Residential Proximity to Naturally Occurring Asbestos and Mesothelioma Risk in California

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Rationale: **Little is known about environmental exposure to low levels of naturally occurring asbestos (NOA) and malignant mesothelioma (MM) risk.**

Objectives: **To conduct a cancer registry-based case control study of residential proximity to NOA with MM in California.**

Methods: **Incident MM cases (n = 2,908) aged 35 yr or more, diagnosed between 1988 and 1997, were selected from the California Cancer Registry and frequency matched to control subjects with pancreatic cancer (n = 2,908) by 5-yr age group and sex. Control subjects were selected by stratified random sampling from 28,123 incident pancreatic cancers in the same time period. We located 93.7% of subjects at the house or street level at initial diagnosis. Individual occupational exposure to asbestos was derived from the longest held occupation, available for 74% of MM cases and 63% of pancreatic cancers. Occupational exposure to asbestos was determined by *a priori* classification and confirmed by association with mesothelioma.**

Main Results: **The adjusted odds ratios and 95% confidence interval for low, medium, and high probabilities of occupational exposures to asbestos were 1.71 (1.32–2.21), 2.51 (1.91–3.30), and 14.94 (8.37–26.67), respectively. Logistic regression analysis from a subset of 1,133 mesothelioma cases and 890 control subjects with pancreatic cancer showed that the odds of mesothelioma decreased approximately 6.3% for every 10 km farther from the nearest asbestos source, an odds ratio of 0.937 (95% confidence interval = 0.895–0.982), adjusted for age, sex, and occupational exposure to asbestos.**

Conclusions: **These data support the hypothesis that residential proximity to NOA is significantly associated with increased risk of MM in California.**

Keywords: Cancer Registry case-control study; GIS; malignant mesothelioma; naturally occurring asbestos; occupational exposure to asbestos

Epidemiologic studies have confirmed that occupational exposure to asbestos causes mesothelioma (1–7). However, almost all population-based studies have found that many mesothelioma cases had no known occupational exposure to asbestos. Some of these cases could be due to domestic and neighborhood exposure to asbestos, or even environmental exposure to naturally occurring asbestos (NOA). An association with domestic or neighborhood exposure to asbestos or other mineral fibers and an increased risk of mesothelioma has been found in several locations including Australia (8), South Africa (9), Italy (10), and New Jersey (11). Studies among residents of two Anatolian villages in Turkey showed that the astounding high incidence of malignant mesothelioma results from environmental exposure to carcinogenic tremolite and erionite, a fibrous zeolite, which is present in the volcanic tuffs that are used as building stone (12). An association between environmental exposure to NOA and mesothelioma has been observed in Cyprus (13), Greece (14), New Caledonia (15), Corsica (16), China (17), and Italy (18), but no research has studied the association of residential distance from environmental (nonoccupational) asbestos and mesothelioma risk (19).

It remains unknown whether environmental exposure to low levels of NOA also causes mesothelioma. Research has failed to find a threshold level below which there is no mesothelioma risk, and low-dose exposure to asbestos can cause mesothelioma (20). Most epidemiologic studies for mesothelioma have failed to find evidence of occupational, domestic, or neighborhood exposure to asbestos in a sizable proportion of mesothelioma cases (7). For example, 25% of mesothelioma cases in a Spanish case–control study had no significant occupational, domestic, or neighborhood exposure to asbestos (3). It is plausible that exposure to NOA may account for a portion of those mesothelioma cases. California has large amounts of serpentinite and other ultramafic rocks that are the predominant but not exclusive source of NOA and are distributed mostly in the Sierra Nevada, Coast Ranges, and Klamath Mountains in Northern and Central California (Figure 1). The most common type of asbestos is chrysotile, but other types including tremolite are also found in California. (21). There have been increasing concerns about whether an increased risk of mesothelioma is associated with environmental exposures to NOA in these areas. Some of these areas include new housing developments and potential exposure to a large number of people.

