

Table 2.1. Case-control studies of asbestos exposure and lung cancer

Reference, study location	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Relative risk (95% CI)*	Adjustment for potential confounders	Comments
Minowa et al.(1991), Yokosuka City, Kanagawa Prefecture, Japan site of a Japanese naval factory	116 male deceased histologically confirmed cases diagnosed in Kyosai Hospital during the period from 1978 to 1982.	86 males without cancer or pneumoconiosis who died in the same hospital of causes other than accident or suicide and whose date of birth was nearest to each of the lung cancer cases were selected as controls	Families were interviewed by investigators using a standardized questionnaire including a detailed work history and smoking history.	Asbestos Not exposed Suspected Exposed	1.00 1.7 2.5 ($p < 0.05$) Mantel trend test $p < 0.01$	Age & smoking.	
Morabia et al. (1992), 9 Metropolitan areas of the US	1793 incident lung cancer cases identified in 9 Metropolitan hospitals between 1980–1989.	3228 patients without lung cancer from same hospitals matched on age, race, hospital and smoking. Subjects having laryngeal, GI and oropharyngeal cancers were excluded.	Structured and standardized questionnaire administered by trained interviewers.	Duration Never < 10 years ≥ 10 years	1.0 2.0 (1.4–2.8) 2.1 (1.6–2.9)	Matching variables and questionnaire type.	The strongest associations were seen among never smokers

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Ahrens et al. (1993), Germany	391 male confirmed incident cases born after 1912, diagnosed within 2 mos. of interview. Cases recruited from 1988 to 1991 in Bremen and Frankfurt/Main.	391 randomly selected controls from municipality records matched to cases on region and age.	1. Supplemental questionnaire 2. LHC-JEM – JEM developed for a European study of Larynx and Hypopharynx. 3. MESO-JEM – JEM developed for a mesothelioma study in France	1. Questionnaire Lifetime hours 0- ≤ 282 283- ≤ 1 400 1 400 – ≤ 5 580 > 5 580 2. LHC-JEM Cumulative asbestos exposure 1 st Quartile (Low) 2 nd Quartile 3 rd Quartile 4 th Quartile 3. MESO-JEM Cumulative asbestos exposure 1 st Quartile (Low) 2 nd Quartile 3 rd Quartile 4 th Quartile	1.1 (0.6–1.9) 1.1 (0.6–2.1) 1.9 (1–3.5) 1.9 (1–3.4) 1.7 (1.0–2.7) 2.3 (1.3–2.8) 2.5 (1.5–4.2) 2.9 (1.7–5.0) 1.3 (0.7–2.3) 2.36 (1.3–3.9) 2.4 (1.3–4.2) 2.5 (1.4–4.4)	Adjusted for matching variables and smoking.	
Brownson et al. (1993), Missouri, USA	429 white women incident cases identified from the Missouri tumour registry from 1986 to 1991	1021 white women controls selected from drivers license and Medicare files matched on age	Interviewer administered questionnaire	Ever < 9 years > 9 years	3.5 (1.2–10.0) 2.5 (0.5–11.7) 4.6 (1.1 –19.2)		
Parkin et al. (1994), Zimbabwe	877 male cases from the Bulawayo, Zimbabwe Cancer Registry that occurred between 1963–1977	4434 male cases of other cancers identified from the same registry during the same time period. Tobacco related cancers were excluded	Interviewer administered questionnaire	Ever < 6 years ≥ 6 years	0.8 (0.5–1.0) 0.7 (0.4–1.0) 0.8 (0.4–1.2)	Time period, birthplace, education, alcohol & smoking	

