

Models and Causal Thinking

CAUSATION

One of the great challenges underlying intervention research is to determine what constitutes proof of causation. The goal of outcomes research is to isolate the effect of treatment on the patient and/or disease being treated. The underlying challenge is to demonstrate that the relationship is causal. Distinguishing cause from association is one of the great challenges of science, especially clinical science.

Much of health services research and outcomes research draws on epidemiology, which is primarily directed at identifying factors associated with illness and identifying its cause. Here we are interested in the causes of improvement that result from defined interventions. Hence, some of the principles work well, but some need extrapolations.

Principles of causation have been around for quite a while, but ironically, they have changed as scientific measurement has improved and science has become more efficient and complex. One of the early philosophers who addressed causation was David Hume (Beauchamp, 1999). He laid out a series of postulates, or criteria, for a causal relationship. For example, to say that **A** causes **B**, the following must be true:

1. **A** must be consistently associated with **B**.
2. **A** must always precede **B**.
3. There must be a theoretical connection of **A** to **B**.

This work was picked up by Jakob Henle and Robert Koch who articulated a set of principles for infection. These principles, known as Henle-Koch's postulates, are as follows:

1. The bacteria must be present in every case of the disease.
2. The bacteria must be isolated from the host with the disease and grown in pure culture.
3. The specific disease must be reproduced when a pure culture of the bacteria is inoculated into a healthy susceptible host.
4. The bacteria must be recoverable from the experimentally infected host.

However, these principles proved difficult to apply as science evolved. We came to recognize that not all persons were equally susceptible and that some agents could not be readily identified. As a result, a new approach to analyzing the chain of causation was needed, one that recognized that the effects of treatment might be mitigated by the characteristics of the patient (and even perhaps by those of the therapist). By the era of viral infection research, Henle-Koch's postulates were examples, not requirements, for causality (Evans, 1976). As knowledge of the immune process increased, the definition of a dangerous bacterium changed.

Debate on how to establish causation continues today. There is no absolute rule about causation but one of the most frequently cited descriptions comes from a famous British epidemiologist, Sir Austin Bradford-Hill. His criteria for distinguishing association from cause are shown in Table 2-1 (Hill, 1965).

Clinical science relies on the randomized clinical trial (RCT) as the highest expression of causal proof. However, the RCT is a relatively new development. Although some go back to the innovation work of James Lind in the 18th century, when he established the cause of scurvy by assigning sailors on some British Royal Navy ships to eat limes while others did not. The first reported RCT usually cited is the 1926 work of Ronald Aylmer Fisher, but it was on agriculture (Fisher, 1926). The first modern medical RCT was the 1948 report by the British Medical Research Council (Medical Research Council, 1948).

Outcomes research relies heavily on epidemiology for its methods. Whereas epidemiology is primarily interested in what causes diseases,

Table 2-1 Bradford-Hill Criteria for Assessing Evidence of Causation

1. **Strength:** Larger effect sizes provide stronger evidence for causation.
2. **Consistency:** Observations should be replicable by different persons at different times and places.
3. **Specificity:** The relationship between the putative cause and putative effect should occur only with them. It is important to distinguish the strength of the association from the clinical importance.
4. **Temporality:** Cause must precede effect.
5. **Biological gradient:** The greater the exposure the greater the effect.
6. **Plausibility:** A reasonable mechanism for the cause and effect relationship is desirable.
7. **Coherence:** Consistency between the epidemiological findings and biological findings strengthens the evidence for causation.
8. **Experiment:** The cause and effect relationship is supported by experimental trials.
9. **Analogy:** Similar effects have been observed with similar exposures.

outcomes research explores the benefits (and harms) of treatment. The modeling is basically the same; only the variables change. Epidemiology talks about risk factors and disease incidence. For outcomes research, the treatment is the risk factor of interest, the disease is the target, and other confounding factors must be considered in the design and analysis of the study (Groenwold, Hak, & Hoes, 2009).

A basic but perplexing distinction is between an association and a cause. The former reflects a consistent pattern of correlations but the latter implies a mechanism. Making the leap from association to cause means taking a big step.