Statewide cancer reporting in California has been mandated by law since 1985, and beginning in January 1988, the California Cancer Registry (CCR) has covered the entire population in California through nine regional population-based cancer registries. The CCR is one of the largest comprehensive population-based statewide cancer registries in the world, covering more than one tenth of the U.S. population. About 300 incident cases of malignant mesothelioma per year are reported in California. It is estimated that more than 98.9% of all mesothelioma cases diagnosed in California are reported to the California Cancer Registry (22). This study used a unique opportunity to evaluate the association between exposure to potential sources of indigenous environmental asbestos and incidence of mesothelioma. California has more serpentinite and ultramafic rocks than other states in the United States, and its distribution is patchy, with exposed areas separated from unexposed areas (23). Additionally, California's large population provided us with an adequate sample size to study this rare cancer.

METHODS

Case Ascertainment and Control Selection

Incident cases of malignant mesothelioma diagnosed from 1988 through 1997 in California were identified from the CCR. The International Classification of Diseases for Oncology, Second edition (ICD-O-2, 1990), was used by the CCR for the period covered by the study (22). The case series consisted of all reported patients ages 35 yr or older

(*Received in original form December 22, 2004; accepted in final form June 19, 2005*)

Supported by the National Cancer Institute (Project Grant IR03CA81615-01).

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Am J Respir Crit Care Med Vol 172. pp 1019–1025, 2005
Originally Published in Press as DOI: 10.1164/rccm.200412-1731OC on June 23, 2005
Internet address: www.atsjournals.org

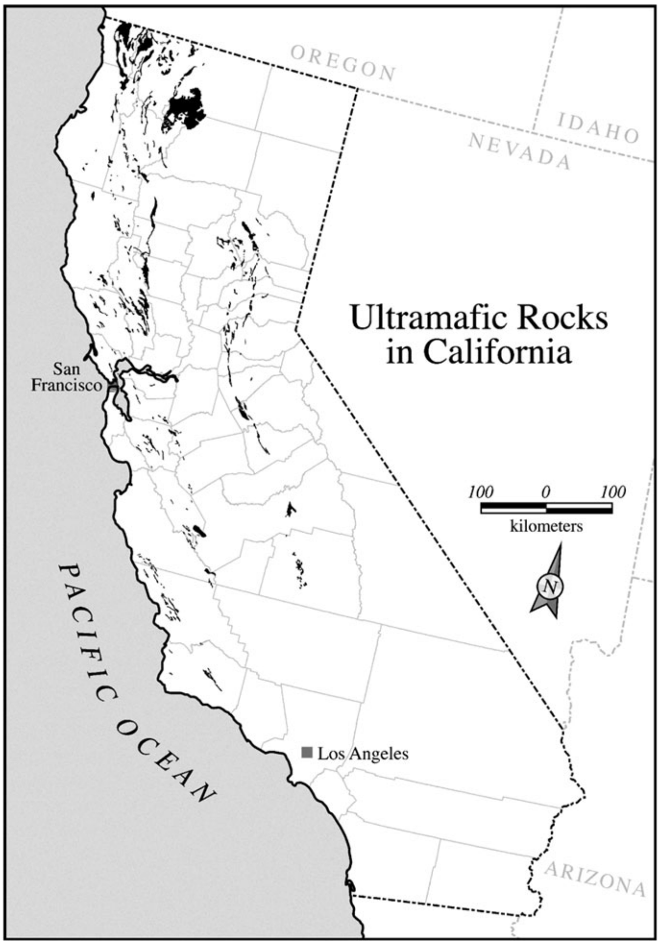

Figure 1. Distribution of ultramafic rocks in California.

diagnosed with malignant mesothelioma (histology ICD-O-2 codes 9050–9053) from 1988 through 1997 in California. For each case, one control frequency-matched by 5-yr age group and sex was selected by stratified random sampling from patients diagnosed with incident malignant pancreatic cancer (primary site ICD-O-2 codes C250–259) reported to the CCR in the same period.

