

## **Understanding Workers' Compensation, Part IV: Determination of Causation in Workers' Compensation**

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March 2013

### **Introduction**

Knowing the workers' compensation system will prepare physicians for caring for patients who claim workplace injury or illness. This fourth in a series of articles about the workers' compensation system covers the determination of causation. Previous articles describe the history of, Vermont statutes and rules governing, and ethics as applied to the workers' compensation system. Forthcoming articles will suggest improvements in the system.

Misunderstanding cause in workers' compensation may misplace blame, condemn the innocent, deprive people of the opportunity to understand and take responsibility for their health or the health problems they create in others, and foster aversion to work. This article defines cause, describes barriers to depending on our perception to determine cause, and describes a hierarchy of medical evidence and approaches to determining cause.

### **Definition of Cause**

A cause is a factor that provides the generative force for something<sup>1</sup> or that produces an effect or action.<sup>2</sup> In medicine, we may consider cause of disease

1. its pathology, or change in structure or function from that which we view as normal to that which creates unpleasant symptoms and/or dysfunction,<sup>3</sup> and
2. personal characteristics or exposures that increase the likelihood of unpleasant symptoms and/or decreased function.<sup>4</sup>

### **Occupational Injuries and Illnesses**

An occupational injury or illness is any harmful work-related change in the body, whether occurring instantaneously or gradually,<sup>5</sup> "arising out of and in the course of employment." In the case of a violent workplace accident with immediate and visible effects, cause and effect are usual clear. An illness arises out of employment when it is caused by "conditions characteristic of and peculiar to a particular trade, occupation, process or employment, and to which an employee is not ordinarily subjected or exposed outside or away from the employment."<sup>5,6</sup> In the case of occupational illnesses, where cause and effect are not immediate and visible, our approach to determination of causation must be analytical to be valid.

### **Fallibility of Perceptions: Cognitive Pitfalls**

Human perceptions are fallible. Humans have thought that the earth was flat<sup>7</sup> and at the center of the universe,<sup>8</sup> that higher forms of life occurred spontaneously without descent from similar organisms,<sup>9</sup> and that disease was caused by demonic possession.<sup>10</sup> Our perception and performance are limited by cognitive pitfalls, for example, by structured biases known as schema,<sup>11,12</sup> a subcategory of which is stereotyping.<sup>13,14</sup> A list of cognitive pitfalls is contained in Appendix A.

The impact of schema can be seen in performance on mathematics tests: When persons from groups who are perceived to do less well in mathematics than white males, such as African Americans,<sup>15,16</sup> Latinos,<sup>17</sup> and females,<sup>17-20</sup> are reminded of their race or gender before taking math tests, they do worse than if not reminded. The effect is particularly strong when the test is challenging and when the examinees are reminded that persons from their group are expected not to perform as well on math tests as white men.

Stereotypes may manifest themselves physically as well as academically. African Americans who are under stereotype threat exhibited larger increases in blood pressure during tests than African Americans who are not under stereotype threat,<sup>16</sup> and their blood pressure was higher blood pressure when they perceived racism.<sup>21</sup>

### **Placebo and Nocebo Effects**

Our expectations of the effect of an exposure shape our reactions to an anticipated exposure. Positive outcomes based on expectation are seen in the placebo effect, which has been documented in many circumstances, including

in treatment of chronic pelvic and abdominal pain,<sup>22, 23</sup> osteoarthritis,<sup>24, 25</sup> headache,<sup>26</sup> fibromyalgia and other body pain,<sup>27-29</sup> diabetic neuropathy,<sup>29</sup> Parkinson's disease,<sup>30</sup> and acne.<sup>31</sup>

The nocebo effect – perception of harm in the absence of harmful exposure – has been documented with treatment of disease and from anticipated exposure to environmental phenomena such as electromagnetic fields. The nocebo effect has been identified during treatment of: fibromyalgia,<sup>28, 29, 32-34</sup> diabetic neuropathy,<sup>29</sup> Parkinson's disease,<sup>30, 37</sup> headaches,<sup>35, 36</sup> and other conditions.<sup>38-41</sup> More nocebo complaints occurred among those who expected than those who did not expect harm from exposure to electromagnetic fields with application of sham electromagnetic fields<sup>42, 43</sup>; and in trials where the anticipated, untoward effects of the intervention were reinforced (told more frequently to participants).<sup>44</sup>

