

Særlige metoder i epidemiologiske studier inden for arbejds- og miljømedicin

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Charlottes udspil...

- Muligheder og begrænsninger
- Hvordan tackler man problemer som healthy worker effekt og confounding
- Hvilke udfald er velegnede at undersøge i registerbaseret forskning?
- Udfordringer med umålt confounding fx rygning

Mit svar...

- Eksempel på projekt med manglende rygeoplysninger og mulig healthy worker bias
- Eksempel på projekt med unik eksponeret kohorte
- Eksempler på projekter med spændende eksponeringsvurderinger!

Konsekvenser af erhvervsmæssig eksponering for organisk støv på astma og KOL – CODUST. Et opfølgningsstudie blandt danske landmænd og træindustriarbejdere.

Vested A, Basinas I, Heederik D, Jacobsen G, Kolstad H, Kromhout H, Omland Ø, Sigsgaard T, Toft G, Thulstrup A, Vestergaard J, Elholm G, Wouters M, I, Schlünssen V

Organisk støv og KOL



Et nyt review om organisk støv og fald i lungefunktion.....

"The results were inconsistent across varying study design and different exposure measures and outcomes. We therefore conclude that there is limited evidence of a causal association between general exposure to organic dust and long-term excess decline in lung function"

Bolund et al OEM 2017

Formål

Undersøge eksponerings-respons sammenhæng
mellem organisk støv og incidens af KOL



Studiepopulation

Alle personer nogensinde ansat i landbrug eller træindustri mellem 1964-2007 ifølge ATP

*Eksklusion af døde,
forsvundne, emigrerede,
KOL ved start af follow-up,*

Udfordring 1: komplet erhvervshistorie?

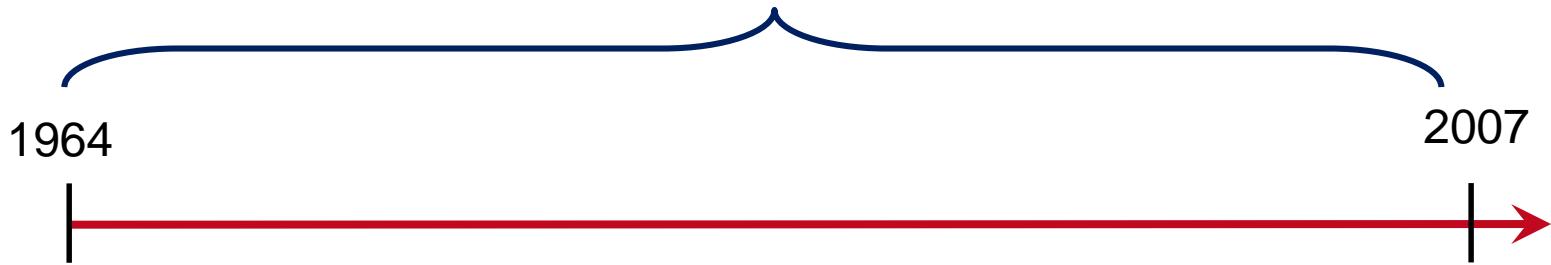
*Personer født før 1950 +
personer med > 15%
missing*

Studie population ca 400.000

Info om branche + to tidsafhængige kvantitative Industri eksponerings matricer...

