Epidemiological Causation Criteria

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Discussion Topics

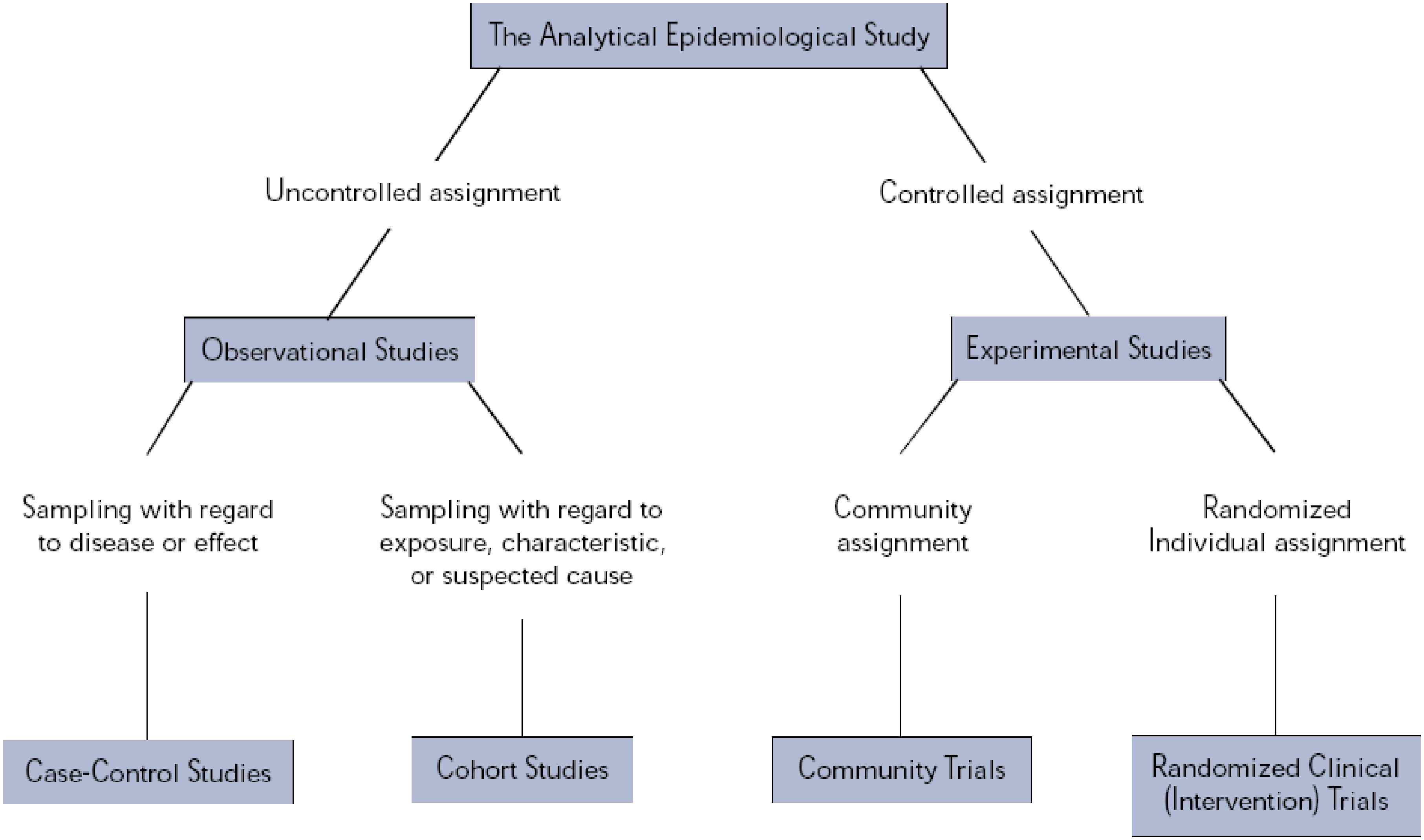
1. Types of epidemiologic studies
2. Epidemiologic science and the media
3. Bradford Hill's "Causation Criteria"
4. Statistical considerations
5. Questions to ask when reviewing an epidemiologic study

