Epidemiology: the big picture

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Why epidemiology?

- To effectively practice medicine and public health, we need evidence/knowledge on 3 fundamental types of professional knowing "gnosis":

Dia-gnosis	Etio-gnosis	Pro-gnosis	For individual (Clinical Medicine)
Dia-gnosis	Etio-gnosis	Pro-gnosis	For community (Public and community health)

All are reflected in the Covid-19 pandemic

- How do we diagnose Covid-19? How good are the tests? How can we detect infection vs disease?
- What is the etiology of Covid-19? Who is likely to die of Covid-19?
- What is the effective treatment for Covid-19? Can we prevent Covid-19 with a vaccine?

Beyond Covid-19

- Does air pollution increase the risk of mortality among people with tuberculosis?
- Does passive smoking increase the risk of spontaneous abortions?
- Are probiotics effective in reducing risk of antibiotic-related diarrhea?
- Does mobile phone use increase the risk of brain cancer?
- Etc, etc.

How do we answer such questions?

- A: Epidemiologic research

- Not perfect, but it is all we have!

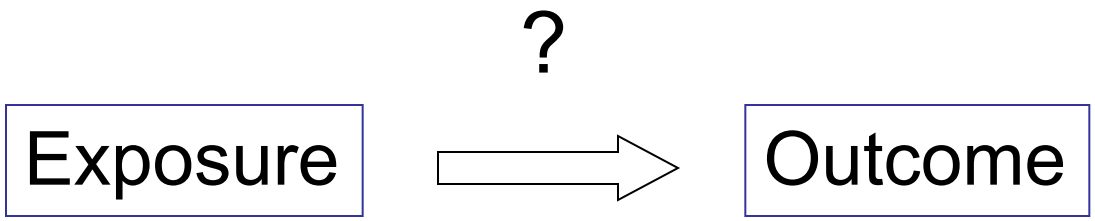
What is epidemiology?

- “Study of the occurrence and distribution of health-related states or events in specified populations, including the study of determinants influencing such states, and the application of this knowledge to control the health problems." [Porta, IEA Dictionary, 2008]

- “Application of the scientific method to health research” [adapted from Rothman KJ, 2002]

Of the 3 types of knowing ("gnosis") etio-gnosis (causality) is the central concern of epidemiology

- Most fundamental application of epidemiology: to identify etiologic (causal) associations between exposure(s) and outcome(s)



Covid-19

Smokers seem less likely than non-smokers to fall ill with covid-19

That may point towards a way of treating it

Bald men at higher risk of severe case of Covid-19, research finds

Researchers suggested that baldness should be considered a risk factor, dubbing it the 'Gabrin sign'

telegraph.co.uk

Zinc can play pertinent role in mitigating COVID-19 : Dr. Soumitra Das

CORONAVIRUS

Indians May Be Partially Immune to COVID-19 Due to BCG Vaccine, Says US-Based Expert

Sunlight destroys coronavirus quickly, say US scientists

Coronavirus pandemic | Study finds link between Vitamin D levels and COVID-19 cases

Causal claims and associations are frequent in the literature & picked up by the media

