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CAUSATION IN DIFFERENT SCIENTIFIC DISCIPLINES: A COMPARISON OF STANDARDS IN OCCUPATIONAL MEDICINE AND PARTICLE PHYSICS

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Abstract

Occupational medical research involves the collection and analysis of data to draw conclusions about the causes and prevention of workplace injuries and diseases. However, there has been criticism that some studies lack rigour in determining causation. This article examines the similarities and differences between occupational medical research and particle physics in terms of their approach to hypothesis testing, statistical methods, and confounder control. The article also explores the use of criteria such as the Bradford Hill criteria to determine causation in occupational medical research. While particle physics is often viewed as a highly rigorous science, occupational medical research also employs rigorous scientific methods to ensure findings are accurate and reliable. However, there is room for improvement in determining causation in occupational medical research, particularly in the use of criteria such as the Bradford Hill criteria to guide the development of more robust studies. It is essential for occupational medical research to adhere to rigorous scientific methods to deliver findings that can help reduce workplace injuries and diseases. The use of criteria such as the Bradford Hill criteria can ensure that the conclusions drawn. Med Pr Work Health Saf. 2023;74(4):333–9.

Key words: occupational medicine, evidence-based medicine, causation, particle physics, levels of evidence, Bradford Hill criteria

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INTRODUCTION

"Association is not the same as causation" [1]. This is a sentiment that, unfortunately, requires repetition in numerous letters to the editor in various journals [1–7]. Scientific rigour in occupational exposure/causation research is essential. Knowledge of causation is a core competency of occupational and environmental medicine and helps various aspects of our specialty, including:

- prevention: identifying hazards that can be controlled to avoid occupational injury and disease,
- dedicolegal: correctly assisting in determination of liability in compensation cases,
- policy: providing advice to governments, organisations, and businesses.

In October 2022, Safe Work Australia published an analysis of the economic impact of work-related conditions between 2008 and 2018, showing an average of 623 663 occupational injuries or illnesses each year, with an estimated annual cost of around AUD 28.6 billion, as well as AUD 37.6 billion in health expenditures and AUD 49.5 billion in other employer costs [8], in a country of <25 million people at the time the data were gathered.

Unfortunately, research in prevention of work-related conditions (particularly musculoskeletal conditions) is filled with examples where the intervention failed to show any convincing or consistent evidence of benefit in primary prevention [9–11]. Is it possible that this is because we are failing to identify true causal links in occupational medical research?

For example, a recent systematic review looked at the efficacy of interventions for lower back pain in nurses [12]. The review found few good quality studies and did not provide any strong evidence of efficacy of interventions for preventing back pain in nursing. However, there is a wealth of evidence that occupational exposures, including lifting and bending and other physical exposures are unlikely to be pathogenic in the development of back pain or degenerative disc disease [13–15]. It should therefore not be surprising that prevention research that focuses on incorrect causation does not yield satisfactory results.

More generally, poor methodology in medical science research has been described as a "scandal" that is tolerated at best and encouraged at worst [16–18].

Does this occur in other scientific fields? In any scientific discipline where there is theoretical research, opinions will be debated and there is always room for interpretation of data, even in fields that can be considered more rigorous than medicine, such as physics [19]. However, in original experimental research, the disciplines of medicine and physics seem to be separated by a gulf of difference in rigour.

Consider the approach to anomalies that seem to contradict the Standard Model of particle physics or another well accepted theoretical principles. In 2011, the world's media reported findings of a pre-published article claiming to have found that neutrinos (weakly interacting subatomic particles) appeared to have travelled faster than light [20]. Prior to pre-publication, the authors rigorously attempted to disprove their own findings. After failing to find a problem with their experiment, they pre-published their article hoping for the wider scientific community to look at their findings in an effort to find what had gone wrong. The assumption was that there was something wrong with the findings.

Obviously if no source of error or bias had been found and if the experiment could be reproduced, it would have represented a fundamental shift in the understanding of modern particle physics and the theory of special relativity. In the end, a technical error was found and a sister experiment found no evidence of faster-than-light neutrinos. A healthy scepticism did not allow the scientific community to unquestioningly accept a finding that would have incorrectly turned physics on its head. This is not a unique story. It is an example of a pattern that allows for robust discussion on theory but also discourages lapses in scientific methodology.

IS OCCUPATIONAL EXPOSURE/CAUSATION RESEARCH THE NEGLECTED COUSIN OF SCIENCE?

Why compare physics and medicine?

