

Review

The Practice of Causal Inference in Cancer Epidemiology

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Abstract

Causal inference is an important link between the practice of cancer epidemiology and effective cancer prevention. Although many papers and epidemiology textbooks have vigorously debated theoretical issues in causal inference, almost no attention has been paid to the issue of how causal inference is practiced. In this paper, we review two series of review papers published between 1985 and 1994 to find answers to the following questions: which studies and prior review papers were cited, which causal criteria were used, and what **causal** conclusions and public health recommendations ensued. Fourteen published reviews on alcohol and breast cancer and 6 published reviews on vasectomy and prostate cancer were examined. For both series of reviews, nearly all available published studies were cited except for ecological studies and prior reviews. Sources of causal criteria were often not provided. When they appeared, all citations were either the 1964 Surgeon General's report or works of Austin Bradford Hill. Reviews often excluded and sometimes altered criteria without giving reasons for these changes. The criteria of consistency and strength of association were almost always used accompanied by dose-response and biological plausibility in a majority of reviews. The criterion of temporality, considered by many methodologists to be a necessary causal condition, was infrequently used. Confounding and bias were often added considerations. Public health recommendations were not discussed in nearly one-half of the reviews.

Introduction

What causes cancer? How much and what kinds of evidence lead to causal conclusions? When should public health recommendations be made? These are central questions of causal inference in cancer epidemiology. Causal inference has been an important methodological focus for at least half a century (1, 2). A classic point of reference is the mid-1960s, when two papers, one by a committee appointed by the Surgeon General (3) and the other by Austin Bradford Hill (4), listed what are usually called causal criteria. These criteria are shown in Table 1. At the time, they were used to support the claim that smoking

causes lung cancer (3) and to guide causal inference for occupational and environmental diseases (4). From 1965 to 1995, many associations have been examined in terms of the central questions of causal inference.

Causal inference is often practiced in review articles and editorials. There, epidemiologists (and others) summarize evidence and consider the issues of causality and public health recommendations for specific exposure-cancer associations. The purpose of this paper is to take a first step toward systematically reviewing the practice of causal inference in cancer epidemiology. Techniques used to assess causation and to make public health recommendations are summarized for two associations: alcohol and breast cancer, and vasectomy and prostate cancer. The alcohol and breast cancer association is timely, controversial, and in the public eye (5). It involves a common exposure and a common cancer and has a large body of empirical evidence; over 50 studies and over a dozen reviews have appeared. The association between vasectomy and prostate cancer also involves a common exposure and a common cancer. It is a relatively recent controversy with a smaller empirical literature and relatively few reviews.

The intent of this "review of reviews" is not to criticize individual reviewers nor to make judgments regarding associations. The limitations of making summary statements from small selected samples are recognized. Recommendations for possible improvements to the practice of causal inference are offered. These are based upon the summary findings and upon our understanding of two areas of related research: the methods and theory of causal inference and the scientific quality of review papers.

Materials and Methods

The MEDLINE and CANCERLIT data bases were searched from 1977 through June 1994, using the keywords "alcohol and breast cancer" and "vasectomy and prostate cancer." Reference lists of primary research studies and reviews identified were perused for mention of relevant articles. Tables of contents from major medical, cancer, public health, and epidemiology journals available at the libraries of the NIH were also examined.

For both associations, three types of review papers were found: editorials in which a review of existing literature was included and either cause or public health recommendations were considered, reviews devoted to the specific association, and "mini-reviews" subsumed within reviews of more general issues. Typically, these mini-reviews were relatively brief sections in papers on alcohol and cancer, diet and cancer, breast (and prostate) cancer epidemiology, and male sterilization. Only editorials and reviews devoted solely to the specific associations are included in this paper, with one exception, an IARC monograph on alcohol and cancer with a review of the alcohol and breast cancer literature (6).

Editorials and reviews are subsequently referred to as "reviews." For each, the following questions were addressed:

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Table 1 Causal criteria as described by A. B. Hill (4) and by the Surgeon General's committee (3)

Consistency ^a
Strength ^a
Dose-response
Biological plausibility
Specificity ^a
Temporality ^a
Experimentation
Coherence ^a
Analogy

^a Criteria described by the Surgeon General's committee (3).

(Which studies are included? (Asked as a check for systematic exclusion.)

(Which causal criteria are used and what sources for these criteria are cited?

(Are other considerations (e.g., study design, bias, and confounding) featured?