There are several measures of association: odds ratio (OR), relative risk (RR), absolute risk (AR), and effect size (ES). Each conveys different information (Austin, 2010). In distinguishing among these measures, it is important to understand the difference between an odds ratio and risk ratio as measures of association. To understand the difference between these measures, it necessary to appreciate how outcomes get counted (i.e., the odds of an outcome versus the risk of an outcome).

The OR quantifies the magnitude of association between the risk factor and the outcome in terms of odds, whereas the RR quantifies the strength

of the association in terms of risk. It assesses the odds of someone with the risk factor developing the outcomes as compared to someone without the risk factor. For example, the OR can be used to compare the occurrence of diabetes mellitus in a population. In the white population, there is one person with diabetes mellitus for every eight individuals without diabetes mellitus. Thus, the odds of diabetes mellitus in the white population are 1 in 8. In the African American community, the odds of diabetes mellitus are closer to 1 in 3. The OR for an association between race and diabetes mellitus is the quotient of the ratios, or 2.67 ($OR = 1/3 \div 1/8$).

Compared with the OR, the RR is based on probability estimates rather than odds. For the previous example, the probability of having diabetes mellitus, expressed as a percent, and being white is 11.1% [$0.111 = 1 / (1 + 8)$]. Among African Americans, the probability of having diabetes mellitus is 33.3%. For this association, the RR is the ratio of the two risks, or 3.00. This example illustrates the important distinction between the OR and RR. The two measures of association give results that are different. In fact, the OR and RR only provide comparable results when the outcome is relatively rare in the population (i.e., less than 10%). This is called the rare disease assumption. Both measures are perfectly acceptable in outcomes research, but it is important to recognize the underlying differences in how the outcomes are quantified (Schmidt & Kohlmann, 2008).

As shown in Table 2-2, the same data can be analyzed to generate an OR and a RR. Customarily, the RR is the preferred measure in prospective studies, where the group under study has been identified by the risk factor. Compared with the RR, the AR is the actual difference between the risk of the outcome with and without the exposure. For many purposes, this is the most important estimate because it speaks most directly to the ultimate impact of the intervention.

To illustrate how these differences can be used, imagine two diseases with treatments. Disease 1 Treatment A improves survival from 1 in 1 million to 2 in 1 million. Disease 2 Treatment B improves survival from 1 in 4 to 1 in 2. The relative risk (or relative benefit) is 2 in both cases. But with Disease 1, the absolute benefit of Treatment A is 1 in 1 million; whereas for Treatment B in Disease 2, it is 1 in 4.

Effect size is similar to relative benefit (or risk) but it adds some new dimensions. Essentially it reflects the distribution of the two groups (i.e., treated and not) and the distribution of outcomes associated with each. It is typically expressed as the difference in the means divided by the standard error.

Table 2-2 Outcomes Analysis Using Cross-tabulated Data

Treatment	Outcome	
	Yes	No
Exposed	<i>a</i>	<i>b</i>
Unexposed	<i>c</i>	<i>d</i>

Risk of the outcome in the exposed = $\frac{a}{(a + b)}$

Risk of the outcome in the unexposed = $\frac{c}{(c + d)}$

Relative risk = $\frac{[\frac{a}{(a + b)}]}{[\frac{c}{(c + d)}]}$

Odds of the outcome in the exposed = $\frac{a}{b}$

Odds of the outcome in the unexposed = $\frac{c}{d}$

Odds ratio = $\frac{[\frac{a}{b}]}{[\frac{c}{d}]}$ or $\frac{ad}{bc}$

Absolute risk = $[\frac{a}{b}] - [\frac{c}{d}]$

Another term encountered is attributable risk. It measures the proportionate excess risk of the outcome that is associated with a risk factor.

$$\text{Attributable Risk} = \frac{\text{Prevalence of Risk Factor} (RR - 1)}{1 + \text{Prevalence of Risk Factor} (RR - 1)}$$

where prevalence of the risk factor in the population is the proportion of those in the population with the risk factor and RR is the relative risk.