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Imbernon et al. (1995)	310 cases that occurred between 1978 and 1989 in a cohort of active male workers in a French gas and electric utility company (EDF-GDF)	1240 controls randomly selected from the cohort who were active and cancer free were matched to cases on year of birth	A Job Exposure Matrix was developed based on expert opinion	Exposed (yes/no) Duration (years) ≤ 10 10–20 20–30 > 30 Cumulative Exposure 0 < 25 th ile 25–50 th ile 50–75 th ile > 75 th ile	4.8 (1.2–19.7) 1.0 1.5 (0.5–4.2) 1.1 (0.4–3.4) 1.4 (0.5–4.3) 1.0 1.1 (0.6–1.9) 0.8 (0.4–1.3) 2.0 (1.3–3.2) 1.9 (1.2–3.0)	Matching variables and SES.	
Wilkinson et al. (1995), London, England	271 patients with histologically or cytologically confirmed lung cancer who were admitted to the London Chest Hospital from September 1992 to March 1993.	678 were patients from the same hospital and time period with non-malignant respiratory diseases or cardiac disease.	Nurse interviewers administered questions on occupational histories. Review of the occupational histories was conducted to group jobs by their probability of exposure to asbestos.	Years of Exposure Entire study 0 < 5 < 10 ≥ 10 ILO score < 1/0 0 < 5 < 10 ≥ 10 ILO score = 0/0 0 < 5 < 10 ≥ 10	1 1.6 (0.9–2.8) 2.2 (1.2–4.3) 1.5 (1.0–2.4) 1 1.0 (0.5–2.1) 2.6 (1.2–5.2) 1.6 (0.9–2.7) 1 0.8 (0.4–1.9) 2.4 (1.1–5.1) 1.6 (0.9–2.8)	Sex, age, smoking & type of referral	

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McDonald et al. (1997), Quebec, Canada	266 lung cancer deaths from a cohort of 10 198 miners and millers born 1 891–1920 who had worked for a month or more in the asbestos mines or mills of Quebec and were followed up to 1992.	Approximately 1 referent for each case was randomly selected from the same cohort matched to cases on survival to the same age, year of birth and year first employed in the industry.	Areas with higher potential exposure to tremolite (central mines) were compared with areas with lower potential (peripheral areas). Exposure within the past 10 years was not considered.	Central mines (high tremolite) Peripheral mines (low tremolite)	2.0 (1.5–2.6) 1.1 (0.8–1.5) LRT = 8.25 (<i>P</i> = 0.004)	Matching variables.	A previous pathologic study showed tremolite levels to be 4 times higher in the lungs of workers from the Central mines than those from the peripheral mines.
Jöckel et al. (1998)	1004 cases from Bremen & Frankfurt/Main in 1988 to 1993 born in or after 1913	1004 controls from Bremen & Frankfurt/Main matched for sex, age, and region of residence	Interviewer administered questionnaire which included job-specific supplementary questions.	Lifetime working hours ≤ 940 940 ≤ 5 280 > 5 280	1.0 (0.7–1.4) 1.4 (1.0–2.0) 1.5 (1.0–2.1)	Matching variables & smoking	
Kreuzer et al. (1999), Germany	2373 male cases from 2 studies 1) Bremen Frankfurt/Main in 1988 to 1993 born in or after 1913 or 2) from Nordrhein-Westfalen, Rheinland-Pfalz and Bayern, the Saarland, Thiiringen, and Sachsen who were residents of study region and lived in Germany for > 25 years.	2348 controls from 2 studies 1) randomly selected from census lists and matched on age, sex and region. 2) population controls who met same study criteria as cases were randomly selected from population registries and frequency matched to cases on age, sex and region	Interviewer administered questionnaire which included job-specific supplementary questions	Age ≤ 45 Ever vs Never Duration: 0–459 460– 1 399 > 1 400 Age 55–69 Ever vs Never Duration: 0–459 460– 1 399 > 1 400	OR 2.4 (1.4–4.0) 2.5 (1.1–5.7) 2.1 (0.9–4.7) 2.7 (1.1–6.6) 1.5 (1.2–1.7) 1.3 (1.1–1.7) 1.4 (1.1–1.8) 1.7 (1.3–2.2)	Age, region & smoking.	

