INDIVIDUAL AND GROUP-BASED EXPOSURE ASSESSMENT

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Purpose of this lecture

1. Exposure modeling in epidemiological studies:
   - individual and group-based exposure assessment
   - attenuation

Exposure modeling in epidemiological studies

Group approach versus individual assessment:

I Exposure assessment at individual level

- largest measurement effort
- should focus on within-worker variance relative to between-worker variance

II Exposure assessment at group level

- more efficient strategy, less measurements
- a priori or a posteriori grouping into sufficiently homogeneous exposure groups; jobs, tasks, work stations, equipment
- are groups homogeneous and distinguishable?

3. Exposure modeling in epidemiological studies

Berkson's error applied to occupational epidemiology:

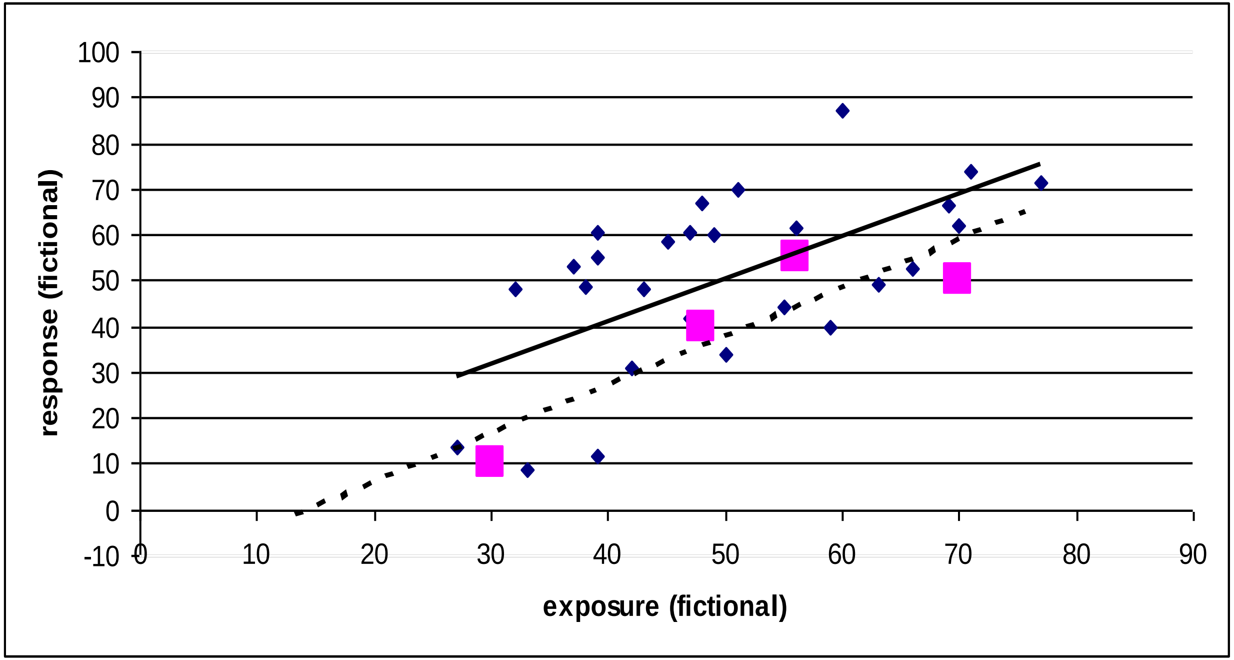
Grouping strategy partly eliminates the effect of random day-to-day variation:

Usually better accuracy but at the cost of a lower precision

Are There Two Regressions?
Author(s): Joseph Berkson
Source: *Journal of the American Statistical Association*, Vol. 45, No. 250 (Jun., 1950), pp. 164-180

