Table 2.3. Cohort and nested case-control studies of nickel and lung cancer

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Andersen *et al.* (1996) Norwegian nickel refinery workers	Cohort of 379 workers with 1st employment 1916–40 and 3 years of employment and 4 385 workers with one year of employment 1946–83.		**Mean exposure (mg/m^3)**			Birth cohort, smoking habits and age	Cumulative exposure to soluble nickel and nickel oxide, considering the two variables simultaneously by multivariate Poisson regression analysis
			A. Soluble Nickel				
			0.1	86	1.0 (Referent)		
			2.3	36	1.2 (0.8–1.9)		
			8.8	23	1.6 (1.0–2.8)		
			28.9	55	3.1 (2.1–4.8)		Workers with unknown smoking habits were excluded (three cases of lung cancer)
			P < 0.001				
			B. Nickel oxide				
			0.4	53	1.0 (Referent)		
			2.5	49	1.0 (0.6–1.5)		
			8.3	53	1.6 (1.0–2.5)		
			44.3	45	1.5 (1.0–2.2)		
			P = 0.05				
Grimsrud *et al.*, 2003, Norwegian nickel refinery workers	Cohort of 5 297 workers employed ≥ 12 months between 1910–1989 and alive > 01/01/1953 followed 12/31/2000	Work history from plant records; nickel exposures from 5 900 measurements for total nickel between 1973–1994 and estimates of specific nickel compounds leading to job exposure matrix.	Period of 1st employment: Total	267	2.6 (2.3 – 2.9)	Smoking habits and	Expected cases based on Norwegian male population rates
			1910 – 1929	17	4.8 (2.8–7.6)	age	
			1930 – 1955	170	2.7 (2.3–3.1)		
			1956 – 1978	75	2.2 (1.7–2.7)		
			1979 – 1989	5	3.7 (1.2–8.7)		
			15+ years emp:				

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Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Grimsrud *et al.*, 2003 (contd)			A. roasting, smelting, calcining	14	3.3 (1.8–5.6)	Smoking and age	
			B. Copper, electrolysis, leaching, Ni sulfate production	13	7.0 (3.7–12.0)		
			C. Ni electrolysis, Cu cementation, electrolyte purification:				
			1st empl 1910–1952	14	5.5 (3.0–9.2)		
			1st empl 1953+	7	4.4 (1.8–9.1)		
	Cohort of 5 297 workers employed ≥ 12 months between 1910–1989 and alive > 01/01/1953 followed 12/31/2000	Work history from plant records; nickel exposures from 5 900 measurements for total nickel between 1973–1994 and estimates of specific nickel compounds leading to job exposure matrix.	Cumulative exposure to: water soluble Ni (mg/m^3 x yr)				
			0.00	13	1.0	Smoking and	
			0.01 – 0.34	68	1.3 (0.7–2.4)	age	
			0.35 – 1.99	94	1.8 (1.0–3.2)		
			2.0+	92	3.1 (1.7–5.5)		
			Ni Oxide				
			0.01 – 0.12	72	1.7 (1.0–3.1)		
			0.13 – 1.99	109	2.5 (1.4–4.4)		
			2.0+	73	2.1 (1.2–3.8)		

Table 2.3. Cohort and nested case-control studies of nickel and lung cancer

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Grimsrud et al., 2002, Norvegian nickel refinery workers	Nested case-control study of 213 lung cancer cases identified in Cancer Registry between 1952–1995 and 525 controls from workforce matched by age, sex and year of birth	Same as Grimsrud et al. (2003) cohort	Cumulative exposure to 4 forms of Ni:			Cigarette smoking and age	
			A. Water soluble				
			Unexposed	9	1.0		
			Low	27	1.3 (0.5–3.5)		
			Low-medium	33	1.8 (0.7–4.5)		
			Medium	36	1.9 (0.8–4.6)		
			Medium-high	42	2.5 (1.0–6.0)		
			High	66	3.8 (1.6–9.0)		
			p-trend = 0.002				
			B. Sulfidic nickel				
			Unexposed	10	1.0		
			Low	27	1.6 (0.6–4.2)		
			Low-medium	48	2.8 (1.1–6.9)		
			Medium	42	2.5 (1.0–6.3)		
			Medium-high	40	2.3 (0.9–5.5)		
			High	46	2.8 (1.1–6.7)		
			p-trend = 0.119				
			C. Oxidic nickel				
			Unexposed	9	1.0		
			Low	29	1.7 (0.7–4.2)		
			Low-medium	42	2.3 (0.9–5.8)		
			Medium	47	2.7 (1.1–6.6)		

