OCCUPATIONAL EXPOSURE ASSESSMENT

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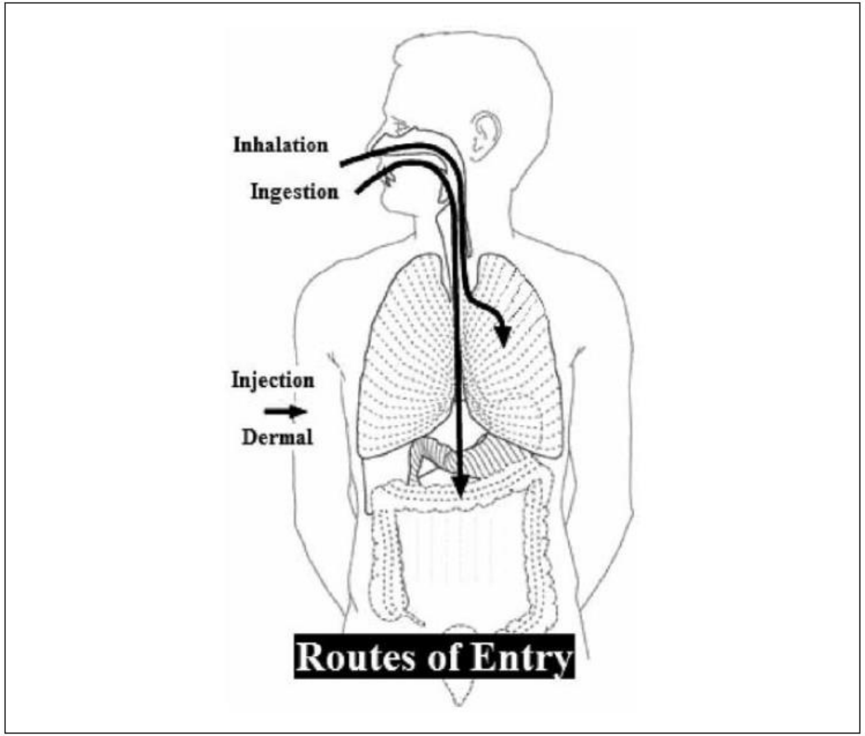
Purpose of this lecture

1. Assessment of occupational exposure
   - definitions and methods
   - exposure assessment and study designs considerations

2. Historical development of analysis of exposure variability:
   - from t-test to mixed effect models
   - new descriptive measures for exposure variability

3. Exposure variability:
   - analysis of trends in exposure across jobs over time
   - repeated measurements in occupational epidemiology study

1. Assessment of occupational exposure



4 different exposure routes

Agent is a chemical, biological, or physical entity that contacts the surface of the human body
Nieuwenhuijsen. Oxford Univ Press 2003

Examples:
Chemical: asbestos, benzene
Biological: microbial dusts, endotoxin
Physical: heat, noise, light

Measurement instruments

Surveys

- Questionnaires
- Interviews
- Diaries
- Walk-throughs

Expert opinions

Registers

Actual measurements

- Environment or worker's contact boundaries
- Blood and/or other biological specimens

Exposure dimensions

- *Intensity – i.e How much?*
- *Duration – i.e. How long ?*
- *Frequency – i.e. How often ?*

Exposure metrics

- *Current exposure*
- *Average exposure*
- *Cumulative exposure*
- *Peak exposure*

Application in different study designs ?

An example: Brisman et al. Occup Environ Med 2004;61:551-3

Table 1 Prevalence ratios for chest and eyes/nose symptoms and a positive SPT to fungal α-amylase in relation to exposure categories for fungal α-amylase allergen

Exposure category	Low	Medium	High
α-amylase allergen level (ng/m^3)			
Arithmetic means (SD)	0.7 (0.8)	10.7 (2.2)	46.7 (16.6)
Number of measurements	225	22	13
Chest symptoms			
Prevalence ratio	1	1.7	3.0
95% CI		0.6 to 4.9	1.1 to 8.1
Number of incident cases	22	5	5
Eyes/nose symptoms			
Prevalence ratio	1	1.9	1.9
95% CI		0.9 to 3.8	0.9 to 4.2
Number of incident cases	56	10	7
SPT positive to α-amylase			
Prevalence ratio	1	3.1	4.0
95% CI		0.6 to 17	0.9 to 18
Number of incident cases	18	2	4

Sex and atopy were confounders in the model.

