Everything you need to know to do a research project in two years!!

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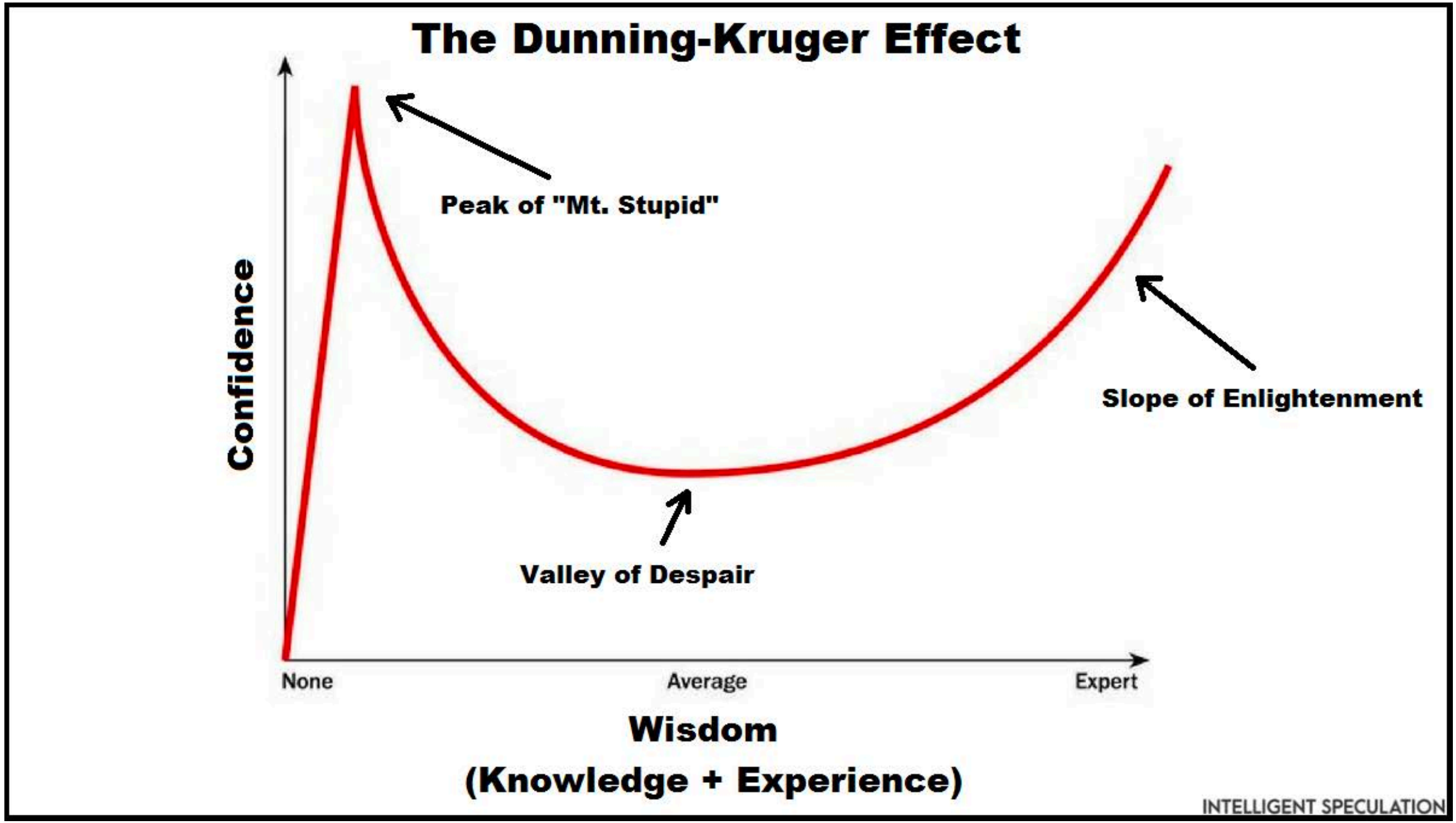
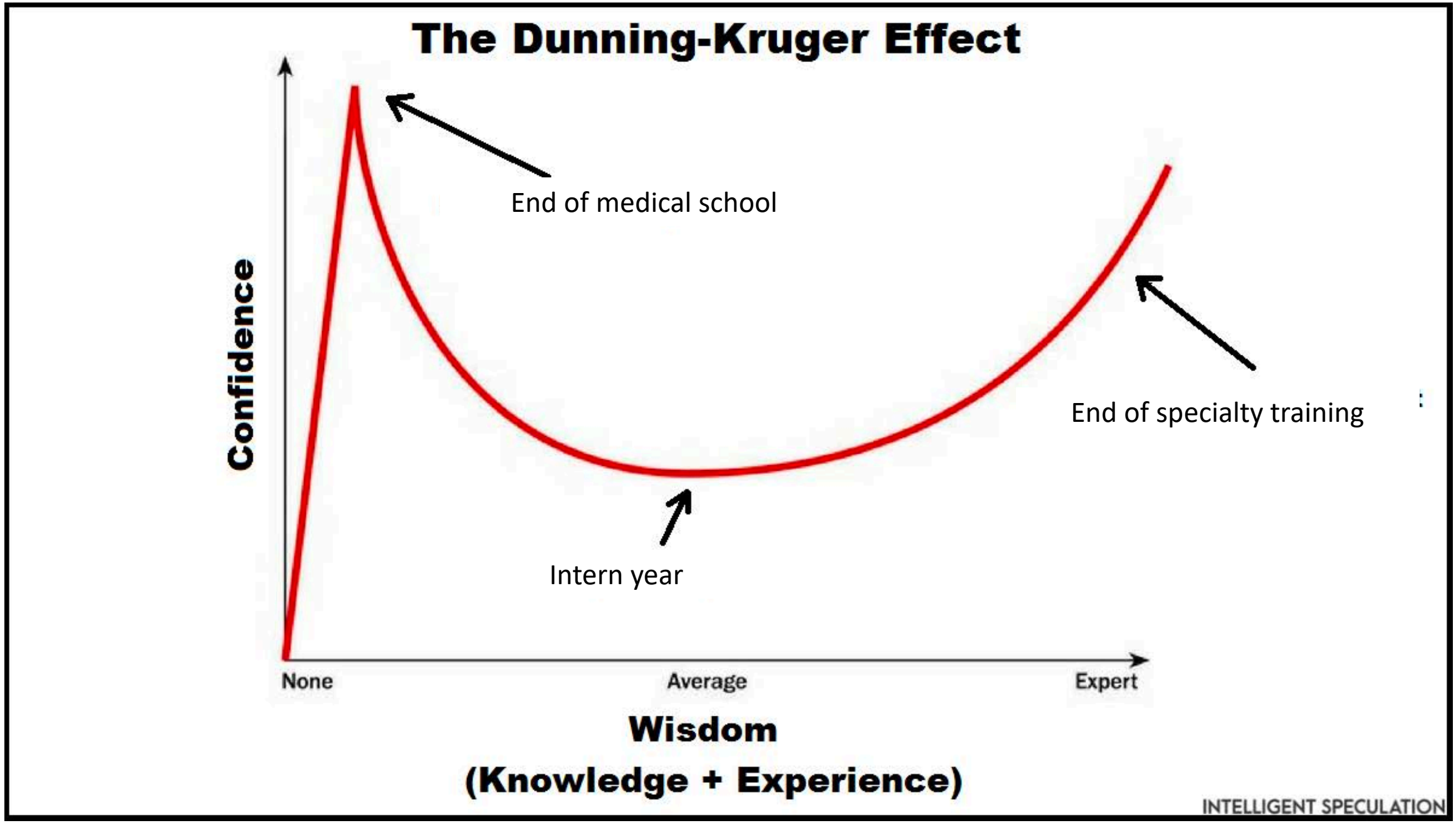
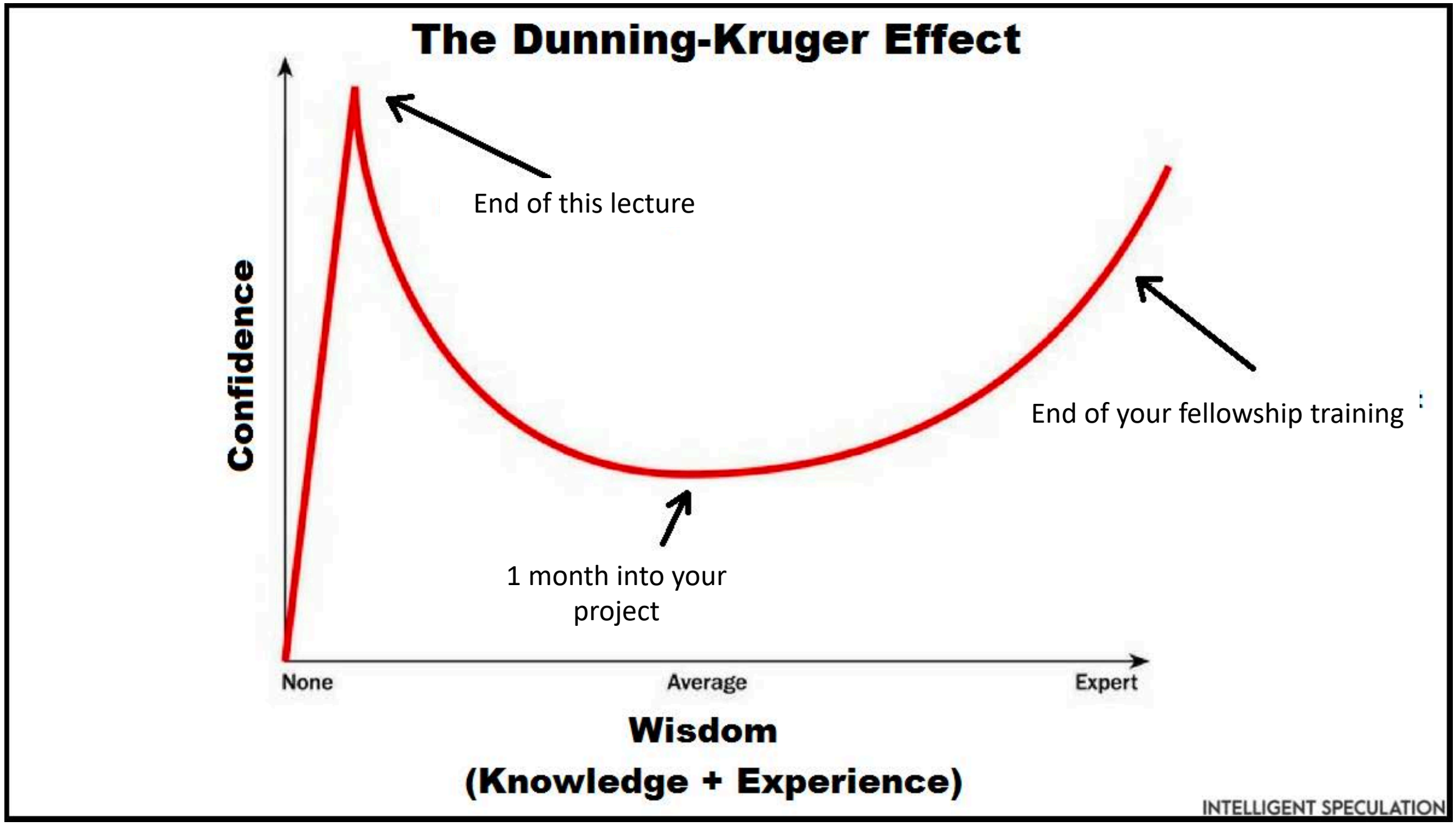
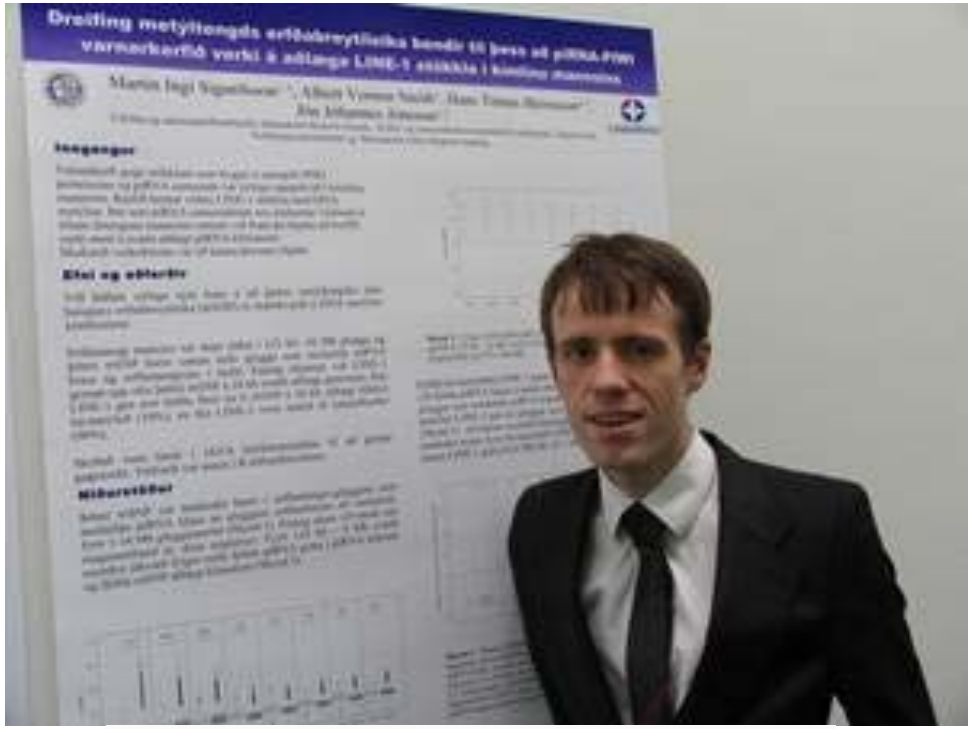
SSAI-OB course 2019


The Dunning-Kruger Effect
Peak of "Mt. Stupid"
Confidence
Slope of Enlightenment
Valley of Despair
None
Average
Expert
Wisdom
(Knowledge + Experience)
INTELLIGENT SPECULATION


The Dunning-Kruger Effect
End of medical school
Intern year
End of specialty training
Confidence
None
Average
Expert
Wisdom
(Knowledge + Experience)
INTELLIGENT SPECULATION


The Dunning-Kruger Effect
Confidence
End of this lecture
1 month into your project
End of your fellowship training
None
Average
Expert
Wisdom
(Knowledge + Experience)
INTELLIGENT SPECULATION

OR



Sigurdsson et al. *BMC Medical Genomics* (2017) 10:25
DOI 10.1186/s12920-017-0270-5

BMC Medical Genomics

RESEARCH ARTICLE Open Access

Post-operative atrial fibrillation examined using whole-genome RNA sequencing in human left atrial tissue

Martin I Sigurdsson[1*], Louis Saddic[1], Mahyar Heydarpour[1], Tzuu-Wang Chang[1], Prem Shekar[2], Sary Aranki[2], Gregory S Couper[2], Stanton K. Sherman[1], Jochen D. Muehlschlegel[1] and Simon C. Body[1]

Sigurdsson et al. *Genome Medicine* (2016) 8:127
DOI 10.1186/s13073-016-0381-1

Genome Medicine

RESEARCH Open Access

Allele-specific expression in the human heart and its application to postoperative atrial fibrillation and myocardial ischemia

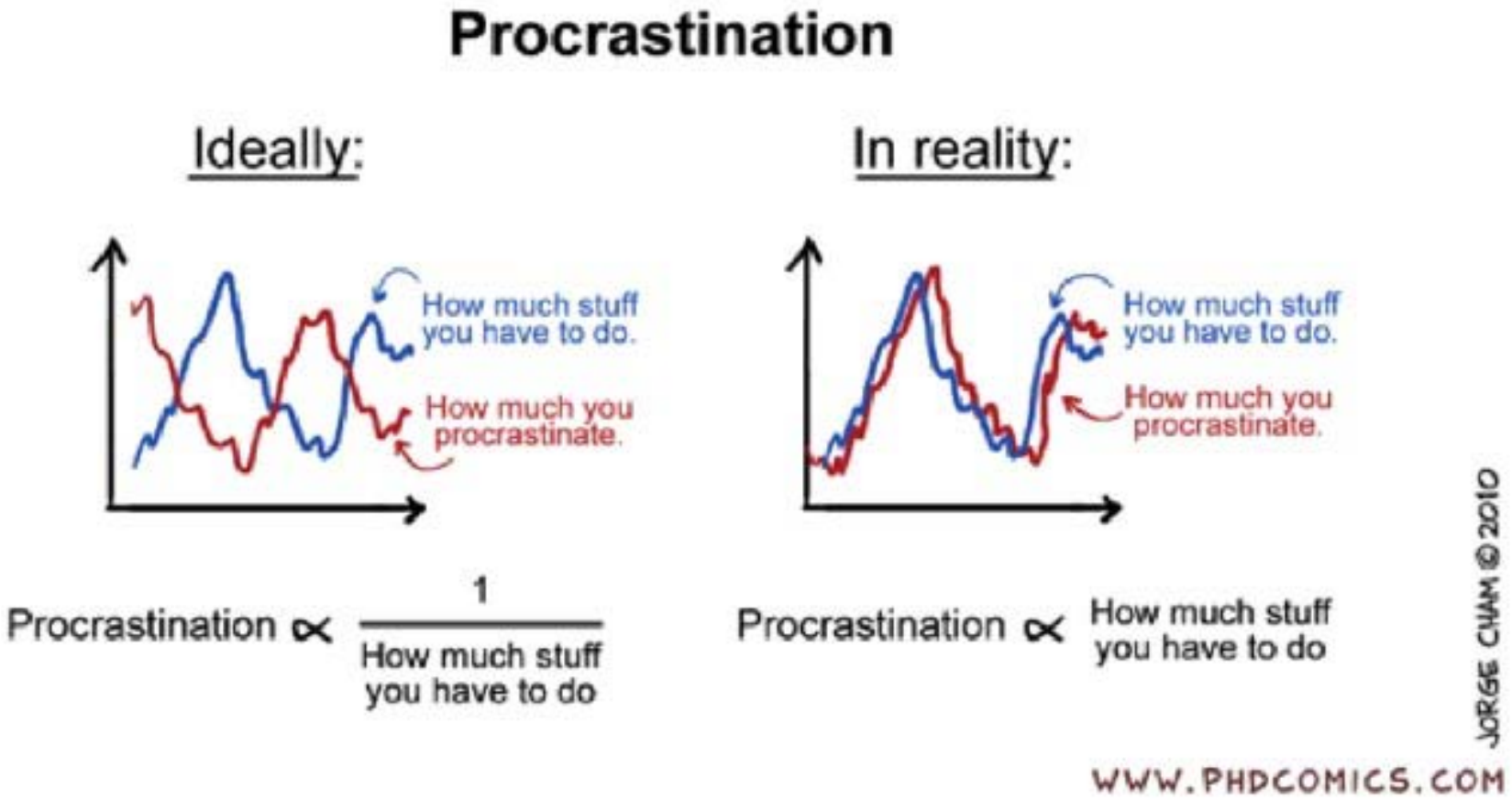
Martin I. Sigurdsson[1*], Louis Saddic[1], Mahyar Heydarpour[1], Tzuu-Wang Chang[1], Prem Shekar[2], Sary Aranki[2], Gregory S. Couper[2], Stanton K. Sherman[1], Jon G. Seidman[3], Simon C. Body[1†] and Jochen D. Muehlschlegel[1†]

