
- So there are 198,000 male elementary schoolteachers

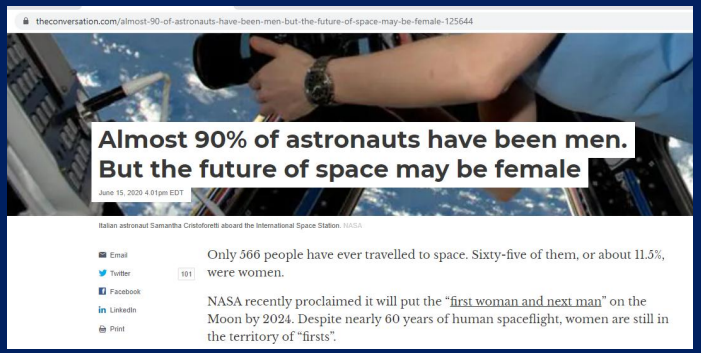


- 566 astronauts
- 89% of these are men
- So there are 501 male astronauts



Person X is a man

- How much more likely is it that he's an elementary school teacher than an astronaut?
  - 198,000 / 501 = 395
  - He's 395 times more likely to be an elementary school teacher than an astronaut

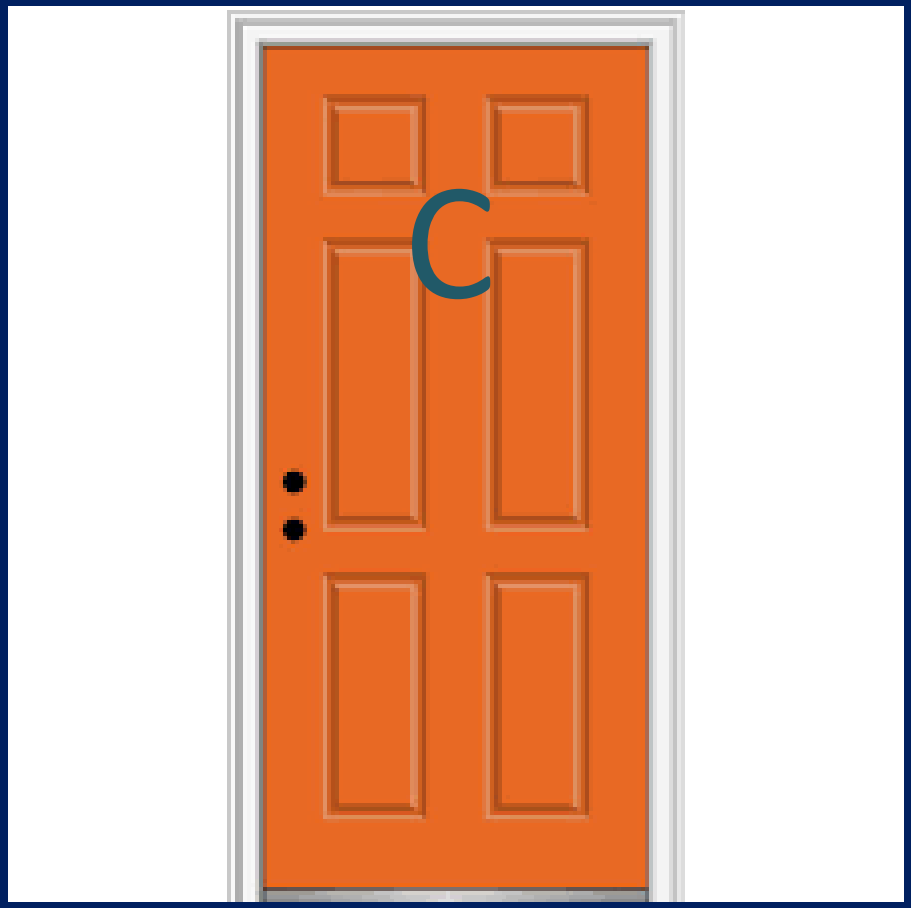


Person Z is a woman

- How much more likely is it that she's an elementary school teacher than an astronaut?
  - (1,8,000*.89) / (566*.11) = 21,935
  - She's 21,935 times more likely to be an elementary school teacher than an astronaut

Astronauts and elementary school teachers

- Astronauts: 89% male
- Elementary school teachers: 11% male



There's 3180x more elementary school teachers than astronauts overall, regardless of gender

There is a man who is an elementary school teacher behind this door

Pretest probability: clinical

- Pretest probability: knowing nothing but the overall prevalence of a particular disease in a specific population, how likely is it that the patient has the disease?
  - You haven't done any evaluation or workup or testing yet
  - No clinical info, just epidemiology

“If you hear hoofbeats, think horses not zebras”

- But: are you at a horse farm in Ocala, or on the Serengeti?
- Underlying prevalence of the condition in the relevant population is key to determining whether the patient is likely to have the condition or not

Pretest probability

- For example:
  - A 30yo woman is admitted to the inpatient psychiatric unit on an involuntary psychiatric hold.
    - What is the pretest probability the patient has schizophrenia?
  - A 30yo woman is admitted to L&D in active labor
    - What is the pretest probability the patient has schizophrenia?

Given that a patient has a new-onset psychosis:

- What is the probability that they have schizophrenia?
- What is the probability that they have dementia?
- Is the patient 18 or 80?
- Age of onset is key

