

A short introduction to epidemiology

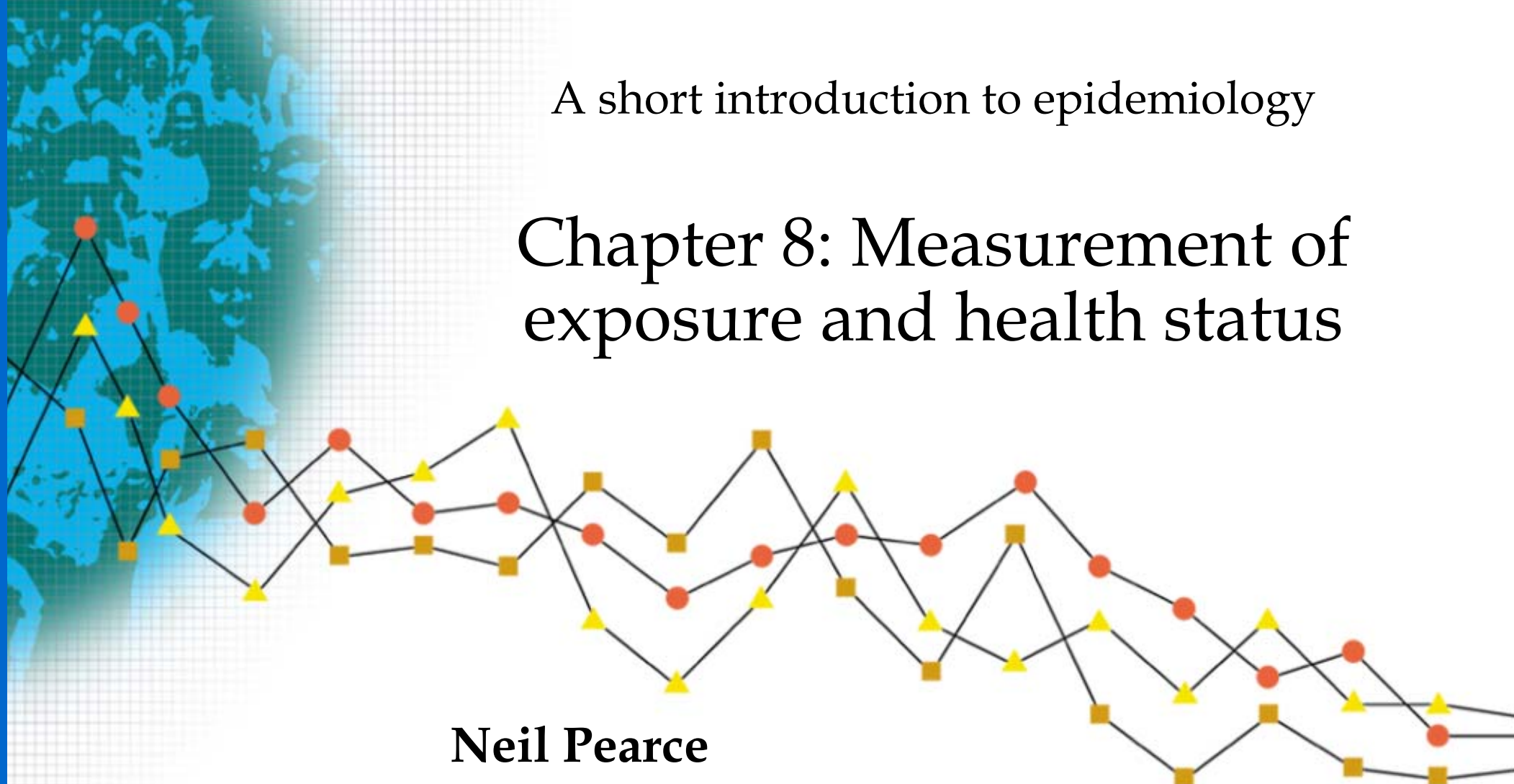
Chapter 8: Measurement of exposure and health status

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Chapter 5

Measurement of exposure and health status

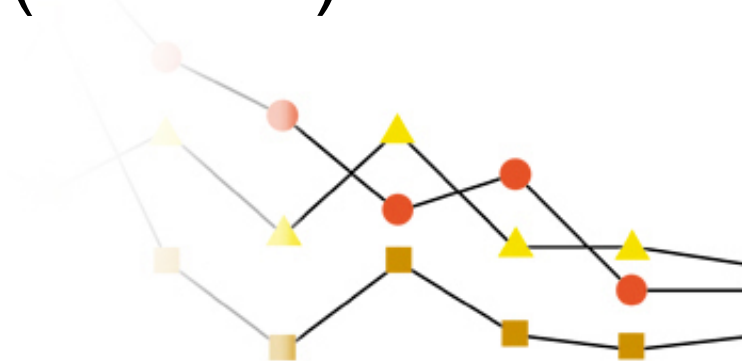
- **Exposure**
 - Exposure and dose
 - Options for exposure assessment
- **Health status**
 - Routine records
 - Morbidity surveys



Exposure and dose

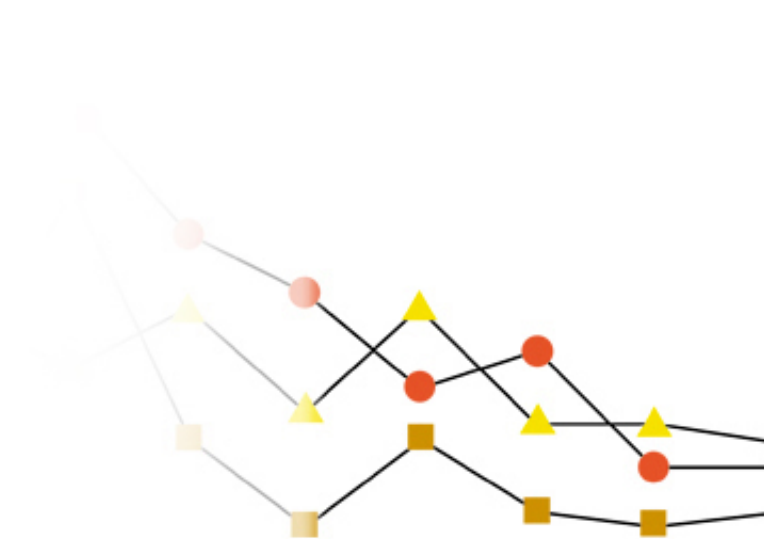
Exposure: the presence of a substance in the environment external to the worker (external/environmental)

Dose: The amount of a substance that reaches susceptible targets in the body (internal)



Measures of exposure

- Intensity of exposure
- Duration of exposure
- Cumulative exposure



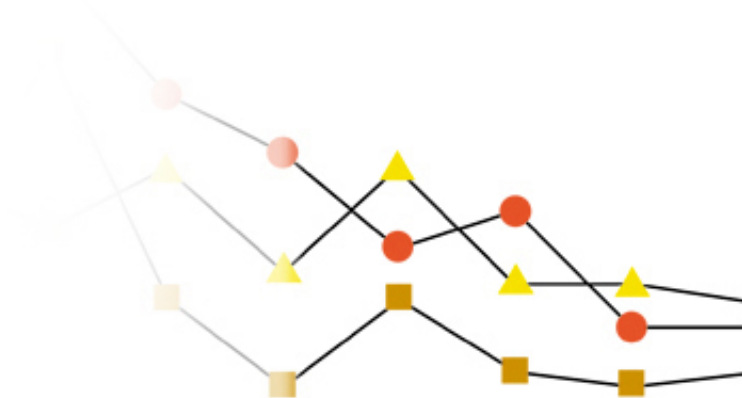
Options for exposure assessment

- Routine records
- Questionnaires
- Environmental measurements and Job-Exposure-Matrices (JEM)
- Quantified personal measurements
- Biomarkers



