Which of the following difference measures is reported as a percentage?

A. Attributable Risk
B. Attributable Fraction
C. Population Attributable Risk
D. Risk Ratio

Which of the following difference measures might be most useful in communicating the need for/value of public health action?

A. Attributable Risk
B. Attributable Fraction
C. Relative Risk
D. Population Attributable Fraction

The attributable risk tells us how much extra disease occurred in the population as a result of the exposure.

A. True

B. False

When a CBC news article communicated that the risk of colon cancer increases by 18% (CI 1.05-1.31) per 50 g portion of processed/red meats consumed per day, this was a measure of?

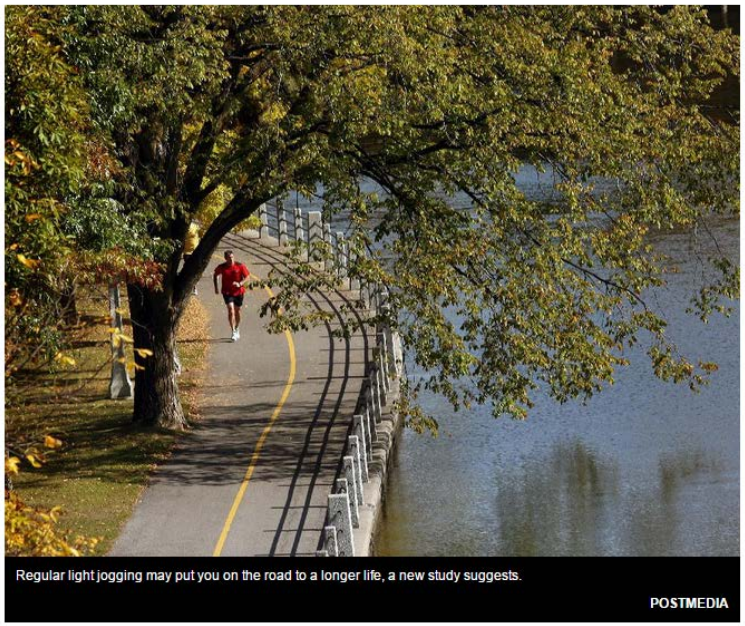
A. Attributable Risk
B. Attributable Fraction
C. Population Attributable Risk
D. Risk Ratio

Review:
Relative vs. Attributable Risk

Measure	What it Does	Uses
Relative Risk (also true for odds ratio)	Evaluates the *strength* of an association between exposure & disease	To help identify risk factors for disease
Attributable Risk	Measures *excess* disease attributable to the exposure *in the exposed group.*	To assess the magnitude of a public health problem associated with an exposure *among those exposed*.

Excessive running could kill you: study

TOM SPEARS, OTTAWA CITIZEN
More from Tom Spears, Ottawa Citizen
Published on: February 2, 2015 | Last Updated: February 4, 2015 12:43 PM EST



Regular light jogging may put you on the road to a longer life, a new study suggests.

POSTMEDIA

Fast running is as deadly as sitting on couch, scientists find

Running a few times a week at a moderate pace is the best way to improve health, say scientists, as they warn against overdoing it

26K 99 171 26K Email

EPI IN THE NEWS

TheUpshot

EXERCISING JUDGMENT

No, More Running Probably Isn't Bad for You

FEB. 5, 2015

Justin Wolfers

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More

Don't run less hard. Don't run less often. Don't run less distance. And don't be persuaded by underpowered medical studies — a habit that really could harm your health.

I say this in response to a recent study suggesting that too much strenuous jogging shortens your life. The conclusions, published in the Journal of the American College of Cardiology, have received wide attention this week.

In fact, the main thing the study shows is that small samples yield unreliable estimates that cannot be reliably discerned from the effects of chance. And the main thing the reaction shows is that perhaps we are all a bit too quick to believe medical studies that tell us what we want to hear.

The study doesn't change what the weight of the evidence shows: Most Americans need to worry about exercising too little, not too much, and it's not clear that any substantial number of people are harming their health by running too much.

Let's start by taking a closer look at what the study actually

LINK TO COMMENTARY

LINK TO ACTUAL PUBLISHED STUDY

What Is *Power*?

- The POWER of a study is the probability of detecting an association *if* one really exists in the general population
- largely affected by sample size (studies with a small sample size have insufficient power to detect real associations)
- If no statistical association is found and the sample size is small, the result should be considered inconclusive due to lack of power
- 80% power is recommended for epidemiologic studies (in this class, you do not need to know how to calculate sample size to achieve this level of power)

Class 11:

Causation and Error in Epidemiology

All that glitters in not gold

RANDOM ERROR

SYSTEMATIC ERROR

THE EFFECT OF ERROR

HILL'S POSTULATES

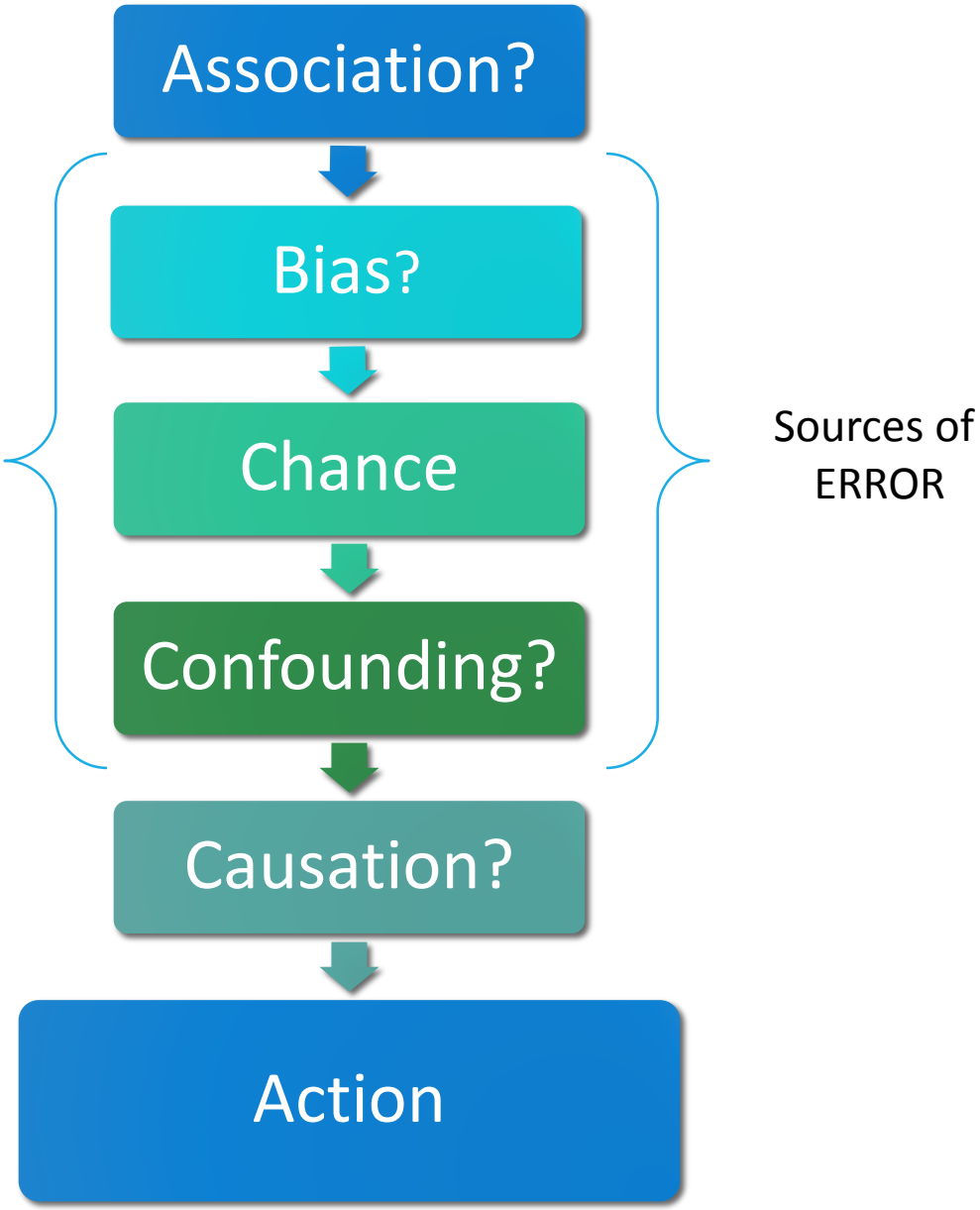
HLSC 2003
Faculty of Health Sciences
University of Lethbridge

Association:

If there is an association, one must ask **“is it real?”**

http://www.freedigitalphotos.net/images/view_photog.php?photogid=732

Process of epidemiological research leading to justifiable public health action.



Internal Validity: The degree to which a particular study is free from error (i.e. random error, bias and confounding)

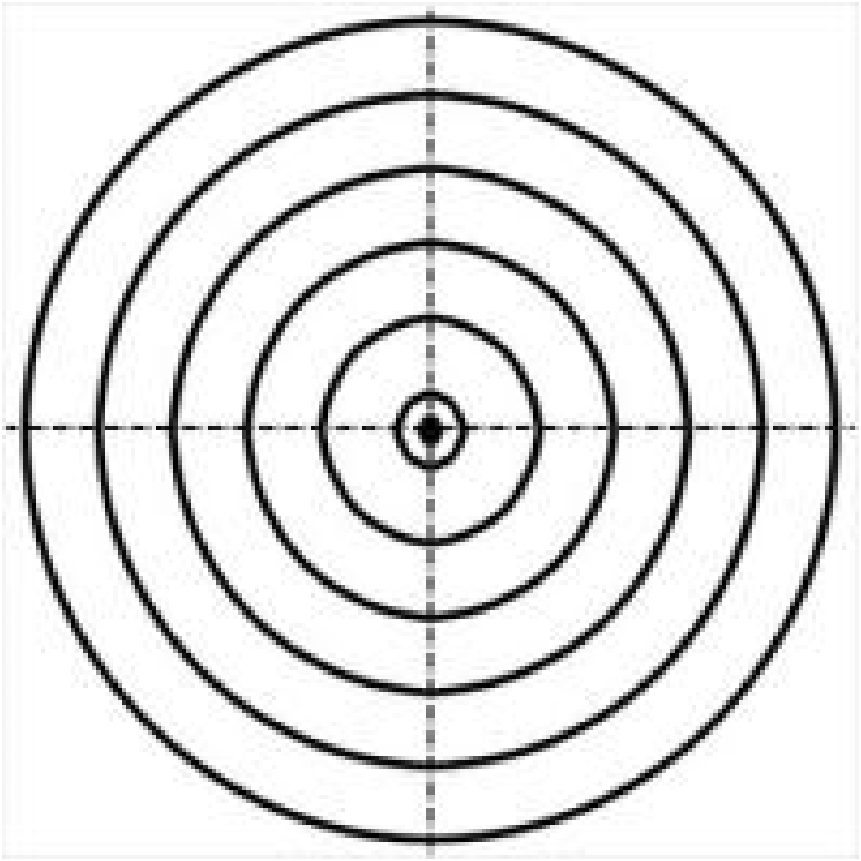
External Validity: the extent to which a particular study can be applied to the broader population (i.e. it is representative of the target population and other potential populations?)

**if a study is not internally valid, it should not be applied to anyone!*

VALIDITY:

