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Mortality Among Sheet Metal Workers Participating in a Medical Screening Program

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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. A study of mortality patterns among screening program participants was undertaken.*

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 2004. Data from the screening program included chest X-ray results by International Labour Office (ILO) criteria and smoking history. Standardized mortality ratios (SMRs) by cause were generated using U.S. death rates and Cox proportional hazards models were used to investigate lung cancer risk relative to chest X-ray changes while controlling for smoking.*

Results *A significantly reduced SMR of 0.83 (95% CI = 0.80–0.85) was observed for all causes combined. Statistically significant excess mortality was observed for pleural cancers, mesothelioma, and asbestosis in the SMR analyses. Both lung cancer and COPD SMRs increased consistently and strongly with increasing ILO profusion score. In Cox models, which controlled for smoking, increased lung cancer risk was observed among workers with ILO scores of 0/1 (RR = 1.17, 95% CI = 0.89–1.54), with a strong trend for increasing lung cancer risk with increasing ILO profusion score >0/0.*

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.* Am. J. Ind. Med. 52:603–613, 2009. *© 2009 Wiley-Liss, Inc.*

KEY WORDS: sheet metal worker; construction; trades; mortality; cancer; lung cancer

BACKGROUND

Sheet metal workers are members of a profession with well-documented exposure to asbestos [Welch et al., 1994]. Sheet metal work involves fabrication or installation of metal products, such as sheet metal 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, railroad industry, and shipyards, as well as in specialized sheet metal production shops. Although the craft of sheet metal work does not itself use asbestos, sheet metal workers in construction were, for many years, exposed to asbestos while working in close proximity to insulation workers, while working in areas that were being sprayed with asbestos for fireproofing, by working on or around beams that had been previously fireproofed with asbestos, and by retrofitting (renovating) asbestos-insulated metal ventilation systems. Very high

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levels of airborne asbestos fibers have been measured during spray application of asbestos before 1973, when this application method was banned [Paik et al., 1983]. Currently, because of stringent regulations on its use, the potential for asbestos exposure in the sheet metal trade generally occurs only during retrofit work in existing buildings. Other respiratory hazards associated with sheet metal work include exposure to welding fumes and manmade mineral fibers, glues, and solvents.

Several studies have examined the prevalence of asbestos-related diseases among sheet metal workers. Baker et al. [1985] reported that 70% of Boston sheet metalworkers with >30 years in the trade had pleural abnormalities, and 4% had parenchymal abnormalities. Among New York City sheet metal workers who belonged to the union for 20 or more years, 29% had radiologic abnormalities consistent with parenchymal and/or pleural asbestos-related disease [Michaels et al., 1987]. Among the 9,605 individuals included in a national asbestos disease screening program Welch et al. [1991, 1994], found that 1,178 (12.3%) had findings consistent with parenchymal disease (International Labour Office, ILO classification score >1/0) and 2,350 (24.5%) pleural abnormalities.

Two prior studies have examined mortality patterns among sheet metal workers. Zoloth and Michaels [1985] examined proportional mortality among New York sheet metal workers using 385 deaths identified from union pension plans. Significantly elevated PMRs were observed for colorectal cancers (PMR = 1.81), lung cancer (PMR = 1.60), non-Hodgkin's lymphoma (PMR = 2.36), and leukemia (PMR = 2.32). Michaels and Zoloth [1988] published an updated analysis based on 331 deaths observed after their initial study. A significantly elevated PMR was observed for lung cancer (PMR = 1.86), stomach cancer (PMR = 2.59), liver cancer (PMR = 2.60), and cancer of lymphatic tissues (PMR = 2.52). Mesothelioma was recorded on the death certificate of 9 of the 716 deaths (1.3%) in the two studies combined, providing strong evidence that sheet metal workers are at increased risk of mortality from asbestos-related disease.

While there is little debate that asbestos exposed workers are at increased risk for, lung cancer, mesothelioma, and other cancers [Nicholson et al., 1982; Helsinki Criteria, 1997; Lee, 2001; Henderson et al., 2004], there is an on-going debate about the risk of lung cancer among workers without asbestosis. Many well-conducted epidemiological studies support a direct relationship between asbestos exposure and risk of lung cancer and show an elevated risk of lung cancer in asbestos-exposed workers without chest X-ray evidence of asbestosis [Liddell and McDonald, 1980; Hillerdal, 1994; Wilkinson et al., 1995; Finkelstein, 1997]. Several studies have shown that the relationship between asbestos exposure and lung cancer is related to both exposure and the presence of underlying asbestosis [Finkelstein, 1997; Cullen et al., 2005; Reid et al., 2005]. The development of lung cancer and asbestosis are confounded because the likelihood of developing both lung cancer and asbestosis increases with the amount of asbestos dust inhaled, because smoking in connection with asbestos exposure is an independent risk factor for asbestosis, and because the diseases have similar latencies. Henderson et al. [2004] carefully examined the weight of the evidence regarding this question and concluded that asbestosis was not a precondition to the development of asbestos-related lung cancer. Nonetheless, the debate about the relative importance of exposure in the absence of asbestosis continues [Banks et al., 1999; Weiss, 1999; Billings and Howard, 2000] and has important medical and public health implications.