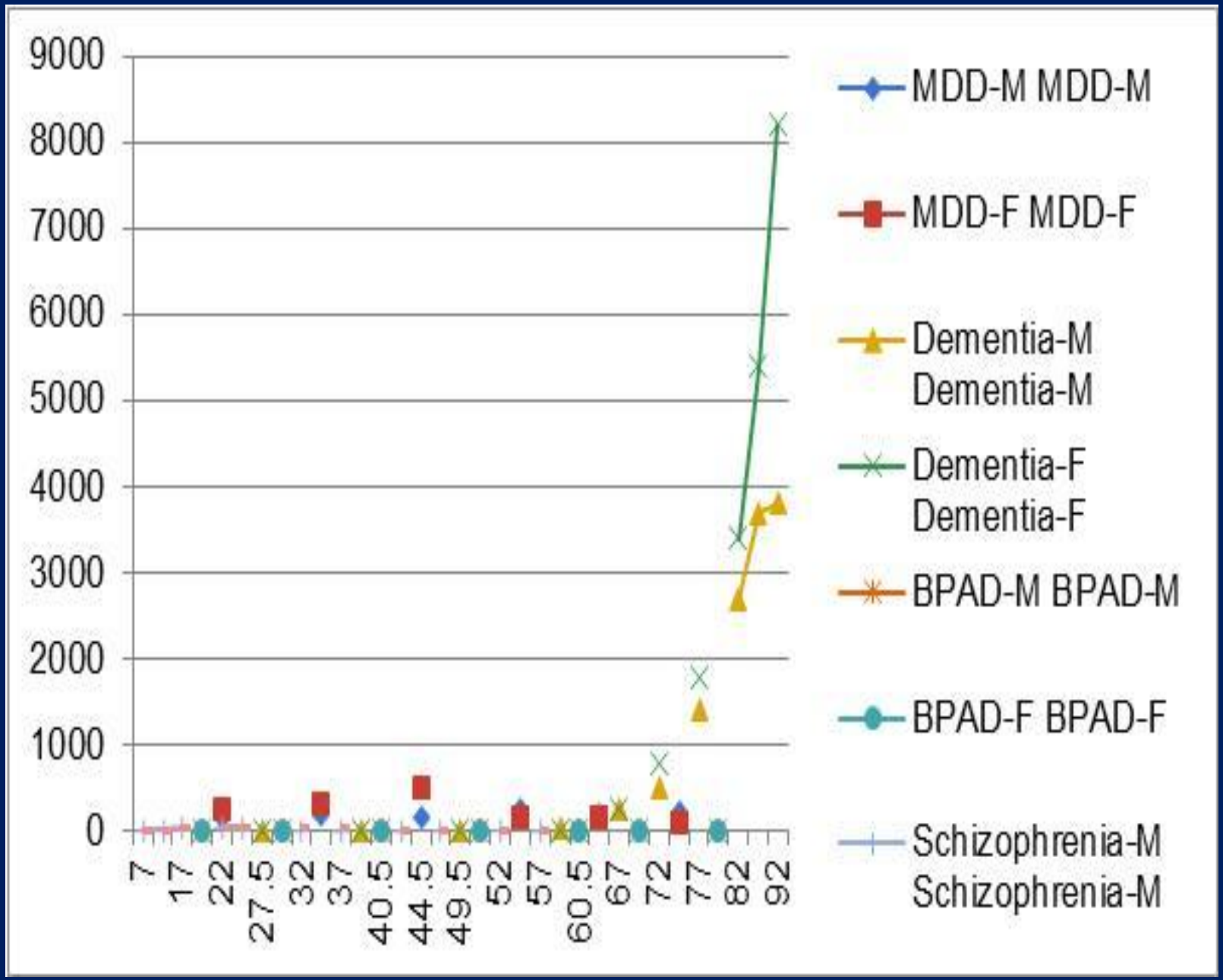
Common things are common, rare things are rare

- Unusual presentation of a common illness (AD) is more likely than a classic presentation of something rare (late-onset schizophrenia)
- But how do we know what's common and what's rare?

Case example 1

- A 75yo man has new-onset hallucinations and delusions
- Medical workup is negative for delirium
- Which diagnosis is more likely?
  - Schizophrenia
  - Dementia

- Observation: patient has hallucinations and delusions
  - In patients with schizophrenia, this observation is almost always true
  - In patients with dementia, this observation is only sometimes true
- But, if the patient is 75:
  - The pretest probability of having new-onset schizophrenia is extremely low
  - The pretest probability of having new-onset dementia is quite high
- Because of this, the most likely diagnosis in this patient is still dementia—regardless of whether the patient has hallucinations and delusions



Rates per 100,000 by age

- In 100,000 75-year-olds:
  - 2.5 will have new-onset schizophrenia
    - If we assume everyone with schizophrenia has hallucinations and delusions:
      - Then 2.5 75-year-olds will have new-onset schizophrenia with hallucinations and delusions
  - 1600 will have new-onset dementia
    - 10%-50% of people with dementia have hallucinations and delusions
      - Then 160-800 75-year-olds will have new-onset dementia with hallucinations and delusions
- Thus, based on pretest probabilities, the patient is 64-320 times more likely patient has dementia

- Extraordinary claims require extraordinary evidence
  - “I saw a cat in my backyard”
  - “I saw an elephant in my backyard”
  - “I saw a unicorn in my backyard”

You’re going to need a LOT of evidence to convince me this isn’t just a horse with a fake horn stuck on its head

- But sometimes people do really have rare/less common diseases!
  - To get that extraordinary evidence to support a rare disease, you need to do additional testing, rule out other more common causes, etc

- New-onset schizophrenia in a 75yo would be so extraordinarily rare that you have to have pretty definitive evidence that more common causes (like dementia) aren't present
  - "When you have eliminated the impossible, whatever remains, however improbable, must be the truth"
  - But, you have to truly eliminate the more likely things first

- We need more evidence to refute the dementia hypothesis
  - Normal neuropsychological testing (even taking into account premorbid functioning)
  - Normal brain imaging
  - Normal medical workup
  - Normal dementia biomarkers

Out of 100,000 75 year olds

- 1600 will have new-onset dementia
  - Of those, 0% will have normal cognitive testing AND normal imaging AND negative workup for dementia biomarkers/cognitively-impairing medical conditions
- So 2.5 out of 100,000 still isn't real likely, but it's more likely than 0 out of 100,000

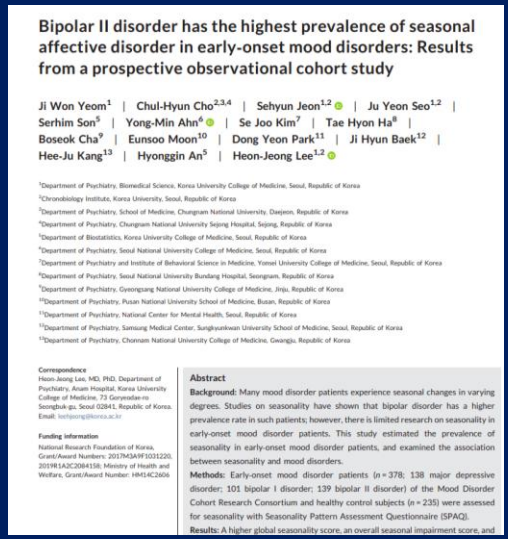
Case example 2

- A 25-year-old woman has depression with seasonal variation
  - You recall hearing that seasonal variation is more common in bipolar disorder than MDD
    - 32% of BPAD II has seasonal variation
    - 10% of MDD has seasonal variation
  - KNOWING NOTHING ELSE AT THIS POINT: what is the most likely diagnosis?