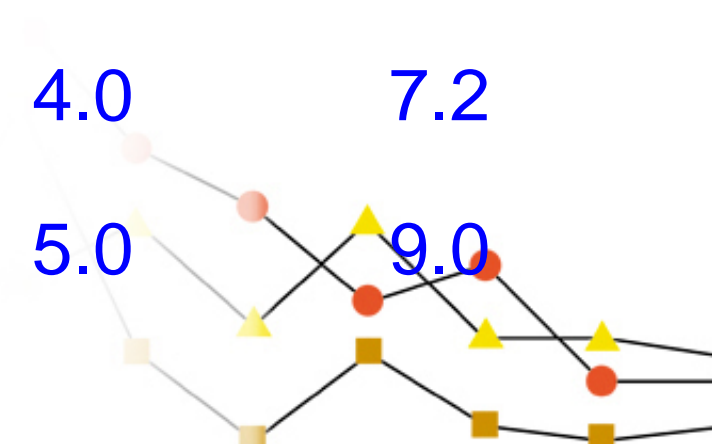
Data sources useful for developing a job-exposure matrix

- Industrial hygiene sampling data
- Process descriptions and flow charts
- Plant production records
- Inspection and accident records
- Engineering control documentation
- Biological monitoring results



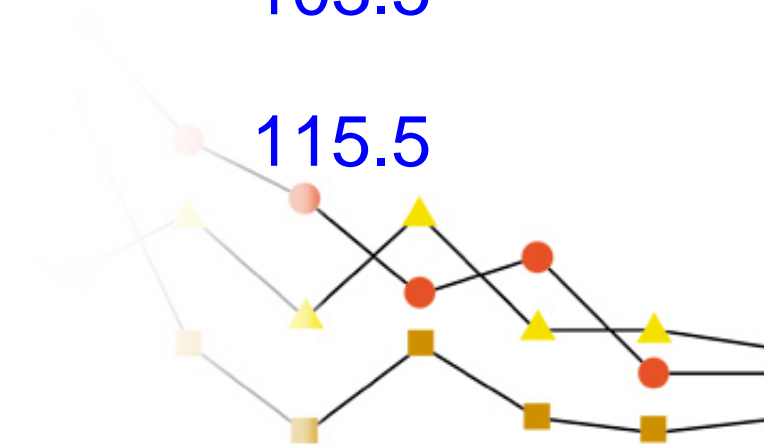
Asbestos concentrations (fibers/cc) in job categories at an asbestos textile plant

Job category	1930-35	1936-45	1946-65	1966-75
General area	10.8	5.3	2.4	4.3
Card operators	13.3	6.5	2.9	5.3
Clean-up	18.1	8.8	4.0	7.2
Raw fiber handling	22.8	11.0	5.0	9.0



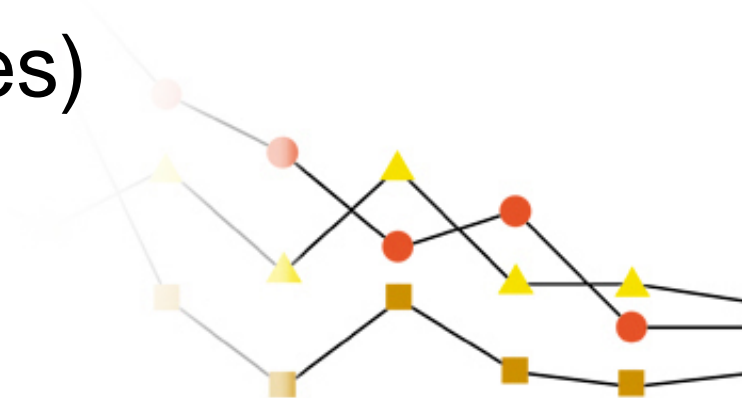
Example of an exposure history

Job	Years	Exposure	Cumulative exposure
Card operator	1933-35	10.8	32.4
Card operator	1936-38	6.5	41.9
Clean-up	1939-45	8.8	103.5
Clean-up	1946-48	4.0	115.5



South Carolina asbestos textile worker study

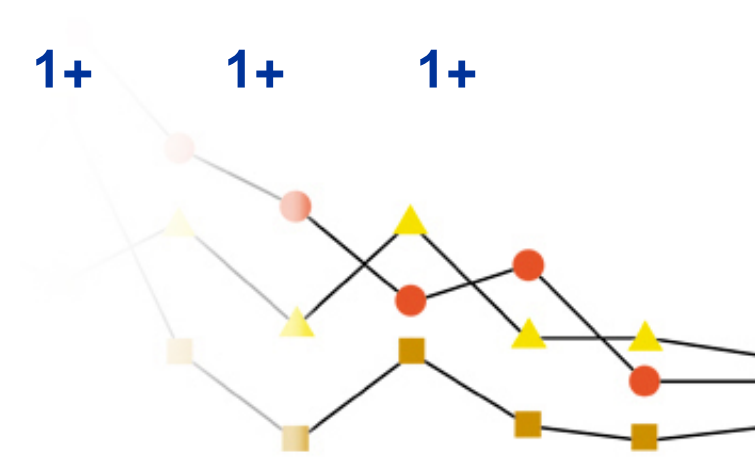
- South Carolina asbestos textile workers
- N=1261
- white males
- followed 1940-1975
- **Exposure:** fibers/cc days (thousands)
- **Outcome:** lung cancer (35 cases)



Employment history of a worker

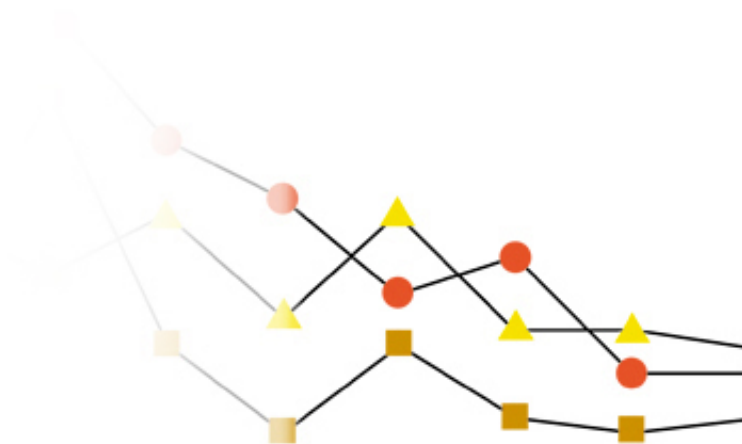


Year	60	61	62	63	64	65	66	67
Exposure	0.1	0.1	0.4	0.6	0.1	0	0	0
Cumulative exposure	0.1	0.2	0.6	1.2	1.3	1.3	1.3	1.3
Cumulative exposure category	<1	<1	<1	1+	1+	1+	1+	1+