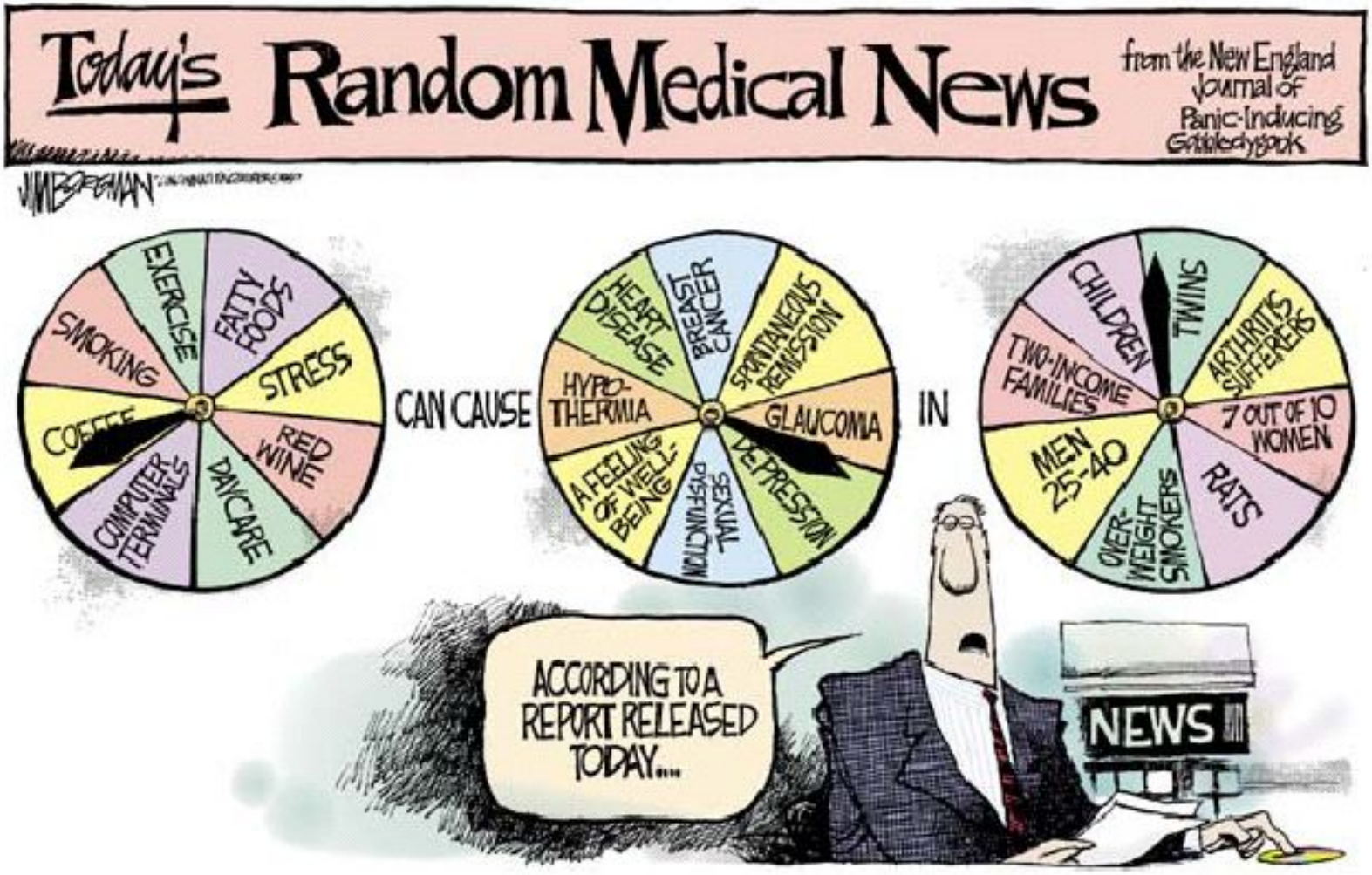
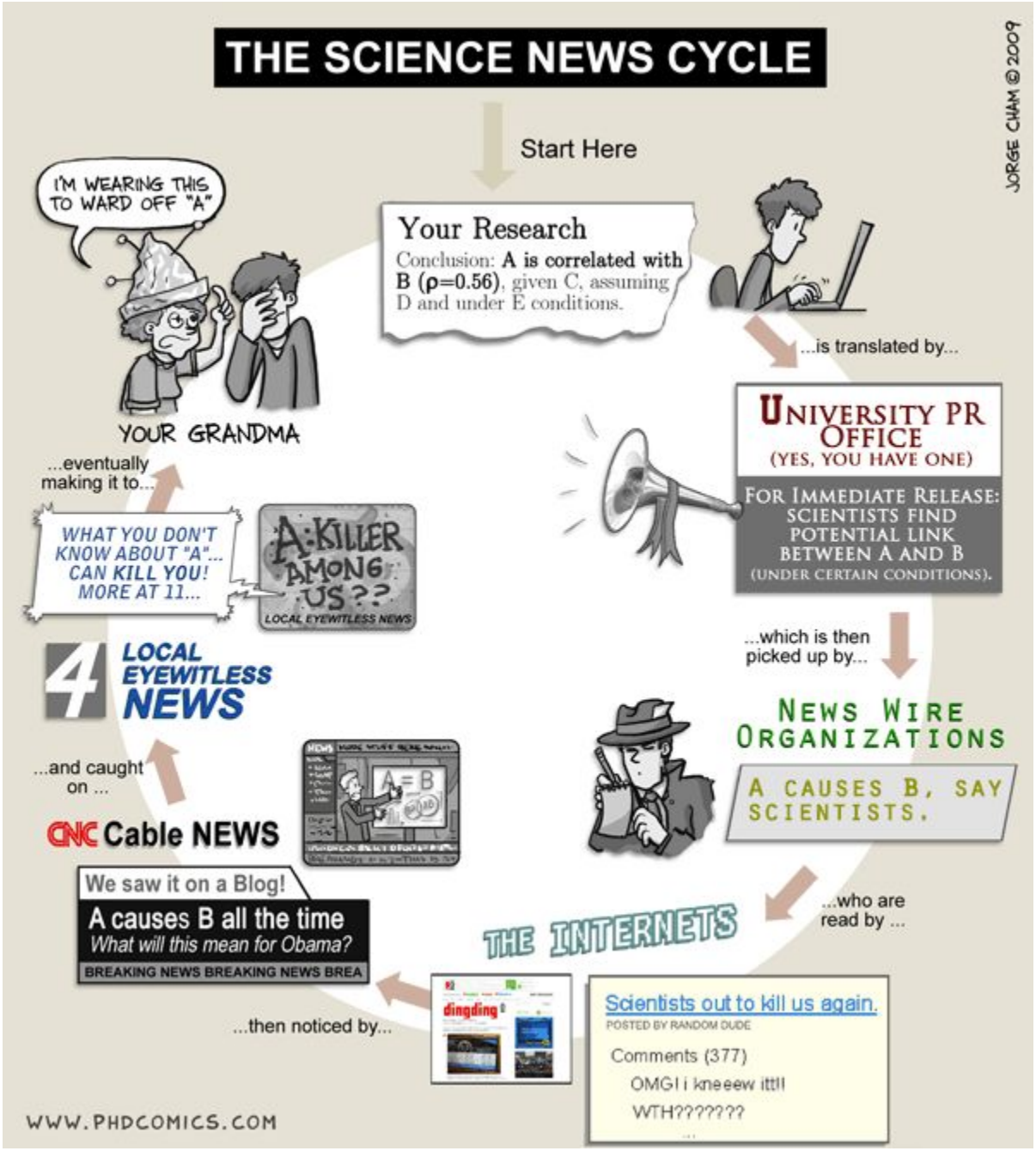


Figure 3: New England Journal of Panic-Inducing Gobbledygook.
Source: Jim Borgman, The Cincinnati Enquirer (27 April 1997, E4).


THE SCIENCE NEWS CYCLE
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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
...eventually making it to...
WHAT YOU DON'T KNOW ABOUT "A"... CAN KILL YOU! MORE AT 11...
A: KILLER AMONG US??
LOCAL EYEWITLESS NEWS
I'M WEARING THIS TO WARD OFF "A"
YOUR GRANDMA
WWW.PHDCOMICS.COM

Poor quality research + bad reporting = chaos

- Too many causal claims; optimism bias is pervasive
- Inconsistency in study findings and too many apparent contradictions
- Causal inferences made on the basis of isolated studies
- Many studies biased or inconclusive
- Fear and panic inducing rather than helpful; media-induced hype