TABLE 2 Comparison of seasonality assessments among the four groups before and after excluding the summer-type

Before excluding summer-type	MDD	BD I	BD II	Control	*p* value	Post hoc
Mean GSS (±*SD*)[a]	4.98 ± 4.79	5.40 ± 4.97	6.88 ± 5.86	3.98 ± 3.96	<.001***	Control, MDD < BD II
Mean overall seasonal impairment score (±*SD*)[a]	1.32 ± 1.31	1.24 ± 1.16	1.72 ± 1.41	0.85 ± 1.07	<.001***	Control < mood disorder BD I < BD II
SAD (%)[b]	14 (10.1)	10 (9.9)	32 (23.0)	15 (6.4)	<.001***	
S-SAD and SAD (%)[b]	30 (21.7)	21 (20.8)	45 (32.4)	29 (12.3)	<.001***	

Specific data taken from this not-very-good paper, though has been shown in some other studies too



Bipolar II disorder has the highest prevalence of seasonal affective disorder in early-onset mood disorders: Results from a prospective observational cohort study

Ji Won Yeom[1] | Chul-Hyun Cho[2,3,4] | Sehyun Jeon[1,2] | Ju Yeon Seo[1,2] | Serhim Son[5] | Yong-Min Ahn[6] | Se Joo Kim[7] | Tae Hyon Ha[8] | Boseok Cha[9] | Eunsoo Moon[10] | Dong Yeon Park[11] | Ji Hyun Baek[12] | Hee-Ju Kang[13] | Hyonggin An[5] | Heon-Jeong Lee[1,2]

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Abstract

Background: Many mood disorder patients experience seasonal changes in varying degrees. Studies on seasonality have shown that bipolar disorder has a higher prevalence rate in such patients; however, there is limited research on seasonality in early-onset mood disorder patients. This study estimated the prevalence of seasonality in early-onset mood disorder patients, and examined the association between seasonality and mood disorders.

Methods: Early-onset mood disorder patients ($n = 378$; 138 major depressive disorder; 101 bipolar I disorder; 139 bipolar II disorder) of the Mood Disorder Cohort Research Consortium and healthy control subjects ($n = 235$) were assessed for seasonality with Seasonality Pattern Assessment Questionnaire (SPAQ).

Results: A higher global seasonality score, an overall seasonal impairment score, and

Population prevalence

- MDD in women: lifetime prevalence 20%
  - A little higher than men
- BPAD in women: lifetime prevalence 1%
  - Same as men

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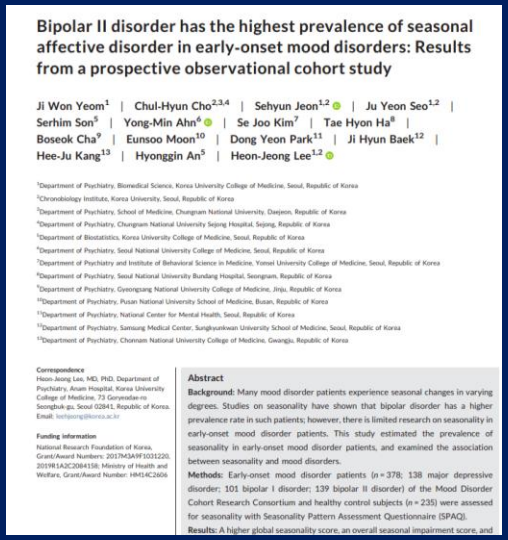

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Results: A higher global seasonality score, an overall seasonal impairment score, and

- 10,000 women
  - 2000 will have MDD
    - 10% of these will have seasonal variation
    - Thus 200 will have MDD with seasonal variation
  - 100 will have BPAD
    - 32% will have seasonal variation
    - Thus 32 will have BPAD with seasonal variation
- 200 / 32 = 6.15
- Thus, if a patient has a mood disorder WITH seasonal variation, it's 6 times more likely to be MDD than BPAD
- If a patient has a mood disorder WITHOUT seasonal variation, it's 26 times more likely to be MDD than BPAD
  - (2000 x 0.9) / (100 x 0.68) = 26.47
- MDD is just overall more common, so wins either way

Moral of the story:

- You can't just look at whether a particular clinical feature (like seasonal variation in mood disorders) is more common in condition A vs condition B
- You ALSO have to look at the overall prevalence of condition A and condition B
- The feature of being male is more common in astronauts than in elementary school teachers
  - But there are over 3,000 more elementary school teachers than astronauts
  - If you meet a man, he's WAY more likely to be an elementary school teacher than an astronaut
- If you see a patient with a mood disorder with seasonal variation, they're several times more likely to have MDD than bipolar disorder
- If you see a 75yo with psychosis, they're WAY more likely to have dementia than schizophrenia

Bayes' theorem can also help us separate good science from bad

- Someone has published a study
- Assume we believe they collected, analyzed, and reported their data properly
- How do we decide if we believe their conclusion actually represents reality, vs being due to chance, unmeasured confounders, etc?
- HINT: it's NOT a p-value!!!
  - Remember, the p-value for the sun exploding was <0.05

Knowing nothing else about the following peer-reviewed published studies except their conclusions, which study's results are more likely to be correct?