Policy implications

- A reduction in α-amylase exposure is likely to reduce the risk for respiratory morbidity in bakery workers.

Study among 300 bakery workers with 260 measurements

How is exposure estimated in this study?

What improvements are possible?

Exposure assessment

1. From single measurement per subject at start of the study to repeated measurements per subject during the follow-up period:
   * how to decide on number of measurements?
   * how to efficiently allocate measurements?

2. From individual-based to group-based exposure assessment strategy:
   * how to group individuals in comparable exposure groups (job, task, etc)?
   * best grouping strategies?

3. From exposure assessment to exposure metrics and exposure models:
   * best exposure characterization in occupational epidemiology study

1. Assessment of occupational exposure

Take home messages 1:

1. Choices in occupational exposure assessment are strongly influenced by study design and, therefore, assumptions of exposure-response relationship

2. The assessment strategy should maximize information on exposure distribution in the occupational group under study

3. Information on sources of variance in exposure is very useful to optimize the measurement strategy and even the epidemiological study

2. Historical example

CHARACTERIZATION OF EXPOSURE TO INHALABLE FLOUR DUST IN SWEDISH BAKERIES

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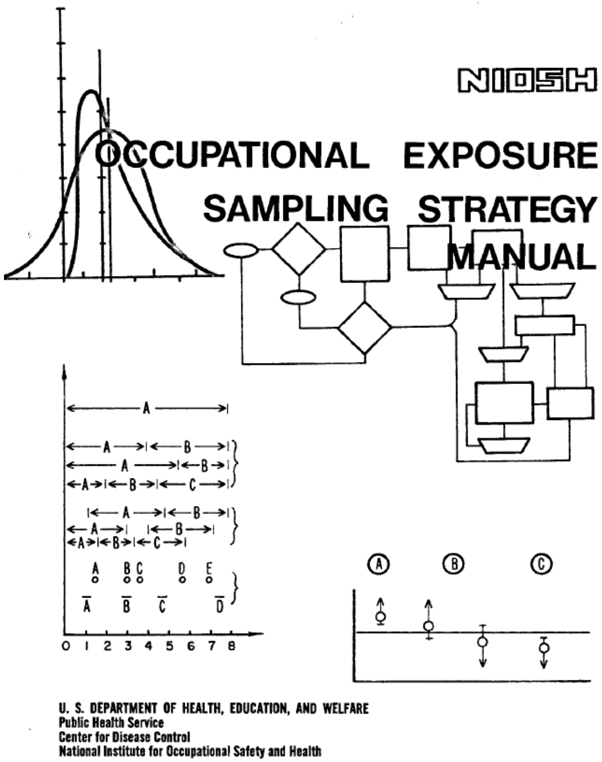
2. Historical example