At first glance, research methods in occupational medical science and particle physics might seem to have little relationship to one another. After all, particle physics research deals with only 17 particles (and their antiparticles) and 4 fundamental forces, whereas occupational medical research deals with countless physical, chemical, biological, ergonomic and psychological hazards interacting with the boundless complexity of the human body and mind. However, upon closer examination, it becomes clear that all scientific fields share commonalities in their underlying approach to research, such as the formulation of testable hypotheses, hypothesis testing, statistical analysis, ruling out bias, etc. It is reasonable to broadly compare 2 disciplines to determine if lessons can be learned.

Physics, the 5-sigma standard and healthy scepticism

Particle physics is a field that demands a very high standard of evidence to claim a discovery. In 2012, the discovery of the Higgs boson (the last remaining unobserved particle of the Standard Model) was announced after years of data collection, analysis, and review, which resulted in a confidence level of 5 standard deviations (5-sigma) above the expected background noise [21,22]. The 5-sigma standard is a statistical threshold that corresponds to a 1 in 3.5 million chance that the observed signal is due to random noise, rather than a real effect or association.

Obviously occupational medical research could never hope to replicate this level of statistical significance. However, that is not the point; in particle physics, even with such a high statistical threshold, there is always a possibility that the observed effect could be due to an error in the experimental design or analysis. It is essential to approach new findings with a healthy scepticism. Physicists do not simply stop at statistical significance and then throw away past theoretical models. Instead, they continue to scrutinise the data for potential bias or errors (sometimes for several years), and search for alternative explanations to ensure the observed effect is real. Failure to do so could lead to false claims, as might have occurred in the faster-than-light neutrino example.

One way particle physicists do this is through the use of a pre-publication repository known as arXiv [23]. ArXiv allows physicists to upload their work for free public view before the standard publication process. This process allows other experts in the field to provide feedback and critique the work, which can improve the final publication and its validity. This is similar and prior to the peer-review process but on a much larger scale and often involves review by experts in an appropriate field and sub-discipline to the research question.

This is what occurred in the example of the faster-than-light neutrinos. The initial results showed a statistical significance of more than 6-sigma, which would have been a ground-breaking discovery if true [24]. However, after pre-publication, a flaw in the experimental setup was eventually discovered, which explained the observed effect as an error rather than a new discovery.

Therefore, healthy scepticism and a rigorous approach to data analysis and peer review are essential in particle physics to ensure that new discoveries are based on solid evidence and not just statistical anomalies or other errors. Obviously, medical research also has these notions, but in physics the dedication to rigorously answer these questions before publication seem to far exceed the medical research equivalent.

Occupational medical research standards for causation

Occupational medical research includes the study of the relationship between occupational hazards, exposures and health outcomes. There are many methods used to study these questions, and there is a hierarchy of evidence levels that are used to determine the quality and strength of the evidence [25]. Some of the more common methods are summarised on Table 1.

In occupational exposure/causation research case-control studies are often used. These are commonly used to investigate the relationship between exposure to a specific occupational hazard and the development of a particular health outcome, where a randomised controlled trial would obviously be unethical [26]. However, the National Health and Medical Research Council of Australia considers this a level III-3 study design (the second lowest level of a 6-level hierarchy of evidence) [27].

It is worth noting that most of this research aims to find associations between occupational hazards and health outcomes, rather than specifically showing causality. Statistical significance is important in establishing whether the association is likely to be real, but it is not sufficient to prove causality. Other factors, such as the biological plausibility of the relationship and the consistency of the findings across multiple studies, also need to be considered when interpreting the results of occupational medical research. It is unfortunately not uncommon for associations to be incorrectly described as causative in occupational exposure/causation research.

Statistical significance is not enough

As has been seen in the particle physics examples, finding an association is not enough. In medical research a p-value of 0.05 is often quoted as a minimum standard for statistical significance. Meanwhile, the particle physics 5-sigma standard in medical terms would be the equivalent p-value of around 0.0000003. While reaching this kind of statistical significance in medical research is unreasonable in most cases, it also demonstrates why finding an association alone is not enough to demonstrate causation. This is particularly the case when one considers the high level of occupational, environmental and biological variability involved in most occupational medical research compared to particle physics research. However, there are tools that focus on identifying whether an association should be accepted as causative.