Objectives of the current study were twofold. First, we explored overall mortality patterns among sheet metal workers participating in the Sheet Metal Occupational Health Institute Trust (SMOHIT) respiratory disease screening program. Second, we explored the effects of exposure, smoking, and chest X-ray evidence of asbestosis on the risk for lung cancer.

METHODS

Cohort Definition

In 1985, the Sheet Metal Workers International Association (SMWIA) and the Sheet Metal and Air Conditioning National Association formed The SMOHIT to examine the health hazards of the sheet metal industry in the U.S. and Canada. SMOHIT contracted with clinical facilities in the United States and Canada to offer a standardized asbestos disease screening program for sheet metal workers. Details of the SMOHIT national screening program for asbestos-related disease have been previously described [Welch et al., 1994, 2007]. 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. 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 ILO classification for pneumoconiosis [ILO, 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].

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 1,582 workers without sufficient demographic data for a search of the National Death Index (NDI). More than 99% of the sheet metal workers who participated in the screening program were white males. All participants were included in the overall mortality analyses; however, more detailed analyses of lung cancer risk factors were restricted to white males.

Ascertainment of Vital Status and Causes of Death

Two sources of information were used to obtain vital status and cause of death data for cohort members: records in the Sheet Metal National Pension Fund (SMNPF), and the NDI. Records of the SMNPF were searched in order to ascertain the vital status as of December 31, 2004 for members covered by this plan. The pension plan covers 70% of the membership of the union and provided data on retired members receiving benefits, on active members contributing towards their pension, and on deceased members who have received a death benefit. Members receiving pension benefits or still actively contributing toward their pension as of December 31, 2004 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, 2004 using the NDI Plus system [Bilgrad, 1995], maintained by the National Center for Health Statistics (NCHS). The NDI provided information on the dates of death for cohort members as well as underlying and contributing causes of death, coded according to the revision of the International Classification of Disease (ICD) in effect at the time of death (9th revision for deaths that occurred before 1999, 10th revision for deaths that occurred since 1999). 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]. The NDI has been shown to provide virtually complete ascertainment of deaths among men and among employed women [Boyle and Decouflė, 1990; Stampfer et al., 1984]; therefore, we assumed that workers not identified as deceased by the SMNPF or the NDI were still alive as of December 31, 2004.

Cohort Mortality Analyses

Mortality data analyses followed traditional epidemiologic methods for occupational cohort studies [Breslow and Day, 1987; Checkoway et al., 1989a,b,c] and included descriptive analyses of the cohort, and calculation of Standardized mortality ratios (SMRs). The Life Table Analysis System (LTAS.Net Version 2.0.8) developed by the National Institute for Occupational Safety and Health (NIOSH) [Steenland et al., 1990] was utilized to compute cause-specific SMRs, comparing the mortality experience of the cohort to that of the U.S. national population, adjusting for age, race, sex, and calendar year. These death rates covered the 10th revision of the ICD codes, with deaths grouped into 119 categories for analyses [Robinson et al., 2006]. 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, 2004. The LTAS program stratified person-years at risk for each worker into strata by race, sex, 5-year age groups, and 5-year calendar time periods. SMRs were calculated as the ratio of observed to expected deaths with 95% confidence intervals for SMRs were computed assuming that the observed number of deaths in the cohort is a Poisson random variable. The Byar approximation was used when the number of cases was six or more and the exact Poisson confidence interval was calculated when the number of cases was fewer than five [Rothman and Boice, 1979; NIOSH, 2008].

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]. In the main analyses, a pleural abnormality was defined as presence of any notations of positive findings in sections 3A–D of the NIOSH ILO coding form.

Multivariate Modeling of Lung Cancer Risk

Within the overall cohort, further analyses were undertaken to examine the association between chest X-ray readings, work history, and smoking and lung cancer mortality risk. These analyses were restricted to 16,068 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. Cox proportional hazards models were used to obtain lung cancer relative risks and 95% confidence intervals. The time axis in these models was the time from the initial screening examination to diagnosis of lung cancer or the last date that the worker was known alive. Covariates included in the baseline model included smoking status at examination (never, past, and current), 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), and 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].

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 a multivariate model. Age, smoking status, pack-years, time since last sheet metal work, and years of sheet metal work were included in baseline model either because they were significantly associated with lung cancer or because their inclusion in the multivariate model changed the parameter estimates for pleural or parenchymal changes more than 10%. Asbestos-related predictors (presence of pleural abnormalities, and ILO parenchymal profusion category) were investigated in the models as categorical variables and tests for trends across parenchymal category were performed by entering the covariate in the model as a grouped linear variable [Rothman and Greenland, 1998]. We investigated two alternative definitions of pleural abnormalities in the models. In the main analyses, pleural abnormalities were defined as presence of any notations of positive findings in sections 3A–D of the NIOSH ILO coding form. An alternate Cox model defining pleural abnormalities as bilateral pleural thickening or plaques, with or without calcification [Cullen et al., 2005] also was investigated.

Cox proportional hazards models were fit using PROC PHREG in SAS Version 9.1.3 [SAS, 2004]. The EXACT method of handing 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 9.1.3 also was used for this purpose.

