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## LETTERS

### Medical Exchanges

Secretary of Health, Education, and Welfare Joseph Califano's efforts to decrease the supply of physicians may have even further repercussions than suggested in R. Jeffrey Smith's article (News and Comment, 16 Feb., p. 630) because the asserted oversupply of physicians is being used as an argument to further discourage foreign medical study by Americans and will doubtless serve as an argument for further increasing the stringency of visa issuance to physicians from other countries. As with most efforts to artificially limit people's choice of occupation, there is a serious chance of throwing out the baby with the bath water. The baby in this case is the mass of physicians from Europe and elsewhere who are as fully qualified as American physicians who would come to the United States for residencies, research, or other training but who will be unable to do so because of visa and licensing difficulties. American medicine has benefited enormously from nonimmigrant medical exchanges; at one time it was even modish for Americans to train abroad. The vigilantes of medicine who would eliminate those underqualified physicians who hope to reap the profits of fee system medicine may also serve to isolate American medicine from the free exchanges of skills and information that have been so important to all concerned in the past. I have no doubt that medical care can only benefit from carefully scrutinizing each practitioner, but with the understanding that other countries have succeeded in producing physicians as qualified as our own.

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### "Low-Risk" Cigarettes:

#### The Debate Continues

In her article of 1 September 1978 (News and Comment, p. 795), Jean L. Marx quotes briefly from our previous letter to *Science* regarding Gio B. Gori's article (17 Dec. 1976, p. 1243) on "low-risk cigarettes." A later article (*I*) builds on the erroneous statistical foundation of the first and includes a misleading table of "critical levels" for low tar and nicotine cigarettes.

Gori's fundamental conceptual error is

equating a (incorrectly computed) lack of statistical significance with the absence of a substantive effect. This is stated by Gori and Lynch (*I*, p. 1256): "The inability to verify this reduced risk might lead to its being considered socially tolerable." By their analysis the risk to the smoker of "critical levels" of cigarettes may be up to 100 percent greater than the risk to the nonsmoker.

In the *Science* article the statistical methodology to which we objected is contained in reference 45. We set forth here some of the methodological errors we believe were made in the handling of Harold A. Kahn's data (2) relating the relative risks of cancer of the lung and bronchus to the number of cigarettes smoked per day.

1) The expression for  $R$  (Gori's equation 2) refers to the risk to a smoker of  $X$  cigarettes per day relative to the nonsmoker (0 per day), that is,  $R$  is the "relative risk." His equation 2 gives  $R = 1.388$  when  $X = 0$ . This says that the risk of a person who smokes zero cigarettes per day (surely a nonsmoker) is 38.8 percent greater than the risk to a nonsmoker! Anyone capable of doing arithmetic should be disturbed by this result and should look with suspicion upon any conclusions drawn from an equation which yields such an answer.

2) In fitting his equation, Gori (3) graphs the relative risk for smokers of one to nine cigarettes per day versus ten, rather than the traditional class interval midpoint—five. He similarly graphs other points at the upper boundary of the interval of cigarette usage. That is, his graphing technique says that the average number of cigarettes consumed per day by persons who consume one to nine cigarettes per day is ten. This has the effect of greatly underestimating the risk of smoking any given number of cigarettes, that is, underestimating the slope of the dose-response curve.

3) Gori fits a quadratic equation to these data where a straight line is appropriate (that is, the quadratic coefficient in his equation is not significantly different from zero and hence should not be included). This inflates the variability of the interpolated values of the relative risk thereby increasing the estimate of number of cigarettes which may be smoked without a "significant" effect. In fact, for the properly fitted straight line and the correct "significance" computations, any number of cigarettes, however small, will yield a "significant" increase in cancer risk. The true "critical" daily number of cigarettes is zero.

The straight line that best fits these data has the equation  $R = 1 + 0.53 X$ ,

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where  $X$  is the number of cigarettes smoked per day. (When  $X = 0$ ,  $R = 1$ , which is what the relative risk to a nonsmoker must be.) This yields the following interpolated increases in risk associated with various values of daily cigarette usage.