Sources of Error: Bias and Chance

Precision vs. Accuracy



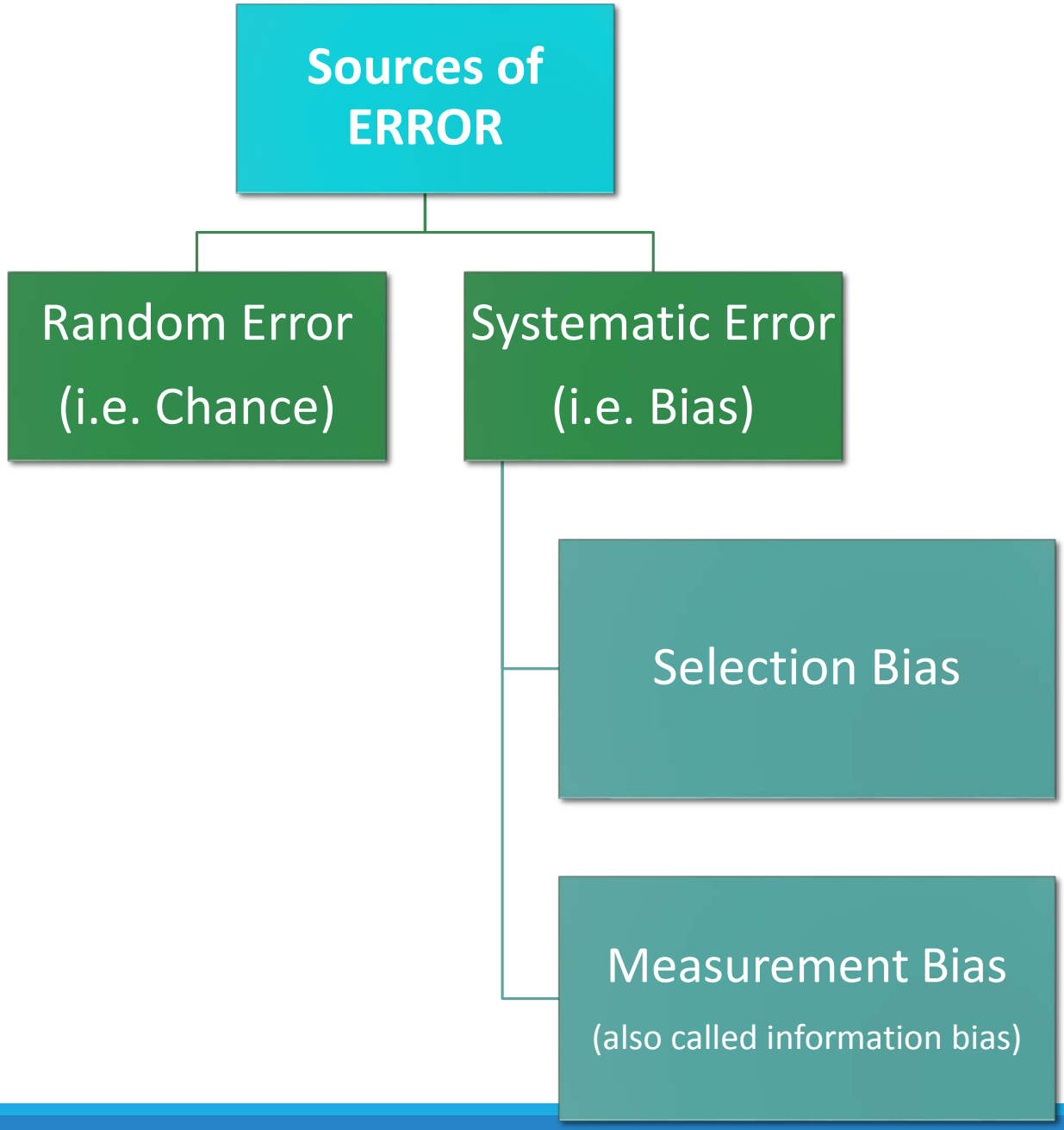
http://www.freeclipartnow.com/signs-symbols/targets/

Precision and Accuracy in Epidemiologic Study Design:

- **Precise and Accurate** – ideal – little random error and little systematic error

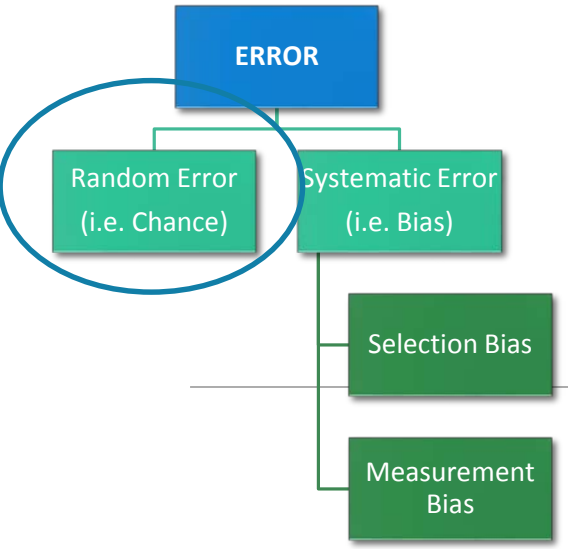
  *(*this would be considered to have a high level of internal validity)*

- **Accurate, but not precise** – random error, little systematic error
- **Precise, but not accurate** – systematic error, little random error
- **Inaccurate AND not Precise** – both random AND systematic error


Sources of ERROR
Random Error (i.e. Chance)
Systematic Error (i.e. Bias)
Selection Bias
Measurement Bias
(also called information bias)

Random Error (i.e. Chance)

*WHEN THE VALUE OF THE SAMPLE MEASUREMENT DIVERGES – **DUE TO CHANCE ALONE** – FROM THAT OF THE TRUE POPULATION VALUE*



- Confidence interval (CI) help determine if an association is statistically significant, suggesting that the association is NOT due to chance alone (narrow CI indicates greater precision – less random error)
- *Random error is inevitable*, but can be controlled somewhat by increasing your sample size (which narrows CI and increases study **"POWER"**)
- **Very little random error would indicate that a study was PRECISE**

Example

Researchers randomly select and interview U of L undergrads. They ask these questions at the same time.

Exposure: Do you exercise ≥3 times a week – yes/no?

Outcome: Are you currently a honor roll student?

Study Type? _____

Incidence or prevalence measured? _____

Measure of association to use? _____

To examine the association between exercise and being an honour roll student, 3 samples were collected at the U of L. **Which is statistically significant?**

i>clicker

A. 10 students: OR = 1.0 (CI = 0.5 to 6.4)

B. 100 students: OR = 1.5 (CI = 1.1 to 1.9)

C. 1000 students: OR = 1.5 (CI = 1.4 to 1.6)

D. A and C

E. B and C

Which of the 3 studies is most precise (has the least amount of random error)?

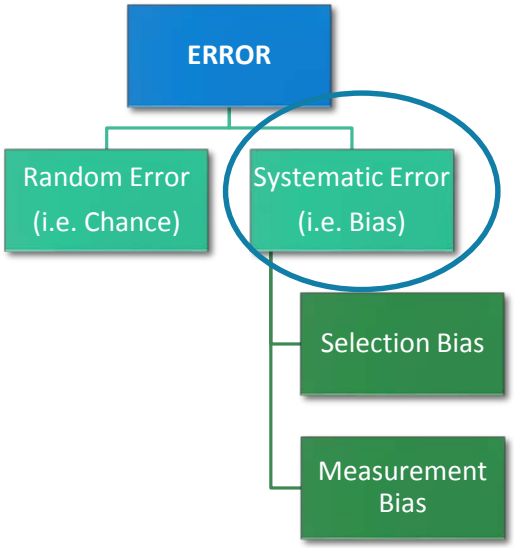
A. 10 students: OR = 1.0 (CI = 0.5 to 6.4)

B. 100 students: OR = 1.5 (CI = 1.1 to 1.9)

C. 1000 students: OR = 1.5 (CI = 1.4 to 1.6)

Systematic Error (i.e. BIAS)

