

Work-Relatedness

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INTRODUCTION

Physicians are frequently requested to determine whether putative risk factors—occupational or nonoccupational—caused an injury, disease, or disorder; therefore, a valid and reproducible method to analyze the available clinical information, epidemiological evidence, and exposure data should be used to determine causation. This determination is not only important to evaluate an individual patient, but also other workers who may be similarly exposed. Interventions to improve the safety of workers by mitigating or eliminating these exposures should be evidence-based. Determination of work-relatedness can determine financial compensation, including past and future expenses of treatment, vocational rehabilitation, permanent or partial disability benefits, and diminution of earning capacity.^{1,2} Because the legal standard for determining work-relatedness may vary jurisdictionally, physicians must be aware of the relevant definition of work-relatedness. Although the legal basis for work-relatedness often differs between jurisdictions, the scientific method for determination of causation or apportionment among occupational, nonoccupational, and personal risk factors remains consistent.

The distinction between establishing medical causation and legal causation is critical:

- *Medical causation* is determined by scientific criteria establishing a causal association between an injury, illness, disease, or disorder and known risk factor(s).
- *Legal causation* is determined by criteria established by legal authority. These criteria vary among jurisdictions. Although the crux of this guideline is the determination of medical causation, a few examples of legal causation follow.

Pursuant to the common law of negligence, *proximate cause* (legal cause) is the primary cause, or that which in a natural and continuous sequence, uninterrupted by any intervening cause, produces injury, and without which the result would not have occurred. An injury is proximately caused whenever a defendant's negligence actually caused the injury, and the injury was either the direct consequence or a reasonably foreseeable consequence of that negligence. Statutory schemes may redefine the conventional common law definition of legal cause.

Under the Federal Employers Liability Act, which applies to interstate railroad carriers, the plaintiff has the burden of proving that the railroad's negligence was the proximate cause, *in whole or in part*, of plaintiff's injury. Courts have construed this statutory language to require mere proof that a railroad's negligence proximately caused a worker's injury, *even to the slightest degree*. This same lenient standard applies to actions prosecuted under the Merchant Marine Act of 1920 (commonly referred to as the "Jones Act").

Pursuant to worker's compensation statutes, state legislatures may create presumptions concerning work-relatedness that establish rights and liabilities, even in the absence of medical causation. Such presumptions almost universally favor a determination of work-relatedness, but are rebuttable by competent contrary evidence. Rarely, agencies may enact a rebuttable presumption that a condition is not work-related. For instance, a state might establish an irrefutable presumption that lung cancers are work-related if they occur among firefighters; accordingly, the development of pulmonary adenocarcinoma by a firefighter would be presumptively work-related. Conversely, a legislature may create a presumption that the development of lung cancer among firefighters who

have at least a 10 pack-year cigarette smoking history is not work-related. Consequently, even a firefighter with significant workplace exposure to a known carcinogen would be presumptively not work-related, if the firefighter's smoking history meets the minimum criterion.

Workers' compensation systems may also weight the opinions of providers differently. A treating physician's causation opinion, regardless of qualifications, may supersede that of a consulting physician with specific subject matter expertise; therefore, the court may disregard a consulting physician's opinion and rely on the treating physician's opinion, irrespective of either the treating physician's qualifications or the rigor of his or her methodology for determination of causation.

DETERMINATION OF CAUSATION

In evaluating traumatic injuries, the etiology of which is not in dispute (eg, fracture or dislocation), or the acute occurrences of disease (eg, acute carbon monoxide toxicity), may not demand the same rigorous evaluation of work-relatedness as an occupational disease. Establishing the causality of disease may be difficult, especially if it is necessary to determine whether an employee's disease was caused by, or alternatively, aggravated by an occupational exposure. In contrast to a traumatic injury, a cause-effect relationship between disease and an occupational exposure may not be clear. Occupational diseases may develop insidiously. Symptoms of disease may be confused with age-related symptoms or effects caused by other relevant factors—personal health attributes or avocational exposures. Information on prior occupational exposures is often unavailable, inadequate, or incomplete. Individual susceptibility to similar exposures to disease-producing agents may influence causation decisions. Avocational exposures may be either a primary or contributory cause.