South Carolina asbestos textile worker study

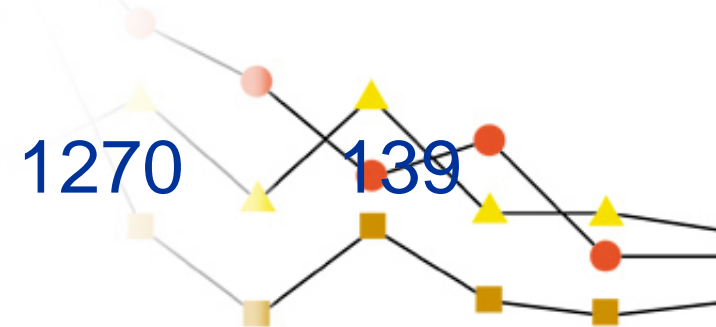
- A separate record is created for each person-year of follow-up
- We get a file with 32,354 person-years and do a cross-tabulation of exposure and the potential confounders



South Carolina asbestos textile worker study (32,354 person-years)

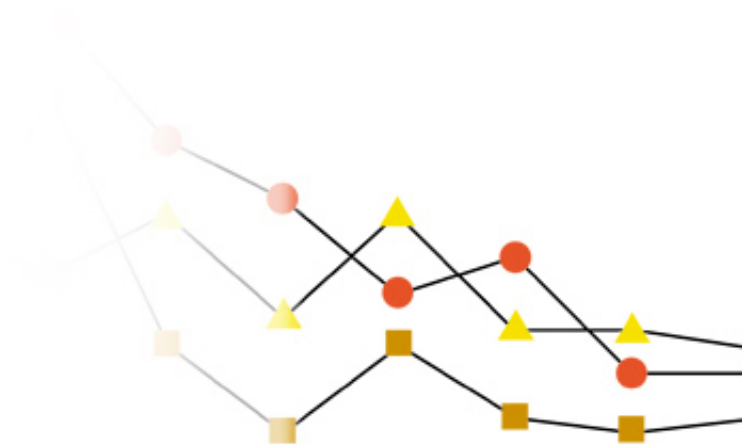
Exposure category

Age	<1	1-9	10-39	40-99	100+
<50	11134	10721	3575	589	62
50-54	964	1024	633	228	27
55-59	570	583	408	226	16
.....					
Total	13146	12823	4976	1270	139



South Carolina asbestos textile worker study

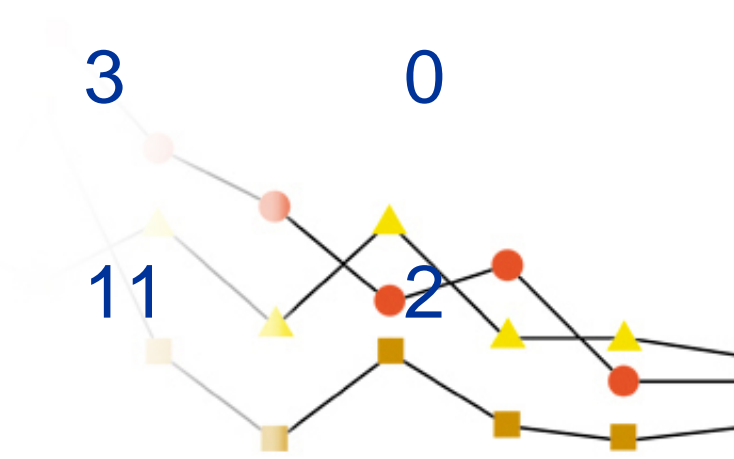
- A separate record is created for each death, classifying the death in the same manner as the person-year in which it occurred
- We get a file with 35 deaths and do a cross-tabulation of exposure and the potential confounders



South Carolina asbestos textile worker study (35 deaths)

Exposure category

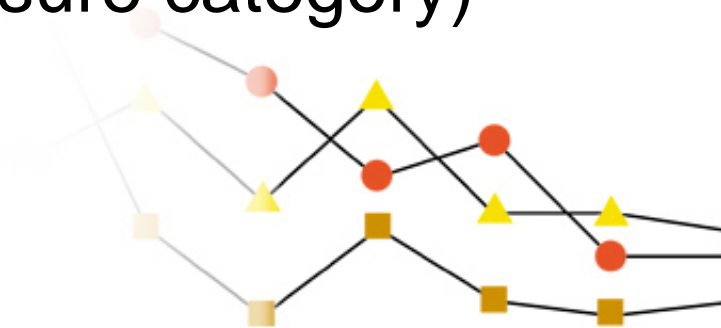
Age	<1	1-9	10-39	40-99	100+
<50	3	2	1	0	0
50-54	1	2	3	3	1
55-59	0	0	3	3	0
.....					
Total	5	10	7	11	2



South Carolina asbestos textile worker study

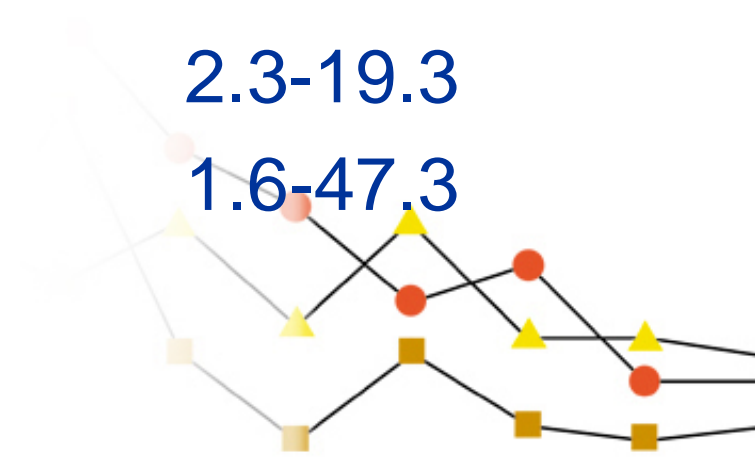
We can then calculate age-standardised lung cancer death rates:

- **SMRs** (comparison with national rates)
- **SRRs** (comparison with lowest exposure category)
- **Poisson regression** can be used to estimate **rate ratios** (comparison with lowest exposure category)

