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Re: "Man-made vitreous fibers and workers' health: An overview of the epidemiologic evidence" by R Saracci, L Simonato.

by [Peterson R](#)

Refers to the following text of the Journal: [1982;8\(4\):234-242](#)

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Re: "Man-made vitreous fibers and workers' health: An overview of the epidemiologic evidence" by R Saracci, L Simonato. *Scand j work environ health* 8 (1982) 234–242.

In the December 1982 issue of the *Scandinavian Journal of Work, Environment & Health* Saracci & Simonato (4) have given an overview of the epidemiologic evidence on the effects of man-made vitreous fibers on workers' health.

The authors reached the following two conclusions from the overview:

1. "...the available evidence indicates that no long-term pathological effects on workers' health have been detectable under the conditions of exposure prevailing in the first 20 a or so after first exposure in the industry producing man-made vitreous fibers [p 240]."
2. "...the answer to the straight question 'Are man-made vitreous fibers fibrogenic or carcinogenic, or not, when inhaled by man?' is not yet in hand ... [p 240]."

These conclusions are wrong. In one of the investigations referred to in the review, evidence of pathological effects was found in the first 20 years after first exposure, and, in the two largest mortality studies referred to, there was a statistically significant ($p < 0.05$) excess mortality of respiratory cancer of 38 and 114 %, respectively, 30 years or more after first exposure.

One of the reasons for the authors' reaching wrong conclusions is that they drew too little attention to the "healthy worker effect." Another reason is that they distinguished between exposure to glass fibers and rockwool fibers. There are however no differences in the chemical, physical, or biological characteristics that could justify such a distinction.

Conclusion 1

To evaluate the hypothesis that exposure to man-made mineral fibers can cause non-malignant respiratory diseases such as chronic bronchitis, the authors referred to ten cross-sectional studies and seven mortality studies. In three of the cross-sectional studies a positive association was found; seven were nonpositive. In four of the mortality studies an excess mortality of nonmalignant respiratory disease was found; three were nonpositive.

Saracci & Simonato drew attention to the fact that: "All cross-sectional studies ... have been carried out on workers still employed, namely, on groups of 'survivors' in an industry with a majority of subjects exposed for not more than 20 a [p 237]." What they mean is that healthy worker selection could explain the number of nonpositive cross-sectional studies.

The authors did not, however, take healthy worker selection into consideration in their discussion of the mortality studies even though the matter was carefully treated in the largest mortality study by Enterline & Marsh (2).

Fig 1 shows the association, found in the study of Enterline & March (2), between the number of years after first exposure and the standardized mortality ratio of nonmalignant respiratory diseases. The standardized mortality ratio of persons with less than 10 years after first exposure was 33, a level statistically significantly lower ($p < 0.05$) than 100. This finding indicates a selection of workers with very healthy lungs into the mineral production industry. Similar results have been found by Bayliss et al (1).

Fig 1 also shows the association between duration of exposure, number of years after first exposure, and the standardized mortality ratio. Workers exposed less than 10 years had a ratio of 177 in the period 10–19 years after first exposure, workers exposed 10–19 years had a ratio of 165 20–29 years after first exposure, and work-

Fig 1. Association between duration of exposure to man-made mineral fibers, number of years after first exposure, and the standardized mortality ratio (SMR) of nonmalignant respiratory diseases (2). [SMR = observed mortality (obs or O) : expected mortality (exp or E)]

Fig 2. Association between number of years after first exposure to man-made mineral fibers and the standardized mortality ratio (SMR) (2). [SMR = observed mortality (obs) : expected mortality (exp)]

ers exposed 20–29 years had a ratio of 242 30 years or more after first exposure. All these standardized mortality ratios were statistically significant ($p < 0.05$). Enterline & March conclude on this base that: “This suggest that some workers may have been terminating because of respiratory problems and this is a reason for the lack of a direct relationship between duration of exposure and respiratory disease. This is one aspect of the healthy worker effect and clouds the meaning of self-determined exposure durations in epidemiologic studies [p 11].”

Before the risk of nonmalignant respiratory diseases in relation to exposure to man-made mineral fibers can be evaluated,

it is necessary to consider the mortality of workers who have terminated employment. As shown, workers exposed less than 10 years had a statistically significant excess mortality of nonmalignant respiratory diseases 10–19 years after their first exposure. The study showed therefore evidence of an excess risk of nonmalignant respiratory diseases even 10–19 years after first exposure. Saracci & Simonato’s first conclusion that: “... no long-term pathological effects on workers’ health have been detectable under the conditions of exposure prevailing in the first 20 a or so after first exposure in the industry producing man-made vitreous fibers [p 240],” is therefore wrong.

Conclusion 2

To evaluate the hypothesis that exposure to man-made mineral fibers can cause respiratory cancer in man, Saracci & Simonato refer to seven mortality studies. In the three smallest, including 416, 596 and 1,448 persons, the results were nonpositive. In the two medium-sized, including 4,399 and 2,576 persons, a nonstatistically significant excess mortality of respiratory cancer was found. The standardized mortality ratio was 170 and 140, respectively. In the two largest studies, including 16,730 and 25,468 persons, the corresponding ratio for respiratory cancer 30 years or more after first exposure was 138 and 214, respectively (2, 5). These ratios were statistically significant ($p < 0.05$).

The sizes of the studies referred to can explain why not all showed positive associations, and it is obvious that the two last-mentioned, and largest, studies must be considered as the most important. In one of these studies the association between the standardized mortality ratio and the number of years after first exposure was calculated. The association is shown in fig 2. It can be seen that the standardized mortality ratio increased with increasing numbers of years after first exposure.

