Different Views

Inappropriate Comparisons of Incidence and Prevalence in Epidemiologic Research

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Abstract: Several epidemiologists have published papers in major medical journals in which they compare incidence rates and prevalence and use these comparisons to support conclusions regarding questions of major public health importance. Although these papers have been criticized in published correspondence, we believe that continued use and advocacy of such comparisons by some epidemiologists has created the need for a full discussion of this practice. In this commentary, we review basic differences between incidence and prevalence and show that direct comparison of these two measures is inappropriate for conceptual, theoretical, and practical reasons. (*Am J Public Health* 1989; 79:1301–1303.)

Introduction

Most epidemiologists recognize that incidence and prevalence measures are not directly comparable because of inherent, fundamental differences. Neverthless, a few epidemiologists[1–3] have published papers in major medical journals in which they compare incidence rates with measures of prevalence and then use these comparisons to support conclusions regarding questions of major public health importance. Moreover, comparison of incidence and prevalence is a fundamental component of a general method which was proposed for addressing surveillance issues in public health.[3] To justify these comparisons, the authors argued that incidence rates reported by tumor registries are not true incidence rates.[1–3]

In one study designed to determine whether the observed association between exogenous estrogen use and endometrial cancer could be explained by selection bias, Horwitz, *et al,*[1] reviewed autopsy results from two major hospitals and estimated the prevalence at death of previously undiagnosed endometrial cancer. They then compared this prevalence with the annual incidence rate of endometrial cancer reported by the Connecticut State Tumor Registry, found the former to be "four to six times greater" than the latter, and concluded that for each detected case of endometrial cancer at least three were undetected prior to death. This conclusion was used to infer a fourfold to fivefold bias in case-control studies of endometrial cancer and postmenopausal estrogen use.

In another study, McFarlane, *et al,*[3] in effect ignored the difference between incidence and prevalence when they proposed a new method for studying secular trends in surveillance data. The method, termed the "epidemiologic necropsy," was developed to distinguish real increases in disease occurrence from those that result from improved diagnostic techniques. As in the study by Horwitz, *et al,*[1] prevalence at death of previously undiagnosed disease was estimated from autopsy data and compared with annual incidence rates reported by the Connecticut State Tumor Registry. They found that the prevalence at death of previously diagnosed lung cancer was about 15 times larger than the incidence rate of lung cancer. They used this and similar comparisons as evidence that "the rise in the reported incidence rates for [lung cancer] may be due more to improved methods of detection than to an absolute increase in the occurrence of the disease" and "that much of the increase in lung cancer occurrence in the past three decades is apparent rather than real." Although their approach has several flaws including the selection bias which can be associated with autopsy series,[4–8] perhaps the most serious from an epidemiologic standpoint was the direct comparison of incidence rates with prevalence.

Feinstein and Esdaile[2] also recommended that incidence rates be compared with prevalence of disease at autopsy. In a commentary, they reviewed definitions of incidence and critiqued methods used to estimate incidence rates. Despite their recognition of differences between incidence and prevalence, they argued that rates reported by tumor registries are not really incidence rates and that such measures are directly comparable to measures of prevalence at autopsy.

In this commentary, we discuss the comparison of incidence rates with autopsy prevalence. First, we review definitions of incidence and prevalence, emphasize differences between the measures, and note why the measures are not directly comparable. Second, we show that, although incidence rates reported by tumor registries may not meet an idealized definition of incidence, they are indeed a form of incidence rate and therefore should not be compared directly to prevalence at autopsy. Although our comments echo those in published correspondence,[7–11] we believe that continued use and advocacy of such comparisons by some epidemiologists has created the need for a full discussion of this practice. Third, we calculate roughly the proportion of lung cancers that are undetected at death. Although our calculations have limitations, they lead to substantially different conclusions than those of McFarlane, *et al.*[3]

Incidence and Prevalence

A *prevalence* is the proportion of a population that has disease at a particular time.[12–14] It measures the frequency of existing disease and has no dimensions or units. By definition, the possible values of prevalence lie between zero and one. Point prevalence is another term sometimes used to denote

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prevalence.[12] The estimates from studies of autopsies in reports by Horwitz, *et al,*[1] and by McFarlane, *et al,*[3] are examples of prevalence measures, the reference point being the moment of death. In this case, the measures estimate the prevalence at death of disease that was not previously diagnosed.