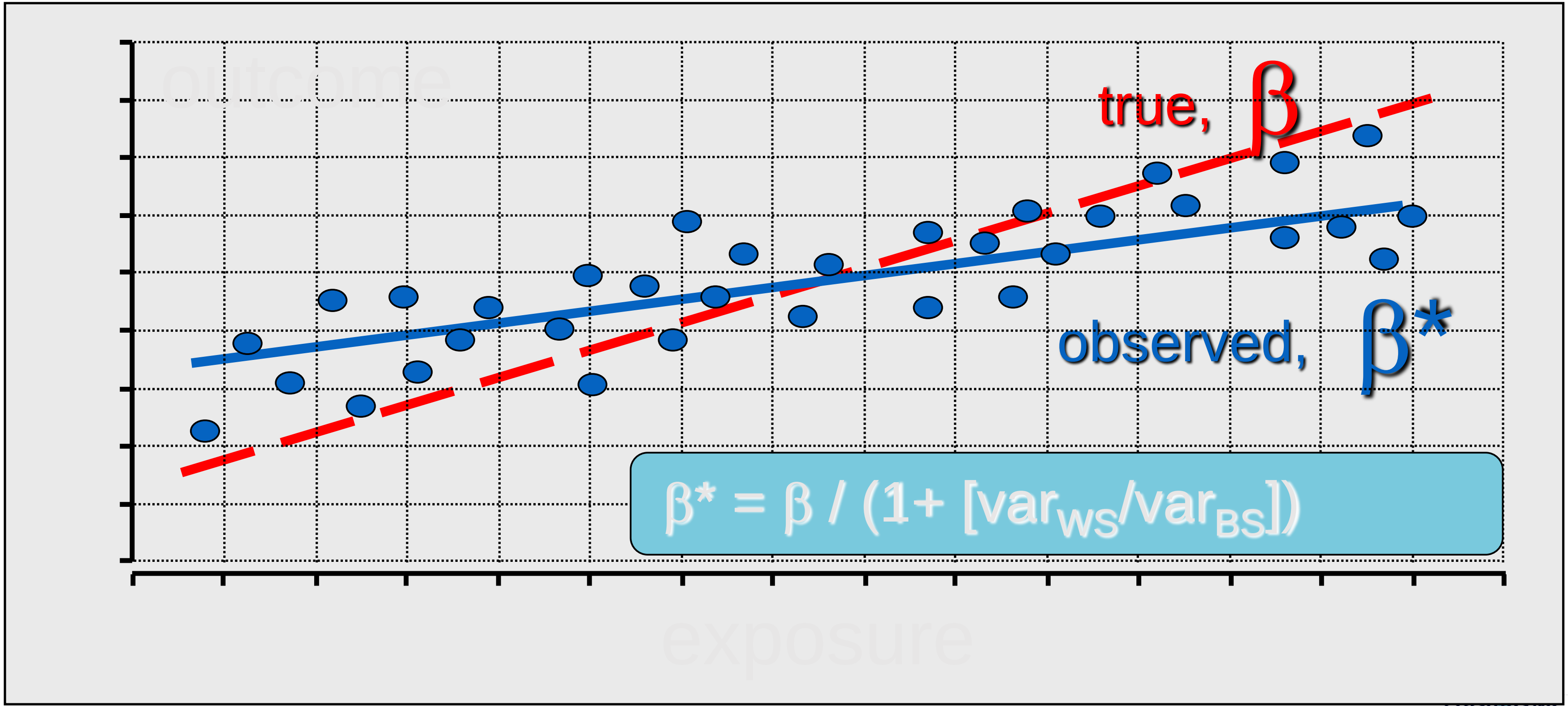
3. Exposure modeling in epidemiological studies

Group approach versus individual assessment (Berkson's error):



3. Exposure modeling in epidemiological studies

Random misclassification in exposure at individual level:



3. Exposure modeling in epidemiological studies

Under certain assumptions, most importantly no systematic errors and equal error variances, the correlation between two measurement methods can be considered as an estimate of reliability of repeated measurements