- Study A:
  - High social support is associated with less depression and anxiety during the COVID-19 pandemic
- Study B:
  - Repeatedly standing in two "power poses" with your limbs spread out for 1 minute each is an effective way to overcome the harms posed by discrimination and poverty

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ELSEVIER

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Original article

The Effect of Social Support on Mental Health in Chinese Adolescents During the Outbreak of COVID-19

Meng Qi, M.S. [a,b,1], Shuang-Jiang Zhou, M.S. [b,1], Zhao-Chang Guo [c], [illegible] [b], Hong-Jie Min [b], Xiao-Min Li, M.S. [a], and Jing-Xu Chen, M.D. [b,*]

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Article history: Received April 21, 2020; Accepted July 1, 2020
Keywords: Adolescent; Depression; Anxiety; COVID-19; Social support; China

ABSTRACT

Purpose: The coronavirus disease 2019 (COVID-19) outbreak impacts physical and mental health. The purpose of this study was to explore the association between the levels of social support and mental health among Chinese adolescents during the outbreak.

Methods: A total of 7,202 adolescents aged 14–18 years completed online questionnaires from Feb. to 15, 2020, in China. Researchers assessed the association between depression symptoms (Patient Health Questionnaire-9), anxiety symptoms (Chinese version of the 7-item Generalized Anxiety Disorder scale), and social support (Social Support Rating Scale).

Results: COVID-19 exposure was associated with higher prevalence of depression symptoms (odds ratio [OR] = 1.38, 95% confidence interval [CI: 1.16–1.66]) and anxiety symptoms (OR = 1.26, 95% CI: 1.04–1.52). Only 24.6% of adolescents reported high levels of social support. Most adolescents (70%) reported moderate levels of support, and 5.4% reported low support. Low support was associated with higher prevalence of depression (OR = 4.24, 95% CI: 3.38–5.33) and anxiety symptoms (OR = 3.18, 95% CI: 2.58–3.98) after controlling for gender, grade, living situation, and COVID-19 exposure; similarly, medium support was associated with higher prevalence of depression (OR = 2.79, 95% CI: 2.48–3.15) and anxiety (OR = 2.19, 95% CI: 1.94–2.48) symptoms.

Conclusions: This study indicates there is a higher prevalence of mental health problems among adolescents with medium and low levels of social support in China during the outbreak of COVID-19.

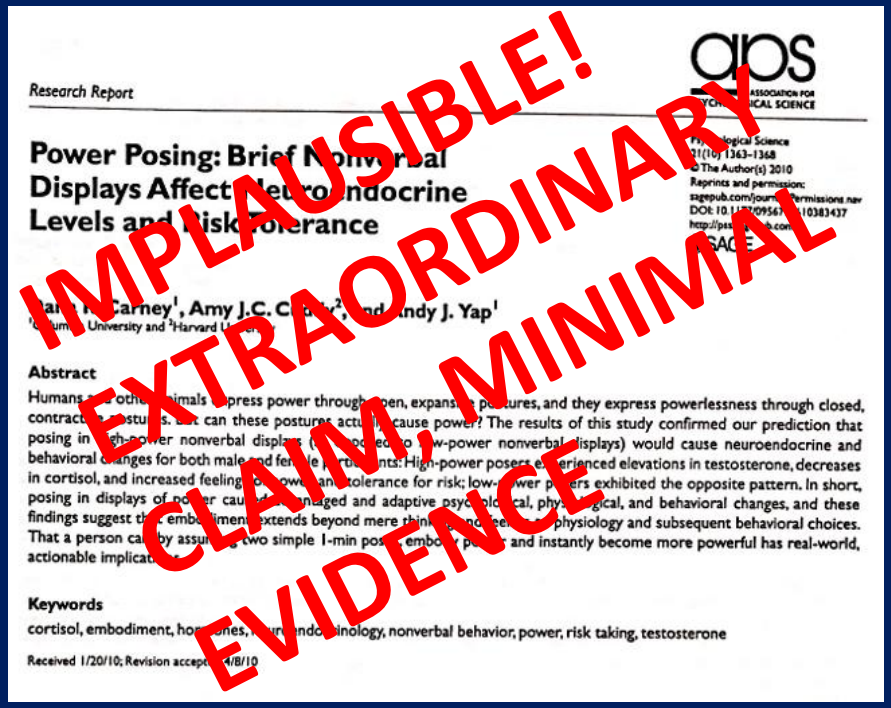
IMPLICATIONS AND CONTRIBUTION

There is a higher prevalence of mental health problems among adolescents with medium and low levels of social support in China during the coronavirus disease 2019 outbreak.

EXTREMELY PLAUSIBLE!

"In the present study, we found a negative correlation between the levels of social support and the severity of depression and anxiety... These findings indicate that social support is a significant important protective factor for mental health among adolescents."

(Study actually examined cortisol and testosterone levels, not long-term effects on general health, wellbeing, SES, or occupationall attainment)



Research Report

aps ASSOCIATION FOR PSYCHOLOGICAL SCIENCE

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Power Posing: Brief Nonverbal Displays Affect Neuroendocrine Levels and Risk Tolerance

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Abstract

Humans and other animals express power through open, expansive postures, and they express powerlessness through closed, contracted postures. But can these postures actually cause power? The results of this study confirmed our prediction that posing in high-power nonverbal displays (relative to low-power nonverbal displays) would cause neuroendocrine and behavioral changes for both male and female participants: High-power posers experienced elevations in testosterone, decreases in cortisol, and increased feelings of power and tolerance for risk; low-power posers exhibited the opposite pattern. In short, posing in displays of power caused hormonal, psychological, physiological, and behavioral changes, and these findings suggest that embodiment extends beyond mere thinking to influence physiology and subsequent behavioral choices. That a person can, by assuming two simple 1-min poses, embody power and instantly become more powerful has real-world, actionable implications.

