ORIGINAL ARTICLE

Mortality from non-malignant respiratory disease in the fibreglass manufacturing industry

L Chiazze, D K Watkins, C Fryar, W Fayerweather, J Kozono, V Biggs

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See end of article for authors' affiliations

Correspondence to: Dr L Chiazze Jr, Department of Family Medicine, 410 Kober Cogan Hall, 3750 Reservoir Road NW, Washington, DC 20007, USA; chiazzel@georgetown.edu

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Objectives: To investigate the question of whether there is an association between workplace exposures and sociodemographic factors and mortality from non-malignant respiratory disease excluding influenza and pneumonia (NMRDxIP) among workers in a fibreglass wool manufacturing facility.
Methods: A case-control study with cases and controls derived from deaths recorded from the Kansas City plant in the Owens Corning mortality surveillance system. The cases are defined as decedents with NMRDxIP as the underlying cause of death. Matched, unadjusted odds ratios (ORs) were used to assess any association between NMRDxIP and cumulative exposure history and sociodemographic factors individually. Matched, adjusted ORs were obtained by conditional logistic regression to estimate the effect of any one variable while controlling for the effect of all the others.
Results: Results of the unadjusted analysis, considering variables one at a time, yielded no significant associations between NMRDxIP and any of the exposure or sociodemographic variables. The smoking OR was substantially increased (OR 5.09; 95%CI 0.65 to undeterimed). Also, there were no significant variables in a conditional logistic regression analysis in which all variables were simultaneously adjusted. ORs for respirable glass fibres were below unity at all concentrations of exposure in the adjusted analysis. For respirable silica there was no consistent relation across all exposure levels. The ORs increased through the first three exposure concentrations but decreased for the highest exposure. However, ORs although not significant, are greater than unity for all respirable concentrations of silica exposure.
Conclusions: The findings for Kansas City show no association between respirable glass fibres and NMRDxIP. The adjusted ORs for all exposures to respirable fibres were less than unity. On the other hand, the ORs for silica exposures were all above unity although there was no clear dose-response relation and none of the ORs were significant. Exposures for all substances considered were very low. Further, given the number of cases and controls, the statistical power to detect relatively small increases in risk, if any increase truly exited, was relatively low. The ORs for exposures to silica were all above unity although there was no clear dose-response relation and none of the ORs were significant. These raised ORs for silica suggest that continued surveillance would be prudent.

The Division of Occupational Health Studies, Department of Family Medicine, Georgetown University Medical Center maintains a mortality surveillance system on behalf of Owens Corning. The mortality surveillance system includes a register of deaths occurring from 1970 among active employees or former employees the deaths of whom Owens Corning would have occasion to know about. They would be those vested in the company insurance plan and are predominately employees with more than 10 years of employment. Also, the mortality surveillance system includes an historical environmental reconstruction of each plant in the company to provide detailed exposure information. A third component of the surveillance system is a nationwide interview survey of both living retirees and of proxies for decedents in the mortality registry. The survey attempts to acquire information on lifetime employment, lifetime residence, smoking and alcohol consumption histories, and other personal and family characteristics which may have an impact on health of employees.

Mortality experience is monitored by comparing the distribution by cause of death in the mortality surveillance system to the distribution of deaths in the local area in which a plant is located (county or local standard) and to the experience of the total United States (national standard) specific for race, sex, and age using the proportionate mortality ratio (PMR).[1] The PMR analyses are conducted annually with an in depth follow up when a PMR is significant over several analysis periods. The PMRs for non-malignant respiratory disease excluding influenza and pneumonia (NMRDxIP) among white men for the Kansas City plant met this criterion.

The Kansas City plant began production of fibreglass wool insulation products in 1946 and employed over 350 workers by 1947. The plant is still in operation today. Through the 1970s and 1980s people employed averaged between 800–900 although more recently this is around 350. Potential exposures are typical of those found in a fibreglass wool insulation plant.