Assessment of Residential Proximity to NOA

No maps exist that illustrate the distribution of NOA in California. However, ultramafic rocks are the principal source of asbestos and may be used as a proxy for its natural occurrence. To locate known bodies of ultramafic rock, we used a digital version of the geologic map of California, at a scale of 1:750,000, created in 1970 by the California Department of Conservation, Division of Mines and Geology (24). Residential proximity to NOA was estimated as the distance to the edge of the nearest known body of ultramafic rock. Distances were measured using the spatial analyst feature in the GIS software ArcView 3.1 (ESRI, Redlands, CA) (25) using the digital geologic map of California and the latitude and longitude of an address at initial diagnosis from the CCR records. The latitude and longitude were obtained from the online Tele Atlas North America's Eagle Geocoding Server (www.geocode.com). The server returned the geocoding results with the original address, standardized address, latitude, longitude, accuracy, and source of the match for every address. Because there are only two small asbestos sources in Southern California, the nearest distance was calculated excluding these two deposits (Figure 1).

Assessment of Occupational Exposure to Asbestos

Occupational exposure to asbestos is a dominant risk factor for mesothelioma, and it is unlikely that the potential weak association between residential proximity to sources of NOA and incidence of mesothelioma would be detectable if we did not control for occupational exposure. Ideally, actual exposure level and duration of each occupation should be considered, but it was impossible to obtain that information for each occupation or job title. In this study, occupational exposure to asbestos was estimated using only CCR records on the longest held occupation or industry. Because there is a significant positive dose–response relationship between the risk of asbestosis and duration and intensity of occupational exposure to asbestos, we ranked occupational exposure to asbestos for some occupations based on asbestosis proportionate mortality ratios (PMR) of these occupations. An occupation with higher asbestosis PMR is assumed to have a higher likelihood of occupational exposure to asbestos. We used data from the Work Lung Disease Surveillance Report by National Institute for Occupational Safety and Health (26), augmented with a study by Cocco and colleagues (27), to rank occupations according to their probability of occupational exposure to asbestos. Occupations with high, moderate, and low probabilities of occupational exposure to asbestos were defined as those that have asbestosis PMR > 15, PMR $= 3$–15, and PMR < 3, respectively. In addition, shipyard workers were considered to have a high probability of occupational exposure (26), and all occupations with no recognizable sources of asbestos were assigned the lowest probability. When a subject had more than one occupation, the probability of exposure to asbestos assigned to an individual was the maximum probability in his or her record. Because asbestosis PMRs were available for a limited number of occupations in the National Institute for Occupational Safety and Health report, a job-exposure matrix for asbestos developed by Cocco and colleagues was also used to rank occupational exposure to asbestos (27). Occupations with high occupational asbestos exposure were shipyard worker, insulator, plumber, pipefitter, steamfitter, and boilermaker (26). Major occupations with moderate probability were mechanic, electrician, sheet metal worker, welder, sailor, navy serviceman, and construction labor (26, 27).

Statistical Analysis

Cases were compared with controls initially by univariate analyses. Chi-square tests were used to compare sex and known occupational exposure, and Wilcoxon rank-sum tests for age and nearest distance from asbestos deposits. Logistic regression was then used to confirm the association between mesothelioma and occupational exposure. Multivariate logistic regression models were used to assess the relationship between mesothelioma risk and asbestos exposure from naturally occurring deposits, adjusted for occupational exposure, age at initial diagnosis (continuous variable), and sex (examined both in pooled models and stratified by sex). The primary models grouped occupation by category of exposure, with unexposed groups as the reference. The influence of occupation was examined both as a confounder and as a potential interaction with residential proximity. Nearest distance in kilometers from naturally occurring deposits was initially examined as a continuous variable, with zero corresponding to residence within a natural asbestos zone. The primary model assumed that the log odds of mesothelioma decreased linearly with distance, so that a 1-km increase in distance was assumed to decrease risk in the odds by a constant percentage, regardless of the location. Results were reported in units of 10-km change for easier interpretation of small coefficients. The assumption of linearity was examined graphically, using plots of locally reweighted smoothed (lowess) log odds versus distance and fractional polynomials (28). Secondary analyses examined alternative relationships to distance, including square root, natural logarithm, and reciprocal transformations of nearest distance; and grouping distance into categories of 50 km, 100 km, and 150 km or more. Model fit was checked by Pearson and Deviance goodness-of-fit statistics and Hosmer and Lemeshow diagnostics (28). All analyses were performed in STATA release 6 (29).