Epidemiology Defined

- *Epi* (upon) = *demos* (people) + *ology* (study of)
- Historical - the study of epidemics of infectious disease
- Modern - the study of the distribution and determinants of health and disease frequency in human populations
- Epidemiology looks for patterns of disease (time, place, personal characteristics)

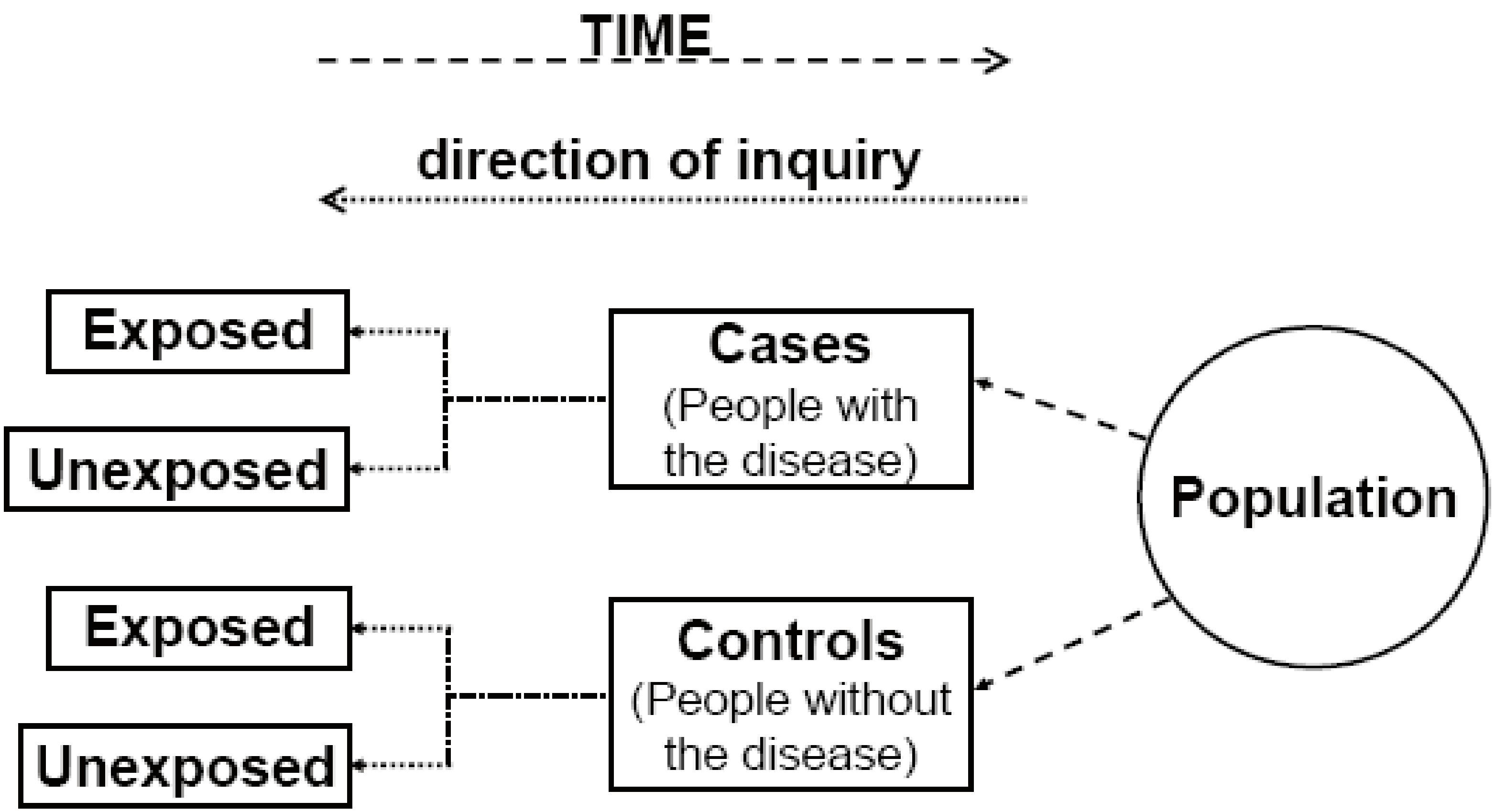
FIGURE 3

Types of epidemiological studies



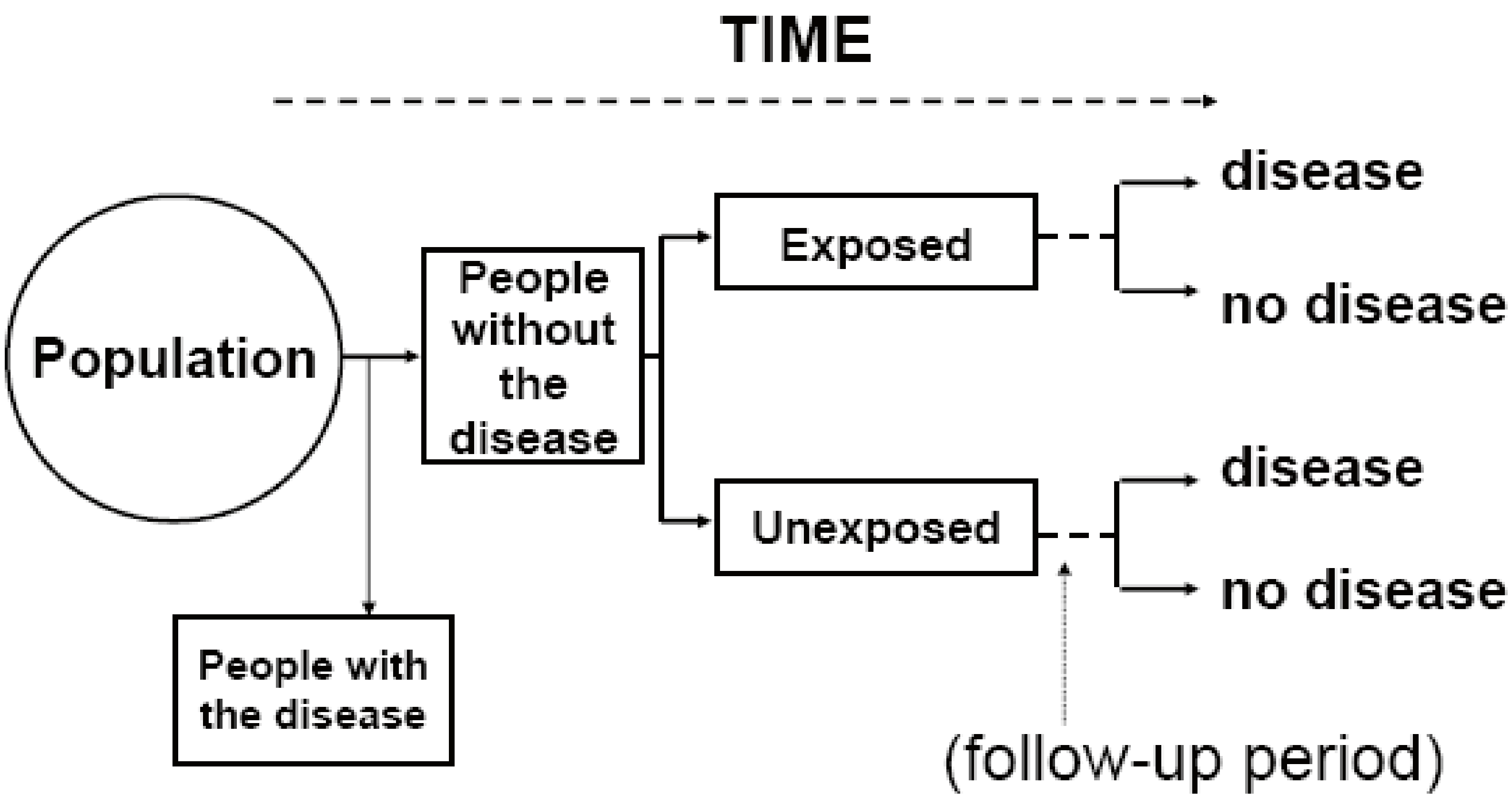
Source: Lilienfeld DE, Foundations of Epidemiology, © D. Lilienfeld 1994 (Used by permission of Oxford University Press)