CONCEPTUAL MODELS

Developing a health outcomes project requires clearly specifying the underlying relationships and understanding what is required to establish a causal relationship. A conceptual model need not be based on disciplinary theory. It simply and clearly explicates what process the investigator believes is occurring, or at least what elements need to be controlled in the analysis. Such a model can be based on clinical experience as well as a review of prior work. Working through the model helps to think about what factors are most important.

Conceptual thinking can readily grow from insightful clinical analysis. Clinical intuition and insight is a valuable gift, which should not

be discarded or devalued in the face of quantitative science. In his autobiography, Colin Powell describes an intelligence unit in Vietnam that received endless amounts of data on the enemy's shelling patterns. All this information was entered into a computer regression model, which eventually produced the result that shelling was heavier on moonless nights, an observation that any combat veteran could have provided (Powell, 1995).

Outcomes research shares some of these problems. On the one hand, if its findings do not agree with clinical wisdom, they are distrusted. On the other hand, if they support such beliefs, they are extraneous. Life is generally too complicated to attempt outcomes analysis without some sort of framework. Some analysts may believe that the data will speak for themselves, but most appreciate the value of a frame of reference. Even more important, with so much information waiting to be collected, one needs some basis for even deciding where to look for the most powerful answers.

Using outcomes wisely requires having a good feel for what question is being asked and what factors are likely to influence the answer. Outcomes research is largely still a clinical undertaking, although it has become sophisticated. At its heart is a clinical model of causation.

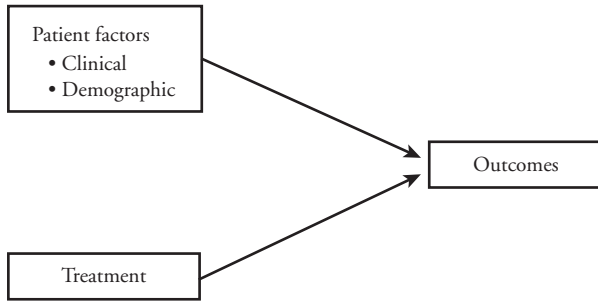
Before an outcomes study can be planned, the investigator needs to develop a clear model of the factors that are believed to be most salient and their relationship to the outcomes of interest. Some factors will play a direct role; others may influence events more indirectly. Each factor needs to be captured and its role defined. This model forms the basis of the analysis plan.

As noted previously, the conceptual model identifies the critical pathways and what other factors are likely to affect them. It should identify which variables, chosen to represent the various components of the basic outcomes equation, are pertinent to the study at hand. The variables themselves, and their relationship both to the outcomes of interest and to each other, should be specified. The process of creating a conceptual model is itself iterative.

A conceptual model is not necessarily the same as a theoretical model. The conceptual model lays out the expected relationship among classes of variables. It may be the result of intuition, of the literature review, or of expert judgment. A theoretical model draws upon some established set of theories that account for the observed associations among major variables.

The starting point is a set of premises based on theory and/or clinical insights. As you flesh out the model and become ever more specific about

Figure 2-1 Basic Conceptual Model



just what is involved, you can begin to think of how to operationalize this model, which may necessitate revisiting the model as it becomes further explicated and refined.

Models can vary in their complexity. Figure 2-1 offers a simple illustration of a conceptual model for looking at the outcomes of care. The two basic components of variables are those reflecting patient characteristics (both clinical and demographic) and the treatment provided. Figure 2-2 takes this model a step further by showing that the treatment may interact with the patient factors to produce an outcome. Figure 2-3 adapts the model to the case of congestive heart failure. Figure 2-4 shows the same model, but the potential relationship (exacerbated in a descriptive study) between patient clinical characteristics and the treatment is stressed. Adjusting for this selection bias will require special analyses.

