health care systems research network

How to Assess Biomedical Literature: A Skeptic's Guide

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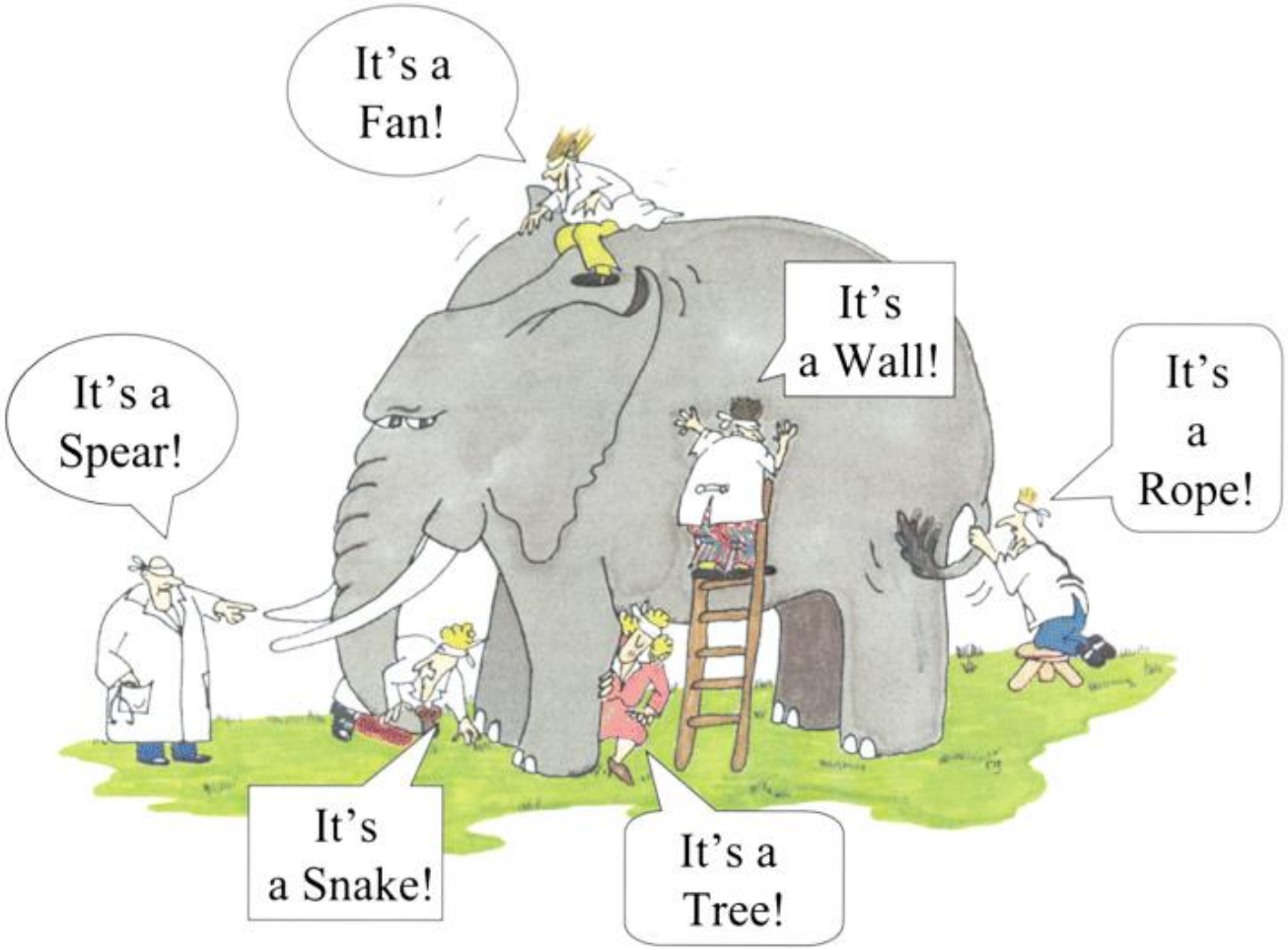
“We have to remember that what we observe is not nature in itself, but nature exposed to our method of questioning.”

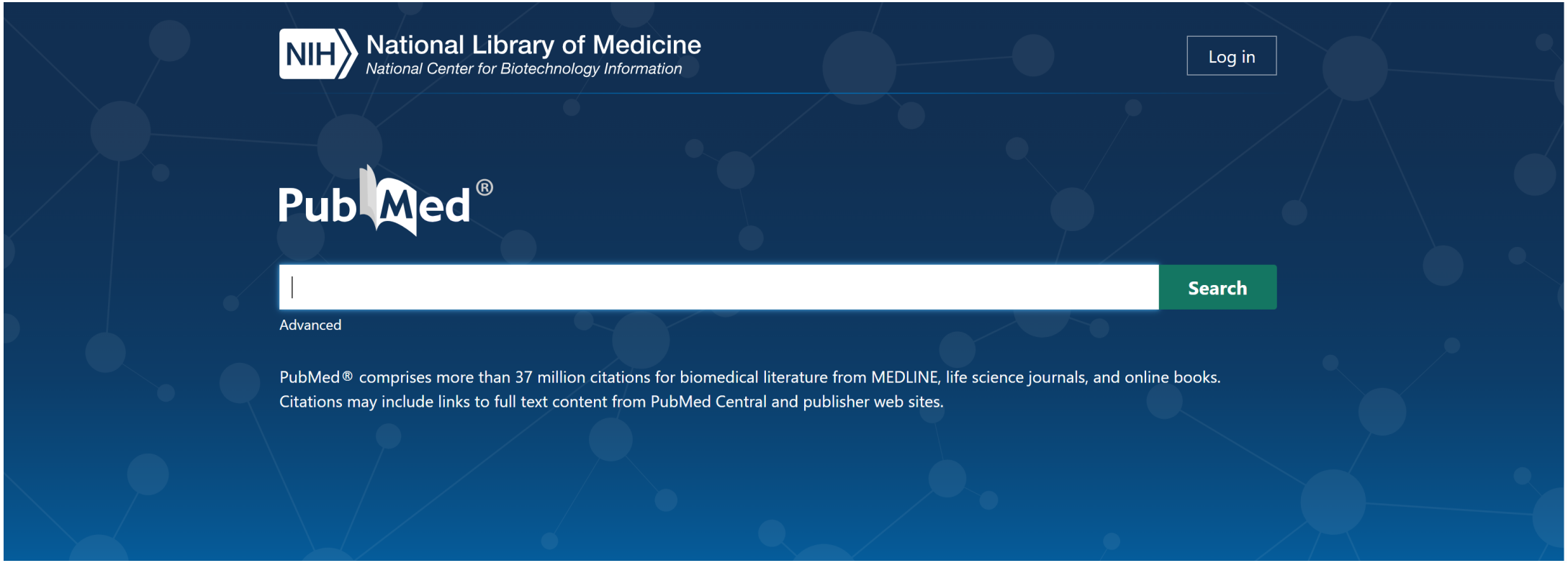
Werner Heisenberg



Can science give us the answers we need?

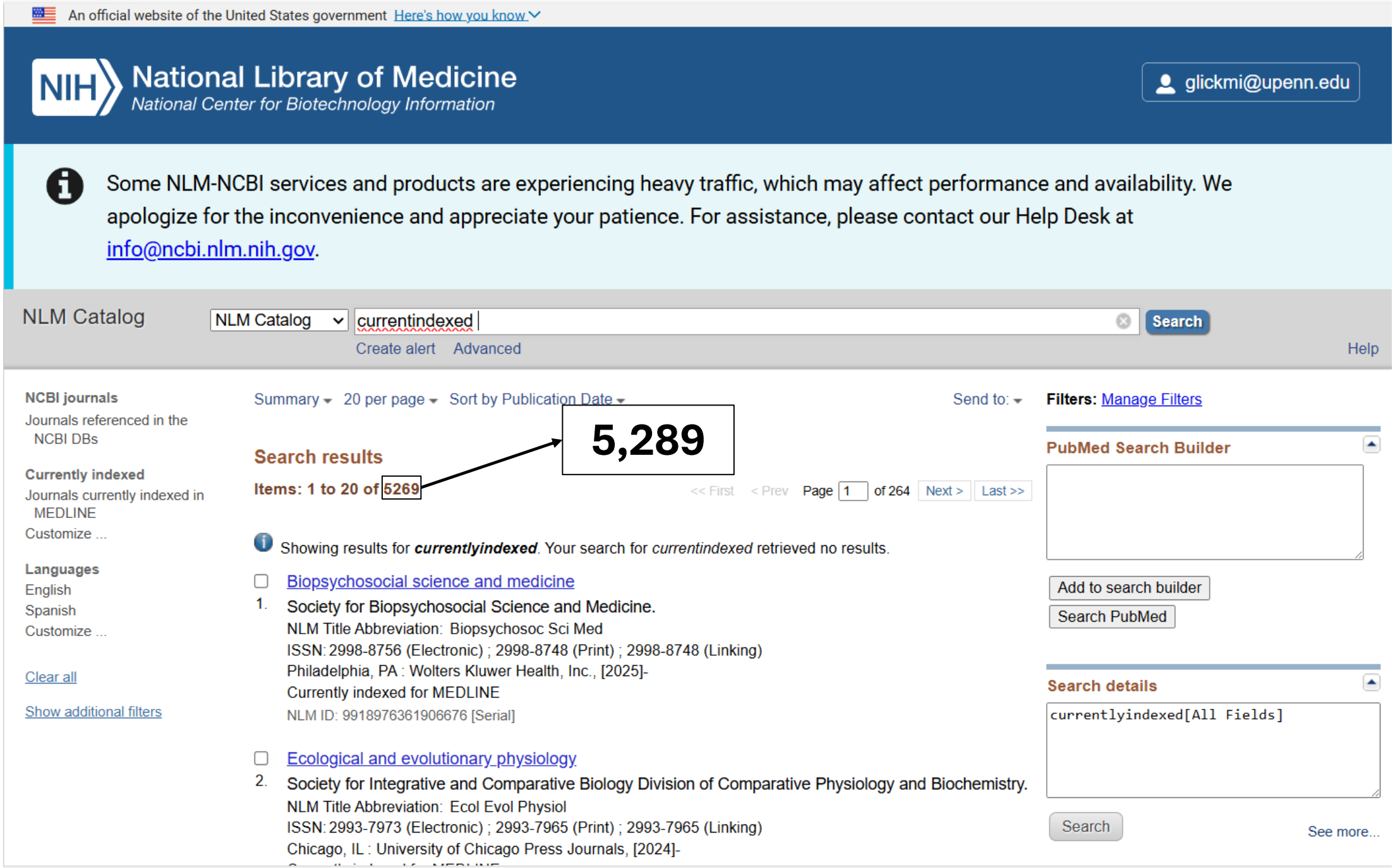
Bad science is a persistent issue—fraudulent studies to poorly conducted research and misinterpretation of research findings.

Publications

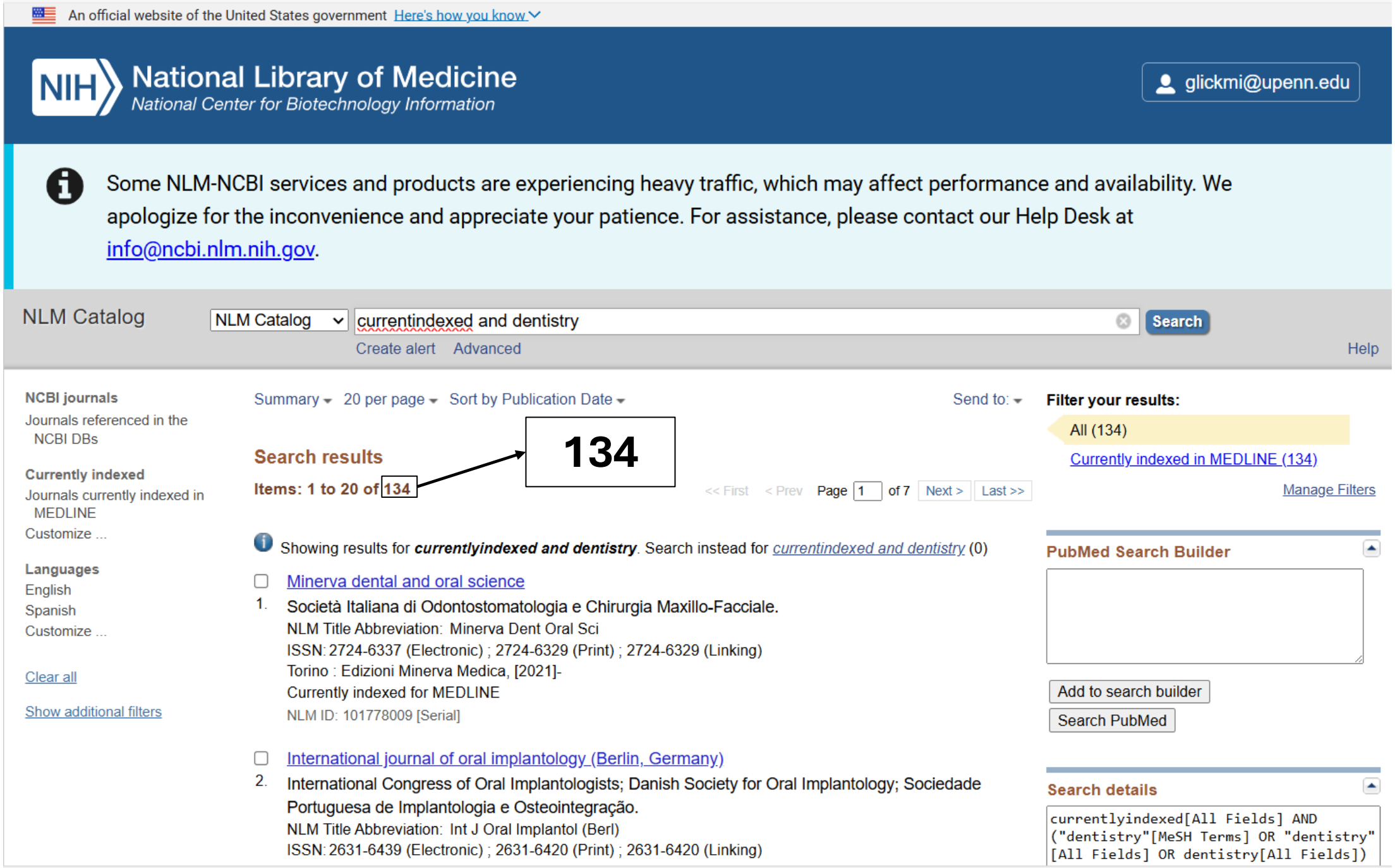


https://pubmed.ncbi.nlm.nih.gov/

Number of indexed journals



Number of indexed dental journals



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Author/Creator

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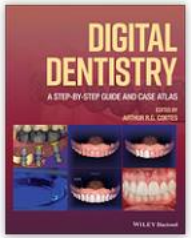
- Muacevic Alexander (4.2k)
- American Dental Association (1.7k)
- United States (1.3k)
- Springerlink (online Service) (890)
- Mickenautsch Steffen (650)

Language



Digital dentistry : a step-by-step guide and case atlas

Author: Arthur R. G. Cortes (Editor)

Summary: "An indispensable introduction to using digital technology in dentistry Digital Dentistry: A Step-by-Step Guide and Case Atlas provides basic information on the use of

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eBook, English, 2022
Edition: First edition
Publisher: John Wiley & Sons, Hoboken, NJ, 2022

Also available as Print Book

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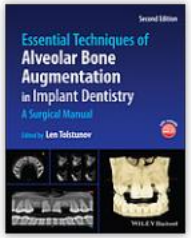

Essential techniques of alveolar bone augmentation in implant dentistry : a surgical manual

Author: Len Tolstunov (Editor)

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Summary: "The second edition of Essential Techniques of Alveolar Bone Augmentation in Implant Dentistry: A Surgical Manual presents a variety of key techniques for ensuring

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eBook, English, 2023
Edition: Second edition
Publisher: John Wiley & Sons, Inc., Hoboken, NJ, 2023

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  - Chapter (22k)
  - Downloadable Article (140k)

Author/Creator

- Ireland Robert (10k)
- Muacevic Alexander (4.2k)
- American Dental Association (1.7k)
- United States (1.3k)
- Springerlink (online Service) (890)
- Mickenautsch Steffen (650)

Language

Content

Peer-reviewed

A systematic review of droplet and aerosol generation in dentistry

Authors: N. Innes, I.G. Johnson, W. Al-Yaseen, R. Harris, R. Jones, S. KC, S. McGregor, M. Robertson, W.G. Wade, J.E. Gallagher

Summary: Objectives: This review aimed to identify which dental procedures generate droplets and aerosols with subsequent contamination, and for these, characterise their

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Article, 2021
Publication: Journal of Dentistry, 105, 202102
Publisher: 2021

Peer-reviewed

Accuracy and consistency of chatbots versus clinicians for answering pediatric dentistry questions: A pilot study

Authors: Rata Rokhshad, Ping Zhang, Hossein Mohammad-Rahimi, Vinay Pitchika, Niloufar Entezari, Falk Schwendicke

Summary: Objectives: Artificial Intelligence has applications such as Large Language Models (LLMs), which simulate human-like conversations. The potential of LLMs in

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Article, 2024
Publication: Journal of Dentistry, 144, 202405
Publisher: 2024

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Format reset

Book

Article, Chapter

- [x] Article (16k)
- [ ] Chapter (46)
- [ ] Downloadable Article (94k)

Author/Creator

- [ ] University Of The Pacific. School Of Dentistry (360)
- [ ] Australian Dental Association. Queensland Branch (270)
- [ ] Illinois State Dental Society (84)
- [ ] American Dental Association (76)
- [ ] Ziegler, Geo. J., M.d (73)
- [ ] Spalding Family (70)

Language

Content

Peer-reviewed

English for Academic Purposes Related to Dentistry: Analyzing the Reading Comprehension Process

Author: Patricia Carabelli

Summary: Abstract The Universidad de la República, in Uruguay, offers reading comprehension in English courses within the career of dentistry for students to access

Show more

Article, 2021
Publication: Profile Issues in Teachers` Professional Development, 23, 202112, 51
Publisher: 2021

Access Free OPEN ACCESS

Gender differences among dentistry conference speakers in Brazil

Authors: Leandro Brambilla Martorell, Ana Luiza Mustafe Silva, Cláudio Rodrigues Leles, Brunno Santos de Freitas Silva, Cristina Vianna Moreira dos Santos, Mirelle Finkler

Summary: ABSTRACT This study aimed to evaluate possible gender differences among the invited speakers of Brazilian dentistry meetings. The selected meetings (n=15) were held in

Show more

Article, 2021
Publication: Saúde em Debate, 45, 202110, 73
Publisher: 2021

Access Free OPEN ACCESS

"No Med School!" Black Resistance to The New Jersey College of

The output of scientific evidence is immense

PubMed search for “dentistry”

