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

Alvan R. Feinstein, MD, MS, Charles K. Chan, MD, John M. Esdaile, MD, MPH, Ralph I. Horwitz, MD, Michael J. McFarlane, MD, and Carolyn K. Wells, MPH

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

From the Clinical Epidemiology Unit, Yale University School of Medicine (Feinstein, Horwitz, Wells). Address reprint requests to Alvan R. Feinstein, MD, Professor of Medicine and Epidemiology, Yale University School of Medicine, P.O. Box 3333, New Haven, CT 06510-8025. Dr. Chan is with the Department of Medicine, University of Toronto; Dr. Esdaile is with the Department of Medicine, McGill University; Dr. McFarlane is with the Department of Internal Medicine, Case Western Reserve University. This paper was invited by the editor on February 17, 1989 and accepted for publication April 27, 1989.

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involves observing those persons, determining that they do not have the "event" when the time-period begins, and following them afterward to demonstrate that the event occurred (or did not occur) during the cited interval. Except for death itself, none of the events cited in the numerators of conventional "incidence" data for disease meets this elementary scientific requirement; and none of the persons cited in any of the denominators is directly observed, followed, or suitably examined for the research. All of the "incidence" data come from groups of statistical information assembled for other purposes.

For almost a century epidemiologists have used a remarkable double standard for research in infectious and non-infectious disease. The infectious-disease researchers, doing active surveys and measurements of serology, have obtained careful scientific evidence to identify "silent" cases of infection that would otherwise be totally missed. The recognition of the many silent cases of infectious disease has allowed accurate estimates of each disease's occurrence, and has led to important scientific concepts (such as the blood-borne viral phase that facilitated development of a polio vaccine). The investigators of non-infectious disease, however, have not done similar research and do not have a simple serologic test for identifying silent cases of cancer, atherosclerosis, and other "chronic" diseases. Without attention to the many silent cases, the statistics about occurrence rates are inevitably too low and misleading, beyond the gross inaccuracies that come from the peculiar tradition of counting the occurrence of diseases from their diagnostic citation on death certificates.

No one can doubt the intellectual splendor of equations such as "$P = I * D/(1 + I * D)$" and the elegance of ideas such as "the proportion of people who have disease at a specific *point* in time." Unfortunately, except in studies of infectious-disease epidemiology, the theoretical splendor and elegance are almost never accompanied by rigorous efforts to observe people directly, examine those people, and get reliable scientific evidence to insert in the equations and ideas.

The history of modern science contains few paradigms that have lingered so long after their original usefulness had vanished. There is no longer any scientific justification for the entrenched custom of calculating incidence rates of non-infectious disease from the grossly inaccurate data that appear on death certificates. This custom may have been accepted during most of the 20th century, but it now has the same scientific validity as archaic old ideas about alchemy and phlogiston.

We make no claim of perfection for any of the new approaches we have proposed. They do have the merit, however, of representing a departure from persistent complacency about the status quo, and of offering potential remedies for some of the egregious scientific defects. Since the existing data have such poor scientific quality, we have tried to see what could be done about getting evidence from persons who have actually been examined, not just counted in a distant census, and whose diagnoses have been actually checked, not just transferred to a compliant computer. We have offered a beginning of efforts to escape from untrustworthy death-certificate diagnoses and to get reasonably accurate data about the occurrence of disease.

This brief commentary is not the place to recapitulate the rationale and justification for the proposed new procedures. We urge interested readers to review the cited papers,[2–4] not only to examine our concepts and methods directly, but also because our proposals have not been correctly cited by Flanders and O'Brien. For example, we offered several cogent reasons[2,4]—not just the inclusion of "cases that were first discovered at autopsy"—for arguing that tumor registry rates are not true incidence rates. As another example, we proposed[4] that suitable investigation be given to both the real and apparent sources of increased occurrence rates for lung cancer. As a third example, we noted[2] that the numerators of "incidence" rates will be distorted by failure to identify "prevalent" cases, but that the error was not a substantial problem in the denominators of those rates.

Flanders and O'Brien have also ignored several important issues of interest to epidemiologists who are concerned more with scientific validity than with mathematical ratiocination:

1) We compared the stratified necropsy occurrence rates with *annual* incidence rates, not with diverse units or durations of "person-years", because the annual rate pertains to denominator people who can be specified, with reasonable accuracy, as having the cited age during that year.

2) The occurrence rate we found[3] at necropsy "screening" for endometrial cancer has now been confirmed[5] by large-scale screening done during life.

3) The phenomena counted as "incidence" of many diseases—ranging from asthma to cancer and from end-stage renal disease to tuberculosis—can be dramatically altered by changes in screening surveillance, diagnostic criteria, diagnostic technology, or therapeutic technology, without any alteration in the true occurrence of those diseases.[2,6,7] If epidemiologists continue to participate in the production of misleading "incidence" data, disillusionment and disrespect will inevitably follow from the general public as well as from policy-makers and funding agencies.

We have clearly stated that the term "incidence rate" does not apply to the occurrence of diseases at necropsy. We await the day when a new generation of scientifically minded epidemiologists and statisticians will recognize that the term "incidence rate" also does not apply to the occurrence of diseases reported either on death certificates or in tumor registry calculations. When these problems become acknowledged, the existing mathematical fantasies can be replaced by scientific standards for data, and by appropriate efforts to get credible evidence. Epidemiologists can then stop wasting useful intellectual energy on statistical polemics about terminology for the occurrence rates of disease, and can settle down to the real scientific challenges, avoided for almost a century, of determining what is happening in nature.

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