Introduction of lognormal distribution in occupational exposure

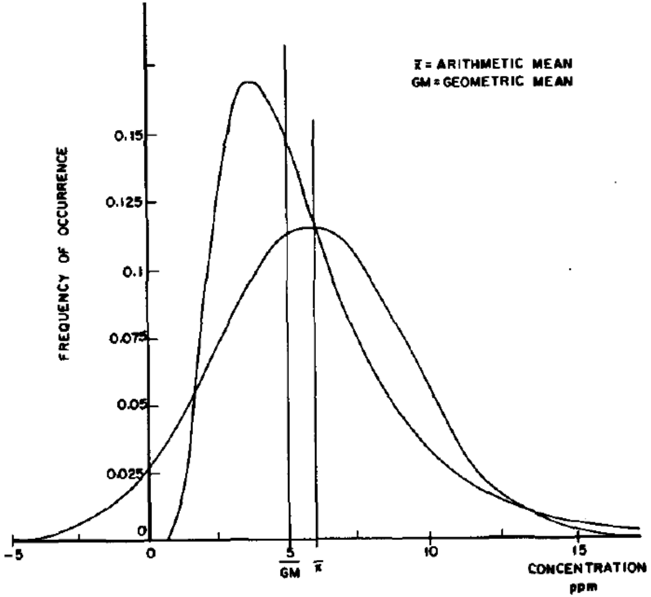
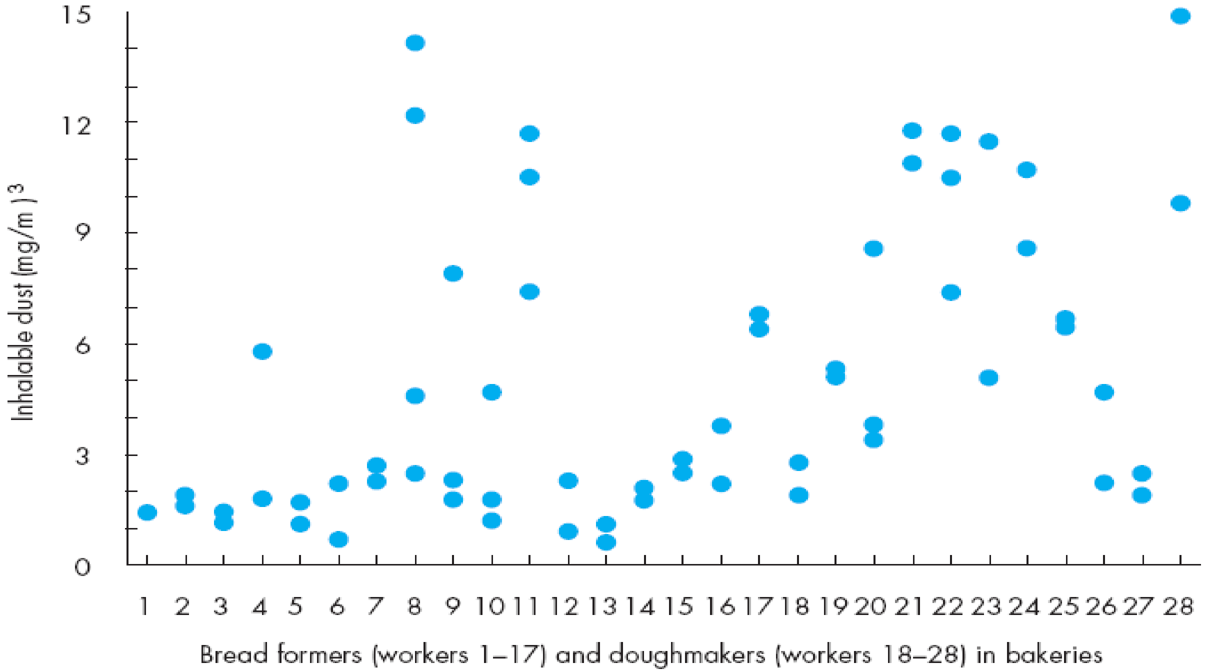


Figure M-1. Lognormal and normal distributions with the same arithmetic mean and standard deviation.

Leidel, Busch, Lynch. Cincinnati, Ohio 1977

2. Historical example



2. Historical example

TABLE 2 MEASUREMENTS OF EXPOSURE TO INHALABLE FLOUR DUST AMONG BAKERY WORKERS BY TASK GROUP. *n* IS THE NUMBER OF MEASUREMENTS AND *N* IS THE NUMBER OF PERSONS MEASURED

Task group	*N*	*n*	AM ($mg\ m^{-3}$)	GM ($mg\ m^{-3}$)	GSD	Range ($mg\ m^{-3}$)
Doughmakers	18	34	6.90	5 46	2.09	1.20–16 90
Bread-formers	41	62	3.39	2 69	1.96	0.60–14.20
Oven workers	7	10	1.59	1.17	2.43	0.20–4.00
Confectionery workers	7	7	0.86	0 58	2.56	0.20–3.00
Packers	6	9	0.63	0.48	2.40	0.10–1.40
Mixed tasks*	5	7	3 09	2.73	1 74	1.20–4 90
Total	84	129	3.83	2 48	2.77	0.10–16.9

*Bread-formers or doughmakers who performed also another task during the measurement.

