British Journal of Industrial Medicine 1992;49:326–331

A case-control study of malignant and non-malignant respiratory disease among employees of a fibreglass manufacturing facility

Leonard Chiazze Jr, Deborah K Watkins, Cheryl Fryar

Abstract

A case-control study was conducted to determine the influence of non-workplace factors on risk of respiratory disease among workers at the Owens-Corning Fiberglas plant in Newark, Ohio. Cases and controls were drawn from a historical cohort mortality study conducted on behalf of the Thermal Insulation Manufacturers Association (TIMA) of workers employed at Newark for at least one year between 1 January 1940 and 31 December 1963 and followed up to the end of 1982. The TIMA study reported a statistically significant increase in respiratory cancer (compared with national death rates). Interviews were completed for 144 lung cancer cases and 299 matching controls and 102 non-malignant respiratory disease cases and 201 matching controls. Unadjusted odds ratios (ORs) were used to assess the association between lung cancer or non-malignant respiratory disease and birthplace, education, income, marital state, smoking with a duration of six months or more, age at which smoking first started, and duration of smoking. Only the smoking variables were statistically significant. For lung cancer, of the variables entered into a conditional logistic regression model, only the smoking OR of 23·4 (95% CI 3·2–172·9) was statistically significant. For non-malignant respiratory disease no variables entered into the final model were statistically significant. Results of the interview portion of our case-control study clearly indicate that smoking is the most important non-workplace factor for risk of lung cancer in this group of workers. Smoking does not seem to play as important a part, however, for non-malignant respiratory disease. Prevalence of cigarette smoking at the Newark plant was estimated for birth cohorts by calendar year. Corresponding data for the United States were compiled from national smoking surveys. Prevalence of cigarette smoking for Newark in 1955 appears to be sufficiently greater than the corresponding United States data in 1955 to suggest that some of the previously reported excess of lung cancer for Newark based on United States mortality may be accounted for by differences in the prevalence of cigarette smoking between white men in Newark and those in the United States as a whole.

Division of Biostatistics and Epidemiology, Department of Community and Family Medicine, Georgetown University School of Medicine, Washington, DC 20007, USA
L Chiazze Jr, D K Watkins, C Fryar

A case-control study was undertaken to investigate risk factors associated with deaths from malignant and non-malignant respiratory disease among employees of the oldest and largest fibreglass manufacturing facility in the United States. This is a follow up to a historical cohort mortality study conducted on behalf of the Thermal Insulation manufacturers Association (TIMA). The TIMA study reported a statistically significant increase in respiratory cancer for production and maintenance workers employed at the Owens-Corning Fiberglas Newark plant for at least one year between 1 January 1940 and 31 December 1963 and followed up to the end of 1982 when compared with national mortality.[1] Earlier studies on the same workers followed up through 1977, also reported an increased (though not statistically significant) standardised mortality ratio (SMR) for respiratory cancer.[2,3] The authors acknowledged the complications in identifying effects on health associated with exposure to manmade mineral fibres (MMMFs) because of "the presence of other substances with possible effects on health in the environment of these workers. These include silica, asphalt, phenol, formaldehyde, ammonia, carbon monoxide, solvent vapours, and heavy metal fumes. Moreover, useful data could not be obtained on the tobacco smoking habits of the populations studied, and this is the most powerful single cause of malignant and non-malignant respiratory disease in the US population."[3]

The overall objective of the study presented here was to determine whether working in a particular area of the plant, production process, or calendar time is associated with an increase in risk of either malignant or non-malignant respiratory disease independent of other possible sources of risk including smoking and other known carcinogens.

The environment of the Newark plant has been and is very complex. The facility has undergone substantial changes over the past 50 years and there are many potential exposures in addition to fibreglass. Furthermore, employee characteristics have changed over time. Previous studies of this plant have attempted to estimate exposure to fibreglass. Neither exposure to other substances nor to non-workplace factors have, however, been dealt with adequately. The current investigation considers these issues.

