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Occupational Exposures to Asbestos: Effects of Unregulated Fibers.

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Final Report

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Abstract

The objective of this project was to draw upon unique existing data for US asbestos workers for whom high-quality estimates of asbestos exposure have been derived by PCM and fiber-size specific estimates of exposure have been derived by TEM in order to estimate the effects of the unregulated fraction of fibers, estimate TEM-based policies that would yield a comparable mortality to that obtained under current OSHA standards, and, estimate alternative TEM-based policies that would yield lower mortality. Occupational standards for asbestos exposure in the US are based on visual counting of particles by phase contrast microscopy (PCM). Only fibers long and thick enough to reliably count using that method are regulated. However, in most occupational settings the majority of asbestos fibers are too small to count by PCM. If asbestos exposure estimates based upon PCM methods were strictly proportional to total exposure to all etiologically-relevant asbestos fibers then a policy that regulated asbestos exposure as measured by PCM might suffice to control etiologically-relevant occupational asbestos exposures. However, there is strong evidence that the proportion of asbestos fibers that are not counted by PCM varies by work activity, fiber quality, and other conditions. This issue has been raised repeatedly by workers and their advocates, who have argued for regulating exposure to asbestos using methods and rules that permit quantification of short (<5 μm) and thin (<0.25 μm) fibers, such as transmission electron microscopy (TEM) analysis of air samples. One obstacle to this has been that most occupational studies of asbestos workers have classified people based on PCM estimates of exposure. Regulators noted that it was unclear what level of exposure, as quantified by TEM, would be acceptable, since TEM estimates of the total number of fibers may not be well correlated with PCM estimates of fiber counts. First, we used hierarchical regression methods to estimate the effects of the unregulated fraction of fibers; second, we used G-methods to estimate TEM-based policies that would yield a comparable mortality to that obtained under current OSHA standards; and, finally we used G-methods to estimate alternative TEM-based policies that would yield less mortality than that obtained under current OSHA standards. The project applied innovative epidemiological methods to estimation of associations between occupational exposures and disease in settings of complex, protracted occupational exposure histories, and potential bias due to health-related selection out of employment.

Section One

Significant Findings

A Bayesian hierarchical regression analysis of US asbestos textile worker data was undertaken; and, a paper describing the findings from this pooled analysis is published {Hamra, 2017 #6007}. We estimated lung cancer risk associated with asbestos fibers of varying length and width, applying an order-constrained prior both to leverage external information from toxicological studies of asbestos health effects. While credible intervals for fiber size-specific risk estimates overlap, our results suggest that some unregulated asbestos fibers may be associated with increased incidence of lung cancer.

In addition, we have successfully completed a paper on application of G-estimation methods, titled "Asbestos standards based on light and electron microscopy: Impact of currently uncounted asbestos fibers on lifetime risk lung cancer". In that report we estimate the lifetime risk of lung cancer for exposure at the regulatory standard; and, we identify policies based on fibers counted using electron microscopy that yield similar lung cancer risk. Given exposure at the current standard, the estimated lung cancer risk was 7.33%, comparable to the risk expected under a standard of 1 fiber/ml counted using electron microscopy (7.30%). The lifetime risk of lung cancer under a standard of 0.1 fiber/ml counted by electron microscopy was estimated to be 7.10%. The results suggest standards based on electron microscopy that yield lung cancer risks that are comparable to, or lower than, that expected under the current standard.

Translation of findings

The work has led to developments for modeling of asbestos exposure-cancer data using a hierarchical model for studies of cancer among workers exposed to hazards that incorporates a prior based on toxicological evidence, as well as insights into use of G-methods for quantifying policy alternatives in terms of lifetime cancer risk. We identify standards based on TEM counting of fibers that yield comparable or lower mortality than current standards based on PCM fiber counting.

Usefulness of Findings

These findings illustrate how useful insights into the association between asbestos exposure and cancer mortality may be obtained via analysis of cohort data in which TEM methods are used characterize fiber dimensions. Modeling of the data via the hierarchical regression model can provide further stabilization of risk estimates; and, G-methods can address policy alternatives while addressing impacts of healthy worker survivor bias.

Section Two

Scientific Report

Background. While asbestos has been regulated by the US OSHA since 1971, asbestos exposure continues in the US due to ongoing importation of asbestos and due to the large asbestos exposure reservoir in US infrastructure that eventually will be removed during remediation, renovations, or demolition. The US Occupational Safety and Health Administration has estimated that 1.3 million workers in general industry continue to be exposed to asbestos in the United States. Significant production and use of asbestos is ongoing in middle-income industrial countries, including Brazil, India, China and Russia. Worldwide consumption of asbestos has been stable since the 1990s at roughly 2 million metric tons per year. Asbestos continues to pose important occupational hazards for workers in the US and worldwide; for example, Rushton et al. estimate that asbestos is responsible for 70% of the occupational cancer deaths in the construction industry.

Currently, airborne asbestos exposure is regulated in terms of concentration of asbestos fibers visually counted using phase contrast microscopy (PCM). Because visual counting of very short and very thin fibers is unreliable, only fibers at least 5 μm long with a width:length ratio of 3:1 are counted.

An alternative is to quantify asbestos fibers as counted by using transmission electron microscopy (TEM). In studies of airborne asbestos that use TEM, it has been found that the majority of airborne fibers are too small and thin to count by PCM. Although fiber characteristics vary between occupational settings, and by fiber type and grade, in prior studies as much as 90% of airborne fibers counted by transmission electron microscopy were short (<5 μm), thin (<0.25 μm) fibers that would not be counted using PCM methods. Of particular concern are long fibers that are too thin to be visible using PCM but are believed to be very hazardous when inhaled.