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AM = arithmetic mean; GM = geometric mean; GSD = geometric standard deviation

2. Historical example

Stages in the statistical analysis:

1. *t-tests between different exposure groups*

Problem: exposure not normally distributed	Solution: log-transformation
Problem: multiple comparisons	Solution: correction (strict)
Problem: variation really random ?	Solution: random sampling
Problem: influence of exposure determinants ?	Solution: stratified t-testing
Problem: how similar are workers within exposure groups ?	Solution: no t-test !!

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2. Historical example

Stages in the statistical analysis:

2. *Linear regression analysis* (....extension of t-test...)

doughmakers	+ 5.47 mg/m^3
breadformers	+ 2.69 mg/m^3
oven workers	+ 1.17 mg/m^3
packers	+ 0.58 mg/m^3
confectionary workers	reference (average = 0.48 mg/m^3)

R^2 = 50% ! Problem: variance within and between workers

2. Historical example

Introduction of new descriptive measures for variability

1. GSDww = geometric standard deviation of within worker variance

   GSDbw = geometric standard deviation of between worker variance

2. $R_{0.95}$ = Range ratio: ratio of 97.5th percentile to 2.5the percentile of the worker's mean exposure (derived from GSDbw)

3. λ = variance ratio: ratio of within-worker over between-worker variance

2. Historical example

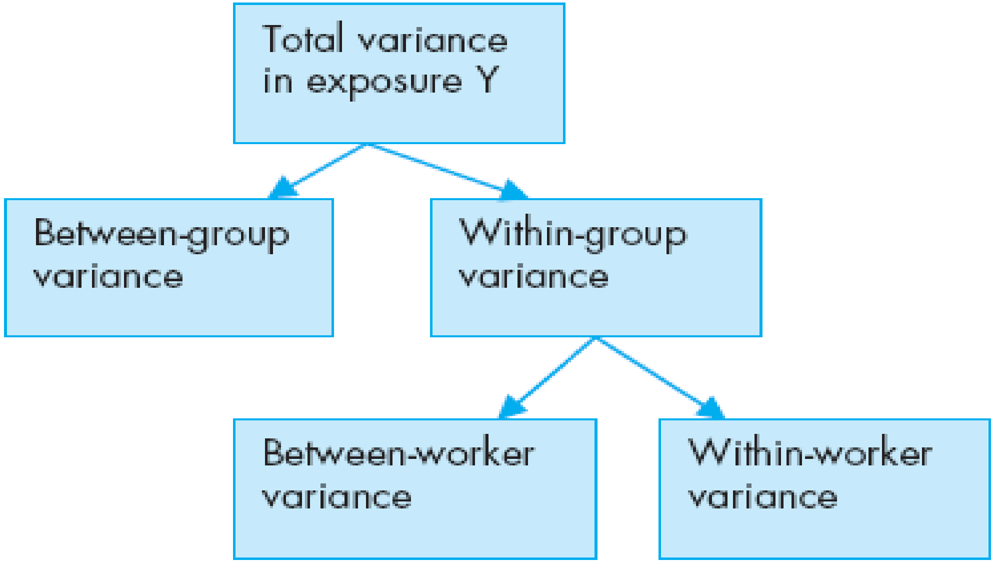
TABLE 3. PARAMETERS TO EVALUATE THE HOMOGENEITY OF TASK GROUPS IN BAKERIES WITH EXPOSURE TO INHALABLE FLOUR DUST. n IS THE NUMBER OF MEASUREMENTS AND N IS THE NUMBER OF PERSONS MEASURED

Task group	N	n	GSD_{bw}*	$R_{0.95}$†	λ‡
Doughmakers	11	27	1.72	8.50	0.45
Bread-formers	17	38	1.77	9.30	0.79
Oven workers	3	6	1.63	6 80	2.07
Packers	3	6	1.64	6.88	1.09
Total	34	77	2.45	33.68	0.30

*GSD between-worker variance.
†Range ratio.
‡Variance ratio.