(What causal conclusions and public health recommendations are made?

(What is the relationship of a conclusion or recommendation to the results of original research studies published by the same author?

(Do reviewers cite the methods, conclusions, or recommendations of earlier reviews?

Results

Alcohol and Breast Cancer

The consumption of alcoholic beverages has been linked with breast cancer since 1974 (7). In the ensuing two decades, ecological studies (8–11), case-control studies (12–50), and cohort studies (51–60) have been published, representing a total of just over 50 studies. Metaanalyses have also appeared (61–63). Reports from a workshop (64–67) and papers discussing aspects of published cohort studies (68, 69) have contributed to the controversy. Twenty-two reviews (63, 70–90) were published between 1985 and 1994, appearing every year except 1986. Fourteen satisfied inclusion criteria (63, 70–82) and are summarized in Table 2; three were published as editorials (70–72).

Studies Included. The vagaries of the publication process make precise determination of studies available to authors difficult, beyond the obvious condition that studies published less than 1 year before publication of the review were probably not available. There is little evidence of systematic exclusion of studies, although ecological studies were irregularly cited, as were abstracts (91–96). Three reviews published since 1991 used methodological criteria to exclude studies from consideration (63, 80, 82). Occasionally, reports were not included in reviews for several years after publication. An example is a case-control study on diet and breast cancer conducted in Greece (21). Published in 1986, this study was cited in reviews published in 1988 (73), 1989 (77), 1991 (80), and 1994 (63) but not in seven other reviews published between 1988 and 1993. A possible explanation is that authors of reviews may not have been aware that in this study alcohol consumption was measured as one component of the diet. A review published in 1994 (63) identified seven case-control studies (43–49) published between 1978 and 1992 that were rarely cited in previous reviews. Six of these seven did not mention "alcohol" in their titles.

Use of Causal Criteria and Sources Cited. Sources of causal criteria were cited in six of fourteen reviews (63, 75, 76, 78–80). Two of the six cited the 1964 Surgeon General's report

(3); in both, the original five criteria were used. The remaining four reviews cited works of Austin Bradford Hill (4, 97). In only one instance was a list of nine criteria used in the assessment (80), although "epidemiological sense" replaced & criterion of coherence of Hill. Chu (76) cited Hill (4) but used only four of his nine criteria: consistency, strength, biological credibility (i.e., plausibility), and experimentation. Longnecker (63) also cited Hill (4) and used a subset comprising consistency, strength, dose-response, and biological plausibility. Lowenfels *et al.* (75) cited Hill (97) and used five criteria. In the eight reviews in which no source for criteria is cited, the number of criteria used varied from one (consistency; Ref. 72) to six of the original nine of Hill (4, 77).

Overall Use of Causal Criteria and Other Considerations.

Because the 1964 Surgeon General's list of causal criteria form a subset of the 1965 criteria of Hill, and because reviewers citing no source nevertheless used many of the same criteria, the overall use of criteria can be examined. Table 3 shows that the criterion of consistency was always used and strength of association was nearly always used in this series of reviews. Dose-response and biological plausibility were also used relatively frequently. In only 4 of 14 reviews was the criterion of temporality discussed. The need for a randomized trial and its ethical and practical feasibility was considered in 3 of the 14 reviews. Coherence and analogy were rarely used. Table 2 reveals that bias (7 of 14) and confounding (11 of 14) were the most common additional considerations in this series.

Causal Conclusions. The question of cause was addressed in 10 of 14 reviews. None claimed cause. Conclusions included reasonably clear rejections of the idea (78, 80, 81) and those that left the issue undecided (70, 73, 74, 77, 82). Two reviewers appeared to lean in the direction of concluding cause. Longnecker (63) for example, argued that the "evidence appears to be growing stronger." Hiatt (79) argued that the data were "not yet sufficient to conclude ... causation."

Public Health Recommendations. Public health recommendations were addressed in 8 of 14 reviews. Three of the eight reviews included recommendations for reductions in alcohol consumption, with an emphasis on women at high risk of breast cancer and without cardiovascular disease risk factors (71, 72, 79). Recommendations were considered premature in two of the eight reviews (76, 80). Another reviewer argued that total abstinence would be required and therefore could not be recommended (75), whereas others would not advocate alcohol beverage consumption at any level (78). One reviewer noted that "before any recommendations are made ... a risk benefit analysis is in order" (63). Perhaps the strongest recommendation to reduce alcohol beverage intake (in high-risk women) was included in a 1987 editorial (71) accompanying the publication of two cohort studies in the same issue of the *New England Journal of Medicine* (53, 54). The author wrote that "whatever can be done...should be done."

