**Supplementary Material:**

# Occupational exposure to nickel and hexavalent chromium and the risk of lung cancer in a pooled analysis of case-control studies (SYNERGY)

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**Supplementary Tables:**

**Table S1.** Description of the studies included in the SYNERGY projects' pooled analysis

| Study (Country) | Cases | | Response | Controls | | Response | Data collection | Source of controls |
|---|---|---|---|---|---|---|---|---|
| | n=16,901 | % | % | n=20,965 | % | % | between years | |
| **Northern Europe** | | | | | | | | |
| AUT-Munich (Germany) | 3,180 | 18.8 | 77 | 3,249 | 15.5 | 41 | 1990-1995 | Population |
| HdA (Germany) | 1,004 | 5.9 | 69 | 1,002 | 4.8 | 68 | 1988-1993 | Population |
| ICARE (France) | 2,739 | 16.2 | 63 | 3,449 | 16.5 | 77 | 2001-2007 | Population |
| PARIS (France) | 169 | 1.0 | 95 | 227 | 1.1 | 95 | 1988-1992 | Hospital |
| LUCA (France) | 280 | 1.7 | 98 | 282 | 1.3 | 98 | 1989-1992 | Hospital |
| LUCAS (Sweden) | 1,014 | 6.0 | 87 | 2,307 | 11.0 | 85 | 1985-1990 | Population |
| INCO/ LLP (UK) | 441 | 2.6 | 78 | 916 | 4.4 | 84 | 1998-2005 | Population |
| MORGEN* (Netherlands) | 43 | 0.3 | N/A | 115 | 0.5 | N/A | 1993-1997 | Population |
| **Southern Europe** | | | | | | | | |
| EAGLE (Italy) | 1,908 | 11.3 | 87 | 2,065 | 9.8 | 72 | 2002-2005 | Population |
| TURIN/ VENETO (Italy) | 1,086 | 6.4 | 79 | 1,489 | 7.1 | 80 | 1990-1994 | Population |
| ROME (Italy) | 326 | 1.9 | 74 | 321 | 1.5 | 63 | 1993-1996 | Hospital |
| CAPUA (Spain) | 559 | 3.3 | 91 | 512 | 2.4 | 96 | 2000-2010 | Hospital |
| **East Europe** | | | | | | | | |
| INCO (Czech Rep.) | 304 | 1.8 | 94 | 452 | 2.2 | 80 | 1998-2002 | Hospital |
| INCO (Hungary) | 391 | 2.3 | 90 | 305 | 1.5 | 100 | 1998-2001 | Hospital |
| INCO (Poland) | 793 | 4.7 | 88 | 835 | 4.0 | 88 | 1999-2002 | Hosp.& Pop. |
| INCO (Romania) | 179 | 1.1 | 90 | 225 | 1.1 | 99 | 1998-2002 | Hospital |
| INCO (Russia) | 599 | 3.5 | 96 | 580 | 2.8 | 90 | 1998-2001 | Hospital |
| INCO (Slovakia) | 345 | 2.0 | 90 | 285 | 1.4 | 84 | 1998-2002 | Hospital |
| **Canada** | | | | | | | | |
| MONTREAL (Canada) | 1,176 | 7.0 | 85 | 1,505 | 7.2 | 69 | 1996-2002 | Population |
| TORONTO (Canada) | 365 | 2.2 | 62 | 844 | 4.0 | 71 | 1997-2002 | Hosp.& Pop. |

* Nested case-control study

**Table S2a.** Lung cancer odds ratios (OR) and 95% CI in relation to cumulative exposure to chromium (VI) and nickel by study region (men)

