Re: Risk Charts: Putting Cancer in Context

In a recent issue of the Journal, Woloshin et al. (1) presented age- and sex-specific 10-year risk charts for various causes of death for current smokers and nonsmokers. We believe that the estimates in the charts could be improved by 1) considering current smokers, former smokers, and never smokers as distinct groups when estimating individual risks from population rates; and 2) considering competing risks by accounting for the fact that a change in the absolute risk of a particular cause of death alters the risk of other causes of death.

One problem with Woloshin et al.’s risk charts is that their estimated risks of lung cancer death among nonsmokers are higher than previously published estimates. For example, for a 70-year-old man who has never smoked, Woloshin et al. report a 10-year risk of lung cancer death of 1.2%. Estimates adapted from the Cancer Prevention Study II (2) and from the second wave of the British Physicians Study (3) are both about 0.4%. What accounts for the difference?

In the latter two studies, death rates were determined prospectively. Woloshin et al., by contrast, estimated risk in reverse, factoring the death rate in the entire population into the rates contributed by each of the risk groups. For example, lung cancer deaths among men in the population were separated into those occurring in current smokers and those occurring in never smokers. The rates of death within each of these groups were determined algebraically, based on both the published relative risks of death for current smokers relative to never smokers and the proportional representation of the two groups in the population. The proportional representation of current smokers was derived from survey data, whereas it appears that the proportional representation of never smokers was set to equal 1 minus this value, which in effect lumped never smokers and former smokers in the never smoker group.

Yet, for estimates of death rates to be accurate, all risk groups that both represent a sizable portion of the population and face a unique level of risk should be considered separately—that is, heterogeneity must be limited. Because former smokers have roughly eight times the risk of lung cancer as never smokers, combining former and never smokers inflates the apparent risk among never smokers, which may cause needless alarm among this very low-risk segment of the population (4).

This omission would be minor if former smokers represented a small fraction of the population. However, in 2000 the majority of men older than 70 years were former, rather than current or never, smokers (Fig. 1). Had Woloshin et al. divided lung cancer deaths into three rather than two categories, the estimated risk of lung cancer among never smokers would have been reduced by about 60% (to about the same level reported in prospective studies). Furthermore, because the relationship between rates of lung cancer death in never smokers and current smokers is fixed by the relative risk, dividing lung cancer deaths into three risk groups reduces the estimated risk of lung cancer death for current smokers to the same extent.

A second problem with the risk charts is that the risk estimates are not individualized to reflect absolute risk. Absolute risk is a real-life metric, in that the probability of an individual dying of one cause is influenced by the risk of dying of another cause (i.e., a competing risk). That is, all other things being equal, an increased risk of death due to one cause lowers the risk of dying of another cause (6). For example, for men aged 75 years, the 10-year risks of death from any cause for never smokers and current smokers are listed as 49% and more than 95%, respectively. However, the risk of accidental death for both groups of men is listed as 1.1%. Had the excess risk of death from any cause among current smokers relative to never smokers been considered in the risk estimation, then the risk of accidental death would have been concomitantly lower in the current smokers (by about 50%). Including a category for former smokers and incorporating individualized estimates of absolute risk would considerably enhance the usefulness of
Woloshin et al.’s risk charts in clinical practice.

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RESPONSE

Bach and Schrag are correct that some of the simplifying assumptions used to create our risk charts introduce imprecision. We tried to make our methods transparent (i.e., avoid the problem of the black box) so others could understand, replicate, and perhaps improve on our work. To determine whether there is a genuine opportunity for improvement, however, it is probably best to review some of the choices we had to make.

Our idea was to create simple charts that could be posted anywhere (on the clinic office wall, for example) and did not require computer hardware. To make the charts easy to use, and to avoid data overload, we wanted to limit them to a single page. Consequently, we had to make pragmatic choices about which causes of death to include, the time frame for the risks, and the age groupings. Because causes of death differ for men and women in important ways, we decided to create separate charts for men and women.

After looking at the initial charts—and, in particular, at deaths from lung cancer—we realized we needed to account for smoking, which is arguably the most important risk factor for many of the causes of death (and all-cause mortality) shown in the charts. The best available estimates we found for the relative risk of death associated with smoking were derived from the American Cancer Society’s Cancer Prevention Study (CPS-II)—the source used in the Surgeon General’s report on the health effects of smoking (1). Nevertheless, we were concerned about the validity of the CPS-II estimates for former smokers because these estimates do not account for why the former smokers stopped smoking. Smokers who quit because they are sick (e.g., have developed lung cancer or have had a heart attack) will have worse health outcomes than “healthy” current smokers; paradoxically, giving up cigarettes will look dangerous. In the latest Surgeon General’s report about women and smoking (2), some efforts have been made to address the former-smoker problem (e.g., excluding former smokers who have quit within the last 2 years and those dying from cancer or heart disease within the first 2 years of the study); however, revised relative risk estimates are not yet available.

To avoid the former-smoker problem and to keep the number of charts manageable, we decided to create charts only for current and never smokers. The problem then was where to put the former smokers; we chose to group them with never smokers. Although this decision adds some imprecision to our estimates, the bias introduced is conservative. That is, we have been careful not to overstate the harm of smoking.

Bach and Schrag also note that we did not account for the fact that whatever increases the chance of dying from one cause must lower the chance of dying from other causes (because you can only die once). Addressing this issue would, however, require a complex model to account for relative changes in risk across diseases and over time. Although such a model might improve the precision of our estimates, it would require another layer of assumptions, potentially threatening the validity of the estimates. In addition, we wanted to keep our methods simple so that the charts could be readily updated to reflect the latest population statistics or expanded to include other conditions.
Finally, validating the charts is difficult because no clear external standards are available. Bach and Schrag use the observed 10-year risk of death among participants in the CPS-II and the British Physicians’ Study to suggest that our estimates (at least for lung cancer) may be slightly high: for a 70-year-old male never smoker, we reported a 12 in 1000 risk, compared with four in 1000 using those external standards. The problem here, however, is generalizability. Participants in both studies were, on average, healthier, of higher socioeconomic status, and more often white than the average American. It is not surprising that the risk of death observed in these selected populations would be a little lower than that of the general U.S. population. In fact, the Surgeon General’s reports recognize this lack of generalizability—their calculations of lives lost from smoking use only the relative risks generated from CPS-II and then apply these to the population risks from the multiple cause of death file (3), just as our calculations did.

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