Clinical evaluations frequently commence with a presumption of work-relatedness, a cursory determination of work-relatedness, or even no evaluation of work-relatedness. Under certain circumstances, clinicians may be concerned primarily with accurate differential diagnosis and prescription of efficacious treatment.³

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The authors acknowledge the assistance of the ACOEM Research Team at the University of Utah. These include: Matthew S. Thiese, PhD, MSPH, Kristine B. Hegmann, MSPH, Emilee Eden, BS, Jenna K. Lindsey, BS, and German L. Ellsworth, MD, MOH.

The authors declare no conflicts of interest.

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DOI: 10.1097/JOM.0000000000001492

However, what appears to be obvious is often subject to controversy, particularly in compensation environments; accordingly, it is important to compile complete and accurate information, if possible, to assure an equitable work-relatedness decision. An inability to identify a nonoccupational cause for the subject condition (eg, an avocational exposure or personal health attribute) should not result in a default conclusion that the adverse health effect is work-related.

GENERAL AND SPECIFIC CAUSATION

Epidemiological evidence establishing that a risk factor is generally capable of causing the plaintiff's adverse health outcome is insufficient evidence that an individual's adverse health consequence was *specifically* caused by the exposures of interest. For example, evidence of an inadvertent chemical release into the ecosystem, coupled with epidemiological evidence of a causal association between such chemicals and the subject disease, is insufficient evidence that the release caused an adverse health consequence, absent evidence that the individual was exposed to a sufficient magnitude of exposure to the chemical to cause the adverse health effect; the temporal (chronological) relationship between exposure and effect is biologically plausible; and other known and biologically plausible causes have been excluded.

PRIMARY CF. MULTIFACTORIAL CAUSATION

The physician may determine that a workplace factor is the primary cause or one of several contributory causes (ie, multifactorial). Each factor could either independently produce a disease or disorder, or there may be a synergy among multiple factors. A direct cause can generally be attributed if both an immediate trauma and the effect are clearly observable. If an obvious and direct relationship exists between an injury and an external energy source, such as a moving or falling object (kinetic energy), a fall (potential energy), a chemical burn (chemical energy), or an electric shock or radiation (electromagnetic energy), a sole direct cause exists.

Health conditions often develop due to a combination of factors, only some of which may be work-related. For instance, hearing loss may occur as a result of aging, cardiovascular disease, and occupational noise exposure. Additionally, occupational and nonoccupational factors may have a synergistic effect (eg, carpal tunnel syndrome developing in the context of simultaneous exertional job requirements,

obesity, and diabetes mellitus). Cases may also develop following exposures arising from both nonoccupational and work-related activities. Personal factors also can be part of the "web of causation." For example, there is evidence that wrist width-depth ratio is a risk for carpal tunnel syndrome.⁴⁻⁶ In these circumstances, physicians are obliged to assess whether causality is truly multifactorial or whether there is a predominant cause among many factors.

Competing causation differs from combined causation in that either a workplace factor or a nonoccupational factor, but not both, is independently responsible for the adverse health effect. For example, because pregnancy, diabetes mellitus, thyroid disorders, tobacco, and repetitive forceful motions have been independently associated with carpal tunnel syndrome (CTS), a patient with diabetes who does very little forceful, repetitive work will most likely develop carpal tunnel syndrome due to the diabetes, not occupational exposure.⁷⁻¹⁸ In both primary and multifactorial causation, it is essential to attain a thorough understanding of the patient's exact work activities, as well as to compare the work activities with exposures reported in the quality epidemiological literature and metrics established by exposure standards, eg, the Occupational Safety and Health Administration (OSHA), International Organization for Standardization (ISO), *American National Standards Institute* (ANSI), and the World Health Organization (WHO) standards and guidelines).

Identifying a condition in coworkers may be informative (particularly when the outcome is rare) in assessing competing and combined causation. For instance, bronchiolitis obliterans among popcorn workers or other diacetyl-exposed workers markedly increases the probability of a causal linkage. When disorders are common and multifactorial, identifying other workplace cases may be meaningful, especially when adjusted rates are valid and statistically elevated. For example, where there are elevated rates of CTS, consideration of occupational and nonoccupational factors permits physicians to understand both the operant biomechanical factors and assess whether the effects are manifest among coworkers, in addition to the patient, although at lesser levels (suggesting combined causation) or limited predominantly to the patient (suggesting competing causation with nonoccupational factors of greater significance than occupational factors).