2. Historical example

Random effect analysis of variance



2. Historical example

TABLE 4 PARTITIONING OF THE TOTAL VARIABILITY IN EXPOSURE TO INHALABLE FLOUR DUST AMONG BAKERY WORKERS USING DIFFERENT GROUPING STRATEGIES

	Grouping strategy					
	A*		B†		C‡	
Source of variability	σ	%	σ	%	σ	%
Between-group variance	0.83	61	0.84	61	1.50	69
Between-worker variance	0 31	22	0.31	22	0 43	20
Within-worker variance	0.23	17	0 23	17	0.23	11

*Grouping strategy A with four groups; doughmakers, bread-formers, oven workers and packers.
†Grouping strategy B with three groups: doughmakers, bread-formers, oven workers + packers.
‡Grouping strategy C with two groups; doughmakers + bread-formers vs oven workers + packers.

2. Historical example

Linear mixed effects model

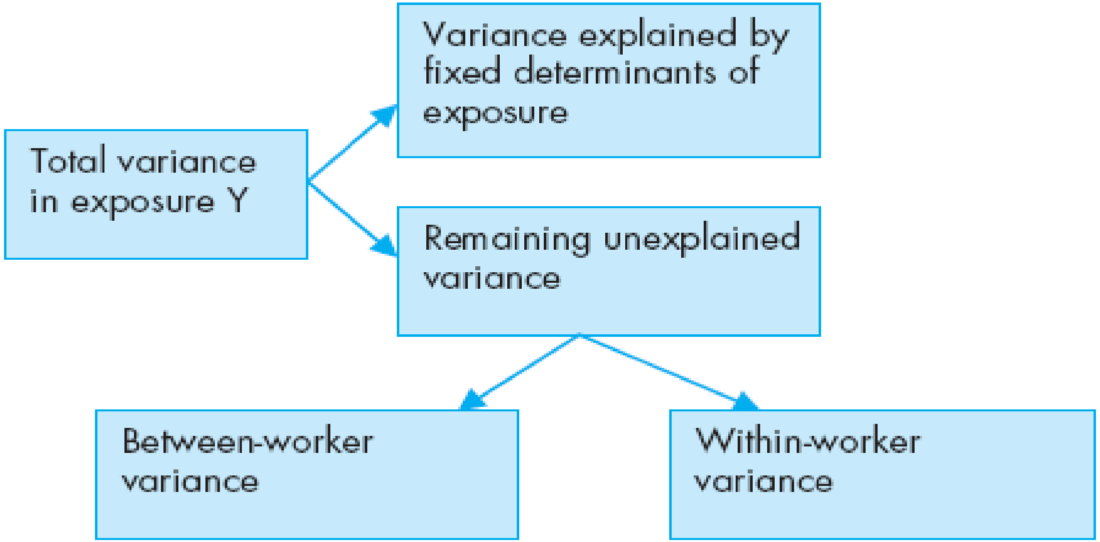


Figure 2 Schematic illustration of dividing the variability in exposure parameter Y into its underlying variance components.

Available in standard software from around year 2000

2. Historical example

Stages in the statistical analysis:

3. Linear mixed effect model (re-analyzed) [regression analysis]

	Linear mixed effect model (re-analyzed)	[regression analysis]
doughmakers	+ 5.47 mg/m^3	+ 5.47 mg/m^3
breadformers	+ 2.61 mg/m^3	+ 2.69 mg/m^3
oven workers	+ 1.19 mg/m^3	+ 1.17 mg/m^3
packers	+ 0.62 mg/m^3	+ 0.58 mg/m^3
confectionary workers	= 0.47 mg/m^3	= 0.48 mg/m^3
	R^2 bW = 60%, R^2 wW = 35%	R^2 = 50%

Why these small differences?