RESULTS

A total of 2,966 incident cases diagnosed with malignant mesothelioma were reported to the California Cancer Registry in the period between 1988 and 1997. There were 17 duplicate records deleted and 41 cases younger than 34 years were removed. The study included 2,908 malignant mesothelioma cases (2,354 men and 554 women). We selected 2,908 control subjects frequency matched by 5-yr age group and sex by stratified random sampling from the 28,123 incident cases of malignant pancreatic cancer reported to the CCR in the same period.

Among 5,816 subjects, mesothelioma cases and control subjects with pancreatic cancer in our study were balanced in vital status (93% versus 97%), percentages of data abstracts from inpatient or outpatient records (96% versus 92%), race/ethnicity, and marital status by sex (Table 1). The percentage of histologic diagnosis of mesothelioma cases was significantly higher than for control subjects with pancreatic cancer (82% versus 56%). Data on the longest-held occupation and industry were available for 74% of mesothelioma cases and 63% of control subjects with pancreatic cancer, respectively. All cases and control subjects were located based on their residential addresses at initial diagnosis. Among these, 93% of geocodes were completed at a house or street level (the most precise), 6% at a geographic centroid of a five-digit zip code, and only 0.3% at a geographic centroid of a city or county (the least precise). Geographic coding rates were comparable in cases and control subjects (Table 1).

Logistic regression analyses were restricted to the subset of 1,133 mesothelioma cases and 890 control subjects with pancreatic cancer who had complete data on residence, age, sex, and occupation. Univariate analyses in this data set showed nearly identical age distributions and proportion of males. The cases had substantially higher frequency of occupational exposures to asbestos (Table 2).

Age-adjusted logistic regression analysis for occupational exposure to asbestos showed that occupations with a high probability of occupational exposure to asbestos in men such as boilermaker, insulator, plumber, pipefitter, steamfitter, sheet metal worker, electrician, and painter were strongly associated with mesothelioma risk, whereas few female cases and control subjects had occupations with a high probability of occupational asbestos exposure. This supported the hypothesis that the difference of mesothelioma incidences between men and women mainly resulted from different occupational exposures to asbestos. Industries with high probability of occupational exposure to asbestos in men such as shipyard and Navy were significantly associated with the elevated mesothelioma risk (Table 2).

In the primary analysis of the association of NOA and mesothelioma, a multivariate logistic regression model was fitted, assuming a constant percent change in the odds of mesothelioma with a 10-km increase in nearest distance, adjusted for the effects of age, sex, and occupational exposure (Table 3). The estimated effect was a 6.3% decrease (computed from the odds ratio as $[(1 - 0.937) \times 100\%]$ in the odds of a mesothelioma case for every 10 km farther away from a NOA source (95% CI, 1.8–10.5%; $p = 0.006$). Occupational exposure, as expected, was the strongest predictor of an increased odds of mesothelioma, with a significant dose–response relationship. Age and sex as major risk factors of mesothelioma and matching factors in this study were included in the final multivariate model to adjust for the impact of imbalance in age and sex from exclusion of cases and controls with unknown occupational exposure and more than 100-km nearest distances.