Why do research at all

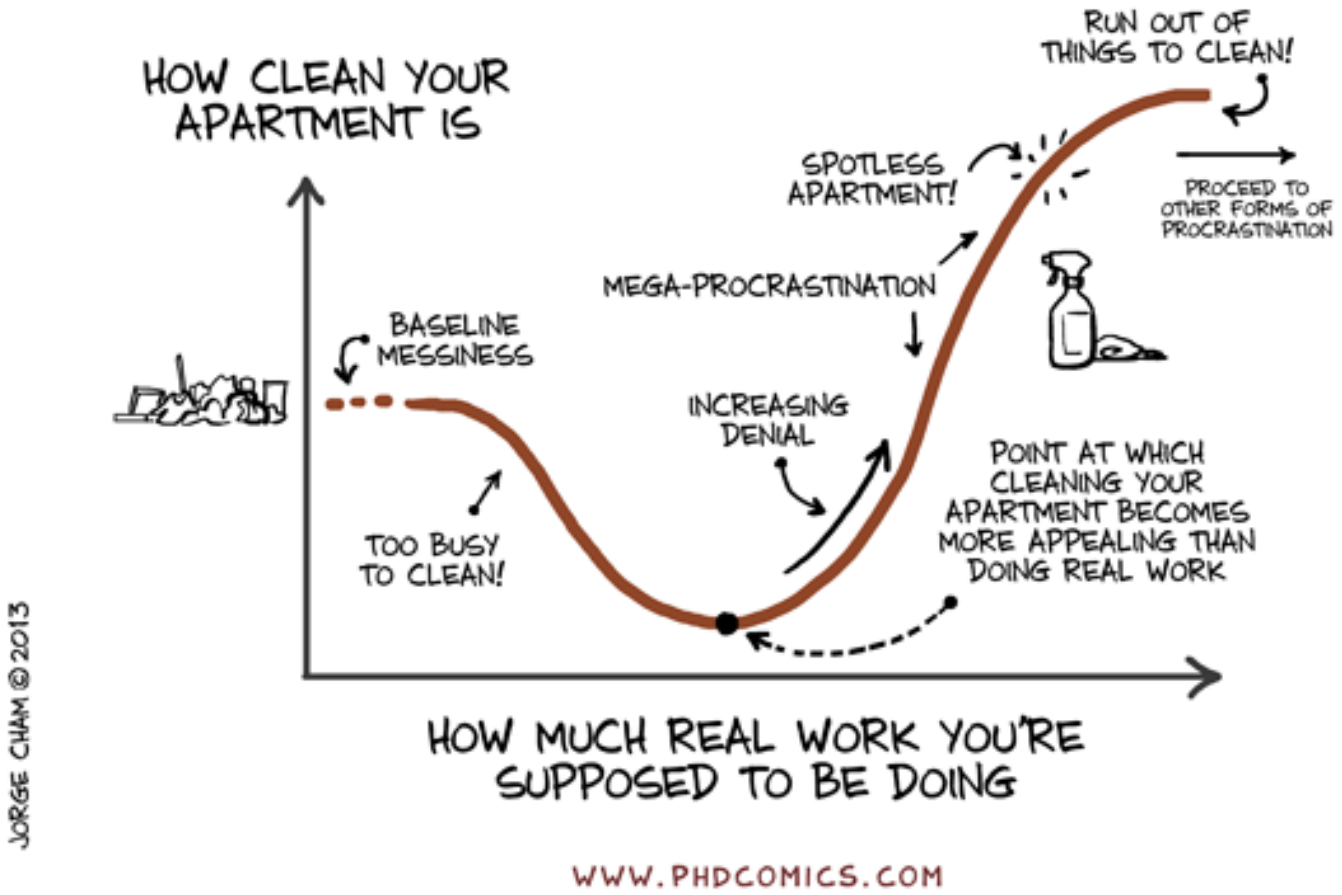
- Good things
  - Exciting
  - Change in your day
  - Always finding something new
  - Collaborations
- Bad things
  - Time consuming
  - Poor instant gratification
  - No “on-call” person

How in the world am I going to do a project in 2 years

Procrastination – no 1. enemy

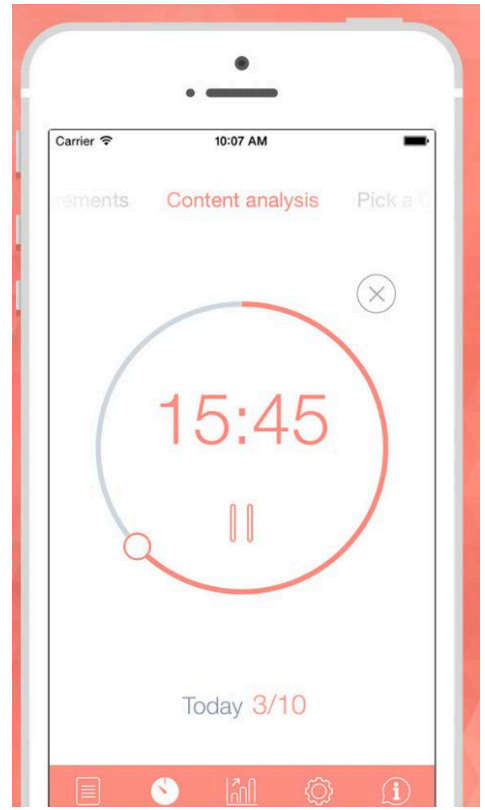


Procrastination – no 1. enemy



Productivity / procrastination avoidance

- 15 min per day vs word (Scrivener)
- Timers (tomato timer)
- Social media blockers (SelfControl)
- Focus apps (BeFocused)



How in the world am I going to do a project in 2 years

- In order of relevance
  - Find a mentor you can work with
    - Ideally track record of successful mentorships
  - Find a topic/project that interests you
    - So you can sell it to others
  - Find a ”support team”
    - Differs (stats, data, research nurse)
  - Scale down the project into ”eatable bites”
    - So you don’t give up in the valley of despair
  - Design the project so you actually answer the question want to answer
    - What data, what stats etc

Find a mentor you can work with

- Almost more important than finding a good project
- Not always the department head
- Identify a rising star

Traits of a Good Mentor

Good mentors often share some of the following personal qualities:

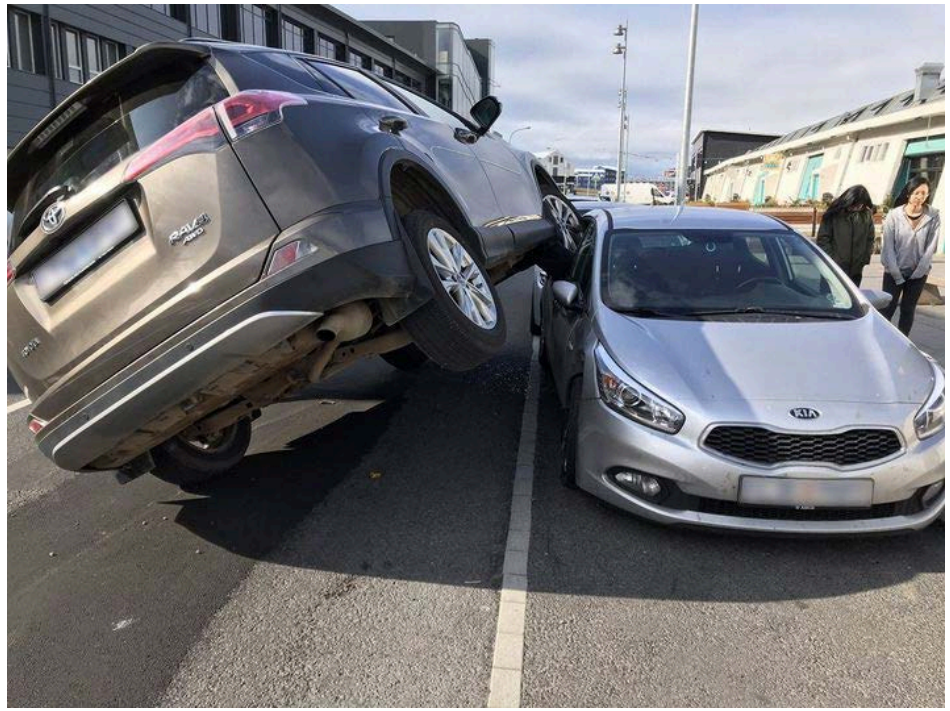
- *Accessibility:* An open door and an approachable attitude.
- *Empathy:* Personal insight into what the trainee is experiencing.
- *Open-mindedness:* Respect for each trainee's individuality and for working styles and career goals different from your own.
- *Consistency:* Acting on your stated principles on a regular basis.
- *Patience:* Awareness that people make mistakes and that each person matures at his or her own rate.
- *Honesty:* Ability to communicate the hard truths about the world "out there" and about the trainee's chances.
- *Savvy:* Attention to the pragmatic aspects of career development.

Find a topic that interests you

- Talk to your colleagues and colleagues in other institutions
- Is there a topic that interests / annoys you
- Do you think you can further knowledge / improve practice with your work

Find a support team

- What is your contribution
  - Driving the boat
  - Other content expertise
- What to you need
  - Data management
  - Statistics
  - Research nurse
  - Colleagues to help you with 24/7 coverage



5 minutes in the library can save you 5 years of work

- What has been done
- What is not known
- What works and does not work
- What is a good setup for my research
- Where should I send it for review

Scale the project down into eatable bites

- Focused project, clear outcomes
- Power analyze your study so you have a chance to answer the study question
- The absence of evidence is not the evidence of absence
- Power depends on
  - How common is the outcome
  - How big of a difference do you (literature) think the intervention is
  - How willing are you to accept the risk of “not finding a significant difference”

Power analysis - example

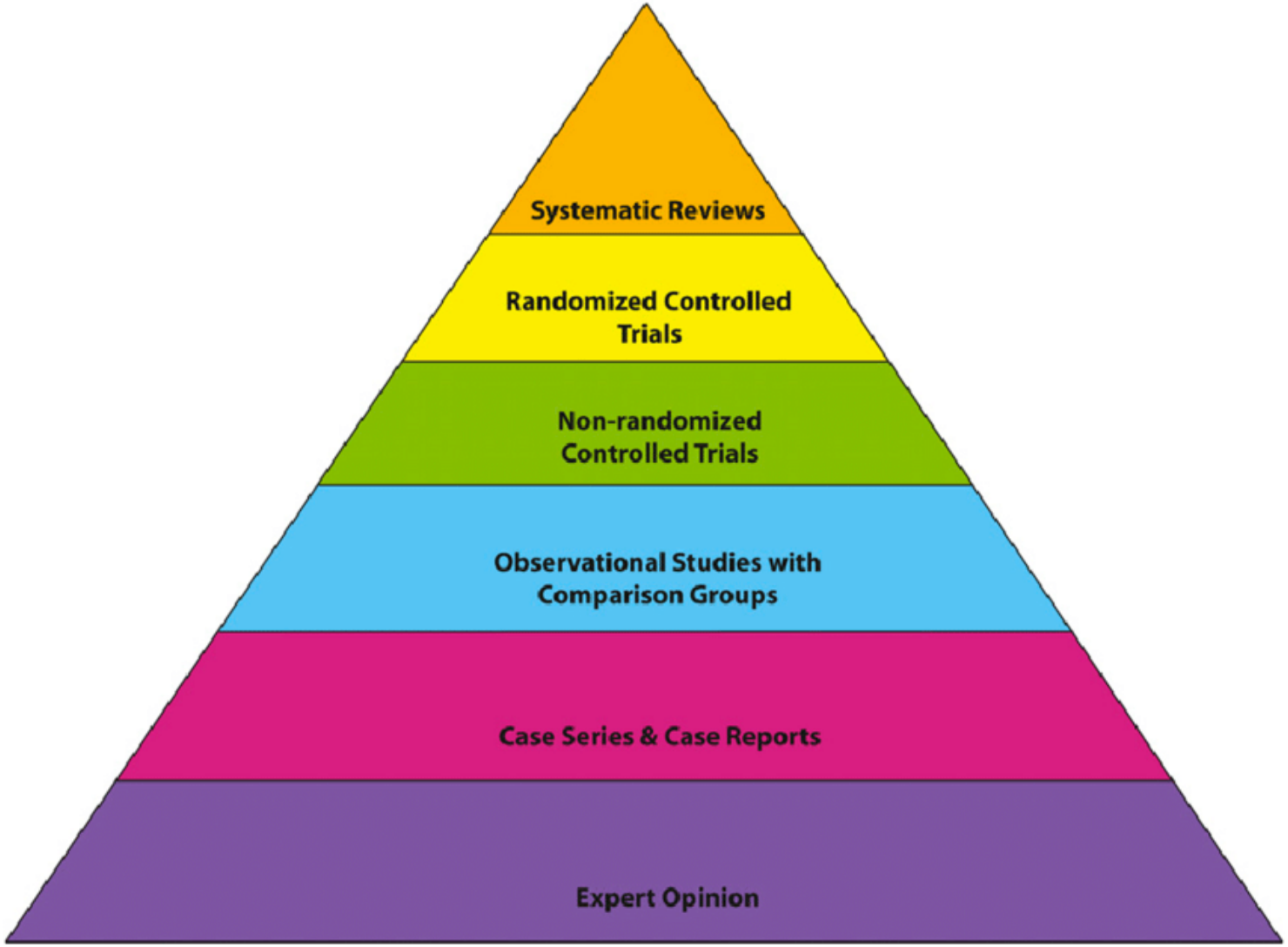
- Very simple (http://biomath.info/power/chsq.htm)
- Project: High vs low concentration bupivacaine in labor epidural on the rate of forceps delivery
- P=0,05, power 80% (common parameters)
- Incidence 50%, think low concentration will reduce to 25% - 65 in each group
- Incidence 50%, think low concentration will reduce to 45% - 1605 in each group
- Incidence 5%, think low concentration will reduce to 2.5% – 984 in each group

Power analysis - example

- Surrogate outcomes can potentially be used to help here
  - Quantified motor strength from 0-100 of high vs low concentration bupivacaine in labor epidural (each patient will be a data point)
  - P=0,05, power 80% (common parameters)
  - Think mean in high is 75, SD 20, and low will be 95 points - 17 in each group
  - Think mean in high is 85, SD 20 and low is 95 – 64 in each group
- Consult statistician to design

What kind of study should I do?

Pyramid of research – what tier should I work



Case report !

THE

BOSTON MEDICAL AND SURGICAL JOURNAL.

VOL. XXXV. WEDNESDAY, NOVEMBER 18, 1846. No. 16.

INSENSIBILITY DURING SURGICAL OPERATIONS PRODUCED BY INHALATION.

Read before the Boston Society of Medical Improvement, Nov. 9th, 1846, an abstract having been previously read before the American Academy of Arts and Sciences, Nov. 3d, 1846.

By Henry Jacob Bigelow, M.D., one of the Surgeons of the Massachusetts General Hospital.

[Communicated for the Boston Medical and Surgical Journal.]

It has long been an important problem in medical science to devise some method of mitigating the pain of surgical operations. An efficient agent for this purpose has at length been discovered. A patient has been rendered completely insensible during an amputation of the thigh, regaining consciousness after a short interval. Other severe operations have been performed without the knowledge of the patients. So remarkable an occurrence will, it is believed, render the following details relating to the history and character of the process, not uninteresting.

On the 16th of Oct., 1846, an operation was performed at the hospital, upon a patient who had inhaled a preparation administered by Dr. Morton, a dentist of this city, with the alleged intention of producing insensibility to

Case series

mbl.is | iceland monitor

LATEST CULTURE POLITICS NATURE FOOD OPINION WEAT

News | Iceland Monitor | Wed 10 Jul 2019 | 13.42 GMT | Modified at 14.06

Share

E. Coli Traced to Farm in Southwest Iceland

Efstidalur II, Southwest Iceland. *mbl.is/Hari*

Case series – words of caution

Early report

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

Early report

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

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Summary

Background We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods 12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

Findings Onset of behavioural symptoms was associated by the parents, with measles, mumps, and rubella vaccination in eight of the 12 children, with measles infection in one child, and otitis media in another. All 12 children had intestinal abnormalities ranging from lymphoid nodular hyperplasia to aphthoid ulceration. Histology showed patchy chronic inflammation in 11 children and reactive ileal lymphoid hyperplasia in seven, but no granulomas. Behavioural disorders included autism (nine), disintegrative psychosis (one), and possible postviral or vaccinal encephalitis (two). There were no focal neurological abnormalities and MRI and EEG tests were normal. Abnormal laboratory results were significantly raised urinary methylmalonic acid compared with age-matched controls ($p=0.003$), low haemoglobin in four children, and low serum IgA in four children.

Interpretation We identified associated gastrointestinal disease and developmental regression in a group of previously normal children, which was generally associated in time with possible environmental triggers.

Introduction

We saw several children who, after a period of apparent normality, lost acquired skills, including communication. They all had gastrointestinal symptoms, including abdominal pain, diarrhoea, and bloating and, in some cases, food intolerance. We describe the clinical findings, and gastrointestinal features of these children.

Patients and methods

12 children, consecutively referred to the department of paediatric gastroenterology with a history of a pervasive developmental disorder with loss of acquired skills and intestinal symptoms (diarrhoea, abdominal pain, bloating and food intolerance), were investigated. All children were admitted to the ward for a week, accompanied by their parents.