Four of the eight reviews in which public health recommendations were considered did not discuss cause (71, 72, 75, 76). Finally, two papers published within 1 year of each other used identical criteria (3) on almost the same data, and yet one reviewer recommended reductions of alcohol intake for high-risk women (79) and the other did not (78).

Authorship of Reviews and Studies. Half of the reviews (7 of 14) were written by individuals who were also authors of studies on the same topic. The author of a positive cohort study argued in a later review that women at high risk should limit their use of alcohol (79) and the authors of two negative case-control studies argued against causation (78) or that rec-

ommendations were premature (76). On the other hand, authors of a positive cohort study (74, 77) and of a positive case-control study (82) made no public health recommendations nor claimed cause. A clear relationship between causal conclusions or public health recommendations and the results of studies conducted by the reviewers was not apparent.

Reviewers Citing Prior Reviews. In only 3 of the 13 reviews was the conclusion of a prior reviewer about causation or public health recommendations mentioned (79–81). Citations of prior reviews were patchy. For example, a review published in 1991 (80) mentioned the opposing interpretations of two reviews published in 1989 (78) and 1990 (79) but did not cite the seven earlier reviews. A review in 1990 (79) mentioned four earlier reviews but conclusions from only two (70, 78). All reviews published in 1989 or earlier made no mention of the conclusions of earlier reviewers about cause or public health. The review by Plant (81) mentioned nearly all prior reviews but included conclusions from only three (71, 77, 78). In some instances, reviewers mentioned biases (82) or possible biological mechanisms (77) discussed in earlier reviews.

Summary of Findings.

(Reviewers appear to cite nearly all available published studies except for ecological designs. Reasons for specific exclusions are infrequently given.

(Reviewers irregularly cite sources of causal criteria. All citations are either the 1964 Surgeon General's criteria (3) or works of Austin Bradford Hill, primarily his classic 1965 paper (4).

(In citing Hill, reviewers often exclude and sometimes alter criteria. Reasons for these changes are not provided.

(Independent of citation status, subsets of the criteria of Hill (4) are most frequently used.

(Consistency and strength are almost always invoked, accompanied by dose-response and biological plausibility in a majority of reviews.

(Confounding and bias are often added considerations.

(Public health recommendations (both for and against changes in current policy or practice) appear without claiming or disclaiming cause.

(Reviewers rarely address the methods or conclusions of prior reviews.

vasectomy and Prostate Cancer

The health effects of vasectomy have been studied since the late 1970s (98). Several prospective studies of morbidity rates in vasectomized men (99–101), case-control studies (102–107), and cohort studies (108–114) have examined the relationship between vasectomy and prostate cancer. Seventeen studies have been published; accompanying them have been 19 publications reviewing or commenting upon the studies (115–133). Six reviews satisfied inclusion criteria (115–120), two of which originally appeared as editorials (115, 116).

The findings from the reviews on vasectomy and prostate cancer matched those from alcohol and breast cancer, with these exceptions:

(Dose-response was not used as a causal criterion because of the all-or-none nature of the exposure.

(Because five of the six reviews were published in the same year, only one earlier review was available for citation. One of the five (118) cited it.

(No reviewers were also authors of original research on the topic.

Discussion

To what extent do these findings accurately represent the practice of causal inference in epidemiology? Has a methodological paradigm been described? We turn to the language popularized by the work of the historian and philosopher of science Thomas Kuhn (134) because it is useful in this context, although we are mindful of its many meanings and possible linguistic devaluation in scientific writing (135, 136). The core idea is that a paradigm is shared by members of a scientific discipline and represents the normal practice of that discipline (137).

The practice of causal inference in only two exposure-cancer associations may not be representative of the practice within cancer epidemiology. Other reviews, summarizing approaches to causal inference for other associations, will help decide the issue. The fact that the findings for alcohol and breast cancer reviews were supported by the vasectomy and prostate cancer series lends support to the idea that a good approximation to a current methodological paradigm has been described. Also important is the fact that no reviewer cited as a source of his or her approach to causal inference any paper after the mid-1960s (the only exception a 1971 version of a 1965 classic by the same author). This situation is consistent with the definition of a paradigm as a classic work [i.e., as an "exemplar" (134, 136)]. Indeed, many papers and textbooks use the original criteria of either the Surgeon General (3) or Hill (4) as the foundation for their treatment of causal inference methodology (138–148). Assuming that a good approximation to the current practice paradigm has been described, we discuss two categories of findings: the use of causal criteria and the "results" that emerge from their use, causal conclusions and public health recommendations.