An analysis excluding the cases with a moderate or high probability of occupational asbestos exposure gave very similar

TABLE 1. CLINICAL FEATURES OF 2,908 MESOTHELIOMA CASES AND 2,908 CONTROL SUBJECTS WITH PANCREATIC CANCER BY SEX, CALIFORNIA, 1988–1997

	Men		Women	
Clinical Characteristics	Cases $n = 2,354$ (%)	Control Subjects $n = 2,354$ (%)	Cases $n = 554$ (%)	Control Subjects $n = 554$ (%)
Age, yr	69.70 ± 10.67	69.75 ± 10.73	68.56 ± 12.44	68.77 ± 12.52
Probability of occupational exposure to asbestos				
None	794 (34)	1068 (45)	303 (55)	282 (51)
Low	367 (16)	259 (11)	19 (3)	8 (1)
Medium	355 (15)	170 (7)	15 (3)	3 (1)
High	287 (12)	27 (1)	6 (1)	1 (0)
Retired	282 (12)	406 (17)	109 (20)	109 (20)
Unknown	269 (11)	424 (19)	102 (18)	151 (27)
Nearest distance (km)* Median	55.2	115.5	112.3	131.4
Range (P5, P95)	2.0, 316.9	2.1, 311.4	2.3, 318.7	2.6, 315.4
Sources of abstract				
Inpatient/outpatient	2,250 (96)	2,162 (92)	526 (95)	514 (93)
Private physician	36 (2)	6 (0)	6 (1)	0 (0)
Laboratory	8 (0)	85 (4)	3 (1)	19 (3)
Nursing home	2 (0)	4 (0)	3 (1)	2 (0)
Autopsy only	25 (1)	35 (1)	8 (1)	2 (0)
Death certificate only	33 (1)	62 (3)	8 (1)	17 (3)
Diagnostic methods				
Histology	1,922 (82)	1,307 (56)	466 (84)	320 (58)
Cytology	265 (11)	374 (16)	65 (12)	87 (16)
Radiography	58 (2)	318 (14)	5 (1)	75 (14)
Clinical	57 (2)	109 (5)	7 (1)	22 (4)
Visualization	5 (0)	110 (5)	0 (0)	22 (4)
Unknown	47 (2)	136 (6)	11 (2)	28 (5)
Types of address matching				
House or street level (the best)	2,170 (92)	2,233 (94)	525 (95)	523 (94)
Centroid of a 5-digit zipcode	177 (8)	113 (5)	26 (5)	29 (5)
Centroid of a county (the worst)	7 (0)	8 (0)	3 (0)	2 (0)
Vital status (dead)	2,195 (93)	2,291 (97)	472 (85)	536 (97)

* Two-sample Wilcoxom rank-sum test for the nearest distance: $p = 0.0141$ for men; $p = 0.0724$ for women.

TABLE 2. AGE-ADJUSTED ODDS RATIOS AND THEIR 95% CI FOR LONGEST-HELD INDUSTRIES OR OCCUPATIONS WITH 25 CASES OR MORE BY SEX: CALIFORNIA, 1988–1997, BASED ON A SUBSET OF 2,146 MESOTHELIOMA CASES AND 1,818 CONTROL SUBJECTS WITH PANCREATIC CANCER

	Men				Women			
Exposure to Asbestos	Cases n = 1,803*	Control Subjects n = 1,524*	OR†	95% CI†	Cases n = 343*	Control Subjects n = 294*	OR†	95% CI†
Industry								
Shipyard	161	12	12.2	6.7–22.0	7	1	6.4	0.8–52.6
Navy	130	26	4.4	2.9–6.8	2	1	1.7	0.2–18.8
Construction	137	68	1.8	1.3–2.4	2	0	—	—
Farming	33	55	0.5	0.3–0.8	1	7	0.1	0.0–0.9
Occupation								
Boilermaker	27	1	23.0	3.1–169	0	0	—	—
Insulator	26	2	11.4	2.7–48.3	1	0	—	—
Plumber, pipefitter, steamfitter	90	16	4.9	2.8–8.3	1	0	—	—
Sheet metal worker	33	6	4.8	2.0–11.5	0	0	—	—
Electrician	53	12	3.8	2.0–7.1	3	1	2.5	0.3–24.6
Painter	31	10	2.6	1.3–5.3	0	0	—	—
Welder	55	25	1.9	1.2–3.0	2	0	—	—
Carpenter	41	28	1.2	0.8–2.0	0	0	—	—
Machinist	35	24	1.2	0.7–2.1	0	0	—	—
Mechanic	46	39	1.0	0.6–1.5	1	0	—	—
Probability of occupational exposure to asbestos								
None	794	1068	1.0		303	282	1.0	
Low	367	259	1.9	1.6–2.3	19	8	2.2	0.9–5.1
Medium	355	170	2.8	2.3–3.4	15	3	4.7	1.3–16.3
High	287	27	14.2	9.5–21.3	6	1	5.9	0.7–49.6