Clinical investigations

We took histories including details of immunisations and exposure to infectious diseases, and assessed the children. In 11 cases the history was obtained by the senior clinician (JW-S). Neurological and psychiatric assessments were done by consultant staff (PH, MB) with HMS-4 criteria.[1] Developmental studies included a review of prospective developmental records from parents, health visitors, and general practitioners. Four children did not undergo psychiatric assessment in hospital; all had been assessed professionally elsewhere, so these assessments were used as the basis for their behavioural diagnosis.

After bowel preparation, ileocolonoscopy was performed by SHM or MAT under sedation with midazolam and pethidine. Paired frozen and formalin-fixed mucosal biopsy samples were taken from the terminal ileum; ascending, transverse, descending, and sigmoid colons, and from the rectum. The procedure was recorded by video or still images, and were compared with images of the previous seven consecutive paediatric colonoscopies (four normal colonoscopies and three on children with ulcerative colitis), in which the physician reported normal appearances in the terminal ileum. Barium follow-through radiography was possible in some cases.

Also under sedation, cerebral magnetic-resonance imaging (MRI), electroencephalography (EEG) including visual, brain stem auditory, and sensory evoked potentials (where compliance made these possible), and lumbar puncture were done.

Laboratory investigations

Thyroid function, serum long-chain fatty acids, and

RETRACTED

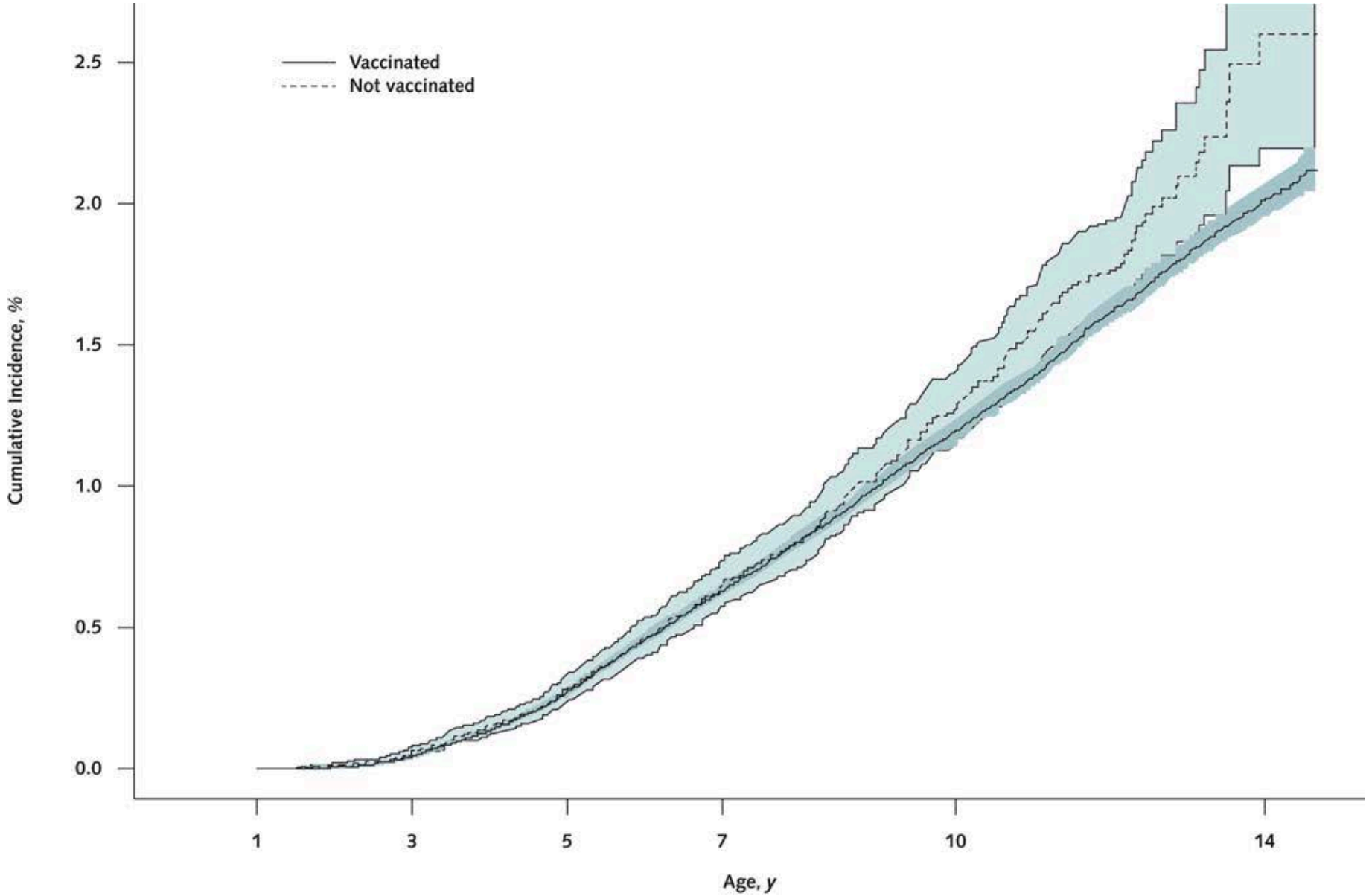
Child	Behavioural diagnosis	Exposure identified by parents or doctor	Interval from exposure to first behavioural symptom	Features associated with exposure	Age at onset of first symptom	
					Behaviour	Bowel
1	Autism	MMR	1 week	Fever/delirium	12 months	Not known
2	Autism	MMR	2 weeks	Self injury	13 months	20 months
3	Autism	MMR	48 h	Rash and fever	14 months	Not known
4	Autism? Disintegrative disorder?	MMR	Measles vaccine at 15 months followed by slowing in development. Dramatic deterioration in behaviour immediately after MMR at 4-5 years	Repetitive behaviour, self injury, loss of self-help	4-5 years	18 months
5	Autism	None—MMR at 16 months	Self-injurious behaviour started at 18 months		4 years	
6	Autism	MMR	1 week	Rash & convulsion; gaze avoidance & self injury	15 months	18 months
7	Autism	MMR	24 h	Convulsion, gaze avoidance	21 months	2 years
8	Post-vaccinial encephalitis?	MMR	2 weeks	Fever, convulsion, rash & diarrhoea	19 months	19 months
9	Autistic spectrum disorder	Recurrent otitis media	1 week (MMR 2 months previously)	Disinterest; lack of play	18 mont	ars
10	Post-viral encephalitis?	Measles (previously vaccinated with MMR)	24 h	Fever, rash & vomiting	15 ths	Not kn
11	Autism	MMR	1 week	Recurrent "viral pneumonia" for 8 weeks following MMR	15 mo	Not kno
12	Autism	None—MMR at 15 months	Loss of speech development and deterioration in language skills noted at 16 months			Not n

MMR=measles, mumps, and rubella vaccine.

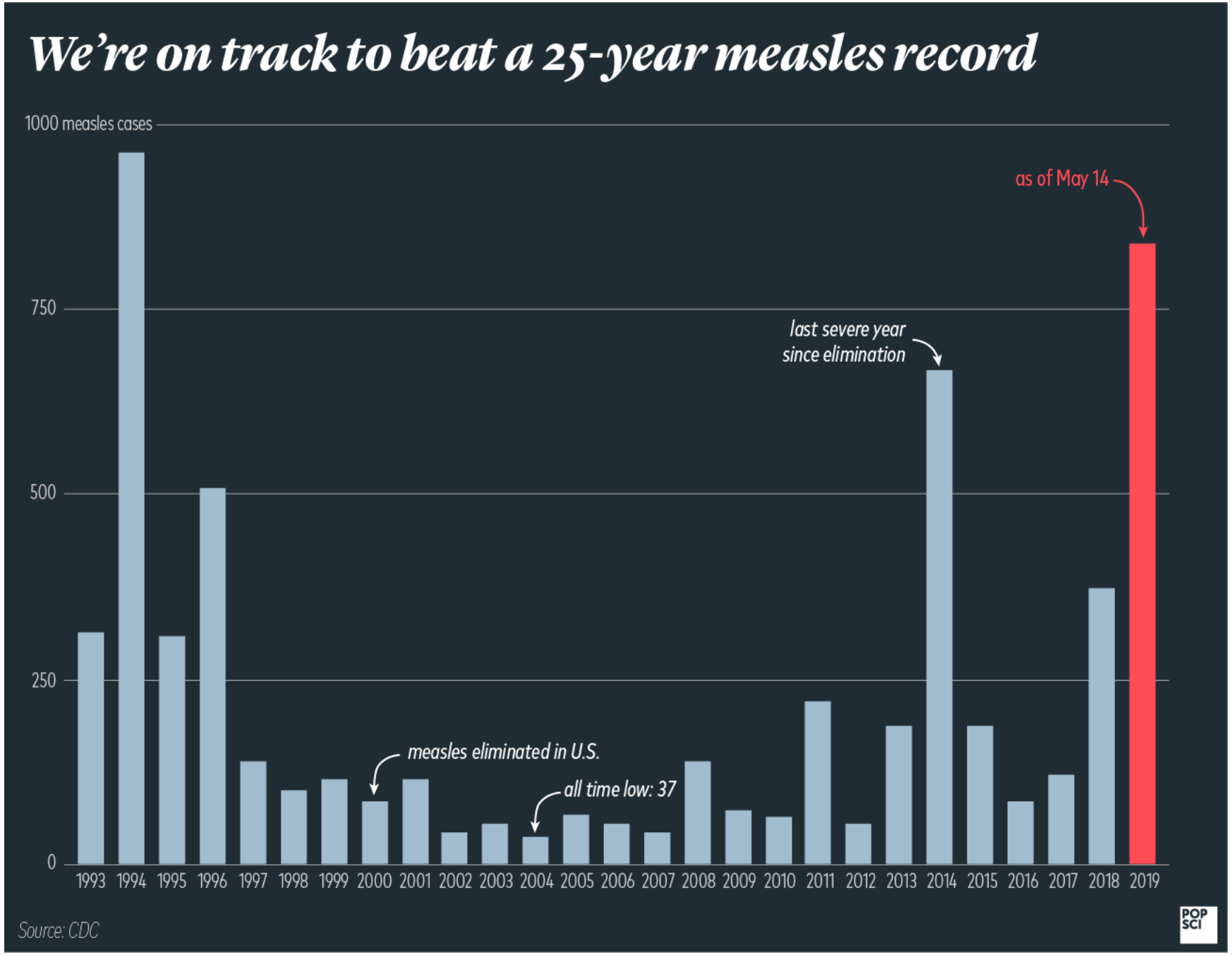
Table 2: **Neuropsychiatric diagnosis**

Following these case series

- Impossible to do a randomized controlled trial
- Retrospective cohort studies ”best thing available”

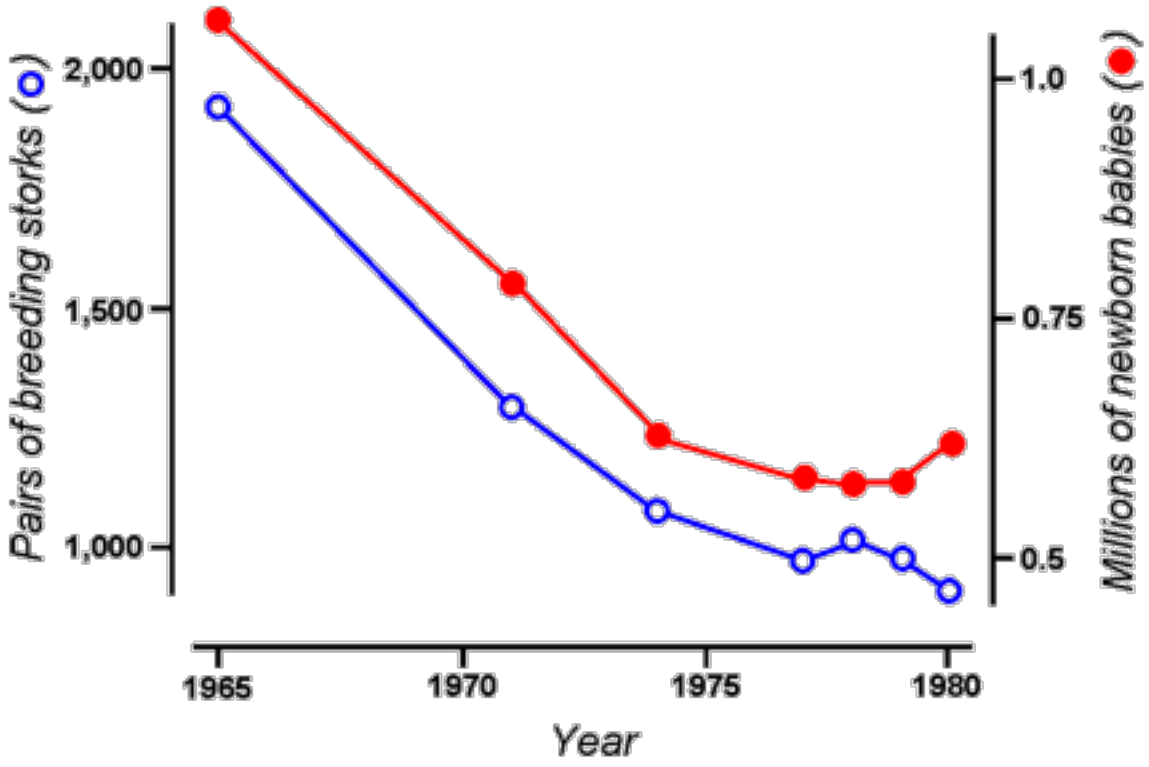


Children at risk, *n*						
Vaccinated:	3457	571 550	493 444	391 259	235 016	37 267
Not vaccinated:	654 004	66 497	36 343	27 392	18 949	823


We're on track to beat a 25-year measles record
1000 measles cases
750
500
250
0
as of May 14
last severe year since elimination
measles eliminated in U.S.
all time low: 37
1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019
Source: CDC
POP SCI

Retrospective cohort studies

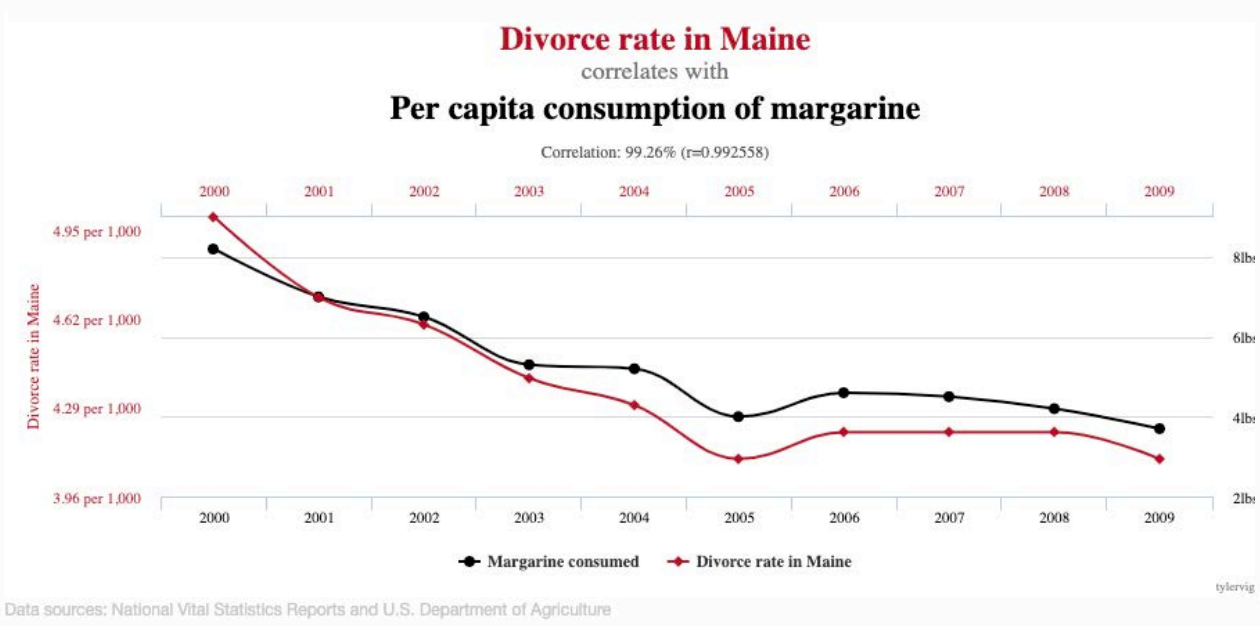
- Common
- ”Cheap” and often not very time-consuming
- Helpful to develop hypotheses
- Hard to interpret findings
- Correlation vs. causation