Our case-control study has two principal components. Work on one component, an historical environmental reconstruction of the Newark plant, is ongoing. This reconstruction will characterise the working environment of the plant from its beginnings as a fibreglass plant in 1934 to the present and will be the subject of a separate communication. The second component, and the subject of this report, is a personal interview survey. The survey obtained information on employee characteristics that may affect the risk of respiratory disease. The questionnaire was designed for use with both subject and proxy interviews and for both in person and telephone interviews. It included questions on demography (date of birth, race, education, marital state, parent's ethnic background, and place of birth), lifetime residence, occupational and smoking histories, hobbies, and personal and family medical history.

Methods

An interview staff working from a field office established in the Newark, Ohio, area administered over 80% of the interviews in person. Telephone interviews were used only when a personal interview was not economically feasible. To avoid potential bias on the part of interviewers, case and control states were masked and no interviewer was a resident of Ohio.

Cases and controls were drawn from the original Newark (TIMA) cohort described previously and followed up to the end of 1982. Cases are those for whom either malignant or non-malignant respiratory disease (excluding influenza and pneumonia) was the underlying cause of death as coded by a qualified nosologist according to the International Classification of Diseases revision in effect at the time of death. Potential controls were any members of the cohort who were not cases but excluded, for ethical considerations, decedents whose cause of death was either suicide or homicide. Controls were matched on year of birth (± two years) and survival to the end of follow up or death (± two years) to allow for comparable time from initial exposure to death or end of follow up.

The goal was to have at least two matched controls for each case. As it was not clear a priori what the

Table 1 Newark case control study tracing and interview results

	Cases		*Controls*	
	No	*%*	*No*	*%*
Malignant respiratory disease				
Attempted to trace	178		415	
Did not meet cohort criteria	2		5	
Controls matched to dropped cases	—		4	
Baseline number	176	100	406	100
Unable to interview	24	14	84	21
Maximum available for unmatched analysis of interview data	152	86	322	79
Maximum available for matched analysis	152	86	276	68
Lung cancer				
Attempted to trace	166		387	
Did not meet cohort criteria	2		4	
Controls matched to dropped cases	—		4	
Baseline number	164	100	379	100
Unable to interview	20	12	80	21
Maximum available for unmatched analysis of interview data	144	88	299	79
Maximum available for matched analysis	144	88	260	69
Non-malignant respiratory disease				
Attempted to trace	112		273	
Did not meet cohort criteria	0		3	
Controls matched to dropped cases	—		0	
Baseline number	112	100	270	100
Unable to interview	10	9	69	26
Maximum available for unmatched analysis of interview data	102	91	201	74
Maximum available for matched analysis	101	90	183	68

success rate would be for tracing proxies for controls who had died several decades ago, four potential matched controls were selected at random for each case and tracing was attempted. If either of the first two selected controls could not be traced and interviewed, the third, or fourth, or both selected controls were utilised.

Tracing was attempted on a total of 978 persons (table 1). During the course of the investigation it was determined that two (lung cancer) cases and eight controls did not meet the criteria for initial inclusion in the cohort. These 10 subjects plus four controls matched to the two excluded cases of lung cancer were dropped from the study.

All cases and 78% of controls were deceased. Proxy respondents accounted for 88% of all interviews including those living subjects who were unable to be interviewed because of illness or disability. Interviews were completed for 86% of cases of malignant respiratory disease (88% for lung cancer) and 79% of their controls and for 91% cases of non-malignant respiratory disease and 74% of their controls (table 1). Reasons for not carrying out interviews among cases of lung cancer were evenly divided between being unable to locate a respondent and proxy refusal. Sixty four per cent of interviews were not completed for potential lung cancer controls because a respondent could not be located. No respondent could be located for nine of the cases of non-malignant respiratory disease and 77% of their controls.

Proxy respondents were predominantly women (72%) with a median age of 65; 92% lived in the same household with the subject at some time but even when not living with the subject, 87% had at least monthly contact with the subject. Ninety nine per cent of proxies believed themselves to be knowledgeable about the subject's residence, work history, hobbies, health, and smoking history.

An advisory committee was appointed to provide ongoing peer review. The committee considered issues including definition of the study question, case definition and control selection, questionnaire development, interview content, subcontractor responsibilities, procedures to avoid bias in tracing and interviewing.