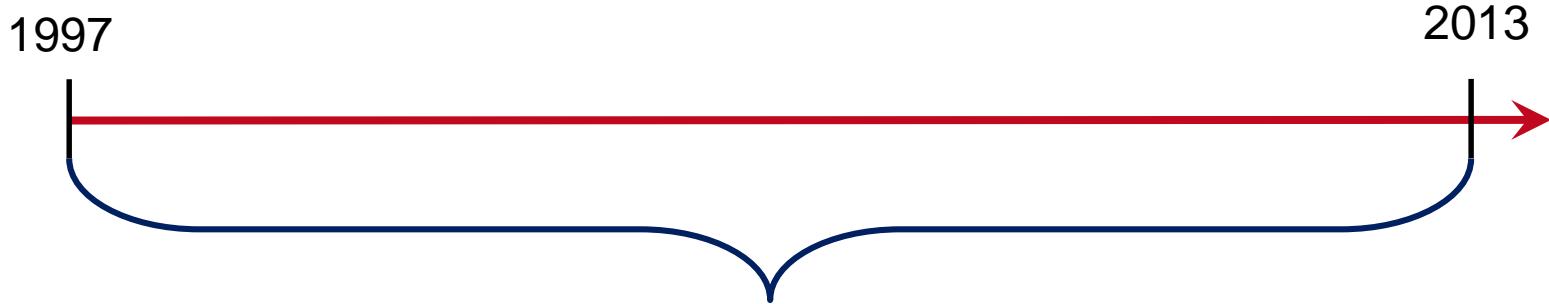
Nace rev. 2	General industry description	
16.10	Sawmilling and planing of wood	
16.21	Manufacture of veneer boards and wood-based boards	
16.22;16.23	Manufacture of builders carpentry and joinery, parquet floors	For hver person et eksponeringsniveau, mg/m ³ pr år
16.24	Manufacture of wooden packaging	
31.01;31.02: 31.09	Furniture industry	
43.32	Carpenter and joiner business/construction	
01.11	Crop farming	
01.41;01.42	Cattle farming	Kauppinen <i>et al</i> Ann Occup Hyg 2006
01.46	Pig farming	Basinas <i>et al</i> JEM 2012
01.47	Poultry farming	Basinas <i>et al</i> JESEE 2013
01.50	Mixed farming	Schlünssen Ann Occup Hyg 2008
01.49.20	Fur-animal farming	

Exposure



- Kumuleret eksponering
- Varighed af eksponering
- Gennemsnitlig eksponering

Outcome



Udfordring 2: Validitet af KOL diagnose i LPR?



available at www.sciencedirect.com



journal homepage: www.elsevier.com/locate/rmed



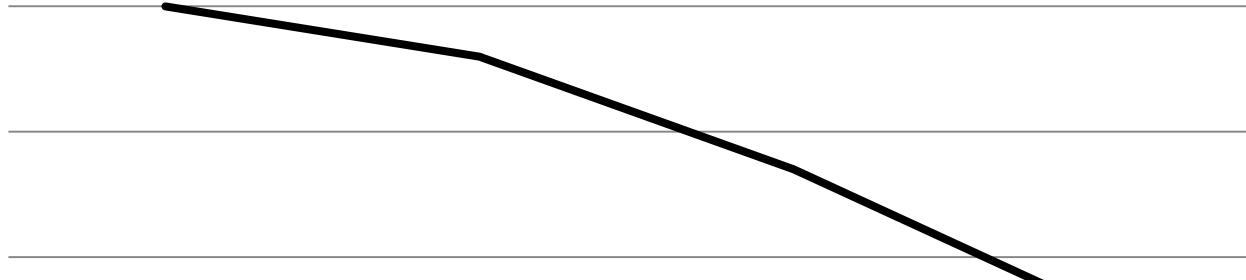
Validity and underrecording of diagnosis of COPD in the Danish National Patient Registry

Reimar W. Thomsen ^{a,*}, Peter Lange ^b, Birthe Hellquist ^c, Ejvind Frausing ^b,
Paul D. Bartels ^d, Birgitte R. Krog ^d, Anne-Marie S. Hansen ^d, Daniel Buck ^a,
Anette E. Bunk ^d

RR for incident KOL i relation til kumuleret eksponering for organisk støv.

RR

Hovedanalyse



Udfordring 3: Ikke eksponerede?

Kun blue collar workers...

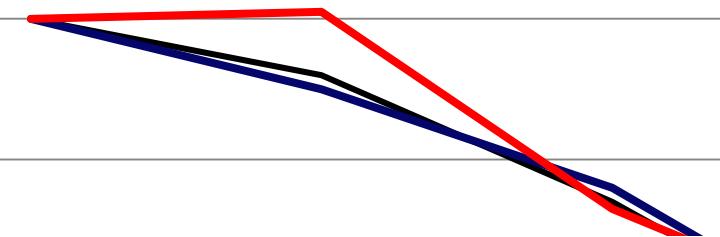
RR

Udfordring 4: selektion ind i kohorten?



Healthy worker hire bias?