Definition of abbreviations: CI: confidence interval; OR: odds ratio.

* Excludes records with "unknown" or "retired" in the longest held industry and occupation data items.

† Adjusted for age at initial diagnosis (continuous).

results. Among all subjects the odds ratio for mesothelioma for a 10-km increase in nearest distance was 0.943 (95% CI, 0.896–0.922). The observed odds ratios for men and women were 0.939 (95% CI, 0.887–0.994) and 0.961 (95% CI, 0.861–1.073), respectively.

Figure 2 illustrates the shift in the log odds of mesothelioma versus pancreatic cancer as the distance from NOA sources increases among men and women. People who lived closer to an asbestos source had a greater chance of having mesothelioma, and the chance decreased steadily as the distance increased. In stratified analyses of men and women, we saw comparable findings, although the results in women were based on small samples and were not statistically significant (results not shown). Fractional polynomial analysis suggested that the nearest distance was reasonably included in the multivariate logistic regression model as a linear continuous independent variable for residential proximity to sources of NOA, which is the assumption for including the distance as a continuous variable in the logistic regression model. Logistic regression diagnostics supported the use of this model, with no evidence for model failure or interactions (results not shown).

We obtained similar results when we repeated the analysis using only subjects with a nearest distance of 50 km or less. When we repeated the analysis using either subjects with 150 km or less or all subjects, using the log-transformed nearest distance rather than the nearest distance in the multivariate logistic regression models, we also found that there was an inverse relationship between the log-transformed nearest distance and risk of mesothelioma (data not shown).

Pleural mesotheliomas accounted for 91% of the total cases. When only pleural mesothelioma cases were used, proximity to NOA was significantly and positively associated with case status for both men and women. On the contrary, when only peritoneal mesothelioma cases were used, proximity to NOA was not significantly associated with case status and did not show a trend with distance.

DISCUSSION

Results of this cancer registry–based case control study for mesothelioma in California demonstrated that residential proximity to geologic sources of NOA in California was independently and positively associated with case status. The odds of being a mesothelioma case are 6.3% lower than the odds of being a control subject for every 10 km farther from the nearest asbestos source. These findings were adjusted for occupational exposure to asbestos, age at initial diagnosis, and sex. The association was observed in both men and women, although the association was statistically significant in men only.

Our study confirmed that some occupations such as shipyard worker, boilermaker, insulator, plumber, pipefitter, and steamfitter, and industries such as shipping, construction, and Navy had higher occupational exposure to asbestos and were strongly associated with an increased risk of malignant mesothelioma, consistent with results from previous studies of mesothelioma (1–6, 30). Although it is likely that occupational exposure misclassification exists, our study did see the expected dose–response relationship between occupational exposure to asbestos and mesothelioma. The method defined by asbestosis PMR for occupations based on the longest held occupation and industry available in CCR data appeared reasonable to classify occupational exposure to asbestos.