Design of Case-Control Study

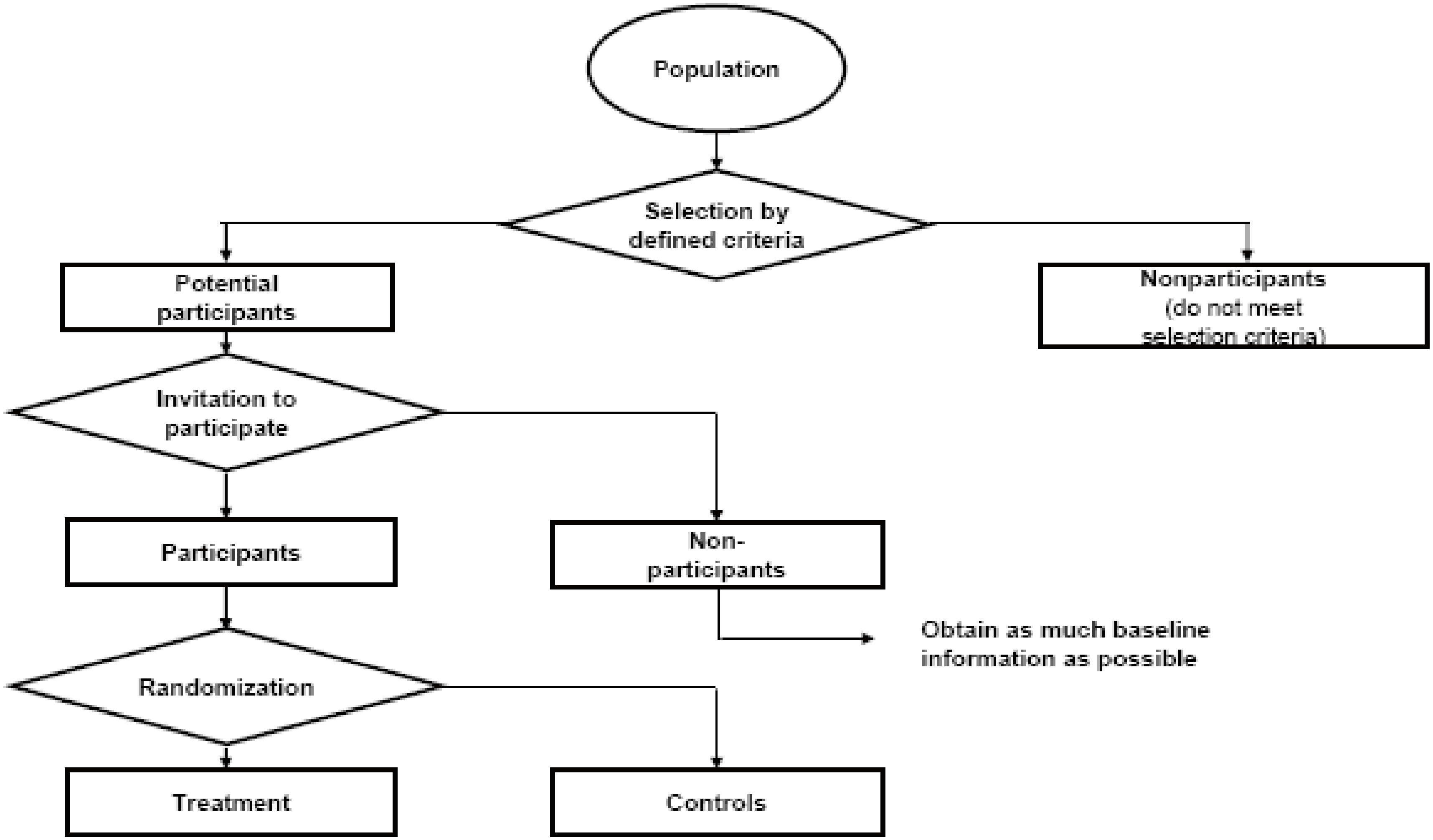



ON SECOND THOUGHT... MAKE MINE HOT CHOCOLATE.
COFFEE

Design of Cohort Study



Design of Experimental Study



Epidemiologic Science and the Media

- Dramatically increased interest in health over the past decade
- What we eat…or don't eat…is always being linked to various diseases, especially obesity and cancer
- Anxiety-provoking media headlines –
  - "Carcinogen-of-the-month" being the most scary to consumers
  - Dietary epi studies always seem to be contradicting each other
- Lots of nutrition nonsense and "food faddism" out there