RR



**Udfordring 5:
selektion ud af kohorten?**

1 kvartil

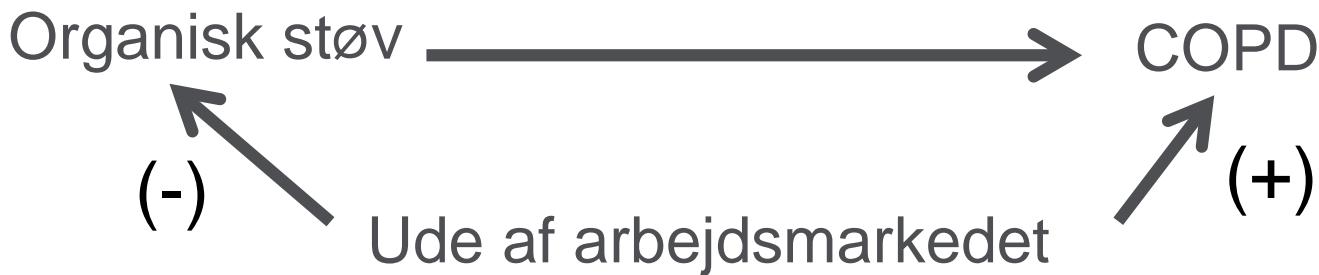
2 kvartil

3 kvartil

4 kvartil

Kumuleret eksponering

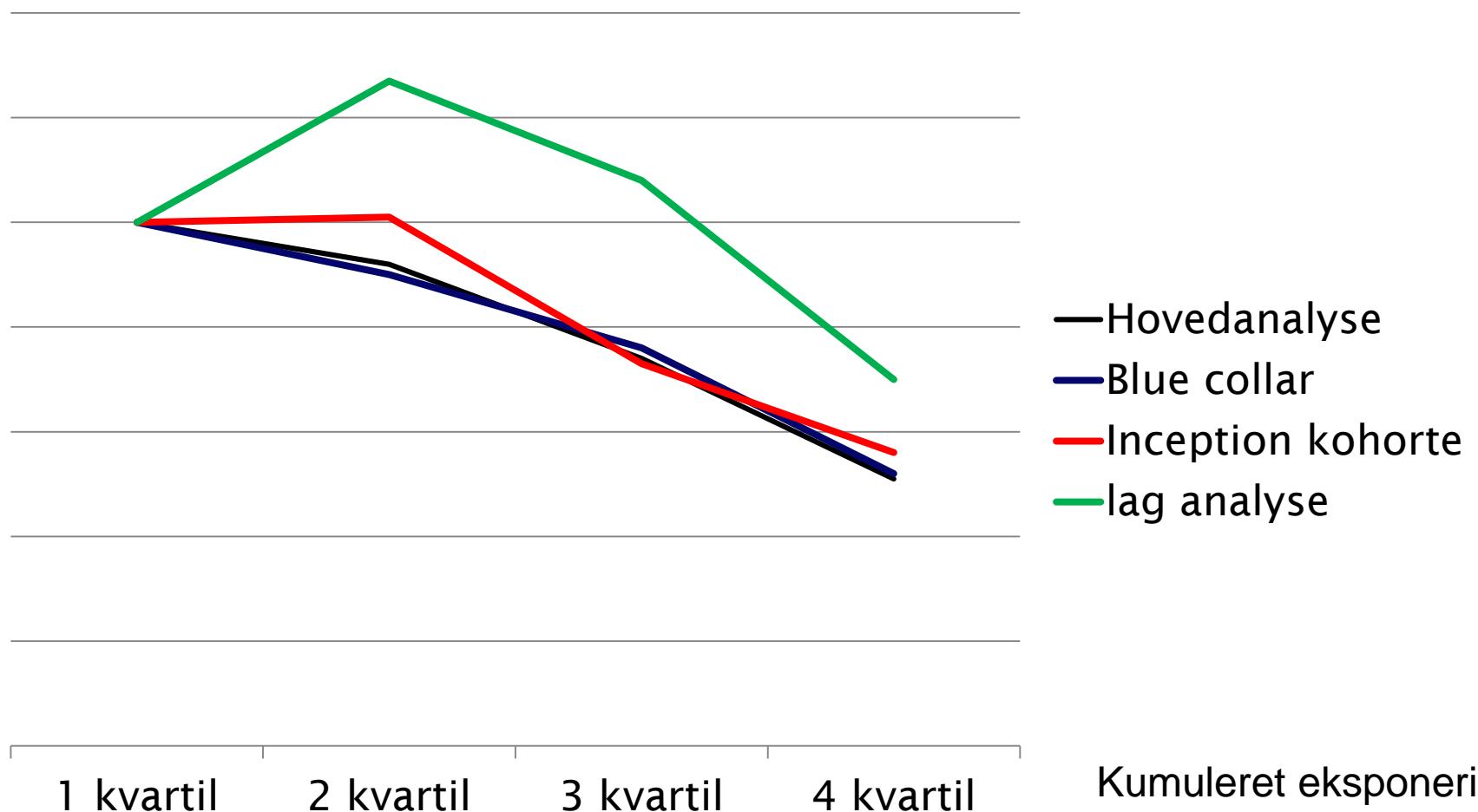
Healthy worker survivor bias?