"…any systematic error in the design, conduct, or analysis of a study that results in a mistaken estimate of an exposure's effect on the risk of disease." -Gordis (2009), p.247

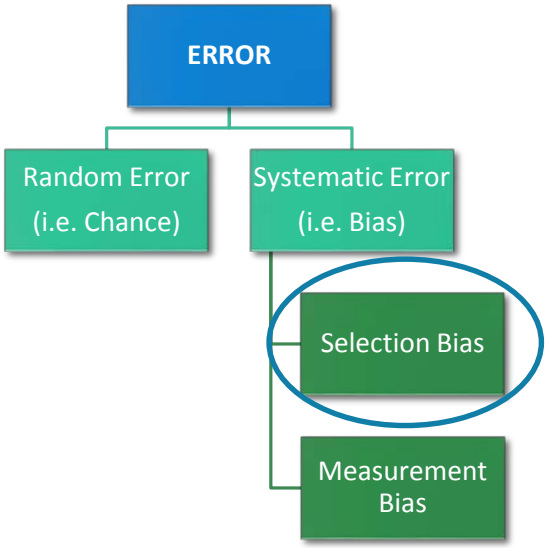


- Can lead to artificially elevated or reduced measures of association
- A study which has very little systematic error is thought to be highly ACCURATE

Selection Bias

Think "Study Participants"

Occurs when there is an error (not due to chance alone) in the selection and involvement of participants…i.e. there is a difference between those selected for the study and those in the target population.



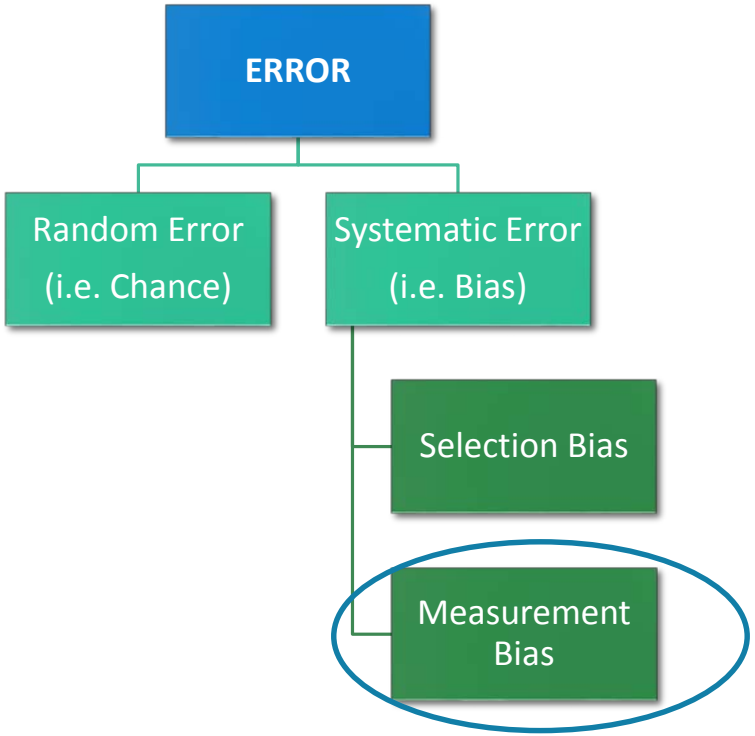
- Volunteer bias
- Low response rates
- Ascertainment/detection bias
- Healthy-worker effect
- Loss to follow-up
- Exclusion criteria

Controlling for Selection Bias:

- Control for selection in the design of the study
- Recognize potential sources of selection bias based on the study design (e.g. loss to follow up in Cohort, elegibility/exclusion criteria and selection of controls in Case Control)
- Once the error has been introduced and the study conducted, cannot easily control for selection bias; you can, and must, however recognize and acknowledge its potential effect on findings

Measurement Bias

Occurs when the an error occurs in the process of data collection



- Recall bias
- Misclassification bias (differential & non-differential)
- Reporting bias
- Surveillance bias
- Interviewer/observer bias

Controlling for Measurement Bias:

- Control for measurement bias in the design, data collection, and execution of the study…eliminate if possible.
- Be clear on definitions (e.g. what is a “heavy smoker”?)
- Use good instruments for measurement and select the right time and place for measurement (e.g. face-to-face vs. telephone interviews; standardizing instruments)
- Blinding investigators
- Be aggressive with follow-up

Potential self-selection bias in a nested case-control study on indoor environmental factors and their association with asthma and allergic symptoms among pre-school children

Carl-Gustaf Bornehag
Jan Sundell
Torben Sigsgaard
Staffan Janson

Abstract

Selection bias means a systematic difference between the characteristics of selected and non-selected individuals in epidemiological studies. Such bias may be introduced if participants select themselves for a study. The present study aims at identifying differences in family characteristics, including health, building characteristics of the home, and socioeconomic factors between participating and non-participating families in a nested case-control study on asthma and allergy among children. Information was collected in a baseline questionnaire to the parents of 14,077 children aged 1—6 years in a first step. In a second step 2,156 of the children were invited to participate in a case-control study. Of these, 198 cases and 202 controls were finally selected. For identifying potential selection bias, information concerning all invited families in the case-control study was obtained from the baseline questionnaire. Results show that there are several possible biases due to self-selection involved in an extensive study on the impact of the home environment on asthma and allergy among children. Factors associated with participating were high socioeconomic status of the family, more health problems in the case families, and health-related lifestyle factors, such as non-smoking parents. The overall conclusion of this study is that there are selection biases involved in studies that need close cooperation with the families involved. One solution to this problem is stratification, i.e. investigating associations between exposures and health in the same socioeconomic strata.

Recall Bias in Melanoma Risk Factors and Measurement Error Effects: A Nested Case-Control Study Within the Norwegian Women and Cancer Study

Christine L. Parr,
Anette Hjartåker,
Petter Laake,
Eiliv Lund and
Marit B. Veierød

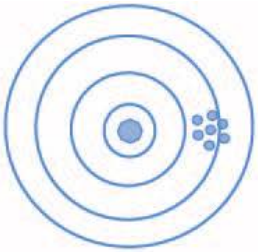
Abstract

Case-control studies of melanoma have the potential for recall bias after much public information about the relation with ultraviolet radiation. Recall bias has been investigated in few studies and only for some risk factors. A nested case-control study of recall bias was conducted in 2004 within the Norwegian Women and Cancer Study: 208 melanoma cases and 2,080 matched controls were invited. Data were analyzed for 162 cases (response, 78%) and 1,242 controls (response, 77%). Questionnaire responses to several host factors and ultraviolet exposures collected at enrollment in 1991–1997 and in 2004 were compared stratified on case-control status. Shifts in responses were observed among both cases and controls, but a shift in cases was observed only for skin color after chronic sun exposure, and a larger shift in cases was observed for nevi. Weighted kappa was lower for cases than for controls for most age intervals of sunburn, sunbathing vacations, and solarium use. Differences in odds ratio estimates of melanoma based on prospective and retrospective measurements indicate measurement error that is difficult to characterize. The authors conclude that indications of recall bias were found in this sample of Norwegian women, but that the results were inconsistent for the different exposures.