PRIMARY CF. CERTAINTY

For medical purposes, different definitions of causation are used depending on the purpose of the assessment of work-

relatedness. In the clinical setting, relatively specific case definitions are used to define occurrence (as described further in the ACOEM guidelines for individual conditions). In clinical practice, action based on the assessment of causal association and on the seriousness of the health effect may be commensurate with the degree of certainty about causation, based on available information on temporal, physiologic, and physical links between exposure and effect. In such cases, analytic reasoning not opinion should be used to link the populations-based epidemiological evidence with clinical findings and exposure data (see Independent Medical Examinations and Consultations guideline); otherwise, preventive efforts are unlikely to be effective.

From a public health perspective, a reasonable probability of causation should lead to preventive actions whenever possible. Physicians can weigh the costs and benefits of the intervention against the degree of certainty of causation (eg, an ergonomics evaluation of a worksite could be triggered by worker complaints of discomfort; whereas, removing a worker from a job generally requires more study and associated certainty). In contrast, bronchiolitis obliterans in a diacetyl-exposed worker should prompt a rapid analysis and preventive interventions.

The physician's opinion on the absolute probability that a disease or disorder is work-related should not be affected by administrative or legal context; however, a statement of probability related to compensability must incorporate both the absolute probability as well as the administrative or legal context. The term "more likely than not" (equal to or greater than 51%) is a legal and not medical term that must be used as defined and intended.

Disorders presented for causal analysis might represent reoccurrence of a previously resolved condition or exacerbation (ie, aggravation) of a pre-existing condition. The distinction between a recurrence, or aggravation of a condition is medically and legally important. Substantial confusion has been engendered by the ambiguous and inconsistent use of such terminology in worker's compensation statutes, which seldom operationally define such terms.

Aggravation could be construed as manifestation of symptoms, exacerbation of symptoms, or a progression, natural or otherwise, of underlying pathology. *Aggravation* and *exacerbation* are synonymous. *Precipitation* could be construed as manifestation, natural or otherwise, of underlying pathology, whether previously recognized or not. Importantly, modulation of symptoms as the result of occupational exposures is characteristic of both occupational and nonoccupational injuries and

diseases. Manifestation of symptoms coincident with occupational activity does not necessarily infer work-relatedness or persistence of “disability.”

Acute trauma can be superimposed on prior work-related and nonwork-related conditions. If an underlying condition is aggravated, it is important to document the impairment due to the aggravating factors. Restoring prior activity levels is a principle goal of treatment. When and if that objective is achieved, the aggravation is deemed to have resolved. Because an aggravation of a pre-existing condition has, by definition, led to a permanent alteration in the patient’s underlying condition, the work-related injury or disease is not cured. Regardless of whether a full return to work occurs, there remains a potential for future recurrence of symptoms. Should symptoms recur, it may, depending upon the workers’ compensation laws involved, be necessary to determine whether recurrence is due to an aggravating incident or exposure or the natural progression of the pre-existing condition.

TYPES OF CAUSATION ANALYSIS

A provisional causation analysis is generally conducted during or immediately after the first clinical encounter. Although the physician is advised to ascertain exposure, information may still be incomplete or inaccurate especially in compensation settings.^{1,19–22} However, a provisional opinion as to causation may be necessary in many jurisdictions to initiate appropriate treatment measures and to determine whether workers’ compensation or other benefits will be provided, even if causation has not yet been definitively determined.

The definitive case analysis is often conducted after reaching a conclusive diagnosis, obtaining considerably more information about individual exposures, and obtaining prior and detailed medical history. Analyzing other pertinent medical information and scientific literature is often necessary. An epidemiologic causal analysis, based on patterns observed in populations of workers, will be important in most instances.

DETERMINING WORK-RELATEDNESS—METHODOLOGY

The approach to the determination of work-relatedness, as published by the National Institute for Occupational Safety and Health (NIOSH),²³ consists of adaptation of the following six-step process:

1. *Evidence of disease.* What is the disease? What certainty is there that the diagnosis is correct? What evidence

supports or fails to support that diagnosis? Is the diagnosis supported using a generally accepted case criteria definition?