- U.S. consumers are specific food & ingredient "avoiders"
- **AVOID or REDUCE**: salt, fat (fries and chips), carbs, coffee/caffeine, MEAT!!

Common Epidemiologic Statistics

- Odds Ratio (OR) = odds of exposure among ill / odds of exposure among well

  - If OR (or RR) > 1, then exposure is a risk factor
  - If OR < 1, then exposure is protective of illness
  - If OR = 1, then there is no association between the exposure and the illness.

- p-value = probability that equal (or more extreme) results can be observed by chance alone; generally set at the 95% level -

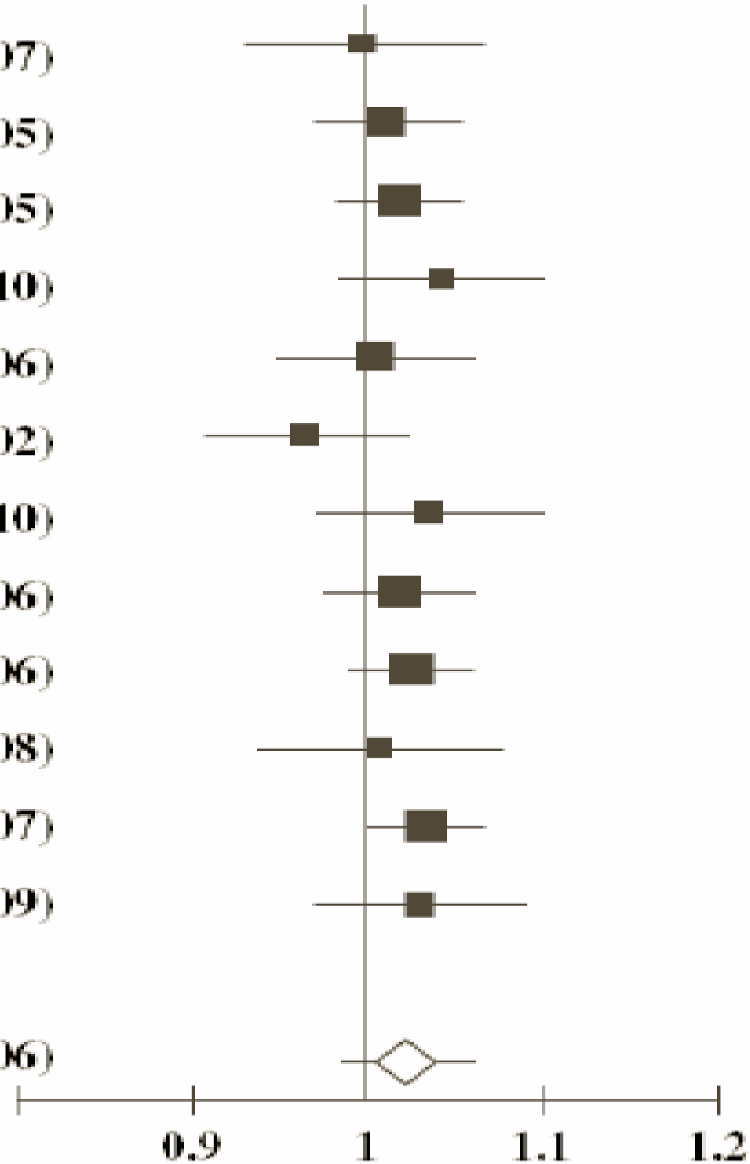
  - $P \leq 0.05$ = significant at the 95% level