Financial awards in workers' compensation claims may create, exacerbate, and prolong symptoms and disability<sup>43</sup>; which may be due to subterfuge<sup>45, 46</sup> and/or nocebo.<sup>47</sup> The phenomenon of poor outcomes in patients who benefit from claiming injury has been termed "compensation neurosis."<sup>48</sup>

### **Cause, Effect, and Medical Evidence and Its Hierarchy**

Given the limitations of human perception, including the limitations of perceptions of persons who claim harm from work, and the potential ulterior motives of persons involved in workers' compensation claims, a rigorous approach using high quality evidence to determine cause and effect is warranted. Rigor and quality of evidence in medicine has been the subject of Evidenced-Based Medicine (EBM). Treatises on EBM<sup>49, 50</sup> often describe a hierarchy of medical evidence, where higher quality evidence compared to lower quality evidence lessens the impact chance and shortcomings of human judgment.

To ensure that chance is not likely to account for differences between exposed and unexposed groups under scrutiny, outcomes undergo statistical analysis and should be reproducible. A single study is of limited use as positive correlations may occur by chance or due to flaws in study design. Positive results of a study, until confirmed by other studies, are nearly always tentative.

When inquiring into cause and effect, a comprehensive search for confirmatory and contradictory studies must be conducted, study outcomes must be abstracted and analyzed, and the aggregated results used to form the conclusion. These reviews should be systematic and be based on good-quality studies.<sup>49, 51-53, 56</sup> If all relevant quality medical literature is not included in the analysis, the conclusions drawn from the analysis are more likely to be biased.

Appendix B describes types of bias. Bias is minimized through *a priori* definition of exposure and outcome, random selection of subjects to be exposed and unexposed, blinding of all study participants, and analysis to adjust for potential biases.

A typical hierarchy of evidence, from highest quality to lowest quality, is<sup>49, 50</sup>:

1. systematic reviews of randomized clinical trials;
2. randomized clinical trials (RCT);
3. controlled cohort studies;
4. case-control studies;
5. cross sectional studies;
6. case series;
7. case studies; and
8. unsupported expert opinion.

In the case of potentially-harmful exposures, RCTs are not conducted, and the highest form of evidence available is the controlled cohort study.

Statistical inference with *a priori* criteria for establishing cause and effect was applied by the United States Surgeon General in determining a relationship between smoking tobacco and its health consequences in a landmark 1964 report.<sup>54</sup> The Surgeon General used criteria of consistency, strength, specificity, temporality, and coherence to judge cause and effect. These criteria were refined by Hill in 1965 when he published nine criteria for determining causation<sup>55</sup> that have become known as "Hill's criteria" and have been specified as the method of determining causation of disease in publications of the American Medical Association<sup>56</sup> (AMA) and the American College of Occupational and Environmental Medicine (ACOEM).<sup>57</sup> Excerpts from Hill's 1965 publication are contained in Appendix C. The importance in determining cause and effect of systematic, statistical analysis relative

to subjective experience can be seen in Hill's consideration of strength, consistency, and specificity of association – outcomes derived from epidemiological studies – as more important than temporality of occurrence. Temporality – presumed cause preceding presumed effect – is a necessary but not sufficient element of determination of cause. Use of temporality as the sole factor for determination of cause is subject to the *post hoc ergo propter hoc* fallacy,<sup>58</sup> a form of illusory correlation.

### **The National Institutes of Occupational Health Approach for Determination of Causation**

In 1979, the National Institutes of Occupational Health and Safety (NIOSH) described an approach for determining causation of workplace health disorders in "A Guide to the Work-Relatedness of Disease," edited by Kusnetz and Hutchinson.<sup>59</sup> The NIOSH approach is:

- "1. consideration of evidence of disease,
- "2. consideration of epidemiologic data,
- "3. consideration of evidence of exposure,
- "4. consideration of validity of testimony,
- "5. consideration of other relevant factors, and
- "6. evaluation and conclusion."