2. *Epidemiology.* What is the epidemiological evidence for that condition? Is there support for a relationship with work?
3. *Evidence of individual exposure.* What objective evidence is there that the level of the patient’s exposure is of the frequency, intensity, duration, and temporal pattern of exposure associated with work-relatedness?
4. *Consideration of other relevant factors.* What other potentially causal factors are present? For example, is the worker with carpal tunnel syndrome (CTS) pregnant or obese?
5. *Validity of testimony.* Are the opinions and sources reliable and credible? If an expert opinion has been rendered, is the person professionally qualified to render that opinion? Is there verification for the basis of the testimony, that is, the importance attributed to various areas of the information reviewed, and the conclusions that were drawn? Is there information that suggests that the information above is inaccurate, for example, from a collateral source (eg, exposure data)?
6. *Conclusions.* This step is a synthesis of the above five steps.

This provides a basic process to follow; however, evaluation of the specific

evidence available is critically important and requires a disciplined process itself.^{24–26}

EVALUATING THE EVIDENCE

For epidemiologic surveillance, a highly sensitive, relatively nonspecific case definition is frequently employed. This may increase the rate of screening yield for study, but generally produces a high rate of false-positives. If surveillance results suggest cause and effect, more formal research can be done to carefully evaluate and better test an apparent association. The epidemiologic research-study definition of causal association is much more rigid, traditionally implying 95% confidence that the purported causal relationship is not statistically spurious. Quality scientific literature about toxicological, musculoskeletal, respiratory, and other occupational disorders defining causal associations with work exposures is frequently lacking, making it difficult to predict whether risk factors statistically associated with or predictive of certain adverse health consequences [or outcomes] are, in fact, *causal* associations.^{27–30} The methodology for inferring a causal association is provided in Table 1.

CRITERIA FOR THE EVALUATION OF EPIDEMIOLOGIC EVIDENCE

The epidemiologic and public health communities have generally accepted criteria to assess the evidence for the work-

TABLE 1. Steps for Evaluating Epidemiological Evidence of a Causal Association

1. Collect all epidemiological literature reported on that disorder
2. Identify the design of each study (see Fig. 1)
3. Assess each study’s methods
 - a. Exposure assessment methods and potential biases
 - b. Disease ascertainment methods and potential biases
 - c. Absence of significant uncontrolled confounders; consideration of residual confounding
 - d. Addressing of other potential biases
 - e. Adequacy of biostatistical methods and analytical techniques
4. Ascertainment of statistical significance—degree to which chance may have produced those results.
5. Assess the studies using the Updated Hill’s Criteria, both applied to individual studies (especially 5a–d) and in aggregate (all)
 - a. Temporality
 - b. Strength of association
 - c. Dose–response
 - d. Consistency
 - e. Coherence
 - f. Specificity
 - g. Plausibility
 - h. Reversibility
 - i. Prevention/Elimination
 - j. Experiment
 - k. Predictive Performance
6. Conclusion regarding the degree to which such a causal association is/not met

Adapted from Hegmann KT, Oostema SJ. Causal associations and determination of work-relatedness. In: Melhorn JM, Ackermann WE III, eds. *Guides to the Evaluation of Disease and Injury Causation*. Chicago, IL: AMA Press; 2014.

relatedness of adverse health effects. These criteria should guide recommendations for preventive measures to evaluate the possible effects of exposures for individuals and groups. See Table 1. The first four of the following criteria are generally considered the most important:

- Temporal association between the exposure or work factor and the health concern (ie, the exposure necessarily precedes the development of disease).
- Strength of the association (eg, how large is the relative risk or odds ratio comparing exposed to unexposed workers?).
- Dose–response (ie, biological gradient) demonstrating progressively increasing risk estimates across at least three levels of exposure).
- Consistency of the association among multiple epidemiological studies.
- Coherence of the association with existing physiologic data, trends in exposure levels over time, and other knowledge.
- Specificity of the association demonstrating that the exposure causes one specific health outcome, rather than a nonspecific group of unrelated outcomes.
- Plausibility of the purported exposure–disease relationship
- Reversibility (eg, that the tissue abnormalities resolve with cessation or reduction of exposure).
- Experimental evidence from animal models.
- Predictive performance of the association in predicting future cases of the disease.

Physicians must be specific about the frequency, intensity, duration, and temporal patterns of purported exposures that might be associated with a specific adverse health outcome.