RESULTS

The final study cohort included 17,345 sheet metal workers who contributed 207, 442 person-years of observation. A total of 9,504 workers (54.8%) entered the cohort before 1990, 6,087 (35.1%) entered between 1990 and 1999, and 1,794 (10.3%) entered the cohort in 2000 or latter. Due to the requirement for 20 years of sheet metal trade work for participation in the asbestos screening program, the cohort average years in the trade was 31.9 years (Table I). Nearly all cohort members were Caucasian and the average age at cohort entry was 57.4 years. Workers who died of lung cancer were on average older at cohort entry (61.2 years).

At entry, 26.0% of the cohort reported to have never smoked, 48.6% were past smokers, and 25.4% were current smokers (Table II). In contrast, only 7% of the workers who died of lung cancer were never smokers and 48.7% reported current smoking at the time of their screening examination.

TABLE I. Sheet Metal Cohort Demographics and Vital Status Follow-Up From Exam Date Through December 31, 2004

Characteristic	Total cohort	Lung cancer deaths
Number of workers	17,345	569
Total deaths, December 31, 2004	4,385	—
Percent male	99.7%	100%
Percent Caucasian	99.2%	99.9%
Age at intake exam (mean (SD))	57.4 (8.7)	61.2 (7.7)
Smoking status at intake exam (no. (%))[a]		
Never smoked	26.0%	7.0%
Past smoker	48.6%	44.3%
Current smoker	25.4%	48.7%
Smoking pack-years for ever smoked (mean (SD))	32.3 (22.4)	45.8 (25.5)
Years of sheet metal trade work (mean (SD))	31.9 (7.2)	33.6 (7.5)
Prevalence of radiographic parenchymal changes[b]	10.4%	19.3%
Prevalence of radiographic pleural changes[c]	21.7%	27.1%

[a]Twenty-four workers missing smoking data.
[b]ILO profusion of small irregular shadows in the lung parenchyma $\geq$ category 1/0.
[c]Any notations of positive findings in sections 3A–D of the NIOSH ILO coding form.

The prevalence of radiographic parenchymal changes (ILO profusion score $\geq$1/0) was 10.4% for the entire cohort and 19.3% for workers whose deaths were attributed to lung cancer. The prevalence of radiographic pleural changes was 21.7% for the whole cohort and 27.1% for the lung cancer cases.

Overall mortality and mortality by cause for the entire cohort are presented in Table II. A total of 4,384 deaths were observed, resulting in a significantly reduced SMR of 0.83 (95% CI = 0.80–0.85) for all causes combined. Significantly reduced mortality was observed for many non-cancer disease groups including diabetes (SMR = 0.47, 95% CI = 0.36–0.60), alcoholism (SMR = 0.41, 95% CI = 0.16–0.84), heart diseases (SMR = 0.73, 95% CI = 0.69–0.77), other circulatory system diseases (SMR = 0.80, 95% CI = 0.72–0.89), diseases of the digestive system (SMR = 0.68, 95% CI = 0.56–0.81), and diseases of the genito-urinary system (SMR = 0.62, 95% CI = 0.46–0.80). While a deficit was observed for all non-malignant respiratory diseases (SMR = 0.87, 95% CI = 0.79–0.95), significantly increased mortality was observed for asbestosis (SMR = 10.61, 95% CI = 6.93–15.54).

Based on 1,558 observed cancer deaths, no overall excess cancer risk was observed. Malignant neoplasms of the digestive organs and peritoneum were significantly reduced (SMR = 0.89, 95% CI = 0.80–0.99). Significant excess mortality was observed for cancers of the pleura (SMR = 8.06, 95% CI = 4.02–14.41) and mesothelioma (SMR = 8.54, 95% CI = 6.27–11.36). A specific disease category for mesothelioma was only available in the 10th revision of the ICD codes starting in 1999; therefore, pleural mesotheliomas

TABLE II. Sheet Metal Worker Overall Mortality Follow-Up From Exam Date Through December 31, 2004