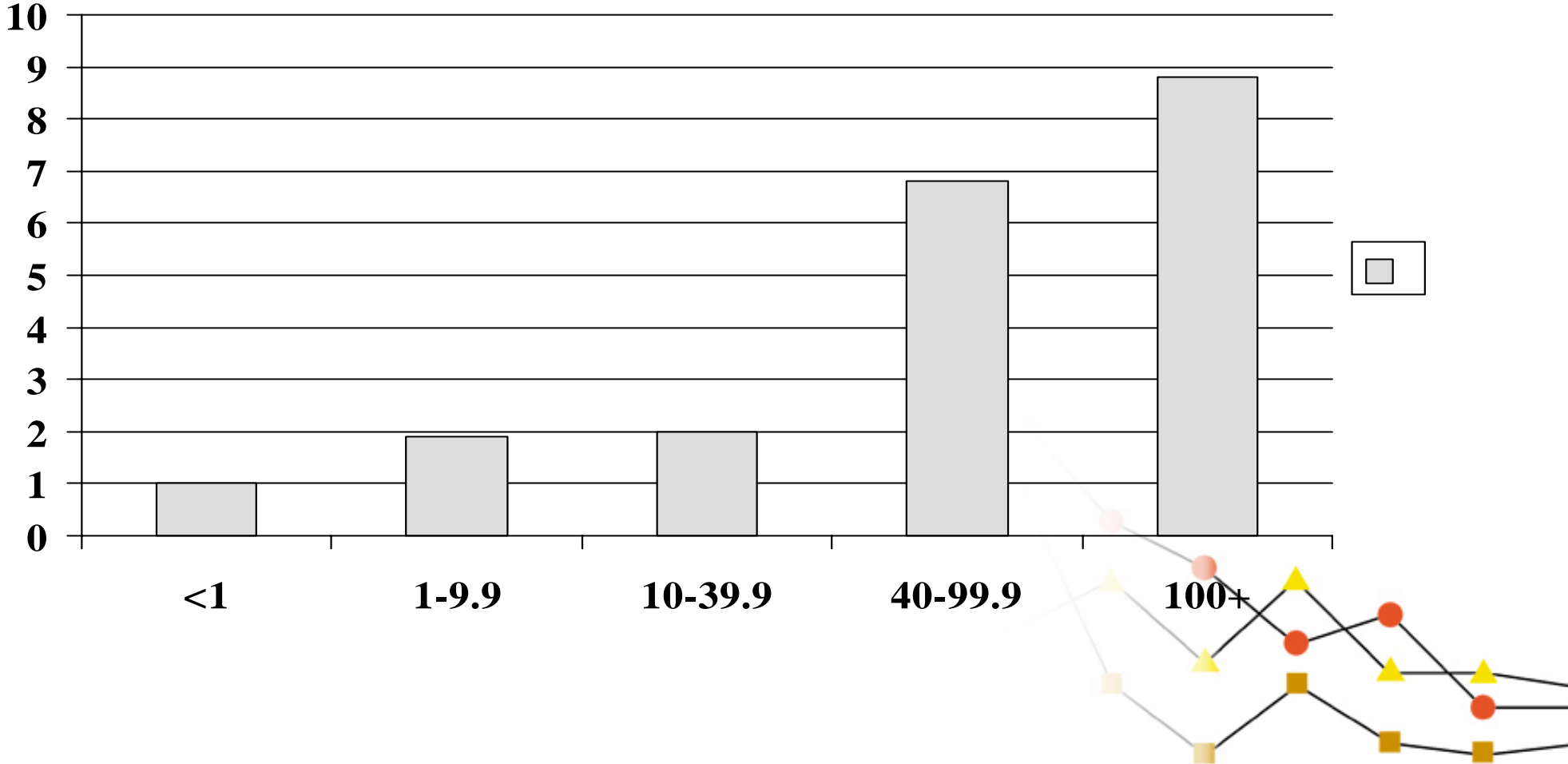


South Carolina asbestos textile worker study

Exposure group	Deaths	Person years	Rate ratio	95% CI
<1	5	13146	1.0	-
1-9	10	12823	1.9	0.6-5.5
10-39	7	4976	2.0	0.6-6.3
40-99	11	1270	6.8	2.3-19.3
100+	2	139	8.8	1.6-47.3

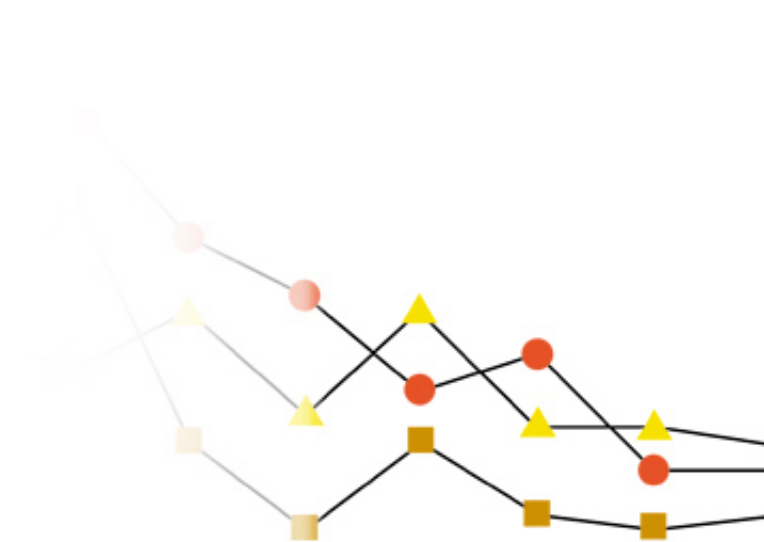


South Carolina asbestos textile worker study



Biomarkers

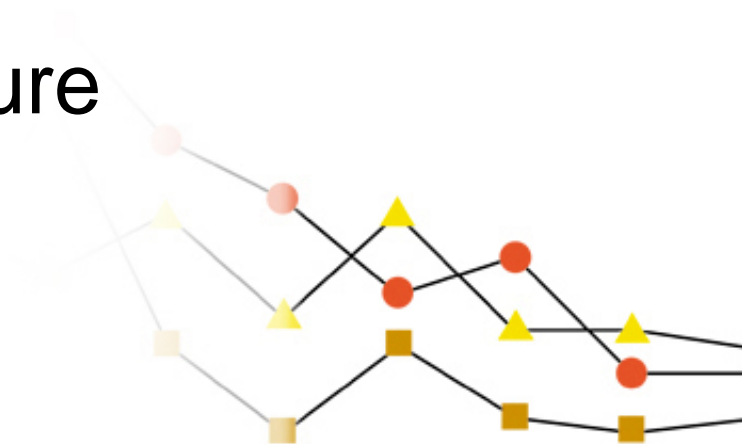
- Exposure
- Early disease
- Individual susceptibility



Biomarkers of exposure

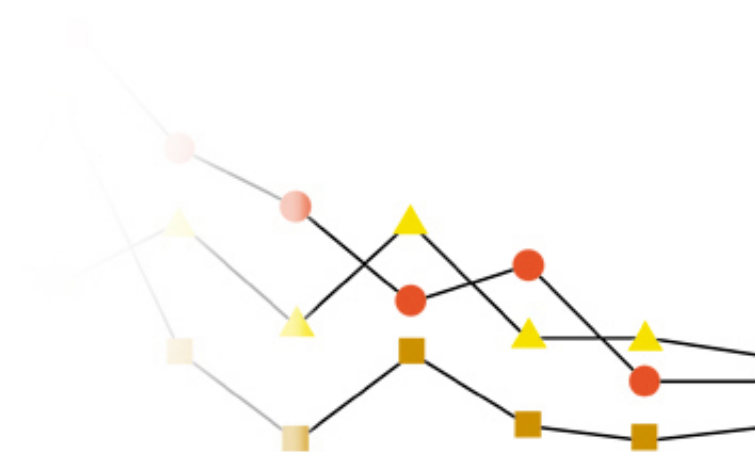
- The concentration of the substance of interest
- The concentration of products of biotransformation
- The biological effects of exposure

(Armstrong et al, 1992)



