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Mary Beth Terry
Alfred I. Neugut
Division of Epidemiology
Joseph L. Mailman School of Public Health
Columbia University
New York, NY 10032

RE: "POPULATION ATTRIBUTABLE FRACTION ESTIMATION FOR ESTABLISHED BREAST CANCER RISK FACTORS: CONSIDERING THE ISSUES OF HIGH PREVALENCE AND UNMODIFIABILITY"

In a recent paper, Rockhill et al. (1) considered the issues of the high prevalence of exposure to recognized breast cancer risk factors and the public health relevance of population attributable fraction (PAF) estimation.

There is a minor error in their description of our findings (2). We estimated a PAF of 0.47 (95 percent confidence interval (CI): 0.17, 0.77) for the First National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study (NHEFS) cohort and a less precise PAF of 0.41 (95 percent CI: 0.016, 0.80) for the US population; we did not estimate a PAF of 0.41 (95 percent CI: 0.16, 0.80) for either the NHEFS or the entire United States.

More importantly, Rockhill et al. highlight key points in showing that both the PAF estimate for several recognized risk factors and the precision of the estimate are sensitive to the definition of "exposed." However, the statement that other reports did not "discuss the issue of [the] scientific or public health value of their estimates" (1, p. 826) is a bit sweeping, since we did comment on these topics (2). Further, while Rockhill et al. find "misleading and even alarmist" (1, p. 832) our statement that our estimates "suggest that a substantial proportion of breast cancer cases in the United States are explained by well-established risk factors" (2, p. 1681), we disagree and do not think the statement is misleading when it is read in context. While most women exposed to recognized risk factors do not develop breast cancer, the fact remains that increases in risk have been consistently reported for family history of breast cancer, later age at first birth, nulliparity, and early menarche.

In our paper (2), we wrote that studying how recognized factors operate might provide useful data for devising strategies to prevent breast cancer. However, many breast cancer cases are probably not attributable to the recognized risk factors we studied. We discussed avenues of research potentially useful for understanding and preventing breast cancer, including the study of dietary, anthropometric, lifestyle, occupational, and environmental factors. We hope that further research will identify factors that can reduce the breast cancer risk of women with and without recognized risk factors.

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Patricia Madigan
Regina G. Ziegler
Jacques Benichou
Celia Byrne
Robert N. Hoover
Epidemiology and Biostatistics Program
Division of Cancer Etiology
National Cancer Institute
Bethesda, MD 20892

THE FIRST AUTHOR REPLIES

We thank Madigan et al. for their comments (1) and for pointing out an error in our paper (2). Although they do not say so directly, it appears that the error they are referring to is our mistake of citing 0.16 rather than 0.016 for the lower bound of the 95 percent confidence interval around their population attributable fraction (PAF) estimate of 0.41 (or, as they have written it in their paper (3), 0.408). The way in which the second paragraph of their letter is written is somewhat confusing, leading one to wonder whether the principal error they refer to involves our interpretation of the PAF of 0.41 as applying to the entire US population. However, this interpretation is clearly correct. We apologize for our typographic error in the lower confidence limit. Our purpose in citing the confidence interval was to point out the great imprecision in PAF estimates that are based on risk factor categorizations that result in a very small proportion of per-

sons in the "unexposed" group (4). The 95 percent confidence interval of 0.016, 0.80 demonstrates an even greater degree of imprecision than our incorrectly cited 0.16, 0.80 and reflects the broad exposure definitions used in the analysis of Madigan et al. (3).

More importantly, Madigan et al. feel it is useful and not misleading to make statements such as "a substantial proportion of breast cancer cases in the United States are explained by well-established risk factors" (3, p. 1681) when referring to risk factors that, by their own calculation, are widely prevalent in the US population and that therefore can do little to elucidate the individual occurrence of cases. Many women greatly overestimate their breast cancer risk and express inordinate fear of this disease, often at the expense of ignoring more prevalent health risks (5–7). We think the declaration that many breast cancers can be "explained" by nulliparity/late age at first birth, higher income, and family history contributes to this disproportionate fear, because many women correctly identify themselves as being exposed to at least one of these factors. If Madigan et al. had considered as a risk factor income level in the upper four fifths of the US distribution rather than income level in the upper two thirds of the US distribution, would they believe it useful (and *not* misleading), from a public health prevention perspective, to state that more of breast cancer incidence is now "explained"? Higher income level is primarily a surrogate for reproductive patterns that are associated with increased risk of breast cancer, such as delayed childbearing or nulliparity (which is already considered in their analysis (3) as one of the three risk factors) and fewer total births. If the purpose of a PAF calculation for breast cancer risk factors is to suggest realistic prevention strategies (whether these strategies are individual or population based), the inclusion of surrogate risk factors such as "higher income" is not helpful in light of the growing knowledge of breast cancer etiology.

"Explained by" is a much vaguer phrase than "caused by," perhaps intentionally so, and for this reason its meaning is open to differing interpretations and misinterpretations. A chief goal of our article (2) was to point out the common confusion between the PAF and the proportion of cases that arise from the segment of the population that is considered "exposed." Madigan et al. conclude their letter by stating, "We hope that further research will identify factors that can reduce the breast cancer risk of women with and without recognized risk factors" (1, p. 543). This is the hope of all breast cancer researchers. This statement, however, may reinforce the misperception held by some that, because the PAFs for breast cancer risk factors are relatively low, a sizeable proportion of breast cancer cases must necessarily arise from those women with no risk factors. For instance, in the analysis of Madigan et al. (3), 90 percent of the (US) population was estimated to be exposed, and the (US) PAF estimate was approximately 0.41. The PAF of 0.41 obviously does not mean that 59 percent of cases are occurring among women with none of the three risk factors considered. It is likely that a very large proportion of breast cancer cases (>90 percent) arose from the 90 percent of US women who were exposed, though it is not possible to calculate this proportion from the data presented in the article by Madigan et al. In fact, in virtually all published PAF calculations for breast cancer risk factors, very few cases have occurred among women with no risk factors, because these factors have usually been defined to include very high proportions of the US population (sometimes as much as 98 percent of the population is exposed to at least one of the factors considered (8)).

Geoffrey Rose (9) made a distinction between the causes of disease incidence and the causes of individual disease cases. For those concerned with developing effective and ethical prevention strategies for breast cancer, the question of the causes of individual cases is assuming scientific prominence. Unfortunately, the three risk factors considered by Madigan et al. (3) can contribute little to the identification of cases in a population where exposure (to at least one of these factors) is highly prevalent, and where the large majority of "exposed" women should *not* be alarmed about breast cancer.

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Beverly Rockhill
Channing Laboratory
Department of Medicine
Harvard Medical School and
Brigham and Women's Hospital
Boston, MA 02115