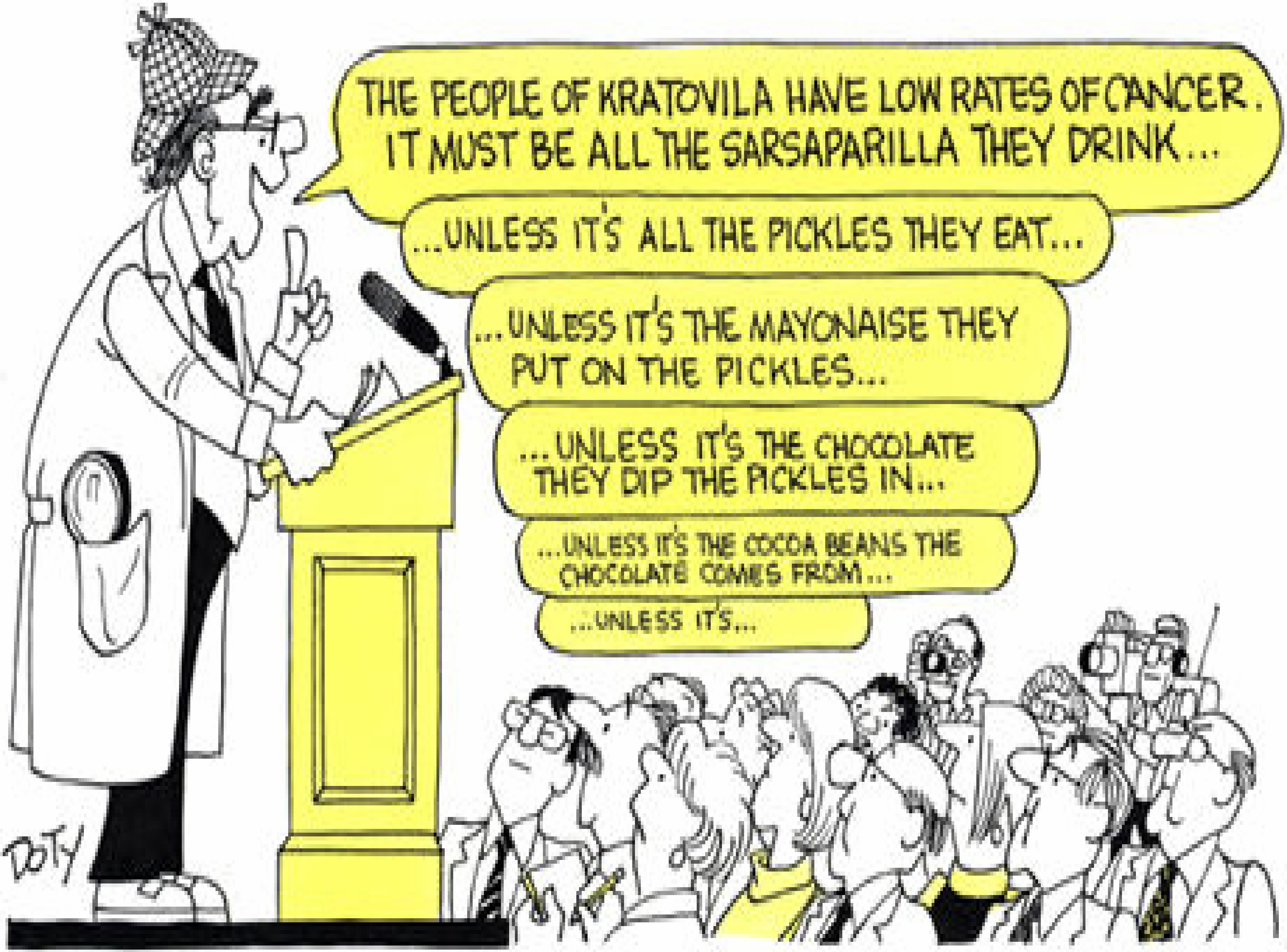
Common Epidemiologic Statistics

- Confidence Interval (C.I.) – used with ORs and RRs
- Width of C.I. tells us about both precision and accuracy and depends on:
  - Amount of variability in the data
  - Dimension of the sample
  - Arbitrary level of confidence (90%, **95%**, 99%)
- Example: OR = 2.3 (1.4 - 3.6)
- If 1.0 is not included in the 95% C.I., the risk is significant.

