

Bradford Hill Criteria

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Austin Bradford Hill (1965). The Environment and Disease: Association or Causation? *Proceedings of the Royal Society of Medicine*, 58, 295-300.

<http://www.edwardtufte.com/tufte/hill>

Correlation vs. Causation?

- *Here then are nine different viewpoints from all of which we should study association before we cry causation.*
- *No formal tests of significance can answer those questions. Such tests can, and should, remind us of the effects that the play of chance can create, and they will instruct us in the likely magnitude of those effects. Beyond that they contribute nothing to the 'proof' of our hypothesis.*

The Criteria

- Strength
- Consistency
- Specificity
- Temporality
- Biological Gradient
- Plausibility
- Coherence
- Experiment
- Analogy

Strength

- How strong is the association between the explanatory and response variables? Statistical measures include correlation and relative risk.
- *To take a more modern... example upon which I have now reflected for over fifteen years, prospective inquiries into smoking have shown that the death rate from cancer of the lung in cigarette smokers is nine to ten times the rate in non-smokers and the rate in heavy cigarette smokers is twenty to thirty times as great.*

Consistency

- Has the explanatory-response association been observed in different studies, at different times, in different places, under different conditions?
- *...the Advisory Committee to the Surgeon-General of the United States Public Health Service found the association of smoking with cancer of the lung in 29 retrospective and 7 prospective inquiries... The lesson here is that broadly the same answer has been reached in quite a wide variety of situations and techniques.*

Specificity

- Is the relationship 1:1? That is, does the outcome only occur with the explanatory variable?
- *... investigations of smoking and [lung] cancer... have been criticized for not showing specificity... But... If other causes of death are raised 10, 20 or even 50% in smokers whereas cancer of the lung is raised 900 – 1000% we have specificity... in the magnitude of the association.*

Temporality

- Does the explanatory variable always precede the response in time? If so, by how long?
- *“... which is the cart and which is the horse? This is a question which might be particularly relevant with diseases of slow development...”*

Biological Gradient

- Is there an increasing dose-response model? That is, does increased exposure to the explanatory variable result in a greater response?
- *For instance, the fact that the death rate from cancer of the lung rises linearly with the number of cigarettes smoked daily, adds a very great deal to the simpler evidence that cigarette smokers have a higher death rate than non-smokers. The comparison would be weakened... if it depended upon, say, a much heavier death rate in light smokers and a lower rate in heavier smokers.*

Plausibility

- Is the relationship biologically plausible? This depends on the current state of knowledge.
- *In short, the association we observe may be one new to science or medicine and we must not dismiss it too light-heartedly as just too odd. As Sherlock Holmes advised Dr. Watson, 'when you have eliminated the impossible, whatever remains, however improbable, must be the truth.'*

Coherence

- Does the association explicitly conflict with current scientific and historical knowledge?
- *... [cancer's] association with cigarette smoking [is] coherent with the temporal rise that has taken place in the two variables over the last generation and with the sex difference in mortality... greatly contributing to coherence [is] histopathological evidence ... isolation from cigarette smoke of factors carcinogenic for... laboratory animals.*

Experiment

- Does controlled manipulation of the explanatory variable result in predictable/sensible changes in the associated dependent variable?
- *Occasionally it is possible to appeal to experimental, or semi-experimental, evidence. For example, because of an observed association, some preventive action is taken... Here the strongest support for the causation hypothesis may be revealed.*

Analogy

- Do similar associations or evidence already exist for related explanatory and response variables?
- *With the effects of thalidomide and rubella before us we would surely be ready to accept slighter but similar evidence with another drug or another viral disease in pregnancy.*