An *incidence* rate is the rate at which new disease occurs in a population.[12–14] It measures the occurrence of new cases and can be defined as the number of new "events" per unit of person-time of observation. Its units are inverse time, typically, though not necessarily, person-year^{-1} or person-months^{-1}. Its possible values include all non-negative numbers. It is estimated as the number of new diagnoses divided by the corresponding number of person-years of observation of people in the population who are candidates for the disease. A person contributes one person-year to the denominator for each year he or she is a member of the population at risk. For example, 10 person-years may represent 10 people who were observed for one year each, or one person observed for 10 years. The terms "force of morbidity" and "incidence density" also denote incidence rate. Rates from the Connecticut State Tumor Registry cited by Horwitz, *et al,* and McFarlane, *et al,* are annual incidence rates.

Incidence rates differ from prevalence measures in many ways.[12–14] They are defined differently, estimated differently, reflect different concepts, have different units, and have different ranges of possible values. These fundamental differences preclude meaningful, direct comparisons. An obvious, yet important obstacle is the difference in units. An incidence rate has units of inverse time, and its apparent magnitude can be changed by choosing different units of time; prevalence, as a simple proportion, has no dimensions and no time units.

Although not directly comparable, prevalence and incidence are interrelated. The relationship is particularly simple under a steady state (that is, if the population is stable and both prevalence and incidence rates remain constant). With these conditions, prevalence and incidence are related by: $P = I \times D/(1 + I \times D)$, which for rare disease reduces to $P = I \times D$, where I denotes incidence, P denotes prevalence, and D denotes the average duration of disease.[12,13]

An incidence rate also differs from cumulative incidence[12,13] or incidence proportion.[15] Cumulative incidence reflects average risk in a population, has no units, and can, if competing risks are negligible, be estimated as a simple proportion. A cumulative incidence differs from prevalence, however, since the former measures the proportion of people who contract disease during some period of time and the latter measures the proportion of people who have disease at a specific *point* in time.

Are rates reported by tumor registries incidence rates?

To justify comparison of incidence with prevalence, Horwitz, *et al,*[1] and McFarlane, *et al,*[3] claim that rates reported by tumor registries are not incidence rates. To support this claim, they observe correctly that rates reported by tumor registries often include cases that were first discovered at autopsy. In spite of their claim, however, this procedure is entirely consistent with the definition of an incidence rate: the "event" used to define tumor registry incidence rates includes all new diagnoses, whether the diagnosis occurred in life or at death. The incidence rate measures the occurrence of *new* diagnoses of disease.

The views of Horwitz, *et al,*[1] Feinstein and Esdaile,[2] and McFarlane, *et al,*[3] might be better understood by emphasizing the difference between an ideal incidence rate and the way incidence rates are estimated in practice. If all incident cases could be identified at the moment of inception or perhaps when first "detectable,"[2,3] an "ideal" incidence rate might then be estimated by dividing these incident cases by the person-years of observation of the population at risk. In this "ideal" situation, the population at risk would exclude people who already have the disease in question. In practice, however, disease cannot be detected at the moment of inception, so the investigator must typically count newly diagnosed cases, some of which may have been diagnosed early and others late in the course of disease. When such newly diagnosed cases are used to estimate the incidence of disease, the resulting measure is technically a rate of occurrence of new diagnosis. Moreover, those with diagnosed disease may not all be excluded from the denominator, although for rare diseases like endometrial cancer, this does not appreciably affect the estimated incidence rate. The key point, however, is that the reported measure is a *rate,*[14] the incidence rate of new diagnoses. As noted previously, incidence rates and prevalences have fundamental differences that preclude meaningful direct comparisons. These fundamental differences exist, even though reported incidence rates may not be "ideal."

As further justification for comparing prevalence with incidence rates, McFarlane, *et al,*[3] claim that, regardless of the definitions, registry rates and the necropsy prevalence are "determined in a relatively similar manner and can be directly compared." Although these measures have some similarities, they also have important differences. Registry incidence rates are estimated from the number of newly diagnosed cases in the observed population divided by *person-time* of observation, whereas the necropsy prevalence measure is calculated by estimating the number of cases newly diagnosed at autopsy divided by the number of deaths among those not known to have disease. These measures are clearly different, precluding direct comparison.