Figure 2-2 Interactive Conceptual Model

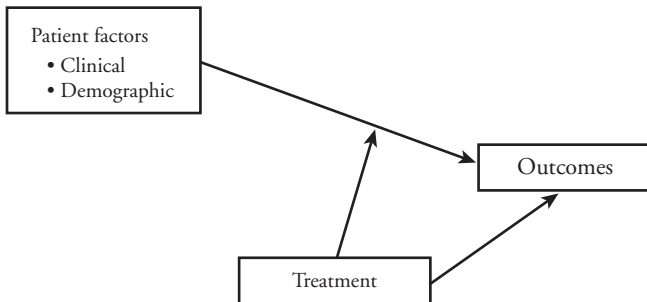
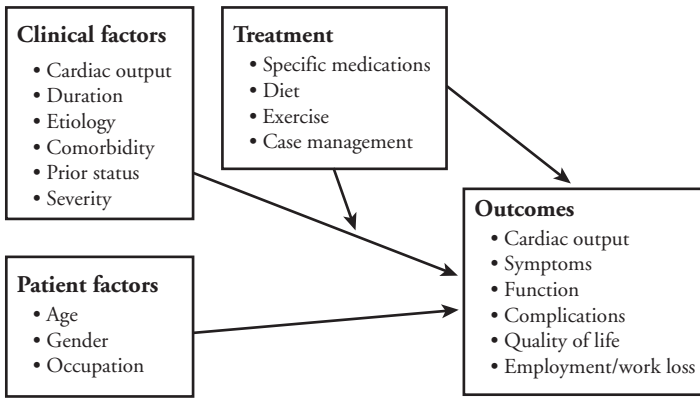


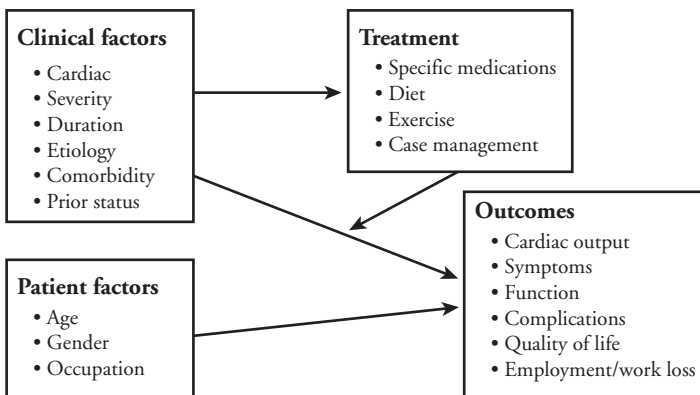
Figure 2-3 Conceptual Model of Treatment and Outcomes for Congestive Heart Failure



The items in the boxes are operationalized aspects of the basic elements that are addressed in the outcomes equation previously described. The arrows indicate an expected effect. In this model, the effects of treatment are expected to interact with the clinical factors to produce outcomes.

A scientific theory is a “construction of explicit explanations in accounting for empirical findings” (Bengtson, Rice, & Johnson, 1999).

Figure 2-4 Conceptual Model of Congestive Heart Failure with Selection Bias



Theory is used to build knowledge and understanding in a systematic and cumulative way, so that our empirical efforts will lead to integration with what is already known, as well as a guide to what is yet to be learned (Bengtson *et al.*, 1999). Theories take time to develop and be tested. Over time they may be rejected when new evidence comes to light that is inconsistent with current beliefs (Kuhn, 1970). By contrast, a model is much simpler. It portrays a picture of how elements may be related to each other. It may be driven by an underlying theory or it may be based on clinical or other observations (some of which may come from previous studies).