Reliability coefficient R_S = $\frac{1}{1 + var_{ww} / k*var_{bw}} = \frac{var_{bw}}{var_{bw} + var_{ww}/k} = \frac{1}{1 + \lambda/k}$

where var_{ww} = within-worker variance

var_{bw} = between-worker variance

k = number of samples per subject

(var_ww and var_bw together:) variance ratio (λ)

Thus, lack of precision (i.e. lower intra-reliability) may be balanced by increasing number of repeats

Increase measurement frequency

Number of measurements versus number of subjects

Example

For demonstrating a 5% difference in exposure level between 2 groups, standard deviation of the exposure in both groups of approx. 10%, significance level of 5% (z=1.96) and power of 90% (z=1.28) without any attenuation of exposure, 84 subjects are required.

Variance Ratio	Reliability coefficient	Number subjects with 1 measurement	Number subjects with 2 measurements
0.25	0.80	105	94
1.00	0.50	168	126
4.00	0.20	420	252

Burdorf. Scand J Work Environ Health 1995;21:15-23

Variability of exposure and individual assessment

American Journal of Epidemiology
Vol. 151, No. 10

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Characterization of Dust Exposure for the Study of Chronic Occupational Lung Disease: A Comparison of Different Exposure Assessment Strategies

Dick Heederik[1,2] and Michael Attfield[2]

Heederik et al Am J Epidemiol 2000;151:982-90.

Variability of exposure and individual assessment

TABLE 3. Regression analysis of the relation between 11-year individual mean exposure to respirable coal dust and 11-year change of lung function (FEV_1) for 1,105 coal miners allowing for age, standing height, and pack-years of tobacco smoked, National Study of Coal Workers' Pneumoconiosis, 1969–1981

Samples/ worker	FEV_1 coefficient (ml per mg/m^3)	SE* (ml per mg/m^3)
All samples	–4.5	1.5
15	–3.8	1.4
12	–3.6	1.4
9	–3.2	1.3
6	–2.5	1.3
3	–1.8	1.1

* SE, standard error.

Variability of exposure and individual assessment

How many samples per worker required for a specific attenuation ?

$\lambda = 3$

$$b = \beta(1 + \lambda/k)^{-1}$$

10% attenuation: approx 30 measurements per worker

75% attenuation: 1 measurements per worker

Individual assessment versus a job exposure matrix

The coal miners study revisited: is more information always better ?

TABLE 4. Regression analysis of the relation between average exposure to coal dust and 11-year change of lung function (FEV_1) for 1,172 coal miners, corrected for age, standing height, and pack-years of tobacco smoked for different exposure assessment strategies, and estimated average cumulative exposure and standard deviation (mg x year/m³), National Study of Coal Workers' Pneumoconiosis, 1969–1981

	FEV_1 coefficient (ml per mg/m³)	SE* (ml per mg/m³)	Correlation†	Average exposure	SD*
Individual	–4.4	1.6	1.0	10.4	7.4
Six categories	–2.2	3.2	0.39	10.0	3.9
Six categories + time (10)‡	–3.2	3.4	0.39	10.3	3.8
Six categories + time (4)	–2.0	3.1	0.39	10.4	3.9
Six categories + mine	–5.9	2.4	0.53	10.0	5.2
Model category + mine	–5.0	1.9	0.51	10.0	4.9
External matrix	–2.0	2.4	0.47	10.2	5.0

* SE, standard error of the regression coefficient; SD, standard deviation.
† Pearson's correlation between average individual exposures using all exposure measurements and the exposure generated with a particular grouping strategy.
‡ Numbers in parentheses, number of categories.