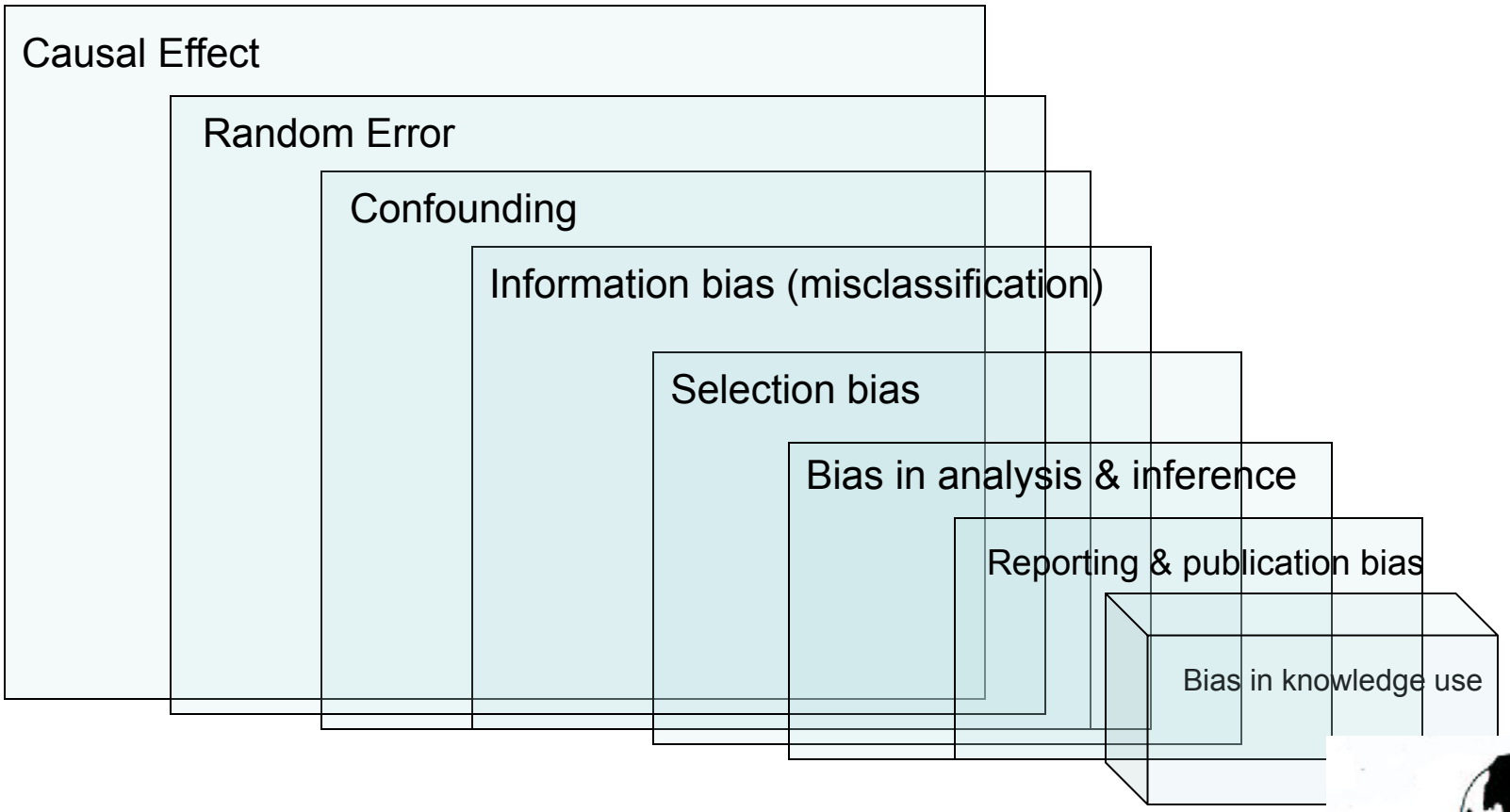
Causality: is it intuitive?

- Most of us intuitively understand causality, even if we have never formally studied it!
- Even as children, we grow up making associations and causal connections
- However, is epidemiology merely applying common sense?

Does anti-snake venom save or kill people?

Dog owners may have lower risk of dying from heart attacks, study says

The long road to causal inference (the "big picture")



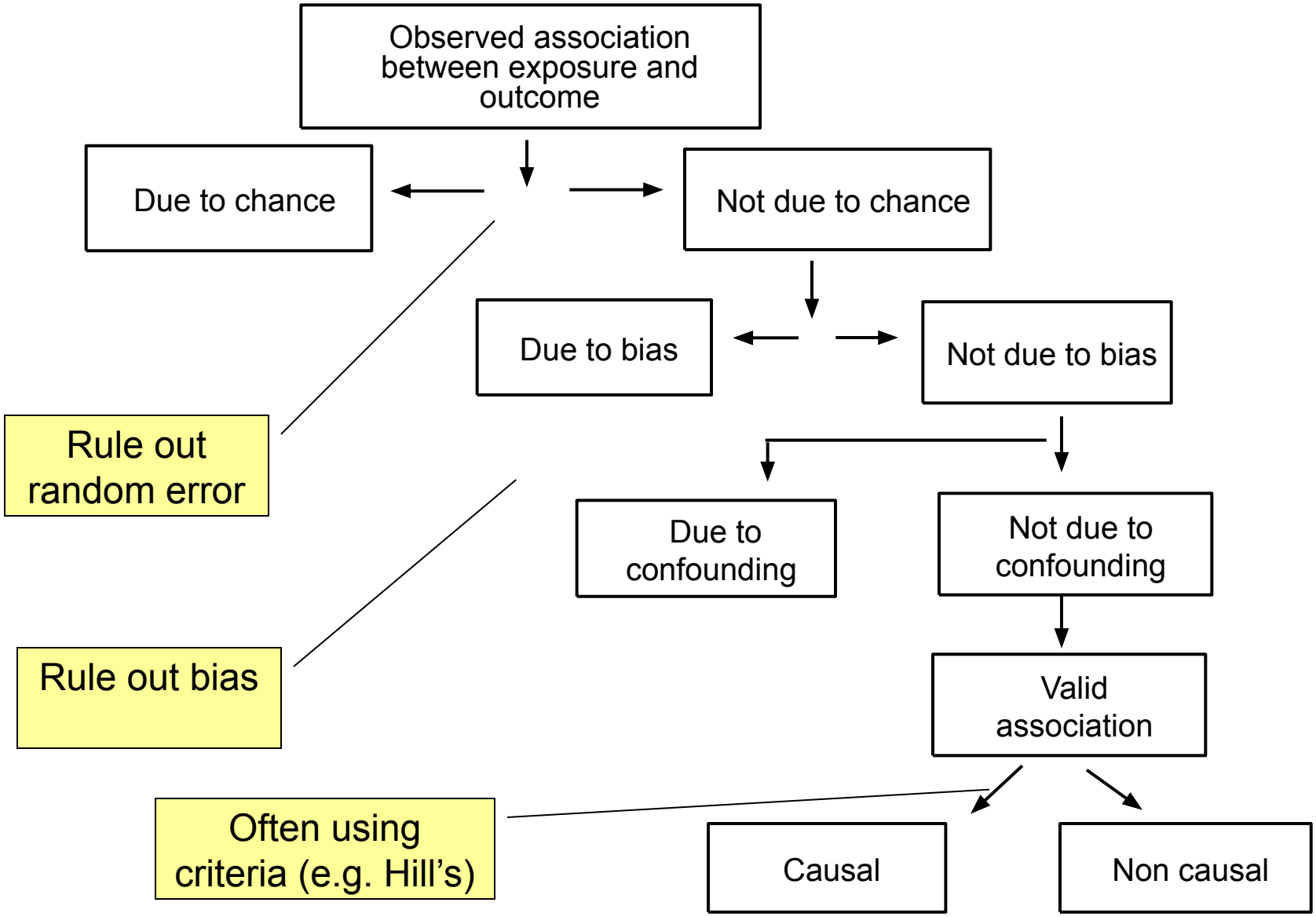
RR_{causal} "truth"

the long road to causal inference…

$RR_{association}$

Adapted from: Maclure, M, Schneeweis S. Epidemiology 2001;12:114-122.