Table 2.3. Cohort and nested case-control studies of nickel and lung cancer

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Grimsrud *et al.*, 2002 (contd)			Medium-high	45	2.3 (1.0–5.7)		
			High	41	2.2 (0.9–5.4)		
			p-trend = 0.201				
	Nested case-control study of 213 lung cancer cases identified in Cancer Registry between 1952–1995 and 525 controls from workforce matched by age, sex and year of birth	Same as Grimsrud *et al.* (2003) cohort	<u>D</u>. Metallic nickel				
			Unexposed	14	1.0		
			Low	31	1.4 (0.6–3.3)		
			Low-medium	37	1.3 (0.6–3.0)		
			Medium	28	1.3 (0.6–3.0)		
			Medium-high	46	1.7 (0.8–3.8)		
			High	57	2.4 (1.1–5.3)		
			p-trend = 0.126				
			Mean exposure (mg/m³)		**OR**	Smoking habits in five categories(never smoker, former smoker, or current smoker of 1–10, 11–20, or > 20 g/day) and for exposure to water-soluble nickel as a continuous variable with natural log-transformed cumulative exposure values (Inf[(cumulative exposure + 1)]	
			<u>A</u>. Sulfidic Nickel				
			Unexposed		1.0		
			Low		1.5 (0.6–3.9)		
			Low-medium		2.2 (0.9–5.5)		
			Medium		1.8 (0.7–4.5)		
			Medium-high		1.3 (0.5–3.3)		
			High		1.2 (0.5–3.3)		
			Likehood ratio test: $P = 0.344$				
			<u>B</u>. Oxidic Nickel				
			Unexposed		1.0		

Table 2.3. Cohort and nested case-control studies of nickel and lung cancer

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Grimsrud *et al.*, 2002 (contd)			Low		1.5 (0.6–3.8)		
			Low-medium		1.8 (0.7–4.5)		
			Medium		1.4 (0.6–3.7)		
			Medium-high		1.5 (0.6–3.7)		
			High		0.9 (0.4–2.5)		
			Likehood ratio test: $P = 0.406$				
			C. Metallic Nickel				
			Unexposed		1.0		
			Low		1.2 (0.5–2.9)		
			Low-medium		1.0 (0.5–2.4)		
			Medium		1.0 (0.4–2.3)		
			Medium-high		1.0 (0.4–2.4)		
			High		0.9 (0.3–2.4)		
			Likehood ratio test: $P = 0.972$				

Table 2.3. Cohort and nested case-control studies of nickel and lung cancer

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Grimsrud *et al.*, 2005, Norvegian nickel refinery workers	Nested case-control study of 213 lung cancer cases identified in Cancer Registry between 1952–1995 and 525 controls from workforce matched by age, sex and year of birth	Same as Grimsrud *et al.* (2003) cohort	Refinery, pyrometallur-gical production (mostly insoluble):			Cigarette smoking, age & other occupational variables as listed	
			Duration (years)				
			0.00	125	1.0		
			0.03–2.1	30	1.3 (0.7–2.4)		
			2.2–7.1	25	1.6 (0.8–2.9)		
			7.2–50.0	33	2.4 (1.3–4.4)		
			Refinery, hydrometallur-gical production (mostly soluble):				
			Duration (years)				
			0.00	84	1.0		
			0.03–2.2	23	1.6 (0.8–3.0)		
			2.3–11.8	44	2.8 (1.5–5.0)		
			12–48	62	5.1 (2.9–9.1)		
			Refinery maintenance work				
			Duration (years)				
			0.00	162	1.0		
			0.13–2.8	17	1.5 (0.7–3.3)		
			2.9–13.0	21	1.5 (0.7–3.1)		
			13.1–47.0	13	1.1 (0.5–2.4)		

Table 2.3. Cohort and nested case-control studies of nickel and lung cancer

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Grimsrud *et al.*, 2005 (contd)			Occupational carcinogenic exposures outside refinery				
			Duration (years)				
			0.00	131	1.0		
			0.03–3.9	27	0.9 (0.5–1.7)		
			4.0–14.4	29	1.2 (0.7–2.2)		
			14.5–49.0	26	1.6 (0.9–3.0)		
			Cumulative exposure to nickel, $\log_e$-transformed, rise in OR per unit of In (mg/m^3):			Smoking, arsenic asbestos, sulfuric acid mist, cobalt, carcinogenic exposure outside refinery	
			Water soluble Ni		2.1 (1.3–3.2)		
			Any form Ni		1.4 (0.6–3.4)		
Sorahan & Williams (2005) Welsh nickel carbonyl refinery	Cohort of 812 workers first employed at a carbonyl refinery between 1953–1992 for 5+ years followed through 2000	Based on chemistry of process	Period from commencement of employment (years)		SMR	Age	National mortality rates as reference
			5–9	1	1.33		
			10–19	1	0.28		
			20+	26	1.65 (1.07–2.41)		
Grimsrud & Peto (2006) Welsh nickel refinery workers	Cohort of workers with 5+ years of employment hired 1902–1969 or between 1953–1992 and followed through 1985 and 2000, respectively	Year of first employment	Period of first employment		SMR	Age	National mortality rates as reference
			1930–1992	62	1.33 (1.03–1.72)		

Table 2.3. Cohort and nested case-control studies of nickel and lung cancer

Reference, location, name of study	Cohort description	Exposure assessment	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Antilla *et al.* (1998) Finnish nickel refinery & copper/ nickel smelter	Cohort of 1 388 workers employed for at least 3 months between 1945–1985 and followed through 1995	Atmospheric measurements available beginning in 1966	Refinery workers:		SIR	Age, gender	Region-specific rates used as reference
			Overall	6	2.61 (0.96–5.67)		
			20+ years latency	6	3.38 (1.24–7.36)		
			Smelter workers				
			Overall	15	1.39 (0.78–2.28)		
			20+ years latency	13	2.00 (1.07–3.42)		