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METHODOLOGIC IMPLICATIONS OF THE PRECAUTIONARY PRINCIPLE: CAUSAL CRITERIA

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Abstract. Applying the Precautionary Principle to public health requires a re-evaluation of the methods of inference currently used to make claims about disease causation from epidemiologic and other forms of scientific evidence. In current thinking, a well-established, near-certain causal relationship implies highly consistent statistically significant results across many different studies, large relative risk estimates, extensive understanding of biological mechanisms and dose-response relationships, positive prevention trial results, a clear temporal relationship between cause and effect, and other conditions spelled out in terms of the widely-used causal criteria. The Precautionary Principle, however, states that preventive measures are to be taken when cause and effect relationships are not fully established scientifically. What evidentiary conditions, as reflected in the causal criteria, will be certain enough to warrant precautionary preventive action? This paper argues that minimum evidentiary requirements for causation need to be articulated if the Precautionary Principle is to be successfully incorporated into public health practice. Two precautionary changes to criteria-based methods of causal inference are examined: reducing the number of criteria and weakening the rules of inference accompanying the criteria. Such changes point in the direction of identifying minimum evidentiary conditions, but would be premature without better understanding how well current methods of causal inference work.

Key words:
Causation, Epidemiology, Inference, Precautionary Principle, Theory

INTRODUCTION

There is a growing interest in the role of the so called Precautionary Principle in public health and much that remains to be done before it can be fully operationalized [1–4]. Consider the following statements from a recent issue of a prominent public health journal:

1. A commonly cited definition of the Precautionary Principle says that (preventive) "measures should be taken even if cause and effect relationships are not fully established scientifically" [1].
2. "The Precautionary Principle is good for public health because it stimulates reevaluation of the methods of public health science" [1].

Together these statements suggest that we should carefully consider how the Precautionary Principle relates to the criteria-based methods used to establish causal relationships in public health. The purpose of this brief commentary is to begin that inquiry, by proposing precautionary changes to the so called causal criteria.

CRITERIA-BASED METHODS OF CAUSAL INFERENCE

Nine causal criteria sit at the center of the current method of causal inference; these were described (as "aspects of" rather than "criteria for" a causal association) in a now-

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classic paper published by Bradford Hill in 1965 [5], one year after a US Surgeon General's Committee declared smoking a cause of lung and laryngeal cancer using five related criteria of judgement [6]. A considerable body of literature about this method has emerged in the ensuing decades [7–9], including discussions in nearly every textbook of epidemiology. Users of this method – and that includes just about anyone charged with judging disease causation from a body of scientific evidence – typically emphasize the following subset of Hill's criteria: strength, dose-response, biological plausibility, and consistency, although considerable variability exists in the choice of criteria and their accompanying rules of inference [10,11].

By "rule of inference" I mean the conditions under which a given criterion is considered to be satisfied. For example, a common though controversial threshold for strength of association is a statistically significant relative risk of 2.0. Using this rule of inference, observed values of relative risk across studies less than 2.0 could be considered "weak" associations, values greater than 2.0 "strong." Not everyone agrees that 2.0 is the appropriate value for distinguishing between strong and weak associations; nevertheless, the numeric value of the summary relative risk is a good example of a rule of inference accompanying the criterion called strength of association. In practice, the available scientific evidence is interpreted in terms of the criteria and their (often unstated) rules of inference: are the summary estimates of relative risk large (strong) or small (weak) in magnitude? Is there a clear increasing relationship between the dose of the exposure and the response, in the pattern of relative risk estimates? Is there a biologically plausible explanation for the relationship, as revealed in laboratory-based basic biological science studies? And, are the published results consistent – similar in direction and magnitude – across studies? Other criteria, such as specificity, coherence, temporality, experimentation, epidemiologic sense, and analogy, are also used although less regularly. Statistical significance, bias, confounding, the extent to which the studies were systematically collected, and, when appropriate, meta-analysis also play a role in current practice [12,13]. More detailed descriptions of this practice can be found elsewhere [14].