Which of the following pictures represents a study with high random error and high systematic error?

(a)

(b)



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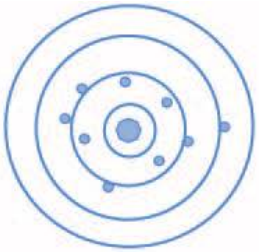

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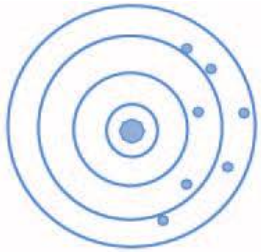
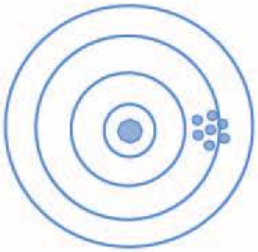
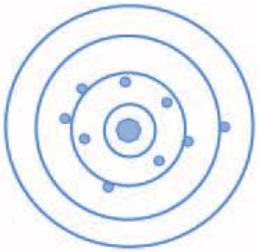
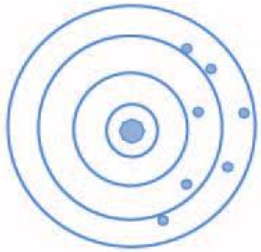


Which of the following pictures represents a study with low random error, but high systematic error?

(a) 

(b) 

(c) 

(d) 

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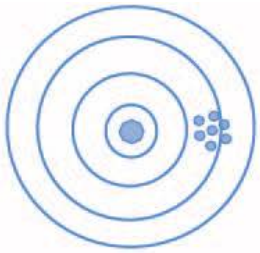
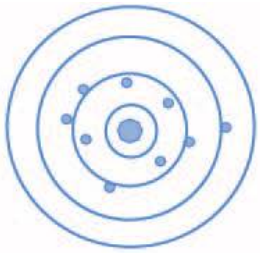
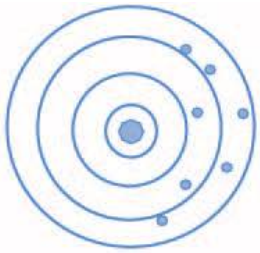
(a) 

(b) 

(c) 

(d) 

*The result of error:

A difference in study results from the true value, leading researchers to overestimate or underestimate association between exposure and outcome variables.

Who cares?

Public health implications of error

Fortunately, most studies with much error are caught in peer review process & never published, but not always…

The most famous example of the adverse public health implications that unrecognized study error can have –THE WAKEFIELD STUDY

- MMR – combined measles, mumps, rubella vaccine given to children.
- In 1998, Wakefield published a paper linking MMR vaccine to autism.

Example

Early report

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

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

Summary

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

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

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

Introduction

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

Patients and methods

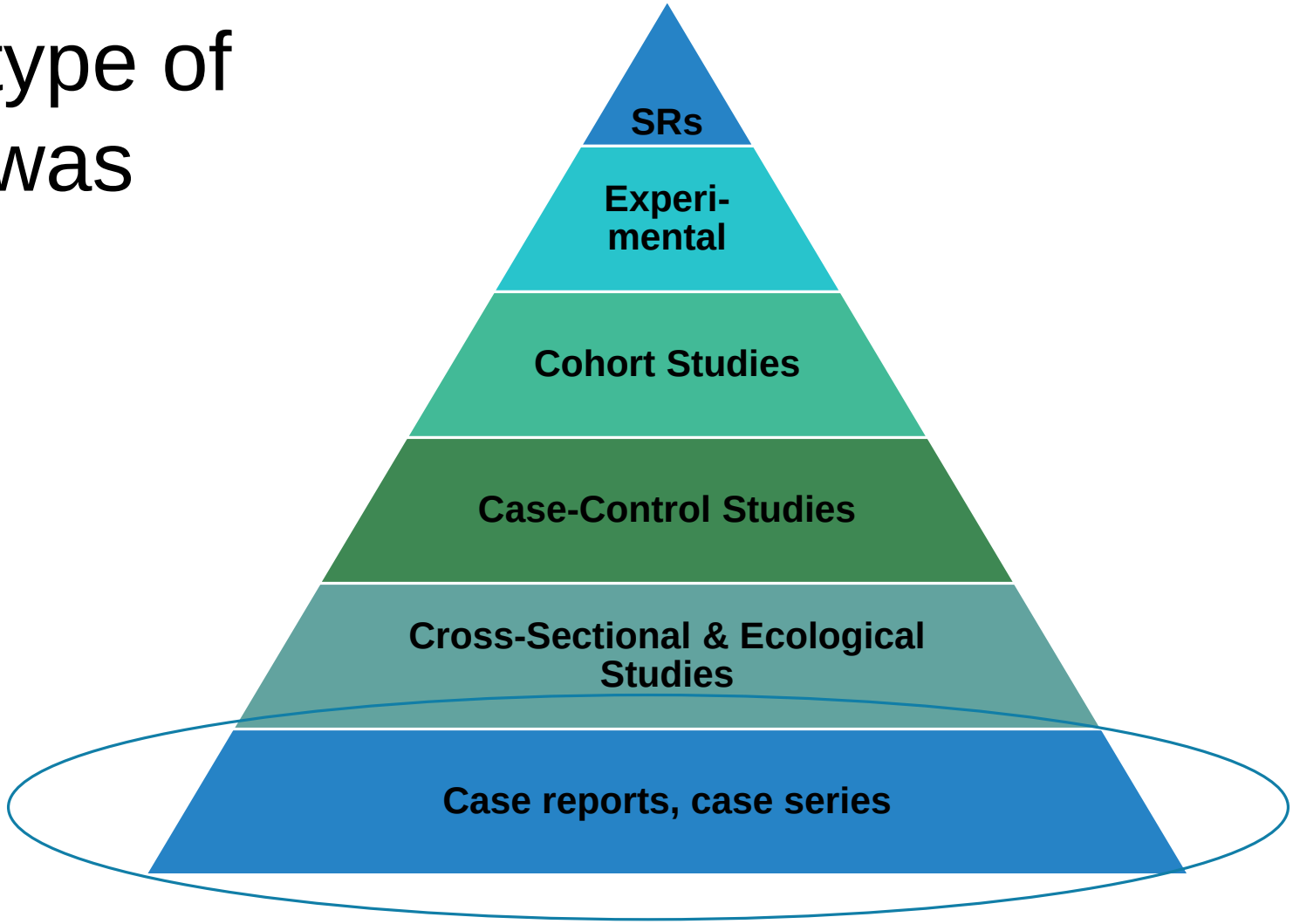
12 children, consecutively referred to the depa paediatric gastroenterology with a history of a developmental disorder with loss of acquired skills an symptoms (diarrhoea, abdominal pain, bloating intolerance), were investigated. All children were adm ward for 1 week, accompanied by their parents.

