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# **MORTALITY AMONG SHEET METAL WORKERS PARTICIPATING IN A RESPIRATORY SCREENING PROGRAM**

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## ABSTRACT

**Background** The Sheet Metal Occupational Health Institute Trust (SMOHIT) was formed in 1985 to examine the health hazards of the sheet metal industry in the U.S. and Canada through an asbestos disease screening program. This investigation updates findings concerning mortality patterns among screening program participants was undertaken and further investigates predictors of increased mortality due to lung cancer, mesothelioma, and COPD.

**Methods** A cohort of 17,345 individuals with 20 or more years in the trade and who participated in the asbestos disease screening program were followed for vital status and causes of death between 1986 and 2010. Data from the screening program included chest x-ray results by ILO criteria, spirometry, and smoking history. Standardized Mortality Ratios (SMR) by cause were generated using U.S. death rates and Cox proportional hazards models were used to investigate predictors of death due to lung cancer, mesothelioma, and COPD

**Results** A significantly reduced SMR of 0.83 (95% CI=0.81-0.85) was observed for all causes combined. Statistically significant excess mortality was observed for pleural cancers, mesothelioma, and asbestosis in the SMR analyses. In Cox models, which controlled for smoking, increased lung cancer risk was observed among workers with ILO scores of 0/1 (RR=1.10, 95% CI=0.86-1.39), with a strong trend for increasing lung cancer risk with increasing ILO profusion score greater than 0/0. Among workers with an ILO profusion score < 1/0, an FEV1 /FVC ratio less than 80% was associated with an increased risk for lung cancer. COPD mortality was predicted by increased interstitial markings on the chest x-ray, FVC below 70% of predicted, FEV1 below 70% of predicted, and an FEV1 /FVC ratio below 70%. The risk of death from cancers of the pleura and mesothelioma also were significantly increased among workers without radiological evidence of asbestosis or pleural abnormalities.

**Conclusions** Sheet metal workers are at increased risk for asbestos-related diseases. This study contributes to the literature demonstrating asbestos-related diseases among workers with largely indirect exposures and supports an increased lung cancer risk among workers with low ILO profusion scores.

**KEY WORDS:** sheet metal worker, construction, trades, mortality, cancer, lung cancer

## KEY FINDINGS

- Statistically significant excess mortality was observed for pleural cancers, mesothelioma, and asbestosis among workers participating in the Sheet Metal Occupational Health Institute Trust (SMOHIT) medical screening program, diseases associated with a history of asbestos exposure.
- After controlling for smoking, increased lung cancer risk was observed among workers with ILO profusion scores of 0/1, with a strong trend for increasing lung cancer risk with increasing ILO profusion score greater than 0/0.
- Among workers with an ILO profusion score < 1/0, an FEV1 /FVC ratio less than 80% was associated with an increased risk for lung cancer.
- COPD risk was predicted by increased interstitial markings on the chest x-ray, FVC below 70% of predicted, FEV1 below 70% of predicted, and an FEV1 /FVC ratio below 70%.
- The risk of cancers of the pleura and mesothelioma also were significantly increased among workers without radiological evidence of asbestosis or pleural abnormalities.

## **BACKGROUND**

Numerous studies have documented the health effects of occupational exposure to asbestos [Becklake, 1976; Nicholson et al., 1982; Selikoff et al., 1978; IARC, 2009; American Thoracic Society, 2004]. Based on the results of studies undertaken in the 1980s [Zoloth and Michaels, 1985; Selikoff and Lilis, 1991], the Sheet Metal Workers International Association (SMWIA) and the Sheet Metal and Air Conditioning National Association formed The Sheet Metal Occupational Health Institute Trust (SMOHIT) to examine the health impact of asbestos exposure in the sheet metal industry. This investigation updates prior reports on findings concerning mortality patterns among screening program participants, and further investigates predictors of increased mortality due to lung cancer, mesothelioma, and COPD.

Sheet metal work involves fabrication or installation of metal products, such as ventilation systems, metal roofing, and metal facades, as well as large-scale production of metal products, such as refrigerators and air conditioners. Sheet metal workers are primarily employed in the construction industry but have also worked in the railroad industry and shipyards, as well as in specialized sheet metal production shops. The craft of sheet metal work handled asbestos-containing materials through the use of gaskets, but at the same time for many years sheet metal workers in construction were exposed to asbestos while working in close proximity to insulation workers applying asbestos containing materials for fireproofing and insulation, by working on or around beams that had been previously fireproofed with asbestos, and by renovating asbestos-insulated metal ventilation systems [Williams et al., 2007]. Very high levels of airborne asbestos fibers were measured during spray application of asbestos before 1973 [Paik et al., 1973], when this application method was banned.

Prior analyses have examined the prevalence of asbestos-related diseases among this cohort of sheet metal workers [Welch et al., 1991; Welch et al., 1994; Welch et al., 2007]. Welch and colleagues [2007] reported that among 18,211 individuals 10.4% had radiographic findings consistent with asbestosis and 21.7% had pleural scarring; the prevalence of asbestos-related radiographic change increased with years worked and with any shipyard work. In a study of mortality in this same cohort [Dement et al., 2009] statistically significant excess mortality was observed for pleural cancers, mesothelioma, and asbestosis. Standardized mortality ratios for both lung cancer and COPD increased consistently and strongly with increasing ILO profusion score. Here we report an extended follow-up of this same group of workers.

