Examples from Occupational Cancer Epidemiology

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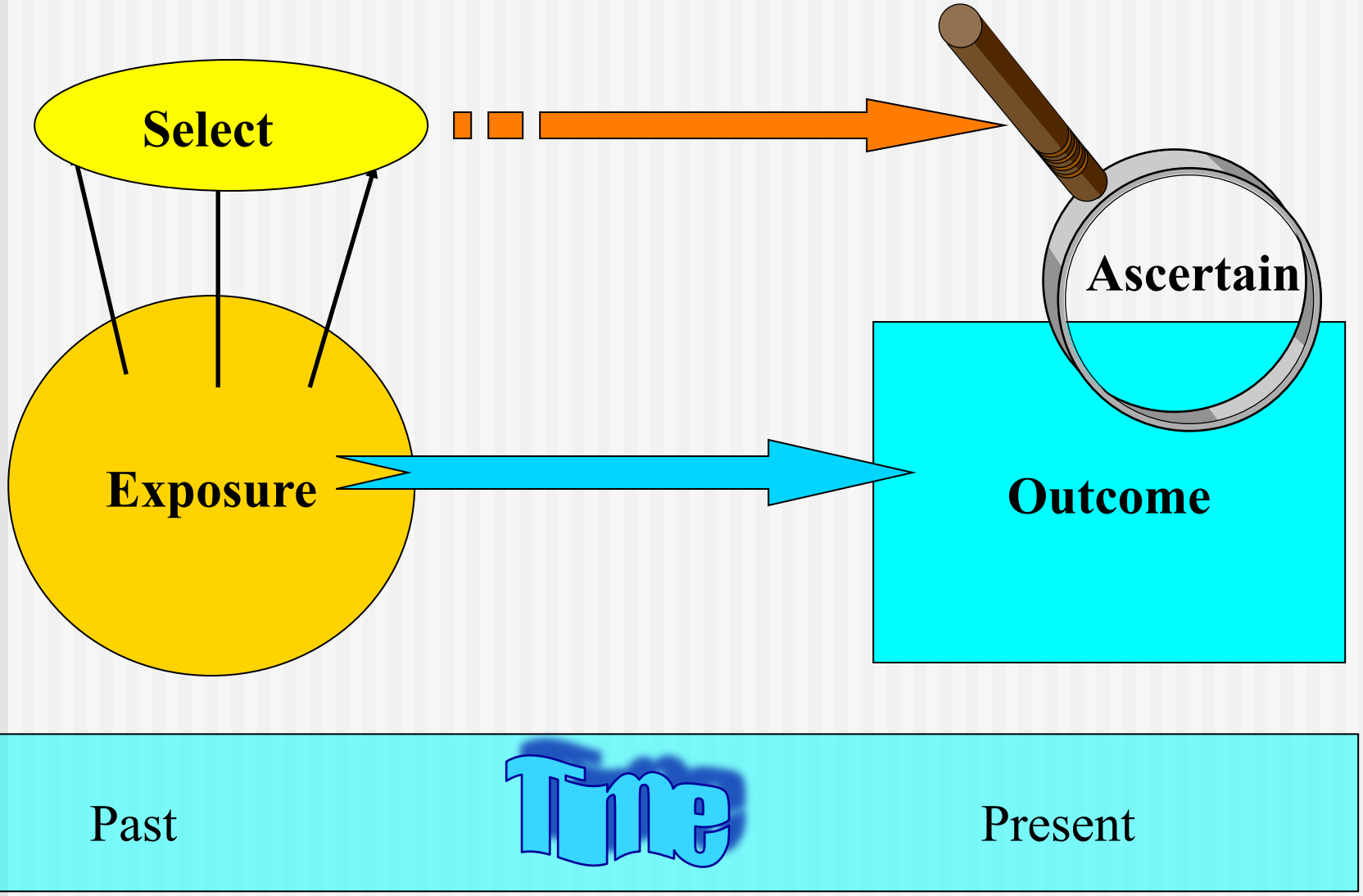
Research Objectives: Motivated to Improve the Public's Health