Clinical investigations

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

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

What type of study was this?



THE LANCET

The Lancet, Volume 351, Issue 9103, Pages 637 - 641, 28 February 1998
doi:10.1016/S0140-6736(97)11096-0 Cite or Link Using DOI

< Previous Article | Next Article >

This article was retracted

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

Dr AJ Wakefield FRCS [a], SH Murch MB [b], A Anthony MB [a], J Linnell PhD [a], DM Casson MRCP [b], M Malik MRCP [b], M Berelowitz FRCPsych [c], AP Dhillon MRCPath [a], MA Thomson FRCP [b], P Harvey FRCP [d], A Valentine FRCR [e], SE Davies MRCPath [a], JA Walker-Smith FRCP [a]

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Findings

Onset of behavioural symptoms was associated, by the parents, with measles, mumps, and rubella vaccination in eight of the 12 children, with measles infection in one child, and otitis media in another. All 12 children had intestinal abnormalities, ranging from lymphoid nodular hyperplasia to aphthoid ulceration. Histology showed patchy chronic inflammation in the colon in 11

Link to retraction

Paper Retracted by Journal

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THE LANCET

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The Lancet, Volume 375, Issue 9713, Page 445, 6 February 2010
doi:10.1016/S0140-6736(10)60175-4 Cite or Link Using DOI

< Previous Article | Next Article >

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

The Editors of The Lancet [a]

Following the judgment of the UK General Medical Council's Fitness to Practise Panel on Jan 28, 2010, it has become clear that several elements of the 1998 paper by Wakefield et al [1] are incorrect, contrary to the findings of an earlier investigation. [2] In particular, the claims in the original paper that children were "consecutively referred" and that investigations were "approved" by the local ethics committee have been proven to be false. Therefore we fully retract this paper from the published r ...

More than error?

- Wakefield did not disclose he was being paid by lawyers acting for parents who believed MMR harmed their children. He had no ethics approval to do study: Link
- It is believed Wakefield altered results, creating the appearance of a link between the vaccine & autism.
- He was striped of his medical licence due to study

Early report

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

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

Lancet 1998; **351:** 637–41
See Commentary page 611

Inflammatory Bowel Disease Study Group, University Departments of Medicine and Histopathology (A J Wakefield FRCS, A Anthony MB, J Linnell PhD, A P Dhillon MRCPath, S E Davies MRCPath) **and the University Departments of Paediatric Gastroenterology** (S H Murch MB, D M Casson MRCP, M Malik MRCP, M A Thomson FRCP, J A Walker-Smith FRCP,), **Child and Adolescent Psychiatry** (M Berelowitz FRCPsych), **Neurology** (P Harvey FRCP), **and Radiology** (A Valentine FRCR), **Royal Free Hospital and School of Medicine, London NW3 2QG, UK**

Correspondence to: Dr A J Wakefield

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

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

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

Laboratory investigations

Thyroid function, serum long-chain fatty acids, and cerebrospinal-fluid lactate were measured to exclude known causes of childhood neurodegenerative disease. Urinary methylmalonic acid was measured in random urine samples from eight of the 12 children and 14 age-matched and sex-matched normal controls, by a modification of a technique described previously.[2] Chromatograms were scanned digitally on computer, to analyse the methylmalonic-acid zones from cases and controls. Urinary methylmalonic-acid concentrations in patients and controls were compared by a two-sample *t* test. Urinary creatinine was estimated by routine spectrophotometric assay.

Children were screened for antiendomyseal antibodies and boys were screened for fragile-X if this had not been done

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EDITORIAL

Wakefield's article linking MMR vaccine and autism was fraudulent

BMJ 2011; 342 doi: http://dx.doi.org/10.1136/bmj.c7452 (Published 6 January 2011)
Cite this as: *BMJ* 2011;342:c7452

MMR

Section PDF

Easy Read

Article correction

Press release

Respond to this article

Statement by Editors of the BMJ

``Clear evidence of falsification of data should now close the door on this damaging vaccine scare… Who perpetrated this fraud? There is no doubt that it was Wakefield. Is it possible that he was wrong, but not dishonest: that he was so incompetent that he was unable to fairly describe the project, or to report even one of the 12 children's cases accurately? No. A great deal of thought and effort must have gone into drafting the paper to achieve the results he wanted: the discrepancies all led in one direction; misreporting was gross.`` Link to full BMJ article

But has this closed the door in the minds of the public?

Why Does the controversy continue?

- **The Problem**: timing of MMR vaccine and when symptoms of autism first appear are close together - seem paired in the minds of parents example

- Assuming that 2 events are associated because one occurs before the other is called a Post-Hoc Fallacy

Why Does the controversy continue?

- **Post hoc fallacy**: derived from the Latin *post hoc ergo propter hoc* (after this, therefore because of this).
- **The role of unbalanced media reports**?
- General lack of ability by the public to critique scientific research

Repercussions? Link

One in five Albertans say vaccines can cause autism

REID SOUTHWICK, CALGARY HERALD
More from Reid Southwick, Calgary Herald

Published on: February 6, 2015
Last Updated: February 6, 2015 6:00 AM MDT

A nurse loads a syringe with a vaccine in Lynwood, California.

ROBYN BECK / AFP/Getty Images

http://calgaryherald.com/news/local-news/one-in-five-albertans-say-vaccines-can-cause-autism

Proving Causation:

Is there a causal relationship?

LINK to story

http://www.stampboards.com/viewtopic.php?f=13&t=8394&start=1600

Cause:

An event, condition, or characteristic or, more often, a combination of these factors that plays an essential role in producing an occurrence of the disease –Webb and Bain (2011), as cited in Rothman (1986).