A major strength of this study was the very large number of incident mesothelioma cases used to assess the potentially weak association between exposure to NOA and mesothelioma inci-

TABLE 3. RESULTS OF MULTIVARIATE LOGISTIC REGRESSION ANALYSIS FOR THE NEAREST DISTANCE ADJUSTING FOR AGE AND OCCUPATIONAL EXPOSURE TO ASBESTOS, BASED ON A SUBSET OF 1,133 MESOTHELIOMA CASES AND 890 CONTROL SUBJECTS WITH PANCREATIC CANCER

Variables	Cases	Control Subjects	OR	95% CI	z	p > |z|
All subjects	*n* = 1,133	*n* = 890				
Distance (every 10 km)			0.937	0.895–0.982	−2.72	0.006
Probability of occupational exposure to asbestos						
Low	185	128	1.712	1.324–2.214	4.10	0.000
Moderate	202	96	2.509	1.908–3.298	6.59	0.000
High	166	13	14.941	8.369–26.674	9.15	0.000
Men	*n* = 962	*n* = 746				
Distance (every 10 km)			0.935	0.888–0.985	−2.55	0.011
Probability of occupational exposure to asbestos						
Low	173	126	1.62	1.25–2.11	3.61	0.000
Moderate	193	95	2.41	1.82–3.18	6.19	0.000
High	165	12	15.79	8.66–28.80	9.00	0.000
Women	*n* = 171	*n* = 144				
Distance (every 10 km)			0.952	0.853–1.062	−0.88	0.381
Probability of occupational exposure to asbestos						
Low	12	2	5.60	1.23–25.52	2.23	0.026
Moderate	9	1	8.06	1.00–64.72	1.96	0.050
High	1	1	0.90	0.06–14.78	−0.07	0.942

Analysis is based on cases and controls with data of occupational exposure, age, sex, and nearest distance range from 0 to 100 km). p > |z| = p value for z-test.

Definition of abbreviations: 95% CI = 95% confidence interval of odds ratio; OR = adjusted odds ratio from multivariate logistic regression analysis = e^b; z = z-score for test of b = 0.

dence. The large size of this study provided us with a unique opportunity to detect relatively low-dose exposures to NOA in the presence of significant occupational exposure to asbestos. Another strength of this study was that GIS approaches were used to characterize potential individual exposure to NOA in a very efficient way. Geocoding of residential addresses provided more accurate assessment of potential environmental exposure to NOA at the individual level than methods using less precise geographic classification.

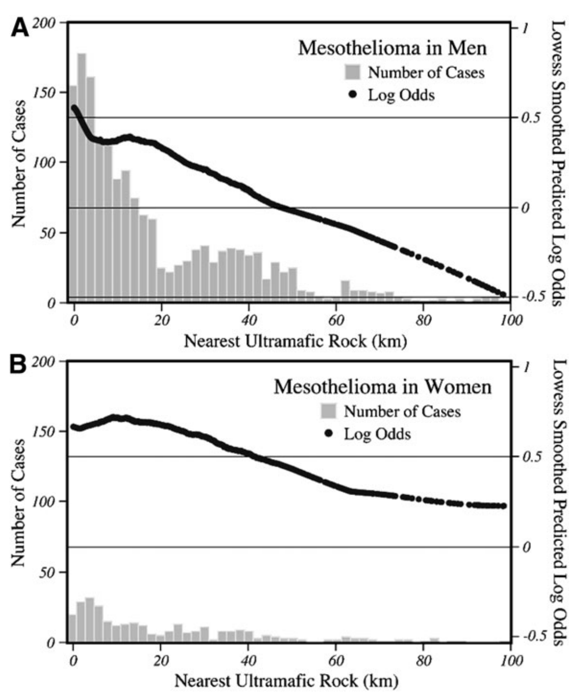

Figure 2. (*A*) Lowess-smoothed predicted log odds of mesothelioma versus nearest distance from naturally occurring asbestos deposits—men (adjusting for age, sex, and occupational exposure) and (*B*) lowess-smoothed predicted log odds of mesothelioma versus nearest distance from naturally occurring asbestos deposits—women (adjusting for age, sex, and occupational exposure).

Selection bias should be limited in our study because the data on mesothelioma and pancreatic cancer were both obtained by the CCR in a comparable way. The data included all registered cases, and the control patients were selected using stratified random sampling from patients with malignant pancreatic cancer in the same time period.