Previously, we examined risk factors for NMRDxIP at the Owens Corning Newark plant, the nation's oldest and largest fibreglass manufacturing factory.[2] We undertook a case-control study of NMRDxIP at the Kansas City plant with information from the mortality surveillance system to deal specifically with the question of whether there is an association between respirable glass fibres, other workplace exposures, and sociodemographic factors and mortality from NMRDxIP among workers at this fibreglass wool manufacturing factory.

METHODS

There are 30 deaths in white men recorded from the Kansas City plant in the mortality surveillance system mortality

Abbreviations: NMRDxIP, non-malignant respiratory disease excluding influenza and pneumonia; PMR, proportionate mortality ratio; ICD-9, international classification of diseases, 9th revision

Table 1 Specific underlying cause of death (ICD-9) for non-malignant respiratory disease (excluding influenza and pneumonia) cases

	Frequency
Chronic bronchitis (491)	3
Emphysema (492)	4
Chronic airways obstruction: not elsewhere classified (496)	22
Pulmonary congestion and hypostasis (514)	1
Total	30

registry for whom the underlying cause of death was NMRDxIP. These 30 deaths, all of whom were long term employees with 10 or more years employment, constitute the case series. The specific causes of death with the 9th revision of the international classification of diseases (ICD-9) codes for all 30 cases are shown in table 1.[3] Twenty two of the 30 cases were concentrated in ICD code 496 (chronic airways obstruction: not elsewhere classified). The rest were: four cases in ICD 492 (emphysema), three cases in ICD 491 (chronic bronchitis), and one case in ICD 514 (pulmonary congestion and hypostasis).

Controls also were drawn from deaths at Kansas City in the mortality surveillance system mortality registry and were matched to cases on year of birth (±2 years) and survival to death (±2 years) or to the end of 1996 to allow controls the opportunity to survive as long as cases. Any death without NMRDxIP or malignant respiratory cancer as the underlying cause of death was eligible to be a control. All eligible controls who met the matching criteria were used resulting in a total of 133 matched controls. There were 18 cases with four controls each, seven cases with three controls each, and five cases with two controls each. Although not included in the matching criteria, the distributions by age when first joining the company and age at death were comparable for cases and controls.

All of the cases were employed for 10 or more years and nearly two thirds were employed for 20 or more years. All but four of the controls were employed for more than 10 years.

The procedure for enumerating exposures and measuring exposure concentrations has been described previously.[2 4] Briefly, an expert exposure assessment committee developed quantitative exposure estimates for workplace substances known or suspected to be respiratory irritants in each manufacturing and non-manufacturing process. Each process was assigned one of four estimated potential exposure concentrations (8 hour time weighed averages) specific for calendar time. This procedure resulted in estimates of the daily exposure to each of the substances over a worker's entire working lifetime. Cumulative exposure to each substance was developed for each employee as the product of the number of days in a process multiplied by the exposure concentration for that process and then summed over all processes and expressed as cumulative exposure. Table 2 gives the number of cases and controls by cumulative exposure-days (concentration multiplied by days of exposure) for each of the exposures in the analysis as well as the numbers for the sociodemographic variables obtained from interviews.

Because the number of cases is limited, we used an exact conditional logistic regression procedure with the LogXact for Windows software package.[5] Matched, unadjusted odds ratios (ORs) were used to find whether there was an association between NMRDxIP and cumulative exposure history or sociodemographic factors one variable at a time (univariate analysis). Matched, adjusted ORs were used to estimate the effect of any one variable while controlling for the effect of all the others. To carry out the adjusted analysis, we used criteria suggested by Siemiatycki *et al* and entered both sociodemographic and exposure variables from the univariate analysis with ORs of 1.5 or greater or 0.67 or less without regard to significance.[6] All tests of significance were two sided and carried out at the $\alpha=0.05$ level.