The Bradford Hill criteria, for example, provide a set of guidelines that can help researchers assess whether a particular association is likely to be causal. Sir Austin Bradford Hill was Professor Emeritus of Medical Statistics at the University of London when he presented his 9 "aspects of association." These are summarised in Table 2, however, the interested reader is recommended

Table 1. Common study types

Evidence type	Summary
Expert opinion	Obtains the views and opinions of subject matter experts in a particular field. This method can be useful in generating a hypothesis or identifying a research question, but it is not a substitute for empirical research. Nevertheless, this is often seen as important in medicolegal practice.
Case study	An in-depth analysis of a single case or a small group of cases. This method can be useful in generating hypotheses or identifying potential risk factors. It is limited in terms of generalisability and cannot establish causality.
Case-control study	An observational study that compares individuals who have a specific health outcome (cases) to those who do not have the outcome (controls). In occupational medicine, this is a commonly used method to investigate the relationship between exposure to a specific occupational hazard and the subsequent development of a particular health outcome. However, these studies are, by definition, retrospective and it is also often difficult to adequately account for bias and confounding factors.
Cohort study	An observational study that follows a group of individuals over time and compares their health outcomes based on exposure to specific workplace hazards. This method can establish a temporal relationship and can be useful in identifying specific risk factors, but it can be challenging to control for confounding factors.
Randomised controlled trial	Randomly assigns individuals to an exposure or control group and compares their outcomes. This is the gold standard method for establishing a strong association and is also useful in establishing the effectiveness of an intervention. In causation studies in occupational medicine, these type of trials would often be unethical [26]. For example it would be unethical to expose a group of workers to a hazard and then compare ill health outcomes to a group that wasn't exposed.
Systematic review and meta-analysis	Systematic reviews involve the comprehensive and systematic identification and analysis of all relevant studies on a specific topic, while meta-analyses involve combining he results of multiple studies to generate estimates of effect size. These methods can synthesise the existing medical evidence and are excellent in determining the strength of association.

Table 2. Summary of Bradford Hill criteria [28]

Aspect of association	Brief summary
Strength of association	The greater the strength of the association between the potential cause and tan effect, the more likely it is that the association is causal
Consistency	The relationship between a potential cause and an effect should be observed repeatedly and consistency in different populations and circumstances
Specificity	The potential cause should produce a specific effect and the effect should be produced only by the potential cause
Temporality	The cause (exposure) should come before the effect (outcome)
Biological gradient	There should be a dose-response relationship between the exposure to the proposed cause and effect
Plausibility	The potential cause should be biologically or scientifically plausible in the context of existing knowledge
Coherence	The relationship between the potential cause and the effect should be compatible with existing knowledge and understanding of the natural history of biological disease or condition
Experiment	Evidence from experimental studies (e.g. randomised controlled trial) can provide stronger evidence for causation than observation studies (if ethical to do so)
Analogy	Similarity to other established causal relationships can strengthen the argument for a potential cause/exposure

to read the original paper [28], where Prof. Hill gave examples for each aspect, some of which will be of historical interest. These criteria include factors such as strength of association, consistency, temporality, coherence, and plausibility, among others. By considering these factors, researchers can develop a more complete understanding of the relationship between 2 variables and determine whether there is evidence of causation.

Despite being well known in "Occupational and Environmental Medicine," the criteria seem to be lacking form much modern research on causation. It may be interesting to note that although it is cited as the "standard reference for occupational epidemiologists" [29], the book "Research Methods in Occupational Epidemiology," second edition by Checkoway, Pearce and Kriebel [30], does not have the term "Bradford Hill" in its index. It does have a small section on causal inferences pages 12–14, but essentially comments that making causal inferences is a difficult and complex process that should ultimately be considered a judgement call. A brief mention is made of some of the Bradford Hill criteria but very little guidance is provided.

There are many other methods that can be applied, and it is beyond the scope of this paper to present or compare them all. A review paper by de Almeida published in 2021 is a primer to some of these methods [31]. The point is that investigation of causation only begins once a robust association is found and that then the scientific process demands further thought, in a similar way to our cousins in particle physics research (even though they enjoy greater statistical significance than we typically do).

Combating folk-aetiologies in occupational medicine

Using the Bradford Hill criteria (or other similar methods) could help combat the spread of folk-aetiologies and a general lay approach to causation.

For instance, let's take the case of "keyboard use and carpal tunnel syndrome (CTS)." It is still a widespread belief that extended computer keyboard usage is a primary cause of CTS. This notion has incorrectly influenced liability decisions and led to various ergonomic interventions in workplaces.

However, when we apply the Bradford Hill criteria to this belief, we may reach a different conclusion:

- Strength: several epidemiological studies demonstrate a weak or no association between keyboard use and CTS, far from the strong correlation one might expect if the belief were true [32].
- Consistency: the results across different studies are inconsistent. While some studies found a slight association, others did not [32].
- Specificity: CTS also occurs in individuals who do not use a keyboard extensively, suggesting that keyboard use is not a specific cause.
- Temporality: it is easy to confuse the cause of a flare-up of symptoms due to the reduced tolerances of an emerging condition with the cause of the emerging condition itself. This makes it a difficult parameter to study in that keyboard use will have predated the onset of symptoms in both scenarios.
- Biological gradient: no clear dose-response relationship is evident. It is not established that longer keyboard usage leads to higher rates of CTS [32]. Again,

it is important not to confuse dose-response of causation on the underlying condition with simply the dose-response of a flare-up.