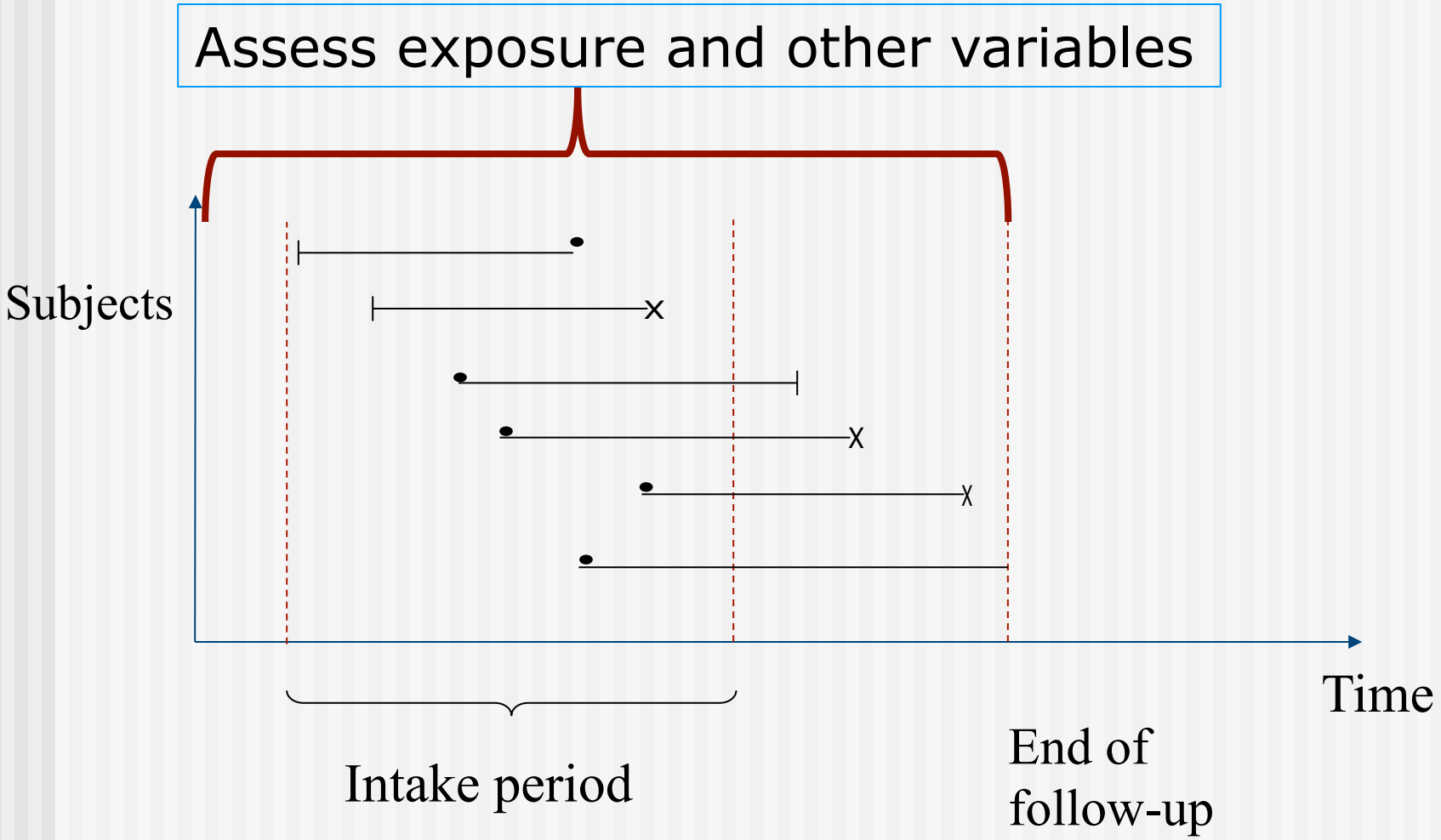
To identify chemical & physical agents in the workplace and in the general environment that cause cancer in humans.