## **MATERIALS AND METHODS**

### **Cohort Definition**

We have previously presented mortality results for this cohort with follow-up through 2004 [Dement et al., 2009]. The current analyses extended the mortality follow-up of this cohort through 2010 and readers are referred to the prior publication for details of the cohort and follow-up methods. Briefly, individuals who were members of the Sheet Metal Workers International Union for 20 years or more as of January 1, 1986 were invited to participate in a medical examination program provided by the Sheet Metal Occupational Health Institute Trust (SMOHIT). Previous reports on this population describe the methods in more detail and present the prevalence of asbestos-related disease on chest radiographs [Welch et al., 1991; Welch et al., 1994; Welch et al., 2007]. Components of the screening program included: 1) completion of an occupational and medical questionnaire, 2) a limited physical examination (blood pressure determination, examination of the heart and lungs, and examination for digit clubbing), 3)

spirometry, performed according to American Thoracic Society (ATS) guidelines [American Thoracic Society, 1987], and 4) PA and lateral chest radiograph, interpreted using the International Labour Office (ILO) classification for pneumoconiosis [International Labour Office, 1980]. Each chest x-ray was classified by one reader who was an A-reader, a B-reader, or a physician with proficiency in the use of the ILO classification but who was neither an A nor a B reader [Welch et al., 2007]. For the current analyses percent predicted FVC and FEV<sub>1</sub>/FVC ratio were calculated based on the prediction equations of Hankinson et al. [1999].)

The current study cohort included 17,345 individuals who were screened for asbestos related disease by chest x-ray at 62 sites nationwide, between 1986 and 2004. We excluded 1582 workers without sufficient demographic data vital status determination.

Two sources of information were used to obtain vital status and cause of death data: 1) records in the Sheet Metal National Pension Fund (SMNPF), and 2) the National Death Index (NDI). Records of the SMNPF were searched and members covered by this plan and those receiving pension benefits or still actively contributing toward their pension as of December 31, 2010 were considered alive. Workers with unknown vital status by match with the SMNPF and workers identified as deceased were followed to identify additional deaths and causes of deaths through December 31, 2010 using the NDI Plus system [Bilgrad, 1995], maintained by the National Center for Health Statistics (NCHS). Record linkage with the NDI was accomplished using probabilistic scores assigned by the NDI and recommended cut-off scores by class for records without a perfect match [Horm, 1996; NCHS, 2013]. We assumed that workers not identified as deceased by the SMNPF or the NDI were still alive as of December 31, 2010 as the NDI provides virtually complete ascertainment of deaths among men and among employed women [Boyle and Decouflè, 1990; Stampfer et al., 1984].

The study was conducted in accord with the recommendations of the Helsinki Declaration (World Medical Association 1975) and was approved by the IRB of CPWR. Each participant signed an informed consent to permit this use of data collected in the examinations.

### **Cohort Mortality Analyses**

The Life Table Analysis System (LTAS.Net Version 3.0.3) developed by the National Institute for Occupational Safety and Health (NIOSH) [Steenland et al., 1990; Robinson et al., 2006] was utilized to compute cause-specific Standardized Mortality Ratios (SMRs), comparing the mortality experience of the cohort to that of the U.S. national population for 119 causes of death, were calculated adjusting for age, race, sex, and calendar year. The chest x-ray date was selected as the starting point for person-years accumulation for each cohort member and person-years accumulated until death or the study cut-off date of December 31, 2010. SMRs were calculated as the ratio of observed to expected deaths and 95% confidence intervals for SMRs were computed assuming that the observed number of deaths in the cohort is a Poisson random variable. The NIOSH LTAS uses the Byar approximation when the number of cases is six or more and the exact Poisson confidence interval when the number of cases was fewer than five [Rothman and Boise, 1979; NIOSH, 2011]

In addition to overall results for the entire cohort, we investigated mortality for selected causes by time since entry into the sheet metal trade, ILO parenchymal profusion category, and presence or absence of pleural changes. Parenchymal profusion categories were group into four categories

as was done by Cullen et al. [2005]. A pleural abnormality was defined as bilateral pleural thickening or plaques, with or without calcification [Cullen et al., 2005]. .

### **Multivariate Modeling of Lung Cancer, Mesothelioma, and COPD Mortality Predictors**

Within the overall cohort, further analyses were undertaken to examine the association between chest x-ray readings, spirometry, work history, and smoking and mortality due to lung cancer, mesothelioma, and COPD. Analyses of the relationship between chest film changes and lung cancer mortality were restricted to Caucasian males with 20 or more years of work in the sheet metal trade and having data on other covariates considered in the models. Females and other race groups were excluded from these analyses due to small numbers. In the main analyses, only workers having spirometry meeting ATS criteria for repeatability between maneuvers were included. Other investigators have suggested that exclusion of workers not meeting reproducibility criteria could introduce bias through exclusion of workers with accelerated loss of lung function [Eisen et al., 1984]. To investigate this issue, we conducted additional sensitivity analyses to determine effects of eliminating workers with spirometry not meeting ATS criteria.