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Variability of exposure

Take home messages 1:

* Variability of exposure has a profound influence on the exposure-response association (both intercept and regression coefficient)

* Reliability of measurement technique (coefficient of variation) should be evaluated against variability of exposure

* Large within-workers variance at individual level: increase number of measurements per worker

Fetal Growth and Prenatal Exposure to Bisphenol A: The Generation R Study

Claudia A. Snijder,[1,2] Dick Heederik,[3] Frank H. Pierik,[4] Albert Hofman,[1,5] Vincent W. Jaddoe,[1,5,6] Holger M. Koch,[7] Matthew P. Longnecker,[8] and Alex Burdorf[2]

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study type	prospective birth cohort study
location	city of Rotterdam
inclusion period	2002 – 2006
participants	9,778 pregnant women and 6,347 partners were enrolled (response 61%, and 71%)
data collection	Extensive assessments during 1st (<18 weeks of gestation), 2nd (18-25 weeks) and 3rd trimester (>25 weeks): examinations, questionnaires, interviews, biological sampling.

Generation R

Exposure modeling in epidemiological studies

Determinant: - urinary bisphenol-A measurements
- measured in a random sample of 236 women
  * 80 women with three measurements (1st, 2nd, 3rd)
  * 40 women with two measurements
  * 116 women with one measurement

Outcome - fetal growth measured by ultrasound
- estimated fetal weight, head circumference during 2nd and 3rd trimester of pregnancy, combined with measurements at birth

Statistics - mixed linear model for repeated measurements

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Reproducibility of Urinary Bisphenol A Concentrations Measured During Pregnancy in the Generation R Study

Todd A. Jusko, PhD[a*], Pamela A. Shaw, PhD[b], Claudia A. Snijder, MD, PhD[c,d], Frank H. Pierik, PhD[e], Holger M. Koch, PhD[f], Russ Hauser, MD, ScD[g], Vincent W.V. Jaddoe, MD, PhD[d,h,i], Alex Burdorf, PhD[c], Albert Hofman, MD, PhD[h], Henning Tiemeier, MD, PhD[j], Matthew P. Longnecker, MD, ScD[k]

Journal of Exposure Science and Environmental Epidemiology

Table 2. Summary statistics for maternal urinary BPA concentrations in the Generation R cohort according to time of measurement.

BPA measure	GM[1]	Min	25th Percentile	Median	75th Percentile	Max
BPA (µg/L) (n=80)						
< 18 weeks	1.3	0.1	0.6	1.1	3.3	14.1
18-25 weeks	1.5	0.2	0.6	1.5	3.2	64.8
> 25 weeks	1.6	0.2	0.8	1.6	2.6	47.5
BPA (µg/g creatinine) (n=65)						
< 18 weeks	3.1	0.9	1.6	3.0	5.5	23.2
18-25 weeks	3.3	0.8	2.0	3.0	4.1	40.4
> 25 weeks	3.2	0.6	1.8	2.6	4.2	43.3

[1]Geometric mean

and a continuous outcome measure, and the observed ratio of within- over between-person variance of 2.5 for BPA measurements in our study population, we estimate that increasing the number of measurements from 1 to 3 per person would reduce the attenuation from 70% to 45%. The BPA–fetal growth relation

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Table 4. Linear regression analyses for repeated measurements of the association between BPA during pregnancy and fetal growth rates according to the number of urine samples analyzed.