Buckley et al *Epidemiology* 2015; Naimi et al *Ann Epidemiol* 2013

Healthy worker survivor bias?

RR



Udfordring 6: Rygning confounder?

- Rygeoplysninger i delpopulation
- Justering for rygeassocierede diagnoser i LPR
- RygeJEM (Sesilje B Petersen EPICOH 2017)
- Axelsons metode (Axelson et al Am J Ind Med 1988)

Cancer Incidence in Workers Exposed to Styrene in the Danish-reinforced Plastics Industry, 1968–2012

Mette Skovgaard Christensen,^{a,b} Johnni Hansen,^c Cecilia Høst Ramlau-Hansen,^d
Gunnar Toft,^{a,e} and Henrik Kolstad^a

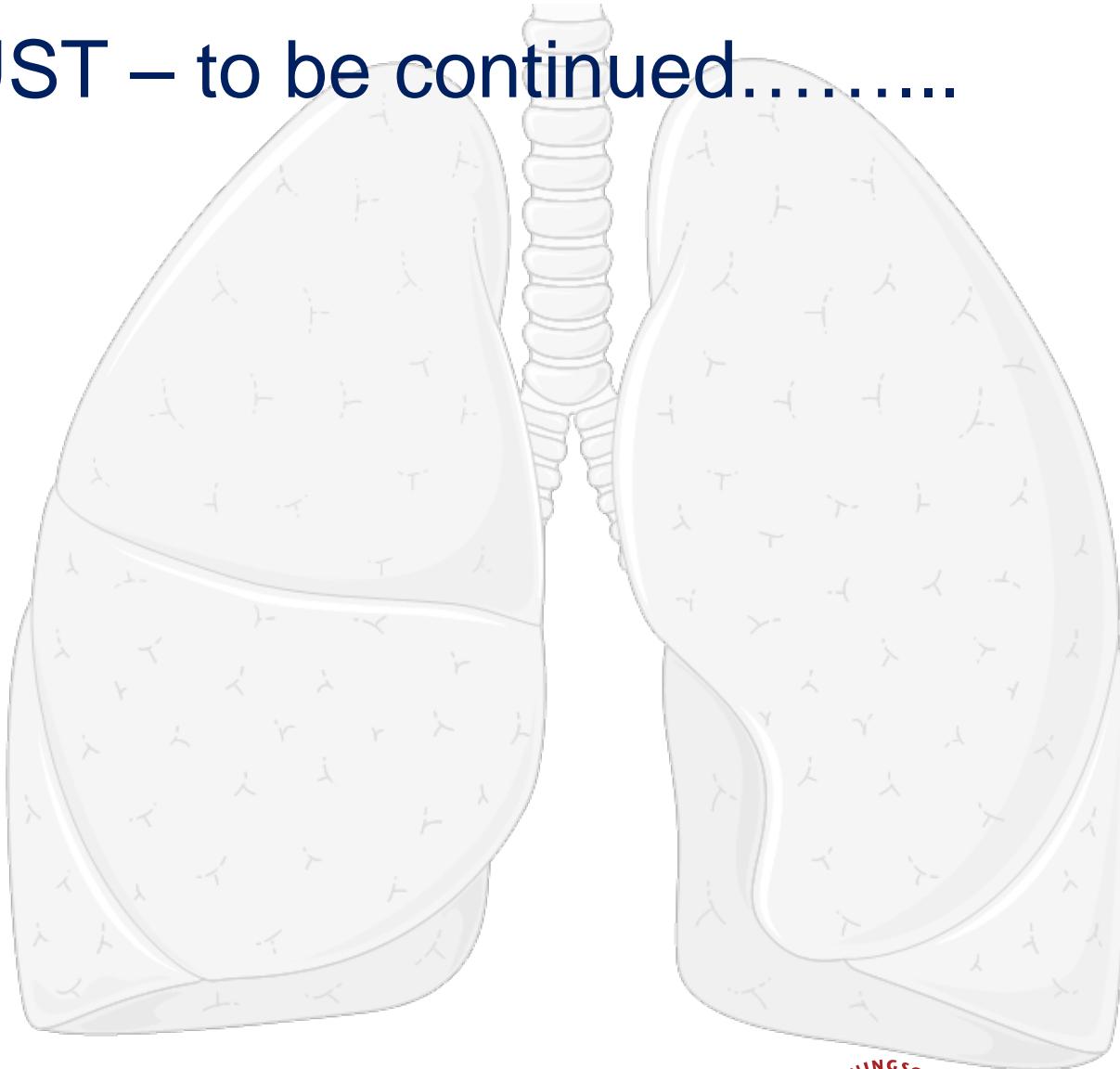
Epidemiology • Volume 28, Number 2, March 2017