Cause	Obs.	Exp.	SMR	95% CI lower	upper
All causes	4,385	5,291.61	0.83**	0.80	0.85
All cancers	1,558	1,557.77	1.00	0.95	1.05
MN buccal and pharynx	23	27.83	0.83	0.52	1.24
MN lip	1	0.33	3.02	0.08	16.82
MN tongue	4	6.40	0.62	0.17	1.60
MN other buccal	9	7.13	1.26	0.58	2.40
MN pharynx	9	13.97	0.64	0.29	1.22
MN digestive and peritoneum	330	369.51	0.89*	0.80	0.99
MN esophagus	41	48.62	0.84	0.61	1.14
MN stomach	34	38.08	0.89	0.62	1.25
MN intestine	111	131.66	0.84	0.69	1.02
MN rectum	18	25.54	0.70	0.42	1.11
MN biliary, liver, gall bladder	35	43.95	0.80	0.55	1.11
MN pancreas	85	77.14	1.10	0.88	1.36
MN peritoneum, other and unspecified sites	6	4.53	1.33	0.49	2.89
MN respiratory	594	577.39	1.03	0.95	1.11
MN larynx	11	16.90	0.65	0.32	1.16
MN trachea, bronchus, lung	568	556.75	1.02	0.94	1.11
MN pleura	11	1.37	8.06**	4.02	14.41
MN other respiratory	4	2.37	1.69	0.46	4.33
MN breast	4	2.12	1.89	0.52	4.84
MN female genital organs	0	0.15	0.00	0.00	24.91
MN male genital organs	133	148.01	0.90	0.75	1.06
MN urinary	77	84.70	0.91	0.72	1.14
MN kidney	34	40.75	0.83	0.58	1.17
MN bladder and other urinary site	43	43.95	0.98	0.71	1.32
MN other and unspecified sites	233	195.91	1.19*	1.04	1.35
MN bone	2	2.27	0.88	0.11	3.19
MN melanoma	22	24.12	0.91	0.57	1.38
MN other skin	8	8.28	0.97	0.42	1.90
MN mesothelioma	47	5.50	8.54**	6.27	11.36
MN connective tissues	4	7.82	0.51	0.14	1.31
MN brain and other nervous	28	34.73	0.81	0.54	1.17
MN eye	1	0.71	1.40	0.04	7.80
MN thyroid	3	2.76	1.09	0.22	3.18
MN other and unspecified sites	118	109.72	1.08	0.89	1.29
MN lymphatic and hematopoietic	164	152.16	1.08	0.92	1.26
Hodgkin's disease	3	3.01	1.00	0.21	2.92
Non-Hodgkin's lymphoma	68	63.27	1.07	0.83	1.36
Multiple myeloma	29	28.31	1.02	0.69	1.47
Leukemia	64	57.57	1.11	0.86	1.42
Benign and unspecified nature neoplasms	14	17.10	0.82	0.45	1.37
Diseases blood and blood-forming organs	17	23.06	0.74	0.43	1.18
Diabetes mellitus	65	138.08	0.47**	0.36	0.60
Mental and psychiatric disorders	40	60.88	0.66**	0.47	0.89
Alcoholism	7	17.21	0.41**	0.16	0.84
Other mental disorders	33	43.67	0.76	0.52	1.06
Nervous system disorders	124	129.25	0.96	0.80	1.14
Heart diseases	1,263	1,736.71	0.73**	0.69	0.77
Other diseases of the circulatory system	347	432.55	0.80**	0.72	0.89

(*Continued*)

TABLE II. (*Continued*)

Cause	Obs.	Exp.	SMR	95% CI lower	upper
Diseases respiratory system	460	530.76	0.87**	0.79	0.95
Acute respiratory infection, except flu, pneumonia	3	0.87	3.43	0.71	10.02
Influenza	3	1.59	1.88	0.39	5.51
Pneumonia	87	129.97	0.67**	0.54	0.83
COPD	284	307.54	0.92	0.82	1.04
Asthma	5	5.89	0.85	0.28	1.98
Asbestosis	26	2.45	10.61**	6.93	15.54
Silicosis	0	0.49	0.00	0.00	7.53
Other pneumoconiosis	1	3.07	0.33	0.01	1.82
Other respiratory diseases	51	78.88	0.65**	0.48	0.85
Diseases digestive system	125	184.35	0.68**	0.56	0.81
Diseases skin and subcutaneous	3	4.63	0.65	0.13	1.89
Diseases musculoskeletal and connective	11	13.73	0.80	0.40	1.43
Diseases genito-urinary system	55	89.11	0.62**	0.46	0.80
Symptoms and ill-defined conditions	21	37.50	0.56**	0.35	0.86
Transportation injuries	50	52.23	0.96	0.71	1.26
Falls	33	28.67	1.15	0.79	1.62
Other injury	37	50.89	0.73	0.51	1.00
Violence	50	67.93	0.74*	0.55	0.97
Other and unspecified causes	111	119.13	0.93	0.77	1.12

*Two-sided $P < 0.05$.
**Two-sided $P < 0.01$.

were often coded as cancers of the pleura in the 9th revision of the ICD codes.

Our cohort permits only limited ability to explore disease risks by work duration due to the requirement of 20 years of sheet metal trade work for screening program eligibility. We did explore trends by time since entry into the sheet metal trade for selected disease categories (lung cancer, cancers of the pleura, mesothelioma, COPD, and asbestosis) and these results are presented in Table III. No clear trends were observed; however, excess mortality was observed for mesothelioma and asbestosis among workers in the lowest category of work duration (20–24 years).

Tables IV and V present mortality patterns for the same disease categories listed above according to radiographic parenchymal and pleural changes on initial examination. Lung cancer risks were significantly elevated for all categories of parenchymal profusion scores $\geq$1/0. Pleural cancers, mesothelioma, and asbestosis mortality were significantly elevated among workers with parenchymal profusion scores <1/0. COPD mortality was significantly elevated among workers with a parenchymal profusion score $\geq$1/0 but significantly reduced among workers with a parenchymal profusion score below 1/0. Workers without radiographic pleural changes were found to be at excess risk for cancers of the pleura, mesothelioma, and asbestosis while COPD was in excess only among workers with pleural changes. Further analyses found excess mortality for cancers of the pleura (SMR = 8.12, 95% CI = 3.27–16.73), asbestosis (SMR = 3.91, 95% CI = 1.43–8.51), and mesothelioma (SMR = 7.00, 95% CI = 4.57–10.26) among workers without parenchymal changes (profusion <1/0) or pleural changes.

Cox proportional hazards model results for lung cancer are presented in Table VI. Tests for the proportional hazard assumption indicated that Cox model assumptions were met for all covariates except smoking category (never, former, current) where the models suggested decreased risk among former smokers over the follow-up period and increased risk among current smokers. To account for these interactions with time, we chose stratified Cox analyses [Allison, 1995] for our final model with strata defined by smoking status (never, former, current).