The approach of Kusnetz and Hutchinson has been recognized and embraced by the AMA,<sup>56</sup> ACOEM,<sup>57</sup> and in a publication of the American Academy of Orthopedic Surgeons,<sup>60</sup>; and has been specified for use in the practice of occupational medicine in the *Practice Guidelines* of the ACOEM.<sup>57, 61</sup>

ACOEM further specified<sup>55, 59</sup> that "[u]nless the causal factor had an immediate and visible effect on the patient, imputing causation to a work factor ... requires that there be reasonable epidemiologic evidence for the association. The coexistence of the exposure and the effects is necessary but not sufficient."

### **Strength of Association Necessary to Satisfy Workers' Compensation Criteria for Causation**

The level of proof to support a health condition as caused by an exposure at the workplace is a preponderance, or more than 50 percent, of evidence.<sup>62, 63</sup> In epidemiological studies, the threshold for showing that a preponderance of the evidence supports a cause-and-effect relationship between an exposure and a health condition is when a particular health condition occurs at more than twice the rate in exposed compared to unexposed populations. Stated in numerical terms, this means that an epidemiological risk indicator (for example, relative risk (RR) in cohort studies) should exceed two.<sup>64, 65</sup> Another way of expressing the strength of the relationship is that the attributable risk should be at least 50 percent.<sup>64-67</sup> For a variety of reasons, including lack of publication of studies that do not show positive results (publication bias) and the sub-optimal quality of most studies, some investigators suggest that epidemiological risk indicators should exceed four before a cause-effect relationship becomes likely.

### **Pathology**

Pathology is important in forming models to explain symptoms and loss of function, and in explaining benefit from or justifying treatment. Pathological anatomic and physiologic changes may be measured by physical examination findings, biochemically, radiographically, histologically, or electrophysiologically. The purported factor causing a specific disease (A) should be significantly-more likely to be found in persons with the disease, and (B) should plausibly explain the symptoms and dysfunction of the disease.

### **Conclusions**

Scientific and technical standards guide the determination of causation, including Hill's criteria<sup>55</sup> and the 1979 NIOSH approach.<sup>57</sup>

Medical evidence has a hierarchy: repeatable RCTs or, in the care of potentially-harmful exposures, cohort studies are the highest quality; and a single case study and unsupported expert opinion are the lowest quality evidence.<sup>49,</sup>

<sup>50</sup> Repeatable, higher quality evidence is less influenced by change and cognitive pitfalls/biases. Many factors can mislead one in establishing a cause effect relationship, and lower-quality evidence, such as case studies depend heavily, on temporality as the basis for claiming cause and effect and are subject to logical fallacies such as the *post hoc ergo propter hoc* fallacy.

Depending on a workers' compensation claimant to define a cause and effect relationship is likewise fraught with risks of misinterpretation, including: misinterpretation that activities that provoke symptoms cause damage, a form of logical fallacy known as an illusory correlation,<sup>68-73</sup> and manipulation by the parties in the claim.

If we care about justice, true workplace safety, providing people with the opportunity to take responsibility for themselves, and the integrity of the workers' compensation process, we cannot rely on anecdotes in determination of cause and effect. It is important to identify causative factors in disease, be they intrinsic (personal characteristics) or extrinsic (exposures), so that when possible, we can modify risk and reduce or eliminate harmful exposure.

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## Appendix A – Cognitive Pitfalls

An incomplete list of cognitive pitfalls follows.