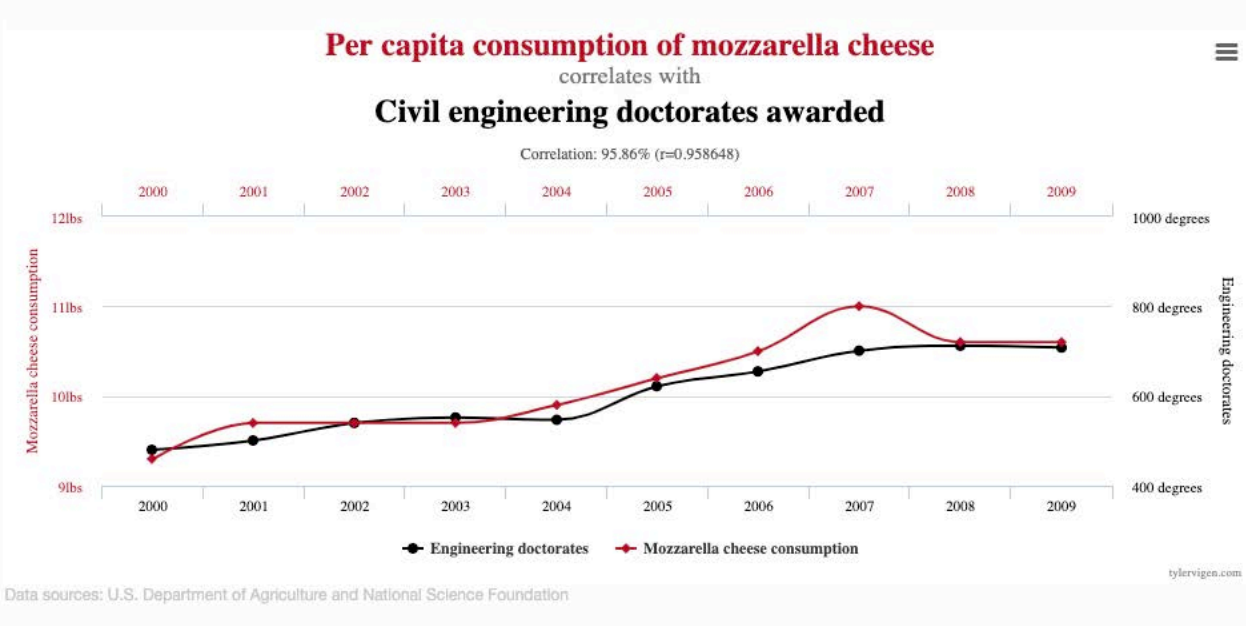


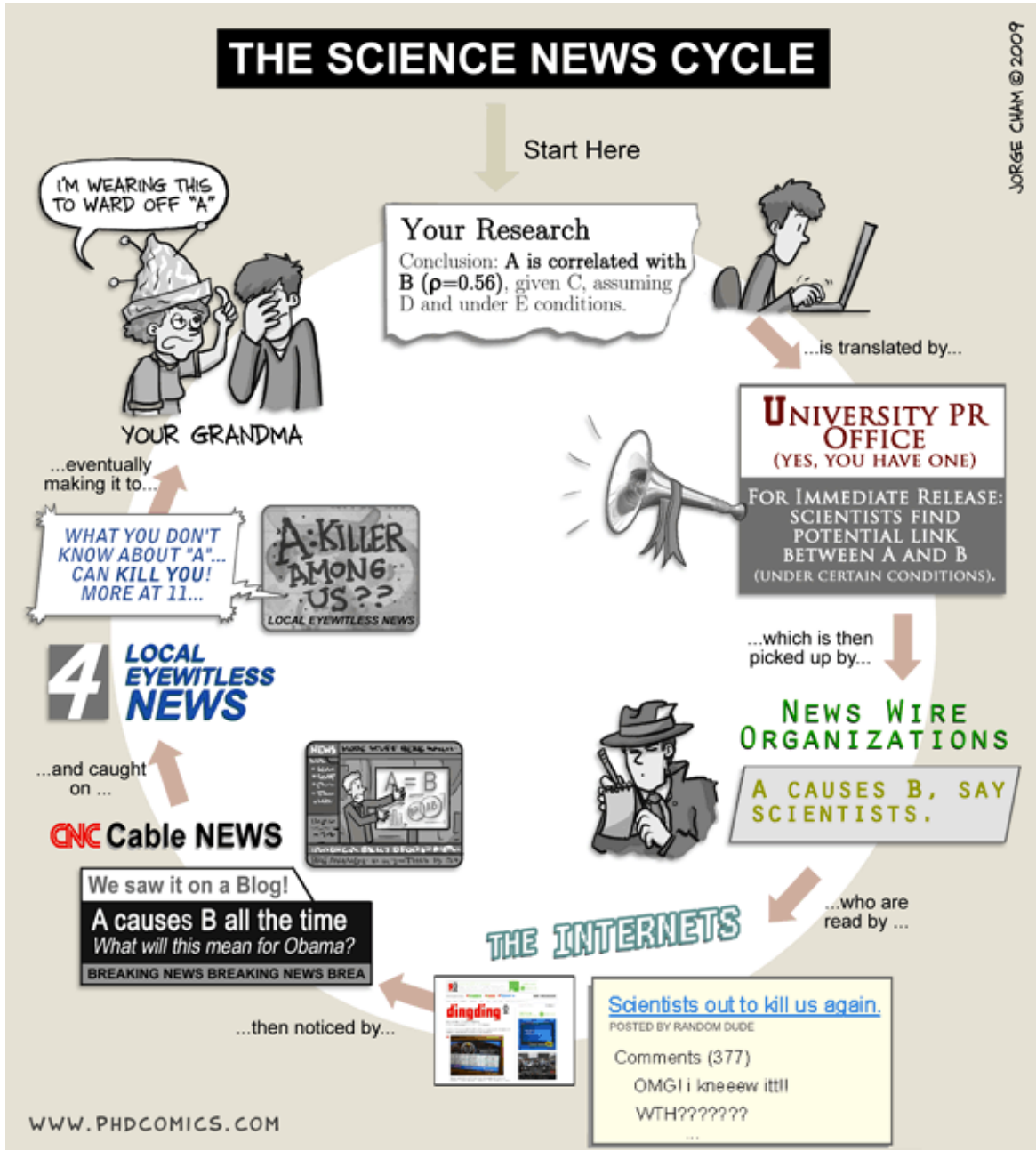
Recommendations for retrospective cohort studies

- Decide on data analysis plan before conducting study
  - Can register the plan at clinicaltrials.gov (often requested)
- Assess power before conducting study
  - Often non-changeable cohort
- Consult guidelines (CONSORT)
- Be careful about your reporting of correlation to not imply causation

Google ”spurious correlation”

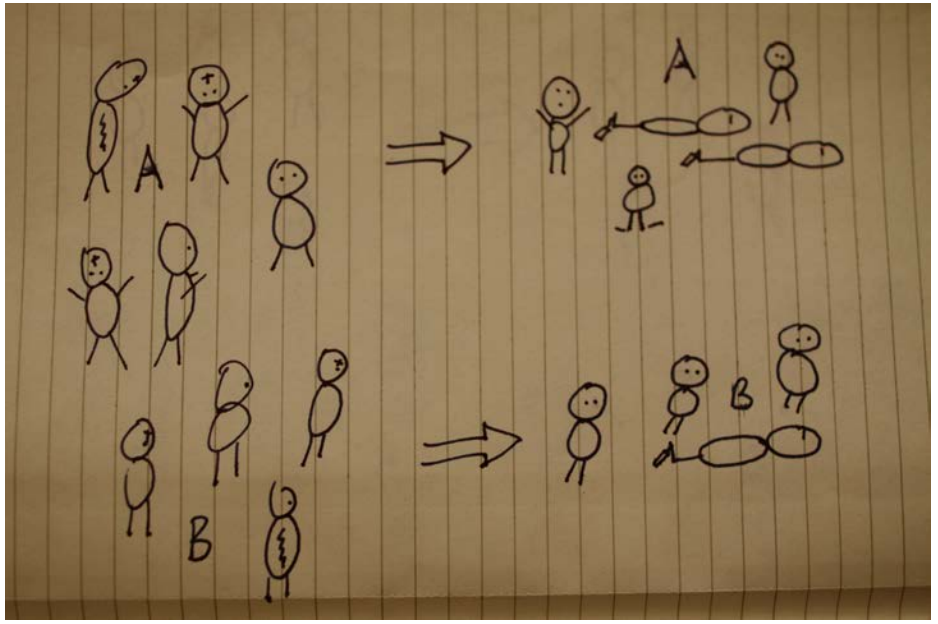





THE SCIENCE NEWS CYCLE
JORGE CHAM © 2009
Start Here
Your Research
Conclusion: A is correlated with B (ρ=0.56), given C, assuming D and under E conditions.
...is translated by...
UNIVERSITY PR OFFICE
(YES, YOU HAVE ONE)
FOR IMMEDIATE RELEASE: SCIENTISTS FIND POTENTIAL LINK BETWEEN A AND B (UNDER CERTAIN CONDITIONS).
...which is then picked up by...
NEWS WIRE ORGANIZATIONS
A CAUSES B, SAY SCIENTISTS.
...who are read by ...
THE INTERNETS
Scientists out to kill us again.
POSTED BY RANDOM DUDE
Comments (377)
OMG! i kneeew it!!!
WTH???????
...then noticed by...
dingding
We saw it on a Blog!
A causes B all the time
What will this mean for Obama?
BREAKING NEWS BREAKING NEWS BREA
...and caught on ...
CNC Cable NEWS
A=B
LOCAL EYEWITLESS NEWS
A: KILLER AMONG US??
LOCAL EYEWITLESS NEWS
WHAT YOU DON'T KNOW ABOUT "A"... CAN KILL YOU! MORE AT 11...
...eventually making it to...
I'M WEARING THIS TO WARD OFF "A"
YOUR GRANDMA
WWW.PHDCOMICS.COM

Randomized control trials

- Prospective
- Blinding (single/double) etc
- Usually expensive and time-consuming
- If you plan on doing one
  - Careful powering of study
  - Expect it to take a while



It can be done in your fellowship!

Obstetric Anesthesiology
Section Editor: Cynthia A. Wong

A Randomized Trial of Dural Puncture Epidural Technique Compared with the Standard Epidural Technique for Labor Analgesia

Eric Cappiello, MD
Nollag O'Rourke, FFARCSI
Scott Segal, MD
Lawrence C. Tsen, MD

BACKGROUND: We designed this prospective, double-blind, randomized study to examine whether a dural puncture without intrathecal drug administration immediately before epidural drug administration would improve labor analgesia when compared to a traditional epidural technique without prior dural puncture.
METHODS: Eighty nulliparous parturients with cervical dilation less than 5 cm were randomly assigned to receive a standardized epidural technique, with or without a single dural puncture with a 25-gauge (G) Whitacre spinal needle. After successful placement of the needle(s) and the epidural catheter, 12 mL of bupivacaine 2.5 mg/mL was administered through the epidural catheter and a patient-controlled epidural infusion of bupivacaine 1.25 mg/mL + fentanyl 2 μg/mL was initiated. The presence of sacral analgesia (S1) and pain scores were compared between groups.
RESULTS: In demographically similar groups, parturients with prior dural puncture had more frequent blockade of the S1 dermatome (absolute risk difference [95% confidence interval] 22% [6–39]), more frequent visual analog scale scores <10/100 at 20 min (absolute risk difference 20% [1–38]), and reduced one-sided analgesia (absolute risk difference [95% CI] 17% [2–330]). The highest median sensory level (T10) was no different between groups.
CONCLUSIONS: Dural puncture with a 25-G spinal needle immediately before the initiation of epidural analgesia improves the sacral spread, onset, and bilateral pain relief produced by analgesic concentrations of bupivacaine with fentanyl in laboring nulliparous patients.
(Anesth Analg 2008;107:1646–51)

Table 2. Analgesic Outcomes[a]

	Dural puncture epidural (n = 39)	Epidural (n = 40)	P
Unilateral block (%)[b]	8	25	0.04
Catheter adjusted (%)	13	28	0.10
Catheter replaced (%)	3	13	0.09
VAS <10 obtained (%) at 20 min	85	65	0.04
VAS <30 obtained (%) at 20 min	90	80	0.22
S1 blocked (%) at 20 min	46	37	0.60
Bilateral S1 blocked (%) at 20 min	41	30	0.31
S1 blocked (%)[b]	92	70	0.01
S2 blocked (%)[b]	77	65	0.24
Bilateral S1 block (% of those with block)[b]	83	82	0.90
Bilateral S2 block (% of those with block)[b]	90	76	0.16
Highest level [median (IQR)][b]	T10 (T9–T11)	T10 (T9–T11)	0.88
Time to S1 block (min), if achieved[b]	25 (10–60)	20 (15–60)	0.91
Time to S2 block (min), if achieved[b]	20 (15–33)	30 (18–90)	0.32
Time to highest block (min)[b]	20 (10–37)	20 (15–83)	0.24
Additional bolus given (%)	53	50	0.81
1st h (%)	16	33	0.18
2nd h (%)	16	21	0.59
3rd h (%)	8	6	0.24
Duration epidural infusion (min)	497 ± 200	415 ± 207	0.07

[a] Values reported as percent, mean ± SD, or median (interquartile range).
[b] Denotes occurrence at any time during labor.
VAS = visual analogue scale.

And if you have more time

Dural Puncture Epidural Technique Improves Labor Analgesia Quality With Fewer Side Effects Compared With Epidural and Combined Spinal Epidural Techniques: A Randomized Clinical Trial

Anthony Chau, MD, MMSc, FRCPC,*†‡ Carolina Bibbo, MD,§ Chuan-Chin Huang, ScD,†
Kelly G. Elterman, MD,‖ Eric C. Cappiello, MD,†‡ Julian N. Robinson, MD,‡§ and Lawrence C. Tsen, MD†‡

BACKGROUND: The dural puncture epidural (DPE) technique is a modification of the combined spinal epidural (CSE) technique, where a dural perforation is created from a spinal needle but intrathecal medication administration is withheld. The DPE technique has been shown to improve caudal spread of analgesia compared with epidural (EPL) technique without the side effects observed with the CSE technique. We hypothesized that the onset of labor analgesia would follow this order: CSE > DPE > EPL techniques.

METHODS: A total of 120 parturients in early labor were randomly assigned to EPL, DPE, or CSE groups. Initial dosing for EPL and DPE consisted of epidural 20 mL of 0.125% bupivacaine plus fentanyl 2 μg/mL over 5 minutes, and for CSE, intrathecal 0.25% bupivacaine 1.7 mg and fentanyl 17 μg. Upon block completion, a blinded coinvestigator assessed the outcomes. Two blinded obstetricians retrospectively interpreted uterine contractions and fetal heart rate tracings 1 hour before and after the neuraxial technique. The primary outcome was time to numeric pain rating scale (NPRS) ≤ 1 analyzed by using Kaplan-Meier curves and Cox proportional hazard model. Secondary outcomes included block quality, maternal adverse effects, uterine contraction patterns, and fetal outcomes analyzed by using the χ^2 test with Yates continuity correction.

RESULTS: There was no significant difference in the time to NPRS ≤ 1 between DPE and EPL (hazard ratio 1.4; 95% confidence interval [CI] 0.83–2.4, $P = .21$). DPE achieved NPRS ≤ 1 significantly slower than CSE (hazard ratio 0.36; 95% CI 0.22–0.59, $P = .0001$). The median times (interquartile range) to NPRS ≤ 1 were 2 (0.5–6) minutes for CSE, 11 (4–120) minutes for DPE, and 18 (10–120) minutes for EPL. Compared with EPL, DPE had significantly greater incidence of bilateral S2 blockade at 10 minutes (risk ratio [RR] 2.13; 95% CI 1.39–3.28; $P < .001$), 20 minutes (RR 1.60; 95% CI 1.26–2.03; $P < .001$), and 30 minutes (RR 1.18; 95% CI 1.01–1.30; $P < .034$), a lower incidence of asymmetric block after 30 minutes (RR 0.19; 95% CI 0.07–0.51; $P < .001$) and physician top-up intervention (RR 0.45; 95% CI 0.23–0.86; $P = .011$). Compared with CSE, DPE had a significantly lower incidence of pruritus (RR 0.15; 95% CI 0.06–0.38; $P < .001$), hypotension (RR 0.38; 95% CI 0.15–0.98; $P = .032$), combined uterine tachysystole and hypertonus (RR 0.22; 95% CI 0.08–0.60; $P < .001$), and physician top-up intervention (RR 0.45; 95% CI 0.23–0.86; $p = .011$).

CONCLUSIONS: Analgesia onset was most rapid with CSE with no difference between DPE and EPL techniques. The DPE technique has improved block quality over the EPL technique with fewer maternal and fetal side effects than the CSE technique for parturients requesting early labor analgesia. (Anesth Analg 2017;124:560–9)

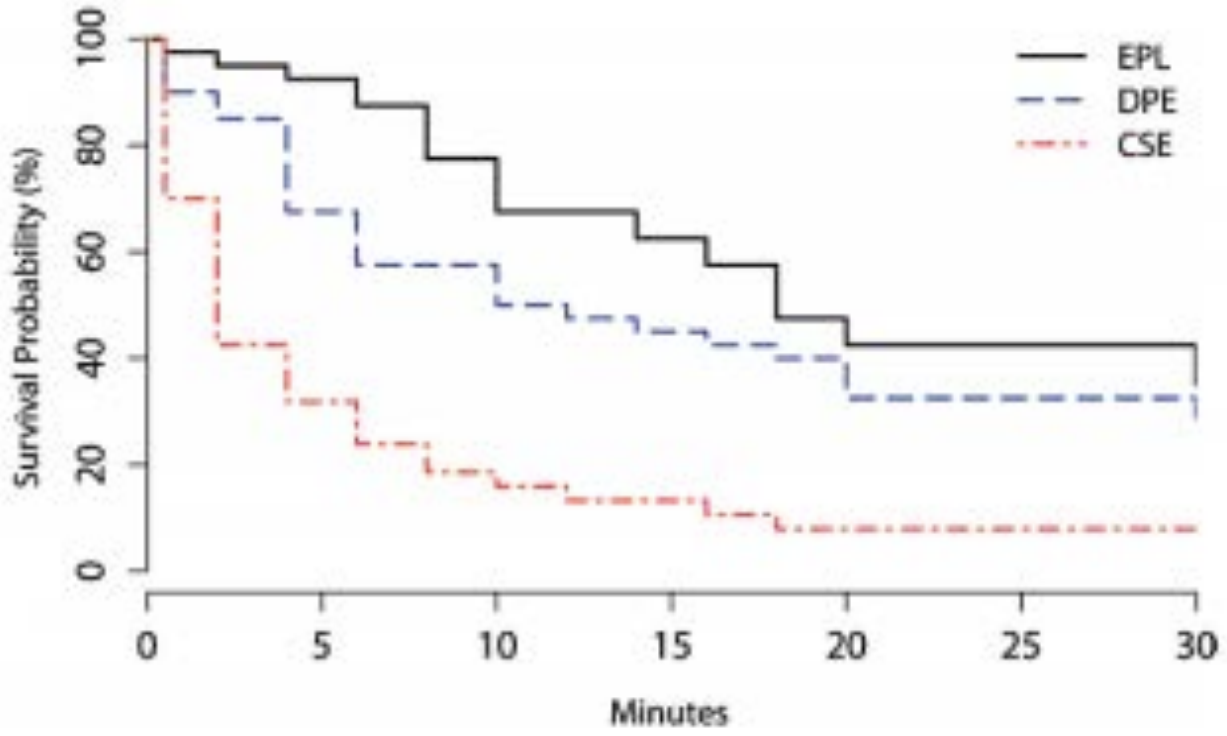


Table 3. Neuraxial Block Quality Parameters and Maternal Outcomes

	EPL (n = 40)	DPE (n = 40)	CSE (n = 40)
Duration of epidural infusion (min)	450 (200)	407 (275)	314 (189)
Sensory block height			
Highest level first 30 min	T4 [T2-T9]	T4 [T3-T8]	T4 [T2-T6]
Highest level any time	T4 [T2-T8]	T4 [T2-T8]	T4 [T2-T6]
Onset of analgesia			
NPRS ≤1 achieved at 0.5 min	1 (2.5)	6 (15)	14 (35)
NPRS ≤1 achieved at 10 min	16 (40)	20 (50)	35 (87.5)
NPRS ≤1 achieved at 20 min	30 (75)	32 (80)	38 (95)
NPRS ≤1 achieved at 30 min	31 (77.5)	35 (87.5)	38 (95)
Thoracic sensory block			
Bilateral T10 at 0.5 min	6 (15)	6 (15)	20 (50)
Bilateral T10 at 10 min	30 (75)	38 (95)	40 (100)
Bilateral T10 at 20 min	40 (100)	40 (100)	40 (100)
Bilateral T10 at 30 min	40 (100)	40 (100)	40 (100)
Sacral sensory block			
Bilateral S2 at 0.5 min	0 (0)	3 (7.5)	11 (27.5)
Bilateral S2 at 10 min	15 (37.5)	32 (80)	38 (95)
Bilateral S2 at 20 min	25 (62.5)	40 (100)	40 (100)
Bilateral S2 at 30 min	34 (85)	40 (100)	40 (100)
No S2 block entire duration	2 (5)	0 (0)	0 (0)
Asymmetric blocks			
First 30 min	23 (57.5)	16 (40)	8 (20)
After 30 min	21 (52.5)	4 (10)	4 (10)
Number of physician top-up interventions			
None	20 (50)	31 (77.5)	20 (50)
One or more	20 (50)	9 (22.5)	20 (50)
Time to first physician top-up (min)	207 (133)	250 (163)	132 (85)
Intervention			
Catheter adjustment	4 (10)	2 (5)	3 (7.5)
Catheter replacement	0 (0)	0 (0)	0 (0)
Motor block			
Bromage score, median [range]	0 [0–3]	0 [0–2]	0 [0–3]
Presence of motor block	15 (37.5)	6 (15)	3 (7.5)
Adverse effects			
Nausea	4 (10)	1 (2.5)	1 (2.5)
Pruritus	4 (10)	4 (10)	27 (67.5)
Hypotension	5 (12.5)	5 (12.5)	13 (32.5)
Postdural puncture headache	0 (0)	0 (0)	0 (0)
Mode of delivery			
Vaginal	28 (70)	31 (77.5)	35 (87.5)
Instrumental (vacuum or forceps)	1 (2.5)	5 (12.5)	3 (7.5)
Cesarean	11 (27.5)	4 (10)	2 (5)

Values are mean (SD), n (%), or median [range].