BASICS OF CAUSATION ANALYSIS

If the ostensible (or purported) causal factor's effect on the patient is immediate and visible (eg, a burn), imputing causation is straightforward. Otherwise, imputing causation to a given physical, biological, or chemical work factor requires credible epidemiological evidence that a purported observation of work-relatedness is ultimately causally associated with an individual's exposure). The co-existence of the exposure and effect is necessary, but not sufficient.

CAUSALITY INITIAL ASSESSMENT—MECHANISM

Although a provisional assessment is often conducted based on limited facts, it

must be conducted carefully as it affects subsequent care, compensability, and state and federal injury recording (eg, federal OSHA injury recording regulations). Information needed to reach a definitive analysis may be available at the time of the first visit, but obtaining additional information is almost always necessary. The minimum initial assessment of causality, for preventive purposes, may be based on a well-informed initial assessment; however, the degree of uncertainty should be clearly communicated to the patient, employer, state or federal agency. The objectives of the initial clinical assessment are to:

- Determine a diagnosis according to specific diagnostic criteria including reported symptoms, clinical signs, and objective diagnostic criteria;
- Evaluate potential causative workplace exposure factors;
- Assess the potential impact (s) of a compensation environment; and
- Assess whether other causal factors are likely.

The initial contact with the patient is usually the best time to acquire time sensitive or unbiased information. The patient's memory of acute events is most accurate immediately following an event. Information needed for the definitive analysis of causation often comes from other sources or is found in medical or employment records, according greatest weight given to the most proximate records.

HISTORY (INITIAL AND INTERVAL)

A careful medical history is essential to consideration of the work-relatedness of a complaint. It emphasizes the organ system (s) that is the focus of the presenting complaint or thought to be the target of the exposure. This includes the elicitation of a description of activity levels, limitations, and symptoms before and after an occupational exposure. This information can provide insight into possible occupational, nonoccupational, psychological, socioeconomic, and premorbid factors that might influence function (ie, global functional response to an injury, disease, or disorder). It is also necessary to obtain a psychiatric history in situations where the patient presents with psychiatric, stress-related, chronic, or recurring complaints. Neuropsychological testing is often necessary when there is a failure of or inadequate response to therapy, interventions, and/or removal from exposure.

One link between exposures and health effects is their temporal relationship. The temporal exposure and trauma and

symptoms onset should be documented. Although the onset of subacute or chronic conditions may be gradual, time estimates should be established. Particular attention should be paid to ascertaining and recording whether the exposure always preceded never followed the onset of symptoms. Although less important, the presence and severity of symptoms overnight, on weekends, on holidays, or other times that the patient is not "exposed," should be critically examined. Determining temporal causality might be difficult for chronic diseases and disorders and certain psychiatric problems. For example, symptoms of post-traumatic stress disorder may be delayed temporally for quite some time relative to the cause of the trauma; and osteoarthritis symptoms often modestly improve over weekends or other periods of nonexposure to physical factors; yet, prescribed activity is actually therapeutic, and the relationship between osteoarthritis and work factors is tenuous.

Workplace exposures need to be objectively quantified by valid and reliable methods. The patient may describe his or her typical workday and any unusual events preceding the onset of symptoms; however, self-reported information concerning both exposure and symptoms is not necessarily reliable in compensation environments.^{1,19–22} Unusual events might include changes in workload, in physical or chemical processes, the absence or breakdown of engineering controls, or personal protective equipment.

The inquiry includes relevant personal habits (especially substances use, tobacco, alcohol, prescription medications (eg, opioids), and others with adverse health effects), coexisting disease states, and family history. The patient should also be asked about similar occupational or nonoccupational problems and their resolution in the past. Nonwork activities should be assessed, particularly regarding the patient's participation in second jobs, recreational activities or hobbies that could precipitate similar symptoms or hinder their resolution. When taking a worker's history, the goal should be to answer:

- Was there a temporal relationship between the exposure and alleged effect? (Did the work exposure occur before the health effect?) If so, was the time that elapsed between the exposure and its putative effect consistent the epidemiological evidence, considering the nature of the exposure (temporal contiguity)?
- Was the amount (frequency, intensity, durations, and temporal patterns) of the exposure sufficient to cause an effect in most workers? If not, was the amount of the exposure sufficient to cause an

effect in this particular worker (ie, does the worker have any immunological sensitization)?