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Mzileni et al. (1999), Northern Province, South Africa	288 male and 60 female incident cancers diagnosed in Garankua Hospital between 1993–1995.	183 men & 197 women selected at the same time as the cases with cancers believed to be unrelated to smoking.	Interviewer administered questionnaire	Asbestos exposure current residence	Women 1.0 1.1 (0.3–3.9) 5.4 (1.3–22.5) $p = 0.02$ Men 1.0 2.1 (1.0–4.4) 2.8 (0.7–10.4) $p = 0.2$	Smoking and dusty industry.	
				Asbestos exposure at birth	Women 1.0 - 2.4 (0.7–7.9) $P = 0.2$ Men 1.0 2.9 (1.2–6.7) 3.1 (0.4–21.4) $P = 0.006$		

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Rosamilia et al. (1999), an oil refinery in Beaumont, Texas	148 male lung cancer deaths were identified from a cohort of 7 119 refinery workers who had worked at least 1 year between 1945–1987 who were followed to 1987.	490 controls were randomly selected from males in the cohort (without replacement) with matching on birth date, and race. Controls had to be alive at time case died and employed at the refinery before that time.	An industrial hygienist classified jobs in terms of their potential for exposure to asbestos into jobs with: 1) background 2) occasional but low 3) occasional but may not be low 4) routine	Duration of occasional or routine (years) 0 < 25 5–34 35+ Test for trend	1.0 0.5 (0.2–1.2) 1.1 (0.6–2.2) 1.3 (0.7–2.7) $P = 0.06$	Analysis conducted ignored the matching variables (i.e. crude analysis)	Only 3 cases and 9 controls were in the “routinely” exposed category.
Brüske-Hohlfeld et al. (2000), Germany	1) 1 004 cases from Bremen & Frankfurt/Main in 1988 to 1993 born in or after 1913 2) 3 180 cases from Nordrhein-Westfalen, Rheinland-Pfalz and Bayern, the Saarland, Thuringen, and Sachsen	1) 1 004 controls from Bremen & Frankfurt/Main matched for sex, age, and region of residence. 2) 3 249 controls from Nordrhein-Westfalen, Rheinland-Pfalz and Bayern, the Saarland, Thuringen, and Sachsen	Interviewer administered questionnaire which included job-specific supplementary questions.	Ever Exposed Duration (years) > 0–3 > 3–10 > 10–20 > 20–30 > 30	1.4 (1.2–1.6) 1.2 (0.9–1.7) 1.2 (1.0–1.5) 1.5 (1.2–1.8) 1.5 (1.1–1.9) 1.9 (1.4–2.4)	Adjusted for matching variables & smoking.	

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Luce et al. (2000), New Caledonia	228 cases identified from the cancer registry of New Caledonia diagnosed between 1993 and 1995 who were older than 18 and had lived in New Caledonia for at least 5 years.	305 population controls randomly selected from the census rolls. Controls were frequency matched to age and sex distribution of cases.	In person interviews were conducted with a questionnaire that included questions on use and living in homes of whitewash ("po") containing tremolite.	Men Ever vs Never Duration < 20 years ≥ 20 years Women Ever vs Never Duration < 20 years ≥ 20 years	0.9 (0.5–1.5) 0.4 (0.2–1.0) 1.4 (0.7–2.8) 2.5 (1.0–6.2) 0.6 (0.2–2.6) 6.8 (2.0–23.1)	Age & smoking	
Gustavsson et al. (2002), Stockholm County, Sweden	1038 male cases age 40–75 identified by the cancer registry between 1985–90	2359 controls 1. Population based referents selected from all men alive at the end of each study period 2. Controls matched on vital status as of 12–31–90. Individuals who died of smoking related causes excluded.	Postal questionnaires supplemented by telephone interviews if answers incomplete.	Asbestos (fibres/ml*years) Never Smokers > 0–0.99 1–2.49 ≥ 2.5 Smokers 1–10 cigs/day > 0–0.99 1–2.49 ≥ 2.5 Smokers 11–20 cigs/day > 0–0.99 1–2.49 ≥ 2.5 Smokers > 20 cigs/day > 0–0.99 1–2.49 ≥ 2.5	RR 1.8 (0.6, 5.5) 2.7 (0.7, 9.5) 10.2 (2.5, 41.2) 18.1 (8.2, 40.4) 12.1 (5.1, 29.3) 13.6 (4.6, 40.0) 17.0 (8.8, 32.7) 29.8 (15.1, 58.6) 86.2 (28.8, 258.2) 38.5 (17.7, 83.4) 36.8 (11.9, 113.7) 80.6 (20.2, 322.0)	Matching variables (age group and year of inclusion), diesel, combustion products, environmental air pollution from road traffic, indoor radon levels, smoking	Interaction between smoking and asbestos was found to be between additive and multiplicative Risk at low exposure was greater than expected based on linear extrapolation from high exposure.