Meat Intake and Colorectal Cancer (EPIC Study) – Norat et al., 2005

Aarhus	56	1.00 (0.93-1.07)
Copenhagen	121	1.01 (0.97-1.05)
France	174	1.02 (0.98-1.05)
Heidelberg	48	1.04 (0.99-1.10)
Postdam	66	1.00 (0.95-1.06)
Italy	101	0.96 (0.91-1.02)
Utrecht	75	1.03 (0.97-1.10)
Spain	110	1.02 (0.98-1.06)
Malmo	194	1.02 (0.99-1.06)
Umea	78	1.01 (0.94-1.08)
UK	172	1.03 (1.00-1.07)
UK Health conscious	68	1.03 (0.97-1.09)
All EPIC	1389	1.02 (0.99-1.06)

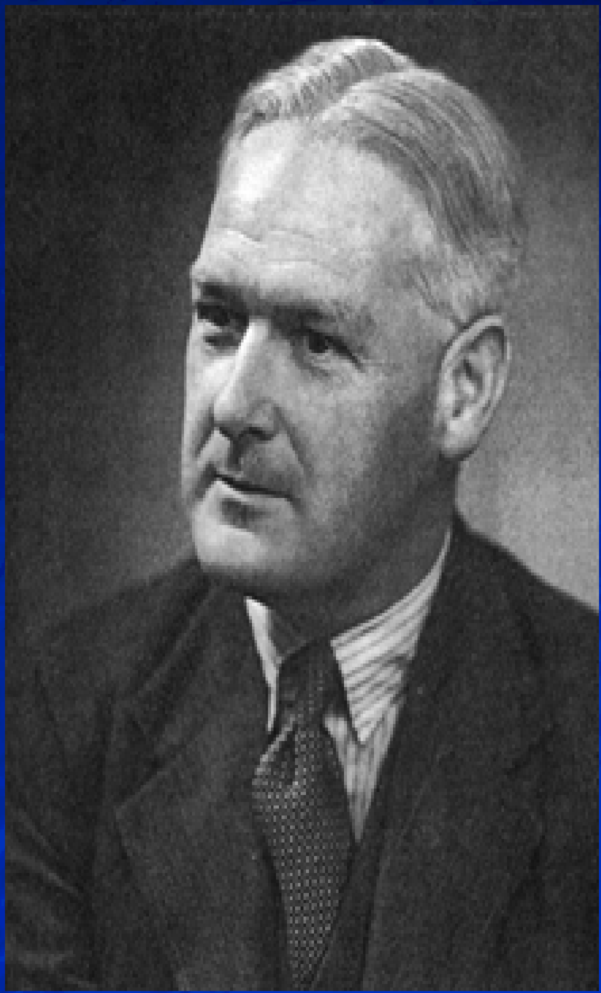



THE PEOPLE OF KRATOVILA HAVE LOW RATES OF CANCER. IT MUST BE ALL THE SARSAPARILLA THEY DRINK...
...UNLESS IT'S ALL THE PICKLES THEY EAT...
...UNLESS IT'S THE MAYONAISE THEY PUT ON THE PICKLES...
...UNLESS IT'S THE CHOCOLATE THEY DIP THE PICKLES IN...
...UNLESS IT'S THE COCOA BEANS THE CHOCOLATE COMES FROM...
...UNLESS IT'S...
DOTY

- A. Bradford Hill was an important 20th century British biostatistician and epidemiologist.

- In 1965 he wrote an often cited article* that laid out nine criteria for evaluating statistical associations.