Samples/women (μg/g crea)		No. of women	Fetal weight β (95% CI)	Fetal head circumference β (95% CI)
Three samples		80		
BPA_{CB}	< 1.54		Reference	Reference
BPA_{CB}	$1.54 < BPA_{CB} < 2.51$		–0.041 (–0.081, –0.001)*	–0.052 (–0.098, –0.006)*
BPA_{CB}	$2.51 < BPA_{CB} < 4.22$		–0.043 (–0.082, –0.004)*	–0.046 (–0.090, –0.003)*
BPA_{CB}	> 4.22		–0.029 (–0.070, 0.012)	–0.066 (–0.113, –0.019)*
BPA_{CB}	Per unit increase in BPA_{CB}		–0.017 (–0.033, –0.001)*	–0.018 (–0.037, 0.000)**
Two samples		120		
BPA_{CB}	< 1.54		Reference	Reference
BPA_{CB}	$1.54 < BPA_{CB} < 2.51$		–0.018 (–0.045, 0.009)	–0.018 (–0.055, 0.018)
BPA_{CB}	$2.51 < BPA_{CB} < 4.22$		–0.029 (–0.056, –0.003)*	–0.013 (–0.049, 0.022)
BPA_{CB}	> 4.22		–0.003 (–0.033, 0.027)	–0.017 (–0.057, 0.023)
BPA_{CB}	Per unit increase in BPA_{CB}		–0.008 (–0.024, 0.008)	–0.005 (–0.024, 0.013)
One sample		219		
BPA_{CB}	< 1.54		Reference	Reference
BPA_{CB}	$1.54 < BPA_{CB} < 2.51$		0.003 (–0.027, 0.032)	–0.011 (–0.049, 0.025)
BPA_{CB}	$2.51 < BPA_{CB} < 4.22$		0.008 (–0.025, 0.040)	0.003 (–0.036, 0.041)
BPA_{CB}	> 4.22		0.025 (–0.002, 0.052)	0.015 (–0.022, 0.051)
BPA_{CB}	Per unit increase in BPA_{CB}		–0.007 (–0.023, 0.010)	0.011 (–0.008, 0.030)

Abbreviations: BPA_{CB}, creatinine-based total BPA concentration; crea, creatinine. Beta coefficient represents the average decrease in SD of fetal weight per gestational week. Adjusted for maternal age, educational level, ethnicity, parity, smoking during pregnancy, alcohol use during pregnancy, height at intake, weight before pregnancy, folic acid supplement use, and sex.
*$p < 0.05$. **$p < 0.10$.

Exposure modeling in epidemiological studies

Take home messages 2:

1. Less subjects and more repeated measurements per subject may improve the quality of the epidemiologic study
2. Insight into variance components should guide the exposure assessment strategy, and, thus, the design of the epidemiologic study

Measurement strategy - Amsterdam vs Rotterdam debate

Measurement by observations at the workplace

Hoozemans et al. Scand J Work Environ Health 2001;27:125-32

Measurement strategy - Amsterdam approach

Frequency of pushing/30 minutes a 135 kg trolley by train stewards and % worktime trunk flexion > 20 degrees
(n=15, 8 hr measurements with 16 periods of 30 minutes)

	no	SD	Within-worker	Between-worker	Variance ratio
Pushing (n=15)	13.4	3.2	90.1%	9.9%	9.1
Flexion (n=15)	3.5%	1.7%	82.8%	17.2%	4.8

⇒ Large within-worker variability to between-worker variability

⇒ Reasonable range (P95-P5 17.7-8.8)

⇒ Strongly increased variability with shorter observation duration

Systematic observation of train stewards

Selection of 15 participants out of 97 train stewards:

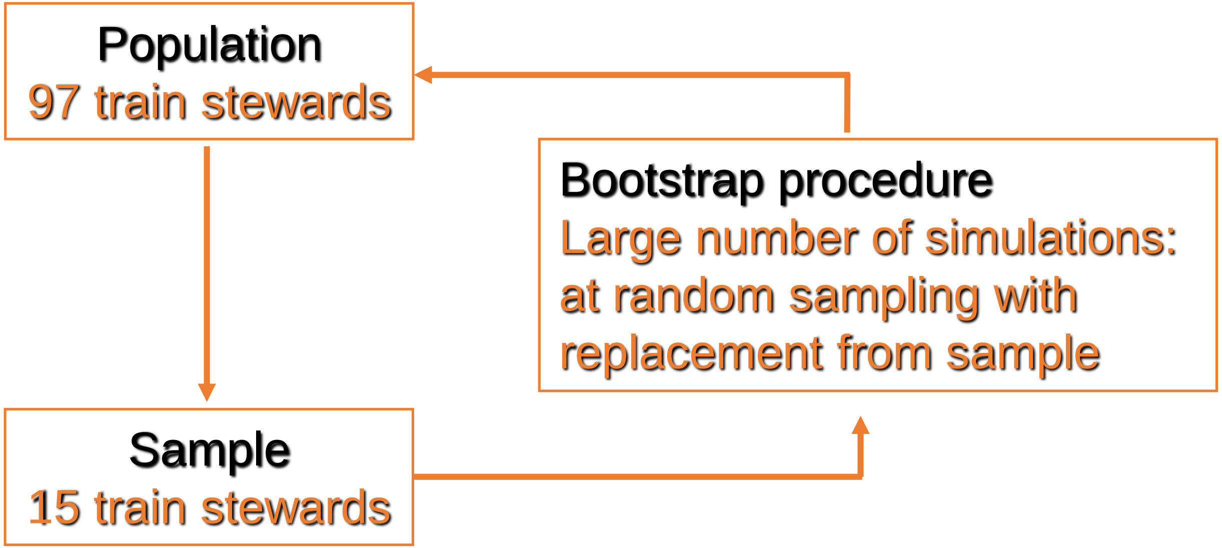
- enough workers sampled ?
- enough periods of 30 minutes (8 hours = 16 periods) ?