Table 2 Number of cases and controls by sociodemographic characteristics and cumulative exposure-days

	Cases	Controls	Total
Subject characteristics:			
Education (y):			
⩾12	17	47	64
8–11	9	41	50
<8	2	12	14
Unknown	2	3	5
Marital status:			
Married	18	79	97
Widowed, divorced, separated	8	22	30
Never married	1	2	3
Unknown	3	0	3
Smoking (cigarettes):			
Never smoked	0	12	12
Smoked for 6 months or more	19	66	85
Unknown	11	25	36
Drinking (alcohol):			
Not regular drinker	9	43	52
Regular drinker	9	34	43
Unknown	12	26	38
Income ($):			
⩾20000	8	27	35
<20000	7	30	37
Unknown	15	46	61
Cumulative exposure days (concentration×days of exposure):			
Respirable fibres (fibres/ml):			
<100	5	20	25
100–299.99	12	20	32
⩾300 (max=687.7)	13	61	74
Unknown	0	2	2
Asbestos (fibres/ml):			
0	16	56	72
0.03–0.99	4	14	18
⩾1 (max=66.7)	10	31	41
Unknown	0	2	2
Talc (fibres/ml):			
0	19	56	75
>0 (max=66.7)	11	45	56
Unknown	0	2	2
Respirable silica (mg/m^3):			
0	3	15	18
0.03–0.999	1	5	6
1 to 9.9	5	17	22
10–99.9	12	29	41
⩾100 (max=6664.8)	9	35	44
Unknown	0	2	2
Formaldehyde (ppm):			
<1000	13	46	59
⩾1000 (max=7514.5)	17	55	72
Unknown	0	2	2

RESULTS

Matched, unadjusted NMRDxIP OR and 95% confidence intervals (95% CIs) for individual sociodemographic and exposure variables are given in table 3. This table also gives the number of observations (cases and controls combined) along with the number of informative strata in producing each OR for the reader to evaluate the extent to which data were complete for any variable. Analyses are based on those cases and controls with available data (table 2). In this analysis, there was no significant relation with any of the exposure variables. There was an increased OR for the lower exposure concentration for respirable glass fibres (OR 2.24; 95% CI 0.54 to 10.97) but an OR less than one for the highest exposure (OR 0.79; 95% CI 0.20 to 3.52). For respirable silica there was no consistent relation: the OR increased through the first three exposure

Table 3 Matched, unadjusted non-malignant respiratory disease (excluding influenza and pneumonia) OR (95% CIs) for sociodemographic and cumulative exposure-days

	OR (95% CI)
Subject characteristics:	
Education (y, observations (n=114), informative strata (n=26)):	
⩾12	1.000
8–11	0.66 (0.23 to 1.77)
<8	0.56 (0.06 to 2.89)
Marital status (observations (n=96), informative strata (n=22)):	
Married	1.000
Widowed, divorced, separated	1.49 (0.50 to 4.12)
Never married	1.51 (0.02 to 30.64)
Smoking (cigarettes, observations (n=22), informative strata (n=6)):	
Never smoked	1.000
Smoked for 6 months or more	5.09 (0.65 to + Inf)
Drinking (observations (n=47), informative strata (n=12)):	
Not regular drinker	1.000
Regular drinker	1.42 (0.36 to 5.63)
Income ($, observations (n=33), informative strata (n=10)):	
⩾20000	1.000
<20000	0.60 (0.13 to 2.81)
Cumulative exposure-days (concentration×days of exposure):	
Respirable fibres (fibres/ml, observations (n=107), informative strata (n=24)):	
<100	1.000
100–299.99	2.24 (0.54 to 10.97)
⩾300 (Max=687.7)	0.79 (0.20 to 3.52)
Asbestos (fibres/ml, (fibres/ml, observations (n=128), informative strata (n=29)):	
0	1.000
0.03–0.99	0.97 (0.13 to 5.13)
⩾1 (max=66.7)	1.10 (0.41 to 2.85)
Talc (fibres/ml, (fibres/ml, observations (n=118), informative strata (n=27)):	
0	1.000
>0 (max=66.7)	0.66 (0.24 to 1.64)
Respirable silica (mg/m^3, observations (n=131), informative strata (n=30)):	
0	1.000
0.03–0.999	1.17 (0.02 to 24.80)
1–9.9	1.58 (0.23 to 14.01)
10–99.9	2.27 (0.46 to 16.03)
⩾100 (max=6664.8)	1.33 (0.27 to 8.94)
Formaldehyde (ppm, observations (n=113), informative strata (n=26)):	
<1000	1.000
⩾1000 (max=7514.5)	1.09 (0.43 to 2.82)