2. Historical example

3. Linear mixed effect model

Univariate analysis, average exposure:

small bakeries	+ 1.14 mg/m^3
medium bakeries	+ 3.20 mg/m^3
large bakeries	+ 1.14 mg/m^3

Relevant differences ?

2. Historical example

Take home messages 2:

1. Statistical analysis of exposure data has developed rapidly in past 30 years

2. Linear mixed effect model is a very powerful statistical tool

3. Reduction in within-worker and between-worker variance due to fixed effects will present important information on exposure determinants and, thus, exposure assignment in occupational epidemiology study

3. Exposure variability

Trends in occupational exposure across jobs over time

368 L. Andersson *et al.*

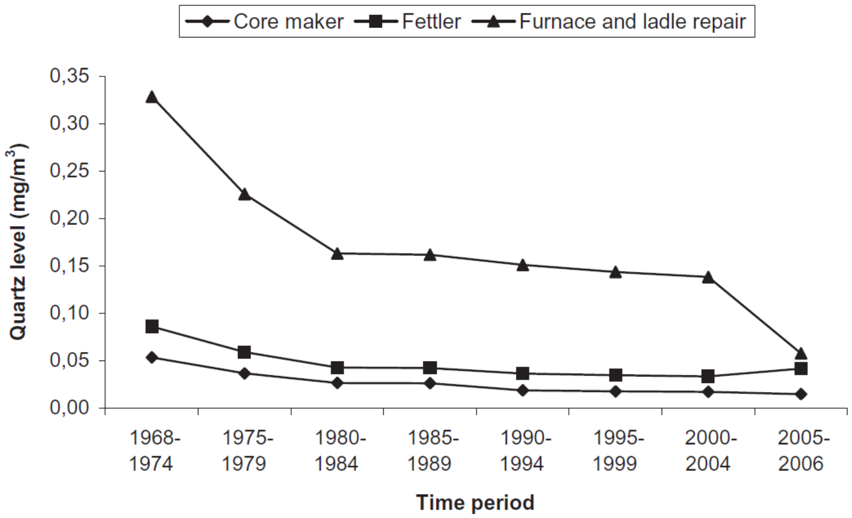


Fig. 1. Long-term trends in exposure to quartz for three typical jobs in medium-sized Swedish foundries between 1968 and 2006.

Determinant	Regression coefficient	
	n	Historical model
Intercept		−4.104 ± 0.102
Time period		
1968–1974	208	0.708 ± 0.116*
1975–1979	237	0.334 ± 0.086*
1980–1984	266	0.009 ± 0.083
1985–1989	398	ref
1990–1994		n/a
1995–1999		n/a
2000–2004		n/a
2005–2006		n/a
Company level		
Small (*n* = 3)	88	0.716 ± 0.134*
Medium (*n* = 4)	270	0.471 ± 0.093*
Large (*n* = 4)	751	ref
Job title		
Caster	35	0.038 ± 0.208
Core maker	118	ref
Fettler	425	0.474 ± 0.109*
Furnace and ladle repair	56	1.812 ± 0.178*
Maintenance	50	0.699 ± 0.168*
Melter	29	0.163 ± 0.215
Moulder	136	0.438 ± 0.137*
Sand mixer	56	0.528 ± 0.181*
Shake out	72	0.222 ± 0.182
Transportation	24	0.651 ± 0.222*
Others	108	0.724 ± 0.136*
Variances (full model)		
σ^2_{WW}		0.267
σ^2_{BW}		0.699
Reduction in σ^2_{BW}		27%

Andersson et al. Ann Occup Hyg 2012;56:362-72.

Purpose of this lecture: revisited

1. Assessment of occupational exposure:
   - choose your exposure measure wisely, depending on study design
   - exposure variability is a source of information

2. Historical development of analysis of exposure variability:
   - from t-test to mixed effect models:
     combined analysis of fixed determinants and random sources of variance
   - new descriptive measures for exposure variability:
     within-subject variance, between-subject variance

3. Exposure variability:
   - analysis of determinants, trends across jobs & over time
   - repeated measurements may be needed in occupational epidemiology study

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Rotterdam, Destroyed city, Zadkine, 1953