Letters to the Editor

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Mesothelioma: An Unwarranted Causal Model

To the Editor: Robert Morgan has proposed a way to calculate the probability that exposure to asbestos in a particular year was the cause of an individual's mesothelioma.[1] He claims his model follows from a formula of Peto, Seidman, and Selikoff (PSS), who fit observed mesothelioma death rates.[2]

This work has been subsequently cited uncritically as using the PSS formula to determine the source of exposure leading to mesothelioma,[3] and—as Morgan recommends—has been used to try to apportion legal liability. In some cases, Morgan's model shifts the responsibility for damages to asbestos-exposed workers away from currently operating companies to bankrupt companies, depriving workers of compensation for illness. But the proposed causal model is scientifically flawed, and does not in fact follow from the work of Peto et al.

Three questionable assumptions are tacitly made in obtaining Morgan's model from the PSS formula. Different, equally arbitrary assumptions yield strikingly different conclusions. First, it is assumed that each worker's mesothelioma has exactly one cause that happened in just one year—ruling out cumulative or interactive causes. Because we do not know the exact mechanism for the development of cancer, the attribution of cause to a single exposure is open to question. Peto et al (who do not make this assumption) discuss various models of carcinogenesis, including multistage models. If, for instance, two stages of exposure to asbestos contribute to the development of cancer, or a higher concentration of fibers is necessary for a cell to go through a particular causal stage, the premise is simply wrong. Evidence that this assumption is wrong exists in the literature.[4]

Second, Morgan takes the probability that *any particular* exposure caused a worker's mesothelioma t years later to be proportional to the incidence of mesothelioma given by the PSS equation $n = bt^k$ in a population an equivalent number of years after *first* exposure. To understand the error in this assumption, refer to the example that Morgan cites of a former insulation worker diagnosed with mesothelioma in 1988, after being exposed to asbestos each year between 1942 and 1944 and again in 1950. The PSS formula approximates the incidence of mesothelioma among large samples of workers who were *first* exposed 46 years, 45 years, 44 years, or 38 years earlier. The members of this population may or may not have been exposed subsequent to their first exposures. Thus, the PSS formula might validly be used to estimate the frequency of observed mesotheliomas in 1988, 1987, 1986, or 1980, given that the first exposure of a population was in 1942. But there is no justification at all for correlating this data with the probability that a particular year of exposure to asbestos, say 1950, caused the worker's mesothelioma in 1988, because 1950 was *not* the worker's first asbestos exposure. Therefore Morgan's second assumption is unrelated to the PSS model; it is simply an arbitrary conjecture.

Morgan's third assumption is that the same values of b and k in the PSS formula apply to all of an individual worker's asbestos exposures, in determining the causal probability. But Peto et al note that the value of b varies from study to study and may be affected by fiber type and the intensity of worker exposure. Thus, Morgan's third assumption directly contradicts the best available information. According to Peto et al, "After exposures for up to 10 years, the risk [determined by the constant factor b] is likely to be roughly proportional to duration."[5] Likewise, k may vary within a range that Peto et al estimate.

All three of Morgan's assumptions bias the outcomes in the direction of apportioning causal probability toward earlier years. For instance, taking b to be constant for each worker over all years of exposure (contrary to the best available information) weights earlier years more heavily. Just to explore the consequences, we recalculated the probabilities for the worker in Morgan's example under two (equally arbitrary) alternative assumptions—first, we let b change from 1944 to 1950 within the range discussed by Peto et al, and second, we let both b and k change within the given ranges. The probability assigned to the year 1950 is .156 under Morgan's assumption, .375 under our first alternative, and .801 under our second alternative. But the alternate models are no more or less arbitrary than Morgan's.

TABLE 1
Causal Probabilities

Exposure	Morgan's Model	Alternate Model 1*	Alternate Model 2†
1942	.303	.225	.071
1943	.281	.208	.066
1944	.260	.192	.062
1950	.156	.375	.801

*Alternate model, in which just 1 of 3 arbitrary assumptions is changed. This model sets $k = 3.5$ and $b = 1.58 \times 10^{-8}$ from 1942 to 1944, and $k = 3.5$ and $b = 5.15 \times 10^{-8}$ in 1950.
†This model sets $b = 1.58 \times 10^{-8}$ and $k = 3.0$ from 1942 to 1944, and $b = 5.15 \times 10^{-8}$ and $k = 3.5$ in 1950. All values are within the range suggested by Peto et al.