Occupational Cancer Epidemiology

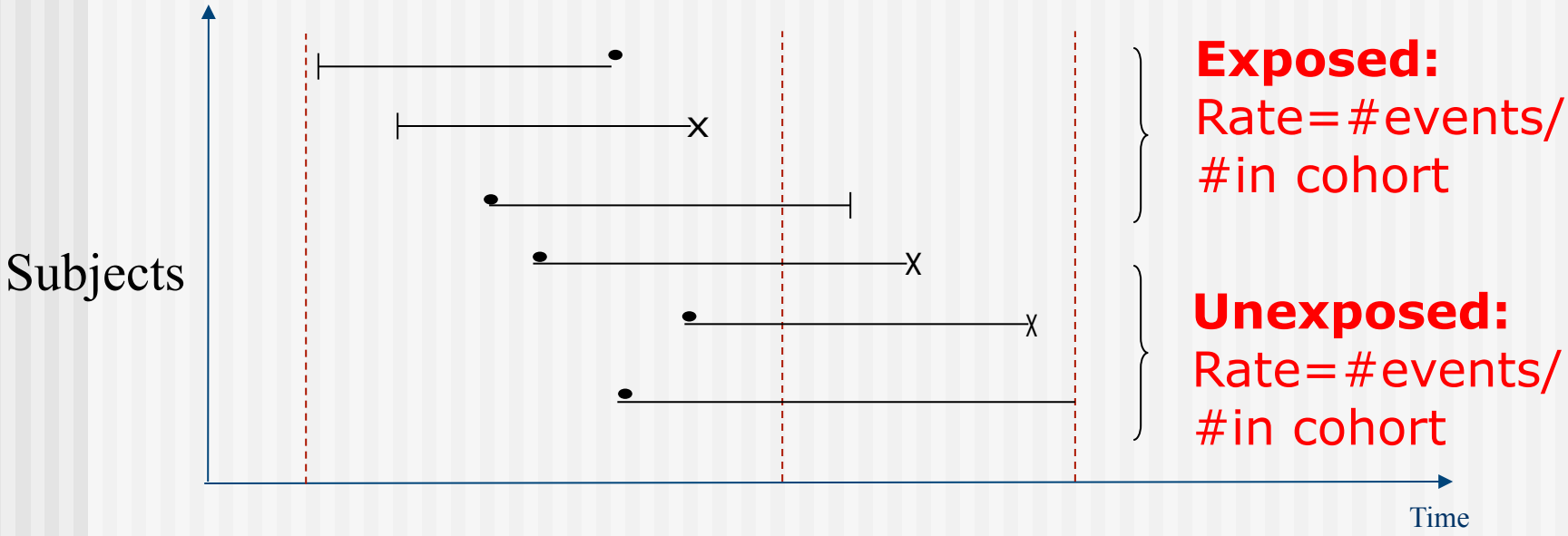
Cohort Studies



Cohort Studies

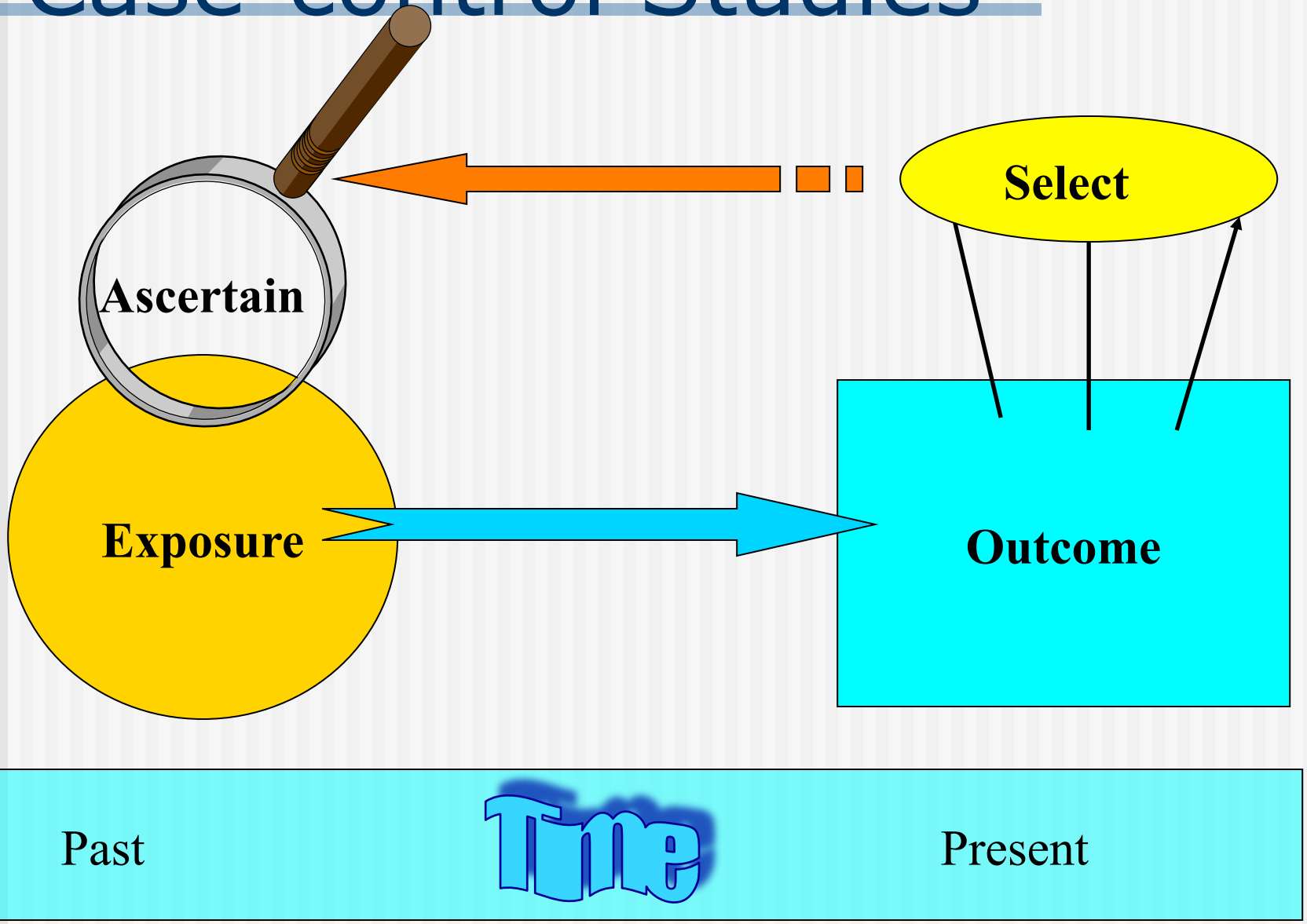


Measure of Association



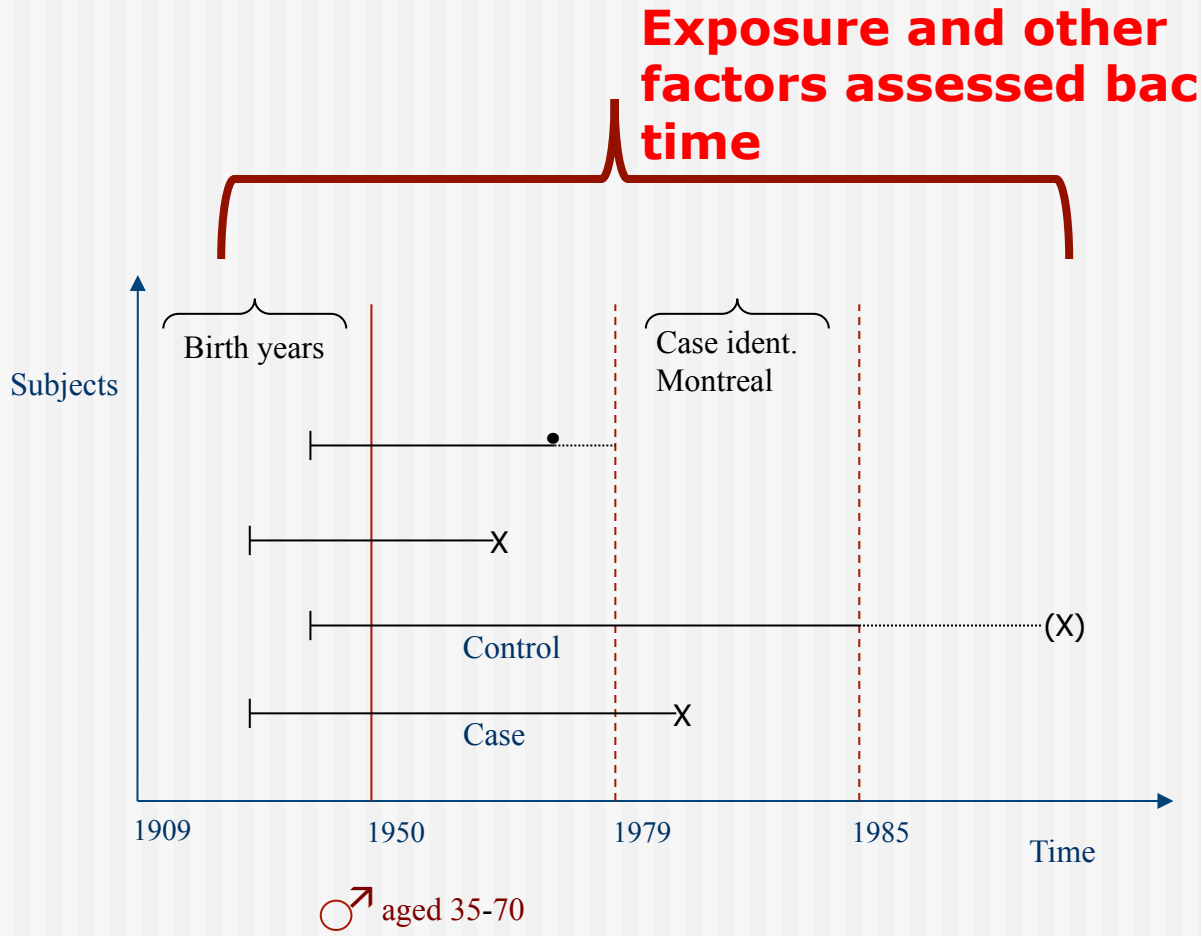
Rate ratio=rate(exposed)/rate(unexposed)

Case-control Studies



Example – Case-Control Studies

- Case-control study of occupational risk factors for cancer on men



Characteristics of the study design

- Siemiatycki, “Risk factors for cancer in the workplace”, CRC Press, 1991
- Men, age 35-70, living in Montreal between 1979 & 1985
- ~20 sites of cancer, <u>confirmed histologically</u>
- Small (~350) population-based series of control subjects

- Interviewer-administered questionnaire for non-occupational risk factors and lifetime occupational histories

Occupational questionnaire

- General questionnaire about each job each subject ever had
- Supplemented with specific questionnaires for selected jobs (e.g. welders)

Please answer the following questions for all positions you have held starting with the most recent, including all major job changes within one company.