While workers and their advocates have argued for regulating exposure to asbestos using methods and rules that permit quantification of short (<5 μm) and thin (<0.25 μm) fibers, such as transmission electron microscopy (TEM) analysis of air samples, one obstacle has been the lack of empirical evidence to support a specific policy based on TEM exposure measures.

We draw on unique data resources developed from a cohort study of US asbestos textile workers for whom high-quality quantitative estimates of exposure to chrysotile, the most common form of asbestos used now and historically, have been derived based on standard PCM-based measures of exposure and fiber-size specific estimates of exposure have been derived based on TEM-methods applied to historical dust samples.

Specific Aims. We proposed three specific aims:

1. Employ hierarchical regression methods to estimate the effects of the unregulated fraction of asbestos fibers. Previous analyses estimated fiber size-specific effects one-at-a-time, yielding estimates of the effect of one fiber size group that were confounded by exposure to fibers of other sizes.

2. Employ G-methods to estimate TEM-based policies that would yield comparable lung cancer mortality to that obtained under current OSHA standards.

3. Employ G-methods to estimate alternative TEM-based policies that would yield less mortality due to lung cancer than that obtained under current OSHA standards.

Results. The South Carolina asbestos cohort includes 3072 men and women employed at an asbestos textile production plant for at least one month between 1 January 1940 and 31 December 1965 (Dement, Brown et al. 1994; Stayner, Smith et al. 1997); 1256 of the workers were white males, 1244 were white females, and 551 were nonwhite males. Workers were followed through December 31, 2001 to determine vital status and cause of death. Vital status through 1978 was determined using information from the Social Security Administration, the Internal Revenue Service, state driver's license files and vital statistics offices. Between 1979 and 2001, the National Death Index was used to obtain vital status. Persons who were confirmed as alive on January 1, 1979, with valid Social Security numbers and not shown to be deceased by the National Death Index between 1979 and 2001 were considered to be alive as of 2001. With follow-up through 2001 the study encompasses 118,513 person-years at risk with 63.8% of the cohort deceased, including 208 deaths due to respiratory cancers of which 198 are cancers of the trachea, bronchus and lung.

Dr. Richardson and collaborators have prepared two manuscripts reporting the findings that address our three aims. Manuscripts include the following: 1) a paper that present the results of hierarchical regression analyses; and 2) a paper that present the results of G-estimation analyses of lung cancer mortality to identify TEM-based policies that would yield comparable lung cancer risk, and lower lung cancer risk, than expected under current regulations.

Aim 1 involved hierarchical regression; results were addressed {Hamra, 2017 #6007}. When we applied a shared mean for the effect of all asbestos fiber exposure groups, the rate ratios for each fiber group per unit exposure appeared mostly equal. Rate ratio estimates for fibers of diameter <0.25 mum and length <1.5 and 1.5-5.0 mum were the most precise. When applying an order-constrained prior, we found that estimates of lung cancer rate ratio per unit of exposure to unregulated fibers 20-40 and >40 mum in the thinnest fiber group were similar in magnitude to estimates of risk associated with long fibers in the regulated fraction of airborne asbestos fibers. Rate ratio estimates for longer fibers were larger than those for shorter fibers, but thicker and thinner fibers did not differ as the toxicologically derived prior had expected. Aim 2 involved identifying TEM based policies that yielded comparable risk to that under PCM based rules;

results are addressed in the forthcoming paper (Richardson et al. forthcoming). Given exposure at the current standard, the estimated lung cancer risk was 7.33%; we found that comparable risk is expected under a standard of 1 fiber/ml counted using TEM (7.30%). Aim 3 involved identifying TEM based policies that yielded lower risk to that under PCM based rules; results are addressed in the forthcoming paper (Richardson et al. forthcoming). We found that the lifetime risk of lung cancer under a standard of 0.1 fiber/ml counted by TEM was estimated to be 7.10%, slightly lower than expected under exposure at the current PCM standard (i.e. 7.33%).

Conclusions. This work has directly contributed to understanding of occupational asbestos exposure health effects, particularly impact of fiber size and dimension through both development of novel methods and empirical data analyses.

Outcomes and outputs

The primary outcomes of this RO3 effort are publications (listed below). In addition, the work has led to increased awareness of occupational health issues related to fiber dimensions.

Additional outputs include use of this research as knowledge for additional research and in discussions of radiation protection. The work will be presented at a symposium at Society for Epidemiologic Research [Richardson DB. Asbestos policy for the 21st Century. Symposium "Putting the Implementation back into Implementation Science. Society for Epidemiologic Research (SER), June, 2017] and was presented at the US National Cancer Institute [Richardson DB. "Impact of currently uncounted asbestos fibers on lung cancer risk" Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology & Genetics, National Cancer Institute, Shady Grove, MD, 2016].

Publications (accepted, under review, and in preparation)

Hamra GB, Richardson DB, Dement J, Loomis D. Lung Cancer Risk Associated with Regulated and Unregulated Chrysotile Asbestos Fibers. Epidemiology 2017;28(2):275-280. PMID: 27922528

Richardson DB, Keil A, Cole SR, Dement J. Asbestos standards based on light and electron microscopy: Impact of currently uncounted asbestos fibers on lifetime risk lung cancer. Occupational and Environmental Medicine (under review).