Because 93% of the cases of malignant respiratory disease were lung cancers, the current analysis focuses on lung cancer and non-malignant respiratory disease. Initial analyses assessed the association between lung cancer or non-malignant respiratory disease and each of the individual variables: place of birth, education, income, marital state, smoking of six months or more duration, age when smoking first started, and duration of smoking. Hobbies were excluded from this analysis because most subjects were reported to have no hobbies. Although employment histories were reasonably complete, dates of employment were often not available, which makes it difficult to incorporate this variable into a systematic, quantitative analysis.

Conditional logistic regression was carried out to

Table 2 Matched, unadjusted lung cancer and non-malignant respiratory disease ORs for risk factors determined by interview

Subject characteristic	*OR (95% CI)*
Lung cancer	
Birthplace:	
Ohio	1·000
Other American states	0·681 (0·392–1·182)
Foreign	2·000 (0·181–22·057)
Education (y):	
12 or more	1·000
8–11	1·749 (1·067–2·868)
<8	1·450 (0·620–3·398)
Income ($):	
<5000	1·000
5000–9999	1·500 (0·251–8·977)
10 000–19 999	0·795 (0·157–4·025)
⩾20 000	2·000 (0·181–22·057)
Marital state:	
Married	1·000
Widowed, divorced, separated	0·953 (0·578–1·571)
Never married	1·125 (0·294–4·303)
Smoking (cigarettes):	
Never smoked	1·000
Smoked for six months or more	14·725 (3·528–61·452)
Age first started smoking:	
Never smoked	1·000
<20 years	19·891 (2·656–148·963)
20 years and over	3·000 (0·312–28·842)
Duration of smoking:	
Never smoked	1·000
40 or fewer pack-years	10·408 (1·328–81·568)
>40 pack-years	13·909 (1·818–106·417)
Non-malignant respiratory disease	
Birthplace:	
Ohio	1·000
Other American states	0·796 (0·401–1·582)
Foreign	1·000 (0·163–6·139)
Education (y):	
12 or more	1·000
8–11	1·269 (0·717–2·247)
<8	1·076 (0·429–2·698)
Income ($):	
<5000	1·000
5000–9999	0·618 (0·055–6·995)
10 000–19 999	2·562 (0·225–29·123)
⩾20 000	2·562 (0·225–29·123)
Marital state:	
Married	1·000
Widowed, divorced, separated	0·833 (0·464–1·496)
Never married	0·366 (0·040–3·346)
Smoking (cigarettes):	
Never smoked	1·000
Smoked for six months or more	2·589 (1·199–5·590)
Age first started smoking:	
Never smoked	1·000
<20 years	4·000 (0·825–19·401)
20 years and over	2·788 (0·559–13·895)
Duration of smoking:	
Never smoked	1·000
40 or fewer pack-years	1·906 (0·363–10·008)
More than 40 pack-years	9·349 (1·173–74·509)

estimate the effect of any one variable while controlling for the effect of all the others.[4] The initial logistic analysis entered individual variables that may have suggested an association (that is, ORs of 1·5 or more or 0·67 or less regardless of significance). A final regression model utilised significant variables from the first step. Matched and unmatched ORs were not completely consistent. As a result, we present only matched analyses to be certain to account for the relation between the matching variables and outcome.

Results

Table 2 shows the unadjusted, matched ORs for each of the subject characteristics obtained at interview. For lung cancer, there were statistically significant ORs for education and each of the smoking variables. Smoking in this analysis was defined as having smoked cigarettes for six months or more. Non-smokers had never smoked cigarettes. Among the characteristics included, cigarette smoking is clearly the overwhelming variable for lung cancer with an OR of 14·7 when those who smoked cigarettes for six months or more were compared with those who never smoked cigarettes. Odds ratios increased with duration of cigarette smoking and decreased as the age at which smoking was started increased. The OR for those who started smoking under 20 years of age was nearly 20 (95% CI 2·7–149).

Only the smoking variables were significant for non-malignant respiratory disease. As with lung cancer, ORs for non-malignant respiratory disease increased with duration of smoking and decreased as the age at which smoking started increased. The highest OR was for those smoking more than 40 pack-years (OR = 9·35, 95% CI 1·2 to 75).