Stratified Cox proportional hazards models were used to obtain lung cancer, mesothelioma, and COPD relative risks and 95 percent confidence intervals. The time axis in these models was the time from the initial screening examination to death due to diseases being studied or the last date that the worker was known alive. Stratified Cox models were fit with strata defined by smoking status at examination (never, past, and current) and covariates considered in the baseline models for each disease included pack-years of smoking (0, 1-19, 20-39, or  $\geq 40$  pack-years), age at start of follow-up (<50, 50-54, 55-59, 60-64, 65-69, 70-74, or  $\geq 75$  years), time since last work in the sheet metal trade (<5, 5-9, or  $\geq 10$  years), years of sheet metal work (20-24, 25-29, 30-34, or  $\geq 35$  years). Age, pack-years, and years of sheet metal work were modeled as grouped linear variables, constructed by assigning ordinal scores to categories based on category median values, and fitted as continuous variables in a manner similar to the study by Cullen et al. [2005]. Asbestos related chest radiographic predictors (presence of pleural abnormalities, and ILO parenchymal profusion category) and spirometry classifications for percent predicted FVC, percent predicted FEV<sub>1</sub>, and FEV<sub>1</sub>/FVC ratio ( $\geq 80$ , 70-79, 60-69, and <60) were investigated in the models as categorical variables and tests for trends across covariate category were performed by entering the covariate in the model as a grouped linear variable [Rothman and Greenland, 1998]. Pleural abnormalities were defined as bilateral pleural thickening or plaques, with or without calcification [Cullen et al., 2005].

After assessing the magnitude of the effect of each single variable on outcome, covariates that were significant in a univariate models (likelihood ratio p-values <0.1) were considered candidate variables for inclusion in multivariate models for each disease. Covariates were retained in the final models if statistically significant based on their Wald Type 3 chi-square or if their inclusion in the multivariate models changed the parameter estimates for pleural changes, parenchymal changes, or spirometry more than 10 percent. We restricted our analyses of spirometry predictors of lung cancer mortality to a sub-cohort with spirometry and with an ILO profusion score <1/0. For analyses of mesothelioma risk, cases included mesotheliomas (ICD-10) and pleural cancers (ICD-9) and parenchymal profusion was dichotomized into <1/0 and  $\geq 1/0$  due to small numbers in higher profusion categories. Analyses of COPD risks were restricted to the sub-cohort with spirometry and parenchymal profusion was dichotomized into <1/0 and  $\geq 1/0$  due to small numbers in higher profusion categories



Cox proportional hazards models were fit using PROC PHREG in SAS Version 9.3 [SAS, 2011]. The EXACT method of handling ties in PROC PHREG was used and the assumption of proportional hazards over the follow-up period was assessed with time-dependent covariates (the product of log-transformed time and the factor of interest). The ASSESS option for testing the proportional hazard assumption available in SAS Version 9.3 also was used for this purpose.

## RESULTS

There were 6,636 deaths as of December 31, 2010 among the 17,345 workers in the cohort (Table I). The cohort was almost entirely male and Caucasian with a mean age of 57.4 years at intake exam. Twenty-six percent of the cohort had never smoke cigarettes, and 25.4% were still smoking at the time of their intake exam. Radiographic parenchymal changes (profusion  $\geq 1/0$ ) were observed in 10.4% of workers and 21.7% had radiographic pleural changes. There were 808 deaths from lung cancer, 85 deaths from mesothelioma with an additional 11 deaths coded to malignant neoplasm of the pleura, and 461 deaths from COPD.

Standardized mortality ratio analyses showed a significant deficit for all causes of death (Table II). The SMR for malignant neoplasm of the trachea, bronchus, and lung was 1.03 which was not significantly elevated. The SMR for mesothelioma and for malignant neoplasms of the pleura were both significantly elevated. The SMR was significantly decreased for a number of causes of death, including heart disease and diseases of the respiratory system, with the exception of a significantly elevated SMR of 11.74 for asbestosis.

Table III displays mortality for selected causes of death by time since entry into the sheet metal trade, a variable that reflects both duration of exposure and latency. The SMR for lung cancer did not increase with time since entry into the trade. The vast majority of deaths from asbestosis, mesothelioma and malignant neoplasm of the pleura occurred after 40 years from first exposure. Table IV displays mortality by increasing amount of parenchymal disease on chest x-ray. The SMRs for lung cancer and asbestosis increased significantly with increasing profusion of parenchymal abnormalities. Table V shows that deaths from asbestosis were significantly higher among workers with pleural changes, but that for the other conditions pleural changes were not associated with a higher SMR.

Tables VI-IX present results of the Cox models for lung cancer, mesothelioma, and COPD. The relative risk for lung cancer death increased significantly as the profusion category on chest x-ray increased, and also increased with, age, smoking, years in sheet metal trade, and years since last sheet metal trade work at exam. A test for linear trend for lung cancer risk by profusion category was highly significant ( $P < 0.001$ ). There is no significant relationship between lung cancer deaths and the presence or absence of pleural abnormalities after parenchymal changes, smoking and other covariates were entered into the model. Among workers with an ILO profusion score  $< 1/0$ , an FEV1 /FVC ratio less than 80% was associated with an increased risk for lung cancer and the relative risk increased as the ratio decreased; there was no such relationship with FVC or FEV1.