A limitation of the registry based study was lack of accurate and complete lifetime occupational histories on individual cases and controls. Incomplete occupational data and lack of duration and intensity of occupational exposure to asbestos in the past made it difficult for us to evaluate occupational exposure to asbestos using common occupational exposure assessments such as job-exposure matrices and expert assessment for exposures. Although the CCR was supposed to record the patient's longest-held occupation and industry, it often listed only current or most recent occupation. Occupational exposure is the predominant cause of asbestos-induced mesothelioma. We should be cautious to explain our results because our assessment for occupational exposure to asbestos was based on incomplete occupational history on individual cases and control subjects.

Another limitation of the study was the lack of a reliable and acceptable job-exposure matrix for asbestos to characterize the potential of individual occupational exposure to asbestos based on occupation or job titles. Therefore we had to derive occupational exposure to asbestos based on incomplete information on occupations and industries. Misclassification for occupational exposure was unavoidable in this study. Although the National Institute for Occupational Safety and Health has reported asbestosis PMR for selected occupations and industries to reflect strength of occupational exposure to asbestos, it included only limited occupations and industries with higher occupational exposure to asbestos and more asbestosis cases (26). The job-exposure matrix for asbestos developed by Cocco and Dosemeci in 1998 lacked validation of occupational exposure to asbestos (27), and too many occupations were defined as exposed in a study of mesothelioma in Australia (31).

The study was also limited by the lack of complete lifetime residential history on individual cases and controls. When we calculated the distance to the nearest NOA from subject residential address at initial diagnosis, we had to assume that subject's residential address at initial diagnosis was the same as the longest residential address in his or her life. Exposure misclassification in our study could either decrease or increase the observed dose–response relationship. Incomplete residential data and lack of residential duration in one's lifetime made it difficult to accurately assess environmental exposure to naturally occurring and other asbestos sources. Reliable assessment of exposure to NOA using GIS approaches ideally depends on accurate and complete residential histories. A field study is needed to examine the relationship between actual asbestos exposure potential and the distance to the nearest asbestos sources. In additionally, consideration should be given to the impact of age of potential exposure, deposit size, residence duration, nature of human disturbance activity, meteorologic conditions, and other geologic/demographic attributes on the actual or potential exposure to NOA.

Our study is based on ultramafic rock-specific GIS map, but not asbestos-specific GIS map for distribution of asbestos sources in California. A new digital map with more accurate and specific information about asbestos sources in California needs to be developed for further studies. It is essential for public health efforts to assess more accurately potential exposure to NOA. Some efforts should be increased to characterize the location of asbestos deposits using imaging spectroscopy to map ultramafic rocks, serpentinites, and tremolite-actinolite–bearing rocks in California (32).

Frequency matching was used to minimize confounding from age and sex. We were unable to control for potential confounding from domestic or residential exposure to asbestos because these data were not available for this study. Selection bias was limited because the data included all eligible cases from the population-based CCR and the control subjects were selected by stratified random sampling from the same population-based cancer registry. The data were collected in a similar manner for cases and control subjects; therefore, information bias from the data collection was limited, although some information bias cannot be avoided. For example, data on the longest occupation and industry were available for 74% of mesothelioma cases and 63% of pancreatic cancer cases in the CCR records. Because patients diagnosed with mesothelioma may be more likely to have been asked about occupational history and asbestos exposure, this may have led to overestimating occupational exposure to asbestos in this study.

We have found that residential proximity to NOA shows an independent and dose–response association with mesothelioma risk. The findings are biologically plausible in view of the known strong association of occupational asbestos exposure and mesothelioma, and the observation of an association of NOA and mesothelioma in other areas of the world (33). A prospective case–control study based on asbestos-specific GIS map in California should be done with incident mesothelioma cases. This would facilitate obtaining accurate and complete lifetime residential and occupational histories. Further research also is needed to develop a model to evaluate relationship between actual environmental exposure to NOA and major influencing factors, and to develop public health strategies to reduce exposure to asbestos from environmental sources.

Conflict of Interest Statement: None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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