- Does the association with work fit logically with previous biologic or statistical evidence as to how the symptom or disorder could develop (termed the coherence of the association)?

Other specifics of the case must also be considered:

- Could other causes (personal, comorbid, or nonoccupational) possibly account for the symptom, illness, or injury in question?
- Could the exposure have been mitigated by engineering controls, personal protective equipment, immunization, or other means?
- Is the health effect causing functional impairment or disability?

WORKPLACE ENVIRONMENT ASSESSMENT

Although causation may be definitely concluded or excluded in many instances based on the patient's history, a more detailed exposure history is necessary to guide the assessment and meet regulatory requirements (in nonacute or nontraumatic situations). This is especially true in cases where the injury or disease is not readily apparent, but rather may be attributable to low-level chronic exposure rather than an acute, readily identifiable event. In such situations, patients should be queried to provide information about workplace physical, chemical, or other exposures.

For musculoskeletal disorders, this particularly includes a detailed description of the exertional demands of the job and, routinely, detailed time study, randomized work sampling, and quantification of the exertional demands of the job. The clinician might inquire about the total force used, local concentration of force (a forcefully applied grasp on a sharp tool handle edge), the frequency of specific motions or tasks, awkward postures, psychological and managerial issues, job satisfaction, and other factors, such as cold temperatures, the presence of vibration, and other factors that might increase the exertional demands of the job. For respiratory and toxicological exposures, questions should be focused on temporality of symptoms, along with the frequency, intensity, duration, and temporal patterns of exposure.

Information obtained directly from the patient should be augmented by quantitative information from the worksite. Descriptions of events from coworkers and supervisors *may* prove useful in corroborating or refuting a patient's recall and history. Summaries of health effects from Safety Data Sheets (SDAs) may prove

TABLE 2. Hierarchy of Exposure Data

Type of Data	Approximation to Actual Exposure
1. Quantified personal/individualized measurement.	Best
2. Quantified surrogate of exposure (another worker used to infer all workers' exposures doing same job)	
3. Quantified pseudo-surrogates of exposure (another worker used to infer all workers' exposures doing similar jobs).	
4. Employment in a defined job category.	Worst
5. Employment in a defined job trade.	
6. Employment in a plant or employer.	

Originally published in Nieuwenhuijsen (2003), then adapted from Hegmann KT, Oostema SJ. Causal associations and determination of work-relatedness. In: Melhorn JM, Ackermann WE III, eds. *Guides to the Evaluation of Disease and Injury Causation*. Chicago, IL: AMA Press; 2008.

helpful in guiding the clinical inquiry and subsequent literature searches. Measuring exposures to chemical, physical, or biological exposures is often necessary to definitively address causation. Although qualitative measurements to determine whether or not a chemical, physical, or biological hazard is present are a common first step, quantitative measurements over time are often required to determine the frequency, intensity, duration, and temporal patterns of exposure.

The appropriate measure(s) for chemical, physical, and biologic agents (eg, daily time-weighted averages cf. peak exposures) are required and guided by relevant epidemiological data or prescribed by federal or state regulations or generally accepted national and international standards (eg, ANSI, ISO, WHO). If possible, measurements should be concurrent with the time course of the problem, rather than using current measurements to impute previous exposure. If current measurements must be used, some assurance that conditions have not materially changed is needed in order to have some degree of confidence that the relationship is plausible. A worksite visit by the physician may be helpful. Depending on the issue, measurements by an appropriately trained ergonomist, industrial hygienist, occupational medicine physician, physical or occupational therapist may be needed to quantify exposure(s).

Personal monitoring data are generally the most useful data to prove and quantify exposure (Table 2). If personal monitoring data or data of a surrogate are unavailable, area monitoring data are the next best option. Ideally, data should be acquired at a time or times when measured exposures would be expected to most closely replicate actual worksite conditions. Any further information that is available for exposure assessment, such as job records (job positions and times held in relationship to timing of disease development), video of job tasks, and monitoring data (work

sampling, personal dosimetry, air monitoring, etc.), can be reviewed. A definitive assessment would require objective, quantified evidence of exposure to proven causative factors at levels known to produce the specific adverse health effects in question.