Parenchymal profusion changes  $\geq 1/0$  and pleural changes were significantly associated with increased risk of mesothelioma mortality (Table VIII). Table IX death from COPD was predicted by increased interstitial markings on the chest x-ray, FVC below 70% of predicted, FEV1 below 70% predicted, and an FEV1 /FVC ratio below 70%. Age, smoking, years in the sheet metal

trade, and years since last sheet metal trade work at exam were also predictive of COPD mortality.

## **DISCUSSION**

Sheet metal workers who participated in this nationwide screening program had a reduced SMR overall compared to the US population, consistent with a healthy survivor effect. No overall increase in lung cancer mortality was observed among this cohort when compared to the US population; however, SMR analyses revealed excess mortality for mesothelioma, malignant neoplasm of the pleura, and asbestosis. Additionally, the SMR analyses demonstrated significant excess risk for lung cancer and COPD among workers with parenchymal changes  $\geq 1/0$  in profusion. The SMR was significantly elevated for pleural cancers, mesothelioma, and asbestosis among workers who did not have parenchymal changes. Cox proportional hazards models controlling for smoking confirmed the excess risk of lung cancer among workers with a profusion score  $\geq 1/0$  and provided compelling evidence for excess lung cancer risk among workers with parenchymal profusion scores  $<1/0$  on the ILO scale.

In addition to smoking and abnormal pulmonary function, which are known risk factors for COPD mortality, both increased interstitial markings on chest x-ray and years in the sheet metal trade were also predictive of death from COPD. These findings suggest a relationship between asbestos exposure and death from COPD. Previous research has shown that asbestos exposure is associated with obstructive disease on lung function testing [ATS, 2004, Dement, et al., 2010]. Exposure to dust, fumes, gases, and vapors is now recognized as a cause of COPD, and of mortality from COPD among construction workers [Bergdahl, 2006]; asbestos is an important component of the dust exposure.

It is well accepted that workers with exposure to asbestos sufficient to cause radiographic changes consistent with clinical asbestosis are at extremely high risk of lung cancer [Coutts et al., 1987; Berry, 1981; Roggli, 1990; Cookson et al., 1985; Liddell and McDonald, 1980; Huuskonen, 1978; Finkelstein et al., 1981; Reid et al., 2005, Reid 2006; Oksa et al., 1997; Karjalainen et al., 1999; Markowitz et al., 2013]. Consistent with the current study, increased lung cancer risk also has been observed among workers without radiological evidence of asbestosis [Markowitz, et al., 2013; Reid, 2006; Wilkinson et al., 1995; Finkelstein, 2010; Anttila et al. 1993; Cullen et al., 2005]. Cullen et al. [2005] conducted a follow-up study of 4060 men with heavy asbestos exposure who participated in a  $\beta$ -carotene and retinol efficiency trial. Parenchymal changes on radiograph were associated with progressively increasing lung cancer risk and workers with a parenchymal profusion of 0/1 were found to have a lung cancer relative risk of 1.48 (0.99-2.22) compared to workers without parenchymal changes. Additionally, the risk of lung cancer increased steadily by duration of heavy asbestos exposure among workers without chest x-ray evidence of asbestosis. Reid reported similar findings in a study of former workers and residents of the Wittenoom mine, finding that both radiographic asbestosis and asbestos exposure were significantly associated with an increased risk of lung cancer, and there was an increased risk of lung cancer reported specifically in those without asbestosis. The most recent study to report on this issue comes from an updated analysis of the North American insulator cohort [Markowitz et al., 2013]. The authors reported that asbestos exposure without radiographic evidence of asbestosis in non-smokers raise the risk of lung cancer by 3.6 fold, and that asbestosis further doubled the lung cancer mortality risk.

Although prior research had found a relationship between the presence of pleural plaque and lung cancer mortality [Loomis et al., 1989; Hillerdal, 1994; Karjalainen et al., 1999; Cullen et al., 2005; Ameile et al, 2011] our study did not find an excess lung cancer risk among workers with pleural changes after adjustment for other model covariates including duration of sheet metal trade work, smoking, presence of parenchymal changes, and time since last sheet metal work at exam. Our failure to find an independent effect of pleural changes on the risk of lung cancer is most likely due to the nature of our cohort, consisting of older workers with 20 or more years of sheet metal work. The prevalence of pleural changes increased markedly with age in our cohort with a low of 9.5% among workers less than 55 years of age to 43.8% among workers older than 70 years. A logistic model (not shown) found both age and duration of sheet metal work to be strong predictors of pleural changes ( $p < 0.001$ ) thus control for both age and years of sheet metal work in our Cox lung cancer models diminished the effects of pleural changes. The presence of pleural plaques may serve as a marker for a higher cumulative asbestos exposure, thus our inability to detect a pleural effect may be due to the requirement that workers have 20 or more years in the sheet metal trade for entry into our cohort, thereby diminishing availability of a reference group with low cumulative asbestos exposure.

One limitation of this study is that the radiologic interpretation and the classification of smoking status were determined at the time of the clinical exam, which could have preceded the date of death by more than a decade. It is possible that some of the workers who were categorized as without asbestosis could have developed parenchymal disease in the interim period. Prior analysis within this same cohort found that only 5% had progression from a normal chest x-ray to one classified as 1/0 or higher over a mean of 9 years [Welch et al., 2007], so misclassification of asbestosis is unlikely to explain the results.