Parenchymal chest X-ray changes were strongly associated with the risk of lung cancer. A test for linear trend for lung cancer risk by profusion category was highly significant ($P = 0.0010$), and an elevated risk was observed among workers with profusion scores of 0/1 (RR = 1.17, 95% CI = 0.89–1.54). The relative risk of lung cancer increased to 6.37 (95% CI = 1.56–25.93) among workers with profusion score of 3/2 or higher. In a separate analysis (not shown) the lung cancer relative risk among those with a profusion score of 1/0 was found to be 1.30 (95% CI = 0.98–1.73). As

TABLE III. Sheet Metal Worker Mortality by Time Since Entry Into Sheet Metal Trade Follow-Up From Exam Date Through December 31, 2004

Disease category	Time since trade entry (years)	Obs.	Exp.	SMR	95% confidence limits lower	upper
Lung cancer	20 to 24	68	55.61	1.22	0.95	1.55
	25 to 29	89	85.26	1.04	0.84	1.28
	30 to 34	138	142.51	0.97	0.81	1.14
	35+	274	273.38	1.00	0.89	1.13
MN Pleura	20 to 24	1	0.14	7.36	0.19	41.00
	25 to 29	1	0.18	5.63	0.14	31.36
	30 to 34	4	0.32	12.48**	3.40	31.94
	35+	5	0.73	6.84**	2.22	15.95
Mesothelioma	20 to 24	4	0.54	7.39**	2.01	18.92
	25 to 29	6	0.83	7.19**	2.64	15.65
	30 to 34	14	1.38	10.11**	5.52	16.96
	35+	23	2.74	8.39**	5.31	12.58
COPD	20 to 24	25	30.78	0.81	0.53	1.20
	25 to 29	42	37.95	1.11	0.80	1.50
	30 to 34	57	69.96	0.81	0.62	1.06
	35+	160	168.87	0.95	0.81	1.11
Asbestosis	20 to 24	6	0.24	25.04**	9.19	54.51
	25 to 29	5	0.28	18.18**	5.90	42.43
	30 to 34	3	0.54	5.51*	1.14	16.09
	35+	12	1.39	8.62**	4.45	15.06

*Two-sided $P < 0.05$.
**Two-sided $P < 0.01$.

TABLE IV. Sheet Metal Worker Mortality by Chest X-Ray Parenchymal Category Follow-Up From Exam Date Through December 31, 2004

Disease category	Parenchymal change category	Obs.	Exp.	SMR	95% confidence limits lower	upper
Lung cancer	0/– to 0/1	459	484.58	0.95	0.86	1.04
	1/0 to 1/2	97	68.34	1.42**	1.15	1.73
	2/1 to 2/3	11	3.65	3.01**	1.50	5.39
	3/2 to 3/+	2	0.19	10.42*	1.26	37.63
MN pleura	0/– to 0/1	10	1.16	8.61**	4.13	15.84
	1/0 to 1/2	1	0.19	5.21	0.13	29.00
	2/1 to 2/3	0	0.01	0.00	0.00	312.93
	3/2 to 3/+	0	<0.01	0.00	0.00	6,499.76
Mesothelioma	0/– to 0/1	37	4.87	7.62**	5.36	10.50
	1/0 to 1/2	10	0.62	16.17**	7.75	29.73
	2/1 to 2/3	0	0.03	0.00	0.00	140.08
	3/2 to 3/+	0	<0.01	0.00	0.00	2,389.78
COPD	0/– to 0/1	210	262.45	0.80**	0.70	0.92
	1/0 to 1/2	62	42.30	1.47**	1.12	1.88
	2/1 to 2/3	11	2.67	4.12**	2.05	7.37
	3/2 to 3/+	1	0.12	8.45	0.21	47.06
Asbestosis	0/– to 0/1	14	2.09	6.69**	3.65	11.22
	1/0 to 1/2	10	0.34	29.71**	14.25	54.64
	2/1 to 2/3	2	0.02	102.82**	12.45	371.42
	3/2 to 3/+	0	<0.01	0.00	0.00	4,028.83

*Two-sided $P < 0.05$.
**Two-sided $P < 0.01$.

TABLE V. Sheet Metal Worker Mortality by Chest X-Ray Pleural Category Follow-Up From Exam Date Through December 31, 2004

Disease category	Pleural changes	Obs.	Exp.	SMR	95% confidence limits lower	upper
Lung cancer	No	415	406.07	1.02	0.93	1.13
	Yes	154	150.70	1.02	0.87	1.20
MN pleura	No	7	0.96	7.27**	2.92	14.99
	Yes	4	0.40	9.92**	2.70	25.40
Mesothelioma	No	31	4.04	7.67**	5.21	10.88
	Yes	16	1.46	10.95**	6.26	17.79
COPD	No	163	214.79	0.76**	0.65	0.88
	Yes	121	92.76	1.30**	1.08	1.56
Asbestosis	No	11	1.70	6.45**	3.22	11.55
	Yes	15	0.75	20.10**	11.24	33.15

**Two-sided $P < 0.01$.

TABLE VI. Cox Model Predictors of Lung Cancer Mortality Among Sheet Metal Workers Follow-Up From Exam Date Through December 31, 2004*