2018 – 29,168

2019 – 30,013

2020 – 35,044

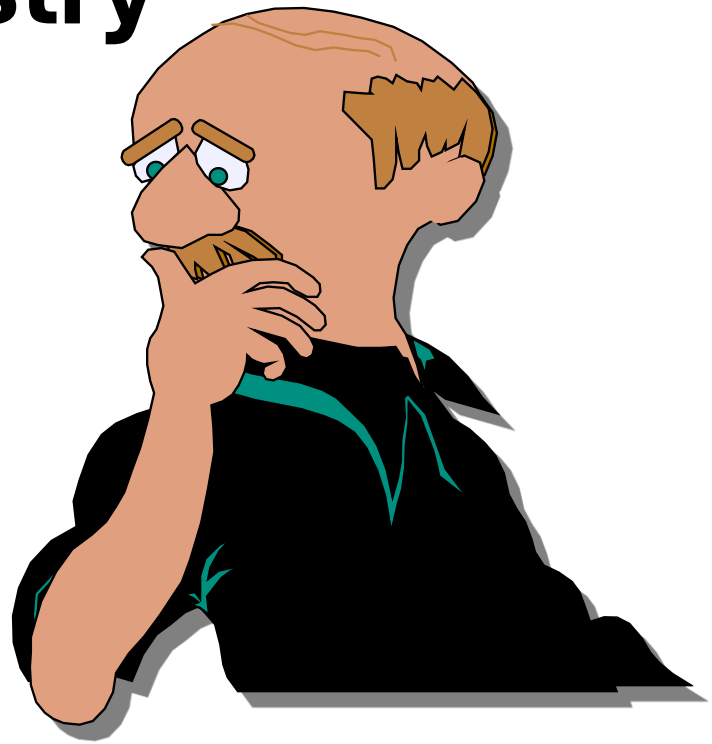
2021 – 39,107

2022 – 38,660

2023 – 37,943

2024 – 40,959

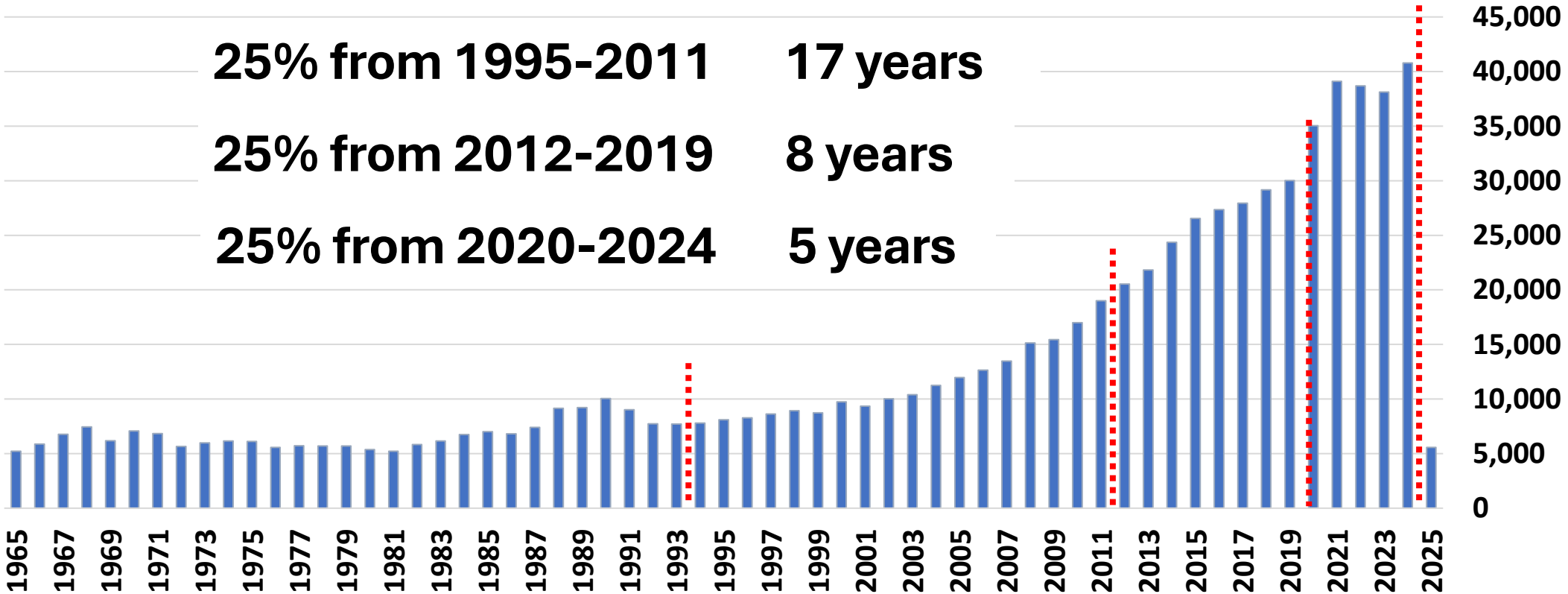
At least 1 dental publication added approximately every 13 minutes!



Total PubMed articles in dentistry — 1965 to 2024

756,973 articles

25% from 1965-1994	30 years
25% from 1995-2011	17 years
25% from 2012-2019	8 years
25% from 2020-2024	5 years

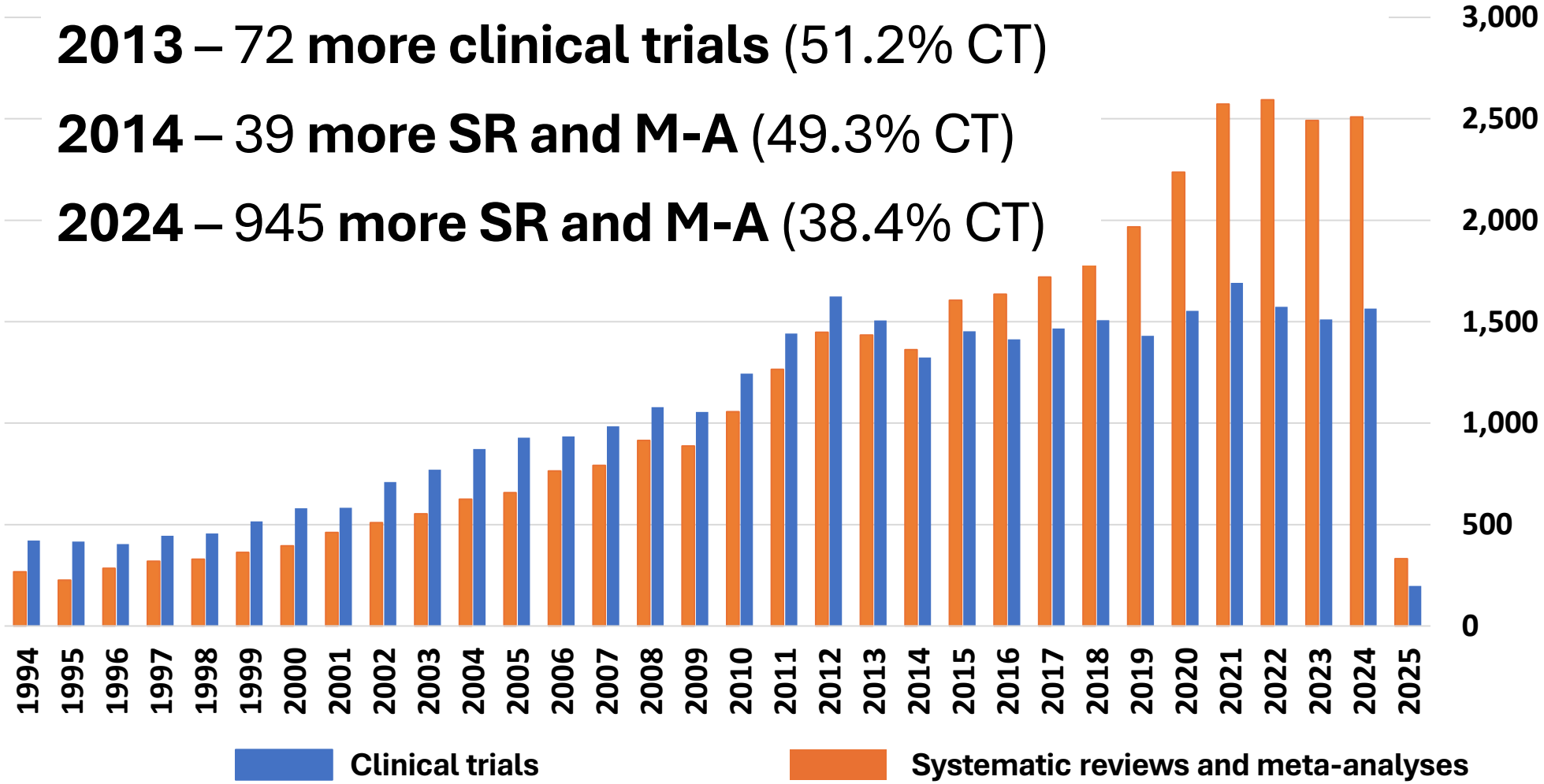


Clinical trials and systematic reviews and meta-analyses — dentistry

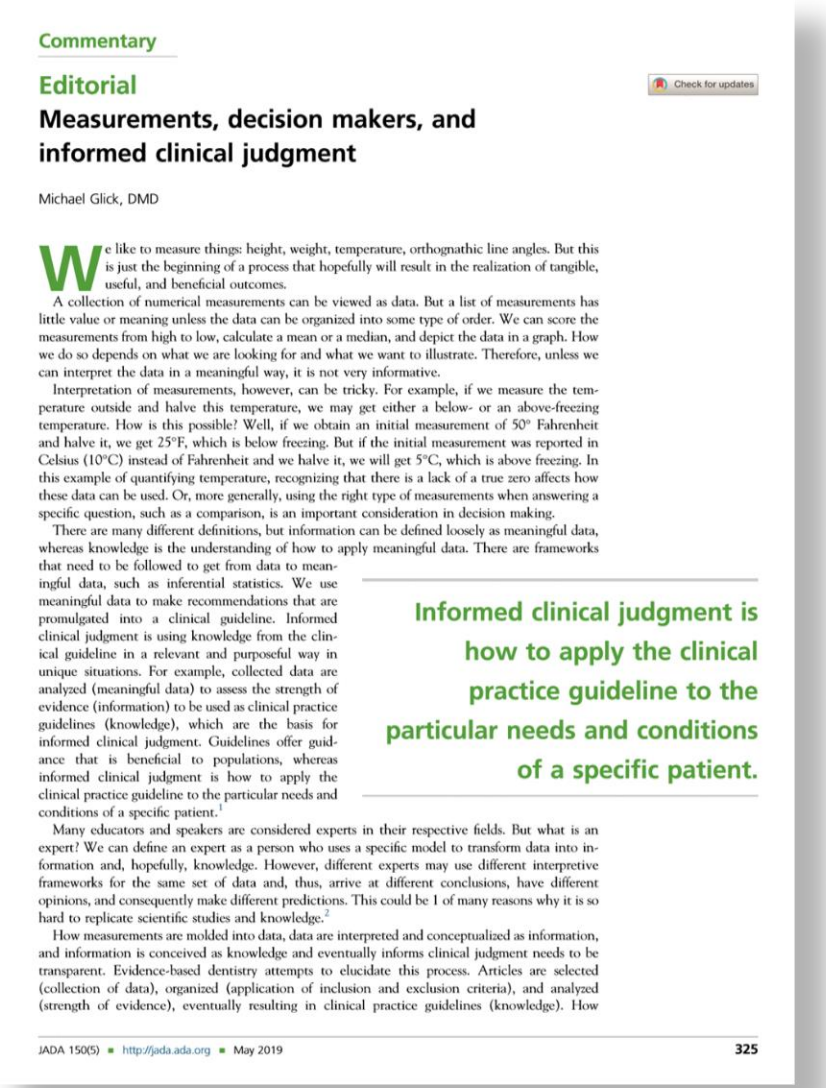
2013 – 72 **more clinical trials** (51.2% CT)

2014 – 39 **more SR and M-A** (49.3% CT)

2024 – 945 **more SR and M-A** (38.4% CT)



How we present and interpret data that can be used for information and eventual knowledge will change over time with the development of better, more sophisticated, and more insightful models.



Commentary

Editorial

Check for updates

Measurements, decision makers, and informed clinical judgment

Michael Glick, DMD

We like to measure things: height, weight, temperature, orthognathic line angles. But this is just the beginning of a process that hopefully will result in the realization of tangible, useful, and beneficial outcomes.

A collection of numerical measurements can be viewed as data. But a list of measurements has little value or meaning unless the data can be organized into some type of order. We can score the measurements from high to low, calculate a mean or a median, and depict the data in a graph. How we do so depends on what we are looking for and what we want to illustrate. Therefore, unless we can interpret the data in a meaningful way, it is not very informative.

Interpretation of measurements, however, can be tricky. For example, if we measure the temperature outside and halve this temperature, we may get either a below- or an above-freezing temperature. How is this possible? Well, if we obtain an initial measurement of 50° Fahrenheit and halve it, we get 25°F, which is below freezing. But if the initial measurement was reported in Celsius (10°C) instead of Fahrenheit and we halve it, we will get 5°C, which is above freezing. In this example of quantifying temperature, recognizing that there is a lack of a true zero affects how these data can be used. Or, more generally, using the right type of measurements when answering a specific question, such as a comparison, is an important consideration in decision making.

There are many different definitions, but information can be defined loosely as meaningful data, whereas knowledge is the understanding of how to apply meaningful data. There are frameworks that need to be followed to get from data to meaningful data, such as inferential statistics. We use meaningful data to make recommendations that are promulgated into a clinical guideline. Informed clinical judgment is using knowledge from the clinical guideline in a relevant and purposeful way in unique situations. For example, collected data are analyzed (meaningful data) to assess the strength of evidence (information) to be used as clinical practice guidelines (knowledge), which are the basis for informed clinical judgment. Guidelines offer guidance that is beneficial to populations, whereas informed clinical judgment is how to apply the clinical practice guideline to the particular needs and conditions of a specific patient.[1]

Informed clinical judgment is how to apply the clinical practice guideline to the particular needs and conditions of a specific patient.

Many educators and speakers are considered experts in their respective fields. But what is an expert? We can define an expert as a person who uses a specific model to transform data into information and, hopefully, knowledge. However, different experts may use different interpretive frameworks for the same set of data and, thus, arrive at different conclusions, have different opinions, and consequently make different predictions. This could be 1 of many reasons why it is so hard to replicate scientific studies and knowledge.[2]

How measurements are molded into data, data are interpreted and conceptualized as information, and information is conceived as knowledge and eventually informs clinical judgment needs to be transparent. Evidence-based dentistry attempts to elucidate this process. Articles are selected (collection of data), organized (application of inclusion and exclusion criteria), and analyzed (strength of evidence), eventually resulting in clinical practice guidelines (knowledge). How

Glick M. JADA. 2019;150(5):325-6

Mistakes were made but not by me 😊

Using the incorrect study design for the research question of interest,

using the wrong study design to claim causality,

not interpretating measures of association correctly, e.g., equating RR with OR,

focusing only on RRD rather than ARD,

not recognizing confounders, mediators, effect modifiers, colliders and other types of bias,

not distinguishing between proportions (ratios) and rates,

confusing incidence with prevalence,

inaccurate protocols for particular study designs (cases and controls),

incorrect interpretation confidence intervals,

incorrect interpretation of p-values,

incorrectly interpreting validity and reliability of outcome measures (questionnaires),

incorrectly equating statistical significance with clinical significance,

incorrectly equating lack of statistical significance with equivalence,

misinterpreting efficacy and efficiency studies,

and more …

Relative risk and interpretations

6-month trial	MI	No MI	Total
Using statins	142	8,759	8,901
Not using statins	251	8,650	8,901
	393	17,409	17,802

Relative risk for **developing** *MI* **when using** *statins*

$$= \frac{\text{AR using } statins}{\text{AR not using } statins} = \frac{142/8{,}901}{251/8{,}901} = \mathbf{0.57}$$

Relative risk for **developing** *MI* **when not using** *stains*

$$= \frac{\text{AR not using } stains}{\text{AR using } stains} = \frac{251/8{,}901}{142/8{,}901} = \mathbf{1.77}$$

Relative risk difference (RRD) $= \frac{142/8{,}901 - 251/8{,}901}{251/8{,}901} = \frac{142/8{,}901}{251/8{,}901} - 1$ = 0.57 - 1 = **-43%**

Relative risk and interpretations

With a *relative risk* of 1.77, which is a correct statement?

"The relative risk of **developing MI** when **not using statins** is 1.77 **that of using statins** over a period of 6 months."

"The relative risk of **developing MI** when **not using statins** is 1.77 **more** than **that of using statins** over a period of 6 months."

A has $100 and B has $120.

B has 1.2 **times that of** A, i.e. $120, but **not** 1.2 **times more** than A.

If B had 1.2 **times more** than A, B would have 100+(1.2x100) = $220.

Relative risk and interpretations

With a *relative risk* of 1.77, which is a correct statement?

"The relative risk of **developing MI** when **not using statins** is 1.77 **that of using statins** over a period of 6 months."

"~~The relative risk of **developing MI** when **not using statins** is 1.77 **more** than **that of using statins** over a period of 6 months.~~"

A has $100 and B has $120.

B has 1.2 **times that of** A, i.e. $120, but **not** 1.2 **times more** than A.

If B had 1.2 **times more** than A, B would have 100+(1.2x100) = $220.

Relative risk and interpretations

What we can state about *relative risk* and *relative risk difference*

"The relative risk of **developing MI** is 0.57, or 57%, **that of not using statins** after 6 months."

"**Using statins** relative to **not using statins** for 6 months is associated with a 43% **decreased risk** of **developing MI**."

"The relative risk of **developing MI** when **not using statins** is 1.77 **that of using statins** over a period of 6 months."

"The risk of **developing MI** when **not using statins** is 77% **times greater** when **using statins** over a period of 6 months."

Odds ratio and interpretations

A study showed that periodontal disease was associated with CVD with an odds ratio (OR) of 3.

Does an OR of 3 mean that there is a 3 times the chance of having CVD if you have periodontal disease?

	CVD(+)	CVD(-)
PD(+)	50	50
PD(-)	25	75

The odds of CVD(+) given PD(+) compared to the odds of CVD(+) given PD(-)

$$\frac{1}{1/3}$$ => an OR = 3

But the risk CVD(+) if PD(+) is 2x as likely, not 3x as likely

How effective is a COVID vaccine?

*"Primary **efficacy** analysis demonstrates BNT162b2 to be **95% effective against COVID-19** beginning 28 days after the first dose;*
170 confirmed cases of COVID-19 were evaluated, with 162 observed in the placebo group versus 8 in the vaccine group."

BioNTech/Pfizer*- mRNA vaccine *BNT162b2

COVID-19 vaccine "95% effective": It doesn't mean what you think it means! | R-bloggers

How effective is a COVID vaccine?

Pfizer selected about 43,000 voluntary participants where about half received the vaccine (22,700) and the other half (the control group; 20,250) received only a placebo, without any active substance.

After about a month after the first dose (i.e. one week after the second dose), they started to count the number of confirmed COVID-19 cases for each group.

In the placebo group 162 cases were confirmed, whereas in the vaccine group only 8 cases appeared.

Scaling proportionally

Vaccinated infection rate is $\frac{8}{22{,}700} = 0.000352$

Unvaccinated infection rate is $\frac{162}{20{,}500} = 0.007902$

Using a common denominator (e.g., per 2,500 people):

Vaccinated per 2,500: $\frac{8}{22{,}700}\ x\ 2{,}500 = 0.88$ (approx. 1 case per 2,500)

Unvaccinated per 2,500: $\frac{162}{20{,}500}\ x\ 2500 = 19.76$ (approx. 20 case per 2,500)

How effective is a COVID vaccine?

1of 2,500 infected despite of vaccine

Vaccinated per 2,500: $\frac{8}{22{,}700}\ x\ 2{,}500 = 0.88$ (approx. 1 case per 2,500)

How effective is a COVID vaccine?

20 of 2,500 infected without vaccine

Unvaccinated per 2,500: $\frac{162}{20{,}500}\ x\ 2500 = 19.76$ (approx. 20 case per 2,500)

How effective is a COVID vaccine?

	COVID(+)	COVID(-)	Total
Vacc(+)	8	2,492	2,500
Vacc(-)	162	2,338	2,500

RR = (8/2,500)/(162/2,500) = 8/162 = 0.05

RRD = (8/162)-(162/162) = RR-1 = -**0.95**

*"Primary **efficacy** analysis demonstrates BNT162b2 to be **95% effective against COVID-19** beginning 28 days after the first dose;*
170 confirmed cases of COVID-19 were evaluated, with 162 observed in the placebo group versus 8 in the vaccine group."

How effective is a COVID vaccine?

*"Primary **efficacy** analysis demonstrates BNT162b2 to be **95% effective against COVID-19** beginning 28 days after the first dose;*
170 confirmed cases of COVID-19 were evaluated, with 162 observed in the placebo group versus 8 in the vaccine group."

Efficacy rate of 95%?

It doesn't mean that 95 out of 100 vaccinated persons will be protected from COVID-19, nor does it mean that it will reduce the severity of the illness in case you contract the virus despite being vaccinated.

How effective is a COVID vaccine?

*"Primary **efficacy** analysis demonstrates BNT162b2 to be **95% effective against COVID-19** beginning 28 days after the first dose;*
170 confirmed cases of COVID-19 were evaluated, with 162 observed in the placebo group versus 8 in the vaccine group."

Efficacy is a proxy, i.e. relative risk-reduction of infections in the **two study groups**. This can give a good indication of the order of magnitude of the real-world effect but is not the same!

What we want to know is the **effectiveness** of the vaccine in the real world, i.e. how well it protects us from contracting the disease.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel

RESULTS

At least 12 days after the booster dose, the rate of confirmed infection was lower in the booster group than in the nonbooster group by a factor of 11.3 (95% confidence interval [CI], 10.4 to 12.3); the rate of severe illness was lower by a factor of 19.5 (95% CI, 12.9 to 29.5). In a secondary analysis, the rate of confirmed infection at least 12 days after vaccination was lower than the rate after 4 to 6 days by a factor of 5.4 (95% CI, 4.8 to 6.1).