A Skeptic's Algorithm for Associations



Data concerns during this pandemic

- Deliberate suppression of information
- Huge variability in testing rates
- Quality of tests is variable
- Each country has its own timeline and dynamic
- Cause of death data are sketchy
- More models & estimates than actual data
- Deliberate misinformation campaigns

Research concerns during this pandemic

- All research is ‘Covidised’ – 23,000 papers+ papers on COVID!
- Deluge of pre-prints, fast-tracked, preliminary, no fact-checking
- Most are not peer reviewed
- Many by researchers with no background/expertise
- Lowering of normal scientific standards
- Tons of correlations based on cross-country comparisons
- Uncontrolled drug studies
- Not enough studies on any given topic
- Single and/or small studies get too much importance
- Policy makers jumping the gun before research is settled

BCG Against Coronavirus: Less Hype And More Evidence, Please

Madhukar Pai Contributor ⓘ
Healthcare
I write about global health, infectious diseases, and equity

Close up of reaction of Bacillus Calmette Guerin or BCG vaccination infants. GETTY

A Skeptic's Guide To Ecologic Studies During A Pandemic

Madhukar Pai Contributor ⓘ
Healthcare
I write about global health, infectious diseases, and equity

24 January 2020, Bavaria, Munich: A face mask and protective goggles are displayed in front of a map ... [+] DPA/PICTURE ALLIANCE VIA GETTY IMAGES

Media reporting: infodemic!

- Media is also ‘Covidised’
- In some areas, media is muzzled
- Sensationalized, hyped coverage (to increase clicks)
- Social media can amplify misinformation easily
- Everyone wants to report ‘breakthroughs’ (want ‘new content’)
- Correlations are presented as causation
- Preliminary findings presented as ‘facts’ (not enough fact checking)
- Uncritical, for most part (lack of epi training)
- Want certainty, when everything is uncertain
- Assumptions underlying models are rarely challenged
- Not able to interview the right experts
- ‘News is bad at communicating risk’

JNCI Journal of the National Cancer Institute Advance Access published November 20, 2009

EDITORIALS

Promoting Healthy Skepticism in the News: Helping Journalists Get It Right

Steven Woloshin, Lisa M. Schwartz, Barnett S. Kramer

Pai Global TB Group

teach epi

a website for learning and teaching epidemiology

COURSES TEACHING RESOURCES FOR MENTORS FOR STUDENTS TEACHING AWARDS

Epidemiology for Health Journalists

Webinar series for health journalists

Description

Webinar series on epidemiology for health journalists presented by Dr. Madhukar Pai

- Session 1 – Epidemiology: the big picture [Slides] [Video]
- Session 2 – Causality & causal inference [Slides] [Video]
- Session 3 – Epidemiologic study designs [Slides] [Video]
- Session 4 – Measuring disease occurrence and association [Slides] [Video]
- Session 5 – Bias in epidemiological studies: the big picture [Slides] [Video]
- Session 6 – Selection bias in epidemiological studies [Slides] [Video]
- Session 7 – Information bias in epidemiological studies [Slides] [Video]
- Session 8 – Confounding in epidemiological studies [Slides] [Video]
- Session 9 – Randomized controlled trials [Slides] [Video]
- Session 10 – Cohort studies [Slides] [Video]
- Session 11 – Case-control studies [Slides] [Video]
- Session 12 – Cross sectional studies [Slides] [Video]
- Session 13 – Ecologic studies [Slides] [Video]
- Session 14 – Diagnostic studies [Slides] [Video]
- Session 15 – Systematic reviews & meta-analysis [Slides] [Video]
- Session 16 – Mathematical modeling [Slides] [Video]

https://www.teachepi.org/courses/epidemiology-for-health-journalists/

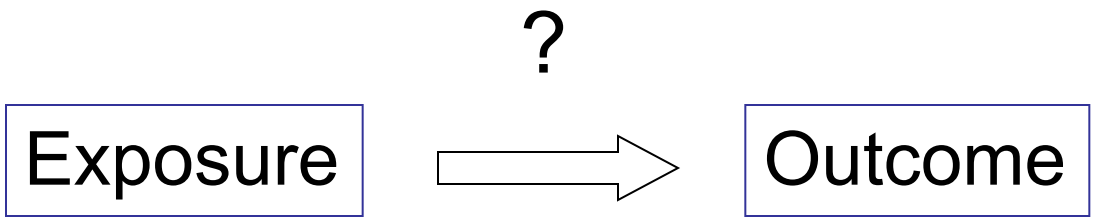
Hence, this course!

Epi concepts that journalists need to understand

- R_0
- Epidemic curve, doubling time, attack rate, etc
- Risk vs Rate vs Odds
- Correlation vs. causation
- Need for randomization & control group
- Sensitivity, specificity, predictive values
- Herd immunity
- Exposure vs infection vs disease
- Incubation period
- Isolation vs quarantine
- Hierarchy of evidence
- Absence of evidence is not evidence of absence
- Statistical vs public health or clinical significance
- Prevalence vs incidence
- Mortality vs case fatality rate vs infection fatality rate
- Confounding & bias
- Relative vs absolute risk
- P-values & confidence intervals
- Vaccine efficacy
- Outbreak, epidemic, endemic, pandemic
- Crude vs adjusted rates
- Importance of denominators
- Mathematical models & their limitations
- Explaining uncertainty

Of the 3 types of knowing ("gnosis") etio-gnosis (causality) is the central concern of epidemiology

- Most fundamental application of epidemiology: to identify etiologic (causal) associations between exposure(s) and outcome(s)



What is a cause?

