

Responses

DIRECTIONALITY, TIMING, AND SAMPLE SELECTION IN EPIDEMIOLOGIC RESEARCH DESIGN

MICHAEL S. KRAMER and JEAN-FRANÇOIS BOIVIN

Department of Epidemiology and Biostatistics, McGill University Faculty of Medicine, Montreal,
Quebec, Canada H3A 1A2

The foregoing commentaries demonstrate wide differences between their authors' choice of terms describing epidemiologic research designs, and in the relative importance they attach to directionality, timing, and sample selection. Nowhere is this more evident than in their discrepant definitions of "prospective" and "retrospective" studies. According to Drs Greenland and Morgenstern, "Prospective studies are based on ascertainment of events (exposures and outcomes) at the time they actually occur; retrospective studies are based on purely historical determinations; thus the distinction is one of timing." By contrast, Dr Abramson uses the same two terms to indicate directionality (prospective = "forward-looking," retrospective = "backward-looking"). Precisely because of this source of confusion, we prefer to avoid these terms entirely.

We applaud Dr Abramson's efforts at simplification, particularly when research design and other epidemiologic principles are presented to students and colleagues without a previous background in epidemiology. But we give an explicit place (as do Greenland and Morgenstern) to the timing of measurement of exposure and outcome in our classification scheme. In our view, timing is important because of both its potential for conceptual "confounding" with directionality and its relevance for apposite and valid measurement of exposure and outcome [1].

In our original article, we defined directionality as "the order in which exposure and outcome are investigated." [1]. As Greenland and Morgenstern surmise, we do indeed conceptualize directionality in terms of order of measurement.

Perhaps our meaning would have been clearer had we used the term "ascertained" instead of "investigated." But in separating directionality from timing, we think it is important to distinguish between when measurements are actually made and when those measurements are *ascertained* by the study investigators. For example, actual exposure measurements may have been carried out by a physician, employer, etc. at the time exposure actually occurred, but the investigators may seek access to the records containing those measurements only at the time of the epidemiologic study. When exposure information is obtained by interviews of the study subjects, the measurement and its ascertainment are of course simultaneous, even if the exposure inquired about occurred in the distant past.

Greenland and Morgenstern appear to agree, then, that the order in which exposure and outcome are ascertained is an important aspect of research design. They also agree that its importance lies in the potential for biased measurement of exposure and outcome. We in no way wish to impugn Greenland's and Morgenstern's knowledge or writings about this source of bias; they have made a number of important contributions in this area. But we share Dr Abramson's point of view that if directionality (order of ascertainment of measurement) is indeed important, as we all appear to agree that it is, then it is logical to include it in a classification system.

Despite apparent overall consensus on the importance of order of ascertainment of exposure and outcome, there remain substantial differences in emphasis. Greenland and Morgenstern

have chosen sample selection as the key "axis" in their classification scheme. They define cohort and case-control studies on the basis of sampling design: "In a cohort study... risk-factor and incidence data are obtained on all source population members..." and "... a case-control study involves gathering data on only a (disease-selective) subset of the source population..." where source population is "... the population at risk that will serve as a source of incident cases for a study." [2]. According to this definition, in a source population of 100,000 subjects in whom 100 cases are observed over a 10-year period, the design would be labelled as cohort if the 100 cases were included along with all 99,900 noncases but as case-control if the 100 cases were included with $99,900 - 1 = 99,899$ noncases. This example shows that in the extreme, the distinction between study designs on the basis of the fraction of noncases selected can become artificial.

By contrast, Abramson uses a "hybrid" classification in his definitions of cohort and case-control studies. For him, "cohort" is a synonym for "prospective," i.e. the definition is based on directionality alone. But "case-control" is based on sample selection: "studies in which cases (of the outcome condition) are compared with controls... they may be backward-directional or nondirectional."

By providing separate axes for directionality, timing, and sample selection, our definitions [1] contain more information about study design. A cohort study is a study in which the ascertainment of measurement of exposure and outcome is forward in direction (exposure \rightarrow outcome); the sample can be selected from the target population either by exposure or by a "representative" approach. A case-control study is a study in which the ascertainment of exposure and outcome is backward in direction (outcome \rightarrow exposure); the sample can be selected either by outcome or by a "representative" approach. In this definition of a case-control

study, 100% of all noncases from the target population can be included in the analysis, and the study remains a case-control study.

We prefer a classification for epidemiologic research design in which directionality (order of ascertainment of measurement), and not sample selection, forms the principal axis, i.e. the basis for defining cohort, case-control, and cross-sectional studies. The world of science has a long and illustrious history documenting the utility of reasoning from effect to cause. This type of inference underlies Sherlock Holmes' methods, the investigation of infectious disease outbreaks, attempts at discovering the causes of airplane crashes, and the entire field of psychoanalysis (although the absence of control groups in the latter setting remains troubling for the epidemiologist).

We can imagine no better illustration of this important difference in emphasis than Greenland's and Morgenstern's own example of a cluster of lung cancers noted in an industrial plant. Instead of historically reconstructing levels of exposure to potentially carcinogenic chemicals for each plant employee, *our* approach would be to identify and locate the cases of lung cancer, identify and locate an appropriate group of plant workers who did not develop lung cancer, and inquire (or consult previous plant records) about prior exposure. The problem (outcome) has already occurred; it seems quite natural to direct our inferential reasoning toward seeking antecedent causes. This baby has been around a long time, and we remain quite reluctant to throw it out with the bath water.

REFERENCES

1. Kramer MS, Boivin J-F. Toward an "unconfounded" classification of epidemiologic research design. *J Chron Dis* 1987; 40: 683-688.
2. Greenland S, Morgenstern H. Classification schemes for epidemiologic research designs. *J Clin Epidemiol* 1988; 41: 715-716.