While the preceding arguments provide theoretical reasons why rates from tumor registries are incidence rates (of diagnosis)[16–18] and are not comparable to autopsy prevalences, a simple numeric example also illustrates why these two measures are not directly comparable. Among the 4,462 women studied by Horwitz, *et al,* who underwent autopsy at the Massachusetts General Hospital between 1952 and 1978, unsuspected endometrial cancer was discovered in 14. Horwitz, *et al,* termed this the "rate of endometrial cancer first detected at necropsy" and reported it as 31/10,000. The authors compared this number to the "rate of detected endometrial cancer as estimated by the [Connecticut State Tumor Registry]," which they noted to be 5.5/10,000. They concluded that "the rate of detection at necropsy is about four to six times greater than the rate of detection during life." However, they failed to note that the actual denominator of the latter measure was 10,000 person-years, in effect ignoring the units of that rate. Although such rates are customarily reported in terms of person-years, the same data could just as accurately be stated as 55/10,000 person-decades or 0.46/10,000 person-months. By arbitrarily choosing and then ignoring the units in the denominator, one could make such rates grow or shrink at will and virtually any desired conclusion could be reached. This untenable situation numerically illustrates the inappropriateness of the comparisons made by Horwitz, *et al,* and by McFarlane, *et al.*

The proportion of cases of lung cancer which are never diagnosed

The epidemiologic necropsy was proposed as a way of distinguishing real increases in incidence from artifactual

increases due to improved diagnosis. The problem addressed by McFarlane, *et al,*[3] occurs because some cases are never diagnosed and are not counted in reported rates. Improvements in diagnostic techniques, they argued, could reduce the number of missed cases, leading to an artifactual increase in rates. McFarlane, *et al,* compared their estimate of the prevalence at death of undetected lung cancer with the reported lung cancer incidence rates and found, by ignoring the time units, that the prevalence was large relative to the incidence rate. They used this comparison to suggest that a large proportion of lung cancer cases are never detected; since other evidence suggested a recent decrease in the prevalence of undetected disease, they argued that recent increases in reported rates were due more to improved diagnostic techniques than to real increases in occurrence.

Although McFarlane, *et al,* claim that a large proportion of lung cancer cases are never detected, their data actually support the opposite conclusion. Specifically, we compared their estimate of the prevalence at death of undetected disease with the prevalence at death of detected lung cancer. In 1975, about 2.3 percent of all deaths among American women over age 20 were certified, on death certificates, as due to lung cancer.[19] After standardizing for age by using the 1970 Connecticut population, the prevalence of (recognized) lung cancer at death was about 3,100 per 100,000. (It would have been even higher if we had included cases not causing death.) In contrast, the prevalence of surprise lung cancer at death reported by McFarlane, *et al,* was only 342 cases per 100,000. Even though the latter estimate may be inflated by selection bias,[4–7] this comparison still suggests that most cases are diagnosed, implying that the number of undetected cases is small relative to the number of recognized cases, undermining the basis of their arguments that improved diagnostic techniques have substantially affected reported lung cancer rates. This evidence, as well as other information such as the threefold to fourfold (300 to 400 percent) increase in reported rates over the past 35 years, the widely accepted role of cigarette smoking as a cause of lung cancer,[20] and the secular trends in smoking habits, suggests that recent increases in lung cancer occurrence are not merely an artifact of improved diagnosis.

In summary, incidence and prevalence are well-defined, well-accepted, and distinctly different measures of disease frequency that are not directly comparable. Tumor registry rates, though imperfect, are incidence rates and therefore cannot be compared directly to prevalence at death or other prevalence measures. The arguments of Horwitz, *et al,*[1] and McFarlane, *et al,*[3] were based on inappropriate comparisons; in fact, the data of McFarlane, *et al,* suggest a conclusion opposite to the one the authors drew. Direct comparison of incidence and prevalence is inappropriate and has no place in epidemiology, medicine, or public health.

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Mathematical Models and Scientific Reality in Occurrence Rates for Disease

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We appreciate the invitation to respond to the preceding paper by Flanders and O'Brien.[1] Their text contains the customary mathematical concepts used by epidemiologists for defining incidence and prevalence, and the customary inattention to the actual evidence[2] that converts the theoretical concepts into credible scientific data.

The evidence for scientific "incidence" involves much more than merely assembling statistics for "the number of new 'events' per unit of person-time of observation." It