- “Cause of a disease event is an event, condition or characteristic that preceded the disease event and without which the disease event either would not have occurred at all or would not have occurred until some other time.”
  - » [Rothman & Greenland, 1998]

Tuberculosis vaccine ‘potential game-changer’ in Covid-19 fight

Countries with high BCG vaccination rates have fewer coronavirus deaths, study shows

Coronavirus: Is TB vaccines a silver bullet in fight against COVID-19

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Correlation between universal BCG vaccination policy and reduced morbidity and mortality for COVID-19: an epidemiological study

Aaron Miller, Mac Josh Reandelar, Kimberly Fasciglione, Violeta Roumenova, Yan Li, Gonzalo H Otazu

doi: https://doi.org/10.1101/2020.03.24.20042937

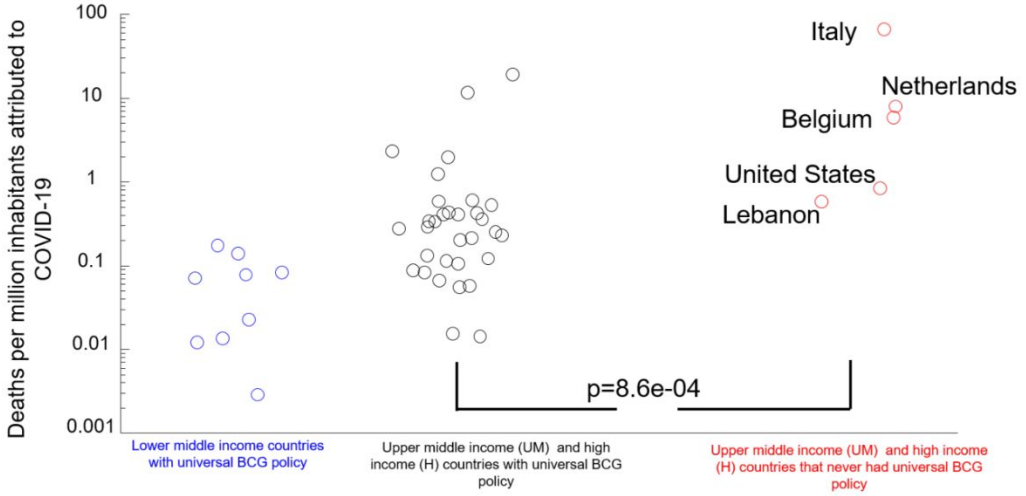


Figure 1: Higher death rates were presented in countries that never implemented a universal BCG vaccination policy.

Covid-19

Smokers seem less likely than non-smokers to fall ill with covid-19

That may point towards a way of treating it

Low incidence of daily active tobacco smoking in patients with symptomatic COVID-19 Preprint v3

Makoto Miyara[1], Florence Tubach[1], Valérie POURCHER[1], Capucine Morelot-Panzini[1], Julie Pernet[1], Julien Haroche[1], Said Lebbah[1], Elise Morawiec, Guy Gorochov[2], Eric Caumes[1], Pierre Hausfater[1], Alain COMBES[1], Thomas Similowski, Zahir Amoura[1]

"Our cross sectional study in both COVID-19 out- & inpatients strongly suggests that daily smokers have a very much lower probability of developing symptomatic or severe SARS-CoV-2 infection as compared to the general pop."

What is a cause?

- Cause
  - Must precede the effect (absolute requirement)
  - Can be either host, agent or environmental factors (e.g. characteristics, conditions, infection, actions of individuals, events, natural, social phenomena)
  - Can be either
    - positive = the presence of an exposure (e.g. radiation)
    - negative = the absence of exposure (e.g. vaccination)

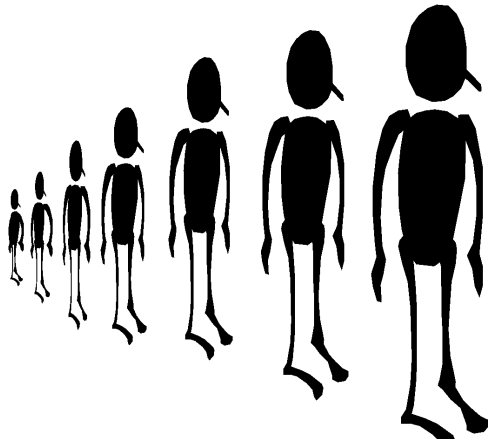
- Should always be set up as a comparison:
  - "Cause is a category of a determinant, in relation to a particular reference category, capable of completing a sufficient cause in some instances in which the reference category is incapable of such completion" [OS Miettinen]

What is a causal effect?

- To determine a causal effect, we always need to set up a causal contrast (against some reference)
- Ideal "causal contrast" between exposed and unexposed groups:
  - "A causal contrast compares disease frequency under *two* exposure distributions, but in *one* target population during *one* etiologic time period"
  - If the ideal causal contrast is met, the observed effect is the "causal effect"

Maldonado & Greenland, Int J Epi 2002;31:422-29

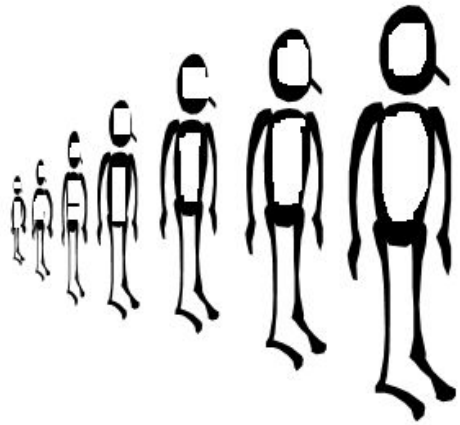
Ideal counterfactual comparison to determine causal effects



I_{exp}

Exposed cohort

"Initial conditions" are identical in the exposed and unexposed groups – because they are the same population!



I_{unexp}

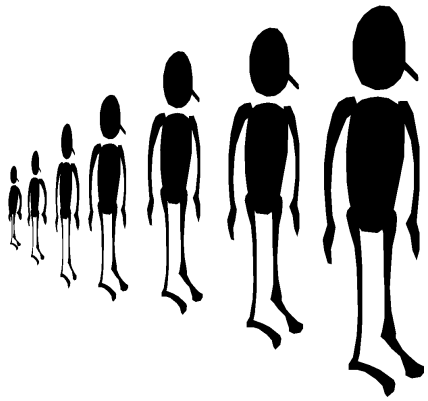
Counterfactual, unexposed cohort

$$RR_{causal} = I_{exp} / I_{unexp}$$

"A causal contrast compares disease frequency under *two* exposure distributions, but in *one* target population during *one* etiologic time period"

Maldonado & Greenland, Int J Epi 2002;31:422-29

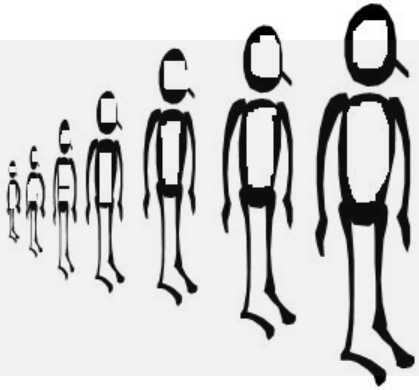
What happens in reality?