The current study provides additional evidence that workers who experienced largely intermittent and indirect exposure to asbestos are at increased risk of asbestos-related diseases and at risk for COPD. The risk of lung cancer risks increased sharply with parenchymal profusion score; however, the study provided compelling evidence for increased risk among workers without radiographic asbestosis. The risk of cancers of the pleura and mesothelioma also were significantly increased among workers without radiological evidence of asbestosis or pleural abnormalities. Our study has several strengths including a large population with chest x-ray data classified by ILO criteria, and smoking histories on each member of the cohort. Nonetheless, our study is limited by a strong healthy survivor effect and an inability to address risks for workers who worked less than 20 years. While our analyses controlled for smoking, it is impossible to entirely exclude a contribution by other unmeasured risk factors such as welding fumes or other occupational lung carcinogens. However, confounding by these unmeasured exposures is unlikely to explain the steep and consistent patterns observed by profusion score.

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**Table I: Sheet Metal Cohort Demographics and Vital Status**

<b>Characteristic</b>	<b>Total Cohort</b>	<b>Lung Cancer Deaths</b>
Number of Workers	17,345	808
Total Deaths, December 31, 2010	6,636	---
Percent Male	99.8%	100%
Percent Caucasian	99.2%	99.4
Age at Intake Exam (Mean, (SD))	57.4(8.7)	61.2 (7.7)
Smoking Status at Intake Exam (No. (%)) <sup>1</sup>		
Never Smoked	26.0%	6.6%
Past Smoker	48.6%	42.7%
Current Smoker	25.4%	50.7%
Smoking Pack-Years for Ever Smoked (Mean, (SD))	32.3 (22.4)	44.3 (24.4)
Years of Sheet Metal Trade Work (Mean, (SD))	31.9 (7.2)	33.5 (7.7)
Prevalence of Radiographic Parenchymal Changes <sup>2</sup>	10.4%	19.7%
Prevalence of Radiographic Pleural Changes <sup>3</sup>	21.7%	26.1%

<sup>1</sup> 24 workers missing smoking data

<sup>2</sup> ILO profusion of small irregular shadows in the lung parenchyma  $\geq$  category 1/0

<sup>3</sup> Any notations of positive findings in sections 3A-D of the NIOSH ILO coding form



**Table II: Sheet Metal Worker Overall Mortality**

Cause of Death	Obs.	Exp.	SMR	95% CI	
				Lower	Upper
<b>All Causes</b>	6636	7972.54	0.83**	0.81	0.85
<b>All Cancers</b>	2224	2271.73	0.98	0.94	1.02
MN buccal & pharynx	31	38.33	0.81	0.55	1.15
MN lip	1	0.45	2.23	0.06	12.45
MN tongue	6	8.92	0.67	0.25	1.46
MN other buccal	12	9.77	1.23	0.63	2.14
MN pharynx	12	19.19	0.63	0.32	1.09
MN digestive & peritoneum	475	540.23	0.88**	0.80	0.96
MN esophagus	60	73.81	0.81	0.62	1.05
MN stomach	51	51.82	0.98	0.73	1.29
MN intestine	139	184.96	0.75**	0.63	0.89
MN rectum	28	37.04	0.76	0.50	1.09
MN biliary, liver, gall bladder	58	68.52	0.85	0.64	1.09
MN pancreas	131	117.79	1.11	0.93	1.32
MN peritoneum, other & unspecified sites	8	6.29	1.27	0.55	2.51
MN respiratory	839	812.78	1.03	0.96	1.10
MN larynx	15	23.21	0.65	0.36	1.07
MN trachea, bronchus, lung	808	784.86	1.03	0.96	1.10
MN pleura	11	1.48	7.42**	3.70	13.27
MN other respiratory	5	3.23	1.55	0.50	3.62
MN breast	5	3.07	1.63	0.53	3.80
MN female genital organs	0	0.20	0.00	0.00	18.28
MN male genital organs	179	225.30	0.79**	0.68	0.92
MN urinary	110	132.48	0.83	0.68	1.00
MN kidney	49	60.02	0.82	0.60	1.08
MN bladder & other urinary site	61	72.46	0.84	0.64	1.08
MN other & unspecified sites	350	291.14	1.20**	1.08	1.33
MN bone	2	3.38	0.59	0.07	2.14
MN melanoma	30	37.20	0.81	0.54	1.15
MN other skin	14	13.22	1.06	0.58	1.78
MN mesothelioma	85	11.58	7.34**	5.86	9.08
MN connective tissues	7	11.57	0.60	0.24	1.25
MN brain & other nervous	48	48.47	0.99	0.73	1.31
MN eye	1	1.02	0.98	0.02	5.45
MN thyroid	3	4.34	0.69	0.14	2.02
MN other & unspecified sites	160	160.35	1.00	0.85	1.17
MN lymphatic & hematopoietic	235	228.19	1.03	0.90	1.17
Hodgkin's disease	5	4.21	1.19	0.39	2.77
Non-Hodgkin's lymphoma	97	92.40	1.05	0.85	1.28
Multiple myeloma	43	42.73	1.01	0.73	1.36
Leukemia	90	88.86	1.01	0.81	1.24
<b>Benign &amp; unspecified nature neoplasms</b>	18	27.05	0.67	0.39	1.05
<b>Diseases blood &amp; blood-forming organs</b>	31	39.17	0.79	0.54	1.12
<b>Diabetes mellitus</b>	112	220.61	0.51**	0.42	0.61
<b>Mental &amp; psychiatric disorders</b>	107	136.79	0.78**	0.64	0.95
Alcoholism	13	22.64	0.57*	0.31	0.98
Other mental disorders	94	114.15	0.82	0.67	1.01