N Engl J Med. 2021;385:1393-400

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel

*At least 12 days after the booster dose, the rate of **confirmed infection** was lower in the booster group than in the nonbooster group by a factor of **11.3** [...] the rate of **severe illness** was lower by a factor of **19.5** [...].*

N Engl J Med. 2021;385:1393-400

Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel:

How effective is a COVID vaccine?

Risk in the booster group => $\frac{6}{2500} = 0.0024$

Risk in the non-booster group => $\frac{64}{2500} = 0.0256$

Relative risk=> $\frac{0.0024}{0.0256} = 0.09375$ or 9.4%

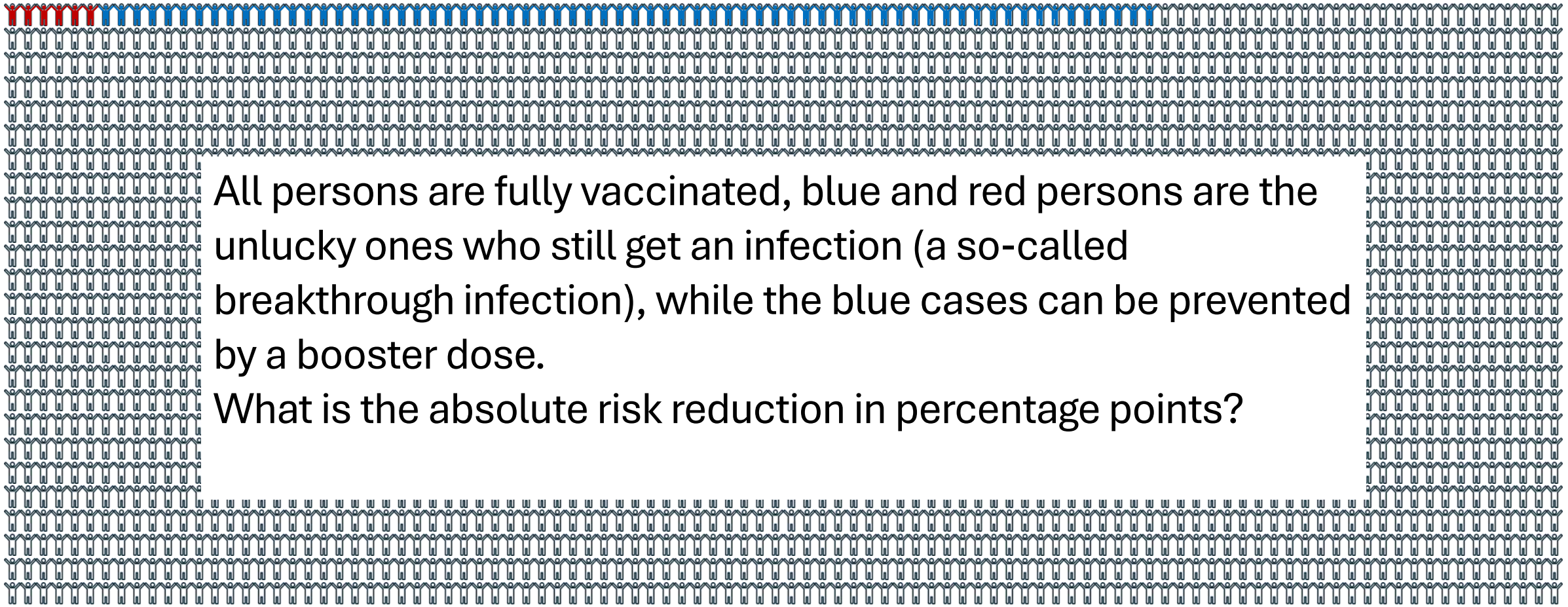
(the reported 11.3 was an adjusted RR)

Absolute risk difference (RRD*risk in the non-booster group)=>

$0.0256 - 0.0024 = 0.0232$ or 2.3 percentage points

How effective is a COVID vaccine?

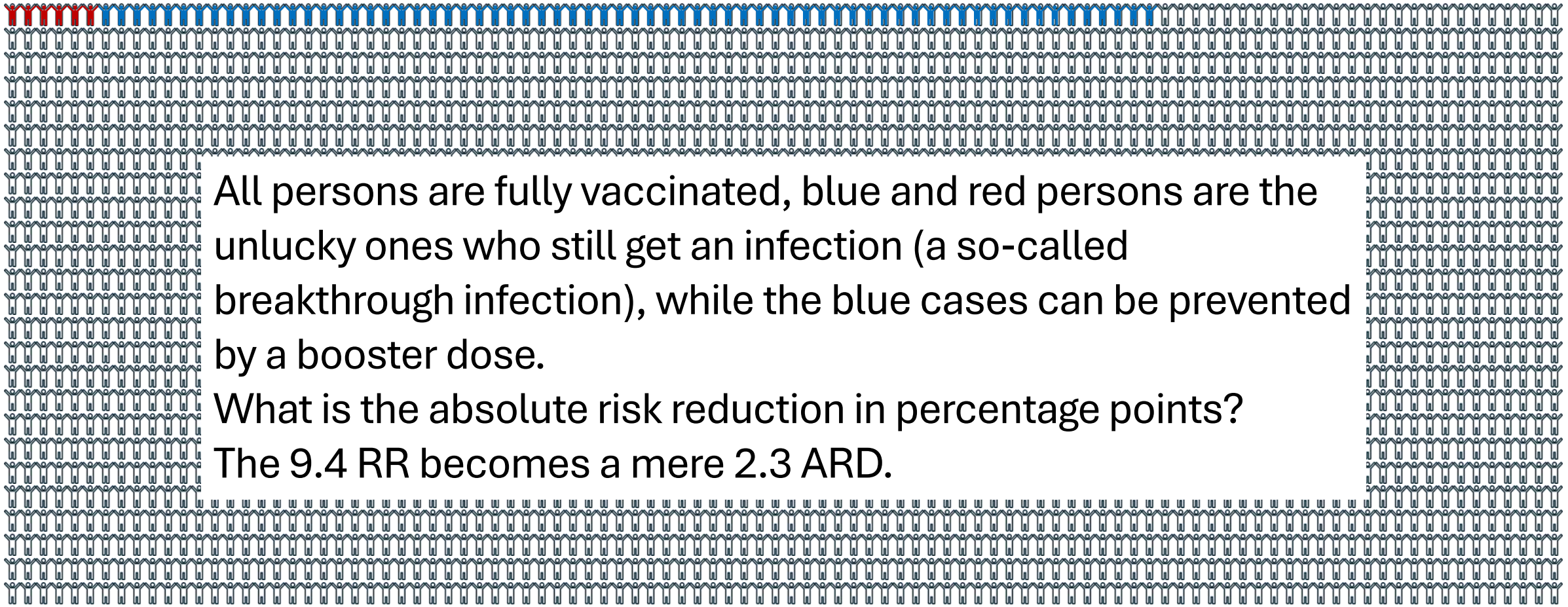
Infections w/o booster: <64/2,500; infection with booster: ≈6/2,500



RR => -9.4 percent

How effective is a COVID vaccine?

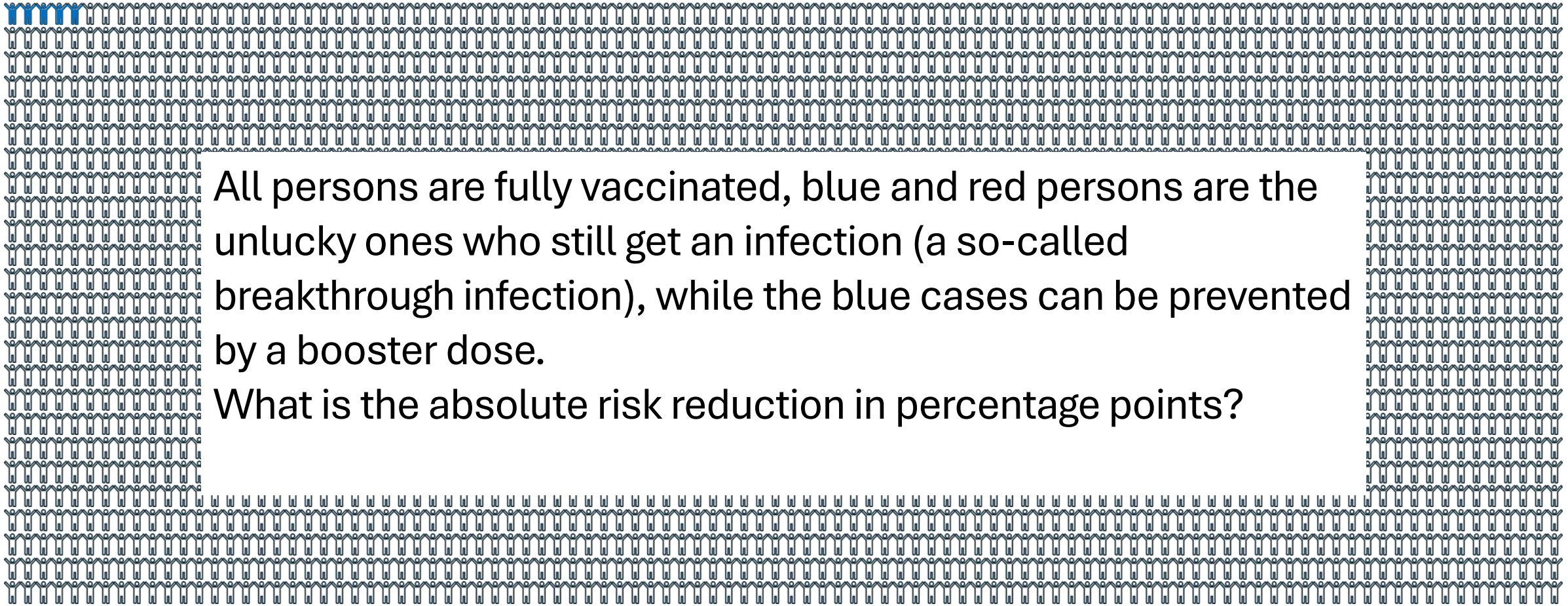
Infections w/o booster: <64/2,500; infection with booster: ≈6/2,500



ARD = 100*64/2500-100*6/2500 => **-2.3 percentage points**

How effective is a COVID vaccine?

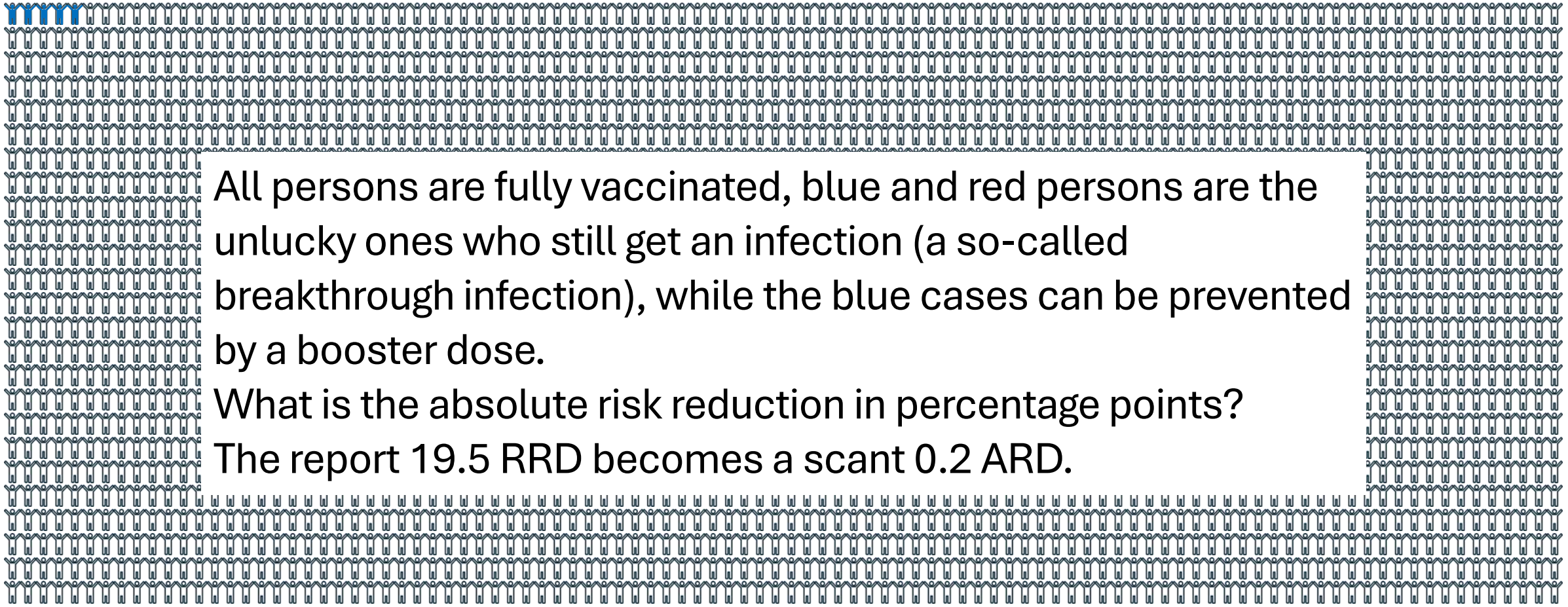
Severe cases w/o booster: < 5/2,500; severe cases with booster: < 1/2,500



RR => -19.5 percent

How effective is a COVID vaccine?

Severe cases w/o booster: < 5/2,500; severe cases with booster: < 1/2,500



ARD = 100*1/2500-100*1

=> **-0.2 percentage points**

Cancer screening

Will oral cancer screening improve mortality rate?

Well, it depends …

Survival rate

About VELscope® Vx Enhanced Oral Assessment

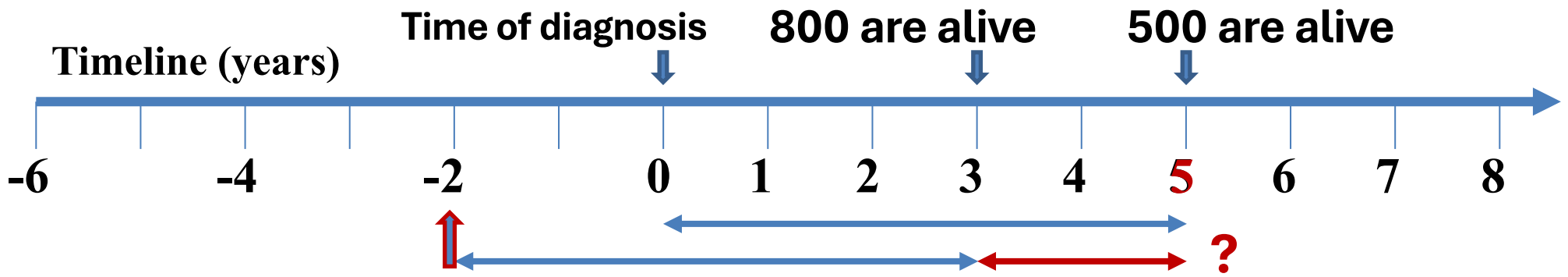
The distinctive blue-spectrum light of the VELscope Vx Enhanced Oral Assessment System

There are more than 40,000 new cases of oral cancer diagnosed in the United States alone every year and early detection is critical for survival; when detected early, the five-year survival rate rises from less than 50% to more than 80%.

mechanism, a key function for referrals and patient records.

There are more than 40,000 new cases of oral cancer diagnosed in the United States alone every year and early detection is critical for survival: when detected early, the five-year survival rate rises from less than 50% to more than 80%. VELscope systems are used during more examinations for oral cancer and other oral diseases than any other adjunctive device. For more information, visit www.velscope.com.

Survival rate



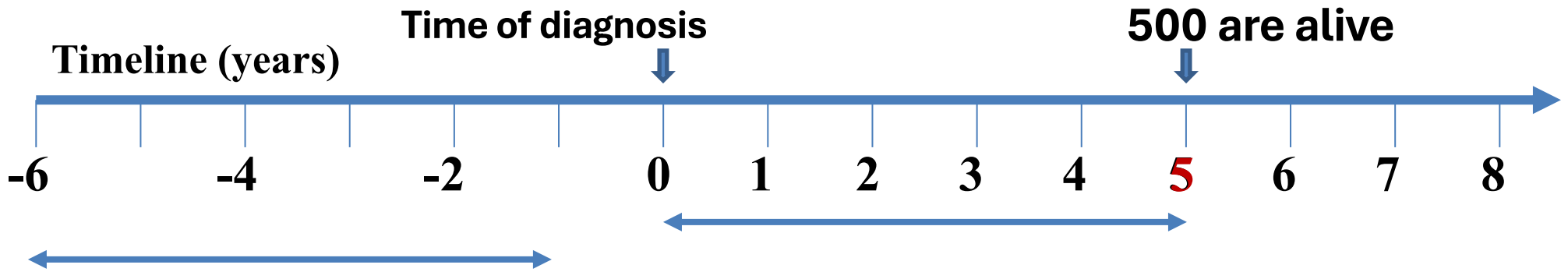
500 out of 1,000 men alive after 5 years (year 5) **=>**
a 50% survival rate 5 years after a *diagnosis* (year 0).
If screening were to be performed 2 years before a diagnosis could have been made (year -2), the survival rate 5 years after *screening* is 80%.

800 of the 1,000 mean would be alive after 5 years (year 3).

The real questions are –
how many of the 800 men are alive at year 5;
how many of the 800 would never have developed the disease?

Impossible to know!

Survival rate



500 out of 1,000 men alive after 5 years (year 5)
represents is a 50% survival rate 5 years after a *diagnosis* (year 0).

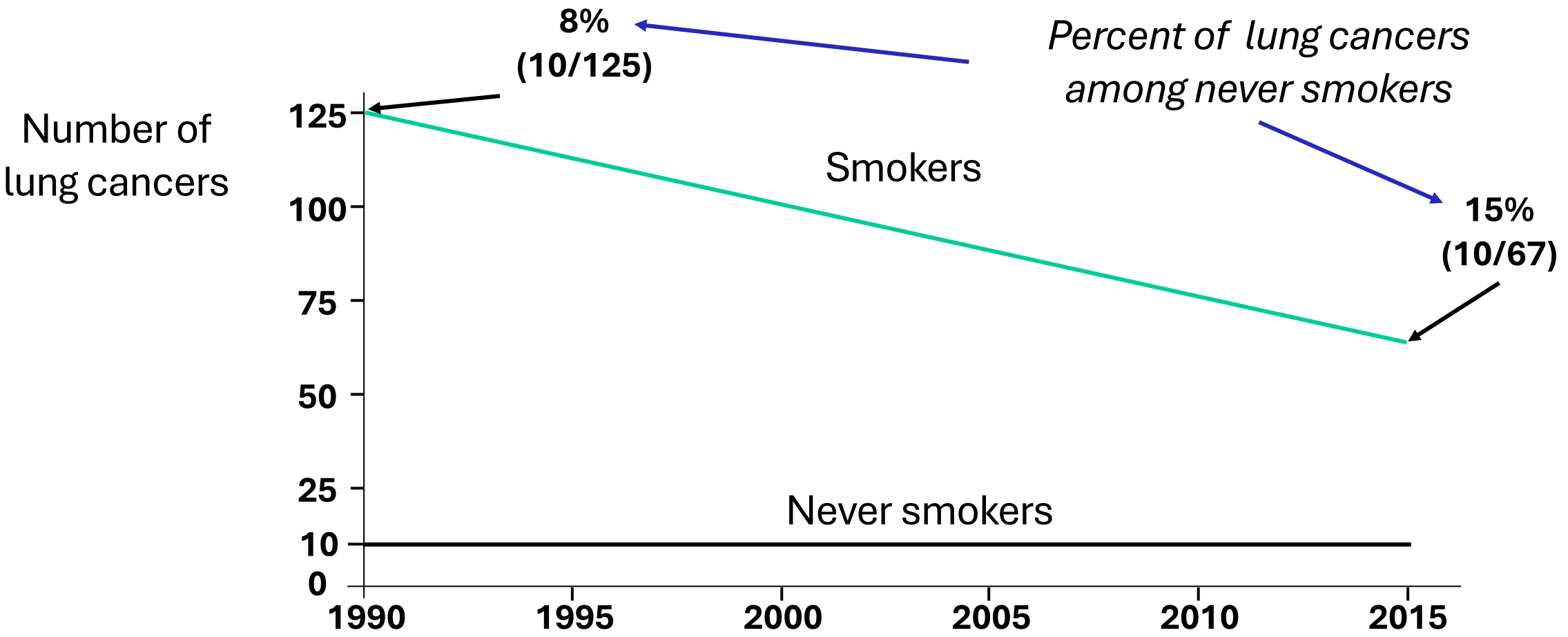
If screening were to be performed 6 years before a diagnosis could have been made (year -6), *1,000 of the 1,000 mean would be alive after 5 years (year -1).*

There is a 100% survival rate with screening! 😊

Survival rate

- **Assumption 1: screening can detect non-progressive cancer**
- **Assumption 2: 10-year survival rate of 5%**
- **Assumption 3: 1 in 5 patients have progressive cancer**
- **With screening: Among 5,000 patients with CA, *1,000* will have *progressive CA;* *4,000* will have *non-progressive CA***
- **Without screening: Among 1,000 patients with *progressive CA*, *50* *will be alive* and 950 will be dead after 10 years**
- **With screening: 4,000 + 50 = 4,050 will be alive after 10 years, which is a 10-year survival rate of 4,050/5,000 = 81%**
- **Screening can increase survival rates without actually saving lives!**
- **Death rate (number of people who have died/all people) is more accurate**

The proportion of lung cancer among never-smokers has almost doubled in the past 25 years.