Current limitations of biomarkers

- Historical exposures
- Individual temporal variation
- Study size



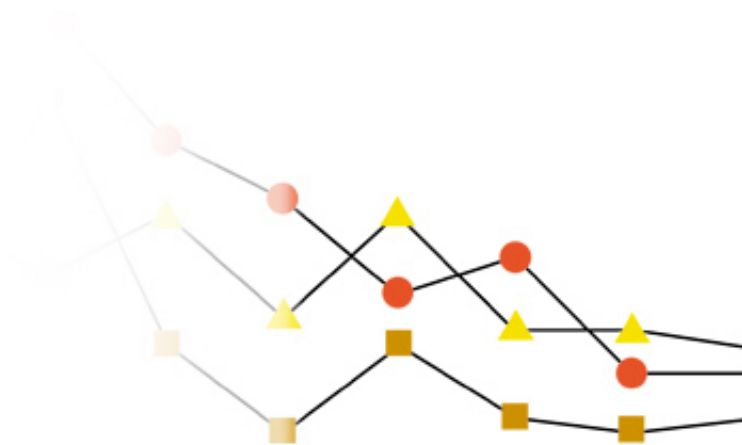
Measuring historical exposures

“A typical case-control study of cancer and chemical exposure could not rely on [DNA-adducts]. The relevant exposures occur many years before disease diagnosis, and any DNA adducts from the relevant exposure period will probably have disappeared or be indistinguishable from adducts formed more recently”
(*Wilcosky and Griffith, 1990*)



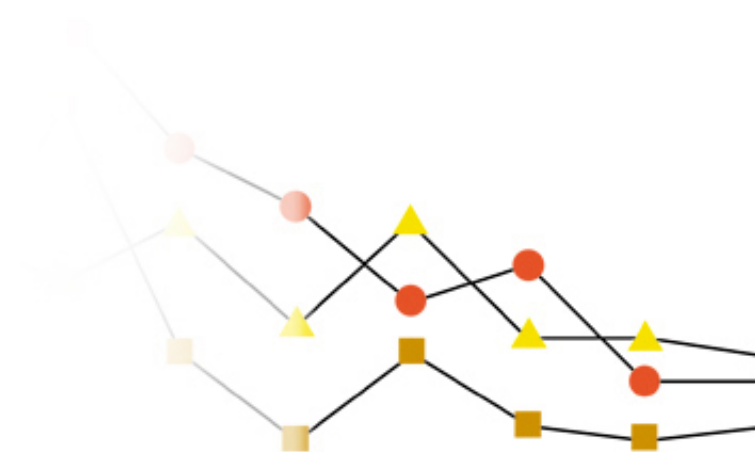
Individual temporal variation

- The variation in exposure levels within an individual (because of day-to-day differences in exposure) may be greater than the variation between individuals



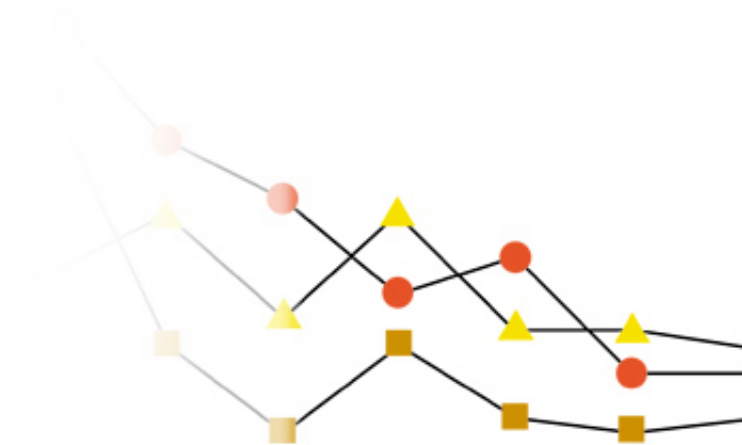
Study size

- The use of biomarkers may severely limit the size of a study; thus, any gains in validity (from better exposure information) may be offset by losses in precision



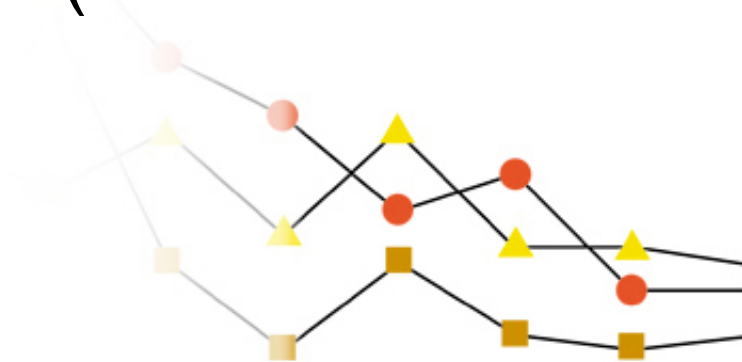
Inherent limitations of biomarkers

- What does a biomarker measure?
- Increased likelihood of confounding
- Public health implications



What does a biomarker measure?

- Exposure or biological response (or disease process)?
- One biological response to one chemical
- Individual response to exposure (individual metabolism)



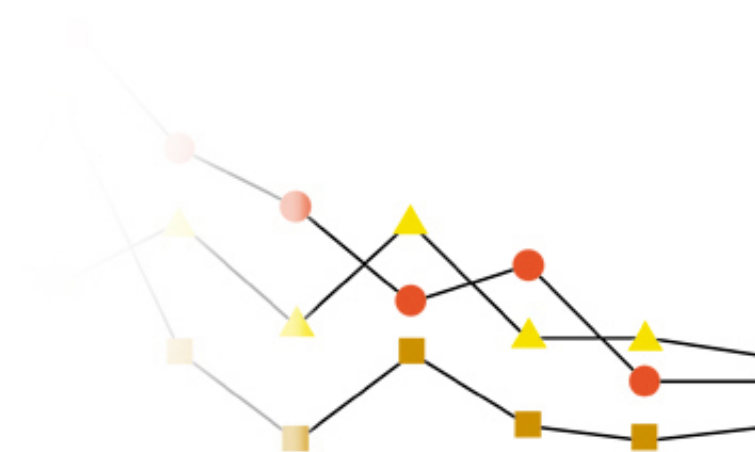
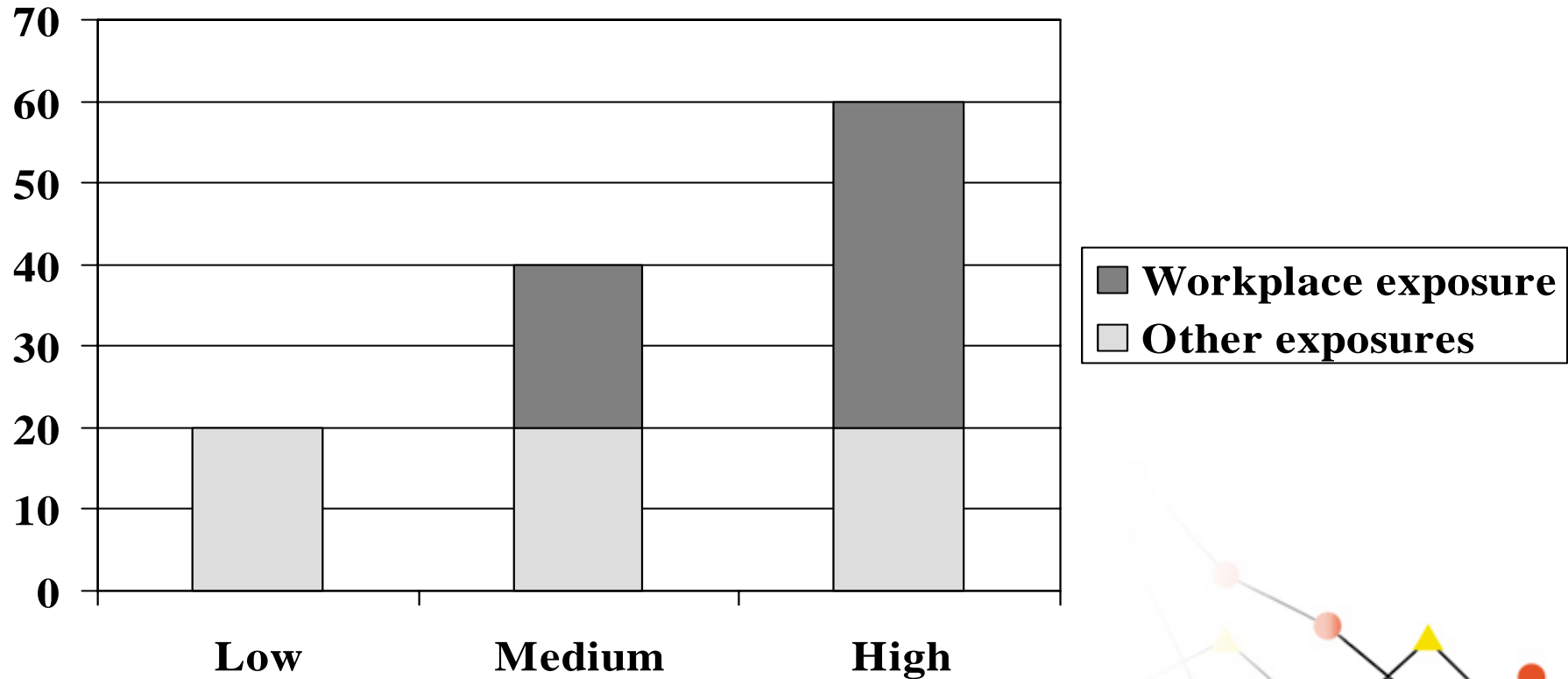
Increased likelihood of confounding