RECORD REVIEW

Definitive causal analysis often requires considerably more information than is available at the time that provisional assessments are made. A detailed and thorough medical history must be obtained, and relevant pre-existing symptoms, injuries, diseases, and disorders should be documented and critically analyzed. The source of information for the history may be the patient, concurrent medical records from other physicians, prior medical records, preplacement testing, or periodic medical surveillance data. Hospital and pharmacy records are usually quite informative. For histories of injuries, the most proximate records are given greater weight than later records with subsequent recall.

LITERATURE REVIEW

In many cases, a critical review of the epidemiologic and/or toxicological literature may be required to clarify the existing evidence linking exposure to health effects. Epidemiologic surveys may be needed to clarify the prevalence of complaints or health effects. A careful review of the published scientific literature may reveal a pattern of association between the apparent exposures and the patient's health effect. In most instances, epidemiologic studies should be based on workers in similar jobs or industries. Study populations may be compared to the circumstances of the patient in question including exposure dose, with higher quality studies utilizing individualized exposure measures (Table 2).

In reviewing the scientific literature, the following questions apply:

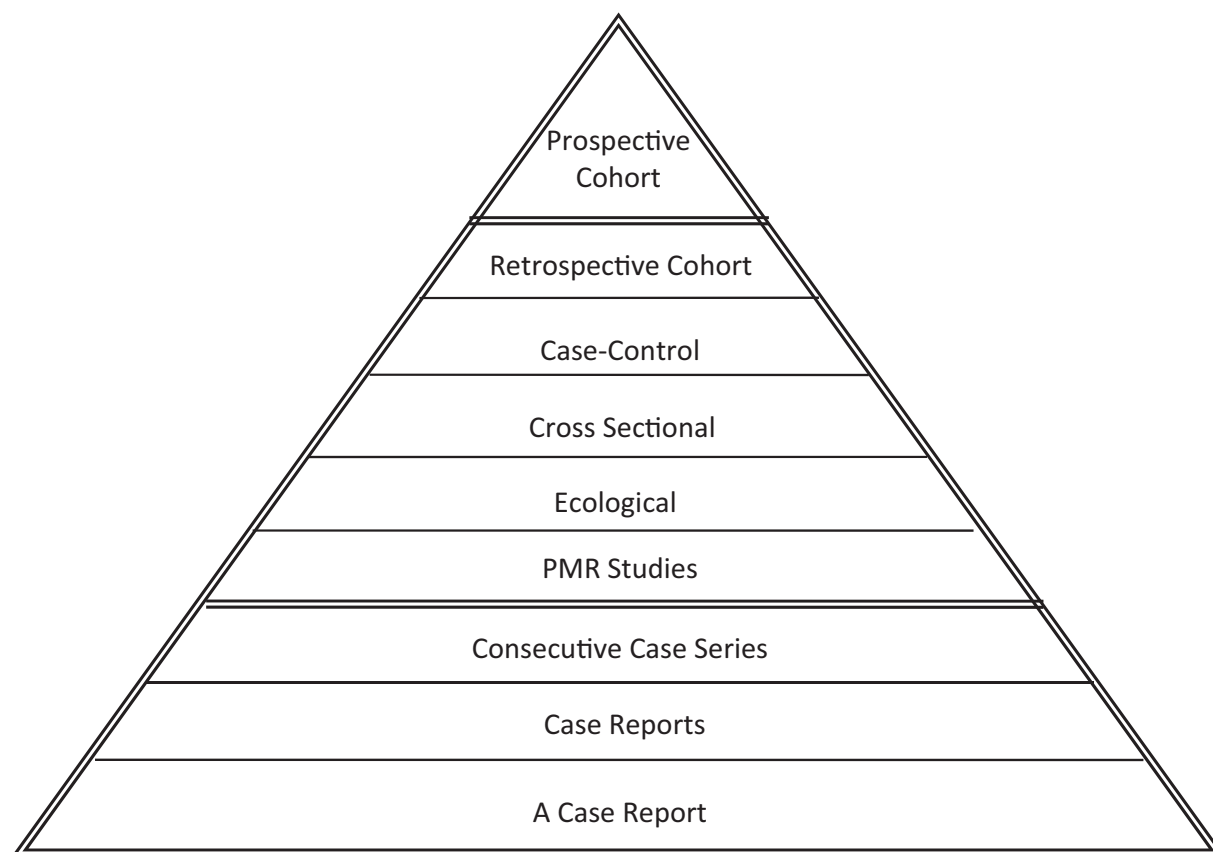


FIGURE 1. Study design pyramid. (Absent randomized controlled trials, the highest quality study is the prospective cohort study. Higher quality studies trump lower quality studies; provided, that they have no major flaws). Adapted from Hegmann KT, Oostema SJ. Causal associations and determination of work-relatedness. In: Melhorn JM, Ackermann WE III, eds. *Guides to the Evaluation of Disease and Injury Causation*. Chicago, IL: AMA Press; 2008.