- **schema**<sup>A-i, A-ii</sup> a structured cluster of pre-conceived ideas that bias observations, a subcategory of which is **stereotyping**,<sup>A-iii, A-iv</sup> applying standardized and simplified conceptions of groups based on prior assumptions, usually not based on objective truth;
- **representativeness**,<sup>A-v</sup> the expectation that whatever qualities are found in a population average will be found in individuals or small samples from the population, a subcategory of which is the “**Law of Small Numbers**,” the expectation that statistical patterns will apply in an orderly fashion;
- **illusory correlations**,<sup>A-vi-xi</sup> the appearance of a relationship when no relationship exists;
- **availability**,<sup>A-xii-xiv</sup> the propensity to make estimates or decision based on what we can remember (heavily influenced by prominent or recent experiences) rather than complete data;
- **confirmatory bias**,<sup>A-xiv, A-xv</sup> a focus of on attention on facts that support one’s assumptions;
- **false consensus**,<sup>A-xvi, A-xvii</sup> the propensity to elicit statements from other supportive of one’s beliefs; and
- **indifference to base rates**,<sup>A-xv</sup> the propensity to focus on positive and ignore negative findings.

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## Appendix B – Types of Bias

### Bias and Confounding

Bias is systematic error in a study that results in an incorrect estimate of the association between exposure and risk of disease. Bias can be broadly classified as selection, observation/information, and confounding.<sup>B-i, B-ii</sup>

#### Selection Bias

Selection bias occurs when the exposure or intervention (treatment) group differs from the control group in ways other than the exposure or intervention. The groups may differ in measured or unmeasured characteristics because of the way in which participants were selected or assigned to groups.<sup>B-iii</sup> Put in another way, selection bias occurs when the subjects studied are not representative of the target population about which conclusions are to be drawn.<sup>B-iv</sup> For example, when comparing mechanical exposures of laborers to non-laborers, those who are better conditioned physically may have chosen jobs as or continued to work as laborers; thus, may be more resistant to the ill effects of mechanical exposure – this is an example of selection bias and the “healthy worker effect.” The healthy worker effect usually biases studies to understate the effect of an exposure; however, biases may also work to exaggerate differences.

#### Information Bias

Information bias is a flaw in measurement of exposure or outcome that results in differential accuracy of information between compared groups<sup>B-ii</sup> and occurs when measuring exposure or disease.<sup>B-iv</sup> Many different biases (recall, reporting, measurement, withdrawal, and so forth) are grouped in this class. As an example, recall bias may occur in a case-control study when asking groups with and without a disease about an exposure. Persons with the disease are likely to have focused more on potential causes of their disease, including exposures, and may be more likely to report exposures than persons without the disease. This bias would exaggerate differences.

#### Confounding

Confounding is a situation in which the intervention effect is biased because of difference between the control and intervention/ exposure groups apart from the intervention/exposure. The confounding differences may be baseline characteristics, prognostic factors, or concomitant interventions/exposures.<sup>B-v</sup> For a factor to be a confounder, it must differ between the comparison groups and predict the outcome of interest. Confounding is a function of the complex interrelationships between various exposures and disease. Confounding can be controlled in the design (randomisation, restriction, exclusion and matching) and in the analysis (stratification, multivariable analysis and matching). The best method to control for unknown confounders is to use a randomised design.<sup>B-ii</sup>

Bias and confounding are not affected by sample size. However, chance effect (random variation) diminishes as sample size gets larger. A small *P* value and a narrow odds ratio/relative risk are reassuring signs against chance effect although they never eliminate that potential. The same cannot be said for bias and confounding.

Confounders may include individual traits, characteristics, physical and psychosocial factors. For example, when the relationship between job title and back pain were compared by Leigh and Sheetz,<sup>B-vi</sup> the seemingly-physically-more-demanding jobs had high odds for back pain as follows:

Job Title	Odds	Job Title	Odds
• Professional or Manager	1.00	• Service Worker	2.67
• Clerical or Sales Worker	1.38	• Farmer or Farm Laborer	5.17
• Craftsman, Operative, or Laborer	2.39		

However, when considering other characteristics of Leigh and Sheetz’s subjects, lower educational level have a stronger association than physical factors.