Exposed cohort

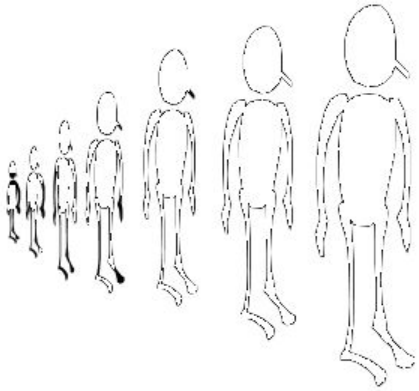
I_{exp}

counterfactual state is not observed (latent)



Counterfactual, unexposed cohort

I_{unexp}



Substitute, unexposed cohort

$I_{substitute}$

A substitute will usually be a population other than the target population during the etiologic time period - INITIAL CONDITIONS MAY BE DIFFERENT

What happens actually?

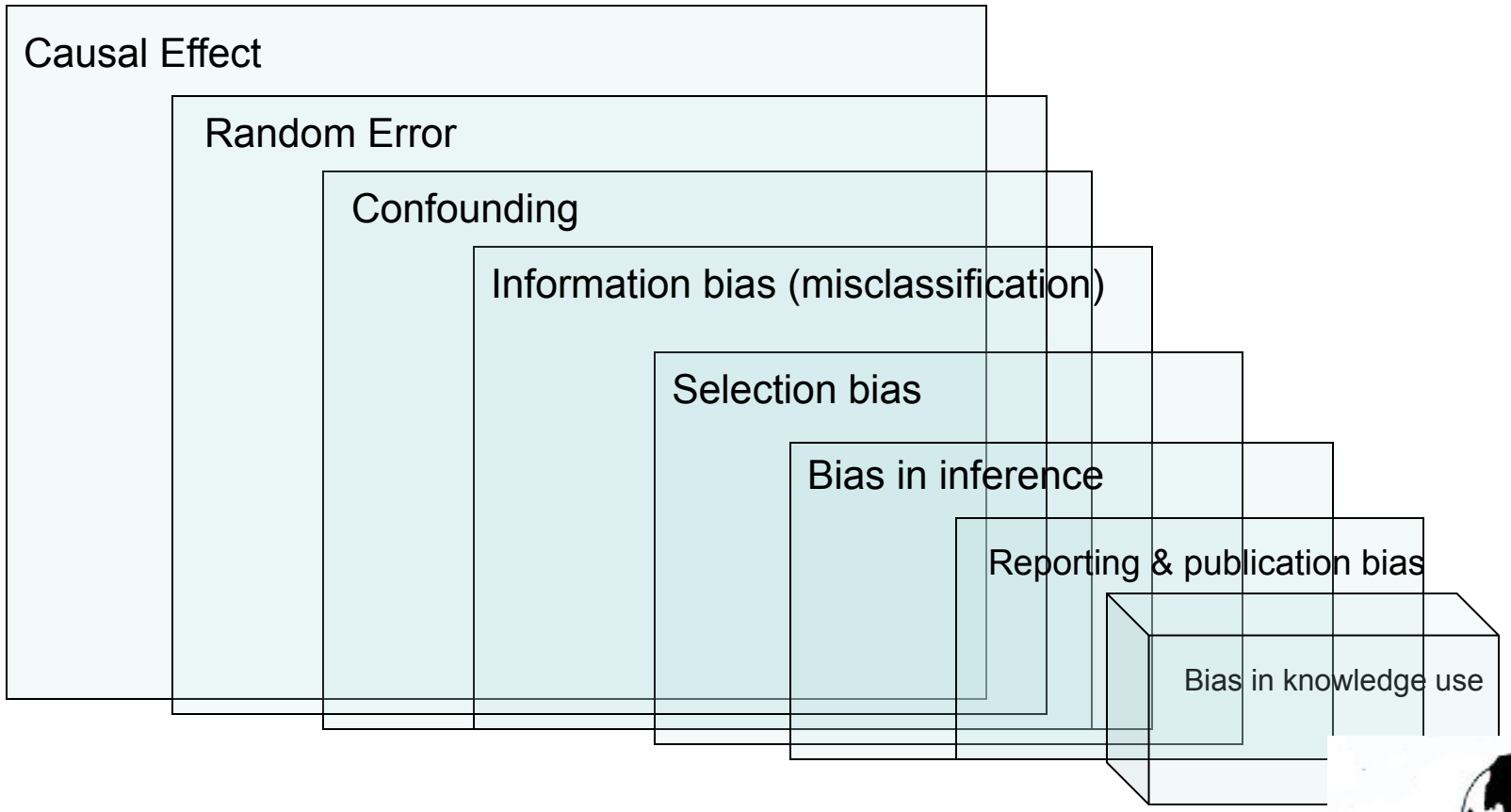
$RR_{causal} = I_{exp} / I_{unexp}$ IDEAL