Daily cigarette usage	Increase in risk compared to that of a nonsmoker (%)
2	106
1	53
0.2	11
0.1	5

That is, smoking two cigarettes per day is associated with an estimated increase in cancer risk of 106 percent, one cigarette per day with a 53 percent increase, and so forth. Gori states in his article that for these data "the critical value lies between 1 and 2 cigarettes per day." Marx reports that "Gori says he redid the analysis in accordance with the suggestions of Gart and Schneiderman and did not find enough difference in the results to warrant changing his conclusions." We find it conceivable that someone might assert that between a 50 to 100 percent increase of cancer is "tolerable" or "acceptable," even though we think these increases are very large and not acceptable to us.

Quite apart from the subjective judgment of what is "tolerable" or "acceptable," we think it important to understand how the estimates were developed and how erroneous techniques lead to untenable conclusions.

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## References and Notes

1. G. B. Gori and C. J. Lynch, *J. Am. Med. Assoc.* **240**, 1255 (15 September 1978).
2. H. A. Kahn, in *Epidemiological Approaches to the Study of Cancer and Other Chronic Diseases*, W. Haenszel, Ed. (Monogr. No. 19, National Cancer Institute, Rockville, Md., 1966), pp. 1-125.
3. Gori gives the intervals of cigarette usage as 1 to 10, 11 to 20, 20 to 39, and > 40. The original study (2, pp. 55-57) gives 1 to 9, 10 to 20, 21 to 39, and > 39.

Gart and Schneiderman address two separate articles, one by me published in *Science*, and the other in the *Journal of the American Medical Association (JAMA)* written with Cornelius J. Lynch (1).

1) They object to equation 2 of the *Science* article, which applies to mortality from lung cancer. They contend that the risk to a nonsmoker is 1, whereas this equation gives a higher estimated value.

However, a risk of 1 is valid for respondents who never smoked. In surveys of U.S. populations, those who report a zero cigarette consumption at any given time include ex-smokers, pipe and cigar smokers, and occasional cigarette smokers. Epidemiological data consistently show that ex-smokers, for example, have relative risks in excess of 1 for as long as 15 years after cessation, even though they report zero cigarette use during this time.

Therefore, estimates of risk in excess of 1 are a more plausible reflection of true conditions than a statistically imposed prejudice.

Moreover, equation 2 refers to an isolated lung cancer study and is given only as a procedural example. It is worth noting that the use of only epidemiological data on lung cancer would have resulted in higher critical values than those estimated in the conclusions of the *Science* article. For those conclusions, the more conservative data referring to overall mortality were used. The estimated risks for zero cigarette consumption in the equations fitted to these studies ranged from 0.95 to 1.06. Values such as these should be viewed as underestimates of reality, because the four studies analyzed (giving over 3 million person-years of experience, almost 50,000 deaths) included a large portion of former cigarette smokers (2) with an ascertained residual risk of 1.4 to 1.5.

2) Gart and Schneiderman object to the choice of the upper boundary of the reported cigarette use interval, as contrasted to using a "traditional class interval midpoint." The midpoint is used when additional information is not available, a practice sometimes referred to as the "equal distribution of ignorance." For tobacco use, however, additional epidemiological information is available. In particular, mean rates of reported tobacco use do not coincide with midpoints of class intervals but usually lie between the 80th and 95th percentiles of the intervals. A review of more than 30,000 respondents of epidemiological studies sponsored by the National Cancer Institute gives a typical frequency distribution of respondents to questions about cigarette use as exemplified in the figure below and indicates that most respondents regard multiple points of five as modes rather than upper boundaries. (Interval means are displayed within the triangles.) It is also well known that respondents to cigarette use questionnaires have an understandable tendency to significantly underreport their consumption (3). For these reasons, the upper boundary is a more realistic statistic