<b>Nervous system disorders</b>	249	263.28	0.95	0.83	1.07
<b>Heart diseases</b>	1871	2486.51	0.75**	0.72	0.79
<b>Other diseases of the circulatory system</b>	509	645.79	0.79**	0.72	0.86
<b>Diseases respiratory system</b>	743	839.70	0.88**	0.82	0.95
Acute resp. infection, except. flu, pneumonia	3	1.22	2.46	0.51	7.19
Influenza	3	2.76	1.09	0.22	3.18
Pneumonia	129	196.57	0.66**	0.55	0.78
COPD	461	485.42	0.95	0.86	1.04
Asthma	5	7.28	0.69	0.22	1.60
Asbestosis	48	4.11	11.68**	8.61	15.48
Silicosis	0	0.68	0.00	0.00	5.44
Other pneumoconiosis	1	4.00	0.25	0.01	1.39
Other respiratory diseases	93	137.67	0.68**	0.55	0.83
<b>Diseases digestive system</b>	194	267.43	0.73**	0.63	0.84
<b>Diseases skin &amp; subcutaneous</b>	5	8.21	0.61	0.20	1.42
<b>Diseases musculoskeletal &amp; connective</b>	14	23.02	0.61	0.33	1.02
<b>Diseases genito-urinary system</b>	109	162.66	0.67**	0.55	0.81
<b>Symptoms &amp; ill-defined conditions</b>	39	59.32	0.66**	0.47	0.90
<b>Transportation injuries</b>	62	71.80	0.86	0.66	1.11
<b>Falls</b>	63	56.42	1.12	0.86	1.43
<b>Other injury</b>	56	75.67	0.74*	0.56	0.96
<b>Violence</b>	65	90.62	0.72**	0.55	0.91
<b>Other &amp; unspecified causes</b>	164	206.96	0.79**	0.68	0.92

\* Two-Sided P < 0.05 \*\* Two-Sided P < 0.01

**Table III: Sheet Metal Worker Mortality by Time since Entry into Sheet Metal Trade**

Disease Category	Time Since Trade Entry (Years)	Obs.	Exp.	SMR	95% Confidence Limits	
					Lower	Upper
Lung Cancer	20 to 29	31	28.18	1.10	0.75	1.56
	30 to 39	142	144.32	0.98	0.83	1.16
	40-49	309	307.80	1.00	0.90	1.12
	50+	326	304.47	1.07	0.96	1.19
MN Pleura	20 to 29	1	0.08	12.15	0.31	67.71
	30 to 39	1	0.32	3.10	0.08	17.25
	40-49	6	0.62	9.73**	3.57	21.17
	50+	3	0.46	6.51*	1.34	19.02
Mesothelioma	20 to 29	1	0.13	7.54	0.19	42.02
	30 to 39	7	1.09	6.43**	2.58	13.24
	40-49	36	3.66	9.84**	6.89	13.63
	50+	41	6.70	6.12**	4.39	8.31
COPD	20 to 29	7	11.67	0.60	0.24	1.24
	30 to 39	29	53.80	0.54**	0.36	0.77
	40-49	131	157.35	0.83**	0.70	0.99
	50+	294	262.54	1.12	1.00	1.26
Asbestosis	20 to 29	2	0.08	24.83**	3.01	89.69
	30 to 39	4	0.36	11.13**	3.03	28.50
	40-49	11	1.19	9.23**	4.60	16.52
	50+	31	2.48	12.51**	8.50	17.75

\* Two-Sided P < 0.05    \*\* Two-Sided P < 0.01

**Table IV: Sheet Metal Worker Mortality by Chest X-Ray Parenchymal Category**

Disease Category	Parenchymal Change Category	Obs.	Exp.	SMR	95% Confidence Limits	
					Lower	Upper
Lung Cancer	0/- to 0/1	649	693.46	0.94	0.87	1.01
	1/0 to 1/2	143	86.85	1.65**	1.39	1.94
	2/1 to 2/3	14	4.28	3.27**	1.79	5.48
	3/2 to 3/+	2	0.26	7.58	0.92	27.38
MN Pleura	0/- to 0/1	10	1.27	7.89**	3.78	14.51
	1/0 to 1/2	1	0.20	4.92	0.12	27.40
	2/1 to 2/3	0	0.01	0.00	0.00	300.99
	3/2 to 3/+	0	<0.01	0.00	0.00	6087.99
Mesothelioma	0/- to 0/1	69	10.37	6.65**	5.18	8.42
	1/0 to 1/2	16	1.16	13.85**	7.91	22.49
	2/1 to 2/3	0	0.04	0.00	0.00	82.29
	3/2 to 3/+	0	<0.01	0.00	0.00	1050.38
COPD	0/- to 0/1	356	423.03	0.84**	0.76	0.93
	1/0 to 1/2	92	58.90	1.56**	1.26	1.92
	2/1 to 2/3	12	3.31	3.63**	1.87	6.33
	3/2 to 3/+	1	0.18	5.52	0.14	30.74
Asbestosis	0/- to 0/1	27	3.58	7.54**	4.96	10.96
	1/0 to 1/2	18	0.50	35.96**	21.30	56.84
	2/1 to 2/3	3	0.03	116.75**	24.08	341.20
	3/2 to 3/+	0	<0.01	0.00	0.00	2446.02