Many different causal models may be *consistent* with an observed set of empirical data, but in general, causality cannot be *determined* merely from correlations or patterns in data, without controlled experimentation. The fact that a specific causal model is consistent with a particular data set does not demonstrate that it correctly attributes cause, nor exclude other models that also fit the data. But a scientifically viable causal model normally generates some predictions (under the assumption that it is correct) that can at least be *compared* with the empirical data to see whether the data are consistent with it or not. But Morgan's causal model, even if assumed to be true, generates no predictions at all that can be compared with the data on mesothelioma death rates or with the PSS formula. This in itself demonstrates that the model is unrelated to the PSS formula, and has no scientific claim to validity.

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2. Peto J, Seidman M, Selikoff IJ. Mesothelioma mortality in asbestos workers: implications for models of carcinogenesis and risk assessment. *Br J Cancer.* 1982;45:124-135.
3. Lamphear BP, Buncher CR. Latent period for malignant mesothelioma of occupational origin. *J Occup Med.* 1992;34:718-721.
4. Mark EJ, Shin DH. Asbestos and histogenesis of lung carcinoma. *Semin Diagn Pathol.* 1992; 9:110-116.
5. Peto J, Seidman M, Selikoff IJ. Mesothelioma mortality in asbestos workers: implications for models of carcinogenesis and risk assessment. *Br J Cancer.* 1982;45:132.

The Author Replies: Thank you for the opportunity of replying to the letter of Egilman et al, commenting on my paper published over 4 years ago.[1] Despite their deliberately political and inflammatory prose, I will respond to their scientific comments.

First, Egilman et al claim that my paper, "...does not in fact follow from the work of Peto et al." This is nonsense, as the Peto et al paper was the direct stimulus for my paper, and I would have been a plagiarist had I claimed credit for the mathematical model on which my paper was based. Readers familiar with the Peto et al model will immediately recognize the link.

I agree with the authors that my method assumes that exposure in any 1 year is sufficient to cause mesothelioma. This assumption is made on the basis of numerous papers that demonstrate that exposures of less than 1 year, when of sufficient intensity, are capable of causing mesothelioma.

I reject the criticism that my calculation of probability is simply arbitrary conjecture; my earlier publication speaks for itself and the "arbitrary conjecture" actually reflects simple probabilities. Although the example I provided was fictional, it is common practice to present fictional sample data to provide a basis for calculations. The b and k values were not arbitrary but were taken from the paper by Peto et al.

I agree with the authors that my paper does not direct the reader as to how to weight varying fiber types and doses. This is an instance in which the user of the model may decide to either vary the exponent used, or apply some weighting factor applied from knowledge of doses or fiber type.

In their table, Egilman et al generate a set of numbers by capriciously changing the b and k values for different times, with no data to support these changes. I will leave the readers to judge this "fun with numbers" approach.

Finally, to answer their last criticism, I make no claims that the Morgan model, as they call it, will predict mesothelioma death rates. I do believe that the precursor Peto model has been shown to be an accurate predictor.

By the way, I prefer to consider my method as an application of the Peto et al model, not as a new "Morgan model," however flattering that may be.

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Students' Perception of Occupational Medicine

To the Editor: I have been intrigued by the paper of Graber and colleagues[1] that reports the view of academic deans about environmental health curricula in US medical schools. This letter is intended to contribute to the debate about the current low profile of environmental and occupational medicine in medical schools by presenting some recent observations from amongst medical students in Italy.

Until 6 years ago, the course of Occupational Medicine (OM) was not compulsory for medical students. In the past, no more than 5% of students had an elective course in OM, and their attendance at the course was primarily because of personal interest in the discipline. The recent introduction of OM in the curriculum as a mandatory course might have caused uncertainty amongst the students as to the clear and correct identification of the discipline and its role in the formation of the profession.[2]

This consideration led me to carry out a survey to investigate students' perception of the discipline in the Medical School of the University of Modena in the academic year 1994-1995.