$RR_{assoc} = I_{exp} / I_{substitute}$ ACTUAL

Chances are…

$RR_{causal} =/= RR_{assoc}$

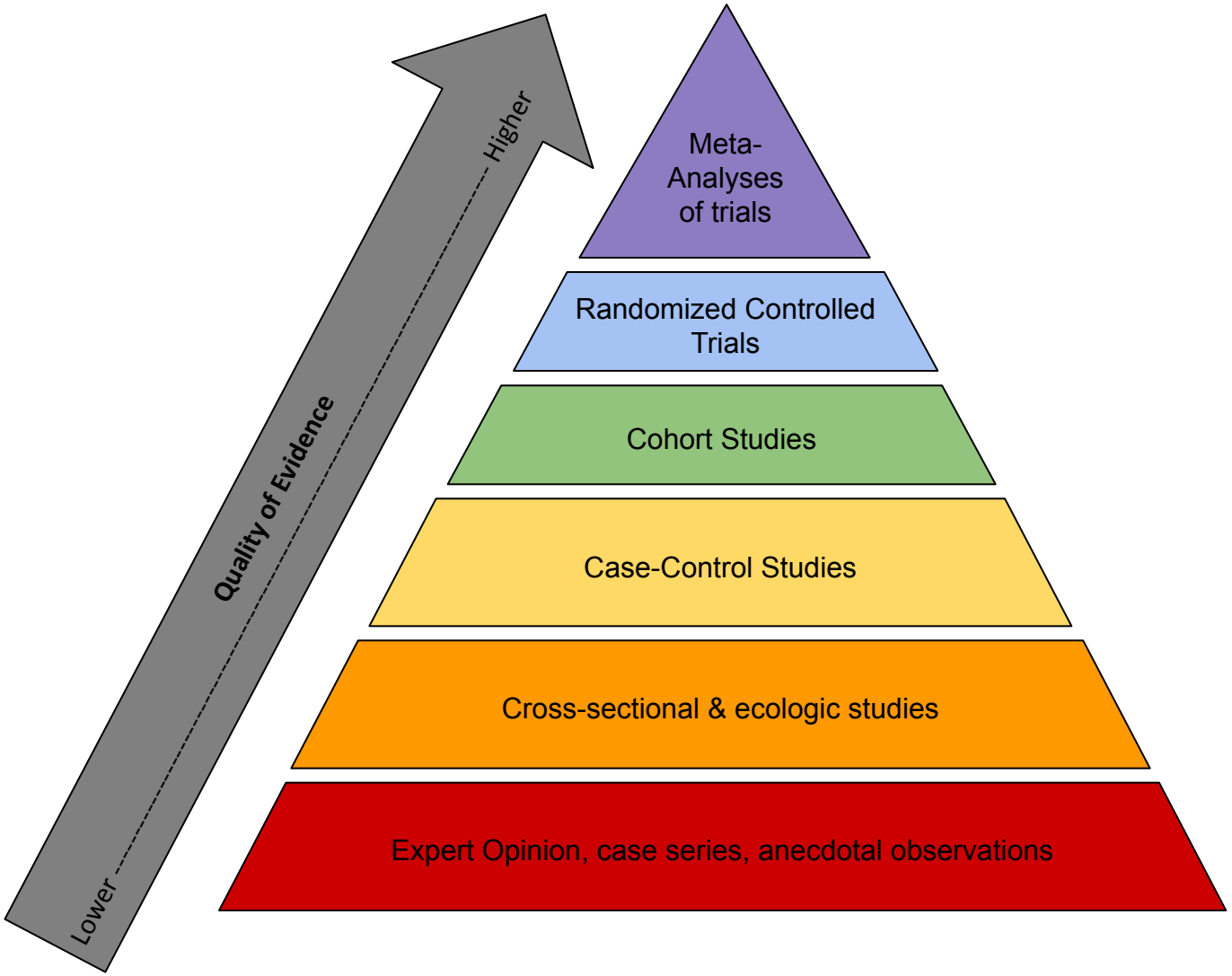
The best epidemiologic study will be one that captures the causal effect with minimal distortion



RR_{causal} "truth" → $RR_{association}$

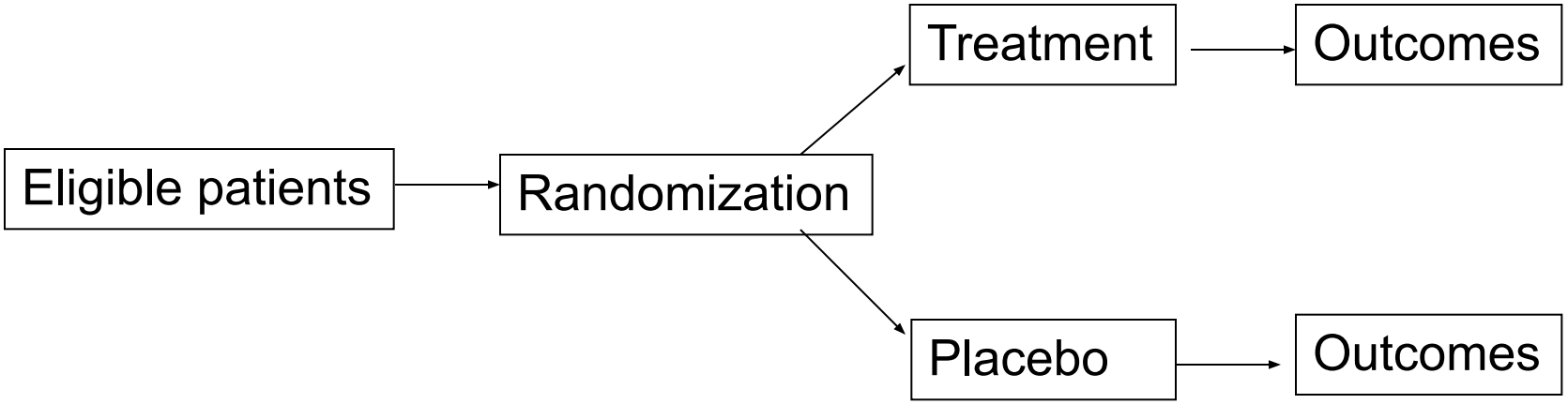
Adapted from: Maclure, M, Schneeweis S. Epidemiology 2001;12:114-122.