\* Two-Sided P < 0.05    \*\* Two-Sided P < 0.01

**Table V: Sheet Metal Worker Mortality by Chest X-Ray Pleural Category**

Disease Category	Pleural Changes	Obs.	Exp.	SMR	95% Confidence Limits	
					Lower	Upper
Lung Cancer	No	597	585.39	1.02	0.94	1.11
	Yes	211	199.47	1.06	0.92	1.21
MN Pleura	No	7	1.05	6.66**	2.68	13.73
	Yes	4	0.43	9.25**	2.52	23.68
Mesothelioma	No	53	8.72	6.08**	4.55	7.95
	Yes	32	2.86	11.19**	7.65	15.79
COPD	No	287	349.36	0.82**	0.73	0.92
	Yes	174	136.06	1.28**	1.10	1.48
Asbestosis	No	21	2.94	7.15**	4.42	10.93
	Yes	27	1.17	23.03**	15.17	33.51

\* Two-Sided P < 0.05    \*\* Two-Sided P < 0.01

**Table VI: Cox Model Chest Radiograph Predictors of Lung Cancer Mortality<sup>1</sup>**

Risk Predictor	Number in Model <sup>2</sup>	No. of Cancer Cases	Relative Risk <sup>2</sup>	95% Confidence Limits	
				Lower	Upper
Profusion Categories <sup>4</sup>					
0/- - 0/0	13066	526	1.00	Ref	Ref
0/1	1341	78	1.10	0.86	1.39
1/0 - 1/2	1559	131	1.48	1.22	1.80
2/1 - 2/3	95	12	2.83	1.59	5.04
3/2 - 3/+	7	2	3.96	0.98	16.05
Pleural Abnormalities					
Negative	13997	635	1.00	Ref	Ref
Positive	2071	114	0.91	0.74	1.11
Years Since Last Sheet Metal Trade Work at Exam					
<1	9880	366	1.00	Ref	Ref
1-5	2942	189	1.33	1.09	1.62
5-10	1884	102	1.21	0.91	1.60
>10	1362	92	2.00	1.43	2.79
Age <sup>3</sup>	16068	749	1.045	1.028	1.061
Smoking Pack-Years <sup>3</sup>	16068	749	1.026	1.021	1.031
Years in Sheet Metal Trade <sup>3</sup>	16068	749	1.026	1.010	1.042

<sup>1</sup> Cox proportional hazard analyses based on 16068 Caucasian males with 20 or more years in sheet metal trade and having data on other model covariates.

<sup>2</sup> Stratified Cox model with strata defined by smoking status (never, past, and current) and adjusted for pack-years of smoking (0, 1-19, 20-39, or  $\geq 40$  pack-years), age at start of follow-up (<50, 50-54, 55-59, 60-64, 65-69, 70-74, or  $\geq 75$  years), time since last work in the sheet metal trade at start of follow-up (<5, 5-9, or  $\geq 10$  years), years of sheet metal work beyond 20 years (20-24, 25-29, 30-34, or  $\geq 35$  years), presence of pleural abnormalities, and profusion category. A pleural abnormality was defined as bilateral pleural thickening or plaques, with or without calcification.

<sup>3</sup> Age, pack-years of smoking, and years of sheet metal work entered as grouped continuous variables.

<sup>4</sup> Test for trend across profusions categories,  $p < 0.0001$ .

**Table VII: Cox Model Spirometry Predictors of Lung Cancer Mortality<sup>1</sup>  
Sheet Metal Workers with ILO Profusion Scores <1/0**

Risk Predictor	Number in Model <sup>2</sup>	No. of Cancer Cases	Relative Risk <sup>2</sup>	95% Confidence Limits	
				Lower	Upper
FVC Percent Predicted <sup>4</sup>					
>=80	7354	226	1.00	Ref	Ref
70-79	1159	66	1.16	0.92	1.65
60-69	471	43	1.54	0.94	2.50
<60	240	28	1.73	0.95	3.16
FEV <sub>1</sub> Percent Predicted <sup>4</sup>					
>=80	7116	176	1.00	Ref	Ref
70-79	1020	70	1.58	1.13	2.22
60-69	47	556	1.38	0.88	2.17
<60	532	70	1.57	0.84	2.92
FEV <sub>1</sub> /FVC <sup>4</sup>					
>=80	3230	51	1.00	Ref	Ref
70-79	4110	137	1.44	1.03	2.00
60-69	1290	100	2.16	1.47	3.18
<60	594	75	2.79	1.69	4.63
Years Since Last Sheet Metal Trade Work at Exam					
<1	6088	186	1.00	Ref	Ref
1-5	1510	93	1.50	1.13	2.00
5-10	973	43	1.12	0.74	1.70
>10	653	41	2.01	1.24	3.25
Age <sup>3</sup>	9224	363	1.033	1.009	1.057
Smoking Pack-Years <sup>3</sup>	9224	363	1.017	1.009	1.025
Years in Sheet Metal Trade <sup>3</sup>	9224	363	1.021	0.999	1.044

Cox proportional hazard analyses based on 9224 Caucasian males with 20 or more years in sheet metal trade and having spirometry data and data on other model covariates. Only workers with spirometry meeting ATS reproducibility criteria were included.

