



# Exposure modelling in a cohort of Swedish hard metal production workers

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## Background

- The International Agency for Research on Cancer (IARC 2006) - cobalt metal with tungsten as “probably carcinogenic to humans (group 2A)”
- International mortality study in the hard metal industry ITIA and University of Pittsburgh (USA, Sweden, UK, Germany, Austria)
- Hard metal-tungsten carbide, cobalt, (nickel and chromium)
- Cohort design-external comparison and exposure response (total 32,354, Sweden 14,768 persons)
- Swedish study on lung cancer - no exposure response by quartiles and exposure classes using internal comparison (Cox proportional regression).
- High cumulative cobalt exposure  $0.4 \text{ mg/m}^3 \cdot \text{years}$



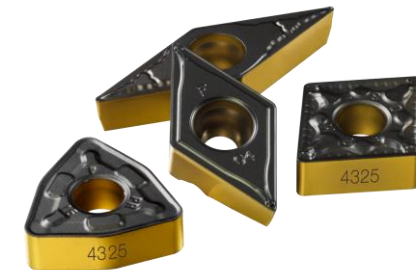
## Aims

- Modelling exposures for time periods with no measurement data (before 1970) using static, linear and exponential extrapolation
- Comparing cumulative and mean exposures for different exposure scenarios
- Calculating hazard ratios, exposure- response using Cox regression analysis with internal comparison for different extrapolation scenarios



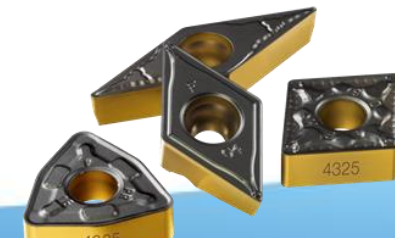
## Study objects and processes

- Three sites (A,B,C) operating since 1931, 1951 and 1942, producing inserts for cutting tools or drills, (C) also produces big parts (rolls for hot rolling)
- Hard metal (tungsten carbide/cobalt). Co content 2-14%, Ni 4-6% for some grades, chromium carbide (Cr after sintering) 0.3-0.9%
- Production of WC-Co powder, (wet milling and mixing, spray – drying, bagging), pressing, shaping and sintering, grinding, blasting and coating (TiC)