A hierarchy of evidence from various study designs



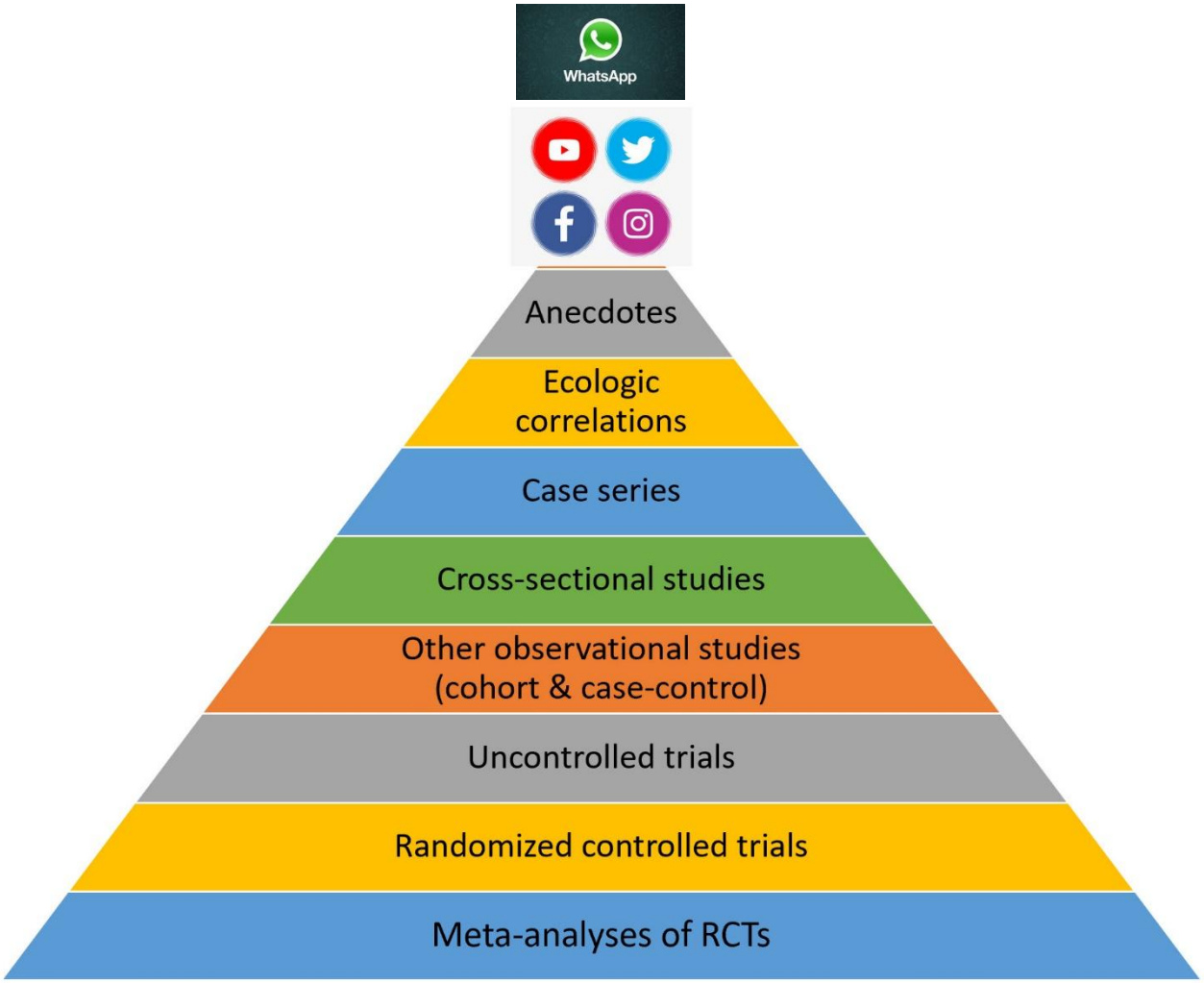
Adapted from UCI Libraries
https://guides.lib.uci.edu/ebm/pyramid

RCTs come close to simulating the counter-factual comparison



Randomization helps to make the groups “comparable” (i.e. similar initial conditions)

During this pandemic, the normal hierarchy of evidence seems inverted!



Single studies are never enough to make a causal inference!

Causal inference using Hill's 'criteria'

Criteria for causation

1. Strength of association
2. Consistency
3. Specificity
4. Temporality
5. Dose-response relationship (gradient)
6. Plausibility
7. Coherence
8. Experimental evidence
9. Analogy

Hill AB. Proc Roy Soc Med 1965

Assessment of the Evidence Suggesting *Helicobacter pylori* as a Causative Agent of Duodenal Ulcers

1. Temporal relationship.
   - *H. pylori* is clearly linked to chronic gastritis. About 11% of chronic gastritis patients will go on to have duodenal ulcers over a 10-year period.
   - In one study of 454 patients who underwent endoscopy 10 years earlier, 34 of 321 patients who had been positive for *H. pylori* (11%) had duodenal ulcer compared with 1 of 133 *H. pylori*-negative patients (0.8%).
2. Strength of the relationship.
   - *H. pylori* is found in at least 90% of patients with duodenal ulcer. In at least one population reported to lack duodenal ulcers, a northern Australian aboriginal tribe that is isolated from other people, it has never been found.
3. Dose-response relationship.
   - Density of *H. pylori* per square millimeter of gastric mucosa is higher in patients with duodenal ulcer than in patients without duodenal ulcer. Also see item 2 above.
4. Replication of the findings.
   - Many of the observations regarding *H. pylori* have been replicated repeatedly.
5. Biologic plausibility.
   - Although originally it was difficult to envision a bacterium that infects the stomach antrum causing ulcers in the duodenum, it is now recognized that *H. pylori* has binding sites on antral cells and can follow these cells into the duodenum.
   - *H. pylori* also induces mediators of inflammation.
   - *H. pylori*-infected mucosa is weakened and is susceptible to the damaging effects of acid.
6. Consideration of alternate explanations.
   - Data suggest that smoking can increase the risk of duodenal ulcer in *H. pylori*-infected patients but is not a risk factor in patients in whom *H. pylori* has been eradicated.
7. Cessation of exposure.
   - Eradication of *H. pylori* heals duodenal ulcers at the same rate as histamine receptor antagonists.
   - Long-term ulcer recurrence rates were zero after *H. pylori* was eradicated using triple-antimicrobial therapy, compared with a 60% to 80% relapse rate often found in patients with duodenal ulcers treated with histamine receptor antagonists.
8. Specificity of the association.
   - Prevalence of *H. pylori* in patients with duodenal ulcers in 90% to 100%. However, it is found in some patients with gastric ulcer and even in asymptomatic individuals.
9. Consistency with other knowledge.
   - Prevalence of *H. pylori* infection is the same in men as in women. The incidence of duodenal ulcer, which in earlier years was believed to be higher in men than in women, has been equal in recent years.
   - The prevalence of ulcer disease in believed to have peaked in the latter part of the 19th century, and the prevalence of *H. pylori* may have been much higher at that time because of poor living conditions. This reasoning is also based on observations today that the prevalence of *H. pylori* is much higher in developing countries.

Data from Megraud F, Lamouliatte H: *Helicobactor pylori* and duodenal ulcer: Evidence suggesting causation. Dig Dis Sci 37:769-772, 1992; and DeCross AJ, Marshall BJ: The role of *Helicobactor pylori* in acid-peptic disease. Am J Med Sci 306:381-391, 1993.