SECTION 1: EMPLOYER IDENTIFICATION

1. Please fill in the table below.

EMPLOYMENT NUMBER: |___|___|	
COMPANY NAME:	_____ ☐ UNKNOWN
PERIOD OF EMPLOYMENT:	From:|___|___|___|___| Year ☐ UNKNOWN To: |___|___|___|___| Year ☐ UNKNOWN
ADDRESS:	_____ MUNICIPALITY _____ PROVINCE *
NUMBER OF WEEKS WORKED PER YEAR (ON AVERAGE):	_____ ☐ UNKNOWN
NUMBER OF DAYS WORKED PER WEEK (ON AVERAGE):	_____ ☐ UNKNOWN
NUMBER OF HOURS WORKED PER WEEK (ON AVERAGE):	_____ ☐ UNKNOWN
PRIMARY ACTIVITY OR PRODUCT OF THE COMPANY:	_____ ☐ UNKNOWN
OTHER ACTIVITIES OR PRODUCTS OF THE COMPANY:	_____ _____ ☐ **UNKNOWN**

SECTION 2: SHIFT WORK

We would like to know what times of the day you worked.

2. Did you always work during the same shift?

- ❍ YES ⇒ GO TO QUESTION 2A
- ❍ NO ⇒ GO TO QUESTION 2B
- ❍ UNKNOWN ⇒ GO TO QUESTION 2B

2A. If you always worked during the same shift please indicate the start and end times.

START: |___|___| : |___|___| **END:** |___|___| : |___|___| ⇒ GO TO QUESTION 3

2B. If you worked in shifts, please indicate the different shifts you worked. If you worked on rotation, please indicate the percentage of time you worked on each shift. For example, in the case of a rotating shift (day/night/evening) indicate 33%.

YEAR	DAY SHIFT	EVENING SHIFT	NIGHT SHIFT
FROM: |___|___|___|___| YEAR ☐ UNKNOWN **TO:** |___|___|___|___| YEAR ☐ UNKNOWN	**START:** |___|___|:|___|___| ☐ UNKNOWN **END:** |___|___|:|___|___| ☐ UNKNOWN **ROTATION:** |___|___| % ☐ UNKNOWN	**START:** |___|___|:|___|___| ☐ UNKNOWN **END:** |___|___|:|___|___| ☐ UNKNOWN **ROTATION:** |___|___| % ☐ UNKNOWN	**START:** |___|___|:|___|___| ☐ UNKNOWN **END:** |___|___|:|___|___| ☐ UNKNOWN **ROTATION:** |___|___| % ☐ UNKNOWN
FROM: |___|___|___|___| YEAR ☐ UNKNOWN **TO:** |___|___|___|___| YEAR ☐ UNKNOWN	**START:** |___|___|:|___|___| ☐ UNKNOWN **END:** |___|___|:|___|___| ☐ UNKNOWN **ROTATION:** |___|___| % ☐ UNKNOWN	**START:** |___|___|:|___|___| ☐ UNKNOWN **END:** |___|___|:|___|___| ☐ UNKNOWN **ROTATION:** |___|___| % ☐ UNKNOWN	**START:** |___|___|:|___|___| ☐ UNKNOWN **END:** |___|___|:|___|___| ☐ UNKNOWN **ROTATION:** |___|___| % ☐ UNKNOWN
FROM: |___|___|___|___| YEAR ☐ UNKNOWN **TO:** |___|___|___|___| YEAR ☐ UNKNOWN	**START:** |___|___|:|___|___| ☐ UNKNOWN **END:** |___|___|:|___|___| ☐ UNKNOWN **ROTATION:** |___|___| % ☐ UNKNOWN	**START:** |___|___|:|___|___| ☐ UNKNOWN **END:** |___|___|:|___|___| ☐ UNKNOWN **ROTATION:** |___|___| % ☐ UNKNOWN	**START:** |___|___|:|___|___| ☐ UNKNOWN **END:** |___|___|:|___|___| ☐ UNKNOWN **ROTATION:** |___|___| % ☐ UNKNOWN
FROM: |___|___|___|___| YEAR ☐ UNKNOWN	**START:** |___|___|:|___|___| ☐ UNKNOWN **END:** |___|___|:|___|___|	**START:** |___|___|:|___|___| ☐ UNKNOWN **END:** |___|___|:|___|___|	**START:** |___|___|:|___|___| ☐ UNKNOWN **END:** |___|___|:|___|___|

3. Which of the following would best describe the place where you usually worked in this job?

- ○ FACTORY OR PLANT
- ○ LABORATORY
- ○ VEHICLE
- ○ CONSTRUCTION SITE
- ○ WAREHOUSE
- ○ GARAGE
- ○ OUTDOORS
- ○ OFFICE
- ○ STORE
- ○ RESTAURANT
- ○ HOTEL
- ○ OTHER, PLEASE SPECIFY _____
- ○ UNKNOWN

4. In what department of the company or organization did you work?

_____

_____

_____

5. We would like you to describe in detail your specific tasks. Try to describe what you did and how you did it. We are particularly interested in any materials that you manipulated or machines that you used.