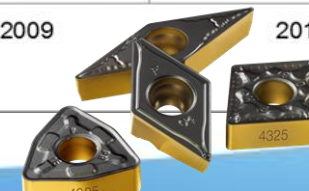
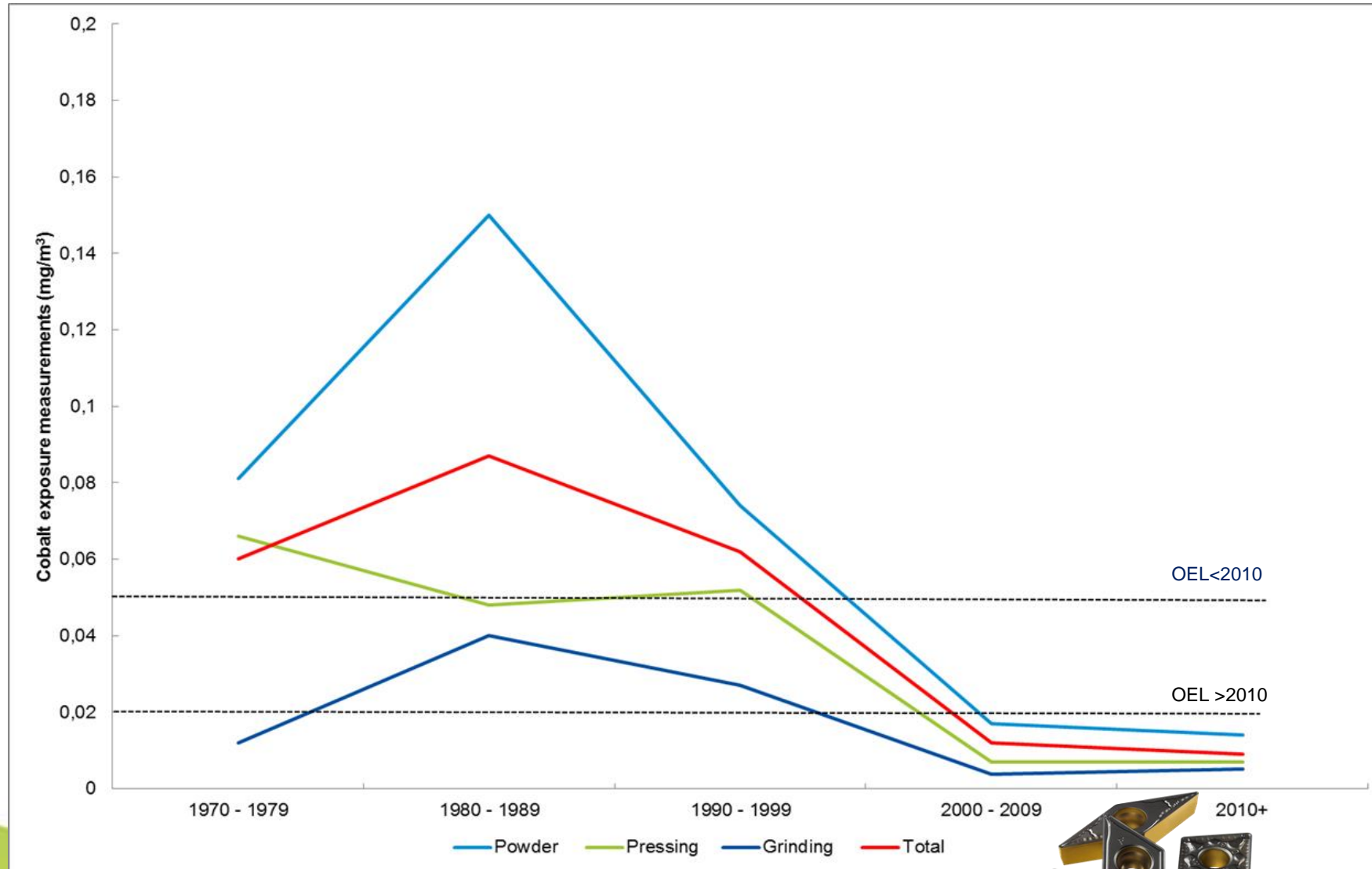
## Measurement data 1969-2012

Chemical agent	N	AM	Median	Min	Max	SD	GM	GSD
<b>Personal</b>								
Co	1210	0.041	0.010	<0.00001	2.8	0.13	0.0090	6.4
W	342	0.15	0.042	<0.0006	5.7	0.43	0.034	6.8
Ni	313	0.036	0.0071	<0.0005	2.8	0.18	0.0054	5.5
Cr	13	0.093	0.040	<0.002	0.54	0.15	0.028	5.8
<b>Total dust</b>	755	0.89	0.37	<0.01	58	2.6	0.36	3.5
<b>Area</b>								
Co	354	0.036	0.0071	<0.000004	1.7	0.14	0.0071	6.8
W	58	0.031	0.0035	<0.00002	0.4	0.075	0.0048	7.5
Ni	142	0.0069	0.00070	<0.00009	0.26	0.026	0.00083	6.6
Cr	15	0.018	0.00071	<0.00009	0.2	0.052	0.00093	10.4
<b>Total dust</b>	497	1.4	0.13	<0.03	102	6.5	0.19	5.2