The association between the cumulative exposure and the standardized mortality ratio has also been calculated. For persons with a cumulative exposure larger than 21.88 fibers/ml $\times$ months, the ratio was 159, ie, statistically significant ($p < 0.05$). For persons with a cumulative exposure of less than 21.88 fibers/ml $\times$ months, the ratio was 102.

The results of the aforementioned studies correspond to what would have been found if the workers had been exposed to asbestos fibers in equivalent doses and times (3) instead of to man-made mineral fibers.

In animal experiments it has been shown that man-made mineral fibers, like asbestos fibers, can cause mesothelioma after intrapleural or intraperitoneal application. As for asbestos fibers the response depends on the diameter and length of the fibers (6).

Therefore both experimental (animal) and epidemiologic evidence exists for the carcinogenic effects of man-made mineral fibers. The second conclusion made by

Saracci & Simonato, ie, that there are no answers to the question of whether man-made mineral fibers are carcinogenic to man, is therefore wrong. There is weighty evidence that man-made mineral fibers, like asbestos fibers, are carcinogenic in man.

References

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Authors' reply

We are not sure we fully understand Dr Petersen's arguments, except of course when he flatly states that the conclusions of our review of man-made vitreous fibers and workers health are wrong both in respect to chronic respiratory disease and respiratory cancer.

As to *chronic respiratory disease*, he starts by immediately merging the results

for mineral wool and fibrous glass plants in one of the two largest studies, ie, that of Enterline & Marsh (1) and finds that for workers employed for less than ten years the standardized mortality ratio of the interval 10–19 years from first employment is 177 ($p < 0.05$). This he considers sufficient to prove wrong our conclusion that "...no long-term pathological effects on workers' health have been detectable under the conditions of exposure prevailing in the 20 a or so after first exposure in the industry producing man-made vitreous fibers ... [p 240]." In fact, the finding just referred to proves nothing for the following reasons:

1. For the same subgroup of workers, ie, those employed for less than ten years, the standardized mortality ratio for the intervals 10–19, 20–29, and ≥ 30 years from first employment are 177, 154, and 130, respectively (the last not being statistically significant), showing a downward trend with time opposite to that expected if an effect related to occupational exposure were present.
2. More generally no trend with time from first employment nor with duration of employment is discernible if one tabulates the merged data (mineral wool plus fibrous glass plants) simultaneously according to these two criteria of classification. As already noted in our overview, the one discernible trend with duration of employment occurs for workers in mineral wool plants 30 years and more after first employment.
3. These considerations prevent the location of a pathological effect of the occupational environment, and of man-made vitreous fibers in particular, in the interval 10–19 years since first employment, when in fact there is not even enough evidence to assert that such an effect exists at any time. The purpose of this analysis should not be to pick up statistically significant standardized mortality ratios here or there, but, first and foremost, to interpret the whole pattern of data of a study in causal terms.

As to *respiratory cancer*, there is (fig 2 in Dr Petersen's letter) a trend towards increasing standardized mortality ratios with time since first employment for the merged data for mineral wool and fibrous glass plants in the Enterline & Marsh paper. However, if one tabulates the data by time from first employment and duration of employment, no relation with the latter emerges. In addition there is no clear relation with cumulative exposure to man-made vitreous fibers, contrary to Dr Petersen's statement. The cut-off point he chooses "a posteriori" (21.88 fibers $\times$ months/ml, which separates the observed deaths into 218 below and 29 above) tends to maximize the difference of the standardized mortality ratios, 102 below and 159 ($p < 0.05$) above the cut-off point, respectively. If, eg, a cut-off of 4.67 fibers $\times$ months/ml had been chosen (which leaves 155 deaths below and 92 above), the two standardized mortality ratios would become rather close, 102 and 114, respectively (neither being statistically significant). This point illustrates the arbitrary character of the dichotomy and offers scarce, if any, support for a relation with cumulative exposure. This statement is confirmed and made clearer by the original tables in the Enterline & Marsh paper.

For mineral wool plants the standardized mortality ratios of the four cumulative exposure classes (< 4.67 , $4.67-21.88$, $21.88-99.99$, and ≥ 100 fibers $\times$ months/ml) are 123, 174, 178, and 138, respectively. For the fibrous glass plants the standardized mortality ratios of the four classes of cumulative exposure (> 2.14 , $2.14-4.67$, $4.67-9.99$, and ≥ 10 fibers $\times$ months/ml) are 104, 93, 86, and 98, respectively. Thus, as to respiratory cancer, the arguments of Dr Petersen are wholly inadequate to change our conclusion, which he quotes, that "...the answer to the straight question 'Are man-made vitreous fibers ... carcinogenic, or not, when inhaled by man?' is not yet in hand" or to alter our other conclusion, which he does not mention, that the existing indications of possible effects (notably respiratory cancer) 20, 30, or more years after first employment are sufficient to require full attention and prompt further investigation to sort out the responsible factors, among which exposure to

man-made vitreous fibers is the first candidate.

The evidence for the carcinogenicity of asbestos may rightly be labeled as "weighty," to use Dr Petersen's own word. To rate on that scale the existing evidence for carcinogenicity of man-made vitreous fibers also as "weighty" denotes, before anything else, a major failure in applying the criteria by which scientific evidence, and epidemiologic evidence in particular, are evaluated and weighted.

To avoid being misunderstood on the possible practical implications of this scientific argument, we also wish to add that one should never wait for "weighty" evidence concerning man before intervening to control hazardous exposures.

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