| Study region | Cumulative Cr(VI) exposure | | | | | | Cumulative nickel exposure | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | [µg/m$^3$-years] | Cases | Controls | OR2 | 95%CI | 99.4%CI° | [µg/m$^3$-years] | Cases | Controls | OR2 | 95%CI | 99.4%CI° |
| | Unexposed | 5,072 | 7,518 | 1.00 | Ref. | Ref. | Unexposed | 5,612 | 7,926 | 1.00 | Ref. | Ref. |
| | >0- ≤15.3 | 511 | 515 | 1.15 | 0.99-1.33 | 0.93-1.41 | >0- ≤11.9 | 265 | 323 | 0.91 | 0.75-1.10 | 0.69-1.19 |
| Northern Europe | >15.3- ≤40.3 | 599 | 541 | 1.32 | 1.14-1.33 | 1.08-1.60 | >11.9- ≤30.9 | 410 | 409 | 1.17 | 0.99-1.38 | 0.93-1.48 |
| | >40.3- ≤99.5 | 595 | 546 | 1.31 | 1.14-1.51 | 1.08-1.60 | >30.9- ≤78.1 | 544 | 486 | 1.21 | 1.04-1.40 | 0.98-1.49 |
| | ≤99.5 | 630 | 560 | 1.41 | 1.23-1.62 | 1.16-1.71 | >78.1 | 576 | 536 | 1.35 | 1.18-1.56 | 1.11-1.66 |
| | Unexposed | 2,269 | 2,627 | 1.00 | Ref. | Ref. | Unexposed | 2,508 | 2,782 | 1.00 | Ref. | Ref. |
| | >0- ≤15.3 | 360 | 345 | 1.06 | 0.88-1.28 | 0.82-1.38 | >0- ≤11.9 | 323 | 346 | 0.92 | 0.77-1.11 | 0.71-1.20 |
| Southern Europe | >15.3- ≤40.3 | 294 | 252 | 1.12 | 0.91-1.37 | 0.83-1.49 | >11.9- ≤30.9 | 204 | 221 | 0.98 | 0.78-1.23 | 0.70-1.36 |
| | >40.3- ≤99.5 | 215 | 211 | 1.06 | 0.84-1.34 | 0.76-1.47 | >30.9- ≤78.1 | 171 | 139 | 1.19 | 0.91-1.55 | 0.82-1.73 |
| | ≤99.5 | 121 | 92 | 1.55 | 1.12-2.14 | 0.98-2.44 | >78.1 | 53 | 39 | 1.81 | 1.10-3.01 | 0.89-3.67 |
| | Unexposed | 1,402 | 1,440 | 1.00 | Ref. | Ref. | Unexposed | 1,502 | 1,521 | 1.00 | Ref. | Ref. |
| | >0- ≤15.3 | 80 | 60 | 1.35 | 0.92-1.99 | 0.78-2.34 | >0- ≤11.9 | 78 | 92 | 0.86 | 0.61-1.22 | 0.52-1.41 |
| East Europe | >15.3- ≤40.3 | 105 | 121 | 0.86 | 0.64-1.17 | 0.56-1.33 | >11.9- ≤30.9 | 114 | 118 | 0.88 | 0.65-1.19 | 0.58-1.35 |
| | >40.3- ≤99.5 | 163 | 144 | 1.00 | 0.77-1.31 | 0.69-1.46 | >30.9- ≤78.1 | 168 | 127 | 1.24 | 0.95-1.64 | 0.84-1.83 |
| | ≤99.5 | 293 | 237 | 1.14 | 0.92-1.41 | 0.84-1.54 | >78.1 | 181 | 144 | 1.20 | 0.92-1.56 | 0.82-1.73 |
| | Unexposed | 731 | 1,046 | 1.00 | Ref. | Ref. | Unexposed | 767 | 1,082 | 1.00 | Ref. | Ref. |
| | >0- ≤15.3 | 14 | 23 | 0.87 | 0.37-1.72 | 0.27-2.38 | >0- ≤11.9 | 6 | 10 | 0.55 | 0.17-1.78 | 0.11-2.87 |
| Canada | >15.3- ≤40.3 | 30 | 36 | 0.94 | 0.53-1.64 | 0.42-2.07 | >11.9- ≤30.9 | 21 | 27 | 0.84 | 0.44-1.62 | 0.34-2.12 |
| | >40.3- ≤99.5 | 44 | 52 | 1.05 | 0.66-1.65 | 0.55-2.00 | >30.9- ≤78.1 | 31 | 38 | 1.07 | 0.62-1.83 | 0.50-2.29 |
| | ≤99.5 | 77 | 85 | 1.16 | 0.80-1.67 | 0.69-1.95 | >78.1 | 71 | 85 | 0.99 | 0.68-1.44 | 0.58-1.68 |

