Asbestos kills – no matter how you cut the data

Asbestos is a term referring to six naturally occurring silicate materials used commercially for their intrinsic properties of high tensile strength, heat and fire resistance, as well as acoustic and thermal insulation. The English name is derived from a Greek term meaning 'inextinguishable'.[1] Aside from its fire retardant properties, humans also discovered early on that asbestos fibres were strong enough to be woven - such that the traditional Chinese character for asbestos 石棉 actually means 'stone cotton'. Asbestos fibres occur in two natural configurations, amphibole and serpentine, with a derivative of the latter (chrysotile), accounting for around 95% of all asbestos used around the world.[2] Being more flexible than the amphibole forms, chrysotile asbestos was the most commonly used variant throughout the 20th Century - often as asbestos cement roofing, wall sheeting, water storage tanks and brake pads. Chrysotile mining began in Quebec, Canada, in the late 1870s,[3] and by the 1980s, consumption of asbestos products in the United States alone, had exceeded half a million tons per year.[4]

The inhalation of asbestos fibres causes several diseases including asbestosis, lung cancer and malignant mesothelioma.[1, 5, 6] The first medical presentation was recorded in the United Kingdom during the late 1890s, with the first case report of

asbestos-related disease being published in a medical journal in 1924.[7] As anatomical knowledge increased during the early 20th Century, scientific understanding of the intricate aspects of lung function had also progressed, in particular, a greater awareness of the human pleura - albeit that malignancies of the pleura, known as mesothelioma, were rarely seen in medical practice at that time.[8] By 1935 further evidence of the dangers of asbestos exposure had begun to emerge when another watershed report was published in the medical literature - this time an unusual case of lung carcinoma and asbestosis.[9] Continual advances in diagnostic technologies throughout the 20th Century, especially x-rays, helped facilitate more effective diagnosis of lung diseases with visible radiographic opacities, including asbestosis. By the 1950s in the US, more and more of these cases began to be seen in clinical practice.[4]

One such clinic was run by a middle-aged chest physician named Irving J. Selikoff (1915-1992), who had earlier made a name for himself in research by receiving the American *Lasker Award* in 1955 for his clinical trials of Isoniazid as a treatment for tuberculosis.[10] As a result, Selikoff was sophisticated in the ways of pulmonary medicine and well understood the intricacies of lung disease. When he opened a lung clinic in New Jersey during the late 1950s, Selikoff began to encounter a series of unusual illnesses among workers from a local asbestos plant.[11] This eventually led to a study involving around 1200 insulation workers in metropolitan New York, including clinical examinations to establish a diagnosis of asbestosis, as well as information on occupational exposure to asbestos for each individual. One of the most striking early observations was that workers who had been exposed to asbestos for less than 20 years displayed normal chest films. Among those who had

been exposed to asbestos for 20 years or more, most chest x-rays were *abnormal*, and in many cases, extensively so. This 20-year time lag between exposure and disease eventually became known as the '20 year rule'.[4]

Asbestos now ranks among the most heavily studied *Environmental and Occupational Health* (EOH) hazards of human history,[12] with Selikoff being one of the worlds' most influential asbestos researchers of the 20th Century.[11, 13, 14] His aforementioned '20 year rule' was based on the analysis of data from a study of New York insulation workers originally published in the *Bulletin of the New York Academy of Medicine* in 1981.[4] We have previously explored Selikoff's pioneering asbestosis data in two earlier articles which examined odds ratios, relative risk and visual interpretation of statistical significance.[15, 16] Part 3 of our series, published in this issue of the *Archives of Environmental & Occupational Health* (AEOH),[17] applies a new statistical measure called the *Aggregate Association Index* (AAI) to Selikoff's published research data, in order to elucidate some additional aspects of his original findings.

Understanding the potential relationship between workplace exposure and whether an individual subsequently contracts disease represents one of the cornerstones of occupational epidemiology.[18] A number of different statistical techniques can be used to analyse these potential associations, such as the calculation of odds ratios, correlations or chi-squared statistics – many of which are undertaken using 2x2 (row and column) matrices.[19] Despite this fact, however, the collection of data is rarely straightforward in EOH, and in many practical situations, one may have knowledge of the row and column totals but have little or no information on the value of the cells

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themselves. This may be because such data were not recorded at the time the study was taken, the data that was collected may have been unreliable or incomplete; or simply because the data that one needs to undertake a thorough analysis were not made public for reasons of confidentiality. In such situations, an analysis of aggregate data can be very useful for deriving a meaningful result from previously 'incomplete' datasets.

In our paper published in this issue of the AEOH,[17] we have demonstrated the application of a new statistical measure, the AAI, which can help elucidate associations between variables when only aggregate data is available. To do so we reanalyse some data from a classic exposure-versus-risk study originally published by Irving Selikoff in the 1980s.[4] One of Selikoff's original key findings was that a worker exposed to asbestos for at least 20 years is more likely to be diagnosed with asbestosis when compared to a worker exposed for less than 20 years. In our current analysis, we have demonstrated that, when the cell values are known, the association between onset of exposure to asbestos and the diagnostic status of asbestosis is positive, thereby statistically confirming the significance of Selikoff's original postulate using modern techniques. Similarly, and somewhat pioneeringly, we have also demonstrated that even if these cell values were *not* known, the 20 year rule still holds true.

It is important to remember that our current finding is more than just a statistical curiosity. It can now be added to an existing body of knowledge all pointing in the same direction - that asbestos kills. Indeed, there are no non-hazardous forms of the material and all types are now proven human carcinogens.[2] Much has been made of

the seemingly less-hazardous chrysotile type, even though it is also a proven human carcinogen and being 'less dangerous' than amphiboles hardly means safe.[12] Although asbestos has now lost its place in modern commerce to safer substitutes, the long lag-time between exposure and disease means that even in countries where its use is now banned, rates of asbestosis have continued to rise.[6] It is unfortunate that despite Selikoff's 20 year rule being proven again and again in theory as in practice, individuals continue to die.

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