Example: PAH exposure in a factory

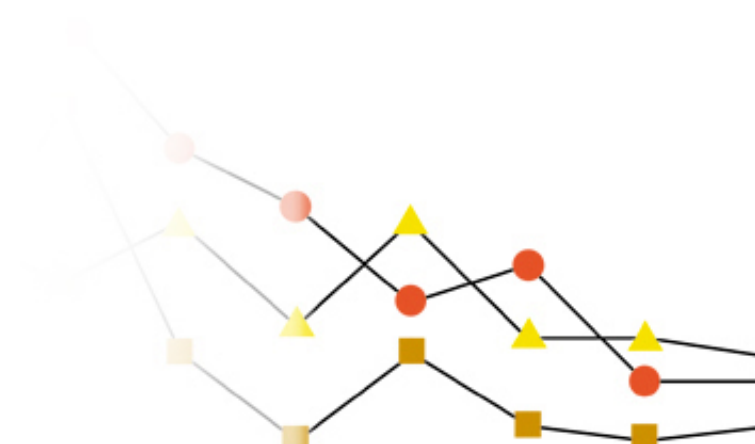
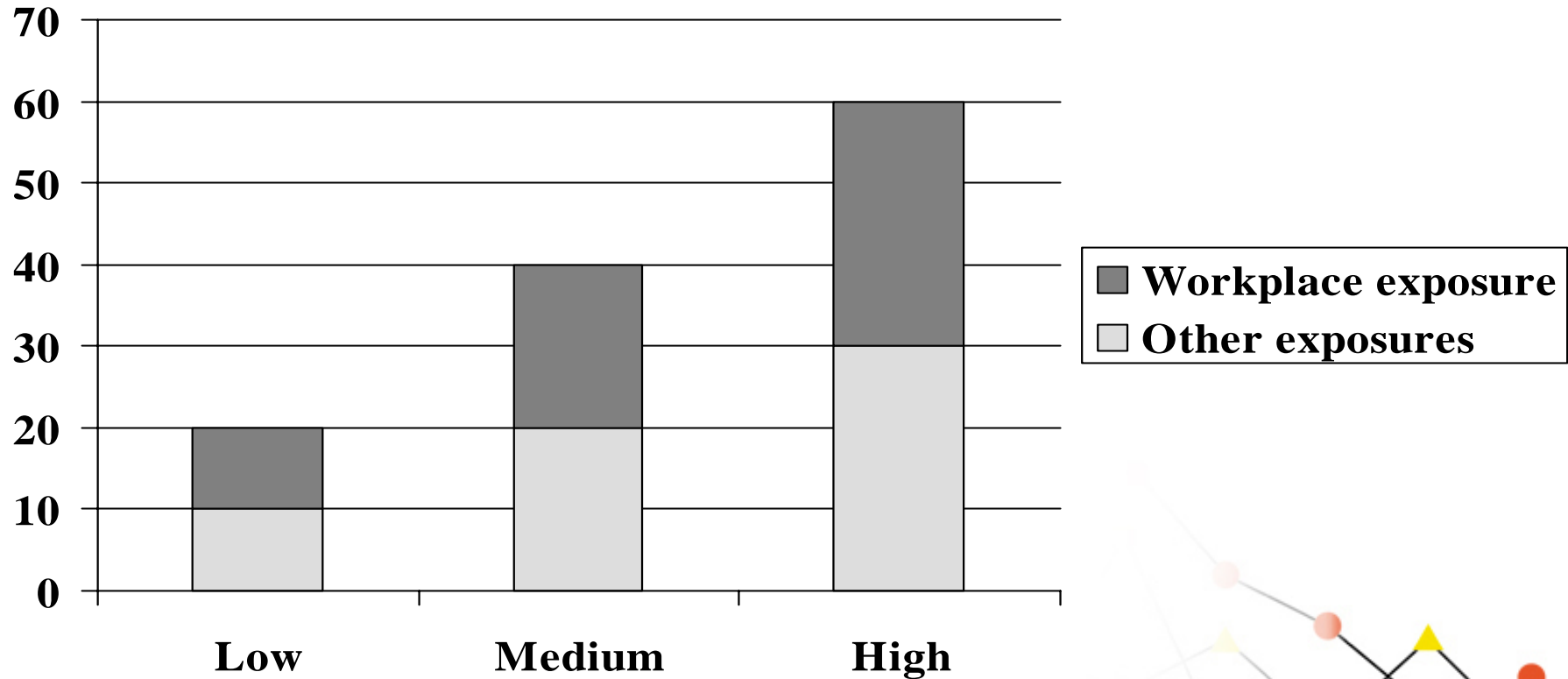
Method of classification	Level of “exposure
Environmental levels in workplace	High Medium Low
PAH-DNA adducts	High Medium Low