Northern Europe (Germany, Sweden, France, UK, The Netherlands); Southern Europe (Italy, Spain); Eastern Europe (Czech Republic, Hungary, Poland, Romania, Russia, Slovakia), Canada

OR2 is adjusted for study, age group, smoking (log(cigarette pack-years+1), time-since-quitting smoking (current smokers, stopping smoking 2-7 years, 8-15 years, 16-25, 26+ years before interview/diagnosis, never smokers)), and list A jobs

° 99.4% CI Bonferroni-corrected for 9 subtests

**Table S2b.** Lung cancer odds ratios (OR) and 95% CI in relation to cumulative exposure to chromium (VI) and nickel by study region (women)

| | Cumulative Cr(VI) exposure | | | | | | Cumulative nickel exposure | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Study region** | **[µg/m³-years]** | **Cases** | **Controls** | **OR2** | **95%CI** | **99.4%C°I** | **[µg/m³-years]** | **Cases** | **Controls** | **OR2** | **95%CI** | **99.4%CI°** |
| | Unexposed | 1,386 | 1,808 | 1.00 | Ref. | Ref. | Unexposed | 1,394 | 1,814 | 1.00 | Ref. | Ref. |
| | >0- ≤15.3 | 32 | 26 | 1.11 | 0.61-2.03 | 0.47-2.60 | >0- ≤11.9 | 24 | 21 | 1.23 | 0.62-2.45 | 0.47-3.25 |
| Northern Europe | >15.3- ≤40.3 | 15 | 18 | 0.73 | 0.32-1.63 | 0.23-2.30 | >11.9- ≤30.9 | 18 | 20 | 0.80 | 0.38-1.69 | 0.28-2.31 |
| | >40.3- ≤99.5 | 19 | 10 | 1.55 | 0.66-3.90 | 0.44-5.43 | >30.9- ≤78.1 | 13 | 5 | 1.62 | 0.56-5.44 | 0.33-7.88 |
| | ≤99.5 | 11 | 5 | 2.29 | 0.74-7.93 | 0.44-11.9 | >78.1 | 14 | 7 | 1.62 | 0.59-4.79 | 0.37-7.05 |
| | Unexposed | 589 | 833 | 1.00 | Ref. | Ref. | Unexposed | 588 | 833 | 1.00 | Ref. | Ref. |
| | >0- ≤15.3 | 15 | 14 | 1.67 | 0.70-3.93 | 0.50-5.62 | >0- ≤11.9 | 20 | 15 | 1.90 | 0.87-4.13 | 0.63-5.73 |
| Southern Europe | >15.3- ≤40.3 | 8 | 7 | 1.85 | 0.57-6.00 | 0.36-9.50 | >11.9- ≤30.9 | 7 | 9 | 1.63 | 0.53-4.79 | 0.35-7.55 |
| | >40.3- ≤99.5 | 6 | 5 | 1.89 | 0.50-7.23 | 0.30-12.0 | >30.9- ≤78.1 | 4 | 3 | 1.91 | 0.35-11.1 | 0.18-20.5 |
| | ≤99.5 | 2 | 1 | 2.83 | 0.22-66.6 | 0.08-107 | >78.1 | 1 | 0 | NA | | |
| | Unexposed | 532 | 634 | 1.00 | Ref. | Ref. | Unexposed | 534 | 643 | 1.00 | Ref. | Ref. |
| | >0- ≤15.3 | 6 | 4 | 1.51 | 0.38-6.52 | 0.21-10.7 | >0- ≤11.9 | 9 | 6 | 1.80 | 0.56-6.20 | 0.34-9.64 |
| Eastern Europe | >15.3- ≤40.3 | 15 | 13 | 0.98 | 0.42-2.34 | 0.29-3.29 | >11.9- ≤30.9 | 13 | 10 | 1.34 | 0.53-3.48 | 0.36-5.00 |
| | >40.3- ≤99.5 | 13 | 18 | 0.70 | 0.30-1.57 | 0.22-2.23 | >30.9- ≤78.1 | 9 | 15 | 0.49 | 0.18-1.31 | 0.12-2.01 |
| | ≤99.5 | 2 | 11 | 0.17 | 0.02-0.80 | 0.02-1.85 | >78.1 | 3 | 6 | 0.47 | 0.09-2.16 | 0.05-4.27 |
| | Unexposed | 630 | 1,093 | 1.00 | Ref. | Ref. | Unexposed | 629 | 1,093 | 1.00 | Ref. | Ref. |
| | >0- ≤15.3 | 3 | 5 | 0.51 | 0.10-2.38 | 0.06-4.61 | >0- ≤11.9 | 1 | 5 | 0.12 | 0.01-0.85 | 0.01-2.86 |
| Canada | >15.3- ≤40.3 | 8 | 3 | 4.59 | 0.96-28.1 | 0.45-47.2 | >11.9- ≤30.9 | 9 | 3 | 4.27 | 0.98-25.2 | 0.46-39.8 |
| | >40.3- ≤99.5 | 2 | 5 | 0.31 | 0.04-1.70 | 0.03-3.87 | >30.9- ≤78.1 | 3 | 5 | 0.61 | 0.10-3.18 | 0.06-6.47 |
| | ≤99.5 | 2 | 1 | 2.04 | 0.12-57.7 | 0.04-119 | >78.1 | 3 | 1 | 3.23 | 0.31-77.2 | 0.09-119 |