Risk predictor	Number in model*	No. of cancer cases	Relative risk[a]	95% confidence limits lower	upper
Profusion categories[b]					
0/− to 0/0	13,066	368	1.00	Ref.	Ref.
0/1	1,341	60	1.17	0.89	1.54
1/0 to 1/2	1,559	87	1.30	1.02	1.65
2/1 to 2/3	95	10	2.91	1.54	5.51
3/2 to 3/+	7	2	6.37	1.56	25.93
Pleural abnormalities[c]					
Negative	12,583	390	1.00	Ref.	Ref.
Positive	3,485	137	0.84	0.69	1.03
Years since last sheet metal trade work at exam					
<1	9,880	242	1.00	Ref.	Ref.
1 to 5	2,942	136	1.26	1.00	1.60
5 to 10	1,884	78	1.11	0.80	1.55
>10	1,362	71	1.80	1.18	2.59
Age[d]	16,068	527	1.051	1.032	1.071
Smoking pack-years[d]	16,068	527	1.026	1.020	1.033
Years in sheet metal trade[d]	16,068	527	1.013	0.995	1.032

*Cox proportional hazard analyses based on 16,068 Caucasian males with 20 or more years in sheet metal trade and having data on other model covariates.

[a]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 (<5, 5−9, or ≥10 years), years of sheet metal work (20−24, 25−29, 30−34, or ≥35 years), and presence of pleural abnormalities.

[b]Test for trend across profusions categories, $P = 0.0010$.

[c]A pleural abnormality was defined as presence of any notations of positive findings in sections 3A−D of the NIOSH ILO coding form. An alternate model defining pleural abnormalities as bilateral pleural thickening or plaques, with or without calcification resulted in a lung cancer relative risk of 0.80 (95% CI = 0.62−1.03).

[d]Age, pack-years of smoking, and years of sheet metal work entered as grouped continuous variables.

expected, pack-years of cigarette smoking was a strong predictor of lung cancer risk. Although workers included in the Cox models had more than 20 years in the sheet metal trade, duration of work beyond 20 years was associated with increased lung cancer risk after adjustment for other model covariates. After control for other model covariates including parenchymal changes, presence of pleural abnormalities was not independently associated with an increased lung cancer risk (RR = 0.85, 95% CI = 0.69–1.05). An alternate model defining pleural abnormalities as bilateral pleural thickening or plaques, with or without calcification [Cullen et al., 2005] resulted in a lung cancer relative risk of 0.80 (95% CI = 0.62–1.03). Inclusion of an interaction term in the final Cox model for smoking pack-years and profusion category suggested some degree of interaction, although not achieving statistical significance ($P = 0.08$).

We tested potential effects of reader type by the ILO system (A-reader, B-reader, and other or missing reader type) in the final Cox lung cancer model by addition of an indicator variable. Among workers included the Cox models 82.7% of chest films were read by B-readers, 11.8% by A-readers, and 5.5% were missing reader type or were read by a physician with proficiency in the use of the ILO classification but who was neither an A nor a B reader. The parameter for reader type was not significant ($P = 0.54$) and did not change the parameter estimates for other model covariates in any meaningful way.

DISCUSSION

Sheet metal workers who participated in the screening programs experienced significantly reduced overall mortality compared to the US population, clearly demonstrating a healthy survivor effect. No overall increase in lung cancer was observed among these workers compared to the US population; however, SMR analyses revealed excess mortality for mesotheliomas, pleural cancers, 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 and excess mortality for pleural cancers, mesothelioma, and asbestosis were observed among all workers, including those 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 evidence for excess lung cancer risk among workers with parenchymal profusion scores $<$1/0 on the ILO scale, a finding consistent with prior research [Finkelstein, 1997; Cullen et al., 2005; Reid et al., 2005].

Clearly, workers who have sufficient exposure to asbestos to cause radiographic changes consistent with clinical asbestosis are at extremely high risk of lung cancer [Huuskonen, 1978; Liddell and McDonald, 1980; Berry, 1981; Finkelstein et al., 1981; Cookson et al., 1985; Coutts and Turner-Warwich, 1987; Roggli, 1990; Reid et al., 2005]. Consistent with the current study, increased lung cancer risk also has been observed among workers without radiological evidence of asbestosis. In their case–control study Wilkinson et al. [1995] observed an odds ratio (OR) for lung cancer of 1.56 (95% CI: 1.02–2.39) among workers exposed to asbestos but not having radiological evidence of fibrosis, after adjustment for sex, age, smoking, and area of referral. Finkelstein [1997] observed a lung cancer SMR of 5.53 (95% CI: 2.9–9.7) among asbestos-cement workers without X-rays changes consistent with asbestosis. These authors also analyzed data from a previous study by Liddell and McDonald [1980] of mortality, during 1967–1975, among 4,559 Quebec chrysotile miners and millers in relation to coding of the most recent radiograph obtained before 1967. These authors found that chrysotile miners and millers without small opacities had a lung cancer SMR was 1.51 (95% CI: 1.21–1.87). Anttila et al. [1993] demonstrated that asbestos causes excess tumors in the lower-lobes of the lungs at relatively low cumulative exposures, independent of pulmonary fibrosis. Cullen et al. [2005] conducted a follow-up study of 4,060 men with heavy asbestos exposure who participated in a β-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.