- Are case definitions consistent among studies? Can a change in symptom or disease be predicted by a change in intensity, duration, body burden, or dose of the chemical, physical, psychological, or biologic factor?
- What is the quality of the available literature? Are the studies descriptive or observational? What is the quality of the study design (eg, randomized clinical trial, prospective cohort study, retrospective cohort study, or cross-sectional study). Greater credence generally accorded to prospective cohort studies for epidemiological questions (see Fig. 1). Were various potential sources of information bias (recall bias, reporting bias, healthy worker effects (attrition rates), volunteer bias, selection bias, or similar sources) recognized and accounted for? Were potentially confounding variables recognized and accounted for?
- What is the specific quantification of the exposure–effect relationship? Is there a statistical significance? Were potential confounders addressed (matched, excluded, stratified, or statistically adjusted)?

- What is the statistical rigor of the study? Is it analyzed correctly? Is it powered adequately?

It is important to conduct a balanced review of the literature rather than relying on a single study or only studies that support a particular point of view (Table 1). If the epidemiologic studies are inadequate, it may be necessary to refer to toxicological studies among animals. In assessing the relevance of animal studies to the patient's situation, the physician may consider the comparability of the specific agent, dose, route of exposure, etc. Interspecies variations (eg, enzyme system differences) need to be taken into account. Similar effects in several species carry more weight than a positive finding in a single nonprimate species.

JOB SITE SURVEYS

In the absence of support in the epidemiological literature for a causal relationship between a disease and a given event, series of events, or injury, the presence of multiple, similarly defined cases in the same worksite may raise a hypothesis of

work-relatedness, but may also indicate clustering due to case ascertainment (eg, highly prevalent conditions such as low back pain, asthma, or carpal tunnel syndrome may result in information biases including reporting and referral biases which are not instructive) or behavioral factors (eg, mass hysteria syndromes, which may be associated with nonspecific complaints such as nausea, headache, and offending odors). Nonetheless, case clusters cannot be ignored without further investigation. If several cases are seen, the attack rate (number of cases/number of employees at risk) can be determined. If clusters are found, more formal surveys of the exposed population and comparison groups should prove useful. Occasionally, the health effect is so rare (eg, vinyl chloride monomer-related angiosarcoma of the liver or bischloromethyl ether-related small cell lung cancer) that calculating the attack rate is not necessary.

SUMMARY

The determination of work-relatedness should utilize a reproducible method

for decision-making including collecting, organizing and appraising medical, occupational, exposure and other evidence. Accurate determinations of work-relatedness are important to assure that: workers receive appropriate benefits (eg, appropriate workers' compensation benefits); resources are appropriately utilized if there is a remediable and causal hazard; as well as to prevent exacerbations and recurrences of the condition where there is increased risk. Where elevated risk is present and when feasible, preventive efforts are needed to help other workers avoid similar problems.

An initial assessment of work-relatedness is usually done at the patient's first clinical encounter. A work-relatedness determination is generally straightforward for acute traumatic injuries, but more complex for subjective complaints and occupational diseases. The initial assessment must, therefore, be considered preliminary. More detailed analyses, including information from the patient, other providers, medical records, exposure records, epidemiological studies, other published literature, and the worksite are usually required for a definitive causal assessment of occupational diseases and disorders.

At the level of the individual worker, assessing work-relatedness may lead to preventive measures, including engineering controls, personal protective equipment, administrative controls, or training. If work causes or contributes to illness and the exposure cannot be controlled, reassigning the worker may be necessary. At the employee group level, preventive efforts may protect workers in similar jobs from hazards and prevent other cases of occupational illness or injury.

Determination of work-relatedness is the determinant for compensation environments. Causation determination should be methodological and evidence-based.

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