Greg Welch, MD

Fragility index or the peril of p's

	No hypertension	Hypertension	
Sleep apnea			60
No sleep apnea			60
			120

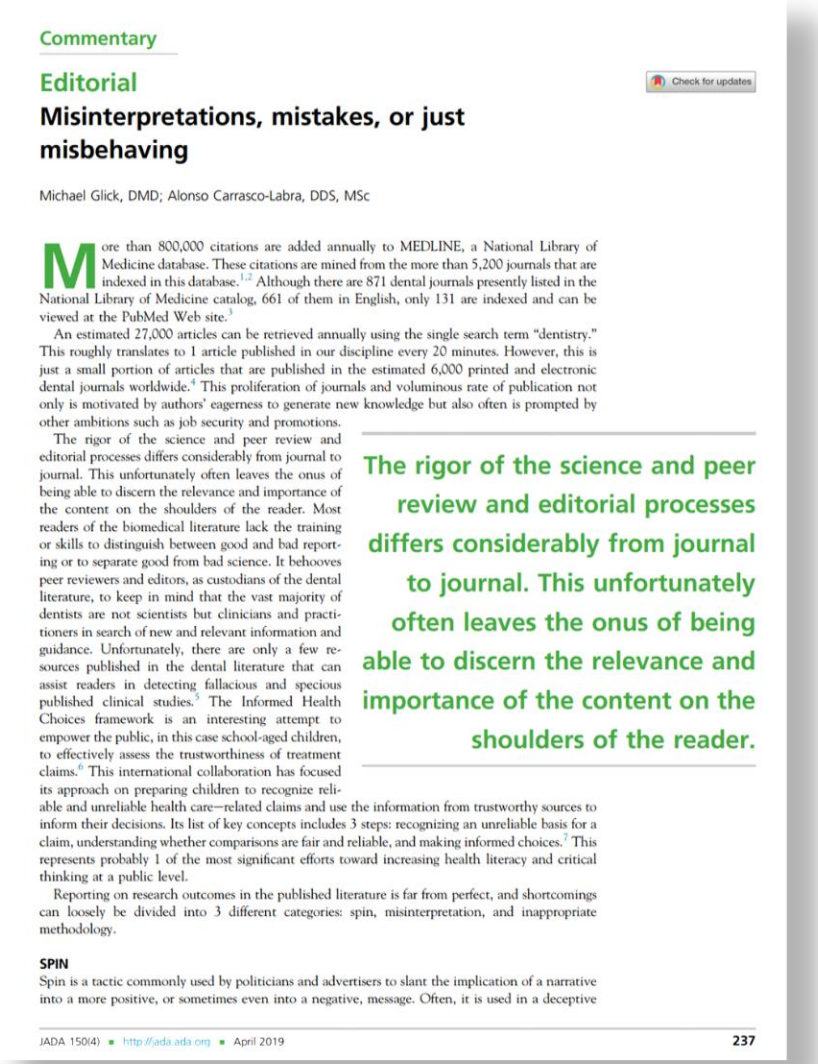
The Chi-square test statistic value is **0.061**. The result is *not* significant at p >0.05.

	No hypertension	Hypertension	
Sleep apnea	50	10	60
No sleep apnea	40	20	60
	90	30	120

The Chi-square test statistic value is **0.035**. The result is significant at p < 0.05.

Fragility index = 1

"The rigor of the science and peer review and editorial processes differs considerably from journal to journal. This unfortunately often leaves the onus of being able to discern the relevance and importance of the content on the shoulders of the reader."



Commentary

Editorial

Check for updates

Misinterpretations, mistakes, or just misbehaving

Michael Glick, DMD; Alonso Carrasco-Labra, DDS, MSc

More than 800,000 citations are added annually to MEDLINE, a National Library of Medicine database. These citations are mined from the more than 5,200 journals that are indexed in this database.[1,2] Although there are 871 dental journals presently listed in the National Library of Medicine catalog, 661 of them in English, only 131 are indexed and can be viewed at the PubMed Web site.[3]

An estimated 27,000 articles can be retrieved annually using the single search term "dentistry." This roughly translates to 1 article published in our discipline every 20 minutes. However, this is just a small portion of articles that are published in the estimated 6,000 printed and electronic dental journals worldwide.[4] This proliferation of journals and voluminous rate of publication not only is motivated by authors' eagerness to generate new knowledge but also often is prompted by other ambitions such as job security and promotions.

The rigor of the science and peer review and editorial processes differs considerably from journal to journal. This unfortunately often leaves the onus of being able to discern the relevance and importance of the content on the shoulders of the reader. Most readers of the biomedical literature lack the training or skills to distinguish between good and bad reporting or to separate good from bad science. It behooves peer reviewers and editors, as custodians of the dental literature, to keep in mind that the vast majority of dentists are not scientists but clinicians and practitioners in search of new and relevant information and guidance. Unfortunately, there are only a few resources published in the dental literature that can assist readers in detecting fallacious and specious published clinical studies.[5] The Informed Health Choices framework is an interesting attempt to empower the public, in this case school-aged children, to effectively assess the trustworthiness of treatment claims.[6] This international collaboration has focused its approach on preparing children to recognize reliable and unreliable health care–related claims and use the information from trustworthy sources to inform their decisions. Its list of key concepts includes 3 steps: recognizing an unreliable basis for a claim, understanding whether comparisons are fair and reliable, and making informed choices.[7] This represents probably 1 of the most significant efforts toward increasing health literacy and critical thinking at a public level.

The rigor of the science and peer review and editorial processes differs considerably from journal to journal. This unfortunately often leaves the onus of being able to discern the relevance and importance of the content on the shoulders of the reader.

Reporting on research outcomes in the published literature is far from perfect, and shortcomings can loosely be divided into 3 different categories: spin, misinterpretation, and inappropriate methodology.

SPIN

Spin is a tactic commonly used by politicians and advertisers to slant the implication of a narrative into a more positive, or sometimes even into a negative, message. Often, it is used in a deceptive

"A meta-analysis of 10 **case-controlled studies** revealed an increased risk of recurrent aphthous stomatitis..."

"A meta-analysis of 21 **case-control studies** revealed that celiac disease is associated with a higher **incidence** of recurrent aphthous stomatitis..."

JAMA. 2024;331(12):1045-1054

Clinical Review & Education

JAMA | Review

Common Oral Conditions
A Review

Eric T. Stoopler, DMD; Alessandro Villa, DDS, PhD, MPH; Mohammed Bindakhil, DDS, MS; David L. Ojeda Diaz, DDS; Thomas P. Sollecito, DMD

IMPORTANCE Dry mouth, oral candidiasis, and recurrent aphthous ulcers are 3 of the most common oral conditions that may be associated with patient discomfort, decreased quality of life, and morbidity.

OBSERVATIONS In a meta-analysis of 26 population-based cohort and cross-sectional studies, the global prevalence of dry mouth symptoms was 23% (95% CI, 18% to 28%), placing individuals at risk of oral candidiasis, dental caries, dysgeusia, masticatory/speech impairment, and oropharyngeal dysphagia. Dry mouth is associated with using more than 3 oral medications per day (odds ratio [OR], 2.9 [95% CI, 1.4 to 6.2]), head and neck radiation, and Sjögren disease. Symptoms may include difficulty swallowing and speaking, thirst, and halitosis. Dry mouth is associated with an 11.5% (95% CI, 3.6% to 27%) higher risk of oral candidiasis, based on a meta-analysis of 6 observational cohorts. Management of dry mouth includes mechanical salivary stimulants, oral moisturizers, and/or systemic sialagogues. Oral candidiasis is an opportunistic fungal infection caused by overgrowth of the *Candida* genus with *C albicans*, which accounts for 76.8% of infections. The prevalence of oral candidiasis is higher in patients who are immunosuppressed, for example, those with HIV (35% [95% CI, 28% to 42%]) and those with salivary gland hypofunction (OR, 3.02 [95% CI, 1.73 to 5.28]). Common risk factors associated with oral candidiasis include use of antibiotics ($P = .04$) and oral mucosal disorders such as lichen planus. Oral burning and dysgeusia are common symptoms of oral candidiasis. Treatment includes addressing risk factors and use of topical and/or systemic antifungal medications. Recurrent aphthous stomatitis is characterized by symptomatic round or oval oral ulcers, which are covered by a gray-white fibrin layer and encircled by an erythematous ring. A meta-analysis of 10 case-controlled studies revealed an increased risk of recurrent aphthous stomatitis associated with polymorphism of IL-1β (+3954C/T) (OR, 1.52 [95% CI, 1.07 to 2.17]) and IL-1β (−511C/T) (OR, 1.35 [95% CI, 1.09 to 1.67]). Another meta-analysis of 9 case-control studies reported that patients with recurrent aphthous stomatitis had a higher frequency of nutritional deficiencies, including vitamin B_{12} (OR, 3.75 [95% CI, 2.38 to 5.94]), folic acid (OR, 7.55 [95% CI, 3.91 to 14.60]), and ferritin (OR, 2.62 [95% CI, 1.69 to 4.06]). Recurrent aphthous stomatitis can be associated with systemic diseases. A meta-analysis of 21 case-control studies revealed that celiac disease is associated with a higher incidence of recurrent aphthous stomatitis (25% vs 11%; OR, 3.79 [95% CI, 2.67 to 5.39]; $P < .001$). Topical corticosteroids are first-line agents to manage recurrent aphthous stomatitis; however, systemic medications may be necessary in more severe cases.

CONCLUSIONS AND RELEVANCE Dry mouth, oral candidiasis, and recurrent aphthous ulcers are common oral conditions that may be associated with patient discomfort, decreased quality of life, and morbidity. First-line treatment includes over-the-counter sialagogues for dry mouth, topical antifungals for oral candidiasis, and topical corticosteroids for aphthous ulcers. Oral conditions that do not improve with first-line treatment may require treatment with systemic medications.

Multimedia

CME at jamacmelookup.com

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"...the use of nystatin was more effective than placebo (relative risk [RR], 0.51 [95% CI, 0.36 to 0.72]), and use of miconazole (lacquer or gel) **did not differ from placebo (RR, 0.73 [95% CI, 0.48 to 1.10])**."

Failing to reject the null hypothesis (i.e., "no significant difference") does not mean the two groups are equivalent — it only means we do not have enough evidence to claim a difference.

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"…reported comparable success rates to traditional denture disinfecting protocols and administration of topical antifungals for the treatment of denture stomatitis (**RR, 1.31 [95%CI, −0.80 to 2.15]**)

"…a meta-analysis of 3 RCTs that investigated probiotics … in the management of recurrent aphthous stomatitis revealed evidence suggesting a reduction of oral pain … with the use of probiotic…" **[compared to …?]**

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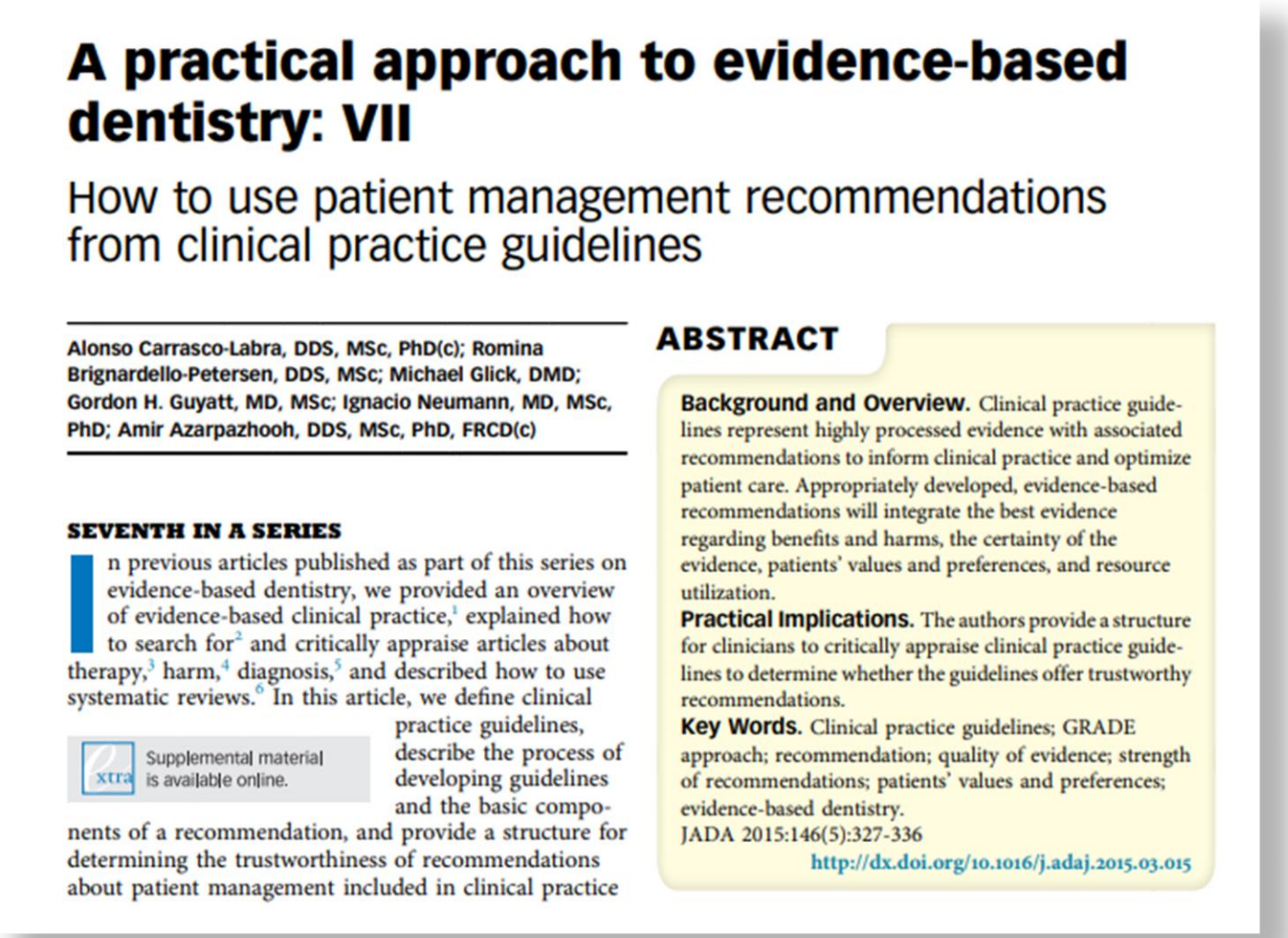
"Clinical practice guidelines represent **highly processed evidence** with associated **recommendations** to **inform clinical practice** and **optimize patient care**.

Appropriately developed, evidence-based recommendations will **integrate the best evidence** regarding **benefits and harms**, the **certainty of the evidence**, **patients' values and preferences**, and **resource utilization**."



A practical approach to evidence-based dentistry: VII

How to use patient management recommendations from clinical practice guidelines

Alonso Carrasco-Labra, DDS, MSc, PhD(c); Romina Brignardello-Petersen, DDS, MSc; Michael Glick, DMD; Gordon H. Guyatt, MD, MSc; Ignacio Neumann, MD, MSc, PhD; Amir Azarpazhooh, DDS, MSc, PhD, FRCD(c)

ABSTRACT

Background and Overview. Clinical practice guidelines represent highly processed evidence with associated recommendations to inform clinical practice and optimize patient care. Appropriately developed, evidence-based recommendations will integrate the best evidence regarding benefits and harms, the certainty of the evidence, patients' values and preferences, and resource utilization.

Practical Implications. The authors provide a structure for clinicians to critically appraise clinical practice guidelines to determine whether the guidelines offer trustworthy recommendations.

Key Words. Clinical practice guidelines; GRADE approach; recommendation; quality of evidence; strength of recommendations; patients' values and preferences; evidence-based dentistry.

JADA 2015:146(5):327-336

http://dx.doi.org/10.1016/j.adaj.2015.03.015

SEVENTH IN A SERIES

In previous articles published as part of this series on evidence-based dentistry, we provided an overview of evidence-based clinical practice,[1] explained how to search for[2] and critically appraise articles about therapy,[3] harm,[4] diagnosis,[5] and described how to use systematic reviews.[6] In this article, we define clinical practice guidelines, describe the process of developing guidelines and the basic components of a recommendation, and provide a structure for determining the trustworthiness of recommendations about patient management included in clinical practice

Supplemental material is available online.

Carrasco-Labra A, et al. J Am Dent Assoc 2015;146(5):327–336

"Guidelines are systematically developed **evidence-based** statements that assist providers, patients, policy makers, and other stakeholders to make informed decisions on health care and public health policy."

"Guidelines should make the **data** (direct evidence, indirect evidence, or purely expert opinion) and their **interpretation fully transparent**."

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Check for updates

TUTORIAL

WILEY Research Synthesis Methods

Using systematic reviews in guideline development: The GRADE approach

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Systematic reviews are essential to produce trustworthy guidelines. To assess the certainty of a body of evidence included in a systematic review, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group has developed an approach that is currently used by over 100 organizations, including the World Health Organization and the Cochrane Collaboration. GRADE provides operational definitions and instructions to rate the certainty of the evidence for each outcome in a review as high, moderate, low, or very low for the effects of interventions, prognostic estimates, values and preferences, test accuracy, and resource utilization. The assessment includes assessing risk of bias, imprecision, inconsistency, indirectness, and publication bias, the magnitude of effects, dose-response relations, and the impact of residual confounding and bias. Summary statistical information and assessments of certainty are presented in GRADE evidence summary tables, which can be produced using GRADE's official GRADEpro software tool (www.gradepro.org/). The evidence summary tables feed into the GRADE Evidence to Decision frameworks which guideline panels can use to produce recommendations.

KEYWORDS
certainty of the evidence, evidence tables, GRADE assessment, guideline, quality of evidence

1 | INTRODUCTION

Guidelines are systematically developed evidence-based statements that assist providers, patients, policy makers, and other stakeholders to make informed decisions on health care and public health policy.[1] There is a consensus that systematic reviews are essential to produce trustworthy guidelines.[1-8] Guideline developers are, however, often concerned about the additional workload associated with systematic reviews when compared to unsystematic identification and appraisal of the available evidence and expert opinion. Expert opinion, defined as a combination of an interpretation and judgments based on the interpretation of relevant data, is nevertheless of crucial importance for guideline development. It is also worthwhile noting the misuse of the term "expert opinion" in guideline development. Empirical evidence suggests that evidence labeled as expert opinion often represents indirect evidence and occasionally represents very-low-quality evidence.[9] In addition, expert opinion, which can be described as a summary of looking at facts (eg, their observations in the world), interpreting these facts, and making judgments about them, is required in the Grading of Recommendations Assessment, Development and Evaluation (GRADE) process, too. The difference lies in being explicit about the type of facts included based on transparent methods and making the interpretation and judgments explicit as opposed to implicit.[10-12] Hence, guidelines should make the data (direct evidence, indirect evidence, or purely expert

"Overall, a conservative estimate is that **50%** of current evidence-based guidelines suffer from either methodological flaws, have questionable content with respect to the primary evidence to which they refer to or documented outcomes diverging from those expected.

On average, guidelines sponsored by medical specialty societies are of lower quality compared with those endorsed by national health agencies."

Evid Based Med 2017;22(1):1-3

Perspective

CrossMark

Wrong guidelines: why and how often they occur

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10.1136/ebmed-2016-110606

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Abstract

Evidence-based guidelines are considered an essential tool in assisting physicians, policymakers and patients when choosing among alternative care options and are considered unbiased standards of care. Unfortunately, depending on how their reliability is measured, up to 50% of guidelines can be considered untrustworthy. This carries serious consequences for patients' safety, resource use and health economics burden. Although conflict of interests, panel composition and methodological flaws are traditionally thought to be the main reasons undermining their untrustworthiness, corruption and waste of biomedical research also contribute. We discuss these issues in the hope for a wider awareness of the limits of guidelines.