Systematic reviews and Meta-analyses

- Can become projects (“cheap” and can be “quick”)
- Require a very thorough knowledge of methodology and a very structured plan
- Do a structured assessment and review of literature
- Assess bias and report
- PRISMA guidelines

Other types of studies that can be done

Anesthesiology 2001; 94:767–72
© 2001 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Dose–Response Study of Epidural Ropivacaine for Labor Analgesia

Bee Beng Lee, M.B.B.S., F.A.N.Z.C.A., Warwick D. Ngan Kee, M.D., F.A.N.Z.C.A.,† Eliza L. Y. Wong, M.P.H.,‡ Justina Y. W. Liu, B.S.N.‡*

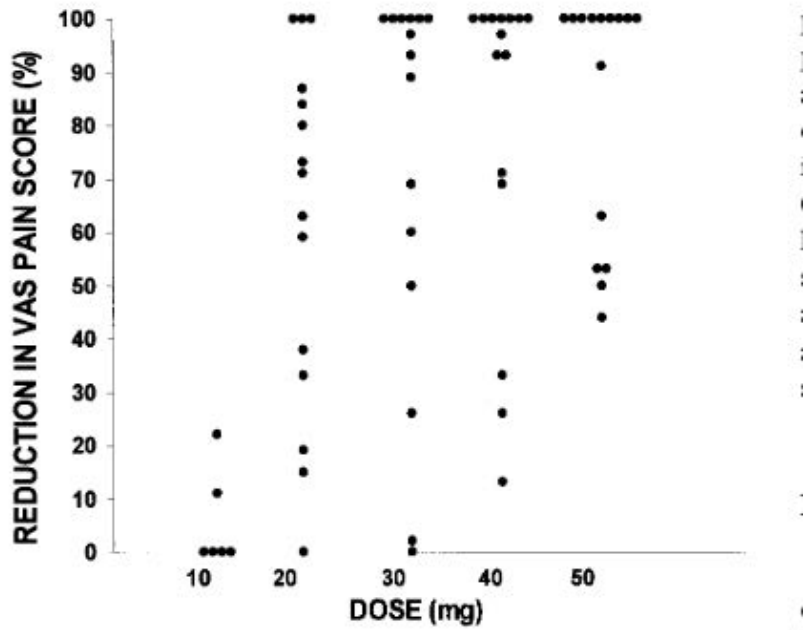
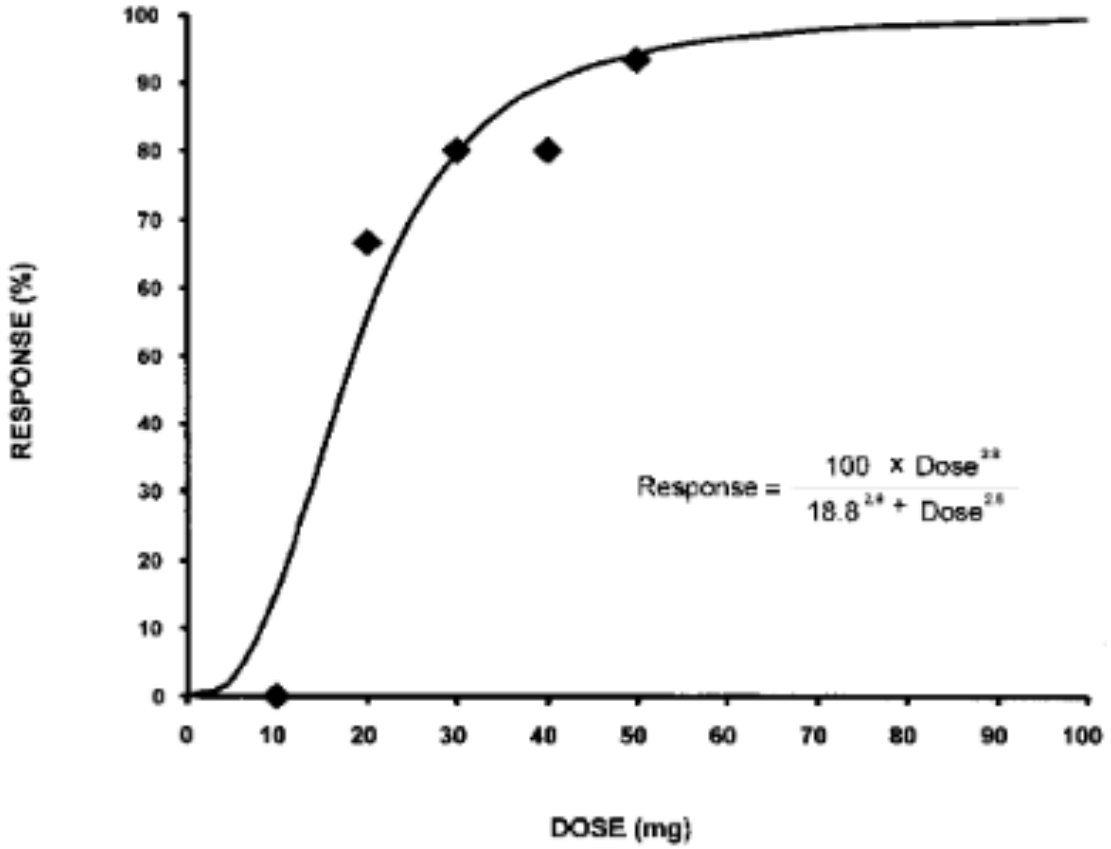


Fig. 1. Percentage reduction in visual analog scale (VAS) pain score for individual patients, with each point representing a patient.



Quality improvement projects

- Differ substantially from “research”
- Usually
  - Smaller cohorts
  - Not statistically complex (although encourage statistical comparison)
  - Often exempt from IRB / ethics committee approval (check !)
  - Very very practical

Example - implementation of PCEA

- **Prior**
  - **4 mL** Marcain 0,25% (2,5 mg/mL)
  - **4 mL** NaCl 0,9%
  - **1-2 ml** Sufentanyl (5 mcg/mL)

Marcain 0,125%

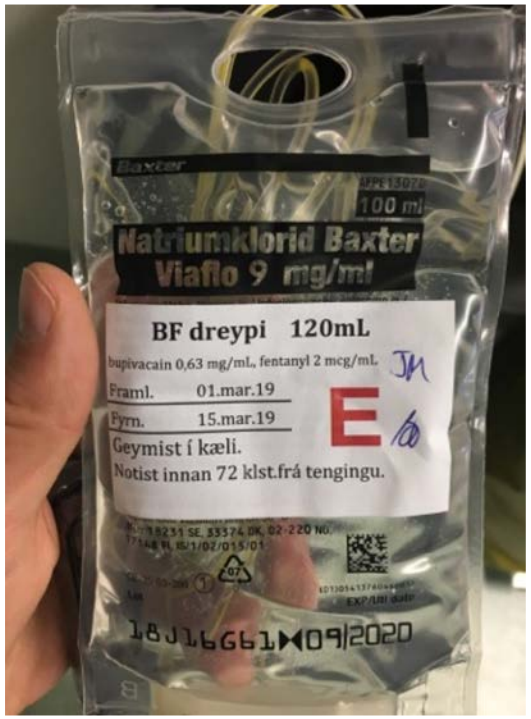
- Boluses by midwife, with consult as needed

New times!

- April **2018**.
- New mix (120 mL):
  - Marcain 0,0625%
  - NaCl 0,9%
  - Fentanyl 2 mcg/mL
- *Clinician bolus*
- *Continuous and bolus doses*

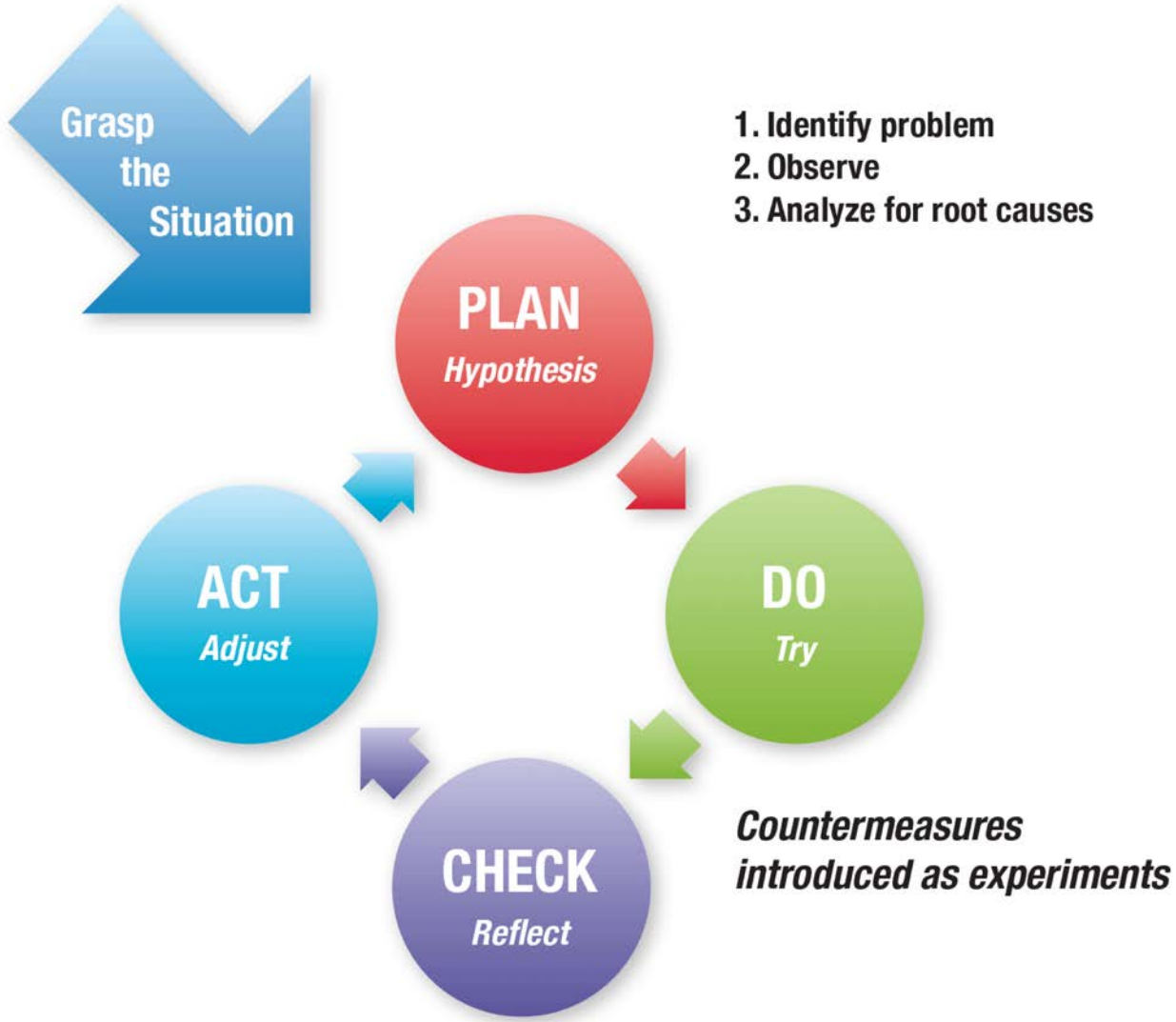
- Problems with pumps
  - Inadequate initial bolus
  - Perceived increased motor block w infusion
  - Concerns about opioids
  - Cost

Marcain 0,0625%



Overall goal - make epidurals great again

The Plan-Do-Check-Act Cycle



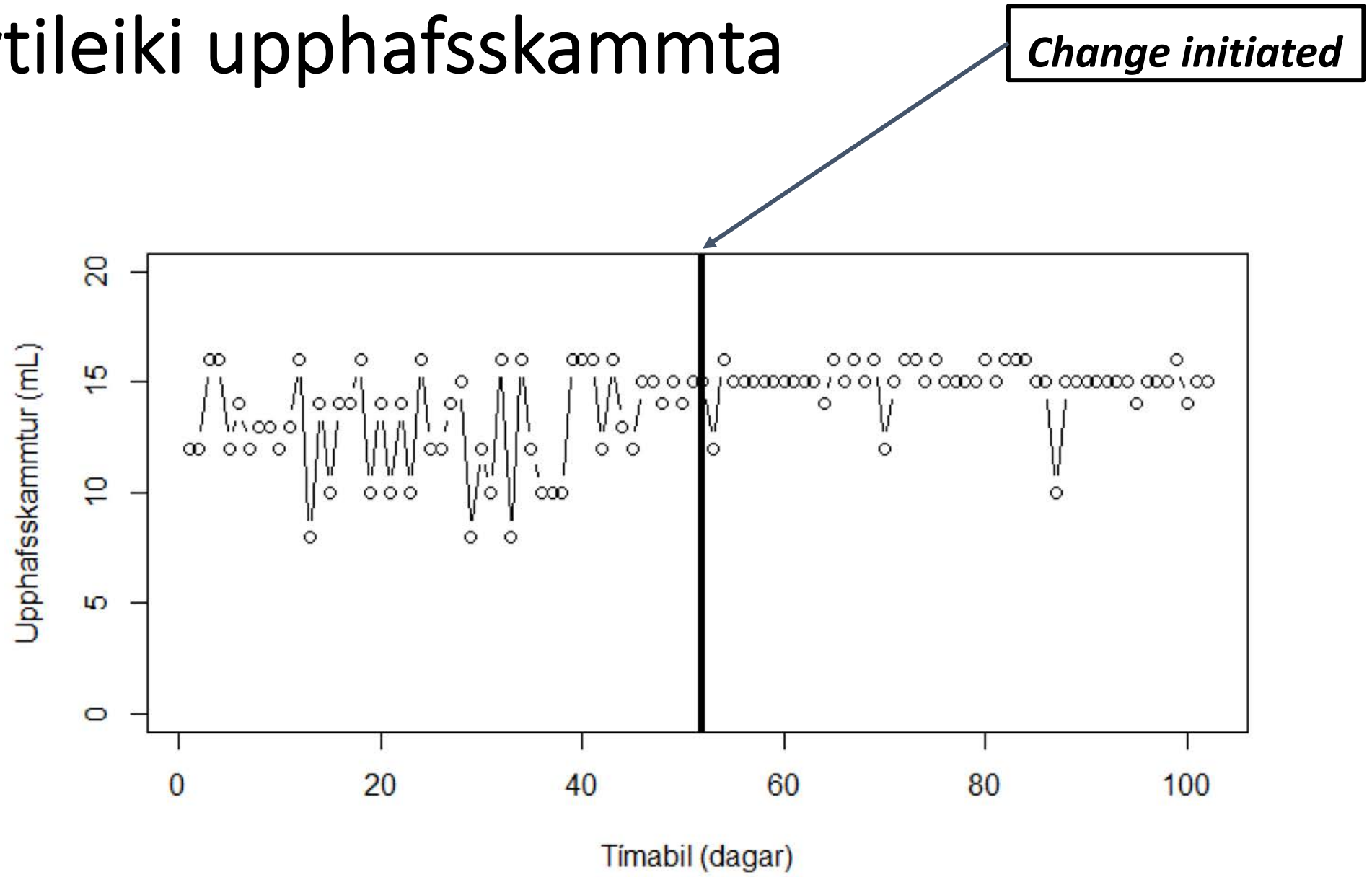
1. Identify problem
2. Observe
3. Analyze for root causes