Regarding causal criteria, the most frequently used were consistency, strength, biological plausibility, and (for alcohol and breast cancer) dose-response. Temporality and experimental evidence were much less frequently used, whereas coherence, analogy, and epidemiological sense were almost never used. We take no issue at this time with the emphasis on consistency, strength, biological plausibility, and dose-response (when appropriate). Nor do we question the relative infrequency with which the criterion of experimental evidence was used, given that no such evidence exists for either association. We are intrigued, however, by the lack of emphasis placed on temporality and coherence.

In the alcohol and breast cancer series, temporality was considered in only 4 of 14 reviews. In the vasectomy and prostate cancer series, temporality was never used. This is a situation in which practice and theory appear to diverge. Both Hill (4) and the Surgeon General's committee (3) recognized the importance of demonstrating the temporal priority of exposures over diseases, especially for slowly developing diseases such as cancer. With rare exceptions (141), recent authors consider temporality to be indispensable (149), crucial (146), a directly deducible (150) *sine qua non* of causality (142), not a sufficient condition for causality but a necessary one (143, 144). In a 1981 list of ranked criteria, temporality is among the top four, after experimentation, strength, and consistency (151). A 1993 textbook puts temporality first in a ranked list (147). Interestingly, Hill (4) argued that "the temporal problem may not arise often." This is a reasonable assertion if temporality refers only to the situation in which a purported cause is really an effect of the disease, so-called "reverse causation" (146). Such a narrow definition of the criterion makes it easily dispensable in some circumstances. In the alcohol and breast cancer series, for example, two reviews claimed that temporality could be considered moot, given cohort evidence demonstrating

Table 2 Characteristics of reviews published on alcohol and breast cancer, 1985-1994

Review	Studies included (by reference)	Criteria invoked (by reference)	Criteria implied (by name/idea)	Other considerations	Causal conclusion	Public health recommendation	Relationship to results
Anonymous, <i>Lancet</i> , 1985 (70)	CC ^a (12-19); CS (52); EC (7-9); RV, NA	None	Consistency, dose-response, strength, biological plausibility	Confounding, study design	"The true effect... lies between no effect... and the small increase in risk evident from the follow-up data"	None	NA
S. Graham, <i>N. Engl. J. Med.</i> , 1987 (71)	CC (12, 14-17) ^b ; CS (52-54); EC, none; RV, none	None	Consistency, dose-response, strength	Bias, confounding, study design	None	"Whatever can be done... should be done"	None
Anonymous, <i>Nutr. Rev.</i> , 1988 (72)	CC (12-20, 22-24); CS (52-54); EC, none; RV (71)	None	Consistency	None	None	"Recommendations from health professionals should be individualized"	NA
IARC Monograph, 1988 (73)	CC (12-21, 23, 24); CS (52-55); EC, none; RV, none	None	Consistency, dose-response, strength	Bias, confounding	"A firm conclusion about a causal relationship cannot be made at present"	None	NA
M. J. Stampfer <i>et al.</i> , <i>Cancer Compr. Ther.</i> , 1988 (74)	CC (12-20, 22, 24); CS (51-54, 91); EC, none; RV (70)	None	Consistency, dose-response, strength, specificity	Bias, confounding, study design, effect modification	"... Evidence insufficient to conclude causation, but no more plausible explanation has been proposed"	None	Authors of positive cohort study (53)
A. B. Lowenfels <i>et al.</i> , <i>Alcohol. Clin. Exp. Res.</i> , 1989 (75)	CC (12-20, 23, 24); CS (52-54); EC (7-9); RV, none	Cite Hill (97), consistency, dose-response, strength, temporality, biological plausibility	No additional	Confounding, special populations	None	"... If there is a link... then complete abstinence would be required... such a recommendation would not appear to be justified."	None
S. Y. Chu, <i>Cancer Prevention</i> , 1989 (76)	CC (12-20, 23-32); CS (52-55, 57); EC, none; RV (70, 71)	Cites Hill (4) but uses consistency, strength, biological credibility, experimentation	Consistency, dose-response, strength, biological plausibility, specificity, experimentation	Confounding	None	"... Recommendations to discontinue modest amounts of alcohol... to reduce breast cancer risk are premature."	Author of negative case-control study (32)
W. C. Willett <i>et al.</i> , <i>Important Advances in Oncology</i> , 1989 (77)	CC (12-26); CS (51-55); EC (7-9); RV (70)	None	Consistency, dose-response, strength, biological plausibility, specificity, experimentation	Bias, confounding, study design, studies in alcoholics	"The present evidence is insufficient to conclude cause and effect, but no more plausible explanation has been proposed"	None	Authors of positive cohort study (53)