Those who assert that the risk of lung cancer among asbestos exposed workers is limited to those who have asbestosis base this opinion on studies which use chest radiography with a profusion $>$1/0 to determine if asbestosis is present. Our study, along with others cited, demonstrates that risk for lung cancer is elevated among asbestos exposed workers with a profusion score $<$1/0. There is widespread agreement that a high resolution CT scan or pathology can detect asbestosis when the chest X-ray is normal. Like other studies based on chest X-ray evidence of asbestosis, our study cannot rule out the presence of histological fibrosis among workers with low profusion scores [Kippen et al., 1987]. Since pathology is rarely medically necessary for clinical diagnosis, few studies of asbestos-exposed cohorts have pathology available, and the available literature cannot precisely determine the risk for lung cancer in asbestos-exposed individuals with and without pathological asbestosis.

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. However, Loomis et al.

[1989] analyzed data from the NHANES I study of the general population and found that individuals with only pleural abnormalities by chest X-ray had a lung cancer relative risk of 3.0 (95% CI: 1.0–9.1). Hillerdal [1994] studied 1,596 men with pleural plaques and followed between 1963 and 1985 and observed an elevated risk of lung cancer for workers with pleural plaques but without parenchymal asbestosis (SMR = 1.4, 95% CI: 1.04–1.97). In β-carotene and retinal efficiency trial population, Cullen et al. [2005] observed a lung cancer relative risk of 1.43 (95% CI = 1.06–1.94) among asbestos-exposed workers with only bilateral pleural thickening or pleural plaques.

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 <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. Cullen et al. [2005] suggested that presence of pleural plaques may serve as a marker for more severe asbestos exposures, 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 lower cumulative asbestos exposure.

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. 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 <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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REFERENCES

Allison PD. 1995. Survival analysis using the SAS system—A practical guide. Cary, NC: SAS Institute, Inc.

American Thoracic Society. 1987. Standardization of spirometry—1987 update. Am Rev Respir Dis 136:1285–1298.

Anttila S, Karjalainen A, Taikina-aho O, Kyyronen P, Vainio H. 1993. Lung cancer in the lower lobe is associated with pulmonary asbestos fiber count and fiber size. Environ Health Perspect 110(2):166–170.

Banks DE, Wang ML, Parker JE. 1999. Asbestos exposure, asbestosis, and lung cancer. Chest 115(2):320–322.

Baker EL, Dagg T, Greene RE. 1985. Respiratory illness in the construction trades: 1. The significance of asbestos-associated pleural disease among sheet metal workers. J Occup Med 27:483–489.

Berry G. 1981. Mortality of workers certified by pemumoconiosis medical panels as having asbestosis. Br J Ind Med 38:130–137.

Bilgrad R. 1995. National Death Index Plus: Coded Causes of Death Supplement to the National Death Index User's Manual, Centers for Disease Control and Prevention.

Billings CG, Howard P. 2000. Asbestos exposure, lung cancer and asbestosis. Monaldi Arch Chest Dis 55(2):151–156.

Boyle CA, Decouflė P. 1990. National sources of vital status information: Extent of coverage and possible selectivity in reporting. Am J Epidemiol 131:160–168.

Breslow NE, Day NE. 1987. Statistical Methods in Cancer Research. Volume II - The Design and Analysis of Cohort Studies. Lyon, International Agency for Research on Cancer. IARC Scientific Publication No. 82.

Checkoway H, Pearce NE, Crawford-Brown DJ. 1989a. Research methods in occupational epidemiology. New York: Oxford University Press.

Checkoway H, Pearce N, Dement JM. 1989b. Design and conduct of occupational epidemiology studies: Part I. Design of cohort studies. Am J Ind Med 15:363–373.

Checkoway H, Pearce N, Dement JM. 1989c. Design and conduct of occupational epidemiology studies: Part II. The analysis of cohort data. Am J Ind Med 15:375–394.

Cookson WO, Musk AW, Glancy JJ, de Klerk NH, Yin R, Mele R, Carr NG, Armstrong BK, Hobbs MS. 1985. Compensation, radiographic changes, and survival in applicants for asbestosis compensation. Br J Ind Med 42(7):461–468.

Coutts JC II, Turner-Warwich M. 1987. Mortality in cases of asbestosis diagnosed by pneumoconiosis medical panel. Thorax 42:111–116.

Cullen MR, Barnett MJ, Balmes JR, Cartmel B, Redlich CA, Brodkin CA, Barnhart S, Rosenstock L, Goodman GE, Hammar SP, Thornquist MD, Omenn GS. 2005. Predictors of lung cancer among asbestos-exposed men in the beta-carotene and retinol efficacy trial. Am J Epidemiol 161(3):260–270.

Finkelstein MM. 1997. Radiographic asbestosis is not a prerequisite for asbestos-associated lung cancer in Ontario asbestos-cement workers. Am J Ind Med 32(4):341–348.

Finkelstein M, Kusiak R, Suranyl G. 1981. Mortality among workers receiving compensation for asbestosis in Ontario. CMA J 125:259–262.

Helsinki Criteria. 1997. Asbestos, asbestosis, and cancer: The Helsinki criteria for diagnosis and attribution. Scand J Work Environ Health 23(4):311–316.