- These criteria have become an informal standard to judge epidemiological research



A. Bradford Hill (1897-1991)

*Hill, A. B. (1965) The environment and disease: association or causation *Proceedings of the Royal Society of Medicine,* 58. 295-300.

Bradford Hill developed his list of "criteria" that continues to be used today. When using them, don't forget Hill's own advice:

"None of these nine viewpoints can bring indisputable evidence for or against a cause and effect hypothesis… What they can do, with greater or less strength, is to help answer the fundamental question - is there any other way of explaining the set of facts before us, is there any other answer equally, or more, likely than cause and effect?"

Cited in Doll, 1991. "Sir Austin Bradford Hill and the progress of medical science." *British Medical Journal* 305, 1521-1526.

The Bradford Hill Criteria

1. Strength of Association
2. Temporality
3. Consistency
4. Theoretical Plausibility
5. Coherence
6. Specificity in the Causes
7. Dose-Response Relationship
8. Experimental Evidence
9. Analogy

Strength of Association

The stronger the relationship between the independent variable (the risk factor) and the dependent variable (the disease), the less likely it is that the relationship is due to an extraneous variable (a confounder).

The lung cancer rate for smokers is about 10 times (RR = 10) higher than for non-smokers, thus arguing in favor of causation.

Temporality

The exposure must precede the disease by a reasonable amount of time, i.e., a cause must precede an effect in time.

Longitudinal studies have shown that a person must smoke for years (decades) before carcinogenesis and cell transformations lead to lung cancer.

Consistency

Multiple observations of an association, with different people under different circumstances and with different measurement instruments, increase the credibility of a causal finding.

Different methods (e.g., ecological, cohort & case-control studies) produced the same result for smokers. The relationship also appeared for different kinds of people (in males & females, in different populations on different continents).

Theoretical Plausibility

It is easier to accept an association as causal when there is a rational and theoretical basis for such a conclusion supported by known biological and other facts.

> The biological theory of smoking causing tissue damage to the respiratory system, which over time results in cancer in the cells, was a highly plausible biological explanation which supported causality.

Coherence

A cause-and-effect interpretation for an association is clearest when it does not conflict with what is known about the variables under study and when there are no plausible competing theories or rival hypotheses. In other words, the association must be coherent with other knowledge.

The conclusion that smoking causes lung cancer, based on epidemiologic, laboratory animal, pharmacokinetic, clinical and other biological data, showed that all available facts stuck together as a coherent whole.

Sources of Uncertainty

- Human variability
- Exposure measurement error
- Uncontrolled confounding
- Selection and recall bias
- Statistical imprecision

Specificity in the Causes

In the ideal situation, the effect has only one cause. In other words, showing that an outcome is best predicted by one primary factor adds credibility to a causal claim.

The evidence has shown that lung cancer is best predicted from the incidence of smoking. Smoking's causal link to other diseases can also be linked to the physical and chemical damage of cigarette smoke on the epithelial cell linings of these affected organs.

Dose-Response Relationship

There should be a direct biological gradient between the risk factor (the independent variable) and people's status on the disease variable (the dependent variable).

Data showed a positive, linear relationship between the number of cigarettes smoked and the incidence of lung cancer.

Experimental Evidence

Any related research (animal, *in vitro*, etc.) that is based on experiments will make a causal inference more plausible.

Tar painted on laboratory rabbits' ears was shown to produce cancer in the ear tissue over time. Hence, it was clear that carcinogens were present in tobacco tar.

Analogy

Sometimes a commonly accepted phenomenon in one area can be applied to another area.

Induced smoking with laboratory rats showed a causal relationship to tumors. It was not a great jump, therefore, for scientists to apply this phenomenon to humans. But analogy is considered to be a weak form of evidence.

Questions to Ask when Reviewing an Epidemiologic Study:

- Are there any methodological flaws in the study that should be considered when making conclusions?
- Does the research design fit the stated purpose of the study?
- What are the inherent limitations of this type of study?
- Are the study's results generalizable to other groups?
- How does this work fit with the body of research on the subject?
- What is the real and statistical significance of these results?
- Are the conclusions supported by the data?
- Could the study be interpreted to say something else?

References

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