Keywords

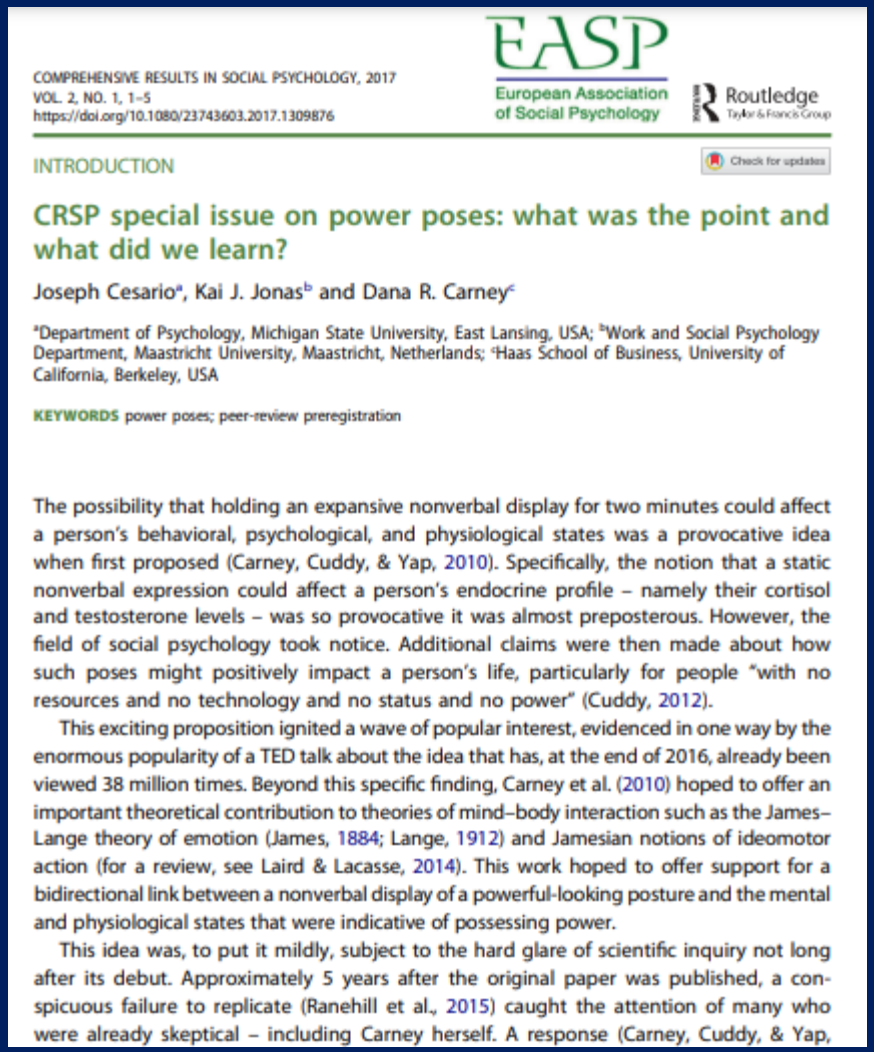
cortisol, embodiment, hormones, neuroendocrinology, nonverbal behavior, power, risk taking, testosterone

Received 1/20/10; Revision accepted 4/8/10

IMPLAUSIBLE! EXTRAORDINARY CLAIM, MINIMAL EVIDENCE

"By simply changing physical posture, an individual prepares his or her mental and physiological systems to endure difficult and stressful situations, and perhaps to actually improve confidence and performance in situations such as interviewing for jobs, speaking in public, disagreeing with a boss, or taking potentially profitable risks. These minimal postural changes and their outcomes potentially could improve a person's general health and well-being. This potential benefit is particularly important when considering people who are or who feel chronically powerless because of lack of resources, low hierarchical rank in an organization, or membership in a low-power social group."

“Power pose” study failed to replicate (unsurprisingly)



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EASP European Association of Social Psychology

Routledge Taylor & Francis Group

INTRODUCTION

Check for updates

CRSP special issue on power poses: what was the point and what did we learn?

Joseph Cesario[a], Kai J. Jonas[b] and Dana R. Carney[c]

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KEYWORDS power poses; peer-review preregistration

The possibility that holding an expansive nonverbal display for two minutes could affect a person's behavioral, psychological, and physiological states was a provocative idea when first proposed (Carney, Cuddy, & Yap, 2010). Specifically, the notion that a static nonverbal expression could affect a person's endocrine profile – namely their cortisol and testosterone levels – was so provocative it was almost preposterous. However, the field of social psychology took notice. Additional claims were then made about how such poses might positively impact a person's life, particularly for people "with no resources and no technology and no status and no power" (Cuddy, 2012).

This exciting proposition ignited a wave of popular interest, evidenced in one way by the enormous popularity of a TED talk about the idea that has, at the end of 2016, already been viewed 38 million times. Beyond this specific finding, Carney et al. (2010) hoped to offer an important theoretical contribution to theories of mind–body interaction such as the James–Lange theory of emotion (James, 1884; Lange, 1912) and Jamesian notions of ideomotor action (for a review, see Laird & Lacasse, 2014). This work hoped to offer support for a bidirectional link between a nonverbal display of a powerful-looking posture and the mental and physiological states that were indicative of possessing power.

This idea was, to put it mildly, subject to the hard glare of scientific inquiry not long after its debut. Approximately 5 years after the original paper was published, a conspicuous failure to replicate (Ranehill et al., 2015) caught the attention of many who were already skeptical – including Carney herself. A response (Carney, Cuddy, & Yap,

- Additional studies did not replicate even the modest actual findings on cortisol and testosterone
- Of course no evidence exists to support the grandiose claims that power poses effectively remedy longstanding inequality
- MAYBE a small effect on self-perceived power, but only among people who had seen the TED talk
  - ie, it’s a placebo effect

Pretest probability for the following hypotheses:

- Social support protects against depression and anxiety

AND

- This protective benefit occurs during stressful situations like the COVID-19 pandemic

Pretest probability for the following hypotheses:

- Standing with your hands on your hips and your feet apart for 2 minutes increases your testosterone level and decreases your cortisol level, and makes you feel more confident

AND

- These physiologic and emotional changes cause you to behave differently in real-world stressful situations