L. Wynder et al., <i>Important Advances in Oncology</i> , 1989 (78)	CC (12-17, 19, 20, 23-25, 92, 93); CS (52-55, 57); EC (7, 8); RV, none	Cite Surgeon General (3), consistency, strength, specificity, temporality, coherence		Publication bias, confounding, studies of heavy drinkers	"... Our evaluation does not support moderate alcohol consumption as an etiologically important factor..."	"... We are not advocating consumption of alcoholic beverages at any level..."	Authors of control s
R. A. Hiatt, <i>Med. Oncol. Tumor Pharmacother.</i> , 1990 (79)	CC (12-27, 35, 92, 93); CS (51-57); EC, none; RV (71, 74, 77, 78)	Cites Surgeon General (3), consistency, strength, specificity, temporality, coherence	Prose reference	Bias in case-control studies	Data are "not yet sufficient to conclude that the relationship is causal"	Women with risk factors for breast cancer but not for heart disease, "may be wise to limit (their) use of alcohol"	Author of positive cohort study (52)
J. Steinberg et al., <i>Breast Cancer Res. Treat.</i> , 1991 (80)	CC (13, 17, 18, 20, 21- 36); CS (52-57); EC (7-9, 11); RV (77, 78)	Cites Hill (4), consistency, strength, dose-response, temporality, specificity, epidemiological sense, biologic plausibility, analogy, experimental	NA	Confounding within context of specificity	"Insufficient evidence to conclude (cause)"	"Probably premature to recommend that women alter their drinking habits as a means of reducing breast cancer risk"	None
M. L. Plant, <i>Mt. J. Addict.</i> , 1992 (81)	CC (13, 14-20, 22-28, 30-36); CS (51-57); EC (7, 10); RV (70-72, 74, 75, 77-78)	e	Consistency, strength, biological mechanism	Reliability of data, confounding, choice of controls	"Evidence of a causal link is lacking"	None	None
L. Rosenberg et al., <i>Epidemiol. Rev.</i> , 1993 (82)	CC (14, 17-20, 22-28, 29, 32, 33, 35-37, 39, 41); CS (51-59); EC, none; RV (77, 79)	None	Biological mechanisms, strength, consistency	Measures of exposure, vulnerable subgroups, confounding	More research is needed to "eventually decide whether alcohol and breast cancer are or are not causally related"	None	Author of positive case- control study (13)
M. P. Longnecker, <i>Cancer Causes & Control</i> , 1994 (63)	CC (12, 13, 15-21, 23-31, 33-37, 39, 41, 42, 44- 49); CS (52-60); EC (10); RV, none	Cites Hill (4) but uses dose-response, biological plausibility, strength, consistency		Bias	"Evidence for alcohol being a cause of breast cancer remains inconclusive"	"Before any recommendations are made... a risk benefit analysis is in order"	Author of metaanalyses (61, 63)

^a CC, case-control study; CS, cohort study; EC, ecological (correlation) study; RV, review; NA, not applicable.

^b Additional studies mentioned but not cited

alcohol consumption before the clinical onset of breast cancer (75, 80).

Why was coherence used so infrequently? The simplest answer is that the reviewers may have equated it with plausibility, thus making it redundant. In the two classic sources, the Surgeon General's committee (3) did not carefully distinguish between the two criteria; plausibility was embedded within coherence. Hill (4), on the other hand, distinguished these criteria on logical grounds. For him, an association is plausible if it is consistent with current biological knowledge; an association is coherent if it does "not seriously conflict with the generally known facts of the natural history and biology of the disease." In the more recent methodological literature, this issue remains unresolved (146,152–155). A recent paper emphasizes plausibility but ignores coherence (146), whereas another favors a broad definition for coherence deemphasizing plausibility (152). Perhaps more important than distinguishing between these two criteria is specifying and categorizing the many types of biological evidence used in causal inference (156).