The prevalence of male smokers in the Danish population 1986–1987 was 49% among the general population, 54% among skilled and unskilled blue-collar workers, and 46% among white-collar workers.²⁹ Using Axelson's method assuming that $\frac{3}{4}$ of the study population were male skilled or unskilled blue-collar workers and $\frac{1}{4}$ were male white-collar workers, and that smokers had a 10-fold increased risk of lung cancer, an increased rate ratio of 1.04 for lung cancer solely due to smoking was expected for the total study population (not tabulated).

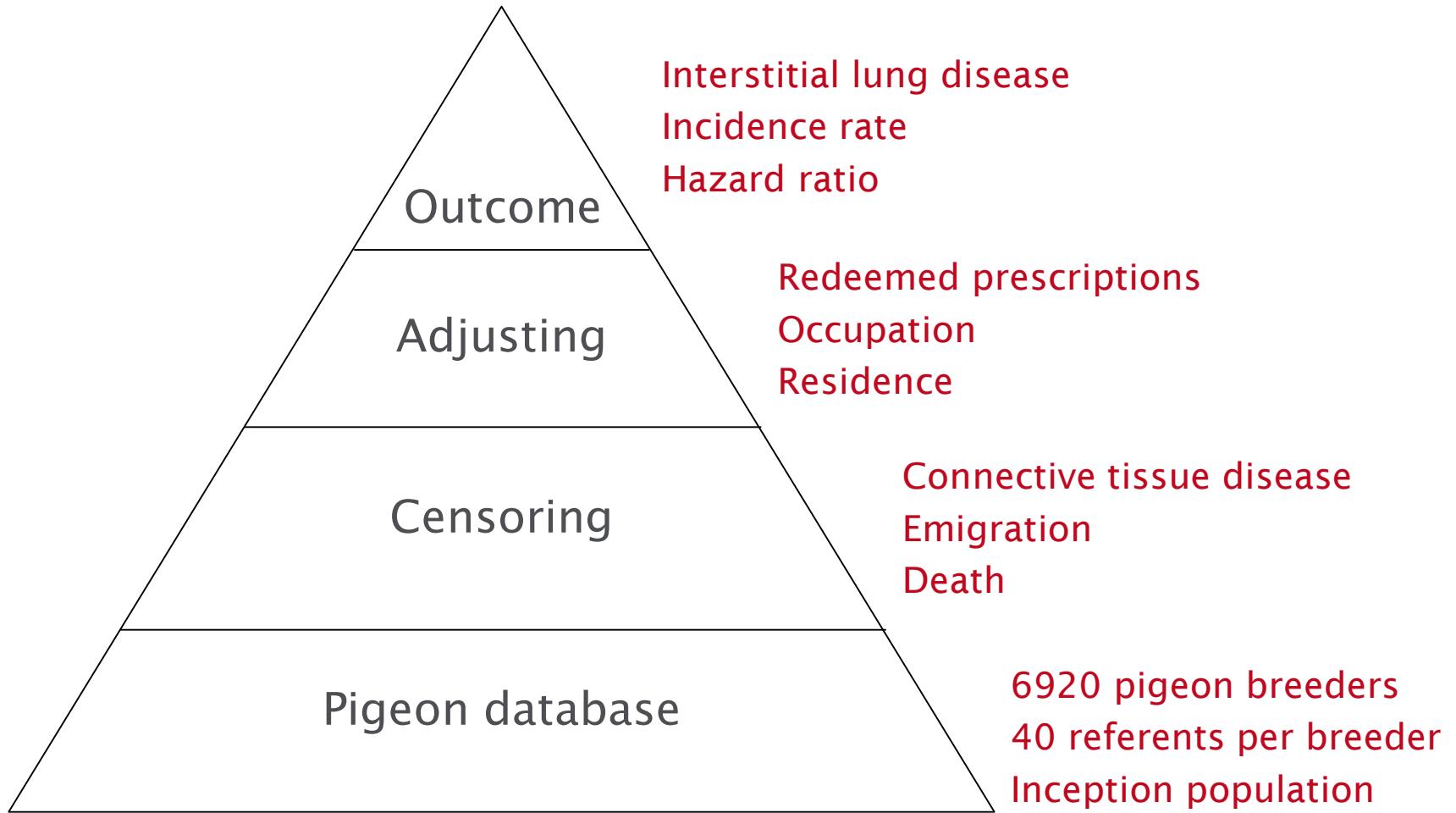
Udfordring 6: Rygning confounder?

