EDITORIAL

Attributable Risk in Practice

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Two papers in this issue, by Wilson et al. (1) and Benichou et al. (2), highlight the use of attributable risk methods to estimate the proportions of disease cases associated with various risk factors, and to assess the potential for preventive interventions. The diseases in question are quite different, cardiac malformations (1) and renal cell cancer (2), and yet the two studies invoke some interesting comparisons with respect to both the methods and their results.

Both studies employ the case-control design, and so have the advantage of being able to examine several risk factors, either individually or in combination, through the use of multivariable logistic regression. Both groups of authors describe sets of risk factors that may or may not be thought of as "causal." Wilson et al. divide their risk factors into those that are "potentially causal" or "not potentially causal," and make adjustments for the latter when considering the former; Benichou et al. describe their factors as "well established" or "speculative," and they calculate attributable risks for both sets.

The authors of both papers propose that calculation of attributable risks may be justified even if causality has not been proved. Wilson et al. suggest that "interventions for potentially causal factors may be implemented even when understanding of biologic causality is limited" (1, p. 414), while Benichou et al. state that "the PAR for the combination of two or more risk factors is usually less than the sum of the PARs for each risk factor" (2, p. 426). The resolution of this apparent discrepancy is related to how the multivariable data are evaluated.

When several risk factors are involved, it is not a trivial matter to decide how or if adjustments should be made for some factors while one considers the attributable risks of other factors. One may wish either to evaluate the factors one at a time or jointly by using a summary or combination attributable risk. The choice is intimately associated with the intended intervention strategy, for instance, whether prevention of several exposures is envisaged, as opposed to removal of only one exposure.

In this context, the authors of these two papers make statements that are, at first glance, contradictory. Wilson et al. indicate that "the sum of the individual extra attributable fractions will generally be less than the summary attributable fraction" (1, p. 417). By contrast, Benichou et al. state in regard to the population attributable risk (PAR), "the PAR for the combination of two or more risk factors is usually less than the sum of the PARs for each risk factor" (2, p. 426). The resolution of this apparent discrepancy is related to how the multivariable data are evaluated.

Wilson et al.'s calculations are based on attributable risks that are fully adjusted for additional effects. Specifically, they use the concept of extra attributable risk, to represent the effect of removing exposure to one risk factor, while leaving all other exposures unchanged. As discussed in more detail elsewhere (3, 4), the simplest possible case of two binary risk factors, A and B, the difference between the summary attributable risk (associated with exposure to at least one factor) and the sum of the (adjusted) attributable risks

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for A and B separately can be expressed as

$$P_{11} (I_{11} - I_{10} - I_{01} + I_{00})/I,$$  \hspace{1cm} (1)

where $P_{11}$ is the proportion of the population exposed to both A and B; $I_{11}$ is the disease incidence in that subgroup; $I_{10}$ is the incidence for individuals exposed only to A, and similarly for the other population subgroups; and $I$ is the overall population incidence.

Expression 1 indicates that the summary attributable risk is greater than the sum of the factor-specific attributable risks if the disease incidences are supra-additive, i.e., if $I_{11}$ in the doubly exposed subgroup is greater than the incidence expected under an additive rate model, given the incidence rates in the other three subgroups. In the special case of disjoint exposures in the population ($P_{11} = 0$), the two methods of calculation give the same result. By adjusting for other effects, Wilson et al.'s estimates may be thought of as partial.

In contrast, Benichou et al.'s statement is based on marginal estimates for each factor, i.e., the factor-specific attributable risks are based on data collapsed over (and hence ignoring) all other factors. In this framework, one may show that the difference between the sum of the marginal attributable risks for two binary factors and the summary (or, in Benichou's terminology, the "combination") attributable risk is given by

$$ (I - I_A - I_B + I_{00})/I,$$  \hspace{1cm} (2)

where $I_A$ and $I_B$ are the (marginal) incidence rates in individuals unexposed to A or B, respectively. While the central component of expression 2 is superficially similar to expression 1, there exists no general rule determining its sign, and hence either method of calculation may give the larger attributable risk value. Even when the incidence rates are multiplicative (which, as Benichou et al. indicate, is implied by the use of the logistic model), no general rule pertains.

Wilson et al.'s method of partial estimation seems preferable for situations where there are sufficient data to fit a valid multivariable risk model. As noted by Wilson et al., attributable risks can be obtained from case-control data using estimates of the appropriate disease odds ratios together with the proportions of cases exposed; direct estimates of population exposure rates are not required. Benichou et al.'s marginal estimates seem preferable either when one has insufficient data to obtain valid adjusted risk estimates or if one wishes to ignore the effects of other factors. As discussed previously (3, 4), in some circumstances, the marginal estimates may provide unbiased assessments of the actual effect of intervention, depending on the extent of confounding and interaction of the various factors. The properties of both the marginal and partial estimates become somewhat more complex when several risk factors are involved, but the same principles apply.

The results of these two groups of investigations form an interesting contrast. Wilson et al.'s cardiac malformation analysis involved a very large number of risk factors, but even the most important factors had small attributable risks of less than 10 percent. The summary attributable risks were also low, being only about 30 percent for a combination of seven factors in the best case. By comparison, Benichou et al.'s renal cancer analysis gave higher attributable risks for both individual factors and in combination, and the three most important factors had a summary attributable risk of about 50 percent.

Wilson et al. conclude that the potential for prevention of cardiac malformations resides with those risk factors that have a high exposure prevalence despite only modest risk elevations. Even so, the high proportion of "unexplained" cases evident in their study limits the potential benefit of any intervention. For renal cancer, the potential gain is apparently much greater, especially if allowance is made for sex-specific effects (e.g., the greater effect of smoking in men).

Despite the disparity in interventional gains indicated by these case-control studies of two diseases, one must also consider the actual interventions that are implied, and their associated costs. The three main factors identified for renal cancer (smoking, hypertension, and body mass index) would likely require long-term and probably expensive programs to achieve substantial reductions, and the benefits might not be achieved for some period of time. By contrast, modification of some of the cardiac malformation factors (e.g., drug use) might be achieved at comparatively low cost, given that exposure needs to be avoided for a relatively short time period (before and during pregnancy) in only a targeted subgroup of the population.

An editorial in another journal (5) suggests that attributable risk calculations are performed all too rarely in epidemiologic studies. The studies by Wilson et al. (1) and Benichou et al. (2) provide useful examples of this type of estimation, both involving multiple risk factors. The particular method of attributable risk calculation requires careful thought, and should be based on the intended programs of preventive interventions. Further work is needed to integrate this type of risk estimate with considerations of cost, feasibility, and time frames to achieve the apparent potential of alternative preventive strategies. The apparent attributable risk will also be reduced by factors related to the number of individuals for whom exposure is actu-
ally influenced by the intervention, and the efficacy in reducing exposure to the desired level (6). A detailed review of adjustment methods for attributable risk estimation in case-control data is provided by Benichou (7).

In the words of British prime minister Harold MacMillan, “To be alive at all involves some risk” (8). Through the use of attributable risk methods, the epidemiologist can go beyond that somewhat negative stance and recognize the potential for improvement in the human condition.

REFERENCES


