

Commentary

When Work is Related to Disease, What Establishes Evidence for a Causal Relation?

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Establishing a causal relationship between factors at work and disease is difficult for occupational physicians and researchers. This paper seeks to provide arguments for the judgement of evidence of causality in observational studies that relate work factors to disease. I derived criteria for the judgement of evidence of causality from the following sources: the criteria list of Hill, the approach by Rothman, the methods used by International Agency for Research on Cancer (IARC), and methods used by epidemiologists. The criteria are applied to two cases of putative occupational diseases; breast cancer caused by shift work and aerotoxic syndrome. Only three of the Hill criteria can be applied to an actual study. Rothman stresses the importance of confounding and alternative explanations than the putative cause. IARC closely follows Hill, but they also incorporate other than epidemiological evidence. Applied to shift work and breast cancer, these results have found moderate evidence for a causal relationship, but applied to the aerotoxic syndrome, there is an absence of evidence of causality. There are no ready to use algorithms for judgement of evidence of causality. Criteria from different sources lead to similar results and can make a conclusion of causality more or less likely.

Key Words: Causality, Occupational medicine, Occupational diseases, Epidemiological studies

Introduction

Establishing a work-related cause of a disease is one of the most challenging aspects of occupational medicine. In practice, physicians face the challenge of making a diagnosis of occupational disease in an individual patient [1]. This constitutes a clinical diagnosis, assessment of the past exposure, and exclusion of other potential causes, which demands specialist skills in both clinical medicine and occupational hygiene. Researchers have to make causal inferences about an occupational origin from observational studies that often leave room for alternative

interpretations [2]. It is therefore conceivable that these difficulties lead to undesirable variations in practice, which is often regarded as a lack of quality such has been described for reporting of occupational diseases in Europe [3].

Currently, it is generally accepted that evidence from scientific research should be used to underpin decisions about health problems to improve the quality of health care. About 20 years ago, this idea was first strongly advocated by Sackett et al. [4]. He applied the idea of what he called *evidence-based medicine* to clinical decision-making at the individual patient level. In mainstream medicine, the most important decisions are about therapy and most of evidence-based medicine has focussed on evidence to support therapeutic decision-making at the individual patient-level.

This raises the question, what establishes evidence to underpin the diagnosis of an occupational disease? Put more precisely, what constitutes evidence for the labelling of a disease as being occupational in origin? For clinical practice, I would

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expect a clinical algorithm that guides the physician in making the decision that there is an occupational cause at work in this disease, in this particular patient. However, I haven't been able to locate articles that describe such a process.

For research, I would expect a similar algorithm that would guide a researcher or a reader through the process of making a decision on work-relatedness when judging a research report on the occupational origin of a disease. Surprisingly little has been published on this topic. In this article, I will restrict myself to the assessment of causality in reports of research.

Therefore in this article, I would like to present arguments for what can be considered evidence for an occupational disease. I will elaborate the various aspects of assessing an occupational disease and the arguments for causation in observational epidemiological studies. Finally, to illustrate the process, I will apply the arguments put forward to two cases of putative occupational diseases.

Occupational Disease

Employment is associated with better health than unemployment. This positive effect of work on health is assumed to be mediated by a higher income, a purposeful social role, and a time structure for those that are employed [5]. On the other hand, workers are exposed to various kinds of health hazards at work. These health hazards may lead to occupational diseases under certain conditions. Occupational diseases can conveniently be defined as diseases that result from exposure during work activities to conditions or substances that are detrimental to health. Thus, occupational diseases can be regarded as an undesirable by-product of working. In most countries, the employer is held responsible for eliminating hazardous exposures at work. If occupational diseases still do happen, it is often regarded as a form of injustice that should be compensated financially by the employer. As part of social security systems, this professional risk is insured but there is a great variation between systems [6]. One of the aspects that varies between systems and countries in which diseases are considered occupational in origin and would need to be financially compensated. One of the main issues here is how big a part of the cause of a given disease should be assigned to occupational in origin. In legal terms, this is often defined as a higher probability of an occupational origin of the disease than of a non-occupational cause. This is then in turn translated to the criterion that more than 50% of the disease should be attributable to work.

To overcome or maybe to avoid the discussion about the amount of attribution to work, occupational diseases have been divided into 'real' occupational diseases and work-related

diseases. The former are then defined as those occupational diseases that are mainly caused by factors at work such as mesothelioma. The work-related diseases are then named multi-causal or diseases in which work plays a minor role in causation such as in occupational back pain. Another way of formulating this is to say that the attributable fraction of work to occupational diseases should be substantial.

When thinking about causes of disease, it becomes quickly clear that this division is difficult to maintain, because all diseases are multi-causal. Even in the case of mesothelioma, it is not just the exposure at work but also more distant factors such as genetic make-up and social circumstances that are causes of the disease. Even without exposure to asbestos, mesothelioma does occur even though the risk of occurrence will be much less. At the individual level, it is therefore impossible to point to one cause as the main cause [7].

Another argument that has been used to distinguish work-related from occupational diseases by their attributable fraction is that the potential for prevention is bigger when the attributable fraction is bigger [1]. The preventive impact is however more dependent on the prevalence of the disease than on the attributable fraction. Preventive interventions at work that have only a small attributable fraction but that are aimed at diseases that are prevalent will prevent a larger number of persons to become ill than those interventions that have a large attributable fraction but where the disease is not very prevalent. Nevertheless, this is only a gradual difference and not a fundamental difference and does not help much in delineating work-related and occupational diseases.

This leaves us with the definition above that defines occupational diseases as any disease that results from exposure at work. There are three important elements in this definition that call for evidence; disease, exposure, and the relationship between these two.

Evidence for Disease

One of the issues that have often led to vigorous debates is what constitutes disease [8]. A disease is diagnosed by means of symptoms, signs, and other data, such as laboratory or imaging results. For some diseases, there is a gold standard, such as certain pathophysiological findings that have to be present to make the diagnosis. Then, the value of other diagnostic information can be judged with the gold standard as the point of reference. However, many diseases lack such a gold standard and thus, diagnosis becomes arbitrary and gives easily rise to debate. The debate concentrates on whether a symptom or a cluster of symptoms constitutes a disease. Repetitive Strain

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