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- Axelsons metode (Axelson et al Am J Ind Med 1988)
- Stratificering

CODUST – to be continued.....



Methods



Hazard ratio for interstitiel lungesygdom (ILD) blandt dueholdere

TABLE 2 Hazard ratios of all interstitial lung diseases (ILDs), hypersensitivity pneumonitis and other interstitial lung diseases among pigeon breeders and referents individually matched on sex and year of birth

	Participants	Person-years	Cases	Incidence rate [#] (95% CI)	Hazard ratio (95% CI)	
					Crude [¶]	Adjusted ^{¶, §}
Total population						
All ILDs						
Pigeon breeders	6920	114 936	89	77.4 (62.9–95.3)	1.61 (1.30–1.99)	1.56 (1.26–1.94)
Referents	276 800	4 566 259	2281	50.0 (47.9–52.0)	1	1
Hypersensitivity pneumonitis						
Pigeon breeders	6920	114 936	17	14.8 (9.2–23.8)	14.53 (8.21–25.70)	14.36 (8.10–25.44)
Referents	276 800	4 566 259	47	1.0 (0.8–1.4)	1	1
Other ILDs						
Pigeon breeders	6920	114 936	72	62.6 (49.7–78.9)	1.33 (1.05–1.68)	1.33 (1.05–1.69)
Referents	276 800	4 566 259	2234	48.9 (46.9–51.0)	1	1
Inception population						
All ILDs						
Pigeon breeders	807	5694	7	122.9	4.61 (2.10–10.15)	4.68 (2.12–10.30)
Referents	32 280	226 587	58	25.6	1	1

Data are presented as n, unless otherwise stated. Results from the total study population and the inception population are presented. The analyses of hypersensitivity pneumonitis and other ILDs, as well as the analyses for the incident members etc. are only adjusted for prescription of medication with ILD as possible side-effect. [#]: per 100 000 person-years; [¶]: adjusted for the matching variables by stratification; [§]: adjusted for residence, occupation and prescription of drugs with pulmonary fibrosis as possible side-effect.