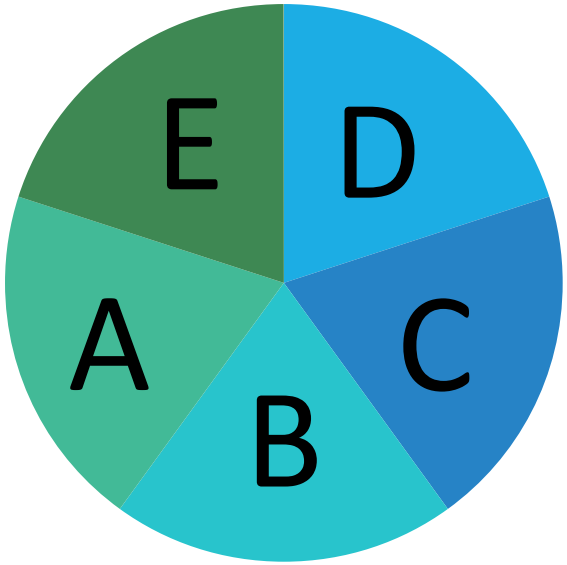
Component cause: a factor that contributes towards disease causation, but is not sufficient to cause disease on its own. (i.e. risk factors)

Sufficient cause: a factor (or combination of several factors) that will inevitably produce disease

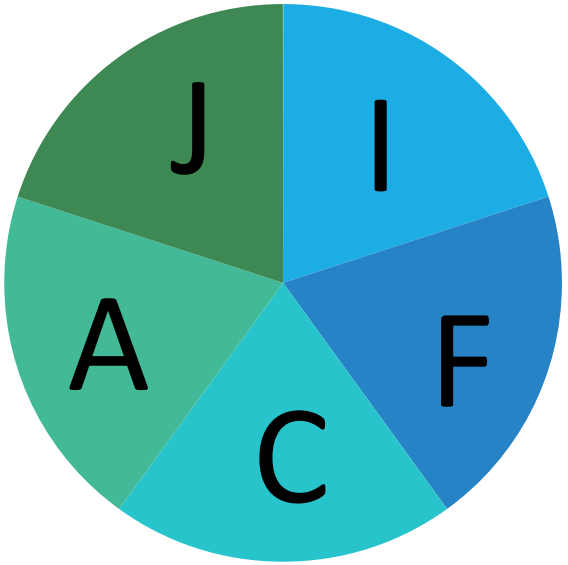
Necessary cause: any agent (or component cause) that is *required* for the development of a disease.

-Webb & Bain (2011)

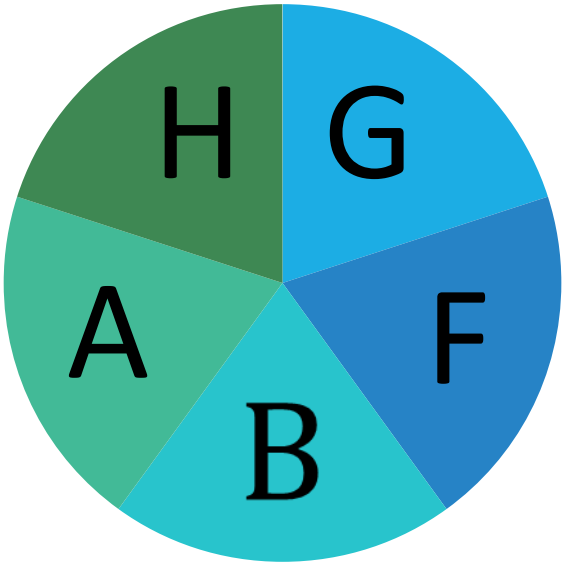
Sufficient Cause I



Sufficient Cause III



Sufficient Cause II



- Rothman & Greenland (2005)

Types of Causal Relationships

1. Necessary and sufficient
2. Necessary but not sufficient
3. Sufficient but not necessary
4. Neither sufficient nor necessary

Sir Austin Bradford Hill

Hill`s Postulates for causation: Top 6

1. Strength of association
2. Repetition
3. Temporal sequence
4. Dose response relationship
5. Biological plausibility
6. Experimental evidence

1. Strength of Association

1. Strength of Association

OR or RR 1+	OR or RR <1	Association strength
5.0 and up	0.3 and lower	Strong
2.0 – 4.0	0.6 – 0.4	Moderate
Under 2.0	0.7 and up	Weak

2. Repetition/Consistency

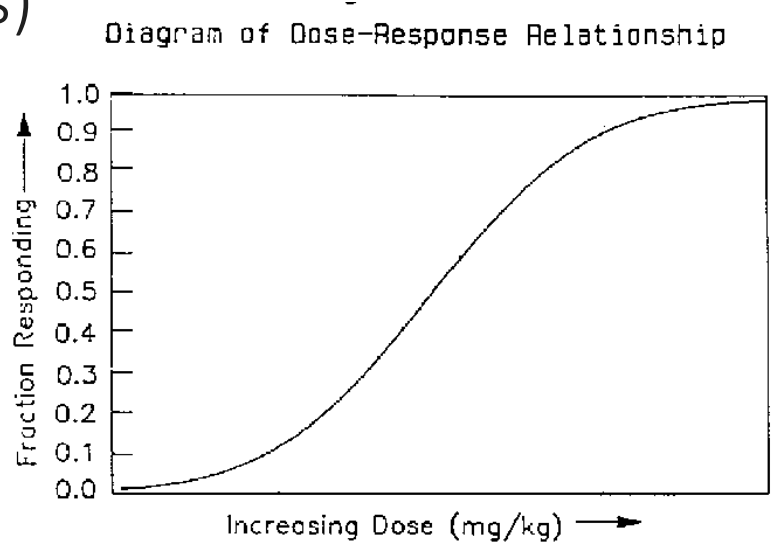
- Has association between exposure and outcome been repeated in previous studies beyond the one you are reviewing – if yes this criteria is met.
- Does not have to be the same study design for this criteria to be met – but studies have to examined the same exposure and outcome.

3. Temporal Sequence

- The exposure must precede the disease (can be difficult to determine, particularly with diseases having long incubation or latent effects)
- Does the design of the study you are reviewing measure prevalence or incidence
- If it measures prevalence – no temporal sequence – this criteria is not met.