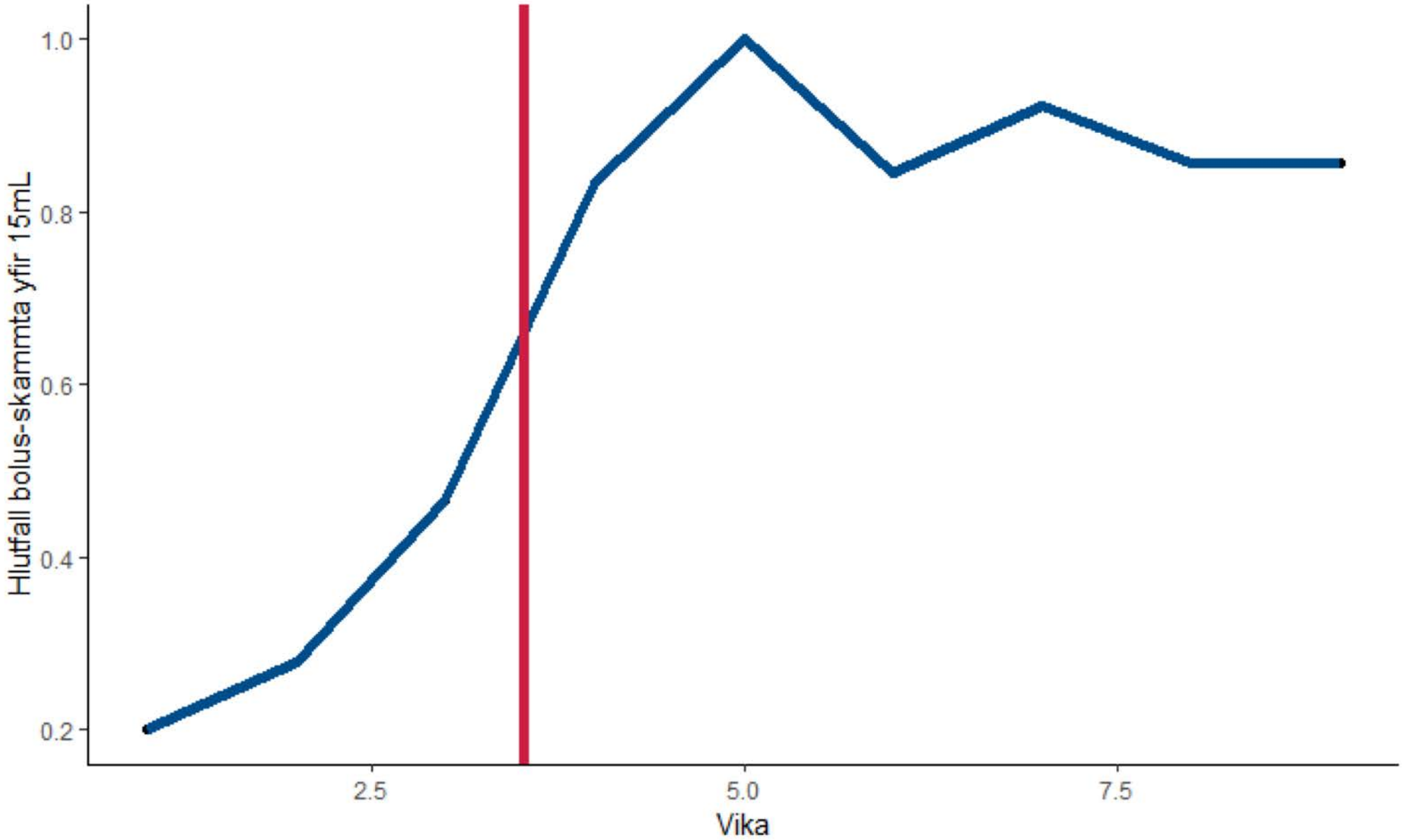
Countermeasures introduced as experiments

Make it small bites and chew one at a time

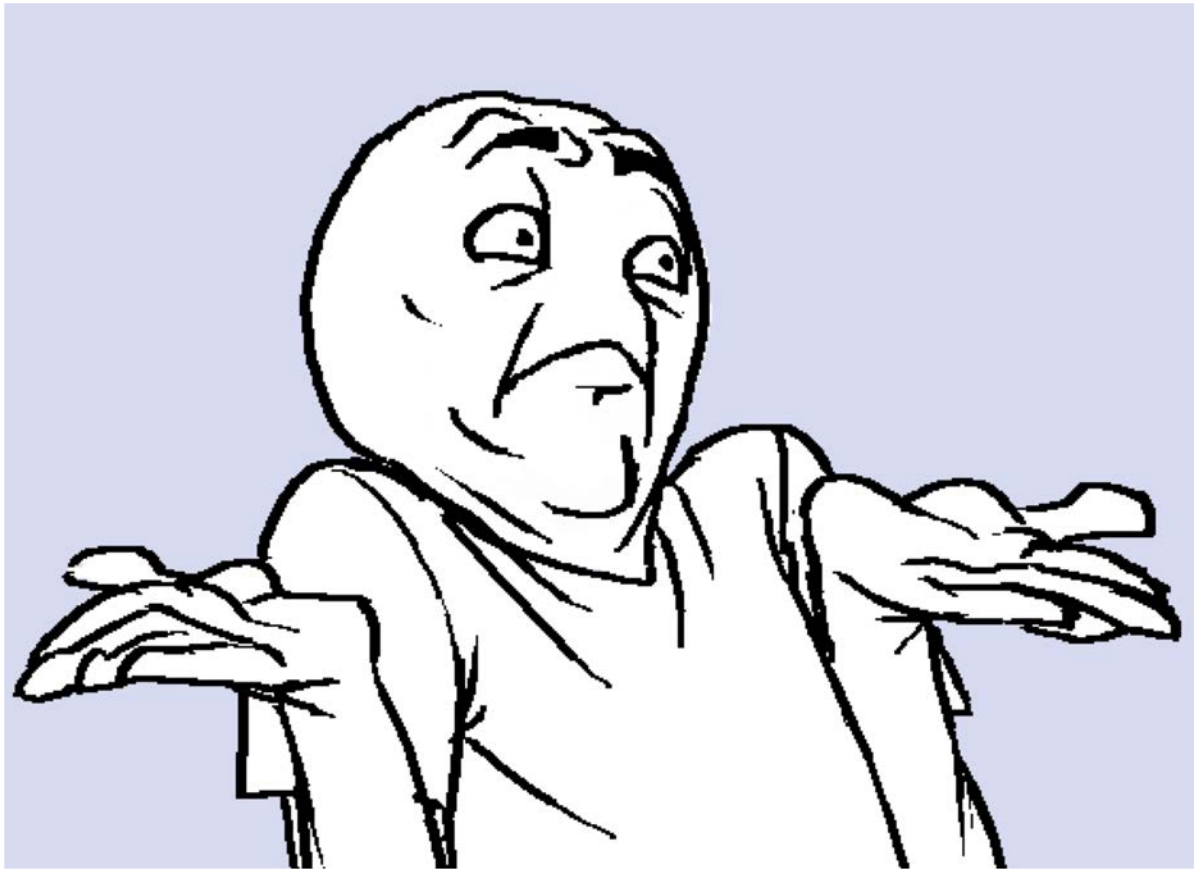
Clinician bolus

Breytileiki upphafsskammta

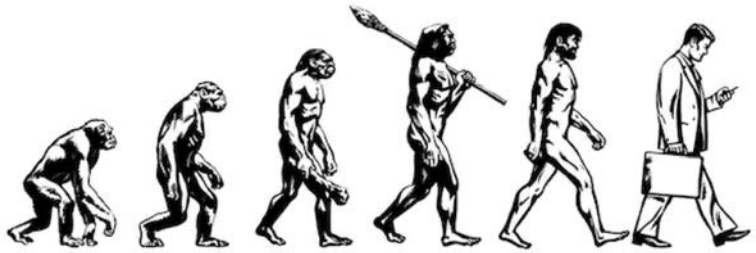



Hlutfall bolus-skammta yfir 15mL
1.0
0.8
0.6
0.4
0.2
2.5
5.0
7.5
Vika

Next bite - maintenance



Evolution



Apríl 2018 | **Mars 2019** | **Júlí 2019**

Prior to pumps

Initial
- **4 mL** Marcain
- **4 mL** NaCl
- **1-2 ml** Sufentanyl

Maintainence PN
- **4-5 mL** Marcain
- **4-5 mL** NaCl

Marcain 0,125 %

Now w pump

Initial
- **10 mL** BF inf
  - Marcain 0,0625%
  - Fentanyl (2 mcg/mL)

Maintenance
- **8 mL/klst** BF sídreypi

Bolus
- **8 mL** bolusar (midwife)

Marcain 0,0625 %

Circle no 1

Initial
- **15 mL** BF inf
  - Marcain 0,0625%
  - Fentanyl (2 mcg/mL)

Maintenance
- **8-10 mL/klst** BF cont

Bolus
- **8-10 mL** bolusar (midwife)

Marcain 0,0625 %

Maintenance

Initial
- **16 mL** BF inf
  - Marcain 0,0625%
  - Fentanyl (2 mcg/mL)

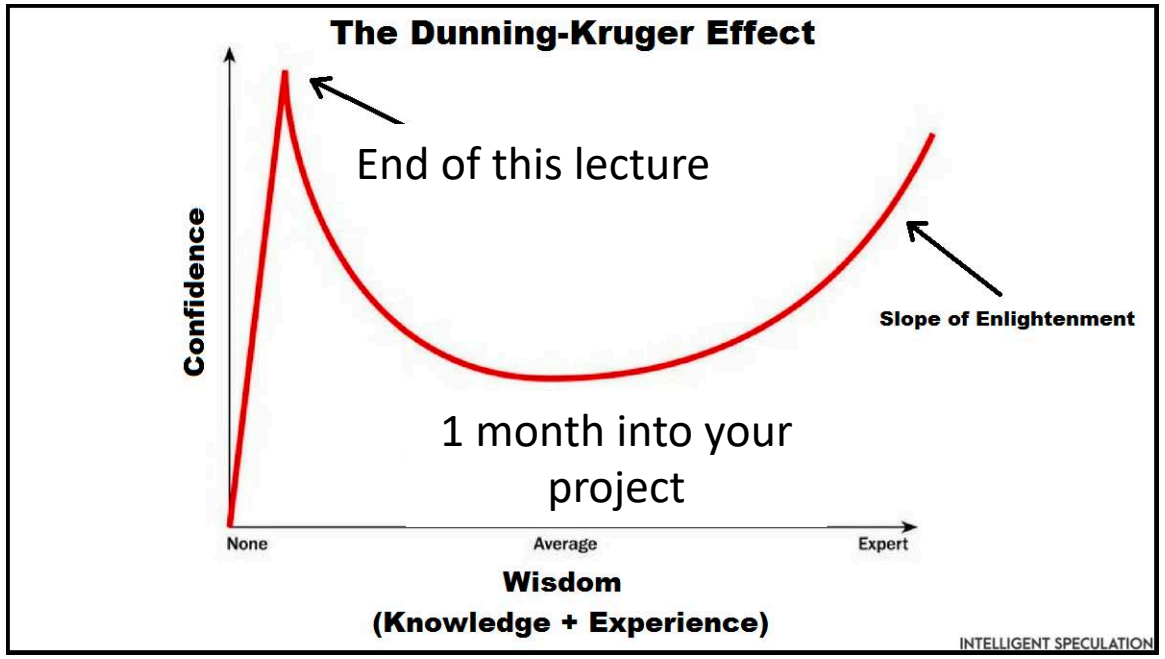
Viðhaldsskammtur
- **1 mL/klst** BF cont

Viðbótarskammtur
- **9,9 mL** bolusar (PCEA)

Marcain 0,0625 %

Summary

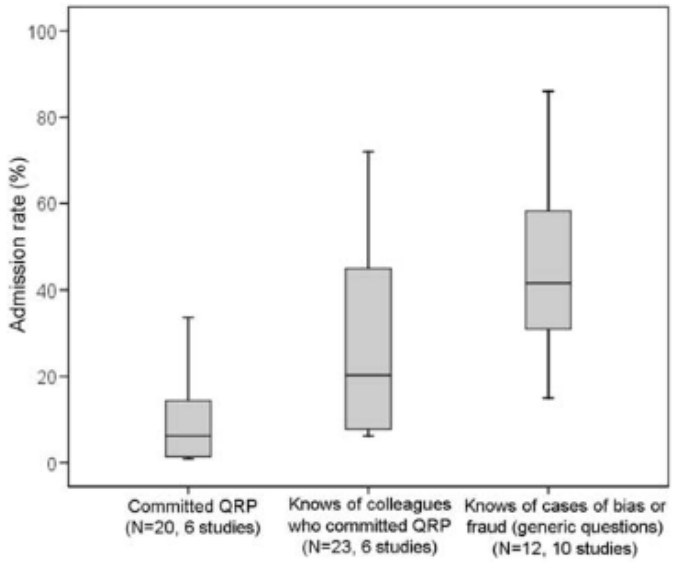
- Mentor and support team
- Power-analyze
- Types of projects
  - Retrospective cohort
  - Small randomized trial with a carefully selected outcome
  - Dose response
  - Quality improvement
  - Metaanalysis/Systematic review



Dishonesty in Science

What is the incidence of dishonesty

- Hard to know
  - Depends on self reporting
- Data fabrication
  - 1.97%
- Plagiarism
  - 1.7% (self-reported)
  - 17% (Analysis of 400 ms by software)
- Authorship problems (Survey of 900 papers in high impact journals)
  - 21%



RESEARCH Open Access

Plagiarism in submitted manuscripts: incidence, characteristics and optimization of screening—case study in a major specialty medical journal

Janet R. Higgins[1*], Feng-Chang Lin[2] and James P. Evans[3]

OPEN ACCESS Freely available online

PLoS on

How Many Scientists Fabricate and Falsify Research? A Systematic Review and Meta-Analysis of Survey Data

Daniele Fanelli*

INNOGEN and ISSTI-Institute for the Study of Science, Technology & Innovation, The University of Edinburgh, Edinburgh, United Kingdom

BMJ

BMJ 2011;343:d6128 doi: 10.1136/bmj.d6128 Page 1 of 7

RESEARCH

Honorary and ghost authorship in high impact biomedical journals: a cross sectional survey

OPEN ACCESS

Joseph S Wislar *survey research specialist, JAMA*, Annette Flanagin *managing deputy editor, JAMA*, Phil B Fontanarosa *executive editor, JAMA*, Catherine D DeAngelis *editor emerita, JAMA*

Dishonesty in anesthesia literature

Leaderboard

Who has the most retractions? Here's our unofficial list (see notes on methodology), which we'll update as more information comes to light:

1. Yoshitaka Fujii (total retractions: 183) See also: Final report of investigating committee, our reporting, additional coverage
2. Joachim Boldt (97) See also: Editors-in-chief statement, our coverage
3. Yoshihiro Sato (84) See also: our coverage
4. Jun Iwamoto (64) See also: our coverage
5. Diederik Stapel (58) See also: our coverage
6. Yuhji Saitoh (53) See also: our coverage
7. Adrian Maxim (48) See also: our coverage
8. Chen-Yuan (Peter) Chen (43) See also: SAGE, our coverage
9. Fazlul Sarkar (41) See also: our coverage
10. Hua Zhong (41) See also: journal notice

https://retractionwatch.com/the-retraction-watch-leaderboard/

Why are people dishonest

- Publish or perish
  - Publishing high-profile paper in a high-impact journal gets you
    - Graduated
    - A good job in academia
    - Promotion
    - Funding
  - It is easier to publish “positive” studies, and ”interesting” stories
  - Journal editors participate in this with “publication bias”
    - Botulinum toxin for prevention of atrial fibrillation story!
- Every scientist wants to have
  - Nature/Science paper featured in the New York Times

Different types of dishonesty

- Plagiarism – probably most common
  - Taking someone's idea/work and presenting it as your own
- Plagiarism
  - Of ideas
  - Plagiarism of data
  - Plagiarism of manuscript text
  - Plagiarism from reviewers!
  - Self-plagiarism

Ophthalmic Research

Editorial

Ophthalmic Res 2004;36:1–3
DOI: 10.1159/000076104

Scientific Misconduct:
From Salami Slicing to Data Fabrication

Stefania M. Mojon-Azzi[a] Daniel S. Mojon[a, b]

[a]Department of Ophthalmology, [b]Scientific Secretary, Swiss Society of Ophthalmology, Kantonsspital St. Gallen, St. Gallen, Switzerland

Plagiarism of manuscript text

- Very common
- Many journals now use automatic software to detect it (usually you are notified of it)
  - Turnitin
- Also commonly used to detect plagiarism in admission essays etc.

Example / case report received for revision

From the submission:
A 24-year-old woman with no other significant co morbidities presented with history of palpitations and breathlessness on exertion of NYHA class III for 6week duration. On examination she was found to have continuous murmur in the right second intercostals space with peripheral signs of aortic run off.

From the published case report A 42-year-old man with no other significant comorbidities presented with history of palpitations and shortness of breath on exertion for 6 years duration. On examination he was found to have continuous murmur in the right second intercostal space with peripheral signs of aortic run off.

From the submission:
Subsequently she underwent aortic root angiography which confirmed aneurysm of right coronary sinus rupturing into right atrium forming a tunnel. Right coronary artery had its origin just above the aneurysm (figure 2, 3).

From the published case report
Subsequently he underwent cardiac catheterisation with oximetry and coronary angiography which confirmed aneurysm of left aortic sinus Valsalva rupturing into right atrium forming a tunnel (figures 3 and and4).4). Left main coronary artery had its origin from the aneurysm.

From the submission:

Patients succumbs to death from congestive heart failure usually occurs within a year after rupture, however longer survival after small slow perforation is well described. SVA can present in various ways such as rupture into cardiac chamber with subsequent cardiac failure, acute coronary syndrome, cardiac tamponade, heart block, aortic regurgitation and right ventricular outflow tract obstruction.[5] Majority of SVA arising from right coronary sinus ruptures in right ventricle and those arising from non-coronary sinus ruptures into RA.[6]

From the published case report:

Death from congestive heart failure usually occurs within a year after rupture, however longer survival after small slow perforation is well described. SVA can present in various ways such as rupture into cardiac chamber with subsequent cardiac failure, acute coronary syndrome, cardiac tamponade, heart block, aortic regurgitation and right ventricular outflow tract obstruction.5

Majority of SVA arising from right coronary sinus ruptures in right ventricle and those arising from non-coronary sinus ruptures into RA.3

Wrote to the editor reccomending rejection – MS promptly rejected

Usually not an isolated case

- Identified a published manuscript by multiple of the same authors, and found the same pattern

Brueck et al. 2009

Objectives: **The aim of the study was to evaluate the safety, feasibility, and procedural variables by the transradial approach compared with the transfemoral access in a standard population of patients undergoing coronary catheterization.**

Sinha et al. 2016

Background and Aim. **The aim of study was to evaluate safety, feasibility, and procedural variables of transradial approach compared with transfemoral approach in a standard population of patients undergoing coronary catheterization** as one of the major criticisms of the transradial approach is that it takes longer overall procedure and fluoroscopy time, thereby causing more radiation exposure.