Northern Europe (Germany, Sweden, France, UK, The Netherlands); Southern Europe (Italy, Spain); Eastern Europe (Czech Republic, Hungary, Poland, Romania, Russia, Slovakia), Canada

OR2 is adjusted for study, age group, smoking (log(cigarette pack-years+1), time-since-quitting smoking (current smokers, stopping smoking 2-7 years, 8-15 years, 16-25, 26+ years before interview/diagnosis, never smokers)), and list A jobs

° 99.4% CI Bonferroni-corrected for 9 subtests

**Table S3a.** Lung cancer odds ratios (OR) and 95% CI in relation to cumulative exposure to chromium (VI) in restricted strata of women in the SYNERGY study

| Cumulative exposure | Population-based studies | | | | | Hospital-based studies | | | | | Blue-collar workers only | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| [µg/m$^3$-years] | Cases | Controls | OR2 | 95%CI | 99.4%CI° | Cases | Controls | OR2 | 95%CI | 99.4%CI° | Cases | Controls | OR2 | 95%CI | 99.4%CI° |
| Unexposed | 2,616 | 3,617 | 1.00 | Ref. | Ref. | 793 | 1,257 | 1.00 | Ref. | Ref. | 1,389 | 1,655 | 1.00 | Ref. | Ref. |
| >0-≤15.3 | 47 | 37 | 1.18 | 0.72-1.95 | 0.58-2.04 | 8 | 7 | 1.26 | 0.41-3.93 | 0.28-4.03 | 55 | 48 | 1.09 | 0.69-1.72 | 0.57-2.08 |
| >15.3-≤40.3 | 29 | 28 | 1.19 | 0.64-2.20 | 0.51-2.33 | 19 | 14 | 1.45 | 0.68-3.18 | 0.52-3.33 | 46 | 40 | 1.17 | 0.71-1.94 | 0.58-2.38 |
| >40.3-≤99.5 | 28 | 21 | 1.17 | 0.61-2.26 | 0.52-2.38 | 15 | 18 | 0.89 | 0.41-1.91 | 0.29-2.06 | 40 | 37 | 1.02 | 0.60-1.73 | 0.49-2.14 |
| >99.5 | 14 | 6 | 2.78 | 0.99-8.54 | 0.80-9.08 | 4 | 12 | 0.42 | 0.11-1.41 | 0.02-1.55 | 17 | 18 | 1.04 | 0.47-2.27 | 0.35-3.14 |
| *Test for trend, p-value* | | | *0.09* | | | | | *0.21* | | | | | *0.77* | | |
| *Excl. never exposed* | | | *0.11* | | | | | *0.22* | | | | | *0.99* | | |