Aim: arrive at the estimate of the group mean with highest precision

Amsterdam approach: few workers over the whole day

Rotterdam approach: many workers over short periods during the day

Bootstrap procedure



Effect of number of workers

Mean 30-minute pushing frequency per worker

Increasing the number of workers to be drawn out of 15 workers with replacement

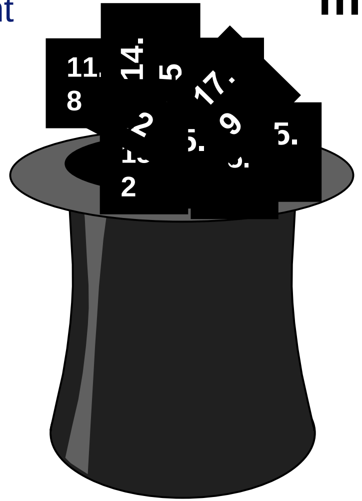
1000 replications

13.4

15.2

15.2

mean

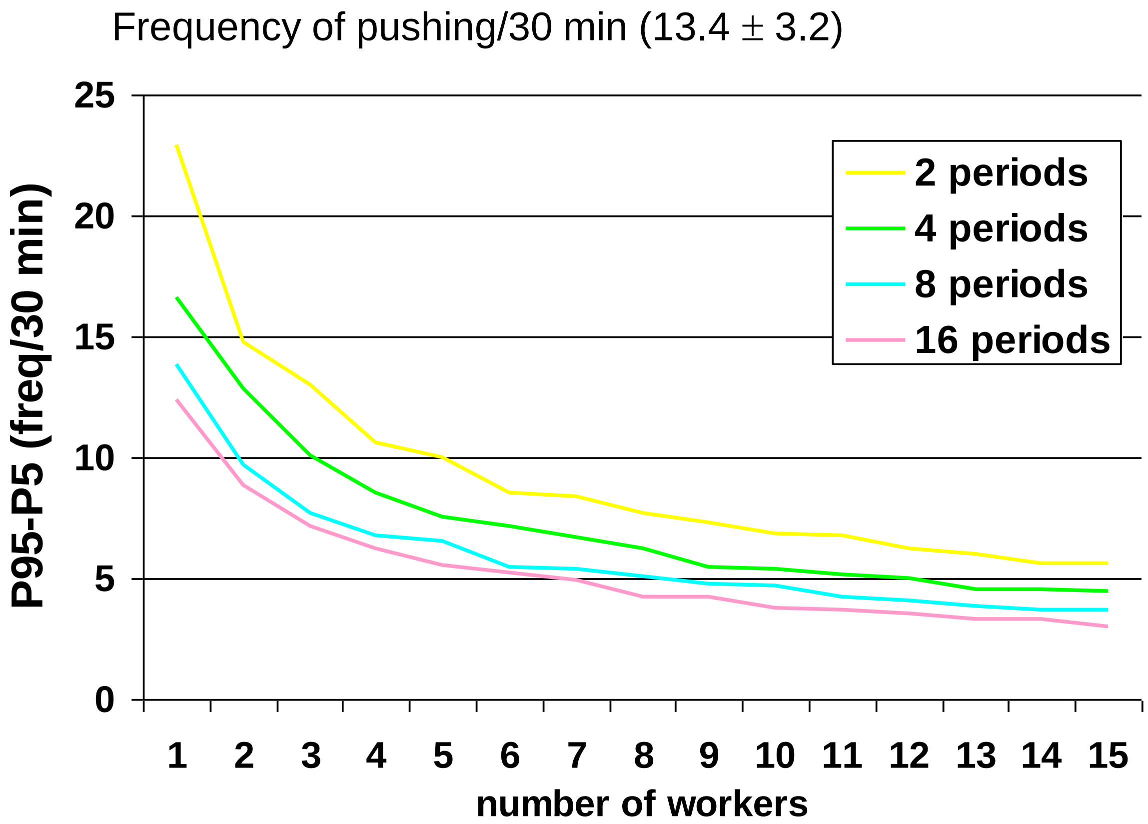


Effect of number of workers *and* measurements per worker

Nested bootstrapping procedure

1. Drawing of predetermined number of workers, with replacement