Although the current practice of causal inference is more qualitative than quantitative and subject to personal, social, and sometimes moral values of its practitioners [15], the results of criteria-based methods are often at the center of important public health controversies. Criteria of causation have been applied to evidence involving environmental and occupational exposures, lifestyle factors, infectious agents, and medical and bio-technologies, precisely the sorts of issues discussed in terms of the Precautionary Principle [16–18].

PRECAUTION AND THE METHODS OF CAUSAL INFERENCE: MINIMUM LEVELS OF EVIDENCE

To begin closing the gap between the Precautionary Principle and the methods used to make causal judgements, it will be important to carefully examine the continuum of uncertainty that stretches from near complete ignorance (e.g., no evidence at all) to 100% certainty. For example, looking to the extreme end of this continuum, we can consider what characteristics of evidence would indicate that the relationship under scrutiny is as close to certainty as possible and thus should be considered "fully established?" Although all versions of the Precautionary Principle caution against waiting until such conditions are met (because it may be too late), sketching out such conditions will be a good starting point for an inquiry applying precaution to methods of causal inference.

In the current practice of causal inference, a "fully established" near-certain causal association implies highly consistent results across many studies of differing designs, large relative risk estimates (i.e., strong associations), extensive understanding of (i.e., highly plausible) biologic mechanisms, monotonically increasing dose-response relationships, a highly specific association (especially for infectious agents), positive results from a randomized prevention (experimental) trial, assurance that the temporal course of events guaranteeing that the cause precedes the effect, and so on.

The Precautionary Principle, however, states that the evidence need not be as close to certainty as possible before action can be recommended [1,3,4,16]. Rather, it

emphasizes anticipatory action to be taken at some point closer to the other, less certain, end of the continuum. A practitioner who applies the Precautionary Principle might reasonably ask: "What is the least amount of evidence – the minimum level of evidence about causation – needed to recommend a public health action?" [19,20]. Answering this question would involve a relatively lower evidentiary point of reference around which public health action is recommended. How much lower, however, is unclear. Certainly, the circumstances of the specific exposure-disease relationship under scrutiny will matter to the decision; as even Hill [5] recognized, weaker evidence might be acceptable for recommending action in the face of highly hazardous exposures and somewhat stronger evidence for exposures whose effects are less harmful. What ties these possibilities together under the Precautionary Principle is twofold: first, that action could be taken when the evidence is certain enough for the particular situation and second, that precaution is about acting earlier than we would have acted in its absence. In any case, we are interested in identifying minimum evidentiary standards (or guidelines) for public health decisions about causal agents. In all such decisions, the costs and benefits of decisions, the political climate, public opinion, and other considerations play important roles. My interest in this paper, however, is to focus upon the scientific evidence and its causal assessment, an integral part of any public health decision, precautionary or not.

PRECAUTIONARY CHANGES TO THE CAUSAL CRITERIA

Translating the precautionary concepts of minimum evidentiary standards and early anticipatory action into more specific methodologic guides is not an easy task. Whereas it is relatively straightforward to describe the conditions under which causal criteria appear to be fully satisfied and similarly those conditions under which causation is clearly not satisfied – e.g., several well-conducted null studies with no shred of biologic evidence – proposing minimum levels of evidence for causation is another matter altogether. Consider, for example, two related changes, both consistent with precaution: reducing the number of criteria and weakening the rules of inference associated with the causal criteria [19].

Reducing the number of causal criteria

One way to ensure that any decision is taken earlier than it would have occurred is to reduce the number of conditions – i.e., criteria – required for making that decision. If, for example, an investigator requires that the evidence be consistent, strong, and biologically plausible, while another investigator requires only that the evidence be consistent and strong, then a decision to declare that evidence "causal" and to act earlier on the basis of that same evidence (all other conditions equal) seems more likely for the second (hypothetical) investigator. Put another way, it is axiomatic that the fewer evidentiary criteria there are, the more likely a claim of causation will be made (all other things equal). Of course, only temporality is a true criterion. Nevertheless, a precautionary change to the causal criteria would be to eliminate some of the so called criteria from consideration. The rationale, however, for eliminating (or discounting) some criteria rather than others is not immediately obvious. For example, causal claims are often made without the results of a randomized prevention trial; analogy, specificity, and coherence are also often ignored. These omissions, however, seem to be based more on personal preference than on theoretical grounds.