concentrations but decreased for the highest. The ORs although not significant, were greater than unity for all exposure concentrations of respirable silica. The OR for any exposure to talc was below unity but not significant (OR 0.66; 95% CI 0.24 to 1.64). The ORs for exposure to both asbestos and formaldehyde were not significant and close to unity for the exposure concentrations analyzed.

As with exposure variables, there were no significant increases or deficits in the univariate analysis for any of the sociodemographic variables including smoking. However, the smoking OR was substantially increased (OR 5.09; 95% CI 0.65 to undetermined). The OR for drinking was increased for regular drinkers (OR 1.42; 95% CI 0.36 to 5.63). The ORs were inversely related to level of income and directly related to education.

Table 4 shows the results of a matched analysis using a conditional logistic regression procedure which was carried out to estimate the effect of any one variable while controlling for the effect of all the others. As already described, variables giving an OR ⩾1.5 or ⩽0.67 for sociodemographic or exposure variables in the unadjusted (univariate) analysis were included in the model. Six variables met the inclusion criteria (income was excluded because of the scarcity of data). Note that the

Table 4 Non-malignant respiratory disease (excluding influenza and pneumonia) matched, ORs (95% CIs) from conditional logistic regression analysis adjusted for sociodemographic and cumulative exposure-days (observations (n=68), informative strata (n=19))

	OR (95% CI)
Subject characteristics:	
Education (y):	
⩾12	1.000
8–11	0.59 (0.00 to 7.57)
<8	0.29 (0.03 to 1.56)
Marital status:	
Married	1.000
Widowed, divorced, separated	2.14 (0.41 to 15.32)
Never married	1.75 (0.04 to + Inf)
Smoking (cigarettes):	
Never smoked	1.000
Smoked for 6 months or more	1.88 (0.24 to + Inf)
Cumulative exposure days (concentration×days of exposure)	
Respirable fibres (fibres/ml):	
<100	1.000
100–299.99	0.63 (0.01 to 19.37)
⩾300 (max=687.7)	0.49 (0.01 to 14.19)
Talc (fibres/ml):	
0	1.000
>0 (max=66.7)	1.31 (0.19 to 17.76)
Respirable silica (mg/m^3):	
0	1.000
0.03–0.999	1.01 (0.00 to 15.85)
1–9.9	1.71 (0.06 to 148.77)
10–99.9	3.96 (0.14 to 431.06)
⩾100 (max=6664.8)	1.77 (0.03 to 183.11)

number of observations was only 68 and the number of informative strata was reduced to 19. As a result, these results should be interpreted with caution.

There were no significant variables in this analysis when all variables were simultaneously adjusted. ORs for respirable glass fibres are below unity at all exposures. The ORs for silica were not significant. These ORs are above unity at all exposure concentrations but there was no evidence of a dose-response relation. Adjusted ORs from conditional logistic regression models which included only smoking and exposure variables were also examined and yielded very similar results.