| Cumulative exposure | Restricted to workers starting job 1960 or later | | | | | Restricted to workers starting job 1970 or later | | | | | Excluding regular welders | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| [µg/m$^3$-years] | Cases | Controls | OR2 | 95%CI | 99.4%CI° | Cases | Controls | OR2 | 95%CI | 99.4%CI° | Cases | Controls | OR2 | 95%CI | 99.4%CI° |
| Unexposed | 1,227 | 1,896 | 1.00 | Ref. | Ref. | 524 | 980 | 1.00 | Ref. | Ref. | 3,137 | 4,638 | 1.00 | Ref. | Ref. |
| >0-≤15.3 | 13 | 16 | 1.15 | 0.47-2.73 | 0.33-3.94 | 7 | 8 | 1.30 | 0.40-4.25 | 0.24-6.96 | 53 | 45 | 1.17 | 0.75-1.85 | 0.62-2.28 |
| >15.3-≤40.3 | 12 | 10 | 1.18 | 0.44-3.27 | 0.29-4.80 | 5 | 2 | 1.51 | 0.27-8.40 | 0.13-17.1 | 44 | 39 | 1.25 | 0.76-2.04 | 0.59-2.44 |
| >40.3-≤99.5 | 14 | 16 | 0.91 | 0.39-2.08 | 0.28-2.94 | 5 | 4 | 1.83 | 0.41-8.15 | 0.22-15.1 | 36 | 35 | 1.04 | 0.62-1.76 | 0.48-2.16 |
| >99.5 | 6 | 9 | 0.68 | 0.20-2.30 | 0.12-3.81 | 2 | 1 | 2.36 | 0.17-32.2 | 0.06-95.3 | 14 | 16 | 0.89 | 0.40-2.01 | 0.28-2.95 |
| *Test for trend, p-value* | | | *0.53* | | | | | *0.26* | | | | | *0.77* | | |
| *Excl. never exposed* | | | *0.52* | | | | | *0.04* | | | | | *0.99* | | |

OR2 is adjusted for study, age group, smoking (log(cigarette pack-years+1), time-since-quitting smoking (current smokers, stopping smoking 2-7 years, 8-15 years, 16-25, 26+ years before interview/diagnosis, never smokers)), and list A jobs

° 99.4% CI Bonferroni-corrected for 9 subtests

**Table S3b.** Lung cancer odds ratios (OR) and 95% CI in relation to cumulative exposure to nickel in restricted strata of women in the SYNERGY study

| Cumulative exposure | Population-based studies | | | | | Hospital-based studies | | | | | Blue-collar workers | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (µg/m³-years) | Cases | Controls | OR2 | 95% CI | 99.4% CI | Cases | Controls | OR2 | 95% CI | 99.4% CI | Cases | Controls | OR2 | 95% CI | 99.4% CI |
| Unexposed | 2,623 | 3,624 | 1.00 | Ref. | Ref. | 795 | 1,266 | 1.00 | Ref. | Ref. | 1,396 | 1,668 | 1.00 | Ref. | Ref. |
| >0-≤11.9 | 38 | 33 | 1.19 | 0.69-2.05 | 0.53-2.21 | 10 | 9 | 1.37 | 0.50-3.81 | 0.34-3.95 | 54 | 47 | 1.21 | 0.76-1.93 | 0.63-2.34 |
| >11.9-≤30.9 | 36 | 31 | 1.33 | 0.76-2.35 | 0.62-2.49 | 17 | 11 | 1.95 | 0.86-4.60 | 0.72-4.78 | 47 | 42 | 1.19 | 0.73-1.94 | 0.60-2.37 |
| >30.9-≤78.1 | 22 | 13 | 1.51 | 0.70-3.38 | 0.56-3.51 | 11 | 15 | 0.76 | 0.31-1.86 | 0.18-1.99 | 29 | 27 | 0.98 | 0.53-1.83 | 0.41-2.36 |
| >78.1 | 15 | 8 | 1.52 | 0.58-4.19 | 0.42-4.32 | 6 | 7 | 1.05 | 0.30-3.67 | 0.13-3.76 | 21 | 14 | 1.19 | 0.54-2.67 | 0.39-3.64 |
| *Test for trend, p-value* | | | *0.60* | | | | | *0.83* | | | | | *0.99* | | |
| *Excl. never exposed* | | | *0.96* | | | | | *0.49* | | | | | *0.75* | | |