Classification based on environmental levels in the workplace



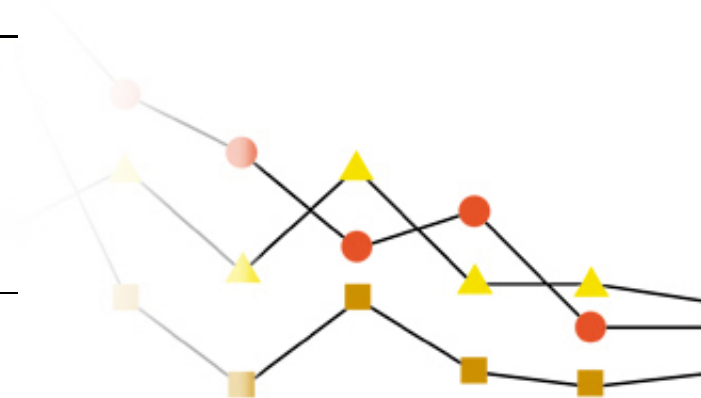
Classification based on PAH-DNA adducts



Increased likelihood of confounding

Example: PAH exposure in a factory

Method of classification	Level of “exposure	% smokers
Environmental levels in workplace	High	Medium
	Medium	Medium
	Low	Medium
PAH-DNA adducts	High	High
	Medium	Medium
	Low	Low



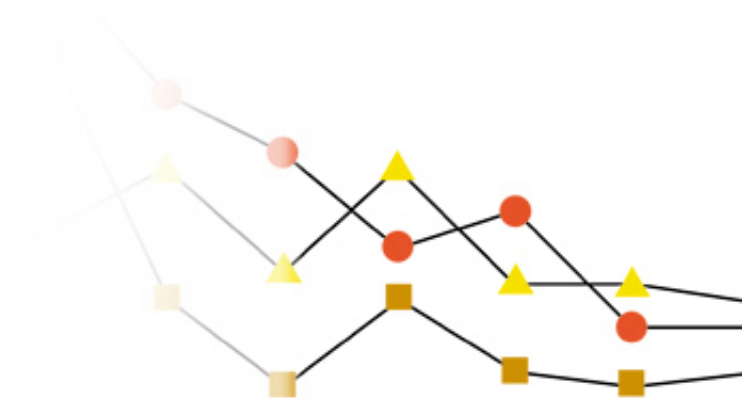
Public health implications

- Technology defines the “problem”
- Regulation is (or should be) based on environmental exposure levels
- Dangers of interventions based in individual susceptibility



Biomarkers, epidemiology and public health

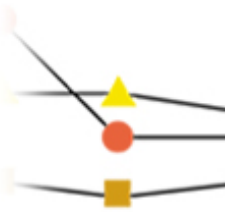
- Relevant to only some of the major public health problems
- In the situations in which they are relevant, biomarkers have both strengths and limitations and are often inferior to more traditional methods of exposure assessment



Chapter 5

Measurement of exposure and health status

- Exposure
 - Exposure and dose
 - Options for exposure assessment
- Health status
 - Routine records
 - Morbidity surveys



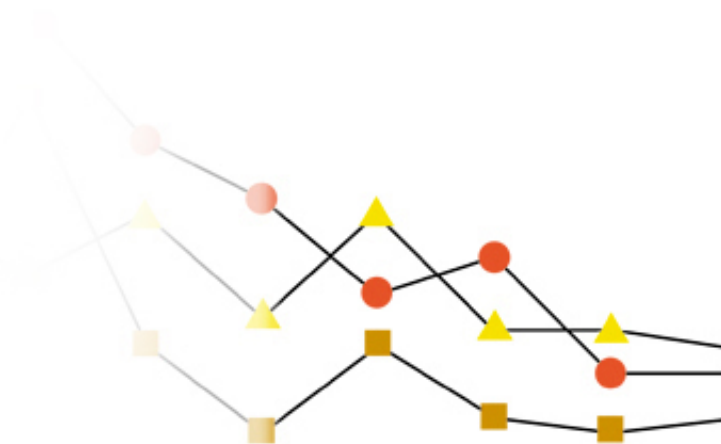
Routine records

- Death registrations
- Disease registers (e.g. cancer, congenital malformations, occupational disease notifications)
- Health system records (e.g. hospital admissions, general practice records)
- Health insurance claims



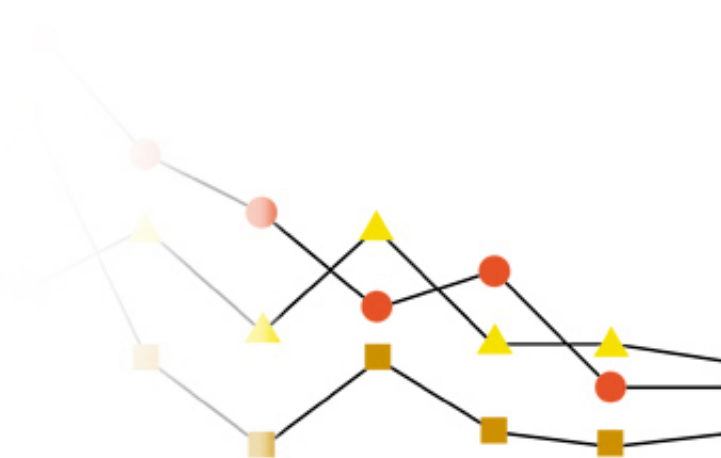
Morbidity surveys

- Standardized questionnaires
 - The ISAAC childhood asthma questionnaire
 - Quality of life questionnaires
 - The Medical Outcomes Study Short Form (SF-36)
- Physiological measurements
 - Lung function testing
- Biological measurements
 - Serum testing (e.g. hepatitis B)



How Do We Decide Which Is the Most Valid Measure to Use?

- The “gold standard” is to give all study participants a full clinical examination
- Survey instruments can be compared to the “gold standard” in terms of their:
 - sensitivity
 - specificity
 - Youden’s Index
 - positive predictive value



Sensitivity and Specificity

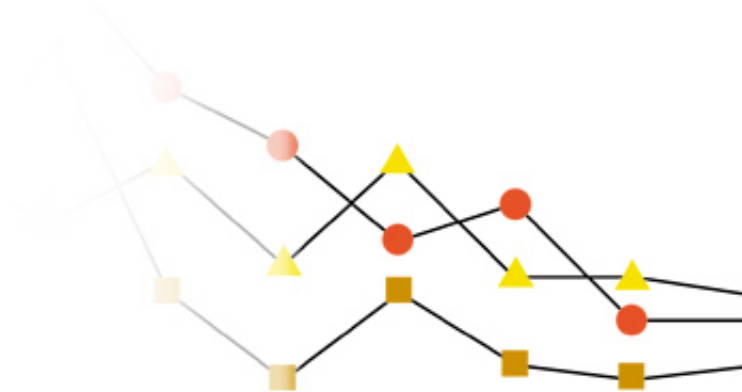
“Gold standard”