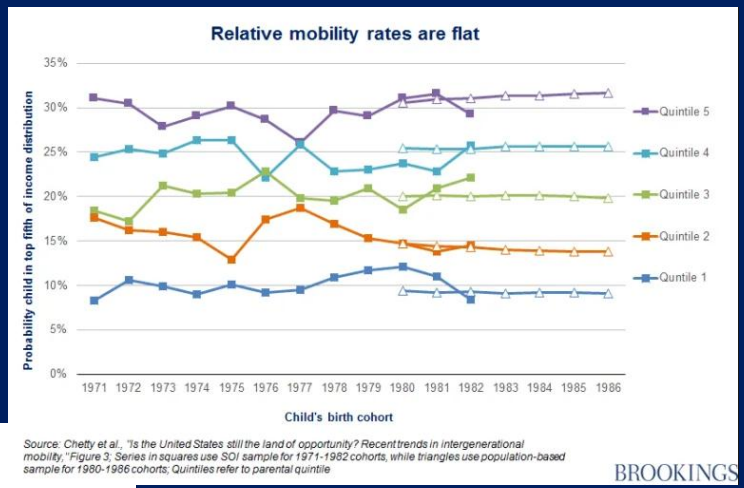
AND

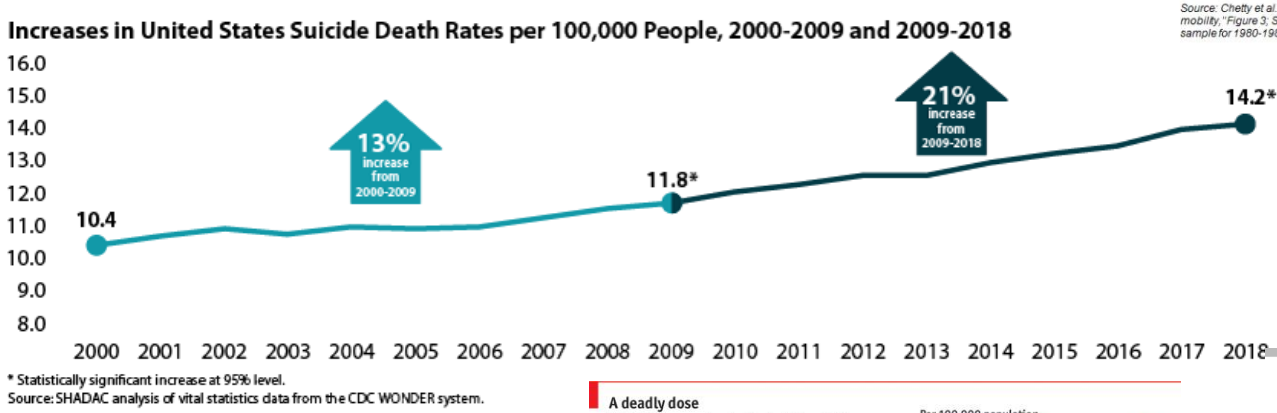
- This change in behavior directly improves your economic status, social status, and health

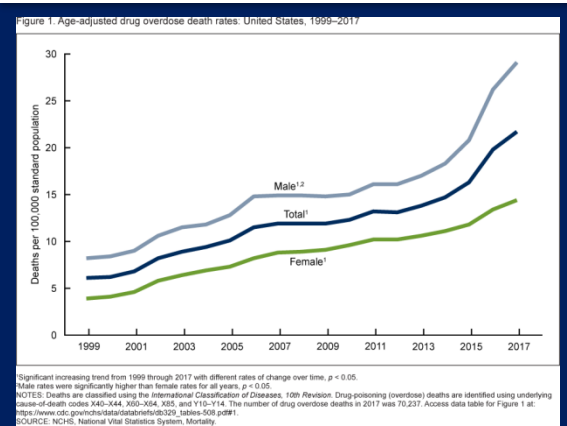
Pretest probability for the following hypotheses:

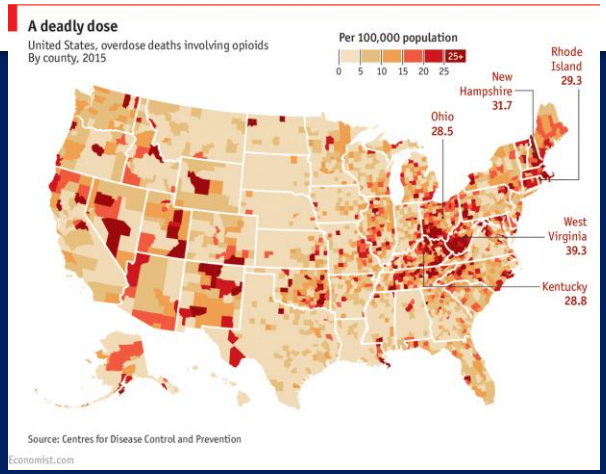
AND

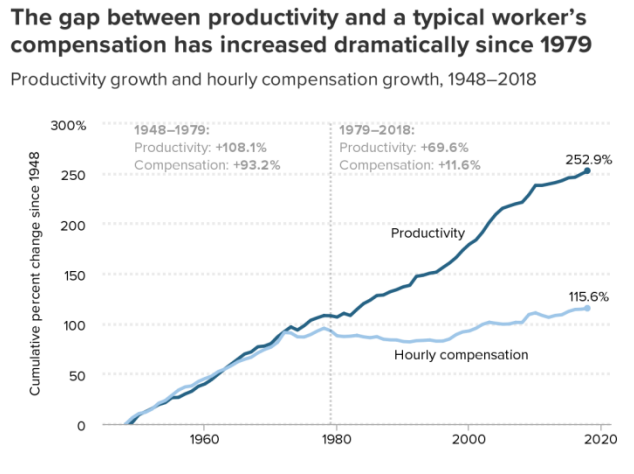
- The magnitude of these improvements is sufficient to ameliorate the harmful effects of structural sources of inequality