With regard to causal conclusions and public health recommendations, it is interesting that reviewers sometimes consider both and sometimes do not mention one or the other. No reviewer in these series offered an explanation for his or her specific choice. In the absence of such, we offer some possibilities. Consider, for example, the reviews in which public health recommendations did not appear. Perhaps reviewers judged that public health actions should not be taken and therefore made no mention of them. Alternatively, reviewers may not include public health recommendations because they see them as policy decisions and therefore as inappropriate to the professional practice of epidemiology (157). There is no way to easily distinguish between these possibilities. Furthermore, some reviewers include public health recommendations without explicitly considering, much less concluding, cause. The *notes* of this practice may be found in the seminal paper of Hill (4). There, he noted that public health action may be recommended in situations in which insufficient evidence exists to firmly conclude causation. Hill also suggested that different levels of evidence may be used for different situations. How to make such judgments, however, remains an elusive methodological problem (2). As a referee pointed out, the summary findings indicate a conservative attitude toward inferring cause.

Because causal conclusions are primarily scientific concerns, whereas public health recommendations are primarily ethical concerns (158), the intended goals of the review may have determined which results were included. Specific goals, however, were not stated in 5 of the 14 alcohol and breast cancer reviews (63, 70–72, 82); in three, the stated purpose did not match the results (76, 77, 81). Certainly, reviews may be written to summarize the studies and to suggest further research without including causal conclusions or public health recommendations. None of the reviews in these series, however, were so limited.

Recommendations for Research. Has epidemiology found the best approach to causal inference? We suspect not. Improvements are important, consistent with the pivotal role of epidemiology in the prevention and control of cancer. Research on several fronts may prove fruitful: examining other series of reviews in light of the techniques of research synthesis (159–163), examining the assumptions embedded within the causal criteria and their accompanying inferential rules (164), and proposing theoretical frameworks, both qualitative and quantitative, from which practical approaches to causal inference may be derived (150, 152, 155, 165, 166). Included within these theoretical efforts are further inquiries into the interrelationships of science and ethics in the practice of causal inference (4,

Table 3 Frequency of the use of causal criteria in 14 published reviews on alcohol and breast cancer, 1985–1994

Criterion	No. of reviews
Consistency ^{a, b}	14
Strength ^{a, b}	13
Dose-response ^a	9
Biological plausibility ^a	8
Specificity ^{a, b}	5
Temporality ^{a, b}	4
Experimentation ^a	3
Coherence ^{a, b}	2
Analogy ^a	1
Epidemiological sense	1

^a Hill, 1965 (4).

^b Surgeon General, 1964 (3)

150, 165). Methods of moral reasoning, for example, may be helpful in making public health recommendations (167, 168).

Recommendations for Practice. The following recommendations do not represent criticisms of the reviews we examined, but rather proposals for future consideration in the multifaceted practice of causal inference. For one component of that practice, namely, citation of studies, a recommendation might seem unnecessary, given that most reviewers cited nearly all available studies. Nevertheless, we recommend that when reviewers exclude studies from consideration, they state their reasons for doing so, using methodological criteria.

We recommend that reviewers clearly state their purpose in writing a review. There are at least three possibilities: to summarize the science and make research recommendations, to make causal conclusions, and to make public health recommendations.

We recommend that when making causal conclusions and/or public health recommendations, reviewers cite a source for their approach to causal inference. In many reviews summarized above, authors used varying subsets of the criteria of Hill (4) without justification for exclusions and changes. This seems a subjective practice (2). Perhaps the use of different subsets stemmed from differences in training, a factor we can examine indirectly in the epidemiological textbooks (138, 140–142, 144, 145, 147, 148, 169–175) published between 1970 and 1995. A remarkable variety of choices regarding the use of criteria are available. Overall, strength (15 of 15), temporality (14 of 15), consistency (13 of 15), biological plausibility (13 of 15), dose-response (13 of 15), and specificity (11 of 15) were the most frequently described. Few lists were ranked.

Finally, we recommend that reviewers examine recent reviews on the same topic and cite when appropriate the causal conclusions and public health recommendations from them. Reviews are increasingly viewed as a legitimate part of the scientific literature, serving to summarize research and to provide answers to the central questions of causal inference for specific associations (163).

Many other facets of this practice remain to be carefully discussed. At its core, causal inference is a complex matter of reasoned judgment informed by science and ethics. It is of central importance to epidemiologists involved in public health and to the public at large.

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