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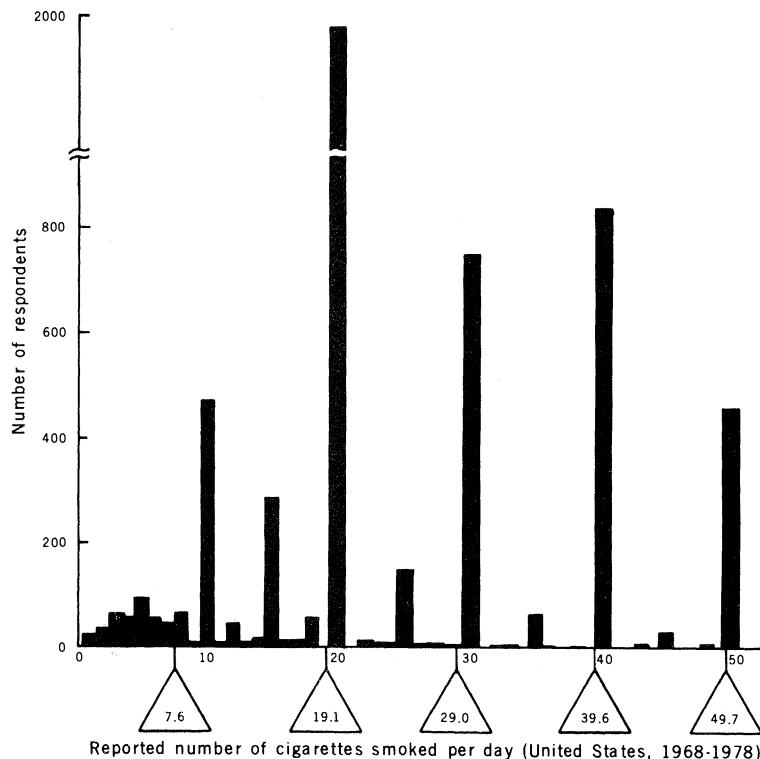
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than the midpoint for the purposes used. Instead of underestimating the risk, as Gart and Schneiderman contend, the use of upper boundaries gives a conservative overestimation of the risk.

3) Objection has been raised to the use of quadratic coefficients in the *Science* article's analysis, even when some of them are not significantly different from zero. It should be noted that there is no preferred statistical criterion for selecting which terms to include in a regression equation. For the equations in the *Science* article, the corrected coefficient of determination, and not significance, was the criterion used. This provides a close fit between reported and estimated data by reducing standard errors.

4) Gart and Schneiderman contend that the *JAMA* article "builds on the erroneous statistical foundation" of the *Science* article. In light of the preceding remarks, I believe that the *Science* article is not only statistically valid, but more important, is epidemiologically valid, as it addresses epidemiological realities of which Gart and Schneiderman may not be aware. The *JAMA* article uses only one statistic from the *Science* article—the average critical value of 2. By this is meant that a daily consumption of cigarettes having toxic yields equivalent to two of the average cigarettes sold in the United States during the late 1950's would not elevate the smoker's observable risk to mortality significantly above that of the average nonsmoker. Independent of the *Science* article, this critical value would

be valid because the four studies upon which it is based had a 0.3 nonresponse bias that results in overestimating the risks (2, p. 116). This bias is larger than the difference in risk between that of nonsmokers and that of two-cigarettes-a-day smokers. Thus it alone would preclude inferring a significant difference in risk between nonsmokers and two-cigarettes-a-day smokers. Consequently, the *JAMA* article could stand on its own merits independent of the statistical foundation of the *Science* article.

I believe the *Science* and *JAMA* articles combined present a realistic procedure for gradually reducing the levels of hazard and addiction for the millions of smokers who persist in their habit despite its known health consequences. Our conclusions were, and still are, that although this would not eliminate the risk to the smoker, it has the potential of reducing the current epidemic of diseases associated with smoking to a considerably less serious public health problem.

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### References

1. G. B. Gori and C. J. Lynch, *J. Am. Med. Assoc.* **240**, 1255 (1978).
2. U.S. Department of Health, Education, and Welfare, *Smoking and Health Report of the Advisory Committee to the Surgeon General of the Public Health Service* (Government Printing Office, Washington, D.C., 1964), p. 93.
3. K. E. Warner, *J. Am. Stat. Assoc.* **73**, 314 (1978).