DISCUSSION AND SUMMARY

A search of the Medline database suggests that publications on the relation of NMRDxIP to occupational exposures is sparse and inconclusive especially for chronic airways obstruction, the predominant cause of death for cases in this case control study. Publications on the relation between NMRDxIP and occupational exposures in the fibreglass manufacturing industry is also sparse, especially when compared with that of malignant respiratory disease, and there is no evidence suggesting an association between NMRDxIP and respirable fibres. Marsh *et al* in an industrywide historical cohort mortality study which included the Kansas City plant state that "analyses by duration of employment, small diameter fiber exposure and cumulative and average intensity of fiber exposure revealed no evidence of a relationship between MMMF exposure and nonmalignant respiratory disease."[7] In the paper by Marsh *et al*, the standardised mortality ratio (SMR) for NMRDxIP for the Kansas City plant was only slightly increased (SMR 114) and not significant.[7] No excess mortality from non-malignant respiratory diseases was found in the International Agency for Research on Cancer historical cohort study of European manmade mineral fibre production workers.[8] A study of Owens Corning's Newark

plant found that smoking was the only significant factor for NMRD although the ORs for respirable fibres and silica were greater than unity for the highest exposure categories.[2]

This study of the Kansas City plant did not show any relation between respirable glass fibres and NMRDxIP. The ORs for respirable glass fibres were below unity when adjusting for smoking and other sociodemographic variables as well as other exposure variables. Even in the univariate analysis, the OR for the highest exposure concentration for respirable fibres was less than unity. On the other hand, the ORs for exposures to silica were all above unity in the adjusted analysis and in the univariate analysis. However, none of the ORs were significant and there was no clear dose-response relation.

It should be pointed out that the exposure concentrations for all substances considered were low. Further, given the number of cases and controls, the statistical power to detect relatively small increases in risk, if any increase truly existed, was relatively low. The study would have required three times as many cases to have an 80% chance of detecting a true doubling in risk in the lowest exposure category. Overall, the findings for Kansas City did not show an association between respirable glass fibres and NMRDxIP. The adjusted ORs for all exposures of respirable fibres were less than unity. The OR for the lower exposures in the unadjusted analysis was increased although not significantly. On the other hand, the OR for the higher exposures was below unity. Obviously a small study such as this cannot provide any definitive answers on the question about any relation between respirable glass fibres and NMRDxIP. On the other hand, given the paucity of literature on this subject, the current study adds some reassurance that no overwhelming risk is present.

The ORs for exposure to silica were all above unity in both the unadjusted and adjusted analyses although there was no clear dose-response relation and none of the ORs were significant. However, these raised ORs for silica suggest that continued surveillance would be prudent.

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Authors' affiliations

L Chiazze, D K Watkins, C Fryar, J Kozono, V Biggs, Division of Occupational Health Studies, Department of Family Medicine, Georgetown University Medical Center, Washington, DC 20007, USA
W Fayerweather, Owens Corning, One Owens Corning Parkway, Toledo, Ohio 43659, USA

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ECHO

Toxic toluidine

Please visit the Occupational and Environmental Medicine website [occenvmed.com] for link to this full article.

Exposure to 5-nitro-*o*-toluidine (5-NT) results in liver damage, Japanese doctors have found. The discovery came after three workers from one factory were referred to the same hospital with liver damage over 13 days. All were working with 5-NT powder in an enclosed factory area. One other worker with liver disease was not admitted.

The coincidence prompted questioning of all 15 workers in that area about symptoms and a hygiene investigation—into working practices; material safety data sheets (MSDS); and the workers' backgrounds, medical history, and previous liver function tests. All had full biochemical analysis for liver function and tests for hepatitis A, B, and C; the three admitted workers had tests for CMV and EBV infection.

Those admitted had severe liver damage, and, 17 days after the first admission, three more workers showed damage and two were admitted. Fortunately, liver function gradually improved. The six most severely affected had handled 5-NT the most—4–5 hours, 12–20 times—compared with the others providing occasional relief, exposed only 1–3 times. Liver damage was not related to any other factor.

The work entailed hand scooping 5-NT powder, unavoidably creating an airborne suspension. The workers were in the habit of loosening their respirators slightly for comfort during short breaks taken in the work section—presumably inhaling the powder.

Toxicity of 5-NT is not proved but highly likely. Despite only one other reported instance of liver damage occupationally—after incidental exposure in one man—Shimizu *et al* believe that those exposed to 5-NT need regular monitoring of their liver function.

▲ *Gut* 2002;**50**:226–270.