Henderson DW, Rodelsperger K, Woitowitz HJ, Leigh J. 2004. After Helsinki: A multidisciplinary review of the relationship between asbestos exposure and lung cancer, with emphasis on studies published during 1997–2004. Pathology 36(6):517–550.

Hillerdal G. 1994. Pleural plaques and risk for bronchial carcinoma and mesothelioma: A prospective study. Chest 105:144–150.

Horm J. 1996. Assignment of Probabilistic Scores to National Death Index Record Matches NDI User's Manual Addendum, Centers for Disease Control and Prevention.

Huuskonen MS. 1978. Clinical features, mortality and survival of patients with asbestosis. Scand J Work Environ Health 4:265–274.

ILO U/C. 1980. International classification of radiographs of pneumoconiosis. Geneva: ILO.

Kipen HM, Lilis R, Suzuki Y, Valciukas JA, Selikoff IJ. 1987. Pulmonary fibrosis in asbestos insulation workers with lung cancer: A radiological and histopathological evaluation. Br J Ind Med 44(2): 96–100.

Liddell FD, McDonald JC. 1980. Radiological findings as predictors of mortality in Quebec asbestos workers. Br J Ind Med 37(3):257–267.

Lee PN. 2001. Relation between exposure to asbestos and smoking jointly and the risk of lung cancer. Occup Environ Med 58(3):145–153.

Loomis DP, Collman GW, Rogan WJ. 1989. Relationship of mortality, occupation, and pulmonary diffusing capacity to pleural thickening in the First National Health and Nutrition Examination Survey. Am J Ind Med 16(5):477–484.

Michaels D, Zoloth S, Lacher M, Holstein E, Lilis R, Drucker E. 1987. Asbestos disease in sheet metal workers: II. Radiologic signs of asbestosis among active workers. Am J Ind Med 12:595–603.

Michaels D, Zoloth S. 1988. Asbestos disease in sheet metal workers: Proportional mortality update. Am J Ind Med 13:731–734.

Nicholson WJ, Perkel G, Selikoff IJ. 1982. Occupational exposure to asbestos: Population at risk and projected mortality—1980–2030. Am J Ind Med 3(3):259–311.

NIOSH. 2008. LTAS Manual, LTAS.Net Version 2.0.8, Downloaded July 7, 2008. http://www.cdc.gov/niosh/LTAS/news.html.

Paik NW, Walcott RJ, Brogan PA. 1983. Worker exposure to asbestos during removal of sprayed material and renovation activity in buildings containing sprayed material. Am Ind Hyg Assoc J 44:428–432.

Reid A, de Klerk N, Ambrosini GL, Olsen N, Pang SC, Berry G, Musk AW. 2005. The effect of asbestosis on lung cancer risk beyond the dose related effect of asbestos alone. Occup Environ Med 62:885–889.

Robinson CF, Schnorr TM, Cassinelli RT, Calvert GM, Steenland NK, Gersic CM, Schubauer-Berigan MK. 2006. Tenth revision U.S. mortality rates for use with the NIOSH life table analysis system. J Occup Environ Med 48:662–667.

Roggli VL. 1990. Human disease consequences of fiber exposures: A review of human lung pathology and fiber burden data. Environ Health Perspect 88:295–303.

Rothman KJ, Boice JD. 1979. Epidemiologic analysis with a programmable calculator. Washington, DC: US Government Printing Office.

Rothman KJ, Greenland S. 1998. Modern epidemiology, 2nd edition. Philadelphia, PA: Lippincott-Raven.

SAS Institute, Inc. 2004. SAS, Version 9. Cary, NC: SAS Institute, Inc.

Stampfer MJ, Willett WC, Speizer FE, Dysert DC, Lipnick RT, Rosner B, Hennekens CH. 1984. Test of the National Death Index. Am J Epidemiol 119:837–839.

Steenland K, Beaumont J, Spaeth S, Brown D, Okun A, Jurcenko L, Ryan B, Phillips S, Roscoe R, Stayner L, Morris J. 1990. New developments in the life table analysis system of the national institute for occupational safety and health. J Occup Med 32: 1091–1098.

Weiss W. 1999. Asbestosis: A marker for the increased risk of lung cancer among workers exposed to asbestos. Chest 115(2):536–549.

Wilkinson P, Hansell DM, Jassens J, Rubens M, Rudd RM, Taylot AN, McDonald JC. 1995. Is lung cancer associated with asbestos exposure when there are no small opacities on the chest radiograph. Lancet 345: 1074–1078.

Welch LS, Michaels D, Zoloth SR. 1991. Asbestos-related disease among sheet-metal workers: Preliminary results of the National Sheet Metal Worker Asbestos Disease Screening Program. Ann NY Acad Sci 643:287–295.

Welch LS, Michaels D, Zoloth SR. 1994. The National Sheet Metal Worker Asbestos Disease Screening Program: Radiologic findings. National Sheet Metal Examination Group. Am J Ind Med 25(5):635–648.

Welch LS, Haile E, Dement J, Michaels D. 2007. Change in prevalence of asbestos-related disease among sheet metal workers 1988–2004. Chest 131:863–869.

Zoloth S, Michaels D. 1985. Asbestos disease in sheet metal workers: The results of proportional mortality analysis. Am J Ind Med 7:315–321.