Table 3 shows the results of the conditional logistic regression analyses. As indicated, variables giving an OR $\geqslant 1{\cdot}5$ or $\leqslant 0{\cdot}67$ in the univariate analysis were included initially in the model. Four variables (place of birth, education, income, and smoking state) met these criteria for lung cancer. When included together, however, the model was inoperable because there were no observations for foreign born cases and only two observations for non-smoking cases. The most adequate estimate of the OR was obtained by including smoking and education. In this model, only the smoking OR of 23·4 (95% CI 3·2–172·9) was statistically significant although the ORs for education were raised. Clearly, in this study, cigarette smoking was such an overpowering predictor for lung cancer that other variables were overwhelmed in any model.

On the other hand, three variables (income, marital state, and smoking state) met the conditional logistic regression model inclusion criteria for non-malignant respiratory disease. Whereas there were raised ORs for each variable, none were statistically significant, including that for cigarette smoking.

Table 3 Lung cancer and non-malignant respiratory disease adjusted ORs from conditional logistic regression analysis for risk factors determined by interview

Subject characteristic	*Adjusted OR (95% CI)*
Lung cancer	
Education:	
⩾12 years	1·000
8–11 years schooling	1·612 (0·970–2·680)
<eight years schooling	1·248 (0·609–2·558)
Smoking (cigarettes):	
Never smoked	1·000
Smoked for six months or more	23·478 (3·189–172·881)
Non-malignant respiratory disease	
Income ($):	
<5000	1·00
5000–9999	3·070 (0·587–16·046)
10 000–19 999	2·688 (0·508–14·217)
⩾20 000	1·312 (0·224–7·704)
Marital state:	
Married	1·00
Widowed, divorced, separated	1·004 (0·474–2·127)
Never married	0·776 (0·069–8·785)
Smoking (cigarettes):	
Never smoked	1·00
Smoked for six months or more	2·105 (0·763–5·802)

Discussion

Historical cohort studies considering the issue of risk of lung cancer among workers engaged in the production of MMMF have been conducted both in the United States[1,2] and in seven European countries.[5] The standardised mortality ratios (SMRs) for lung cancer in both the United States and European studies were statistically significantly raised when based on national rates but not when based on local rates.

The Newark plant constitutes 38% of all MMMF workers in the TIMA study. The current case control study was undertaken to determine the extent to which exposures to substances in the Newark plant environment, to non-workplace factors, or to a combination may play a part in risk of mortality from respiratory disease among workers in this plant. Although work to characterise exposures to substances other than fibreglass is ongoing, results to date indicate the necessity for taking potential confounders into consideration before ascribing any excess of observed over expected deaths from lung cancer to exposure to fibreglass alone. As well as fibreglass, there has been potential exposure to a variety of substances—for example, asbestos, silica, and formaldehyde. Furthermore, many of the employees included in the Newark cohort study worked at Newark for comparatively short periods and their non-Newark working environment has not been taken into consideration in interpreting increased SMRs.

Results of the historical cohort mortality study carried out on behalf of TIMA were not adjusted for the possible confounding effect of smoking. A nested case-control study for the entire TIMA cohort showed a significant association between lung cancer and smoking among production workers but not between lung cancer and dosage of fibre.[1] If there were differences in prevalence of smoking between the TIMA cohort and the United States population upon which the standard death rates were based, some of the excess of observed over expected deaths could be accounted for by differential prevalence of smoking between the TIMA cohort and the United States population. The same is true for any individual plant. The number of interviews in the TIMA nested case-control study was too small, however, to give meaningful estimates of the prevalence of smoking by plant.[1]

Lung cancer SMRs for the Newark cohort (followed up to the end of 1982) based on national death rates were significantly raised. Those based on local rates were also raised, though not significantly. Table 4, which shows that most subjects in the case-control study were smokers, suggests that the potential impact of differential smoking prevalence on SMRs for Newark needs to be examined.

Our interview study obtained smoking histories on a total of 751 subjects (some 13% of the original Newark cohort of 5720). It affords an opportunity to estimate the prevalence of those who ever smoked in the Newark cohort and perhaps provide some insight into the impact of smoking on the SMRs for lung cancer for the Newark plant.