Yes

No

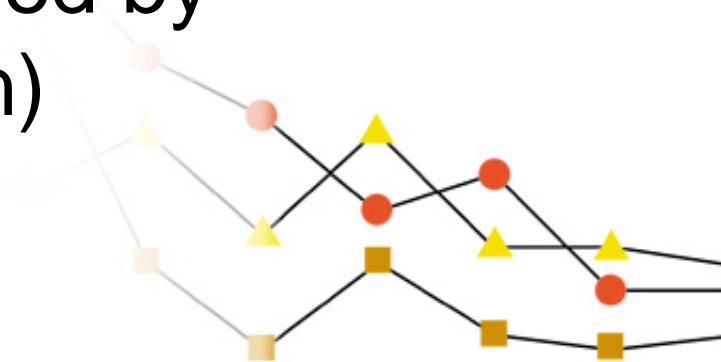
Instrument	Yes	a (Sensitivity)
	No	1-a

	b (Specificity)
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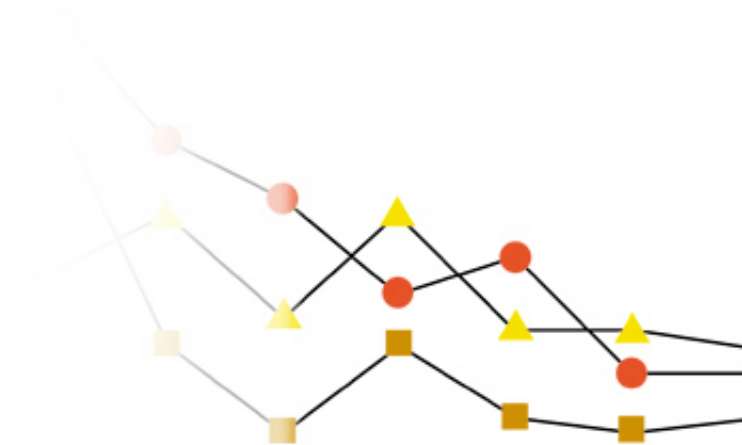
Validation of Survey Instruments

- Sensitivity = a
- Specificity = b
- Youden's Index = $a + b - 1$
- All these three measures have a range of 0 to 1 (Youden's Index can be less than 0, but only if the sensitivity and specificity are worse than would be obtained by chance with a random definition)



Validation of Survey Instruments

- Suppose that we are doing a survey in a population in which the true prevalence is P
- The observed prevalence is:
$$aP + (1-b)(1-P) = P(a+b-1) + (1-b)$$



Validation of Survey Instruments

If we compare two populations, then the observed prevalences are:

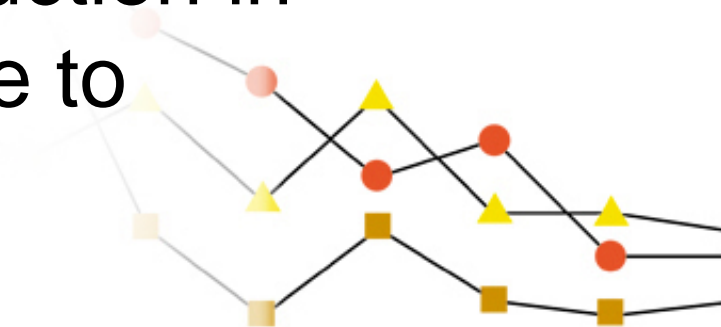
$$P_1(a+b-1) + (1-b)$$

$$P_0(a+b-1) + (1-b)$$

the observed prevalence difference is:

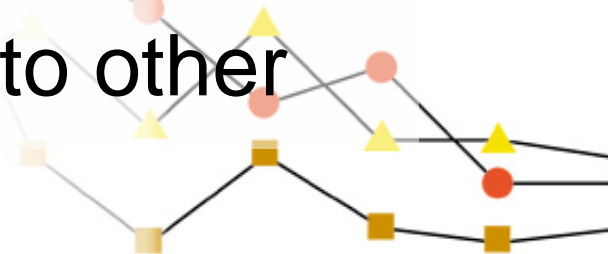
$$(P_1 - P_0)(a+b-1)$$

Youden's Index indicates the reduction in the true prevalence difference due to misclassification



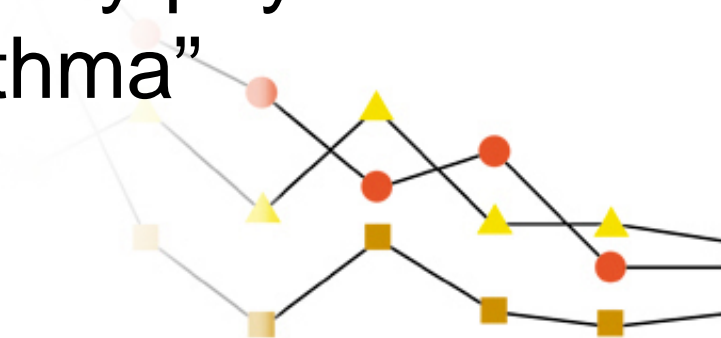
Validation of Survey Instruments

- In population-based prevalence surveys, *Youden's Index* is the most appropriate measure of validity
- In etiologic studies (e.g. cohort studies, case-control studies), the *positive predictive value* is also important. However, a “severe” and restrictive definition of asthma may have a good positive predictive value, but the findings may not be generalisable to other asthmatics



Example: Jenkins et al (1996)

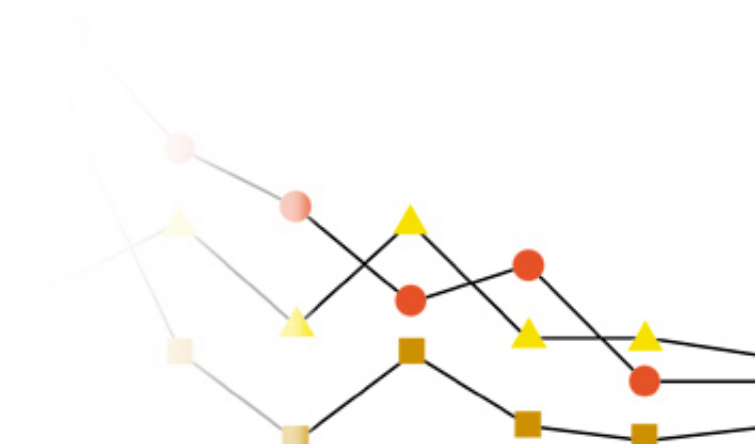
- 361 children in Melbourne given ISAAC questionnaire
- 93 adults in Melbourne given similar questionnaire
- Bronchial challenge with hypertonic saline
- Interviewed by pediatric respiratory physician and diagnosed with “current asthma”



Example: Jenkins et al (1996)

Findings in Adults

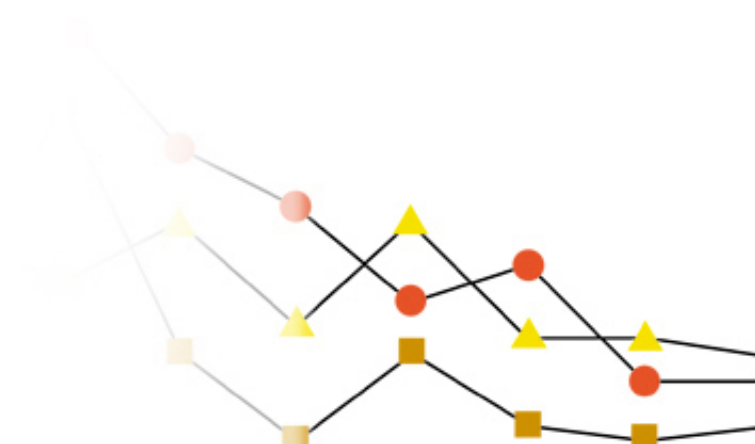
	Sensitivity	Specificity	Youden's Index
Symptoms	0.80	0.97	0.76
BHR	0.39	0.90	0.29
Symptoms + BHR	0.37	0.99	0.36



Example: Jenkins et al (1996)

Findings in Children

	Sensitivity	Specificity	Youden's Index
Symptoms	0.85	0.81	0.66
BHR	0.54	0.89	0.43
Symptoms + BHR	0.47	0.94	0.41



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