## Cobalt exposures by time



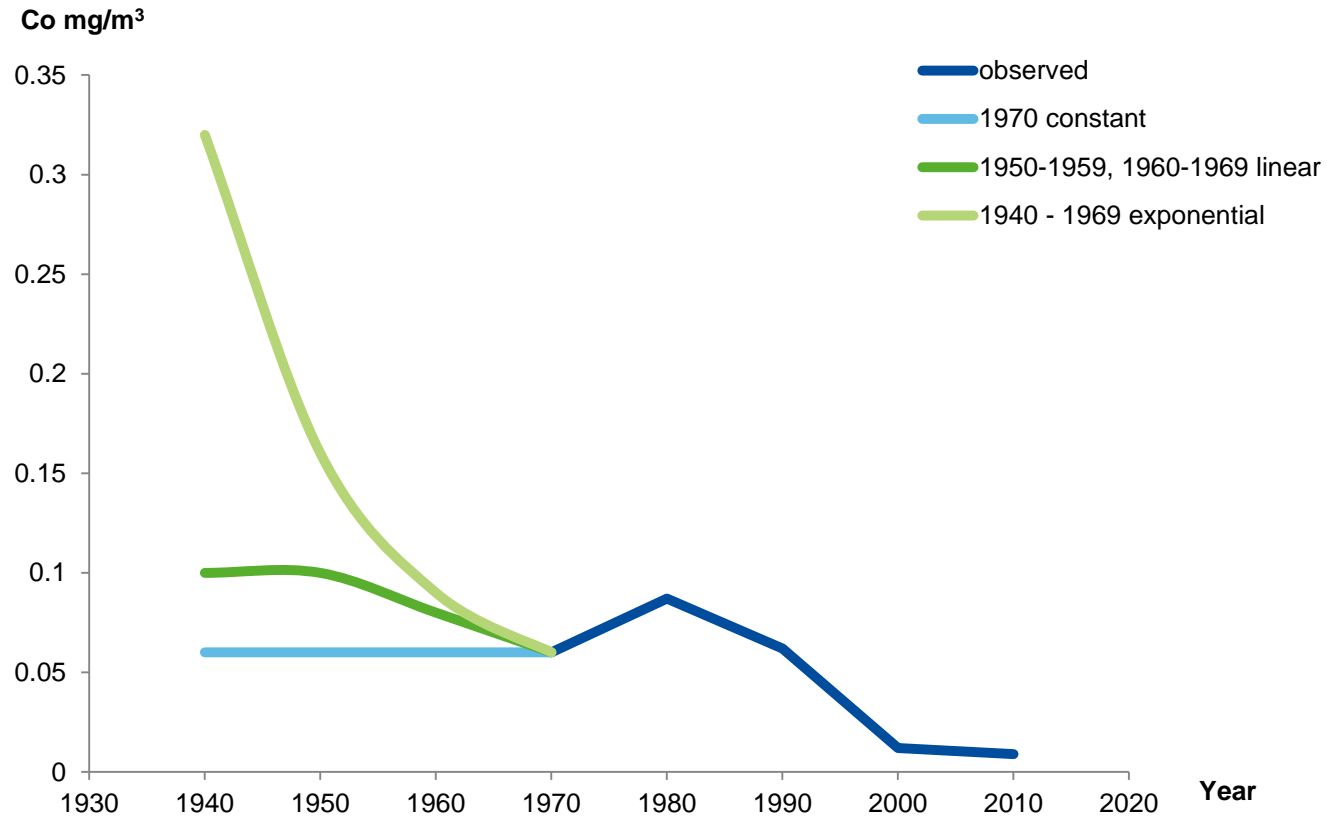
## Exposure model and measures multiple linear regression

- $\text{Ln}(\text{cobalt}) = b_0 + b_1 * [\text{Site}] + b_2 * [\text{Time-period}] + b_3 * [\text{Job class}]$
- Cumulative exposure  $\text{CE}(j) = \sum E_k(jk) T(jk) \text{ mg/m}^3 \cdot \text{years}$
- Mean exposure  $\text{CE}(j) = \sum E_k(jk) T(jk) / \sum T(jk) \text{ mg/m}^3$





## Exposure extrapolation?



## Exposure model, blue collar, aggregated jobs, 1970-2012

	<b>B</b>	<b>95 % CI</b>	
(Constant)	0.0038	0.0027	0.0056
<b>Company</b>			
A ref <sup>1)</sup>	1		
B	1.9	1.5	2.4
C	2.4	1.9	3.2
<b>Year</b>			
1970-1979 ref <sup>1)</sup>	1		
1980-1989	1.1	0.81	1.5
1990-1999	0.84	0.65	1.1
2000-2009	0.23	0.17	0.30
2010+	0.19	0.14	0.27
<b>Job class</b>			
I Grinding ref	1		
D Powder	5.5	4.2	7.2
E Pressing, forming	2.1	1.6	2.7
F Slow moving operations	0.62	0.34	1.1
G Coating	0.22	0.11	0.44
H Rolls (big pieces)	4.8	2.7	8.3