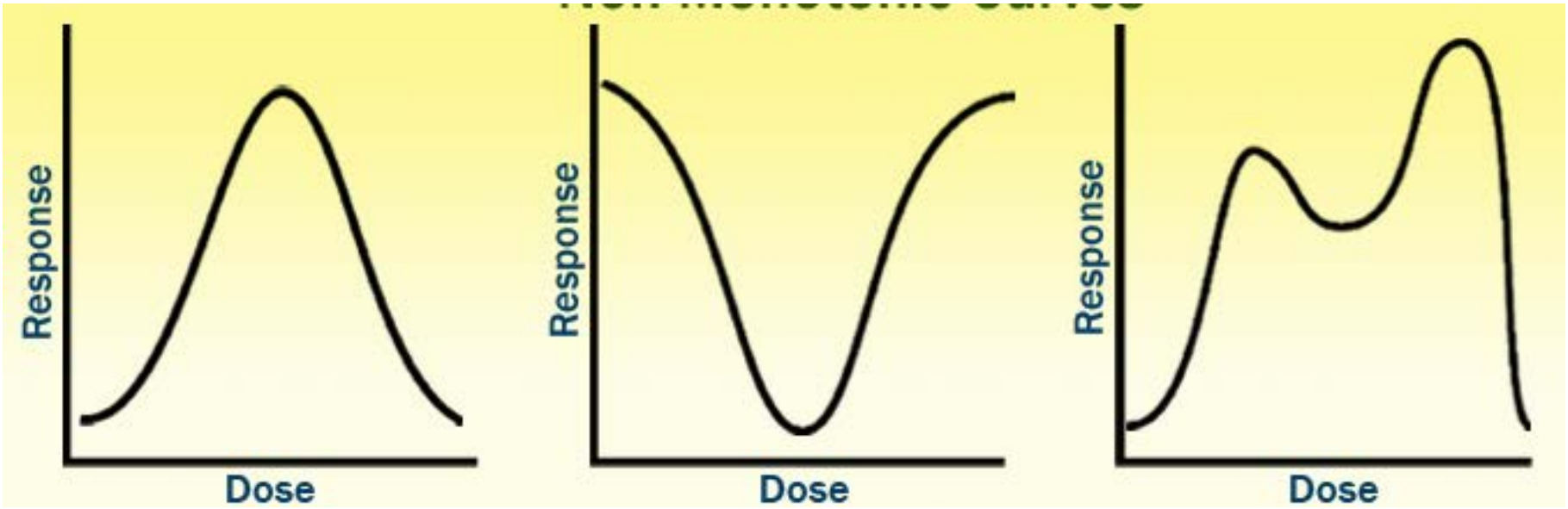
4. Dose response relationship

- Risk increases with increasing level of exposure
- May be a “threshold” below which no outcomes will result or above which will not exacerbate effect
- Some levels of exposure may actually be positive (poisons vs remedies)



4. Dose response relationship

Some examples of non-dose response relationships



5. Biological plausibility

- Is the association in a study biologically possible – what evidence does the study give to indicate the association has a biological basis
- This is limited by the current level of understanding in the biologic sciences

6. Experimental evidence

- Studies which are randomized controlled trials offer the strongest evidence for causation
- Is the study you are reviewing an experimental or observation study
- If observational study – this criteria is not met

Does H. Pylori cause Stomach cancer?

I.E. IS IT "CAUSAL," OR MERELY AND ASSOCIATION?

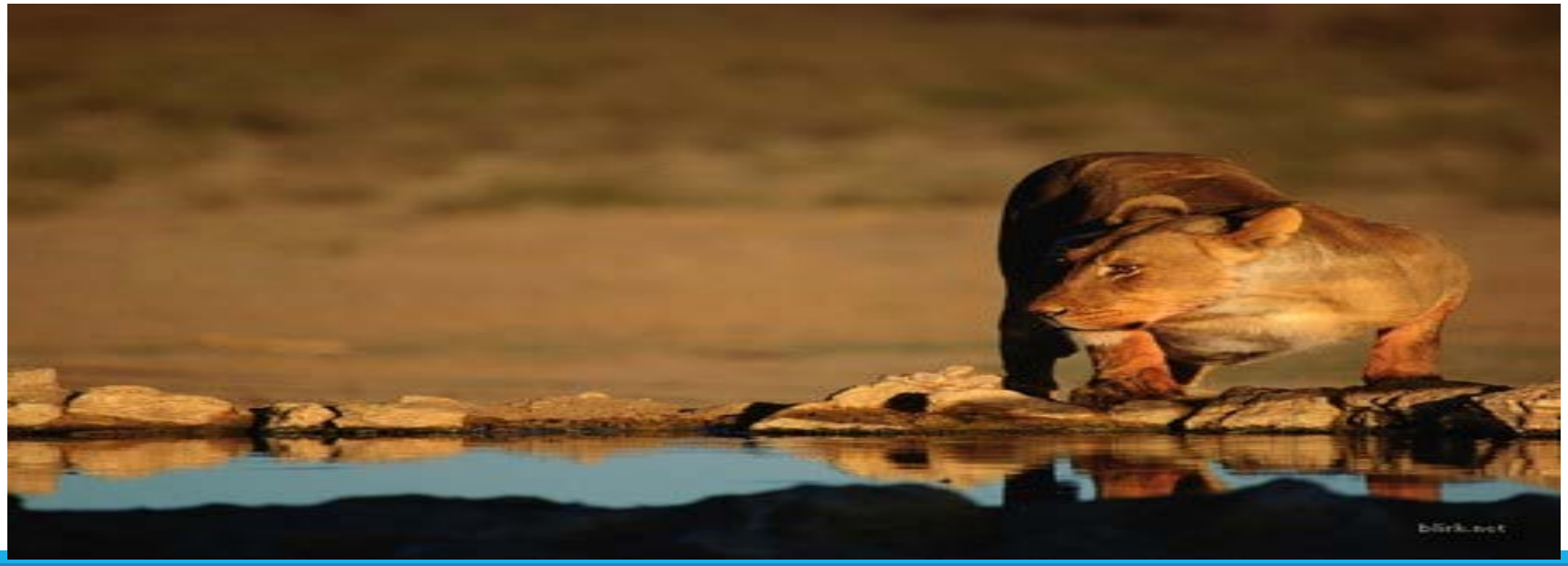
Why Study Design Matters:

Study Design	Ability to 'prove' causation.
Randomized Clinical Trials	Strong
Cohort Studies	Moderate
Case-control Studies	Moderate
Ecological (correlational) Studies	Weak
Cross-sectional Studies	Weak

CONSUMERS BEWARE:

Be Skeptical.
Just because it glitters, doesn't mean it's gold.
Ask Questions.
Look for the unobvious.
Acknowledge limitations.

NEXT CLASS…Confounding



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