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Hauptmann et al. (2002)	1) 1 004 from Bremen & Frankfurt/Main in 1988 to 1993 born in or after 1913 2) 2 225 from Nordrhein-Westfalen, Rheinland-Pfalz and Bayern, the Saarland, Thiiringen, and Sachsen who were < 76 age, resident of study region and lived in Germany for > 25 years.	1) 1 004 randomly selected from census lists and matched on age, sex and region. 2) 2 216 population controls who met same study criteria as cases were randomly selected from population registries and frequency matched to cases on age, sex and region	Interviewer administered questionnaire which included job-specific supplementary questions.	Duration 0–1 years 1–2 years 3–7 years ≥ 8 years Fibre-years 0–4 5–17 18–49 ≥ 50 Continuous duration of exposure (change in OR for one year)	1.0 1.1 (0.8–1.5) 1.0 (0.7–1.4) 1.3 (0.9–1.8) 1.0 1.3 (0.9–1.8) 1.1 (0.8–1.6) 1.6 (1.1–2.4) 1.02 (1.01–1.04)	Adjusted for active smoking [for exsmokers], and history of previous lung diseases Matching variables & smoking	
Pohlabeln et al. (2002) Germany	839 male cases from hospitals in Bremen & Frankfurt/Main between 1988 to 1993 born in or after 1913	839 male controls from from hospitals in Bremen & Frankfurt/Main between 1988 to 1993 born in or after 1913. Individually matched on age and region.	Two stage design 1) All subjects: Interviewer administered questionnaire which included job-specific supplementary questions 2) For a validation sample further assessment by a panel of Industrial Hygienists	Two Stage Analysis 0 ≤ 1 fibre-years 1 ≤ 10 fibre-years 10 + fibre-years	0.9 (0.6–1.3) 1.3 (0.8–2.2) 1.9 (1.1–3.4)	smoking	

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Menvielle et al. (2003), New Caledonia	228 cases identified from the cancer registry of New Caledonia diagnosed between 1993 and 1995 who were older than 18 and had lived in New Caledonia for at least 5 years.	305 population controls randomly selected from the census rolls. Controls were frequency matched to age and sex distribution of cases.	In person interviews were conducted with a questionnaire that included questions on use and living in homes of whitewash ("po") containing tremolite and exposure to field dust.	Women Field Dust Ever/Never < 25 th %ile 25–75 th %ile > 75 th %ile Exposed to po & field dust Men Field Dust Never Exposed to Po < 90 th %ile > 90 th %ile Ever Exposed to Po < 90 th %ile > 90 th %ile	2.1 (0.8–5.1) 1.0 (0.2–4.8) 1.8 (0.6–5.5) 4.0 (1.1–15.0) 3.3 (2.4–4.5) 0.9 (0.5–1.7) 2.0 (0.5–7.8) 1.9 (0.6–6.3) 5.7 (1.1–29.7)	Age, tobacco consumption and ethnicity	
De Stefani et al. (2005) Uruguay	338 male lung adenocarcinomas from 4 hospital between 1994 to 2000	1014 hospital controls from individuals without tobacco related diseases	Interviewer-administered questionnaire	Ever 1–20 21+	1.5 (1.1–1.9) 1.8 (1.3–2.6) 1.2 (0.8–1.7) Test trend = 0.09		