<sup>2</sup> Stratified Cox model with strata defined by smoking status (never, past, and current) and adjusted for pack-years of smoking (0, 1-19, 20-39, or ≥ 40 pack-years), age at start of follow-up (<50, 50-54, 55-59, 60-64, 65-69, 70-74, or ≥ 75 years), time since last work in the sheet metal trade at start of follow-up (<5, 5-9, or ≥ 10 years), years of <sup>1</sup> sheet metal work beyond 20 years (20-24, 25-29, 30-34, or ≥ 35 years). Pleural abnormalities were not significantly associated with lung cancer in the adjusted model (p=0.38).

<sup>3</sup> Age, pack-years of smoking, and years of sheet metal work entered as grouped continuous variables.

<sup>4</sup> Test for trend across categories for percent predicted FVC (p=0.0472), FEV<sub>1</sub> (p=0.0971) and FEV<sub>1</sub>/FVC (p<0.0001).

**Table VIII: Cox Model Predictors of Mesothelioma Mortality**

Risk Predictor	Number in Model <sup>1</sup>	No. of Cancer Cases	Relative Risk <sup>2</sup>	95% Confidence Limits	
				Lower	Upper
Profusion Categories					
< 1/0	14407	72	1.00	Ref	Ref
≥ 1/0	1661	17	1.77	1.03	3.05
Pleural Abnormalities <sup>2</sup>					
Negative	13997	67	1.00	Ref	Ref
Positive	2071	22	1.79	1.09	2.94
Age <sup>3</sup>	16068	89	1.063	1.034	1.092

<sup>1</sup> Cox proportional hazard analyses based on 16068 Caucasian males with 20 or more years in sheet metal trade and having data on other model covariates. Smoking (p=0.24), years of sheet metal work beyond 20 years (p=0.73), years since last sheet metal work (p=0.41), percent predicted FVC (p=0.16), and percent predicted FEV<sub>1</sub>/FVC (p=0.19) were not significant predictors of mesothelioma mortality and were eliminated from the final model.

<sup>2</sup> An alternate model with pleural abnormalities defined as any indication of pleural change on the ILO recording form resulted in slightly greater risk (RR= 1.97, 95% CI=1.36-3.06).

<sup>3</sup> Age entered as grouped continuous variables.



**Table IX: Cox Model Predictors of COPD Mortality<sup>1</sup>**

Risk Predictor	Number in Model <sup>2</sup>	No. of COPD Cases	Relative Risk <sup>2</sup>	95% Confidence Limits	
				Lower	Upper
Profusion Categories					
< 1/0	9224	187	1.00	Ref	Ref
≥ 1/0	1032	59	1.39	1.03	1.88
FVC Percent Predicted <sup>4</sup>					
≥80	7979	102	1.00	Ref	Ref
70-79	1353	50	1.17	0.76	1.78
60-69	597	48	1.83	1.12	2.97
<60	327	46	1.61	0.96	2.70
FEV1 Percent Predicted <sup>4</sup>					
≥80	7678	58	1.00	Ref	Ref
70-79	1208	28	1.44	0.88	2.37
60-69	674	36	1.87	1.10	3.17
<60	696	124	325	1.71	6.19
FEV <sub>1</sub> /FVC <sup>4</sup>					
≥80	3512	14	1.00	Ref	Ref
70-79	4542	45	1.49	0.81	2.75
60-69	1471	54	3.36	1.78	6.35
<60	731	133	10.61	5.35	21.02
Years Since Last Sheet Metal Trade Work at Exam					
<1	6588	77	1.00	Ref	Ref
1-5	1723	61	1.75	1.21	2.54
5-10	1152	61	2.17	1.34	3.53
>10	746	47	3.29	1.89	5.75
Age <sup>3</sup>	10256	246	1.072	1.041	1.104
Smoking Pack-Years <sup>3</sup>	10256	246	1.022	1.012	1.033
Years in Sheet Metal Trade <sup>3</sup>	10256	246	1.042	1.013	1.071

<sup>1</sup> Cox proportional hazard analyses based on 10256 Caucasian males with 20 or more years in sheet metal trade, spirometry, and having data on other model covariates. Only workers with spirometry meeting ATS reproducibility were included. Pleural changes (p=0.73) were not significantly associated with COPD mortality and this parameter was dropped from the final model.

<sup>2</sup> Stratified Cox model with strata defined by smoking status (never, past, and current) and adjusted for pack-years of smoking (0, 1-19, 20-39, or ≥ 40 pack-years), age at start of follow-up (<50, 50-54, 55-59, 60-64, 65-69, 70-74, or ≥ 75 years), time since last work in the sheet metal trade at start of follow-up (<5, 5-9, or ≥ 10 years), years of sheet metal work beyond 20 years (20-24, 25-29, 30-34, or ≥ 35 years), and presence of pleural abnormalities.

<sup>3</sup> Age, pack-years of smoking, and years of sheet metal work entered as grouped continuous variables.

<sup>4</sup> Test for trend across categories for percent predicted FVC (p=0.0244), FEV<sub>1</sub> (p=<0.0001) and FEV<sub>1</sub>/FVC (p<0.0001).