## Regression coefficients, different extrapolation scenarios

Model	Time period, B-values		
	1950-59	1960-69	1970-79 ref
Static (the same as 1970-79)	1	1	1
Linear	1.6	1.3	1
Exponential	1.9	1.6	1





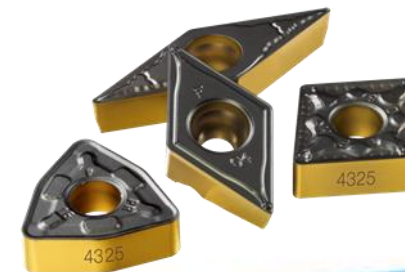
## Cumulative exposures Co mg/m<sup>3</sup>, blue collar > 1 year, different extrapolations for 1950-69

Job	N	Static		Linear		Exp	
		AM	SD	AM	SD	AM	SD
Several jobs	534	0.083	0.11	0.085	0.12	0.087	0.12
D Powder	258	0.27	0.34	0.29	0.38	0.40	0.78
E Pressing	739	0.10	0.14	0.11	0.16	0.15	0.29
F Slow moving op	224	0.03	0.038	0.035	0.044	0.049	0.079
G Coating	243	0.0082	0.010	0.0083	0.0098	0.009	0.012
H Rolls production	57	0.33	0.38	0.33	0.39	0.39	0.53
I Grinding	1673	0.047	0.058	0.049	0.061	0.053	0.079
Total	3728	0.079	0.15	0.084	0.16	0.10	0.28



## Cox regression for different exposure scenarios

	N	Exposure	HR	95 % CI
<b>Static</b>	39	<0.20	1	
	4	0.21-0.40	0.38	0.23-2.0
	4	0.41+	0.89	0.29-2.7
<b>Linear</b>	39	<0.20	1	
	4	0.21-0.40	0.68	0.22-2.0
	4	0.41+	0.89	0.29-2.7
<b>Exponential</b>	36	<0.20	1	
	6	0.21-0.40	1.0	0.41-2.5
	5	0.41+	0.80	0.28-2.3





## Conclusions

- Exposure modelling using static, linear and exponential extrapolation for early time periods with no existing measurement data is useful for historical cohorts
- Exposure measures based on different extrapolation assumptions could be used for an outcome sensitivity analysis
- For our cobalt cohort, no significant changes of risk were determined for the different extrapolation models



## Publications

- Marsh G et. al. Mortality among hardmetal production workers-pooled analysis JOEM 2017;59 (12) e342-364
- Wallner P et. al. Mortality among hardmetal production workers-a retrospective cohort study in the Austrian hardmetal Industry JOEM 2017;59 (12) e282-287
- Morfeld P et. al. German Historical Cohort Studie- German Historical Cohort Study JOEM 2017;59 (12) e289-295
- Marsh G et.al. Mortality among hardmetal production workers-US Cohort and Nested Case-Control Studies JOEM 2017;59 (12) e306-26
- Westberg H et. al. Mortality among hardmetal production workers-the Swedish cohort JOEM 2017;59 (12) e263-74
- Mc Elvenny D et. al. Mortality among hardmetal production workers- UK Cohort and Nested Case–Control Studies JOEM 2017;59 (12) e275-81
- Svartengren M et.al. Cancer Incidence Among Hardmetal Production Workers-the Swedish cohort JOEM 2017;59 (12) e365-373
- Kennedy K et. al. Mortality among hardmetal production workers-occupational exposures JOEM 2017;59 (12) e297-305
- Westberg H et. al. Mortality among hardmetal production workers-Swedish measurement data and exposure assessment JOEM 2017;59 (12) e327-341