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Carel et al.(2007) Europe a. Central & eastern Europe (CE) b. United Kingdom (United Kingdom)	Total 2 205 incident male cases, < age 75 a.2057 CE b. 148 from United Kingdom	2305 population or hospital frequency matched on age and gender a. 2 154 CE b. 151 United Kingdom	Interviewer-administered questionnaire	a. CE Ever exposed Intensity (fibres/m) Low Medium High Cumulative exp (fibres/ml*hr) < 41.99 < 125.98 < 699.95 > 699.95 b. United Kingdom Ever exposed Intensity (fibres/m) Low Medium High Cumulative exp (fibres/ml*hr) 41.99 125.98 < 699.95 > 699.95	a. CE 0.92 (0.73 to 1.15) 0.88 (0.68 to 1.13) 1.08 (0.67 to 1.73) 0.95 (0.36 to 2.47) Test trend $P = 0.46$ 1.05 (0.70 to 1.59) 0.87 (0.57 to 1.31) 0.70 (0.45 to 1.09) 1.07 (0.70 to 1.63) Test trend = 0.35 b. United Kingdom 1.85 (1.07 to 3.21) 2.01 (1.08 to 3.76) 1.66 (0.71 to 3.85) 1.53 (0.51 to 4.54) Test trend $P = 0.20$ 1.66 (0.72 to 3.85) 2.03 (0.87 to 4.76) 2.95 (1.05 to 8.26) 1.49 (0.67 to 3.33) Test trend = 0.95		

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Dodic Fikfak et al. (2007), Slovenia	58 histologically confirmed cases employed in an asbestos cement factory on December 31, 1946 and worked at least 1 day between 1964 and 1994	290 controls from the same cohort matched to cases on date of birth, gender and year of hire	Work histories & an asbestos JEM	All asbestos: Ever Above Median Above 90%ile Chrysotile: Ever Above Median Above 90%ile Amphibole: Ever Above Median Above 90%ile	0.8 (0.4–1.6) 0.9 (0.5–1.7) 1.5 (0.6–3.9) 0.8 (0.4–1.6) 1.1 (0.6–2.1) 1.6 (0.6–4.1) 0.9 (0.5–1.6) 0.8 (0.4–1.5) 2.0 (0.9–4.7)	Controlled for matching variables	
Yiin et al. (2007), Portsmouth, New Hampshire, USA	1097 lung cancer deaths identified in a cohort study of 37 853 workers at a naval shipyard between 1952 and 1992 with followup through 1996.	3291 controls matched on age and selected using incidence density sampling from the same cohort.	Employment histories were used with a job exposure matrix for asbestos that was developed by a panel of industrial hygienists.	Cumulative exposure (fibre/ml*days) < 120 120 – 240 240–480 480+	1 1.35 (0.92, 1.95) 1.33 (0.93, 1.86) 1.26 (1.02, 1.55)	age	

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Pintos et al. (2008), Montreal	Incident & histologically confirmed lung cancer cases from all major Montreal hospitals from 2 studies. a. Study I: 857 male cases age 35 to 70 from 1979 to 1986 b. Study II: 741 male cases age 35 to 75 from 1996 to 2001	Study I: 533 population based controls & 1 349 cancer patient controls from the same years and hospitals as cases frequency matched by age and area of residence. Study II: 899 population based controls recruited according to the distributions of age, sex, and area of residence of lung cancer cases	Interviewer-administered questionnaire	a. Study 1 Any level of exposure Non substantial level Substantial level Substantial < 20 yrs Substantial > 20 yrs Any level of amphiboles Non substantial level Substantial level b. Study 2 Any level of exposure Non substantial level Substantial level Substantial < 20 yrs Substantial > 20 yrs Any level of amphiboles Non substantial level Substantial level Pooled Analysis: Any level of exposure Non substantial level Substantial level Substantial < 20 yrs Substantial > 20 yrs Any level of amphiboles Non substantial level Substantial level	OR 1.29 (0.97–1.71) 1.20 (0.89–1.61) 2.25 (1.09–4.65) 1.43 (0.55–3.76) 3.90 (1.24–12.25) 1.12 (0.75–1.67) 1.05 (0.69–1.59) 1.96 (0.64–5.93) 1.18 (0.85–1.64) 1.14 (0.81–1.62) 1.48 (0.66–3.30) 1.11 (0.41–3.05) 2.37 (0.63–8.85) 1.41 (0.75–2.65) 1.40 (0.68–2.88) 1.46 (0.43–4.96) 1.21 (0.98–1.49) 1.14 (0.91–1.42) 1.90 (1.11–3.24) 1.37 (0.69–2.74) 2.98 (1.28–6.96) 1.18 (0.85–1.63) 1.11 (0.78–1.58) 1.66 (0.74–3.73)	Age, ethnicity, schooling level, census tract median family income, smoking, respondent status, and man made mineral fibres.	