(Operation and maintenance of machines, vehicles; loading, unloading containers; cleaning; substances or chemicals used – probe for functions and names)

TASKS	EQUIPMENT, IF APPLICABLE

SECTION 3: WORK ENVIRONMENT

DUST

9. Was there dust in the environment where you worked? (For example, coal dust, metal dust, insulation material dust, wood dust, grain dust, textile fibres, plastic dust)

- ○ YES ⇒ GO TO QUESTION 9A
- ○ NO ⇒ GO TO QUESTION 10
- ○ UNKNOWN ⇒ GO TO QUESTION 10

9A. Please describe the source of the dust, frequency and duration of your exposure and whether the materials which created the dust were being used by you or by others nearby?

NAME/DESCRIPTION	DURING HOW MANY WEEKS OF THE YEAR WERE YOU EXPOSED	FOR HOW MANY HOURS PER WEEK	WHERE WAS THIS DUST COMING FROM	USED BY YOURSELF OR BY OTHERS
☐ UNKNOWN	☐ UNKNOWN	☐ UNKNOWN	☐ UNKNOWN	○ MYSELF ○ OTHERS ○ UNKNOWN
☐ UNKNOWN	☐ UNKNOWN	☐ UNKNOWN	☐ UNKNOWN	○ MYSELF ○ OTHERS ○ UNKNOWN
				○ MYSELF ○ OTHERS

- Similar questions for:
  - Smoke, fumes, gases
  - Oils, solvents, other chemicals
  - Fungicides, insecticides, herbicides, wood preservatives

ELECTRICAL OR ELECTRONIC TOOLS, MACHINES OR EQUIPMENT

13. Did you use or work less than 6 feet (1.8 meters) from any electrical motor or equipment? This would include small or large tools or appliances such as drills, sanders, washers, dryers, furnaces, machine-tools or equipment as well as conveyers, elevators, photocopying machines, large mainframe computers, etc. Do not consider a *personal computer*.

- ○ YES ⇒ GO TO QUESTION 13A
- ○ NO ⇒ GO TO QUESTION 14
- ○ UNKNOWN ⇒ GO TO QUESTION 14

13A. Please specify which tools, appliances or equipment were used as part of your job and indicate on average how many hours per day they were used.

TYPE OF TOOLS, APPLIANCE OR EQUIPMENT	HOURS PER DAY
_____ _____ _____ ☐ UNKNOWN	|___|___| hours per day ☐ UNKNOWN
_____ _____ _____ ☐ UNKNOWN	|___|___| hours per day ☐ UNKNOWN
_____ _____ _____	|___|___| hours per day ☐ UNKNOWN

- Other questions on:
  - Ventilation
  - Protective equipment
  - Environmental tobacco smoke

Occupational Coding

- Team of chemists & industrial hygienists reviewed each job history & attributed exposure to ~300 agents

- Coded:
  - Lifetime occupations (as coded by job and industry titles)
  - Lifetime exposure to ~300 agents in the workplace

- Exposure variables
  - Start/end dates of job; duration
  - Concentration, coded on a 4-level ordinal scale

None	
Low	- Background exposure
Medium	- In between
High	- Handling product in concentrated form

- Frequency, coded on 4-level interval scale

  None

  Low - 1-5%

  Medium - 5-30%

  High - >30%

- Route of exposure, nominal
  - Respiratory
  - Cutaneous
  - Both
- Confidence of exposure, ordinal
  - “Possible”
  - “Probable”
  - “Certain”

CHEMICAL CODE SHEET

I.D.: _____ **Job no.:** ___ **Dates:** 19___ to 19___ **US SIC:** _____ **DOT:** _____

Can SIC: _____ **CCDO:** _____

Legend:

Physical Aspect = Dust, Fume, Vapor/gas, Mist, Radiation.
R = reliability
Y_i = year in
Y_o = year out
P = % of working days exposed over the period

F_{R1} = % of the day (frequency) for respiratory exposure at conc. 1
F_{R2} = % of the day (frequency) for respiratory exposure at conc. 2
F_{R3} = % of the day (frequency) for respiratory exposure at conc. 3
P_k = peak exposure (Y or N)
F_C = % of the day (frequency) of cutaneous exposure

Skin: Potential for skin absorption (S: ACGIH Skin notation ●: Droz, dermal toxiciy ○: Droz, dermal absorption **A, B, C**