2. For each worker: drawing of predetermined number of 30-minute periods, with replacement

Measurement strategy - bootstrapping approach



Purpose of this lecture: revisited

Exposure modeling in epidemiological studies:

- consider individual and group-based exposure assessment
- insight into attenuation is crucial
- Exposure assessment considerations are as important as design issues and power calculations in an epidemiological study (ever seen this in a grant application ?)

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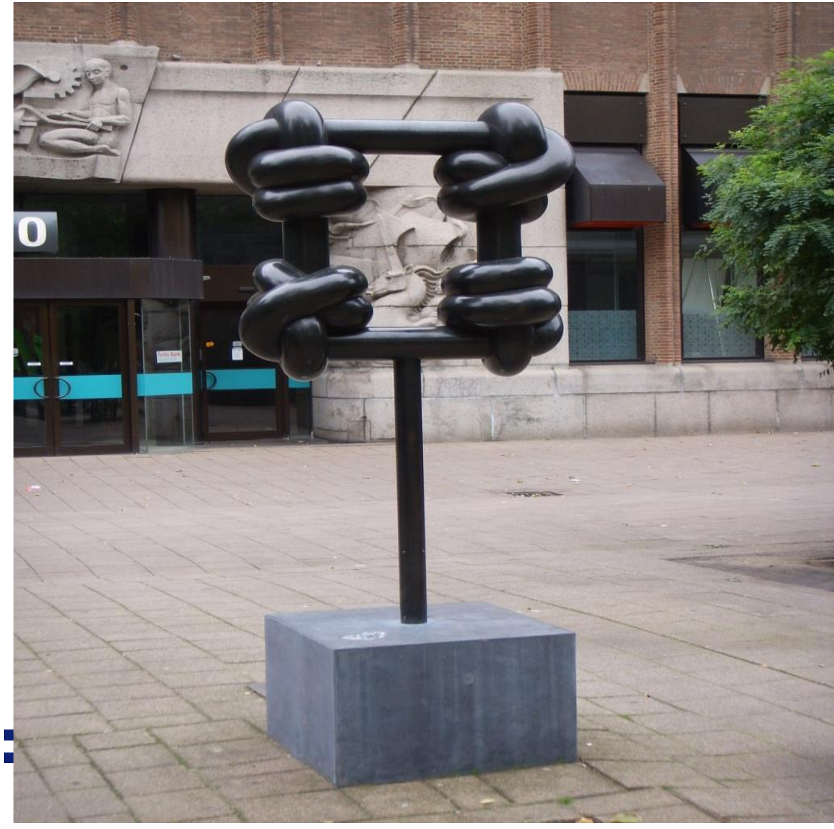

Knot, Tajiri, 1981