Introduction

Produced by panels of renowned experts according to formal processes and rules, evidence-based guidelines are considered unbiased and valid, having the same level of certainty of the conventional scientific method.[1] However, in spite of the efforts set forth to produce reliable guidelines, several concerns about their trustworthiness have been recently raised.[2] Although the exact magnitude of this phenomenon is still unknown, it is essential to establish the degree and impact of unintended and harmful clinical effects triggered by the adoption of flawed guidelines, and moreover, the implications of the significant waste of resources, and generalised damage to the evidence-based 'quality mark'. Understanding why and how often guideline errors occur will encourage users to cautiously handle clinical guideline recommendations and will promote the use of different strategies to tackle this challenge successfully.

When is a clinical guideline wrong?

Formulating a judgement on the validity of a guideline is not straightforward, since producing a guideline is a very complex process involving technical skills (searching for primary evidence efficiently), value judgements (rating that evidence) and social aspects (managing discussion and achieving consensus within the guideline panel group).[3] Broadly speaking, any guideline failing to offer the right advice should be considered erroneous and, conversely correct 'if, when followed, they lead to the health and cost outcomes projected for them, with other things being equal'.[4] However, judging guidelines only once the effects derived from their adoption are known, is rarely possible. More often, we consider to what extent 'the projected health outcomes and costs of alternative courses of action, the relationship between the evidence and recommendations, the substance and quality of the scientific and clinical evidence cited, and the means used to evaluate the evidence'[4] are convincing. That is how we measure the reliability of guidelines assessing the methods followed for producing them (*methodological trustworthiness*) and/or their content, whether primary evidence was correctly searched, evaluated, synthesised and translated onto a given recommendation (*content trustworthiness*).

Epidemiology of untrustworthy guidelines

Irrespective of how we define their reliability, an 'epidemiology' of wrong guidelines still needs to be written (see online supplementary file). Interestingly, claims of methodological untrustworthiness were raised since their first appearance. In 2000, only 22 of 431 (5%) guidelines screened by Grilli *et al*[5] fulfilled 3 basic quality criteria, whereas 221 (54%) of them did not meet any quality criterion. Similarly, the mean overall adherence to a more complex quality checklist was 47% among a set of 279 guidelines in another study published in 1999.[6] Quality did not subsequently improve, with little or no progress found over the course of the next two decades, since in 2012 less than half of 130 guidelines met more than 50% of the Institute of Medicine (IOM) standards,[7] a finding independently confirmed. Content trustworthiness was not assessed to the same extent, but substandard results have been frequently reported.

Overall, a conservative estimate is that 50% of current evidence-based guidelines suffer from either methodological flaws, have questionable content with respect to the primary evidence to which they refer to or documented outcomes diverging from those expected. On average, guidelines sponsored by medical specialty societies were and still continue to be of lower quality compared with those endorsed by national health agencies.

Why do errors occur in evidence-based guidelines?

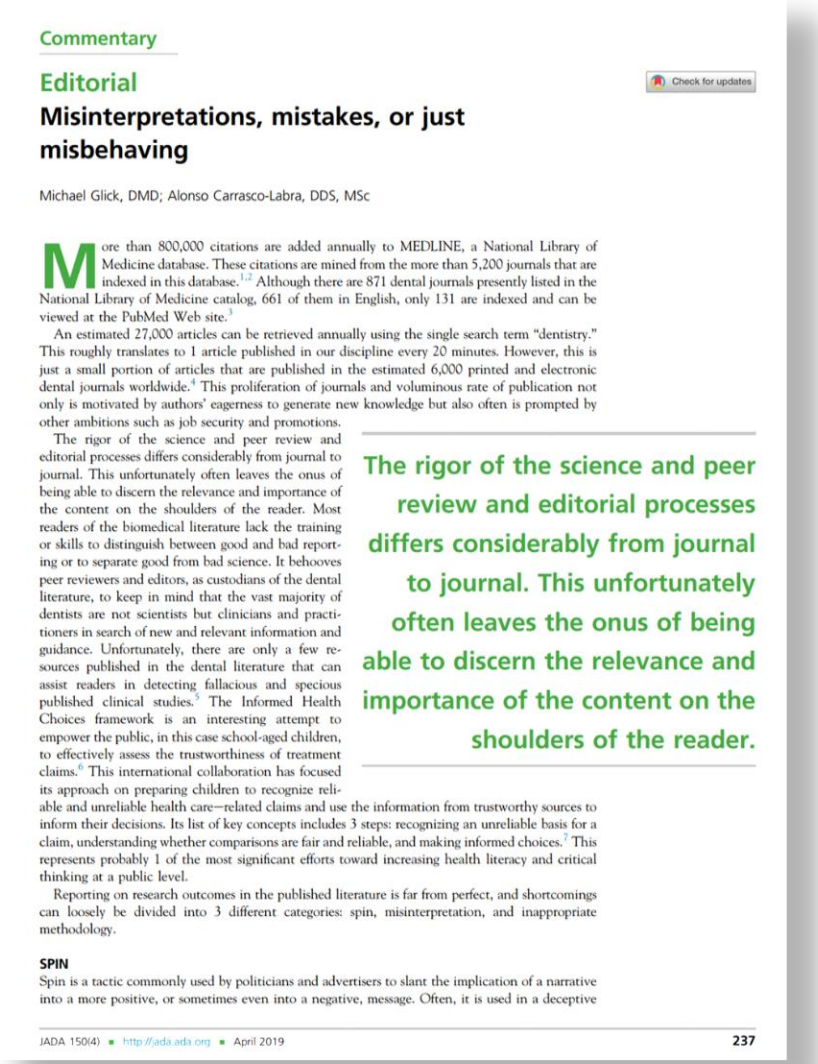
Early consensus-based guidelines considered evidence in a variable and unpredictable way and were particularly at risk of errors, whereas more recent evidence-based guidelines should ensure more balanced and reliable recommendations (figure 1). However, despite the desirable features of these newer guidelines produced since the early 1990s,[7] their quality remained largely unsatisfactory, with the occurrence of one or more of the following factors related to the guideline making process: (1) limited and unbalanced panel composition with excess of specialists and content experts favouring new treatments and interventions disproportionately,[8] (2) stacking of panels with experts with (known) prejudices about what was to be evaluated,[9] (3) lack of formal consensus management methods within the panel groups with prevalence of dysfunctional decision paths, (4) oversimplified, opaque and inconsistent methods for rating evidence and making consistent, clear and

Linked

► http://dx.doi.org/10.1136/ebmed-2016-110607

"**Spin** can be found in the results and conclusion sections of abstracts, as well as in the results, discussion, and conclusion sections in the main text.

A study of nonrandomized studies found at least 1 example of spin in the abstract of 107 of 128 assessed articles (84%), with erroneous use of causal language identified in 68 (53%) of abstracts."



Commentary

Editorial

Check for updates

Misinterpretations, mistakes, or just misbehaving

Michael Glick, DMD; Alonso Carrasco-Labra, DDS, MSc

More than 800,000 citations are added annually to MEDLINE, a National Library of Medicine database. These citations are mined from the more than 5,200 journals that are indexed in this database.[1,2] Although there are 871 dental journals presently listed in the National Library of Medicine catalog, 661 of them in English, only 131 are indexed and can be viewed at the PubMed Web site.[3]

An estimated 27,000 articles can be retrieved annually using the single search term "dentistry." This roughly translates to 1 article published in our discipline every 20 minutes. However, this is just a small portion of articles that are published in the estimated 6,000 printed and electronic dental journals worldwide.[4] This proliferation of journals and voluminous rate of publication not only is motivated by authors' eagerness to generate new knowledge but also often is prompted by other ambitions such as job security and promotions.

The rigor of the science and peer review and editorial processes differs considerably from journal to journal. This unfortunately often leaves the onus of being able to discern the relevance and importance of the content on the shoulders of the reader. Most readers of the biomedical literature lack the training or skills to distinguish between good and bad reporting or to separate good from bad science. It behooves peer reviewers and editors, as custodians of the dental literature, to keep in mind that the vast majority of dentists are not scientists but clinicians and practitioners in search of new and relevant information and guidance. Unfortunately, there are only a few resources published in the dental literature that can assist readers in detecting fallacious and specious published clinical studies.[5] The Informed Health Choices framework is an interesting attempt to empower the public, in this case school-aged children, to effectively assess the trustworthiness of treatment claims.[6] This international collaboration has focused its approach on preparing children to recognize reliable and unreliable health care–related claims and use the information from trustworthy sources to inform their decisions. Its list of key concepts includes 3 steps: recognizing an unreliable basis for a claim, understanding whether comparisons are fair and reliable, and making informed choices.[7] This represents probably 1 of the most significant efforts toward increasing health literacy and critical thinking at a public level.

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Reporting on research outcomes in the published literature is far from perfect, and shortcomings can loosely be divided into 3 different categories: spin, misinterpretation, and inappropriate methodology.

SPIN

Spin is a tactic commonly used by politicians and advertisers to slant the implication of a narrative into a more positive, or sometimes even into a negative, message. Often, it is used in a deceptive

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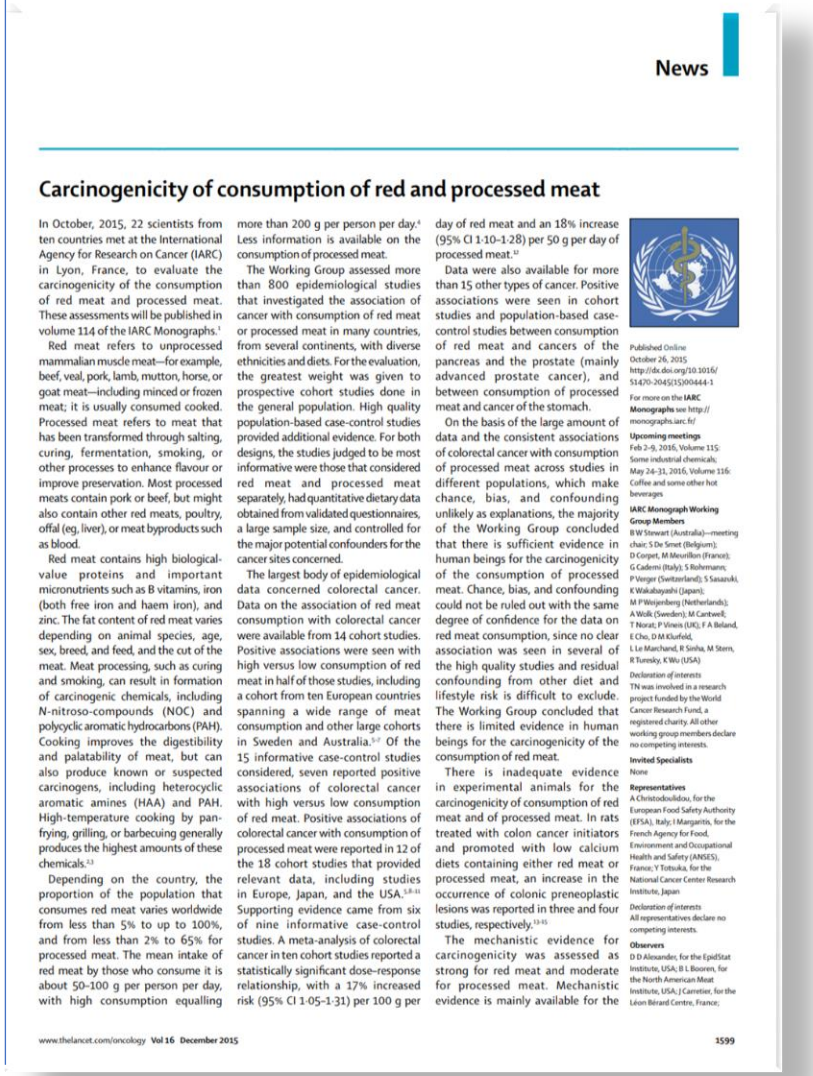

News

Carcinogenicity of consumption of red and processed meat

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Red meat contains high biological-value proteins and important micronutrients such as B vitamins, iron (both free iron and haem iron), and zinc. The fat content of red meat varies depending on animal species, age, sex, breed, and feed, and the cut of the meat. Meat processing, such as curing and smoking, can result in formation of carcinogenic chemicals, including *N*-nitroso-compounds (NOC) and polycyclic aromatic hydrocarbons (PAH). Cooking improves the digestibility and palatability of meat, but can also produce known or suspected carcinogens, including heterocyclic aromatic amines (HAA) and PAH. High-temperature cooking by pan-frying, grilling, or barbecuing generally produces the highest amounts of these chemicals.[2,3]

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The Working Group assessed more than 800 epidemiological studies that investigated the association of cancer with consumption of red meat or processed meat in many countries, from several continents, with diverse ethnicities and diets. For the evaluation, the greatest weight was given to prospective cohort studies done in the general population. High quality population-based case-control studies provided additional evidence. For both designs, the studies judged to be most informative were those that considered red meat and processed meat separately, had quantitative dietary data obtained from validated questionnaires, a large sample size, and controlled for the major potential confounders for the cancer sites concerned.

The largest body of epidemiological data concerned colorectal cancer. Data on the association of red meat consumption with colorectal cancer were available from 14 cohort studies. Positive associations were seen with high versus low consumption of red meat in half of those studies, including a cohort from ten European countries spanning a wide range of meat consumption and other large cohorts in Sweden and Australia.[5–7] Of the 15 informative case-control studies considered, seven reported positive associations of colorectal cancer with high versus low consumption of red meat. Positive associations of colorectal cancer with consumption of processed meat were reported in 12 of the 18 cohort studies that provided relevant data, including studies in Europe, Japan, and the USA.[3,8–11] Supporting evidence came from six of nine informative case-control studies. A meta-analysis of colorectal cancer in ten cohort studies reported a statistically significant dose–response relationship, with a 17% increased risk (95% CI 1·05–1·31) per 100 g per day of red meat and an 18% increase (95% CI 1·10–1·28) per 50 g per day of processed meat.[12]

Data were also available for more than 15 other types of cancer. Positive associations were seen in cohort studies and population-based case-control studies between consumption of red meat and cancers of the pancreas and the prostate (mainly advanced prostate cancer), and between consumption of processed meat and cancer of the stomach.

On the basis of the large amount of data and the consistent associations of colorectal cancer with consumption of processed meat across studies in different populations, which make chance, bias, and confounding unlikely as explanations, the majority of the Working Group concluded that there is sufficient evidence in human beings for the carcinogenicity of the consumption of processed meat. Chance, bias, and confounding could not be ruled out with the same degree of confidence for the data on red meat consumption, since no clear association was seen in several of the high quality studies and residual confounding from other diet and lifestyle risk is difficult to exclude. The Working Group concluded that there is limited evidence in human beings for the carcinogenicity of the consumption of red meat.

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Feb 2–9, 2016, Volume 115: Some industrial chemicals;
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Declaration of interests
TN was involved in a research project funded by the World Cancer Research Fund, a registered charity. All other working group members declare no competing interests.

Invited Specialists
None

Representatives
A Christodoulidou, for the European Food Safety Authority (EFSA), Italy; I Margaritis, for the French Agency for Food, Environment and Occupational Health and Safety (ANSES), France; Y Totsuka, for the National Cancer Center Research Institute, Japan

Declaration of interests
All representatives declare no competing interests.

Observers
D D Alexander, for the EpidStat Institute, USA; B L Boonen, for the North American Meat Institute, USA; J Carretier, for the Léon Bérard Centre, France;

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[IARC Monographs evaluate consumption of red meat and processed meat (who.int)]

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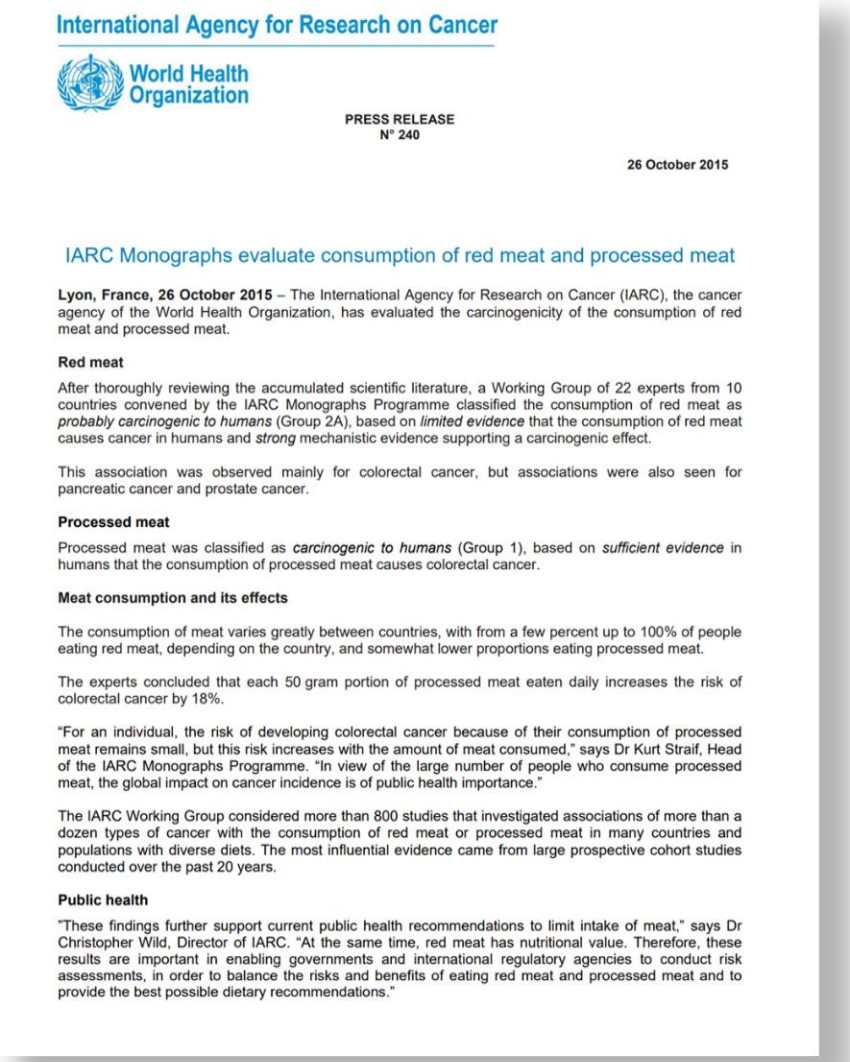

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World Health Organization

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Meat consumption and its effects

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The experts concluded that each 50 gram portion of processed meat eaten daily increases the risk of colorectal cancer by 18%.

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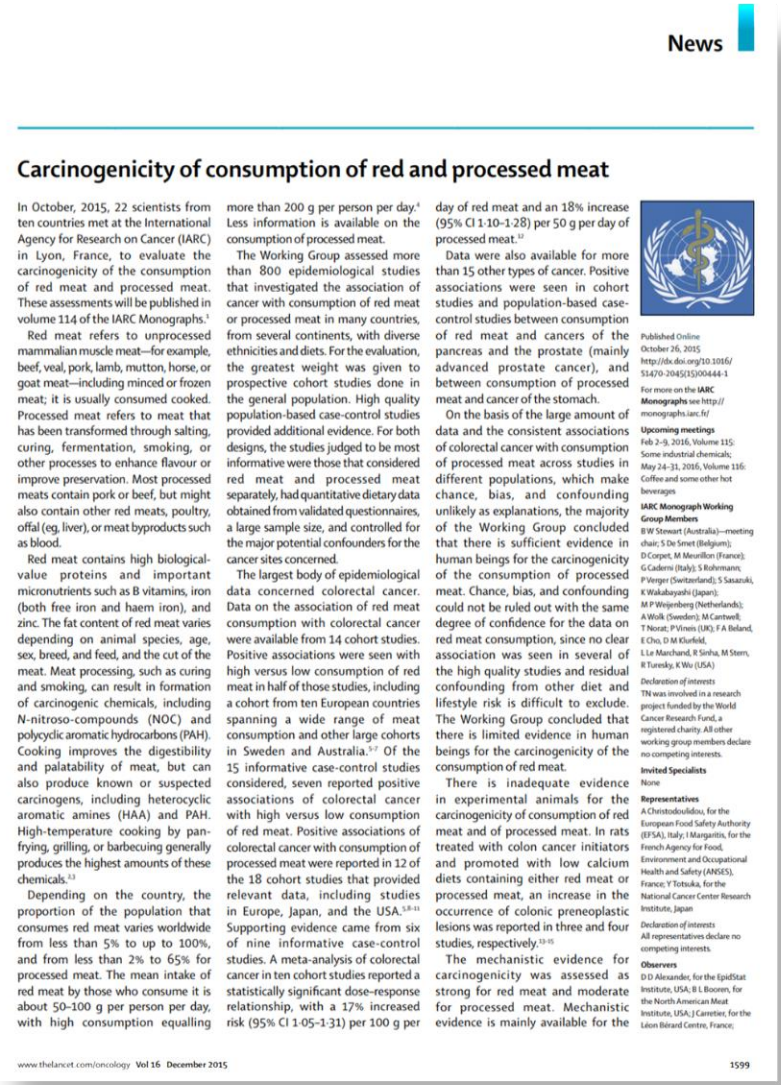

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May 24–31, 2016, Volume 116: Coffee and some other hot beverages

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B W Stewart (Australia)—meeting chair; S De Smet (Belgium); D Corpet, M Meurillon (France); G Caderni (Italy); S Rohrmann; P Verger (Switzerland); S Sasazuki, K Wakabayashi (Japan); M P Weijenberg (Netherlands); A Wolk (Sweden); M Cantwell; T Norat; P Vineis (UK); F A Beland, E Cho, D M Klurfeld, L Le Marchand, R Sinha, M Stern, R Turesky, K Wu (USA)

Declaration of interests
TN was involved in a research project funded by the World Cancer Research Fund, a registered charity. All other working group members declare no competing interests.