CODE	EXPOSURE	Phys. Aspect	R	Y_i	Y_o	P	F_{R1}	F_{R2}	F_{R3}	P_k	F_C	Remarks
	SOLIDS											
	INORGANIC SOLIDS											
110001	Abrasives dust											
110009	Crystalline silica											
111301	Alumina											
111401	Silicon carbide											
117401	*Tungsten carbide*											
110005	Metallic dusts											
110018	Bronze dust											

Statistical Analysis

- Wish to estimate odds ratios
- Odds ratios in a case-control study approximate rate ratios or relative risks

Example of a 2X2 contingency table

	Cases	Controls	Total
Exposed	112	93	205
Not exposed	1890	5690	7580
Total	2002	5783	7785

Odds **OR=(112/1890)/(93/5690)=3.5**

Confounding

- We want to ensure that other factors do not “distort” these estimates
- We use a regression model that is designed for binary outcomes (cases/ controls) and can account for other factors (adjustment) [logistic regression]

Example of confounding

- We want to estimate the OR for the incidence of lung cancer and exposure to asbestos
- Smoking causes lung cancer
- If people exposed to asbestos smoke more than those not exposed, then smoking can confound the OR
- Solution: include smoking in the regression model

Coding of exposure for analysis

- Exposure indices
  - Duration at medium/high concentrations
  - Cumulative = $\sum_{\text{jobs}} \text{conc} * \text{freq} * \text{duration}$

Coding:

conc= {0,…,3}

freq= {0,…,3}

  - "Substantial$_1$" - { conc ≥ medium (2); freq ≥ high (3) }
  - " Substantial$_2$" - { conc * freq > 3; duration > 5 yr prior to 5 years before diagnosis }

Selected Results

Site	Agent	OR $_{(subst_2)}$	90% CI
Lung	Crysotile asbestos	1.9	1.1-3.2
	Crystaline silica	1.4	1.0-1.8
	Wood dust	1.3	1.0-1.7
Rectum	Rayon fibres	3.5	1.6-7.8
Stomach	CO	2.4	1.6-3.7
Rectum	Synthetic fibres	2.5	1.1-5.7

Aspects of the design

Strengths

- Population-based
- Relatively large case series
- Histological confirmation
- Control subjects
- Lifetime exposure data
- Confounders

Limitations

- Low prevalence of exposure
- Control subjects
- Confounders

Example: Postmenopausal Breast Cancer and Occupational Exposures to Extremely Low Frequency Magnetic Fields

Context

- Postmenopausal breast cancer case-control study
- Montreal, 1996-7
- Main aim was to estimate risks for occupational exposures

Study Design

- Cases/controls: pathology departments and cancer registries from the 18 major hospitals
- age 50–75, 1996-97
- Cases: malignant breast neoplasm
- Controls: 32 different types of cancer from the same hospitals as the cases

Study Design

- Frequency-matched by hospital and age.
- Excluded: liver and intrahepatic bile duct, pancreas, lung, bronchus and trachea, brain and central nervous system, leukemias, lymphomas, non-melanoma skin cancer
- Confirmed histologically

Design

- Telephone & face-to-face interviews
- Most accepted or suspected risk factors
- Detailed estimates of exposure for ~300 occupational agents
- Address at time of diagnosis

Some Relevant Findings

- Response rates:
  - Cases 81%
  - Controls 76%

TABLE I. Distribution of Selected Risk Factors for Incident Female Postmenopausal Breast Cancer, With Associated Age-Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI), Montreal, Canada, 1996–1997

	Interquartile range[a]	Age-adjusted	
		OR	95% CI
Family history (Yes/No)	—	2.2	1.6–3.1
Benign breast disease (Yes/No)	—	3.3	2.5–4.3
Years of schooling	5	1.4	1.2–1.6
Age at menarche	2	0.9	0.8–1.0
Age at 1st full-term pregnancy	5.6	1.2	1.0–1.4
Number of full-term pregnancies	2	0.9	0.8–1.0
Cumulative duration of breastfeeding (weeks)	79	0.9	0.7–1.0
Later age at bilateral oophorectomy	22	0.2	0.1–0.4
Duration of hormonal replacement therapy (months)	60	1.1	1.0–1.3
Oral contraception use (years)	7	0.9	0.8–1.2
Body mass index (kg/m^2)[b]			
1st quartile—mean (26.1)	3.6	1.1	1.0–1.2
Mean—90th centile (32.3)	6.2	0.9	0.7–1.1

TABLE II. Risks for Binary Indices of Occupational Exposure to Magnetic Fields for Incident Postmenopausal Breast Cancer, Montreal, Canada, 1996–1997

