Re: Population Attributable Risk for Breast Cancer: Diet, Nutrition, and Physical Exercise

Mezzetti et al. (1) reported population attributable risks (PARs) for breast cancer in Italy with respect to lifestyle factors. As a multivariate analysis of PARs for modifiable risk factors, their study was especially interesting. We want to raise some questions regarding the interpretation of the PARs in general and for breast cancer in particular.

Some major findings in the study by Mezzetti et al. (1) are summarized in Fig. 1, using the graphical approach of Eide and Gefeller (2). The combined PAR percentage for any set of three out of the four risk factors analyzed was approximately 30%, with indications that β-carotene and physical activity were the most important risk factors. For an
Overall assessment, the combined PAR for all four variables would be very interesting, but such data were not provided by Mezzetti et al. (1).

All PARs reported by Mezzetti et al. (1) were also adjusted for age, center, educational level, calorie intake, and menopausal status. Tavani et al. (3) found from the same study sample that approximately 50% of the breast cancer risk could be attributed to the reproductive factors, as acknowledged in (1). From these results (1,3), one might easily be misled to believe that 80% of the breast cancer risk can be attributed to the combined effect of lifestyle and reproductive factors. However, even if the sets of lifestyle and reproductive factors were statistically independent, PARs cannot be summed to give the combined PAR for all factors (4,5). Furthermore, a potential confounding effect of reproductive factors on the association between breast cancer risk and certain lifestyle factors might change the PARs. Only analyzing all factors jointly can yield similar results for the PARs. Mezzetti et al. (1) stated, “The PAR for each factor describes the theoretical percent of cases that would be prevented if all subjects were moved into the exposure level associated with the lowest risk for that factor.” However, in their Table 3 (1), PARs were reported for the highest risk level of each lifestyle factor only. What is the correct interpretation when each factor has three levels? If only two levels were considered, are the PARs underestimated in relation to the models underlying Table 2 (1)?

PARs are increasingly getting more attention in the evaluation of preventive strategies. It is important to realize that the context is crucial for their interpretation. PARs are reported sometimes for nonmodifiable factors (3) and sometimes for modifiable ones (1). Strategies for prevention can be rationally discussed only by using correct methodology (6,7). Furthermore, concepts like sequential and average attributable risks (2) may be of substantial help in discussing implications of PAR estimates.

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References


Notes

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Response

We thank Dr. Eide and co-workers for their interest in PARs and in our study in particular. Estimation of adjusted PARs for combination of several variables is not computationally possible because of the small number of subjects in the various strata. This fact makes it impossible to obtain PARs and, more importantly, to estimate their variances on which confidence intervals are based. The same line of reasoning applies to subgroup analyses, including those restricted to nulliparous women (402 case patients and 383 control subjects). It is clear, in any case, that the combined effect of various factors does not lead to a PAR that is the sum of each single factor, due to the intercorrelations between various factors. In most cases, as shown in Table 3 of our article, the combination of various factors leads to a PAR that is less than the sum of the PARs of each single factor, although, in rare cases, such a combination may lead
to a PAR that is greater than the sum (1). To estimate PAR for the combination of several factors, it is possible to obtain odds ratio estimates for each stratum with the use of a multiplicative logistic model in the absence of controls in one or more strata. This model does not allow us, however, to estimate the corresponding variance (2).

Finally, we thank Dr. Eide and colleagues for noting a mistake in the first footnote to our Table 3, which should read: “For β-carotene, this meant more than 5053.2 μg/day; for vitamin E, more than 11.7 mg/day; for alcohol, nondrinkers; for physical activity, high levels.”

A D R I A N O D E C A R L I  
M A U R A  M E Z Z E T T I  
C A R L O  L A  V E C C H I A

REFERENCES


N O T E S

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