EXPLANATORY MODELS

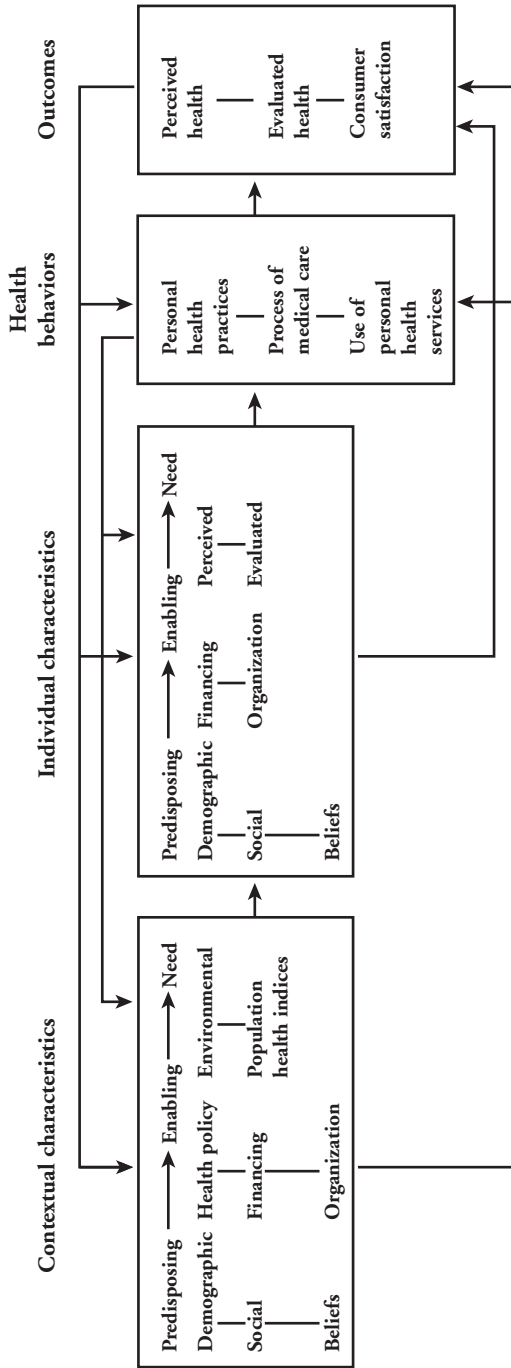
A number of explanatory models can be used in outcomes research. They may guide the actual creation of an analytically driven conceptual model or they may offer insights into how behavior can affect outcomes. Two of the most widely used are the Andersen–Aday model of utilization (Aday & Andersen, 1974; Phillips, Morrison, Andersen, & Aday, 1998) and the Health Belief Model (Stretcher & Rosenstock, 1997). The Andersen–Aday model is widely cited because it is so inclusive (Aday & Andersen, 1974). It has undergone many iterations (Andersen, 2008). The most recent version is shown in Figure 2-5. It identifies three major groups of factors that account for utilization of health resources.

1. Predisposing characteristics (demographic, social support, health beliefs)
2. Enabling resources (personal/family, community)
3. Need (perceived, evaluated)

Its strength is its weakness. It is so inclusive that almost anything can fit it. Hence, it is very attractive to people looking for a justification for their research. However, its breadth often means it explains little. Researchers may find themselves pushing variables into pigeonholes in the model to create a rationale for their inclusion when a simple, straightforward approach might work better.

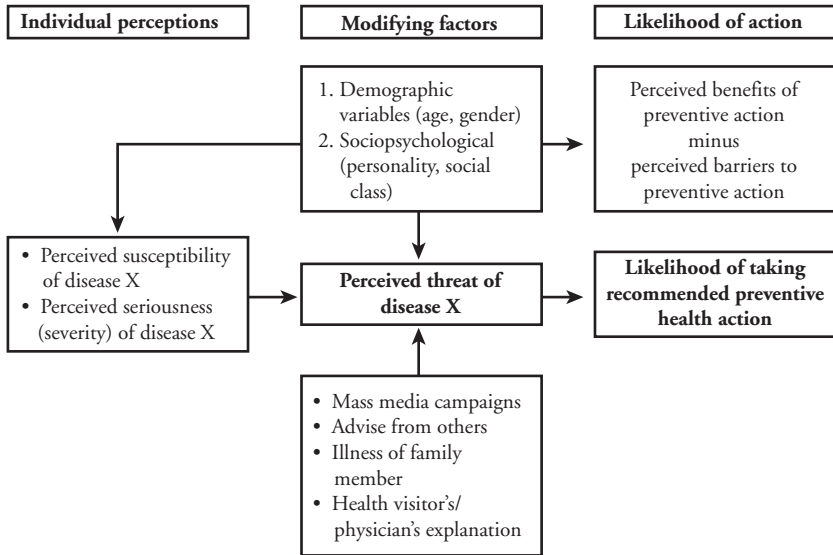
The Health Belief Model (see Figure 2-6) was originally developed to explain preventive behaviors (Becker & Maiman, 1975; Stretcher &