Weakening the rules of inference for causal criteria

A related precautionary approach is to weaken the rules of inference accompanying the causal criteria. The more quantitative criteria such as strength and consistency can be used to illustrate this approach. If, for example, an investigator considers a relative risk of 2.0 to be the threshold at which one distinguishes between "weak" and "strong" associations, then that same investigator could consider changing that threshold to some smaller value, less than 2.0. Similarly, if by consistent evidence it is meant at least 75 per cent of the studies are statistically significant and in the "positive" direction (relative risk greater than 1.0), then a precautionary change to this rule would

be to change that threshold to some other (smaller) number. Weakening a rule of inference for any given criterion could involve, at the extreme, completely eliminating that criterion from further consideration, thus linking the two precautionary approaches outlined here.

RESEARCH QUESTIONS AND STRATEGIES

Precautionary changes to existing criteria-based methods of causal inference are deceptively easy to outline and difficult to defend. At the heart of both approaches proposed above are two untested presumptions: that we know how well the current method works, i.e., how well that method distinguishes between truly causal and truly non-causal associations, and second, that the causal criteria are reflective of (derivable from) theoretical causal models.

Put another way, making precautionary changes to the criteria-based methods of causal inference may need to wait until we can better answer several related research questions: how much evidence does it take to ensure a valid causal claim? In actual practice, which causal criteria were dispensable when used to examine exposure-disease relationships known to be causal? What rules of inference were employed? Does it make sense to discuss minimum conditions for all the current criteria? And finally, how can we examine the impact of precautionary changes to these methods on the health of populations?

Answering these questions will require conceptual and theoretical research into the assumptions underlying the criteria, the definitions (models) of causation, and the relationship of causal definitions and models to the criteria. Retrospective research examining the past use of causal inference methods and the subsequent outcomes of preventive interventions will also be important. The goal of these more historical inquiries will be to better understand how much (and what kinds of) evidence were present when causal judgements were made and preventive interventions were recommended. Studies of how epidemiologists use these methods in hypothetical situations may also be helpful. From the results of these studies we may be able to describe the level of evidence actually used to make causal claims in terms of the causal criteria and to assess whether it would have been reasonable to make such claims earlier, consistent with a precautionary approach. Finally, techniques for estimating the effects of precautionary methodologic changes on subsequent population-based measures of health status (e.g., incidence, mortality, well-being, and so on) will be needed.

CONCLUSIONS

This paper does not advocate for precautionary changes in the causal criteria; rather, it suggests that if precaution is to be successfully incorporated into public health practice, changing the way the causal criteria are used and interpreted is an approach worth considering. Acting earlier, on less certain evidence, is not necessarily a good idea; such actions may have undesirable effects, such as the immense economic costs of evacuating miles of an Atlantic Ocean beachfront to avoid the effects of a hurricane (Floyd) that never arrived. On the other hand, acting earlier may also save many lives and reduce much suffering. My purpose here is not to examine those tradeoffs. Rather, I suggest that a careful examination of the use of causal criteria and the subsequent success (or not) of preventive interventions is likely to yield important information that will improve the practice of causal inference and, ultimately, the health of the public.

Primary disease prevention in public health relies upon the identification of disease-causing agents or factors through careful scientific study and active intervention. Finding a cause, removing it, and reducing the incidence and mortality of subsequent disease in populations are hallmarks of public health science and practice. The Precautionary Principle emphasizes that these preventive actions should be anticipatory, that is, actions should be taken as early as possible in order to reduce the subsequent harm. Put another way, precaution emphasizes that we should act earlier that we would have acted in its absence. One approach to achieving precautionary public health would be to change some aspects of the ways we interpret scientific evidence by altering the methods used to make inferences about disease causation. Specifically, we should search for the minimum levels of scientific evidence needed to infer causation and to recommend prevention. Several

anticipatory "minimum-evidentiary-level" approaches are possible, including: reducing the number of causal criteria or weakening the rules of inference aligned with each criterion. Such changes should only be undertaken after a careful research program has examined how well the current methods of causal inference work.

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