

**MULTICENTRIC CASE-CONTROL STUDY ON
MALIGNANT MESOTHELIOMA AND NON-
OCCUPATIONAL EXPOSURE TO ASBESTOS**

Magnani et al, Br J Cancer 83: 104, 2000

TOPICS TO DISCUSS BY THE STUDENTS

- ▶ **What is the aim of the study?**
- ▶ **What is the design of the study and why is this chosen?**
- ▶ **What are the methods of the study?**
 - ▶ **How are cases identified?**
 - ▶ **How are controls identified?**
 - ▶ **What can you say about exposure assessment?**
 - ▶ **Which statistical analysis were performed?**
- ▶ **What are the results of the study?**
- ▶ **Discussion: which potential sources of bias can be identified?**



SOURCES OF NON-OCCUPATIONAL EXPOSURE

- ▶ **Workers exposed to asbestos bring home fibres with their clothes**
- ▶ **Exposure also results from residence in the vicinity of asbestos mines, mills or factories**
- ▶ **The soil may be rich in asbestiform fibres (e.g. in Cappadocia, Turkey)**



WHY A CASE-CONTROL STUDY?

- ▶ **No cohort easily identifiable**
- ▶ **Multiple exposure sources**
- ▶ **Rare disease, but relatively frequent exposure in particular areas**



CASE IDENTIFICATION

- ▶ **Six areas in 3 European countries where asbestos exposure is highly prevalent: Torino, Casale, Prato, Firenze, Barcelona, Cadiz, Geneve**
- ▶ **Cases: all newly diagnosed primary malignant pleural mesotheliomas (~1995-1996)**
- ▶ **Identification through cancer/mesothelioma registries; cases histologically confirmed and revised by a panel of pathologists**



CONTROL SELECTION

- ▶ **Controls: random sample from the general population except in Spain where they were patients discharged from hospitals (excluding asbestos- related diagnoses)**
- ▶ **Frequency-matching for age and sex, with sample size twice the number of cases**



EXPOSURE ASSESSMENT- 1

- ▶ **Cases and controls interviewed at home or at the hospital by trained interviewers.**
- ▶ **Relatives provided information for deceased subjects : 98% of controls interviewed in person, while a proxy was used for one third of cases (implications?)**
- ▶ **Interview lasted 6 min for cases and 52 min for controls (why?)**



EXPOSURE ASSESSMENT- 2

- ▶ **Occupational and non-occupational (domestic and environmental) exposure assessment made *blindly* by expert industrial hygienists on the basis of a structured questionnaire**
- ▶ **Scales of *Probability* (high, middle, low, no exposure, unkown) and *Intensity* (same)**
- ▶ **see Appendix**



EXPOSURE ASSESSMENT- 3

Non-occupational exposure defined on the basis of dwelling characteristics, heating and air conditioning systems, insulation and other asbestos uses, cohabitants working in jobs with asbestos exposure



STATISTICAL ANALYSIS

- ▶ **53/215 cases and 232 /448 controls not occupationally exposed to asbestos**
- ▶ **Relative risk estimated by unconditional logistic regression**
- ▶ **All estimates adjusted by centre, sex and age**



RESULTS AMONG NON-OCCUPATIONALLY EXPOSED

Exposure Probability		OR (95% CI)
Domestic	low	2.0 (0.8-5.1)
	middle-high	4.8 (1.8-13.1)
Environmental	low	2.7 (0.9-8.4)
	middle-high	11.5 (3.5-38.2)



RESULTS AMONG NON-OCCUPATIONALLY EXPOSED

Exposure Intensity		OR (95% CI)
Domestic	low	2.0 (0.8-5.1)
	middle	5.7 (1.4-23.3)
	high	7.8 (1.7-36.2)
Environmental	low	2.2 (0.7-7.6)
	middle	9.5 (2.5-36.5)
	high	45.0 (6.4-318)



BIAS - POPULATION

- ▶ **Mean age at start of exposure** cases 14 years
controls 21 years
- ▶ **Mean duration** cases 39 years
controls 27 years
- ▶ **Participation rates** cases 94%
controls 82%



BIAS - METHODS

- ▶ **inaccurate occupational histories from individuals with low education (and potentially greater exposure): overestimation of non-occupational risks**
- ▶ **low quality of responses from proxy responders; these are more among the cases, with potential underestimation of risks**
- ▶ **better recall of exposure from cases (aware of the study hypothesis)?**
- ▶ **Interviews lasted 66 min for cases and 52 min for controls**



Validation study

In Barcelona 18 cases were interviewed, then after their deaths a proxy was asked the same questions: kappa index of 0.59 (0.79 for spouses)

Classification of subjects by the panel of experts did not change using either sources of information



**Original observation: mesothelioma in
asbestos roofing in Barcelona?**