Characteristic	Odds	Characteristic	Odds
Education		Physical Effort – as designated by respondent	
• 8th Grade or less	2.18	• Much	1.68
• 9th to 11th grade	1.45	• Not “Much”	1.00
• 12th grade	1.05	Repetitious Work – as designated by respondent	

- Over 12th grade 1.00
- Much 1.20
- Not “Much” 1.00

### Minimization of Bias

Bias may be minimized by various means, including:

- randomization of subjects if possible (usually this is not practicable in epidemiological studies), restriction and/or matching of exposed and unexposed subjects, and stratification during analysis to minimize confounding;
- measurement of potential confounders;
- careful selection of study groups so that participants are selected from populations that differ only in whether or not they are exposed;
- multivariate analysis, which may help correct for confounding if potential confounders can be identified and measured;
- arrangement of reliable follow-up to minimize loss of participants;
- blinding of subjects, evaluators, and data analyzers to minimize effects of prejudices about exposure measurement and reporting bias;
- rigorous, standardized, objective quantification of exposure and outcome to minimize measurement bias; and
- application of identical measurement tools to all study groups to minimize measurement bias.

### Appendix B References

- B-i. Analysis of epidemiologic studies: evaluating the role of bias. In Hennekens CH, Buring JE. *Epidemiology in medicine*. Pages 272-286. Little, Brown and Company. Boston. 1987.
- B-ii. Dorak MT. Bias and Confounding. <http://www.dorak.info/epi/bc.html>. Accessed December 1, 2008. (Associated Lecture at <http://www.dorak.info/epi/bc.ppt>.)
- B-iii. Selection bias. Glossary. The Trial Bank Project: complete CONSORT Plus guideline. University of California San Francisco. <http://rctbank.ucsf.edu/BaT/html-files/glossary.html>. Accessed December 26, 2008.
- B-iv. Coggon D, Rose G, Barker DJP. Epidemiology for the uninitiated: measurement error and bias. <http://www.bmj.com/epidem/epid.4.dtl#pgfId=1002291>
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## Appendix C – Hill’s Criteria

### Hill’s Criteria for Determination of Causation

From Austin Bradford Hill’s 1965 paper, with minor format changes: “[A]n association between two variables, perfectly clear-cut and beyond what we would care to attribute to the play of chance” should be decided by the following.

- "1. **Strength:** First upon my list I would put the strength of the association. To take a very old example.... ‘the mortality of chimney sweeps from scrotal cancer was some 200 times that of workers who were not specially exposed to tar or mineral oils....’
- "2. **Consistency:** Next on my list of features to be specially considered I would place the consistency of the observed association. Has it been repeatedly observed by different persons, in different places, circumstances and times?
- "3. **Specificity:**.... If... the association is limited to specific workers and to particular sites and types of disease and there is no association between the work and other [diseases], then clearly that is a strong argument in favor of causation.
- "4. **Temporality:**.... Does a particular diet lead to disease or do the early stages of the disease lead to those particular dietetic habits? Does a particular occupation or occupational environment promote infection by the tubercle bacillus or are the men and women who select that kind of work more liable to contract tuberculosis whatever the environment – or, indeed, have they already contracted it? This temporal problem ... certainly needs to be remembered, particularly with selective factors at work....
- "5. **Biological gradient:**... or dose-response curve.... adds a very great deal to the simpler evidence.... [If dose-response is not present and proportional between exposure and disease, w]e should then need to envisage some much more complex relationship to satisfy the cause and effect hypothesis....
- "6. **Plausibility:** It will be helpful if the causation we suspect is biologically plausible. But this is a feature I am convinced we cannot demand. What is biologically plausible depends upon the biological knowledge of the day....
- "7. **Coherence:**... [T]he cause-and-effect interpretation of our data should not seriously conflict with the generally known facts of the natural history and biology of the disease....
- "8. **Experiment:** Occasionally it is possible to appeal to experimental, or semi-experimental, evidence. For example, because of an observed association some preventive action is taken. Does it in fact prevent? The dust in the workshop is reduced, lubricating oils are changed, persons stop smoking cigarettes. Is the frequency of the associated events affected? Here the strongest support for the causation hypothesis may be revealed.
- "9. **Analogy:** In some circumstances it would be fair to judge by analogy. 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.”

### Appendix B References

C-i. Hill AB. The Environment and Disease: Association or Causation? *Proc Royal Society Med* 58:295-300. 1965.