Kategori A/B
Farm 134
Fodde 3
Vægt 07595
Størrelse
Løbning

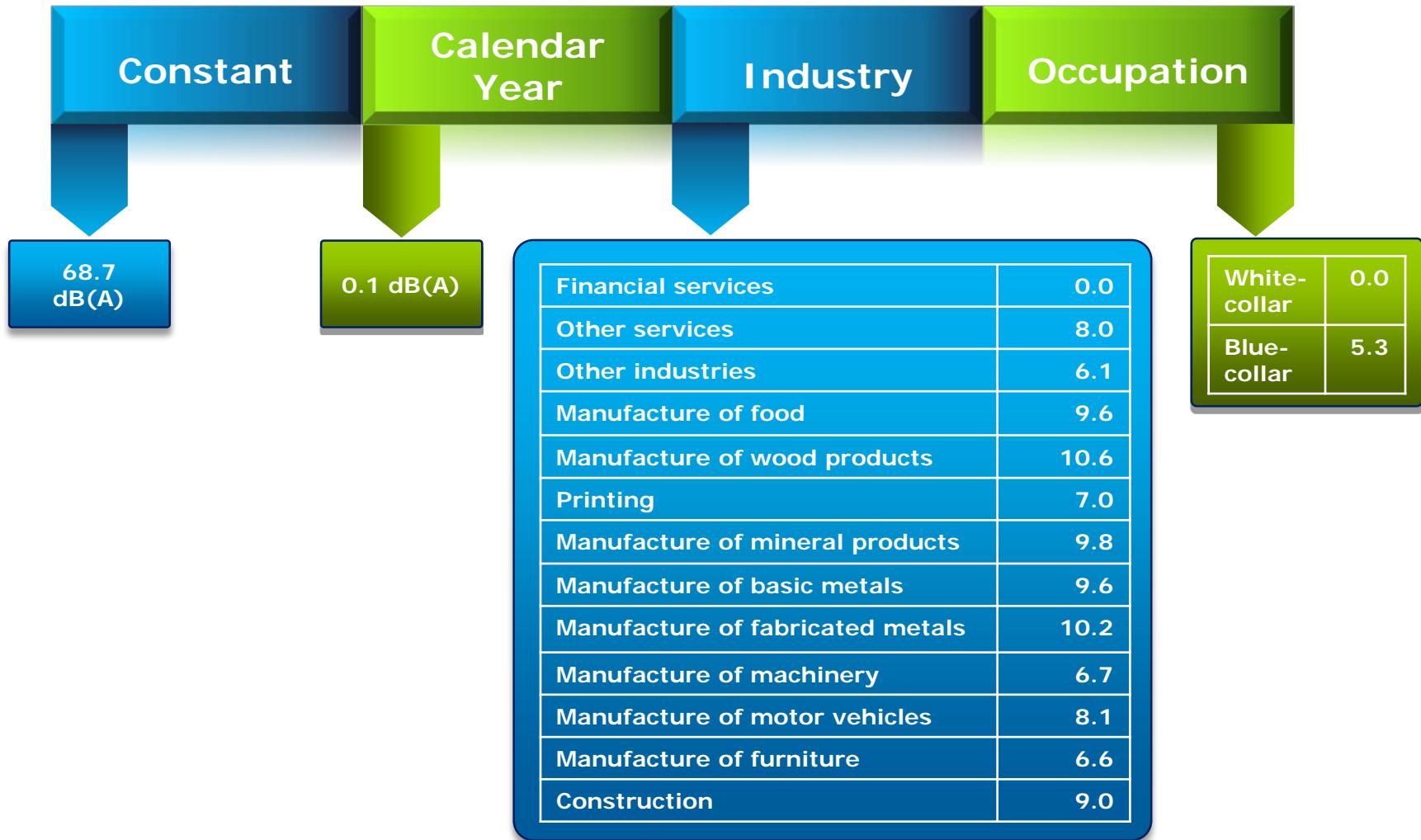
Kategori A/B
Farm 134
Fodde 3
Vægt 07595
Størrelse
Løbning 40

Kategori A/B
Farm 134
Fodde 3
Vægt 07595
Størrelse
Løbning

En støveksponeret erhvervskohorte 2001-2007: Nationale register data

Register	Information	Classification	Observations
Danish Occupational Health Authority (At)	Industries: 2001-2007	NACE	12
The Central Business Register (CVR)	Companies: 2001-2007	CVR	725
Supplementary Pension Fund (ATP)	Workers' work histories 1964-2007	CPR	145,000
Integrated Database for Labor Market Research (IDA)	Occupation: 1991-2007 SES: 1980-2007	DISCO	145,000
Civil Registration system	Vital status: 2001-2007	-	145,000
National Patient Register	Stroke diagnoses: 1997-2007	ICD-8 ICD-10	1200

Exposure Assessment – Exposure Matrix



Average noise/year= 68.7 + (Calendar year * 0.1dB(A)) + Industry + Occupation

Occupational Noise Exposure and the Risk of Stroke

Zara A. Stokholm, MD; Jens Peter Bonde, DMSc; Kent L. Christensen, MD;
Åse M. Hansen, PhD; Henrik A. Kolstad, MD

(*Stroke*. 2013;44:3214-3216.)