- Plausibility: while it may seem plausible for repetitive movements to cause CTS, a clear biologically plausible mechanism has not been suggested, particularly considering other explanations including genetic predisposition, hormonal factors, and other physical factors.
- Coherence: the proposed cause-and-effect interpretation does not necessarily align with the current knowledge of the natural history and biology of CTS.
- Experiment: ergonomic interventions designed to minimise keyboard usage have not consistently demonstrated a significant decrease in CTS incidence [32].
- Analogy: there is no other analogous condition that does not also suffer from similar problems in causation research.

Using the Bradford Hill criteria, we can see that the assumed causation between keyboard use and CTS is not justified. This critical application of Bradford Hill criteria could influence administrative decisions and lead to a more effective allocation of resources for prevention and treatment for other conditions such as non-specific lower back pain, tendinosis, hernias, non-specific neck pain, de Quervain's tenosynovitis, subacromial pain syndrome, lateral/medial epicondylalgia and more.

It is important to note that there is research that uses the Bradford Hill criteria and other methods to try to determine causation, such as the systematic review of systematic reviews on back pain causation by Swain et al. in 2019 [14]. However, this seems to be the exception rather than the rule with a search of PubMed for the terms "Bradford Hill" and "systematic review" yielding only 75 results (as opposed to 309 709 results when "Bradford Hill" was removed as a search term) [33]. While this is obviously not a rigorous search, the magnitude of the difference is alarming.

DISCUSSION

Both particle physics and occupational medical research involve the collection and analysis of data to draw conclusions. In both cases, it is essential to establish a hypothesis and use statistical methods to test it rigorously. Furthermore, in both disciplines, researchers must consider factors that could potentially bias their findings and rule out confounding factors. This approach helps ensure that the conclusions drawn from the data are as accurate and reliable as possible and should not be forgotten in occupational medical research.

Incorporating methods like the Bradford Hill criteria more comprehensively into occupational medical research can substantially elevate the rigour of our studies. By providing a systematic framework for assessing associations, it can allow researchers to take a step beyond merely identifying correlations to robustly evaluating potential causal relationships. This more rigorous approach could pave the way for more accurate understanding of occupational risks and the development of effective prevention and intervention strategies, ultimately leading to improved health outcomes for workers.

Moreover, a more widespread application of the Bradford Hill criteria could provide a structured framework to critically assess and challenge prevailing folk-aetiologies that pollute our research as well as our practice. These are the commonly held but unproven beliefs about the causes of diseases in specific occupational settings. Folk-aetiologies, while they sometimes provide helpful starting points for investigation, can also lead to misconceptions, stigmatisation, and the diversion of resources away from addressing the true underlying risks. By systematically examining the strength, consistency, specificity, and coherence of the evidence, the Bradford Hill criteria can help researchers discern between genuine risk factors and folk-aetiologies. Consequently, this can prevent misguided preventative efforts and foster more effective strategies for occupational health and safety. Such shifts in research practice could redefine the landscape of occupational medical research and bolster its impact on policy, prevention, and practice.

The widespread acceptance of folk-aetiologies and a lack of rigorous application of principles like the Bradford Hill criteria can indeed lead to misguided research efforts and wasted resources. This can be illustrated by the example of prevention research into back pain in nurses.

Research driven by folk-aetiologies that have been perpetuated over time represent a considerable waste of resources, including time, money, and workforce capacity, which could have been more effectively utilised to address other aspects of occupational health.

Further, acceptance of folk-aetiologies can seriously impact medicolegal decisions. When unverified causations are blindly accepted, it can lead to unjustified compensation decisions and wasted time in legal proceedings when medical experts disagree on causation. It is critical that medicolegal experts are able to base their conclusions on sound research.

CONCLUSIONS

Overall, there is no reason why particle physics and occupational medical research cannot both be considered rigorous disciplines.

It is past time for occupational medical research to get serious about methods for determining causation.

The medical literature should be reviewed to determine if unjustified conclusions have been adopted and perpetuated; adoption of folk aetiologies should be discouraged without strong evidence.

Researchers should remember that research on causation does not end at finding an association in a systematic review. The Bradford Hill criteria and other methods should be widely employed in helping to determine causation in occupational medical research.

By demanding greater rigour in determining causation, researchers and clinicians can improve the design of original research and enhance the credibility of the field.

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