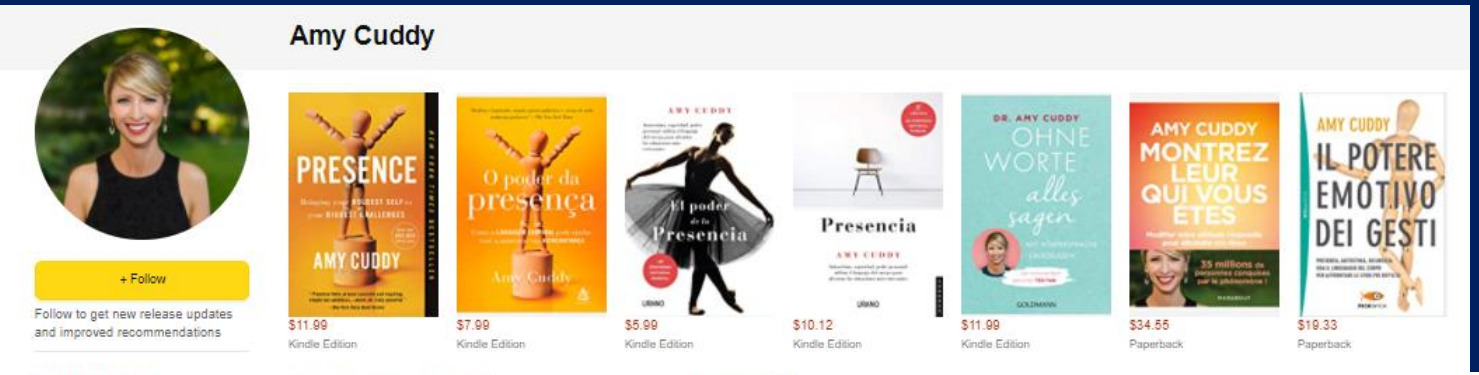


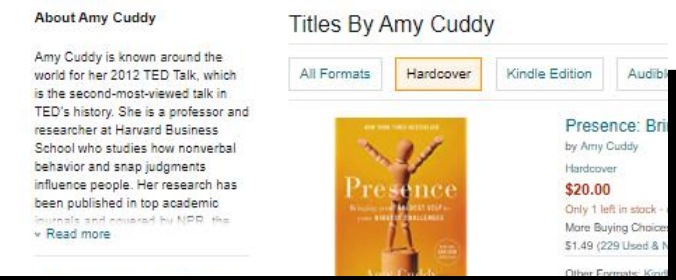


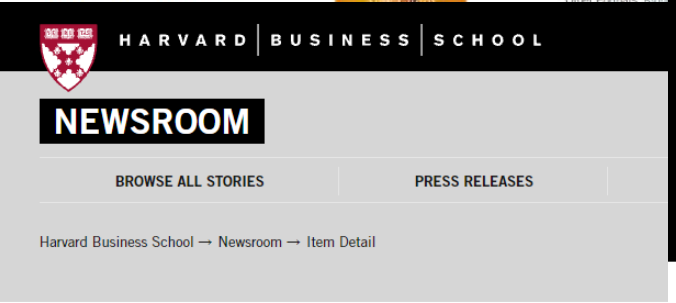
But all this is obvious, right? Why do we need a formal theory of Baysean statistics to come to these conclusions?

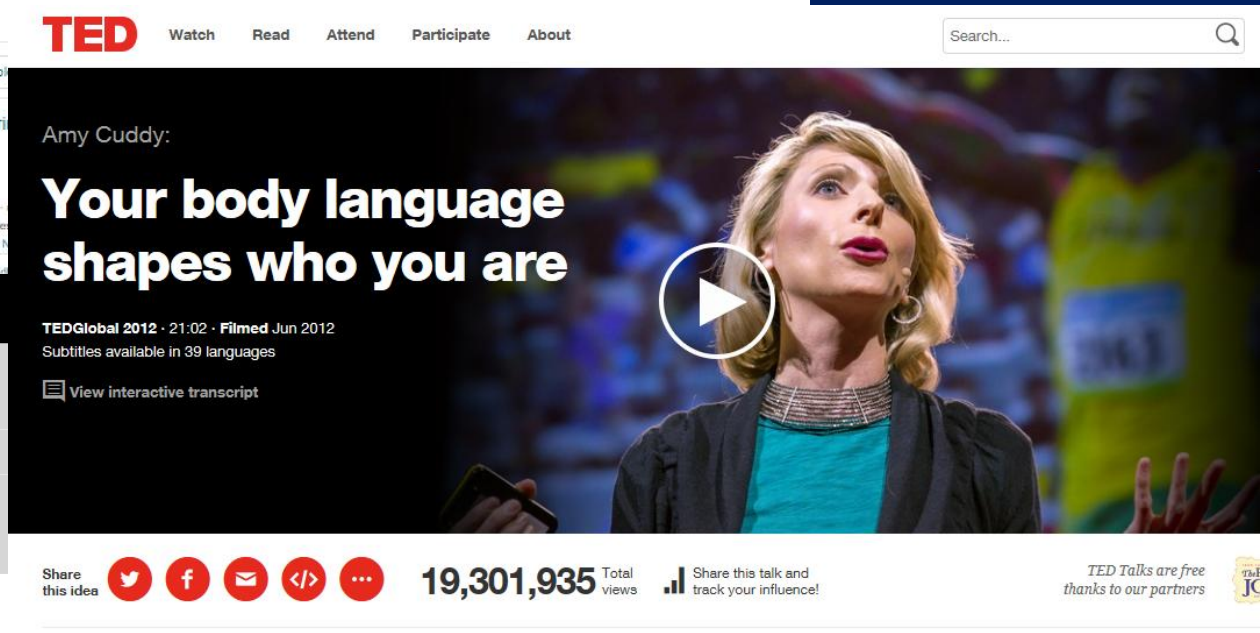
- Because the mistakes that lead to this type of bad diagnosis and inaccurate research are all to easy to make if we don't consciously take into account the base rate of the condition / the pretest probability that the hypothesis is true
- If we don't keep Bayes' theorem in mind, it's easy to fixate on the details and overlook the big picture
  - ie, focusing only on specific symptoms or statistical tests

Power pose media—and academic-- sensation









Faculty News | CNN | 10 OCT 2010

Power Poses: Certain positions boost testosterone & confidence

Re: Amy J.C. Cuddy

The researchers started their work after noticing some of their female students seemed to participate less in class. They tested these poses on subjects who did not know the intent of the research. CNN's Don Lemon spoke with Professor Amy Cuddy of Harvard Business School and Professor Dana Carney of Columbia Graduate School of Business, the authors of "Power Posing: Brief Nonverbal Displays Affect Neuroendocrine Levels and Risk Tolerance."