Invited Specialists
None

Representatives
A Christodouldidou, for the European Food Safety Authority (EFSA), Italy; I Margaritis, for the French Agency for Food, Environment and Occupational Health and Safety (ANSES), France; Y Totsuka, for the National Cancer Center Research Institute, Japan

Declaration of interests
All representatives declare no competing interests.

Observers
D D Alexander, for the EpidStat Institute, USA; B L Booren, for the North American Meat Institute, USA; J Carretier, for the Léon Bérard Centre, France;

Lancet Oncology. 2015;16(16):1599-1600

Know the Facts

Colorectal Cancer

The Average Lifetime Risk for Men = 1 in 23.
The Average Lifetime Risk for Women = 1 in 25.

The third most commonly diagnosed cancer in men and women combined in the U.S.

The second leading cause of cancer death in men and women combined in the U.S.

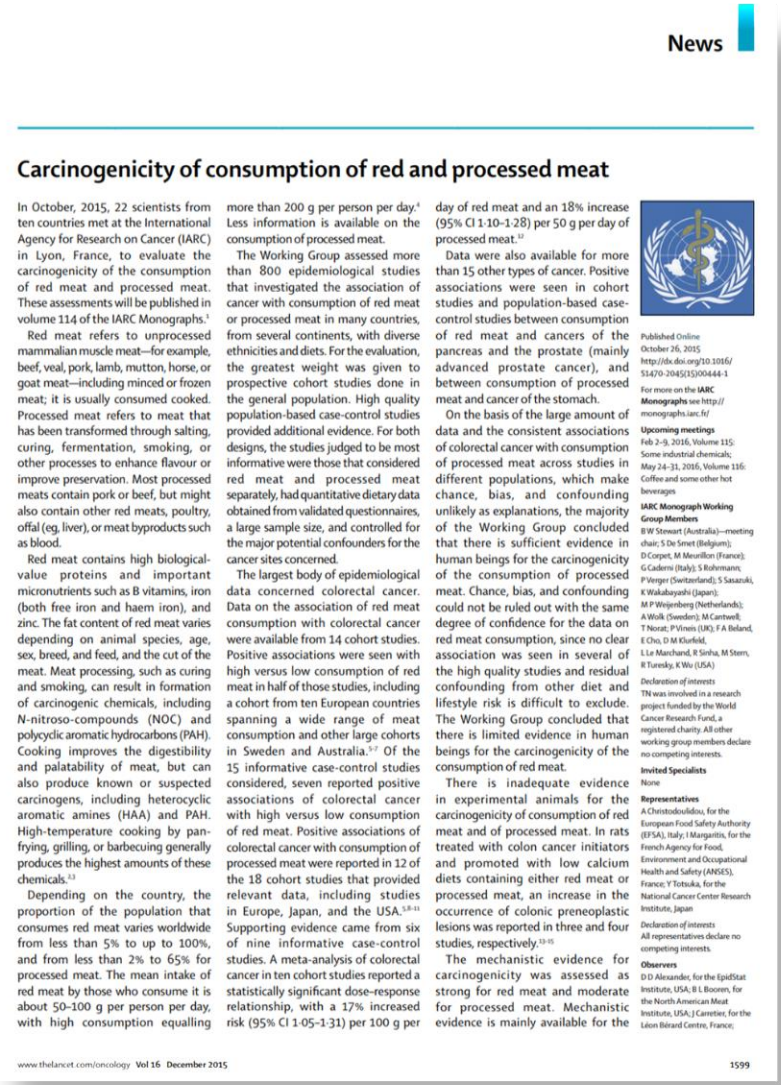
Relative Risk – 18%

Absolute Risk (no processed meat) => 4%

Absolute Risk (processed meat) => 4% x 1.18 ≈ 5%

Conclusions:
Over a lifetime, eating 2 slices of bacon every day versus no bacon will result in an estimated **1 additional person developing colorectal cancer among 100 individuals**.

Lancet Oncology. 2015;16(16):1599-1600



News

Carcinogenicity of consumption of red and processed meat

In October, 2015, 22 scientists from ten countries met at the International Agency for Research on Cancer (IARC) in Lyon, France, to evaluate the carcinogenicity of the consumption of red meat and processed meat. These assessments will be published in volume 114 of the IARC Monographs.[1]

Red meat refers to unprocessed mammalian muscle meat—for example, beef, veal, pork, lamb, mutton, horse, or goat meat—including minced or frozen meat; it is usually consumed cooked. Processed meat refers to meat that has been transformed through salting, curing, fermentation, smoking, or other processes to enhance flavour or improve preservation. Most processed meats contain pork or beef, but might also contain other red meats, poultry, offal (eg, liver), or meat byproducts such as blood.

Red meat contains high biological-value proteins and important micronutrients such as B vitamins, iron (both free iron and haem iron), and zinc. The fat content of red meat varies depending on animal species, age, sex, breed, and feed, and the cut of the meat. Meat processing, such as curing and smoking, can result in formation of carcinogenic chemicals, including *N*-nitroso-compounds (NOC) and polycyclic aromatic hydrocarbons (PAH). Cooking improves the digestibility and palatability of meat, but can also produce known or suspected carcinogens, including heterocyclic aromatic amines (HAA) and PAH. High-temperature cooking by pan-frying, grilling, or barbecuing generally produces the highest amounts of these chemicals.[2,3]

Depending on the country, the proportion of the population that consumes red meat varies worldwide from less than 5% to up to 100%, and from less than 2% to 65% for processed meat. The mean intake of red meat by those who consume it is about 50–100 g per person per day, with high consumption equalling more than 200 g per person per day.[4] Less information is available on the consumption of processed meat.

The Working Group assessed more than 800 epidemiological studies that investigated the association of cancer with consumption of red meat or processed meat in many countries, from several continents, with diverse ethnicities and diets. For the evaluation, the greatest weight was given to prospective cohort studies done in the general population. High quality population-based case-control studies provided additional evidence. For both designs, the studies judged to be most informative were those that considered red meat and processed meat separately, had quantitative dietary data obtained from validated questionnaires, a large sample size, and controlled for the major potential confounders for the cancer sites concerned.

The largest body of epidemiological data concerned colorectal cancer. Data on the association of red meat consumption with colorectal cancer were available from 14 cohort studies. Positive associations were seen with high versus low consumption of red meat in half of those studies, including a cohort from ten European countries spanning a wide range of meat consumption and other large cohorts in Sweden and Australia.[5–7] Of the 15 informative case-control studies considered, seven reported positive associations of colorectal cancer with high versus low consumption of red meat. Positive associations of colorectal cancer with consumption of processed meat were reported in 12 of the 18 cohort studies that provided relevant data, including studies in Europe, Japan, and the USA.[5,8–11] Supporting evidence came from six of nine informative case-control studies. A meta-analysis of colorectal cancer in ten cohort studies reported a statistically significant dose-response relationship, with a 17% increased risk (95% CI 1·05–1·31) per 100 g per day of red meat and an 18% increase (95% CI 1·10–1·28) per 50 g per day of processed meat.[12]

Data were also available for more than 15 other types of cancer. Positive associations were seen in cohort studies and population-based case-control studies between consumption of red meat and cancers of the pancreas and the prostate (mainly advanced prostate cancer), and between consumption of processed meat and cancer of the stomach.

On the basis of the large amount of data and the consistent associations of colorectal cancer with consumption of processed meat across studies in different populations, which make chance, bias, and confounding unlikely as explanations, the majority of the Working Group concluded that there is sufficient evidence in human beings for the carcinogenicity of the consumption of processed meat. Chance, bias, and confounding could not be ruled out with the same degree of confidence for the data on red meat consumption, since no clear association was seen in several of the high quality studies and residual confounding from other diet and lifestyle risk is difficult to exclude. The Working Group concluded that there is limited evidence in human beings for the carcinogenicity of the consumption of red meat.

There is inadequate evidence in experimental animals for the carcinogenicity of consumption of red meat and of processed meat. In rats treated with colon cancer initiators and promoted with low calcium diets containing either red meat or processed meat, an increase in the occurrence of colonic preneoplastic lesions was reported in three and four studies, respectively.[13–15]

The mechanistic evidence for carcinogenicity was assessed as strong for red meat and moderate for processed meat. Mechanistic evidence is mainly available for the

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For more on the **IARC Monographs** see http://monographs.iarc.fr/

Upcoming meetings
Feb 2–9, 2016, Volume 115: Some industrial chemicals;
May 24–31, 2016, Volume 116: Coffee and some other hot beverages

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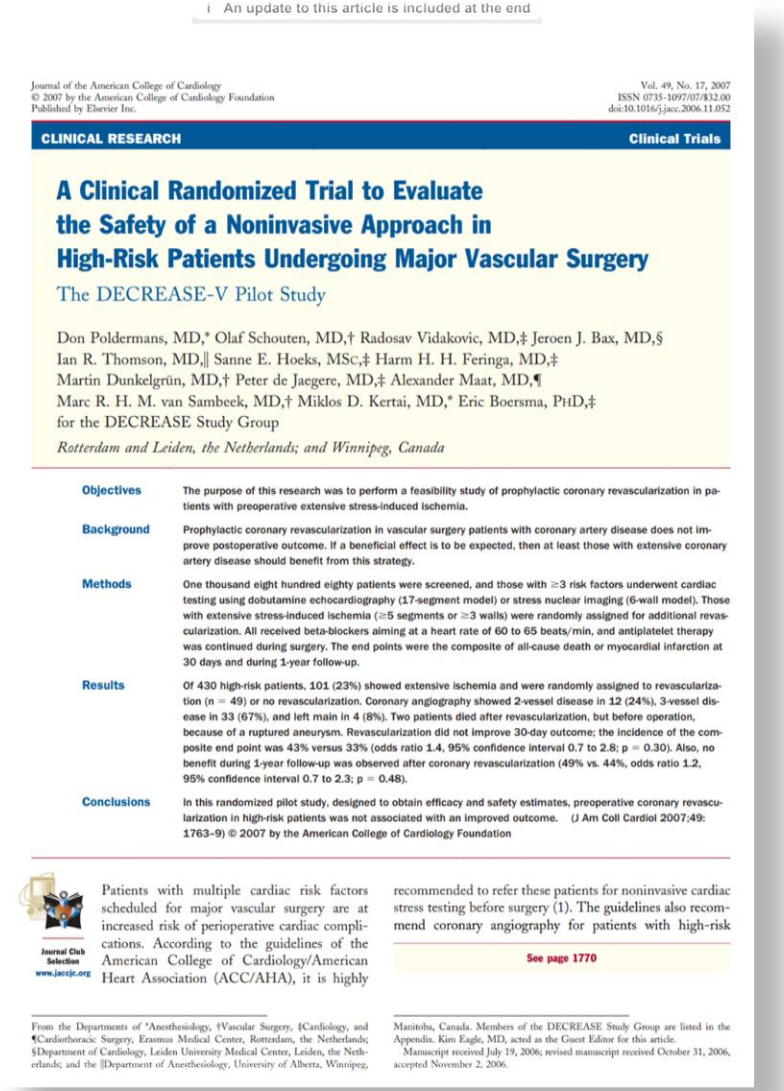
Research was led by **Dr. Don Poldermans**, a Dutch cardiologist, and claimed that using beta-blockers in patients undergoing non-cardiac surgery significantly reduced their risk of heart complications.

These findings were included in **European Society of Cardiology (ESC) guidelines (2009)**, which recommended perioperative beta-blocker use.

As a result, **hospitals and physicians across Europe and the UK adopted beta-blockers as a standard pre-surgical treatment**.



i An update to this article is included at the end

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CLINICAL RESEARCH — Clinical Trials

A Clinical Randomized Trial to Evaluate the Safety of a Noninvasive Approach in High-Risk Patients Undergoing Major Vascular Surgery

The DECREASE-V Pilot Study

Don Poldermans, MD,* Olaf Schouten, MD,† Radosav Vidakovic, MD,‡ Jeroen J. Bax, MD,§ Ian R. Thomson, MD,‖ Sanne E. Hoeks, MSc,‡ Harm H. H. Feringa, MD,‡ Martin Dunkelgrün, MD,† Peter de Jaegere, MD,‡ Alexander Maat, MD,¶ Marc R. H. M. van Sambeek, MD,† Miklos D. Kertai, MD,* Eric Boersma, PhD,‡ for the DECREASE Study Group

Rotterdam and Leiden, the Netherlands; and Winnipeg, Canada

Objectives The purpose of this research was to perform a feasibility study of prophylactic coronary revascularization in patients with preoperative extensive stress-induced ischemia.

Background Prophylactic coronary revascularization in vascular surgery patients with coronary artery disease does not improve postoperative outcome. If a beneficial effect is to be expected, then at least those with extensive coronary artery disease should benefit from this strategy.

Methods One thousand eight hundred eighty patients were screened, and those with ≥3 risk factors underwent cardiac testing using dobutamine echocardiography (17-segment model) or stress nuclear imaging (6-wall model). Those with extensive stress-induced ischemia (≥5 segments or ≥3 walls) were randomly assigned for additional revascularization. All received beta-blockers aiming at a heart rate of 60 to 65 beats/min, and antiplatelet therapy was continued during surgery. The end points were the composite of all-cause death or myocardial infarction at 30 days and during 1-year follow-up.

Results Of 430 high-risk patients, 101 (23%) showed extensive ischemia and were randomly assigned to revascularization (n = 49) or no revascularization. Coronary angiography showed 2-vessel disease in 12 (24%), 3-vessel disease in 33 (67%), and left main in 4 (8%). Two patients died after revascularization, but before operation, because of a ruptured aneurysm. Revascularization did not improve 30-day outcome; the incidence of the composite end point was 43% versus 33% (odds ratio 1.4, 95% confidence interval 0.7 to 2.8; p = 0.30). Also, no benefit during 1-year follow-up was observed after coronary revascularization (49% vs. 44%, odds ratio 1.2, 95% confidence interval 0.7 to 2.3; p = 0.48).

Conclusions In this randomized pilot study, designed to obtain efficacy and safety estimates, preoperative coronary revascularization in high-risk patients was not associated with an improved outcome. (J Am Coll Cardiol 2007;49:1763–9) © 2007 by the American College of Cardiology Foundation

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Patients with multiple cardiac risk factors scheduled for major vascular surgery are at increased risk of perioperative cardiac complications. According to the guidelines of the American College of Cardiology/American Heart Association (ACC/AHA), it is highly recommended to refer these patients for noninvasive cardiac stress testing before surgery (1). The guidelines also recommend coronary angiography for patients with high-risk

See page 1770

From the Departments of *Anesthesiology, †Vascular Surgery, ‡Cardiology, and ¶Cardiothoracic Surgery, Erasmus Medical Center, Rotterdam, the Netherlands; §Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands; and the ‖Department of Anesthesiology, University of Alberta, Winnipeg, Manitoba, Canada. Members of the DECREASE Study Group are listed in the Appendix. Kim Eagle, MD, acted as the Guest Editor for this article.

Manuscript received July 19, 2006; revised manuscript received October 31, 2006, accepted November 2, 2006.

Fabricated and Manipulated Data

- An investigation found that **patient data was either fabricated or selectively manipulated**.
- Poldermans failed to obtain ethical approvals for some of his work.

Lack of Proper Randomization and Controls

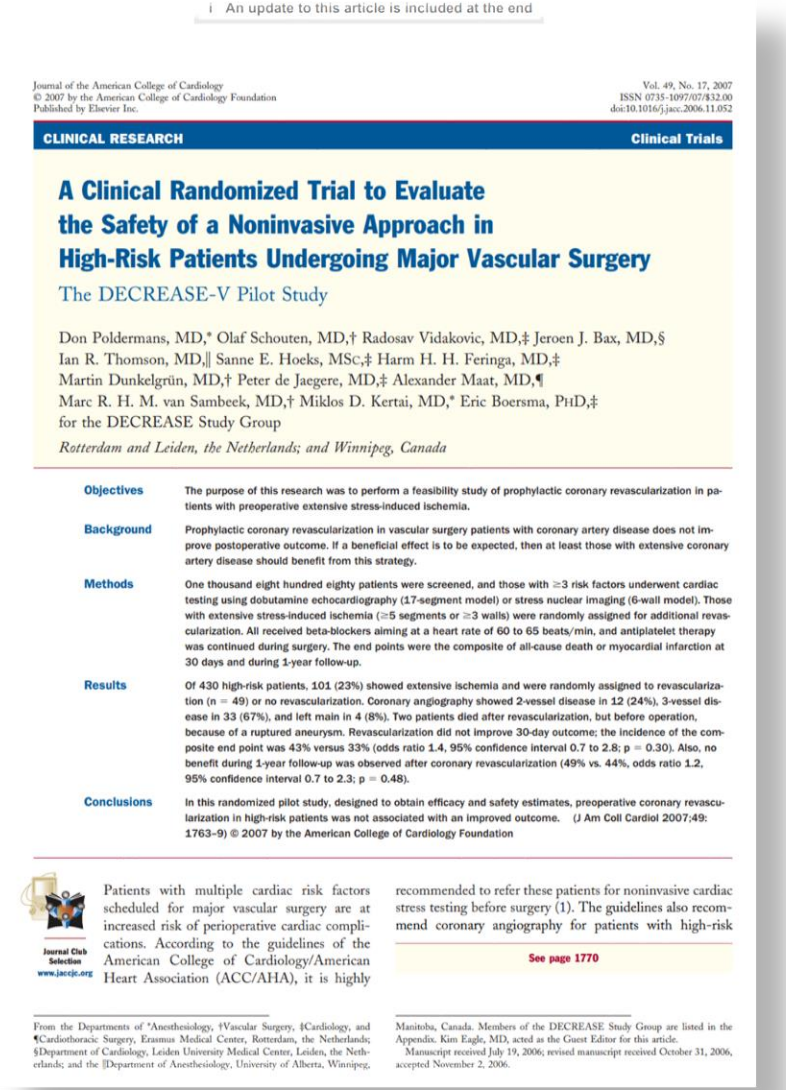
- The trials lacked proper **randomization and double-blinding**.
- Many patients included in the study were not properly tracked.

Lack Contradictory Findings in Later Research

- Subsequent **randomized controlled trials (RCTs) showed increased risks associated with perioperative beta-blockers**, contradicting Poldermans' claims.
- A major **2013 meta-analysis published in the British Medical Journal (BMJ)** found that beta-blocker use in non-cardiac surgery **increased the risk of stroke and death by 27% and 33%, respectively**.

The **Dutch Beta-Blocker Study Scandal** is a striking example of how flawed or misleading medical research can lead to widespread harm. The study in question was **the trial**, which was later found to be based on fabricated and manipulated data.

The consequences of this fraudulent study contributed to an estimated 10,000 deaths in the UK alone.