Brueck et al. 2009

Results: **Successful catheterization was achieved in 494 of 512 patients (96.5%) in the transradial and in 511 of 512 patients (99.8%) in the transfemoral group (p < 0.0001).** Median procedural duration (37.0 min, interquartile range [IQR] 19.6 to 49.1 min vs. 40.2 min, IQR 24.3 to 50.8 min; p = 0.046) and median dose area product (38.2 $Gycm^2$, IQR 20.4 to 48.5 $Gycm^2$ vs. 41.9 $Gycm^2$, IQR 22.6 to 52.2 $Gycm^2$; p = 0.034) were significantly lower in the transfemoral group compared with the transradial access group. A median amount of contrast agent was similar among both groups. Vascular access site complications were higher in the transfemoral group (3.71%) than in the transradial group (0.58%; p = 0.0008)

Sinha et al. 2016

Result. **Successful catheterization was achieved in 1045 of 1076 patients (97.1%) in the transradial group and in 918 of 921 patients (99.7%) in the transfemoral group (*p*= 0.001).** Comparing the transradial and transfemoral approaches, fluoroscopy time (2.46 ± 1.22 versus 2.83 ± 1.31 min; *p* = 0.32), procedure time (8.89 ± 2.72 versus 9.33 ± 2.82 min; *p* = 0.56), contrast volume (67.52 ± 22.54 versus 71.63 ± 25.41 mL; *p* = 0.32), radiation dose as dose area product (24.2 ± 4.21 versus 22.3 ± 3.46 $Gycm^2$; *p* = 0.43), and postprocedural rise of serum creatinine (6 ± 4.5% versus 8 ± 2.6%; *p* = 0.41) were not significantly different while vascular access site complications were significantly lower in transradial group than transfemoral group (3.9% versus 7.6%; *p* = 0.04).

18 months later!

Sara Elzafarany <sara.elzafarany@hindawi.com>
to me, Martin.Brueck

Dear Dr. Sigurdsson,

My name is Sara Elzafarany; I am a Research Integrity Specialist at Hindawi Publishing Corporation. Thank you for bringing this matter to our attention. We are investigating this in order to take the necessary actions.

Best regards,

Sara

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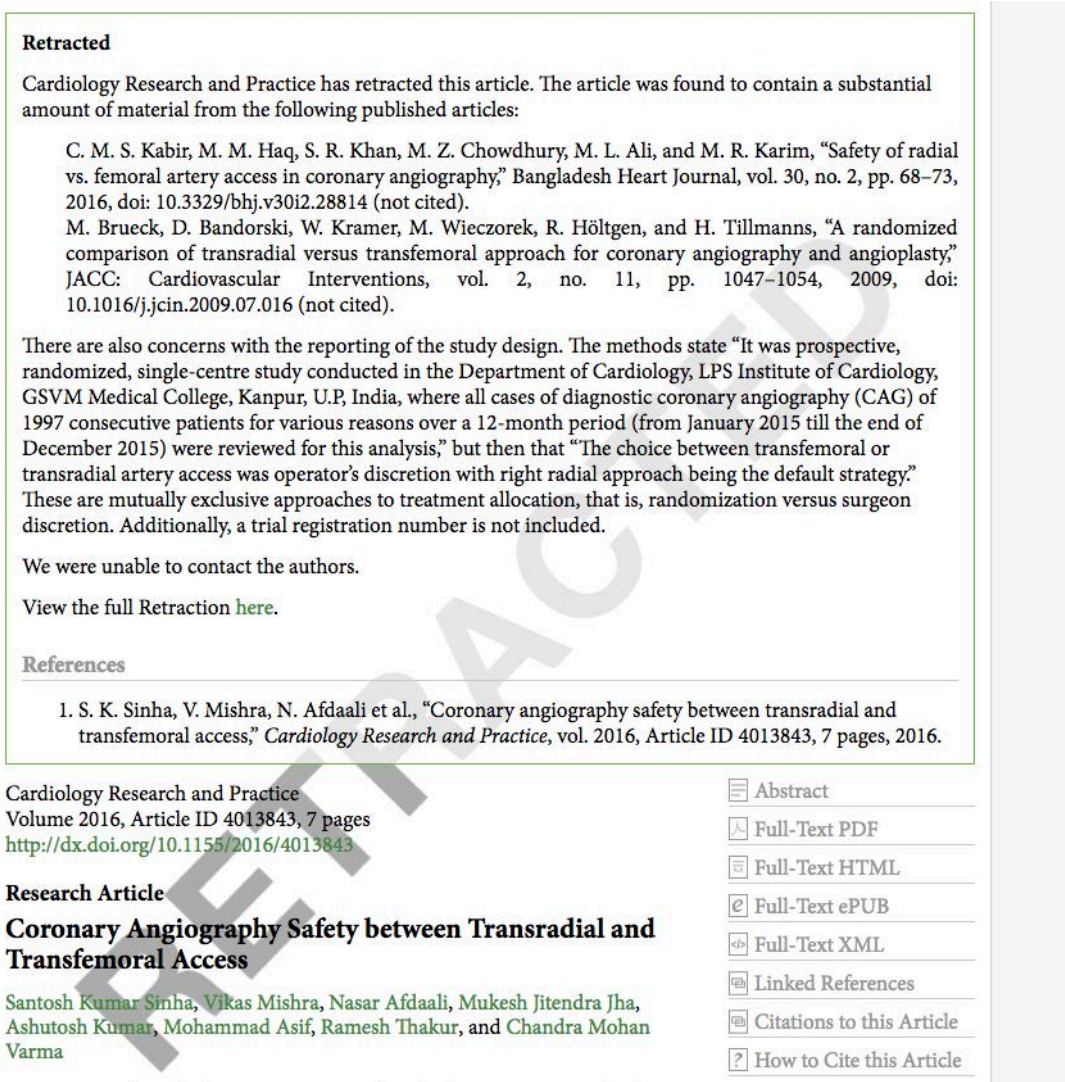
****
Sara Elzafarany
Research Integrity Specialist
Hindawi Publishing Corporation
http://www.hindawi.com
****



Retracted

Cardiology Research and Practice has retracted this article. The article was found to contain a substantial amount of material from the following published articles:

C. M. S. Kabir, M. M. Haq, S. R. Khan, M. Z. Chowdhury, M. L. Ali, and M. R. Karim, "Safety of radial vs. femoral artery access in coronary angiography," Bangladesh Heart Journal, vol. 30, no. 2, pp. 68–73, 2016, doi: 10.3329/bhj.v30i2.28814 (not cited).

M. Brueck, D. Bandorski, W. Kramer, M. Wieczorek, R. Höltgen, and H. Tillmanns, "A randomized comparison of transradial versus transfemoral approach for coronary angiography and angioplasty," JACC: Cardiovascular Interventions, vol. 2, no. 11, pp. 1047–1054, 2009, doi: 10.1016/j.jcin.2009.07.016 (not cited).

There are also concerns with the reporting of the study design. The methods state "It was prospective, randomized, single-centre study conducted in the Department of Cardiology, LPS Institute of Cardiology, GSVM Medical College, Kanpur, U.P, India, where all cases of diagnostic coronary angiography (CAG) of 1997 consecutive patients for various reasons over a 12-month period (from January 2015 till the end of December 2015) were reviewed for this analysis," but then that "The choice between transfemoral or transradial artery access was operator's discretion with right radial approach being the default strategy." These are mutually exclusive approaches to treatment allocation, that is, randomization versus surgeon discretion. Additionally, a trial registration number is not included.

We were unable to contact the authors.

View the full Retraction here.

References

1. S. K. Sinha, V. Mishra, N. Afdaali et al., "Coronary angiography safety between transradial and transfemoral access," *Cardiology Research and Practice*, vol. 2016, Article ID 4013843, 7 pages, 2016.

Cardiology Research and Practice
Volume 2016, Article ID 4013843, 7 pages
http://dx.doi.org/10.1155/2016/4013843

Research Article

Coronary Angiography Safety between Transradial and Transfemoral Access

Santosh Kumar Sinha, Vikas Mishra, Nasar Afdaali, Mukesh Jitendra Jha, Ashutosh Kumar, Mohammad Asif, Ramesh Thakur, and Chandra Mohan Varma

Abstract
Full-Text PDF
Full-Text HTML
Full-Text ePUB
Full-Text XML
Linked References
Citations to this Article
How to Cite this Article

RETRACTED

Self – plagiarism (text recycling)

- Using text from a prior manuscript in a current one
  - Often materials an methods
  - Note that publication wrights are handed to publisher

- COPE guidelines (https://publicationethics.org/text-recycling-guidelines)
  - If minor and identified during review, offer rewriting, if major reject
  - If minor and identified after publication, correction vs retraction
- Recommend rewriting all text for every publication
  - Including methods
  - Cite previous work!

How to prevent this

- Write entire paper at all times
  - Including methods
- Use plagiarism checker
  - Before submitting!
  - When reviewing
- Cite generously all papers
  - In particular prior papers relied on during data collection/analysis and manuscript writing

Dishonesty during data collection and analysis

- Fabrication
  - Making up data or results and record them or report them
- Falsification
  - Manipulating research materials or results, changing data, omitting data or results
  - This can include intentional incorrect statistical methods

Fabrication example – Yoshitaka Fujii

- https://retractionwatch.com/category/yoshitaka-fujii/
- Over 100 published papers with fabricated data
- Discovered by a reader of his paper (John Carlisle)

Anaesthesia 2012, 67, 521–537 doi:10.1111/j.1365-2044.2012.07128.x

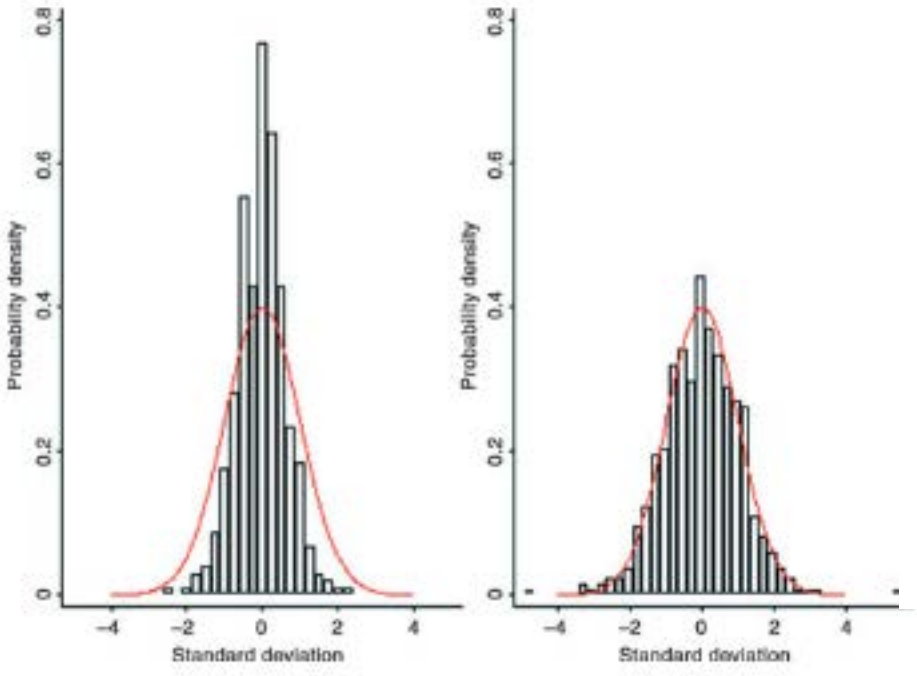
Special Article

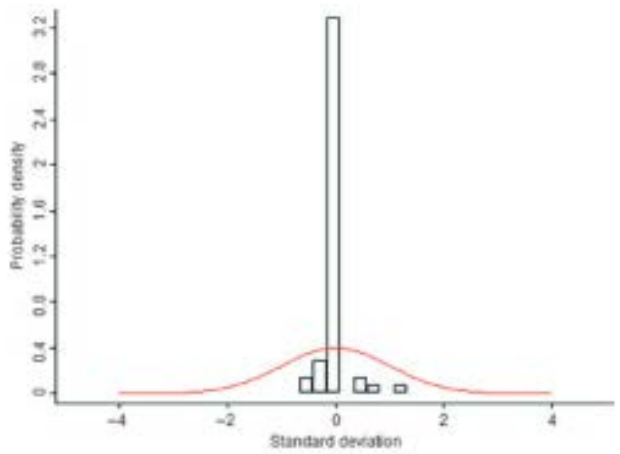
The analysis of 168 randomised controlled trials to test data integrity

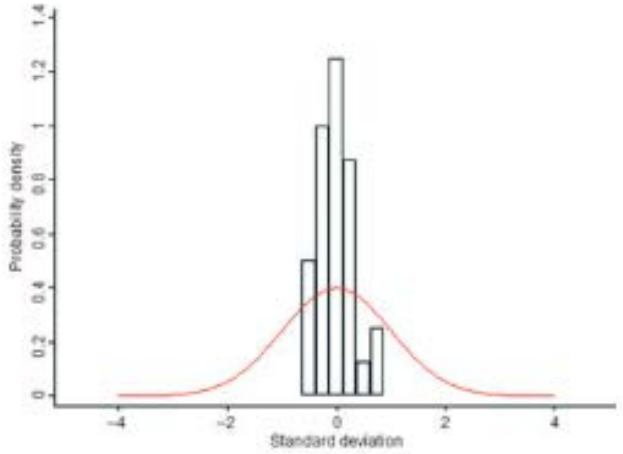
J. B. Carlisle

Consultant Anaesthetist, Torbay Hospital, South Devon NHS Foundation Trust, Torquay, UK

Fujii et al – complete fabrication of data sets







More common – falsification of data

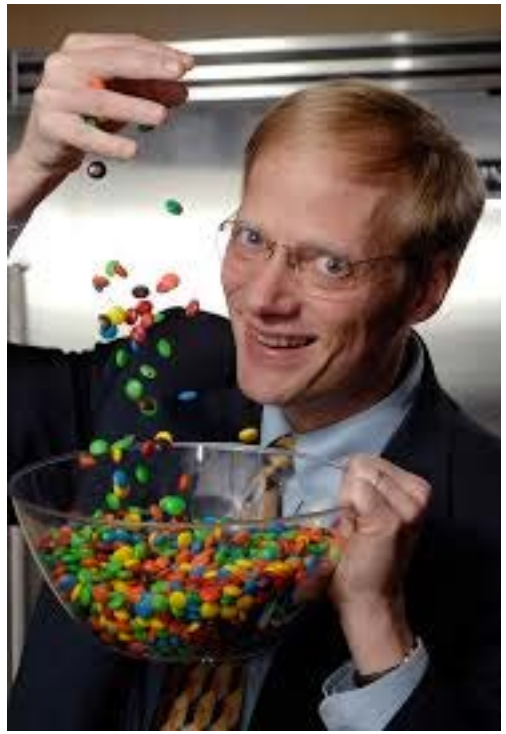
- Removing “outliers”
- Removing or adding data points to fit with theory
- Adding or reusing control samples inappropriately
- Changing the statistical analysis plan (p-hacking)

P-hacking

- Exploring same dataset for trends of “statistically significant” findings, and then conduct a story around the finding
- If you do 20 statistical tests on a data set, one of them will be less than 0.05 by random
- Importance of adjusting for multiple testing

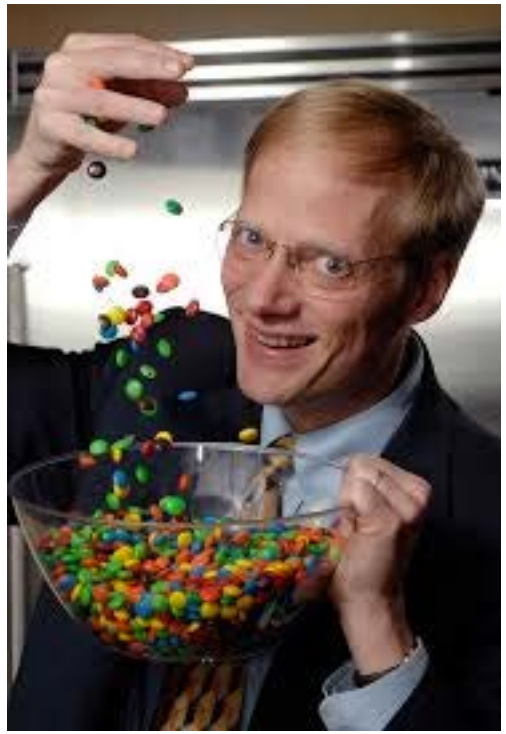
Brian Wanshink

- 20,000 citations. High-profile food/nutrition researcher
- Head of Cornell´s food phychology research unit
- New York Times, Oprah etc



P-hacking example Brian Wanshink

- https://retractionwatch.com/?s=wansink
- In 2016:

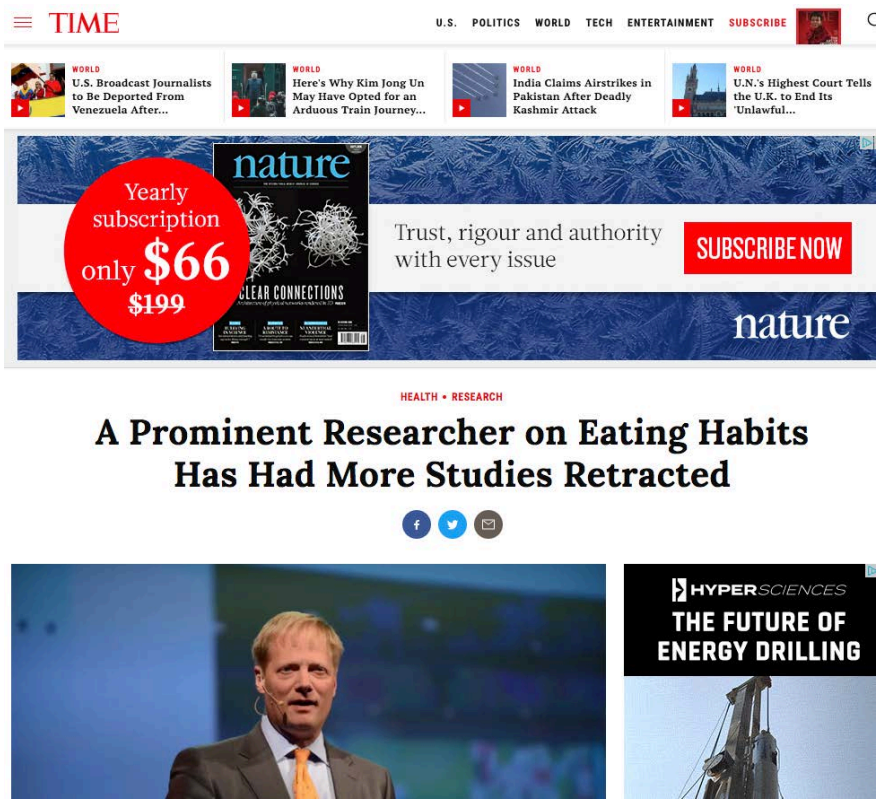


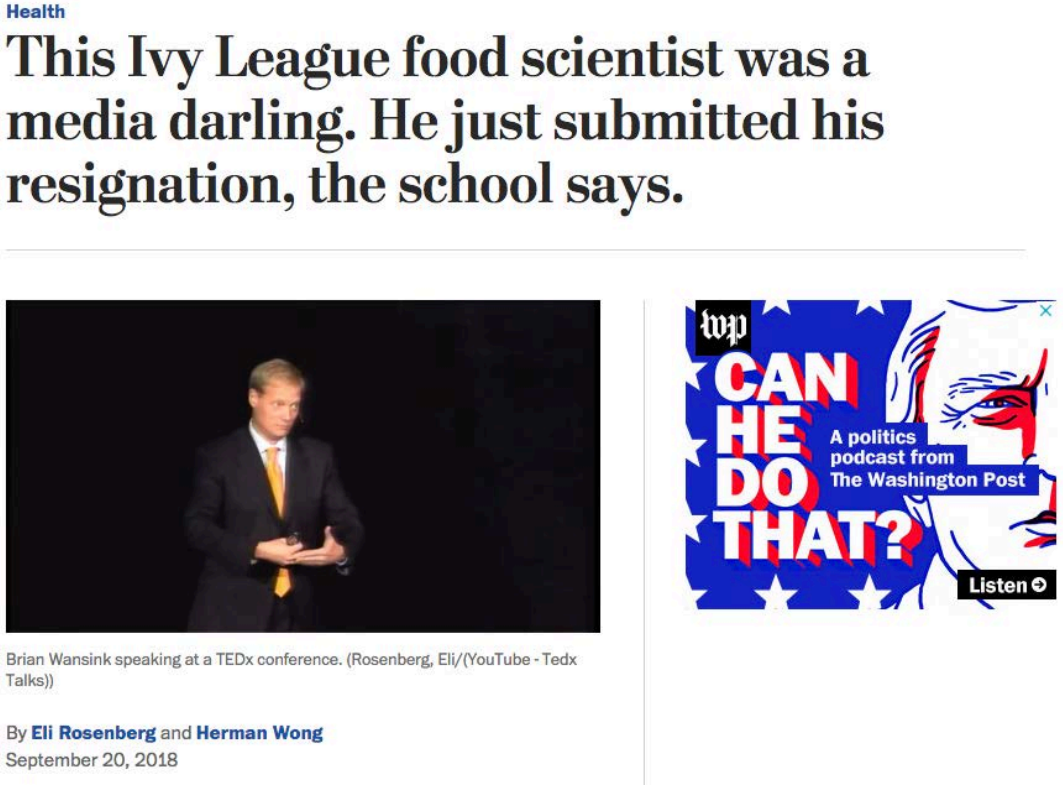
Here is a description of the original research, from Wansink's November post:

> *When [the graduate student] 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 ½ 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.*

This started review of all of his papers

- http://www.timvanderzee.com/the-wansink-dossier-an-overview/





Solution

- Pre-registering trials including analysis plan
  - Even publishing protocol a priori
- Adjustment for multiple testing
  - And honesty in reporting what was tested
- Disclaiming any concerns
  - i.e. reusing controls, combining trials etc

During writing / publication of the manuscript

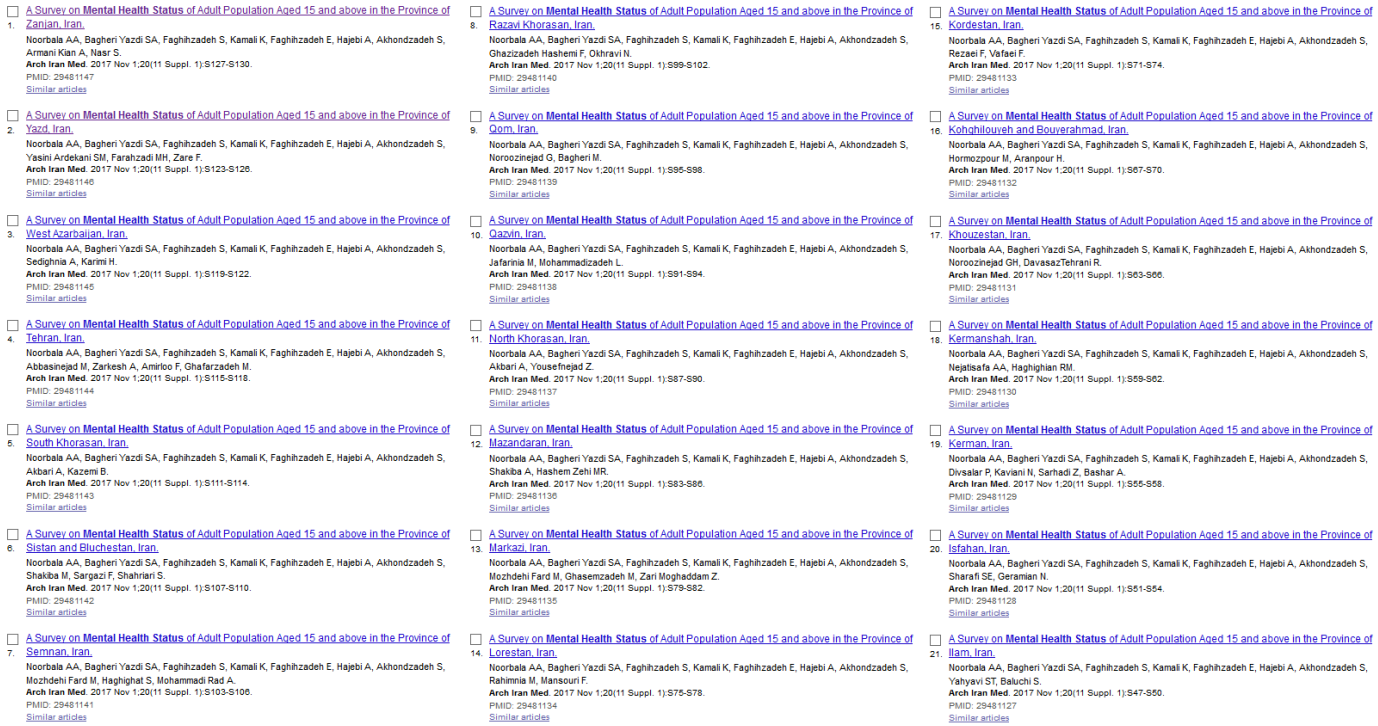
- Salami slicing
- Double publication
- Authorship issues
- Sham reviews

Salami slicing

- Utilizing “least publishable unit” to the edge
  - Smallest measurable amount of information that can be used to generate a peer-reviewed paper
- Splitting up data into multiple smaller publications without scientific reason

Salami slicing

- https://www.ncbi.nlm.nih.gov/pubmed/?term=noorbola+aa%2C+Kamali



1. A Survey on **Mental Health Status** of Adult Population Aged 15 and above in the Province of Zanjan, Iran.
Noorbala AA, Bagheri Yazdi SA, Faghihzadeh S, Kamali K, Faghihzadeh E, Hajebi A, Akhondzadeh S, Armani Kian A, Nasr S.
Arch Iran Med. 2017 Nov 1;20(11 Suppl. 1):S127-S130.
PMID: 29481147
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2. A Survey on **Mental Health Status** of Adult Population Aged 15 and above in the Province of Yazd, Iran.
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PMID: 29481144
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Arch Iran Med. 2017 Nov 1;20(11 Suppl. 1):S111-S114.
PMID: 29481143
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Arch Iran Med. 2017 Nov 1;20(11 Suppl. 1):S107-S110.
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PMID: 29481141
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PMID: 29481140
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Arch Iran Med. 2017 Nov 1;20(11 Suppl. 1):S95-S98.
PMID: 29481139
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PMID: 29481138
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Arch Iran Med. 2017 Nov 1;20(11 Suppl. 1):S87-S90.
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Noorbala AA, Bagheri Yazdi SA, Faghihzadeh S, Kamali K, Faghihzadeh E, Hajebi A, Akhondzadeh S, Shakiba A, Hashem Zehi MR.
Arch Iran Med. 2017 Nov 1;20(11 Suppl. 1):S83-S86.
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Noorbala AA, Bagheri Yazdi SA, Faghihzadeh S, Kamali K, Faghihzadeh E, Hajebi A, Akhondzadeh S, Rezaei F, Vafaei F.
Arch Iran Med. 2017 Nov 1;20(11 Suppl. 1):S71-S74.
PMID: 29481133
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Noorbala AA, Bagheri Yazdi SA, Faghihzadeh S, Kamali K, Faghihzadeh E, Hajebi A, Akhondzadeh S, Hormozpour M, Aranpour H.
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Noorbala AA, Bagheri Yazdi SA, Faghihzadeh S, Kamali K, Faghihzadeh E, Hajebi A, Akhondzadeh S, Noroozinejad GH, DavasazTehrani R.
Arch Iran Med. 2017 Nov 1;20(11 Suppl. 1):S63-S66.
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Noorbala AA, Bagheri Yazdi SA, Faghihzadeh S, Kamali K, Faghihzadeh E, Hajebi A, Akhondzadeh S, Nejatisafa AA, Haghighian RM.
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- Ghost authorship
- Gratuitous authorship
- Input from industry sponsor
- Ghost writer
- Unfair order of authors

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- https://publicationethics.org/authorship

International Committee of Medical Journal Editors (ICMJE)

The ICMJE recommends that an author should meet all four of the following criteria:

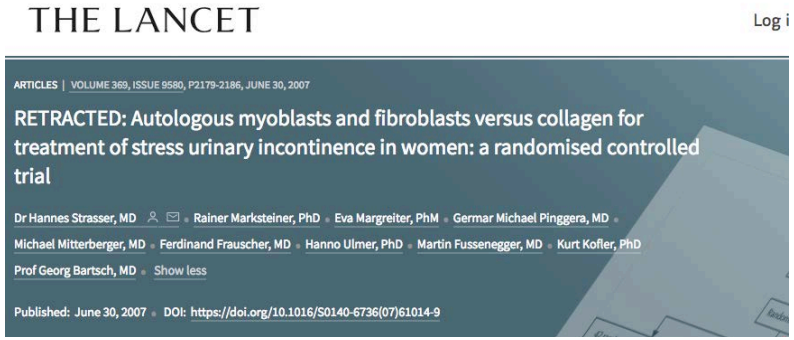
- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work;
- Drafting the work or revising it critically for important intellectual content;
- Final approval of the version to be published;
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved."

Ghost authorship

- Someone writes the manuscript but is not listed as an author
- Often related to publications for industry
- Often related in large-scale trials
- Should be acknowledged
  - Then technically is not ghost authorship
- Also
  - Someone who should be an author is left out of the author lists

Gratuitous (gift) authorship

- Adding someone to the author list as a favor to them
- No contribution to the work
- Do not accept gift authorship!
  - Responsible for content of paper
  - https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(08)61320-3/fulltext
  - Here a paper was retracted for no consent, no ethics committee approval, forged documents etc.
  - Senior author: Had no part in study, requested his name to be removed from paper during investigation



Guest authorship

- Including a famous / senior scientist as a coauthor without contribution from them
  - Hope to get approved to a better journal
- Same concerns regarding guest and gift authorship
  - Do not accept
  - Do not add them
  - And obviously all authors should agree to be authors prior to submission

Unfair order of authors

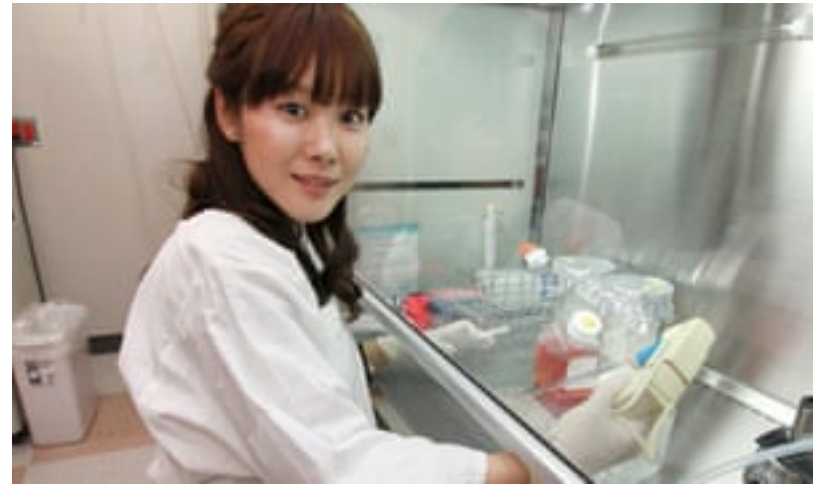
- Exceedingly common cause for dispute, occasionally results in retraction of papers
- https://publicationethics.org/authorship
- General tips
  - Behave ethically
  - Discuss authorship when planning research
  - Decide authorship before you start each article

Misleading citations

- Biased
  - By author (self-citations)
  - By institution
  - By country
  - By continent
- Dishonesty by reviewers / journal editors
  - Requesting referrals to specific journal
  - Requesting citations to own publications

STAP story

- https://www.newyorker.com/magazine/2016/02/29/the-stem-cell-scandal
- Charles Vacanti
  - Stem cell researcher and chair of Anesthesiology at Harvard Medical School/Brigham and Women´s Hospital
  - Idea on how to generate stem cells by “harsh treatment” of other cells (acid treatment, harsh pipetting)
  - STAP - stimulus-triggered acquisition of pluripotency
  - Gets a postdoc from Riken institute to work on project
- Haruko Obokata
  - Post-doc from prestigious Riken institute in Japan
    - PhD on spore-like cells (close to STAP cells)
  - Starts work on generating and proving STAP cells
- Wakayama – prominent researcher included in project



STAP story

- Sasai
  - Prominent stem cell researcher at Riken, starts collaborating to get results published (after Nature rejection)
  - "With a magic spell that Haruko discovered, the chain of ‘epigenetic curse’ of differentiation is unexpectedly broken,” he wrote. “Under your admirably generous support, Haruko unveiled it with her God-given ingenuity and developed the research to this highest level.”
- 2014
  - Nature publishes two back-to back papers on STAP cells
  - Widespread attention – Nobel prize thoughts etc
  - Obokata becomes a star in Japan

STAP story

- Immediately
  - Duplicated images found in papers
  - More images from PhD thesis found in papers
  - Obokatas PhD thesis found to be plagiarized
  - Noone can replicate cells (protocol published)
- Riken starts investigating
  - Obokata is supposed to generate cells under video surveillance
- Four months later
  - Nature retracts both paper (seven high-impact labs fail to replicate)

STAP story

- Vacanti
  - Resigned as chair of the department at Harvard/ Brigham and Women´s
- Obokata
  - Lost her PhD
  - Admitted to psychiatric institution
  - Published a book claiming supervisors were responsible
- Sasai
  - Committed suicide in 2014
  - Letter: “make sure you reproduce STAP cells”

Summary - discussions

- There is a wide range of research dishonesty
- Distribute authorship fairly and ahead of time
- Take care in reusing text even written by yourself

martin@Landspitali.is

Few “horror” stories

LaCour - Science 2014

- https://retractionwatch.com/2015/05/20/author-retracts-study-of-changing-minds-on-same-sex-marriage-after-colleague-admits-data-were-faked/
- PhD student – LaCour
  - Short conversation can change the mindset towards same-sex marriage
- 2014 Science paper – NY times, NPR, Wall Street Journal picked up

Science 2014

- Two other graduate students at UC Berkeley wanted to extend study
  - Very high test-retest reliability, and response rate very high
  - Unable to get the same response
    - Contacted firm responsible for conducting the study – firm did not do study
    - Re-analysis of raw dataset shows distribution of variables between two studies by same first author is identical
- Contacted senior author – concerned
  - First author claims database was accidentally deleted – incorrect
  - First author will not release information on survey responders for participation verification
  - Cash incentives for study participations did not exist
- Senior author requests retraction, looses a grant
- First author looses post-graduation academic job
- Graduate students replicate study and get a Science paper!

Anil Potti

- Duke cancer researcher
- Gene expression signatures to predict response to chemotherapy
  - Multiple high-impact publications: JAMA, NEJM, PNAS, Lancet
- Large sums of money by funding agencies
- Prospective trials started based on results
  - Randomizing patients to different chemotherapies based on their expression profile

Anil Potti

- Takes a 3rd year medical student into his laboratory (Dr. Bradford Perez), who applies lab methodology to a novel dataset and submits a manuscript
- Perez gets a concerns from reviewers that methodology is not valid
- When he critically starts analyzing, finds great concerns
  - Validation set only tests most significant finding of original set after removing samples who do not fit the model
  - Thus validation sets are not blinded, and virtually guaranteed to validate predictions made by original sets

Anil Potti

- http://med.stanford.edu/content/dam/sm/cancer/documents/Cancer%20Letters/TCL010915.pdf
- After being unable to get Dr. Pottis attention, goes to his supervisor with a strongly worded letter of concerns (2008)
  - Witdraws from lab, repeats third year of medical school
  - Removes his name from publications he was involved in
  - Supervisor asks him not to send letter further, will investigate

Anil Potti

- 2009
  - Various biostatisticians and cancer researchers have voiced their concerns, asking for reanalysis of data
  - Various replication attempts continue
- 2010
  - Inaccuries in Dr. Pottis CV revealed
  - 31 biostatisticians write a letter to the National Cancer Intitute
  - Internal investigation inisitate
  - Multiple retractions
  - Potti resigns from his position

Anil Potti

- 2011
  - Institute of Medicine investigates
  - FDA investigates
  - Lawsuits by patients included in studies based on results, many settled
  - Duke refunds grants