Real patient case

- Well-educated and premorbidly well-functioning woman in her 60s
- Over 1-2 years, developed a severe functional decline such that she went from working at a professional job to living in a SNF because she couldn't care for herself
- Also had a few episodes of auditory hallucinations over this course
- Seen by another clinician before me, who wrote in their note that:
  - The patient couldn't have DLB, as the hallucinations would be constant then
  - So, she must have late-onset schizophrenia
    - And people with late-onset schizophrenia tend to have higher premorbid functioning, so it all fits!!!

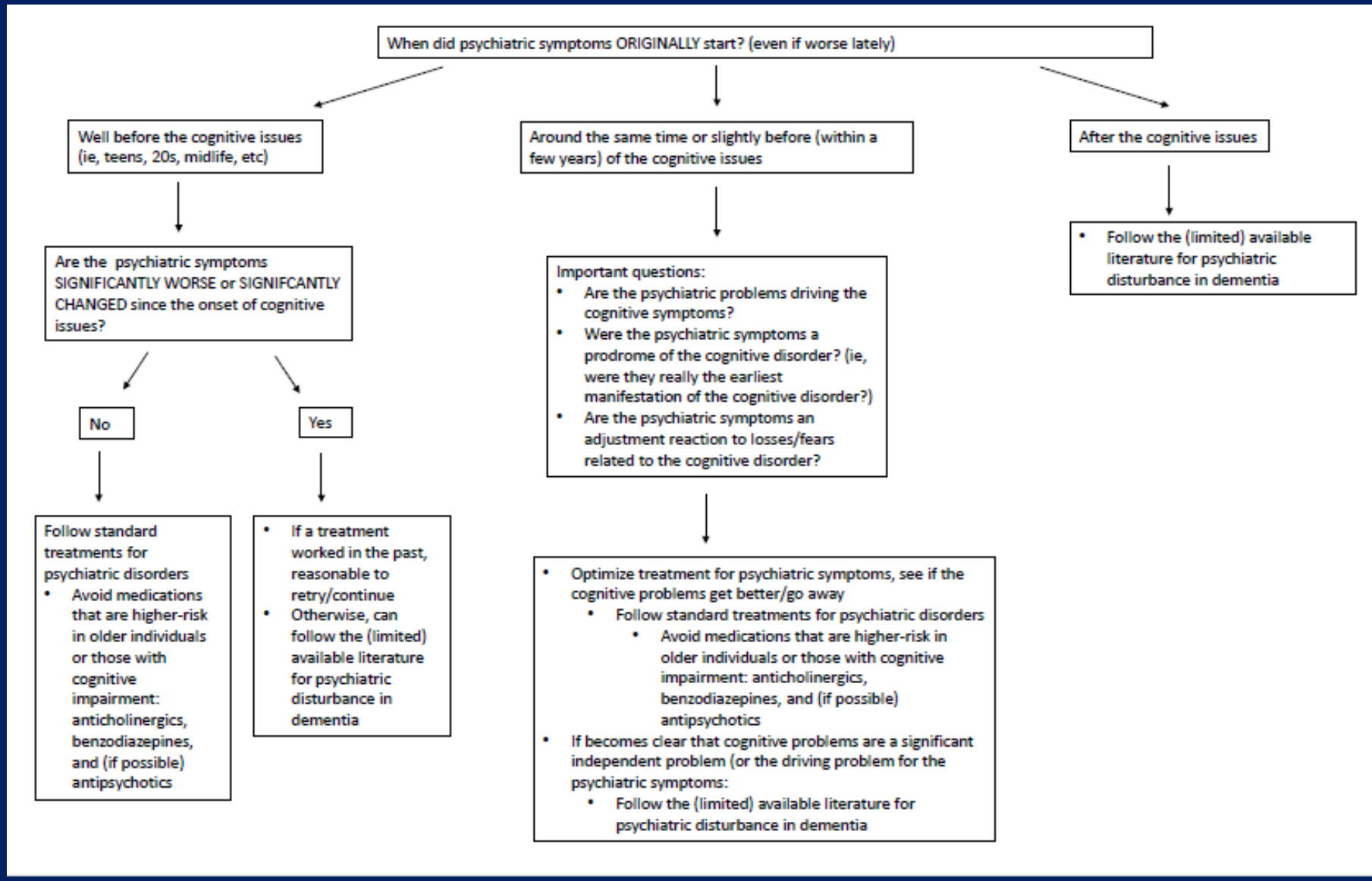
So much wrong it's hard to know where to begin

- Causes of psychosis besides DLB and schizophrenia exist
- Someone with schizophrenia ALSO wouldn't only have hallucinations 2-3x over the course of a year
- High premorbid functioning is NOT a risk factor for schizophrenia in general
  - The correct statement would be that, AMONG INDIVIDUALS WITH SCHIZOPHRENIA, individuals with late onset tend to have higher premorbid functioning than individuals with early-onset
- The BIGGEST mistake—that perhaps could have prevented these other errors—is not taking into account the incidence of schizophrenia vs dementia in someone in their 60s

In Neuropsychiatry clinic and Behavioral Neurology clinic:

- Knowing that the pretest probability for dementia is 64-320 times more likely than the pretest probability for schizophrenia in a person in their 60s with psychosis:
  - Further investigation for dementia was undertaken
- Patient had brain imaging which showed temporal and parietal atrophy
- CSF biomarker positive for Alzheimer disease
- Able to give patient/family more accurate prognosis and avoid unnecessary treatments with high potential for harm (antipsychotics)

Older adult with psychiatric symptoms



Look for treatable etiologies

- Unclear if someone has late-onset MDD or early neurodegenerative dementia?
  - Only one of those has disease-modifying treatment
- Some cognitive/neuropsychiatric disorders DO have disease-modifying treatments
  - Delirium: treat underling cause
  - Neurosyphilis, HIV dementia: treat infection
  - Vascular dementia/cognitive impairment: secondary stroke prevention (BP control, antiplatelets/anticoagulation, statin, treatment of DM, smoking cessation)
  - Catatonia: needs benzodiazepines, ECT
  - Seizures: AEDs