Ideally, to account for any contribution of differential prevalence of smoking to the excess of observed over expected deaths, one would want the age-race-sex-specific prevalence of smoking for both Newark and the comparison population for comparable calendar periods. Data on the prevalence of smoking by calendar year and birth cohort for the United States are limited. A smoking survey reported by Fortune magazine in 1935 indicated that 65·5% of men under age 40 and 39·7% of men over age 40 were cigarette smokers.[6] This shows that the prevalence of smoking was increasing over the period most important for its potential impact on the SMRs in the TIMA study.

Table 4 Cases and matched controls by smoking state

Smoking state	*Cases no (%)*	*Controls no (%)*
Lung cancer		
Smoking history obtained	143 (100)	259 (100)
Smoked cigarettes for six months or more	139 (97)	209 (79)
Never smoked cigarettes	4 (3)	47 (18)
Non-malignant respiratory disease		
Smoking state:		
Smoking history obtained	99 (100)	181 (100)
Smoked cigarettes for six months or more	88 (89%)	135 (75)
Never smoked cigarettes	10 (10)	41 (23)

Table 5 Estimated prevalence of cigarette smoking (%) for the United States and Newark by birth cohort for 1955 and 1965

Birth cohort	*US†*	*Newark*	
		Controls only	*Controls plus cases*
	*1955**		
1921–30	72	94	96
1911–20	73	88	92
1901–10	70	78	84
1891–1900	60	63	70
<1891	41	47	54
	1965‡		
1921–1930	79	94	96
1911–1920	—	87	91
1901–1920	76	83	87
1901–1910	—	77	83
1891–1900	—	60	70
<1891–1900	56	57	67
<1891	—	47	57

*Derived from Haenszel *et al*; appendix table 4.[9]
†Regular plus occasional cigarette smokers.
‡Source: Health US, 1986, table 40.[10]

Harris has produced widely used estimates of smoking prevalence for the United States by birth cohort for calendar years from 1900 to 1980 based on data from the National Health Interview Survey (HIS) special smoking supplements for 1978–80.[7] His estimates are based on self respondents and are not race specific. Further, his estimates of prevalence of smoking for calendar years pertinent to the TIMA cohort are underestimates of past smoking prevalence because of (1) differential mortality between smokers and non-smokers and (2) possible underreporting by respondents due to increases in the "perceived . . . social stigma associated with smoking."[8] In correcting for differential mortality, Harris provided the prevalence of current smokers by calendar year. It is the prevalence of those who have ever smoked rather than of current smokers, however, that is most pertinent to the impact of smoking on the SMRs.

Two sources are available that provide age-race-sex-specific data on the prevalence of those who ever smoked for the United States population for two years near the mid-point of the period for which the expectations were calculated in the TIMA study. The study by Haenszel *et al* of tobacco smoking patterns in the United States provides data with the greatest detail on the proportion of the United States white male population in 1955 who ever smoked by birth cohort.[9] The second source provides more limited data for 1965 by birth cohort.[10] Unlike the Harris estimates, these surveys are not likely to be biased by underreporting as they were done before the first report of the Surgeon General on Smoking

Table 6 Estimated prevalence of cigarette smoking (%) for Columbus, Ohio and Newark by birth cohort for 1947

Birth cohort	Columbus*	Newark	
		Controls only	Controls plus cases
1918–27	84	92	95
1908–17	84	84	89
1898–1907	82	75	81
1888–97	78	58	67
1878–87	61	56	55

*Derived from table 4.[11]

and Health in the mid-1960s at a time when smoking was more socially acceptable.

Table 5 presents estimates of the prevalence of ever smoked among white men by birth cohort for both the Newark plant population and the United States in 1955 and 1965. Prevalence of smoking for Newark may be overestimated by using both cases and controls because of the inclusion of a number of subjects whom we know eventually died of lung cancer or non-malignant respiratory disease. On the other hand, the data of Haenszel *et al* also include subjects who will eventually die from these causes although in lesser proportion than the combined case-control data. Use of controls only will tend to underestimate prevalence of smoking in Newark and minimise differences between Newark and the United States.