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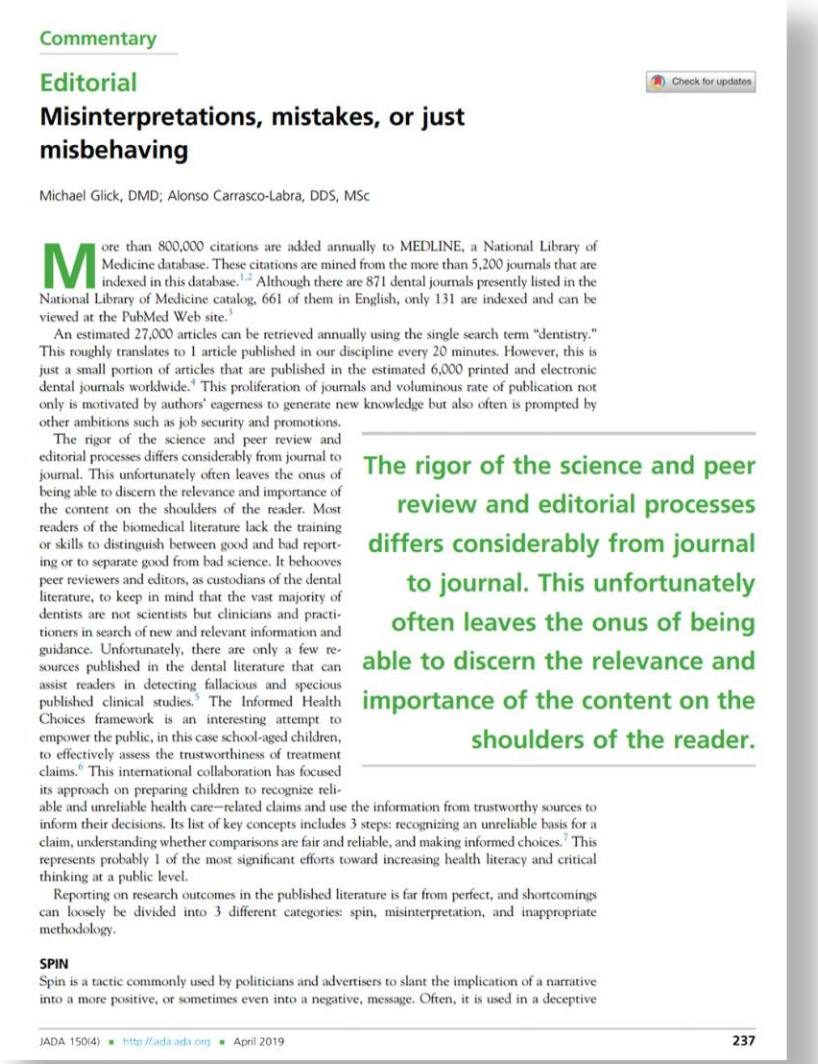
Inappropriate methodology

- HARKing (hypothesizing after the results are known);
- JARKing (justifying after the results are known);
- P-hacking;
- using the wrong study designs for specific research aims;
- using inappropriate statistical tests;
- inappropriate data and analyzes.



Commentary

Editorial

Check for updates

Misinterpretations, mistakes, or just misbehaving

Michael Glick, DMD; Alonso Carrasco-Labra, DDS, MSc

More than 800,000 citations are added annually to MEDLINE, a National Library of Medicine database. These citations are mined from the more than 5,200 journals that are indexed in this database.[1,2] Although there are 871 dental journals presently listed in the National Library of Medicine catalog, 661 of them in English, only 131 are indexed and can be viewed at the PubMed Web site.[3]

An estimated 27,000 articles can be retrieved annually using the single search term "dentistry." This roughly translates to 1 article published in our discipline every 20 minutes. However, this is just a small portion of articles that are published in the estimated 6,000 printed and electronic dental journals worldwide.[4] This proliferation of journals and voluminous rate of publication not only is motivated by authors' eagerness to generate new knowledge but also often is prompted by other ambitions such as job security and promotions.

The rigor of the science and peer review and editorial processes differs considerably from journal to journal. This unfortunately often leaves the onus of being able to discern the relevance and importance of the content on the shoulders of the reader. Most readers of the biomedical literature lack the training or skills to distinguish between good and bad reporting or to separate good from bad science. It behooves peer reviewers and editors, as custodians of the dental literature, to keep in mind that the vast majority of dentists are not scientists but clinicians and practitioners in search of new and relevant information and guidance. Unfortunately, there are only a few resources published in the dental literature that can assist readers in detecting fallacious and specious published clinical studies.[5] The Informed Health Choices framework is an interesting attempt to empower the public, in this case school-aged children, to effectively assess the trustworthiness of treatment claims.[6] This international collaboration has focused its approach on preparing children to recognize reliable and unreliable health care–related claims and use the information from trustworthy sources to inform their decisions. Its list of key concepts includes 3 steps: recognizing an unreliable basis for a claim, understanding whether comparisons are fair and reliable, and making informed choices.[7] This represents probably 1 of the most significant efforts toward increasing health literacy and critical thinking at a public level.

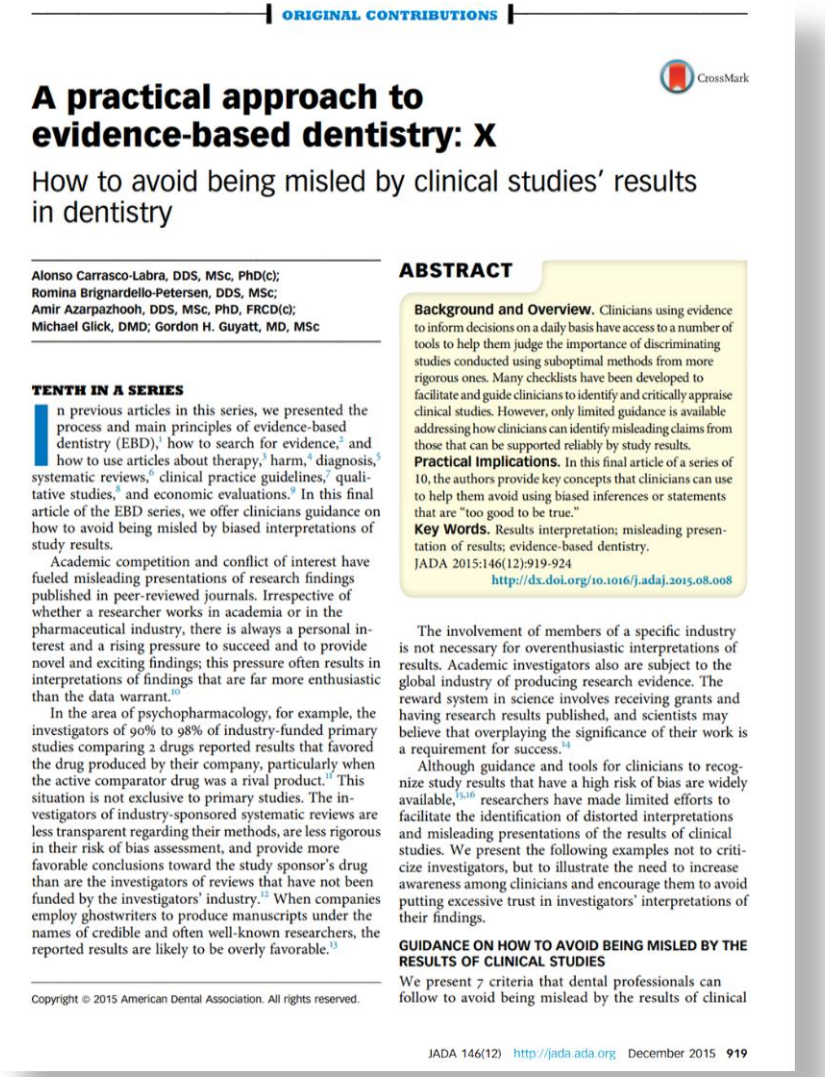
The rigor of the science and peer review and editorial processes differs considerably from journal to journal. This unfortunately often leaves the onus of being able to discern the relevance and importance of the content on the shoulders of the reader.

Reporting on research outcomes in the published literature is far from perfect, and shortcomings can loosely be divided into 3 different categories: spin, misinterpretation, and inappropriate methodology.

SPIN

Spin is a tactic commonly used by politicians and advertisers to slant the implication of a narrative into a more positive, or sometimes even into a negative, message. Often, it is used in a deceptive

"Although clinicians have available a number of guides to critically appraise the risk of bias associated with clinical studies, little guidance exists addressing how to protect patients and clinicians from being misled by the interpretations offered by the authors of clinical studies."



ORIGINAL CONTRIBUTIONS

A practical approach to evidence-based dentistry: X

How to avoid being misled by clinical studies' results in dentistry

Alonso Carrasco-Labra, DDS, MSc, PhD(c); Romina Brignardello-Petersen, DDS, MSc; Amir Azarpazhooh, DDS, MSc, PhD, FRCD(c); Michael Glick, DMD; Gordon H. Guyatt, MD, MSc

ABSTRACT

Background and Overview. Clinicians using evidence to inform decisions on a daily basis have access to a number of tools to help them judge the importance of discriminating studies conducted using suboptimal methods from more rigorous ones. Many checklists have been developed to facilitate and guide clinicians to identify and critically appraise clinical studies. However, only limited guidance is available addressing how clinicians can identify misleading claims from those that can be supported reliably by study results.

Practical Implications. In this final article of a series of 10, the authors provide key concepts that clinicians can use to help them avoid using biased inferences or statements that are "too good to be true."

Key Words. Results interpretation; misleading presentation of results; evidence-based dentistry.

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TENTH IN A SERIES

In previous articles in this series, we presented the process and main principles of evidence-based dentistry (EBD),[1] how to search for evidence,[2] and how to use articles about therapy,[3] harm,[4] diagnosis,[5] systematic reviews,[6] clinical practice guidelines,[7] qualitative studies,[8] and economic evaluations.[9] In this final article of the EBD series, we offer clinicians guidance on how to avoid being misled by biased interpretations of study results.

Academic competition and conflict of interest have fueled misleading presentations of research findings published in peer-reviewed journals. Irrespective of whether a researcher works in academia or in the pharmaceutical industry, there is always a personal interest and a rising pressure to succeed and to provide novel and exciting findings; this pressure often results in interpretations of findings that are far more enthusiastic than the data warrant.[10]

In the area of psychopharmacology, for example, the investigators of 90% to 98% of industry-funded primary studies comparing 2 drugs reported results that favored the drug produced by their company, particularly when the active comparator drug was a rival product.[11] This situation is not exclusive to primary studies. The investigators of industry-sponsored systematic reviews are less transparent regarding their methods, are less rigorous in their risk of bias assessment, and provide more favorable conclusions toward the study sponsor's drug than are the investigators of reviews that have not been funded by the investigators' industry.[12] When companies employ ghostwriters to produce manuscripts under the names of credible and often well-known researchers, the reported results are likely to be overly favorable.[13]

The involvement of members of a specific industry is not necessary for overenthusiastic interpretations of results. Academic investigators also are subject to the global industry of producing research evidence. The reward system in science involves receiving grants and having research results published, and scientists may believe that overplaying the significance of their work is a requirement for success.[14]

Although guidance and tools for clinicians to recognize study results that have a high risk of bias are widely available,[15,16] researchers have made limited efforts to facilitate the identification of distorted interpretations and misleading presentations of the results of clinical studies. We present the following examples not to criticize investigators, but to illustrate the need to increase awareness among clinicians and encourage them to avoid putting excessive trust in investigators' interpretations of their findings.

GUIDANCE ON HOW TO AVOID BEING MISLED BY THE RESULTS OF CLINICAL STUDIES

We present 7 criteria that dental professionals can follow to avoid being mislead by the results of clinical

Spurious relationships?

The NEW ENGLAND JOURNAL of MEDICINE

OCCASIONAL NOTES

Chocolate Consumption, Cognitive Function, and Nobel Laureates

Franz H. Messerli, M.D.

Dietary flavonoids, abundant in plant-based foods, have been shown to improve cognitive function. Specifically, a reduction in the risk of dementia, enhanced performance on some cognitive tests, and improved cognitive function in elderly patients with mild impairment have been associated with a regular intake of flavonoids.[1,2] A subclass of flavonoids called flavanols, which are widely present in cocoa, green tea, red wine, and some fruits, seems to be effective in slowing down or even reversing the reductions in cognitive performance that occur with aging. Dietary flavanols have also been shown to improve endothelial function and to lower blood pressure by causing vasodilation in the peripheral vasculature and in the brain.[3,4] Improved cognitive performance with the administration of a cocoa polyphenolic extract has even been reported in aged Wistar–Unilever rats.[5]

Since chocolate consumption could hypothetically improve cognitive function not only in individuals but also in whole populations, I wondered whether there would be a correlation between a country's level of chocolate consumption and its population's cognitive function. To my knowledge, no data on overall national cognitive function are publicly available. Conceivably, however, the total number of Nobel laureates per capita could serve as a surrogate end point reflecting the proportion with superior cognitive function and thereby give us some measure of the overall cognitive function of a given country.

METHODS

A list of countries ranked in terms of Nobel laureates per capita was downloaded from Wikipedia (http://en.wikipedia.org/wiki/List_of_countries_by_Nobel_laureates_per_capita). Because the population of a country is substantially higher than its number of Nobel laureates, the numbers had to be multiplied by 10 million. Thus, the numbers must be read as the number of Nobel laureates for every 10 million persons in a given country.

All Nobel Prizes that were awarded through October 10, 2011, were included. Data on per capita yearly chocolate consumption in 22 countries was obtained from Chocosuisse (www.chocosuisse.ch/web/chocosuisse/en/home), Theobroma-cacao (www.theobroma-cacao.de/wissen/wirtschaft/international/konsum), and Caobisco (www.caobisco.com/page.asp?p=213). Data were available from 2011 for 1 country (Switzerland), from 2010 for 15 countries, from 2004 for 5 countries, and from 2002 for 1 country (China).

RESULTS

There was a close, significant linear correlation ($r=0.791$, $P<0.0001$) between chocolate consumption per capita and the number of Nobel laureates per 10 million persons in a total of 23 countries (Fig. 1). When recalculated with the exclusion of Sweden, the correlation coefficient increased to 0.862. Switzerland was the top performer in terms of both the number of Nobel laureates and chocolate consumption. The slope of the regression line allows us to estimate that it would take about 0.4 kg of chocolate per capita per year to increase the number of Nobel laureates in a given country by 1. For the United States, that would amount to 125 million kg per year. The minimally effective chocolate dose seems to hover around 2 kg per year, and the dose–response curve reveals no apparent ceiling on the number of Nobel laureates at the highest chocolate-dose level of 11 kg per year.

Hypothesis

Since chocolate consumption could hypothetically improve cognitive function not only in individuals but also in whole populations, I wondered whether there would be a correlation between a country's level of chocolate consumption and its population's cognitive function. To my knowledge, no data on overall national cognitive function are publicly available. Conceivably, however, the total number of Nobel laureates per capita could serve as a surrogate end point reflecting the proportion with superior cognitive function and thereby give us some measure of the overall cognitive function of a given country.

Messerli FH. N Engl J Med. 2012 (Oct. 10)

Results

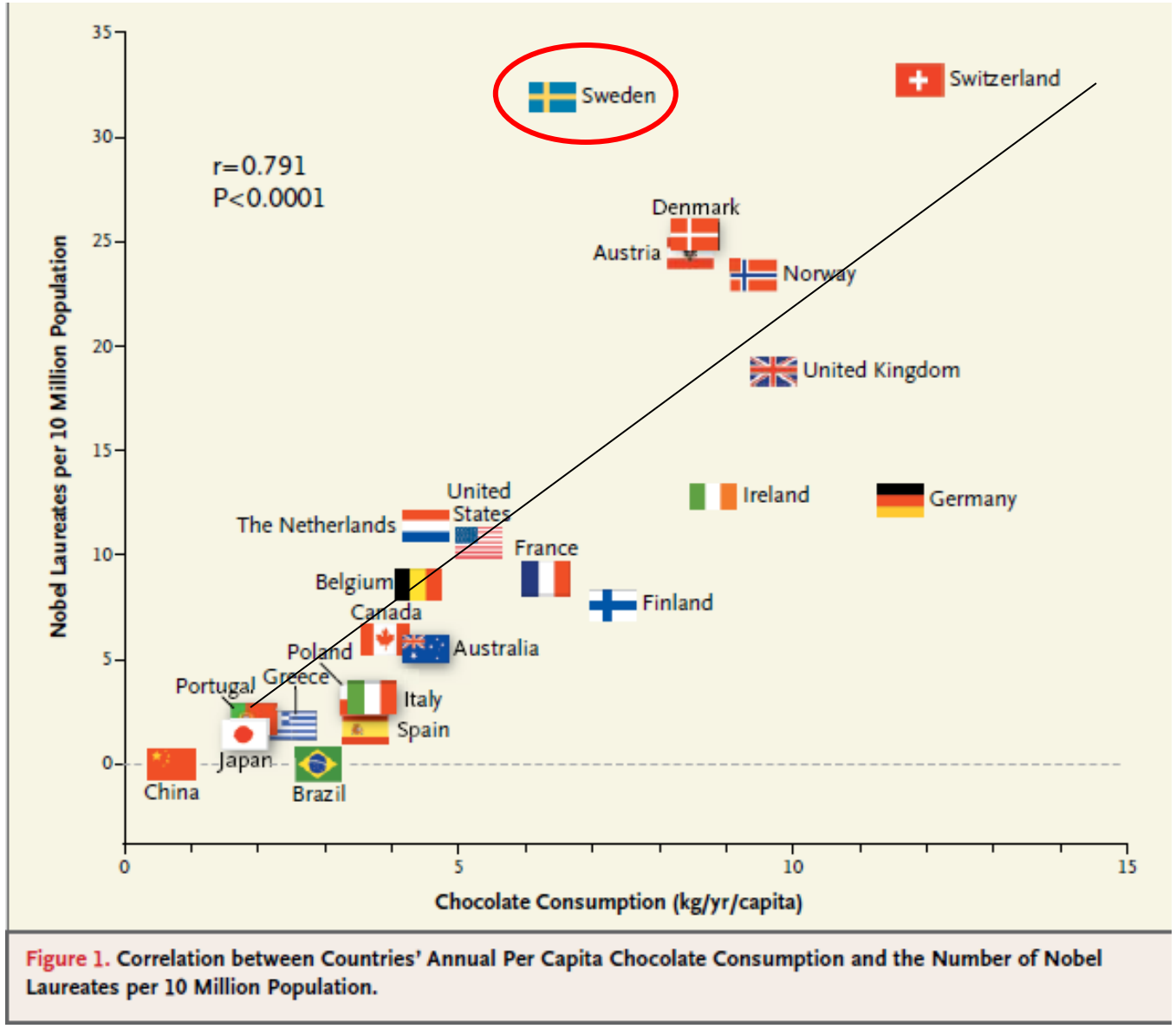


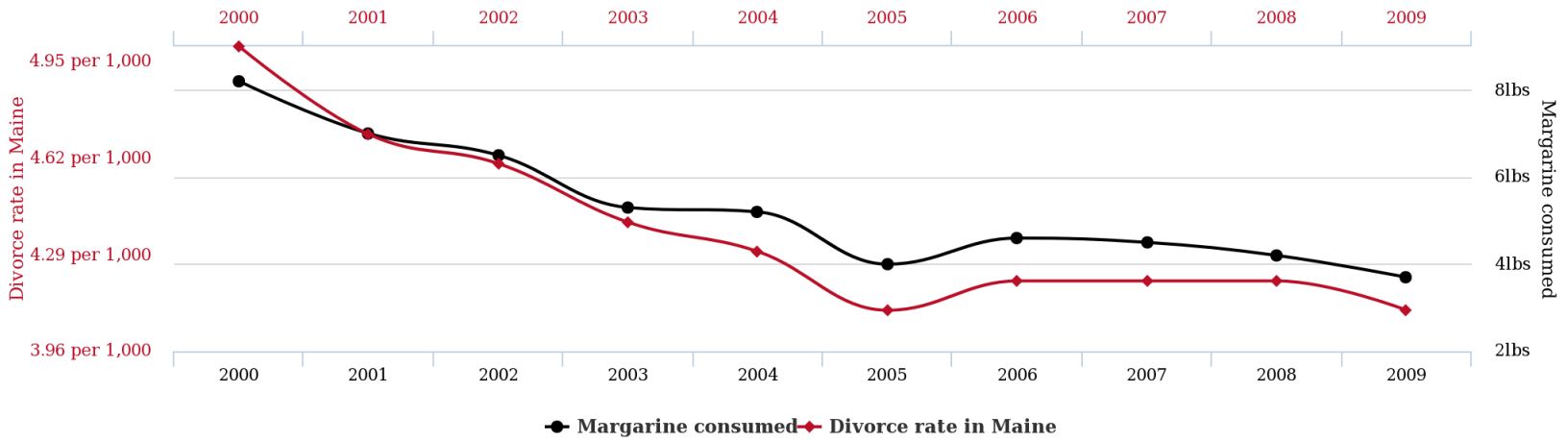
Figure 1. Correlation between Countries' Annual Per Capita Chocolate Consumption and the Number of Nobel Laureates per 10 Million Population.

Discussion

Finally, as to a third hypothesis, it is difficult to identify a plausible common denominator that could possibly drive both chocolate consumption and the number of Nobel laureates over many years. Differences in socioeconomic status from country to country and geographic and climatic factors may play some role, but they fall short of fully explaining the close correlation observed.