Figure 2-5 Andersen–Aday Behavioral Model of Health Services Use



Source: (Andersen, 2008)

Figure 2-6 Health Belief Model



Rosenstock, 1997). Its predictive capacity has been challenged but it continues to offer a useful basic framework that suggests that people's adherence behavior is driven by their perceptions of the seriousness of a disease and their susceptibility to it. In the context of outcomes, this might be transformed into a belief in the efficacy of treatment. Thus, they conduct a crude benefit calculation that weighs the risks against the potential benefits. This calculation is susceptible to external influences.

SUMMARY

It is important but often difficult to distinguish causation from association. Various tests of association should be used deliberately and carefully. Theoretical models provide general guidance to explain phenomena, but conceptual models can offer specific details that guide the analysis of a research study. Some conceptual models are derived from theory; others may come from practice or insight. Models are simply ways of displaying what the researcher believes is happening as the basis for explicating and testing research questions.

REFERENCES

- Aday, L. A., & Andersen, R. (1974). A framework for the study of access to medical care. *Health Services Research, 9*(3), 208–220.
- Andersen, R. M. (2008). National health surveys and the behavioral model of health services use. *Medical Care, 46*(7), 647–653.
- Austin, P. C. (2010). Absolute risk reductions, relative risks, relative risk reductions, and numbers needed to treat can be obtained from a logistic regression model. *Journal of Clinical Epidemiology, 63*(1), 2–6.
- Beauchamp, T. L. (Ed.). (1999). *An enquiry concerning human understanding*. New York: Oxford University Press.
- Becker, M. H., & Maiman, L. A. (1975). Sociobehavioral determinants of compliance with health and medical care recommendations. *Medical Care, 13*(1), 10–24.
- Bengtson, V. L., Rice, C. J., & Johnson, M. L. (1999). Are theories of aging important? Models and explanations in gerontology at the turn of the century. In V. L. Bengtson & K. W. Schaie (Eds.), *Handbook of Theories of Aging* (pp. 3–20). New York: Springer Publishing Company.
- Evans, A. S. (1976). Causation and disease: The Henle-Koch Postulates revisited. *Yale Journal of Biology and Medicine, 49*(2), 175–195.
- Fisher, R. A. (1926). The arrangement of field experiments. *Journal of Ministry of Agriculture, 33*, 500–513.
- Groenwold, R. H., Hak, E., & Hoes, A. W. (2009). Quantitative assessment of unobserved confounding is mandatory in nonrandomized intervention studies. *Journal of Clinical Epidemiology, 62*(1), 22–28.
- Hill, A. B. (1965). The environment and disease: Association or causation. *Proceedings of the Royal Society of Medicine, 58*, 295–300.
- Kuhn, T. S. (1970). *The Structure of Scientific Revolutions* (2nd ed.). Chicago: University of Chicago Press.

- Medical Research Council. (1948). Streptomycin treatment of pulmonary tuberculosis: A Medical Research Council investigation. *British Medical Journal*, 2, 769.
- Phillips, K. A., Morrison, K. R., Andersen, R., & Aday, L. A. (1998). Understanding the context of healthcare utilization: Assessing environmental and provider-related variables in the behavioral model of utilization. *Health Services Research*, 33(3), 571–596.
- Powell, C. L. (1995). *My American journey* (1st ed.). New York: Random House.
- Schmidt, C. O., & Kohlmann, T. (2008). When to use the odds ratio or the relative risk? *International Journal of Public Health*, 53, 165–167.
- Stretcher, V., & Rosenstock, I. M. (1997). The health belief model. In K. Glanz, F. M. Lewis, & B. K. Rimer (Eds.), *Health behavior and health education: Theory, research, and practice* (2nd ed., pp. 41–59). San Francisco: Jossey-Bass.