Prevalence of cigarette smoking for Newark in 1955 appears to be sufficiently greater than the corresponding United States data in 1955 to suggest that some of the previously reported excess of lung cancer for Newark (based on United States mortalities) may be accounted for by differences in the prevalence of cigarette smoking between white men in Newark and the United States.

As indicated above, the SMR for lung cancer for Newark based on a local standard was raised though not significantly so. Data on local smoking prevalence that would allow investigation of the impact of smoking on locally based SMRs are not available. Limited data are available, however, for that of a nearby area—namely, Columbus, Ohio.[11] These data may provide a basis for evaluating the impact of smoking on those SMRs based on the local standard. Table 6 provides a comparison by birth cohort of the Newark estimates of prevalence of smoking and those from Columbus. Prevalence of smoking is somewhat higher in Newark only for the most recent birth cohort, which accounted for 21% of the Newark lung cancer deaths. For the earlier birth cohorts, prevalence of smoking is higher in Columbus. If data for Columbus are similar to those in the four county area which comprises the local standard, differences in prevalence of smoking between Newark and the local population would not appear to account for the observed excess based on a local standard. Of course, there is no way of determining whether prevalence of smoking in Columbus is at all similar to that of the Newark area.

The issue of how much of the excess in risk of lung cancer can be accounted for by differential prevalence of smoking between the Newark cohort and either the United States in 1955 or the Columbus data for 1947 provides a matter for further investigation. Results of the interview portion of our case control study clearly indicate that smoking is by far the most important non-workplace factor in distinguishing between lung cancer cases and controls in this group of workers. The smoking ORs for lung cancer are large and nearly all of the lung cancer cases were smokers. On the other hand for non-malignant respiratory disease among these workers, smoking does not seem to be as important a non-workplace factor as it is for lung cancer. It remains to be seen what effect smoking has for both malignant and non-malignant respiratory disease when added to the information on exposure being developed.

This study was supported by a grant to Georgetown University from the Owens-Corning Fiberglas Corporation. The authors gratefully acknowledge the contributions of Olga Alsheimer, Cynthia Moore, and members of the Advisory Committee—Dr Patricia A Buffler, University of Texas at Houston, Dr John Higginson, Georgetown University, and Dr Genevieve Matanoski, the Johns Hopkins University School of Hygiene and Public Health.

1 Enterline PE, Marsh GM, Henderson V, Callahan C. Mortality update of a cohort of US man-made mineral fiber workers. *Ann Occup Hyg* 1987;31:625–56.
2 Enterline PE, Marsh GM, Esmen NA. Respiratory disease among workers exposed to man-made mineral fibers. *Am Rev Respir Dis* 1983;128:1–7.
3 Enterline PE, Marsh GM. The health of workers in the MMMF industry. In: Guthe T, ed. *Biological effects of man-made mineral fibers*. Vol 1—Proceedings of a WHO/IARC conference. Denmark: World Health Organisation, 1984:311–39.
4 Breslow NE, Day NE. *Statistical methods in cancer research*. vol 1. *The analysis of case-control studies*. Lyon: International Agency for Research on Cancer, 1980.
5 Simonato L, Fletcher AC, Cherrie JW. The International Agency for Research on Cancer historical cohort study of MMMF production workers in seven European countries—extension of the follow-up. *Ann Occup Hyg* 1987;31:603–23.
6 Fortune Magazine. The Fortune survey. III. Cigarettes. *Fortune* 1935;12:68, 111.
7 Harris JE. Cigarette smoking among successive birth cohorts of men and women in the United States during 1900–80. *J Natl Cancer Inst* 1983;71:473–9.
8 Warner W. Possible increases in the underreporting of cigarette consumption. *Journal of the American Statistical Association* 1978;73:314–8.
9 Haenszel W, Shimkin MB, Miller HP. *Tobacco smoking patterns in the United States*. Washington DC: US Government Printing Office, 1956. (Public Health Service (No 463)).
10 National Center for Health Statistics: *Health, United States, 1986*. Washington DC: US Government Printing Office, 1986. (DHHS pub no (PHS) 87–1232).
11 Mills CA, Porter MM. Tobacco-smoking habits in an American city. *J Natl Cancer Inst* 1953;13:1283–97.

Accepted 16 September 1991