Index	No. of exposed cases	No. of exposed controls	Adjusted[a]		Adjusted for textiles[b]	
			OR	95% CI	OR	95% CI
No exposure	119	150	1		1	
Ever	437	450	1.06	0.75–1.49	1.03	0.72–1.47
Intensity > low	134	151	1.27	0.81–2.00	1.90	0.99–3.65
Substantial exposure (>5 years)						
Any	94	110	1.10	0.71–1.71	0.96	0.56–1.67
Lag of 10 years before diagnosis	91	104	1.18	0.75–1.85	1.11	0.63–1.94
Exposure before age 35 years	69	73	1.34	0.80–2.24	1.12	0.59–2.10

TABLE III. Risks for Duration of Occupational Exposure to Magnetic Fields for Incident Postmenopausal Breast Cancer, Montreal, Canada, 1996–1997

	Age-adjusted	Adjusted[b]		Adjusted for textiles[c]	
Duration at > low intensity	OR[a]	OR[a]	95% CI	OR[a]	95% CI
Lifetime exposures[d]	1.04	1.13	0.94–1.35	1.21	0.97–1.49
Lag of 10 years before diagnosis	1.08	1.20	0.98–1.48	1.31	1.03–1.68
Exposures before age 35 years	1.18	1.40	0.98–2.02	1.54	1.00–2.36

a Odds ratios (OR) evaluated across the interquartile range (6,000 hr).
b OR and associated 95% confidence intervals (CI) were evaluated across the interquartile range of duration of exposure and were adjusted for age, family history, age at oophorectomy, education, ethnicity, age at menarche, oral contraception use, duration of hormone replacement therapy use, total duration of breastfeeding, smoking status, alcohol consumption status, body mass index, age at first full-term pregnancy (35 weeks), and proxy respondent status.
c Adjusted for the same factors as in footnote "b," but also for ever/never working in the textile industry.
d Lifetime exposures were computed by adding up hours of exposure to medium or high levels of ELF-MF

across all jobs until the date of diagnosis, regardless of age at exposure.

Additional slides

RADIATION AND RADIOACTIVE MATERIALS

14. Was radiation or radioactive materials (X-rays, U.V., microwave, radar, laser, etc.) used by you or near where you worked?

- ○ YES ⇒ GO TO QUESTION 14A
- ○ NO ⇒ GO TO QUESTION 15
- ○ UNKNOWN ⇒ GO TO QUESTION 15

14A. What type(s) of radiation was(were) used?

_____

_____

○ UNKNOWN

14B. How did you work with it and how often (hours per day)?

_____

_____

|___|___| hours per day

○ UNKNOWN

14C. How far were you from the radiation source?

|___|___|___| metres or |___|___|___| feet

○ UNKNOWN

14D. Did you wear a radiation badge (dosimeter)?

- ○ YES
- ○ NO

PROTECTIVE EQUIPMENT

15. Did you have to wear any protective equipment while at work?

- ○ YES ⇒ GO TO QUESTION 15A
- ○ NO ⇒ GO TO QUESTION 16
- ○ UNKNOWN ⇒ GO TO QUESTION 16

15A. Please specify what protective equipment was used and the task for which it was used?

PROTECTIVE EQUIPMENT	ACTIVITY FOR WHICH IT WAS USED?
GOGGLES	
FOOTWEAR	
APRON	
SIMPLE DUST MASK (PAPER MASK)	
FILTER CARTRIDGE RESPIRATOR	
AIR-SUPPLIED RESPIRATOR OR SELF-CONTAINED BREATHING APPARATUS	
RUBBER OR PLASTIC GLOVES	
ASBESTOS GLOVES	

WORK AREA

We would like to know about your main worksite, work area or office (or the most typical if there were many).

17. What was the size of your general work area?

☐ WORKED OUTDOORS ⇒ IF WORKED OUTDOORS, GO TO QUESTION 17A

ROOM SIZE

○ TYPICAL OFFICE / LIVING ROOM	100 FT^2 OR 9 M^2
○ SMALL STORE / CLASSROOM	600 FT^2 OR 55 M^2
○ DRUGSTORE	1000 FT^2 OR 81 M^2
○ LARGE GROCERY STORE	METRO/PROVIGO
○ WAREHOUSE STORE	COSTCO/WAL-MART
○ UNKNOWN	

CEILING HEIGHT

○ TYPICAL OFFICE / LIVING ROOM	10 FT OR 3 M
○ LARGE GROCERY STORE (METRO/PROVIGO)	15 FT OR 4.5 M
○ WAREHOUSE STORE	20 FT OR 6 M
○ UNKNOWN	

17A. How many people were performing the same tasks as you in your work area?

|___|___|___|___|
NUMBER OF PEOPLE

☐ UNKNOWN

18. What other work was being done around you?

_____

_____

_____

_____

_____

_____

19. What machines or processes were used by others in your work area?

_____

_____

_____

_____