Table 1. Association of Stroke With Cumulative Noise Exposure for Industrial and Financial Workers

Cumulative Noise Exposure (dB(A)-year)	Person-Years	Cases	Crude RR (95% CI)	P Value	Adjusted RR (95% CI)	P Value
<75	93 424	47*	1.00		1.00	
75-79	139 819	90	1.16 (0.81-1.65)	0.420	0.80 (0.56-1.15)	0.223
80-84	192 520	206	1.95 (1.42-2.68)	<0.001	1.04 (0.75-1.44)	0.834
85-89	182 837	199	1.97 (1.44-2.72)	<0.001	1.11 (0.79-1.55)	0.559
90-94	240 630	300	2.09 (1.53-2.86)	<0.001	1.08 (0.77-1.51)	0.673
95-99	69 334	124	3.01 (2.14-4.23)	<0.001	0.99 (0.68-1.42)	0.939
≥100	3235	15	7.88 (4.39-14.15)	<0.001	1.49 (0.82-2.73)	0.193
Trend RR†	921 799	981	1.04 (1.03-1.05)	<0.001	1.01 (0.99-1.02)	0.129
Trend RR excluding financial workers†	644 813	746	1.05 (1.03-1.06)	<0.001	1.00 (0.98-1.01)	0.915

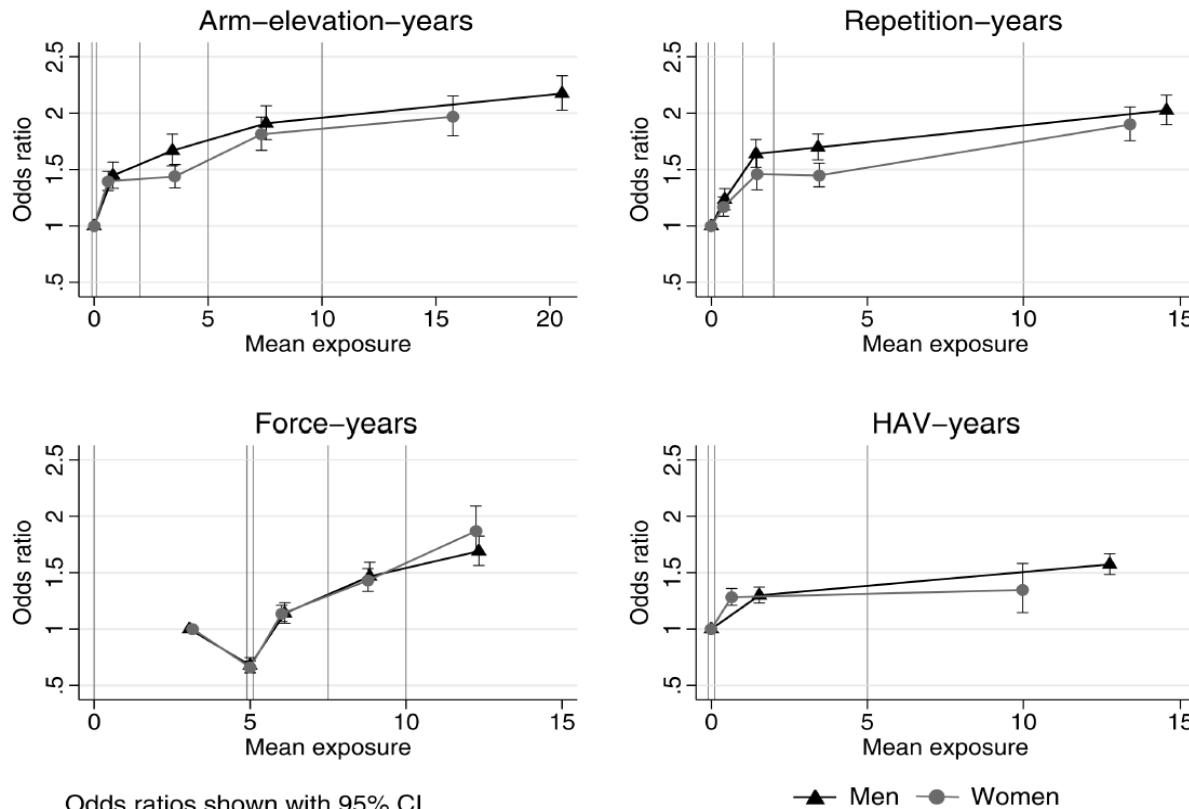
Adjusted for age, sex, socioeconomic status, calendar year, and employment status.



Cumulative occupational shoulder exposures and surgery for subacromial impingement syndrome: a nationwide Danish cohort study

Annett Dalbøge,¹ Poul Frost,¹ Johan Hviid Andersen,² Susanne Wulff Svendsen²

Figure 2 Adjusted odds ratios* for surgery for subacromial impingement syndrome in relation to mean exposures within categories of cumulative exposures for men and women. Adjusted for time varying age (five age categories), sex, region of residence (five regions) and calendar year at start of follow-up. HAV, hand-arm-vibration



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