Messerli FH. N Engl J Med. 2012 (Oct. 10)

Divorce rate in Maine
correlates with
Per capita consumption of margarine



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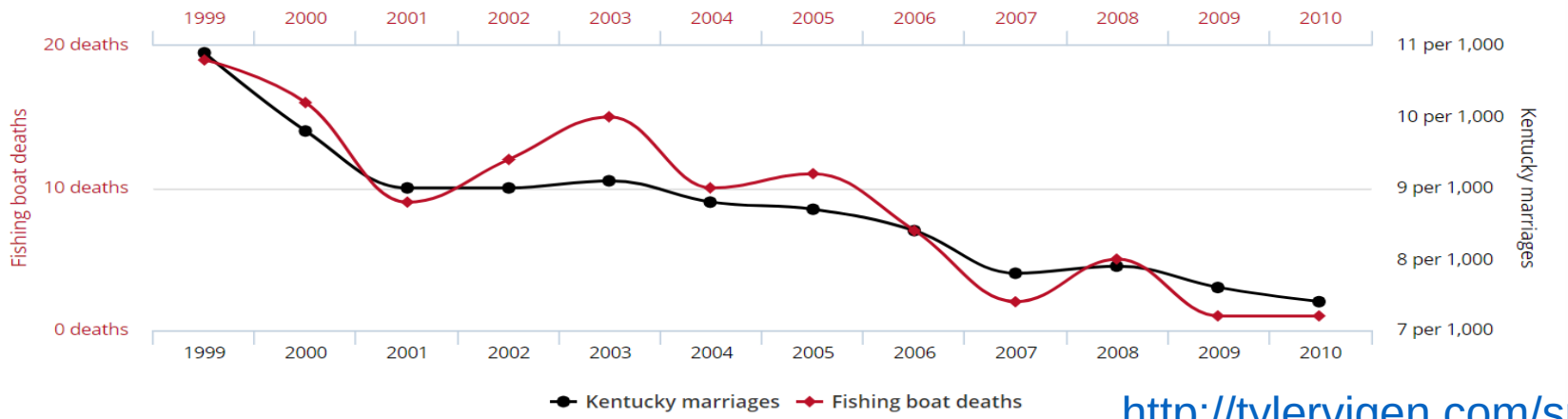
People who drowned after falling out of a fishing boat
correlates with
Marriage rate in Kentucky

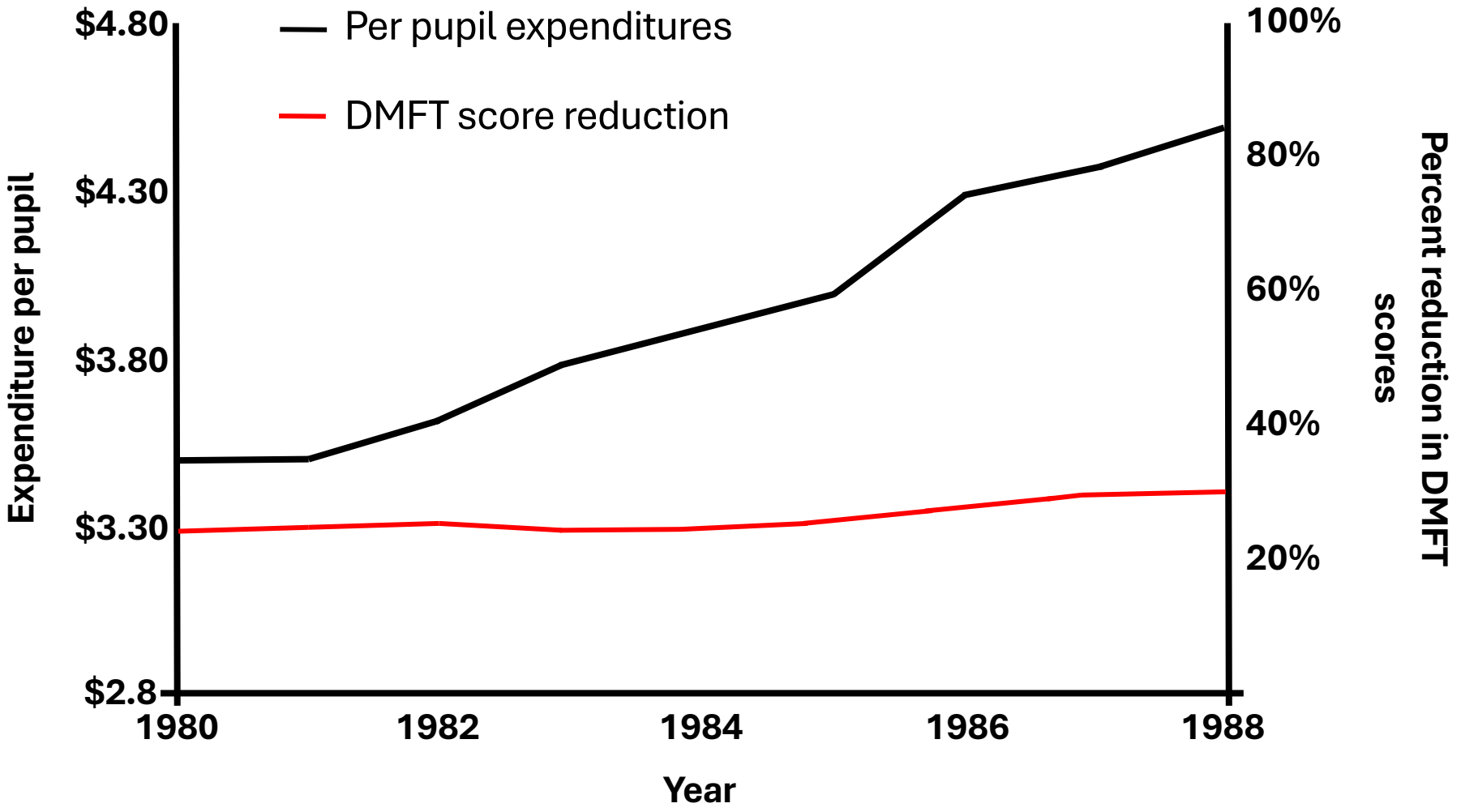
Correlation: 95.24% (r=0.952407)



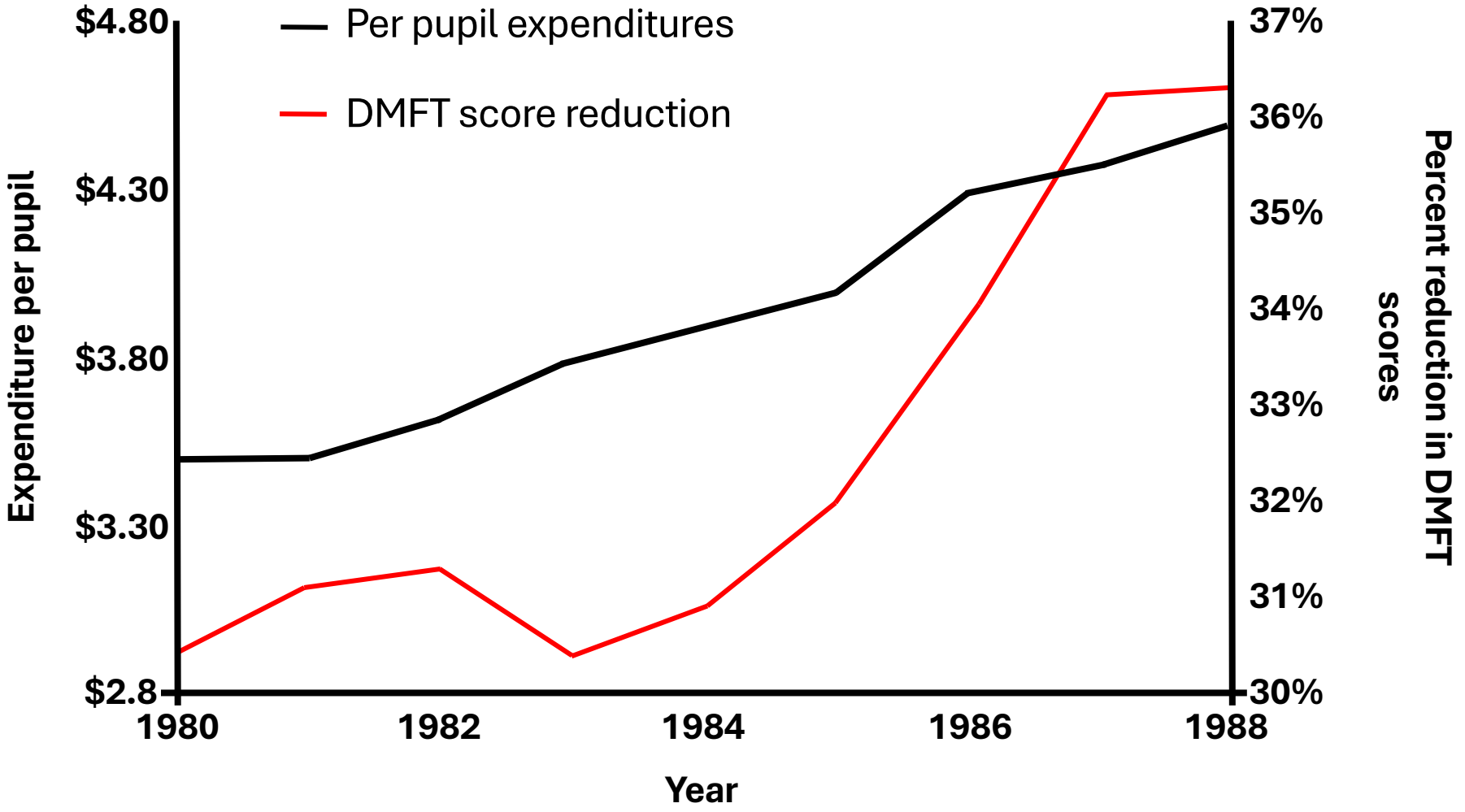
Data sources: Centers for Disease Control & Prevention and National Vital Statistics Reports

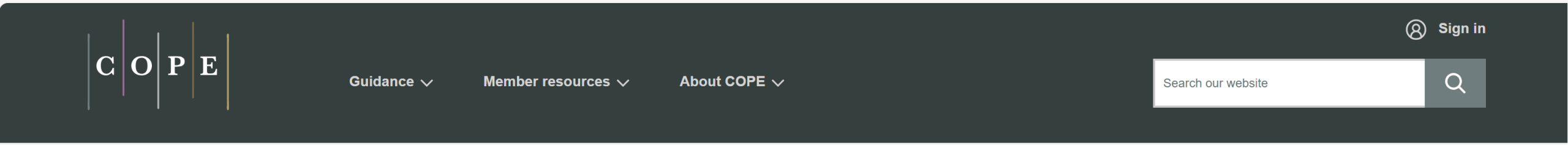
http://tylervigen.com/spurious-correlations

Oral health expenditures vs. DMFT score reduction



Oral health expenditures vs. DMFT score reduction





Home

Potential paper mills

Potential “paper mills” and what to do about them – a publisher’s perspective

Potential paper mills | COPE: Committee on Publication Ethics

Paper mills

Generate manuscripts based made-up, fraudulent, manipulated or plagiarized data

Sell fake manuscripts

Sell authorships, positions and citations

Guarantee publication in reputable journals

Engineers the peer review process

Estimates suggest paper mills are responsible for 2% to 20% of all published academic papers, particularly impacting the biomedical literature.
Prices can be high, with authorship on papers targeting high-impact journals costing up to 30,000 EUR

Detection and Prevention

Publishers and the academic community are working to combat paper mills through:

Training editors to identify suspicious manuscripts

Developing AI tools to detect paper mill products

Implementing stricter authorship verification processes

Collaborating across publishers to share information on suspected paper mills

Predatory publishing

DOI: https://doi.org/10.24318/cope.2019.3.6

The COPE predatory publishing discussion document introduces issues, and analyses potential solutions, around predatory publications. COPE welcomes comments which add to this ongoing debate.

Common features of the phenomenon include deception and lack of quality controls, and there are a range of warning signs to look for when assessing a journal. Problems for authors, readers, and other stakeholders are also discussed, as well as an examination of established interventions and solutions to address the problem. COPE presents 30 insightful suggestions to tackle, avoid, and raise awareness of the problem of predatory journals.

Document

Predatory publishing, discussion document PDF 693 KB

[Predatory publishing | COPE: Committee on Publication Ethics]

Predatory journal

- Accept articles quickly with little or no peer review
- Notify authors of fees only after paper acceptance
- Aggressively solicit submissions and editorial board memberships
- Editorial board: not listed; lists academics without permission; comprises dead or retired scholars or scholars who are not specialized in the topic; appoint fake academics to editorial boards
- Mimic names or websites of established journals
- Make misleading claims about impact factors or indexing

Predatory journal

- Advertises very fast times from submission to publication
- Publishes out-of-scope articles
- Publishes nonsense articles
- Poor or non-existent editing of articles (many spelling mistakes or very poor grammar)
- Hides information on charges
- Lack of information on the policies of the journal, such as peer review, licensing and copyright

Fake impact factors

Academic Resource Index (ResearchBib)

Asian Science Citation Index (ASCI)

CiteFactor

Cosmos Impact Factor

Eurasian Scientific Journal Index (ESJI)

I2OR Publication Impact Factor (PIF)

Index Copernicus International

International Scientific Indexing (ISI)

Journal Factor

Scientific Indexing Services (SIS)

Scientific Journal Impact Factor (SJIF)

Scope Database

List of Predatory Indexers and Fake Impact Factors *Updated (predatoryjournals.org)

Predatory publisher

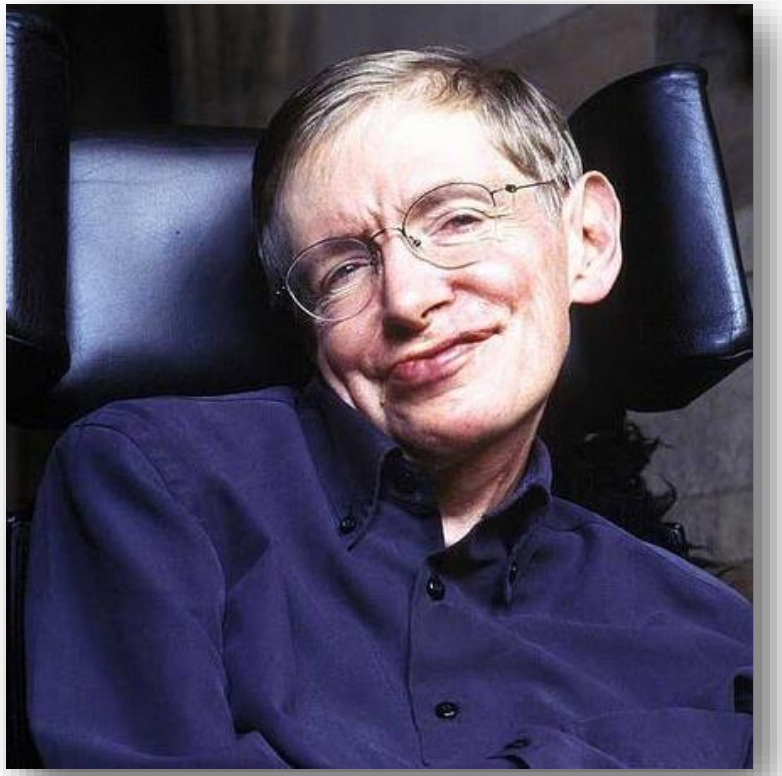
- Charge publication fees to authors without providing proper peer review or editorial services
- Accept articles quickly with little or no quality control
- Aggressively solicit submissions from academics
- Make misleading claims about their reputation, impact factor, or indexing
- Appoint fake academics to editorial boards or list academics without permission
- Mimic the names or websites of legitimate journals

Predatory publisher

The special editions model was also responsible for the exponential growth of **MDPI**, founded just 13 years ago and today the fourth largest scientific publisher in the world. The company published around 20,000 articles in its first 15 years, but began to multiply production in 2015. In 2021, there were 240,500 articles, charging an average processing fee of 1,258 Swiss francs (CHF) per paper (US$ 1,300). In 2023, its two main titles, **Sustainability** and **International Journal of Molecular Sciences**, are expected to publish around 3,500 special editions each – nine per day!

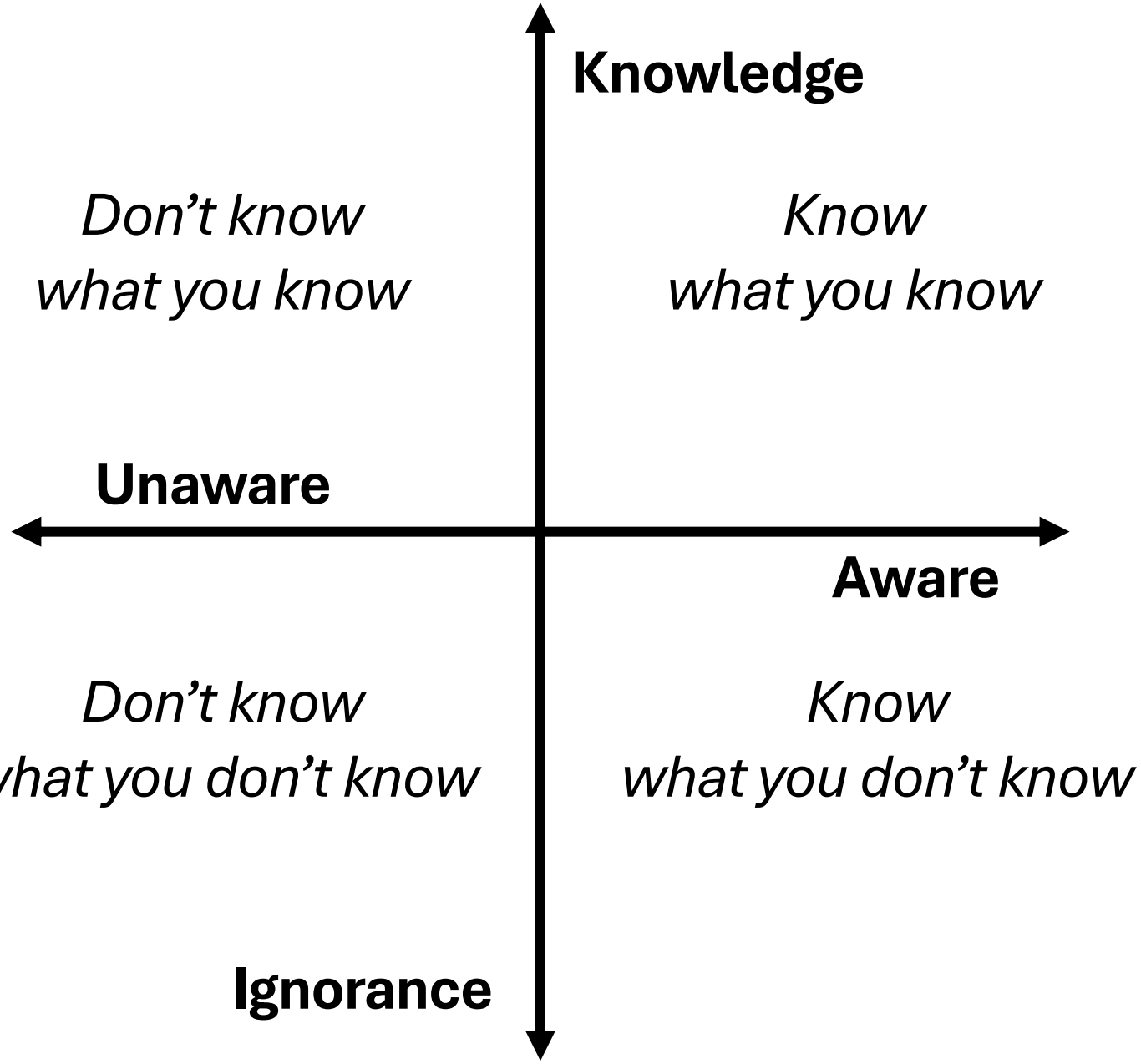
Signs a journal or publisher might be "predatory"

- The journal is **not** listed in the **Directory of Open Access Journals (DOAJ)**
- It is **not** listed in **Ulrichs**, which is an authoritative source on publisher information, including Open Access titles
- The publisher is **not** a member of the **Open Access Scholarly Publishers Association (OASPA)**
- It's **not** widely available within **major databases**
- The publisher lists an **Impact Factor** but the journal is not listed in **Journal Citation Reports** or **Scopus CiteScore.**



"The greatest enemy of knowledge is not ignorance, it is the illusion of knowledge."

Stephen Hawking


Knowledge
Don’t know
what you know
Know
what you know
Unaware
Aware
Don’t know
what you don’t know
Know
what you don’t know
Ignorance

Questions?