| Cumulative exposure | Restricted to workers starting job 1960 or later | | | | | Restricted to workers starting job 1970 or later | | | | | Excluding regular welders | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (µg/m³-years) | Cases | Controls | OR2 | 95%CI | 99.4%CI° | Cases | Controls | OR2 | 95%CI | 99.4%CI° | Cases | Controls | OR2 | 95%CI | 99.4%CI° |
| Unexposed | 1,230 | 1,901 | 1.00 | Ref. | Ref. | 527 | 983 | 1.00 | Ref. | Ref. | 3,145 | 4,383 | 1.00 | Ref. | Ref. |
| >0-≤11.9 | 11 | 15 | 1.47 | 0.58-3.64 | 0.41-5.34 | 5 | 6 | 1.64 | 0.41-6.50 | 0.23-11.5 | 48 | 43 | 1.21 | 0.76-1.94 | 0.61-2.38 |
| >11.9-≤30.9 | 13 | 9 | 1.63 | 0.62-4.43 | 0.41-6.43 | 4 | 1 | 8.96 | 0.71-113 | 0.25-325 | 44 | 37 | 1.40 | 0.86-2.31 | 0.69-2.87 |
| >30.9-≤78.1 | 12 | 16 | 0.75 | 0.31-1.82 | 0.22-2.62 | 5 | 5 | 0.93 | 0.24-3.62 | 0.14-6.36 | 27 | 28 | 0.93 | 0.51-1.69 | 0.38-2.16 |
| >78.1 | 6 | 6 | 0.84 | 0.23-3.24 | 0.13-5.40 | 2 | 0 | - | | | 20 | 12 | 1.44 | 0.65-3.22 | 0.43-4.41 |
| *Test for trend, p-value* | | | *0.92* | | | | | *0.32* | | | | | *0.59* | | |
| *Excl. never exposed* | | | *0.42* | | | | | *0.64* | | | | | *0.67* | | |

OR2 is adjusted for study, age group, smoking (log(cigarette pack-years+1), time-since-quitting smoking (current smokers, stopping smoking 2-7 years, 8-15 years, 16-25, 26+ years before interview/diagnosis, never smokers)), and list A jobs

° 99.4% CI Bonferroni-corrected for 9 subtests

**Table S4.** Lung-cancer odds ratios (OR) and 95% CI in relation to cumulative exposure to chromium (VI) and nickel - Lagged analysis

| | Cumulative chromium (VI) exposure | | | | | | Cumulative nickel exposure | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Lag period** | **[µg/m³-years]** | **Cases** | **Controls** | **OR2** | **95%CI** | **99.4%CI°** | **[µg/m³-years]** | **Cases** | **Controls** | **OR2** | **95%CI** | **99.4%CI°** |
| | **Men** | | | | | | **Men** | | | | | |
| | Unexposed | 9,491 | 12,643 | 1.00 | Ref. | Ref. | Unexposed | 10,399 | 13,320 | 1.00 | Ref. | Ref. |
| | >0-≤15.3 | 958 | 940 | 1.11 | 1.00-1.24 | 0.95-1.29 | >0-≤11.9 | 677 | 767 | 0.94 | 0.83-1.06 | 0.79-1.12 |
| 5 years | >15.3-≤40.3 | 1,030 | 948 | 1.20 | 1.08-1.34 | 1.04-1.40 | >11.9-≤30.9 | 729 | 773 | 1.03 | 0.92-1.17 | 0.87-1.23 |
| | >40.3-≤99.5 | 986 | 949 | 1.15 | 1.04-1.28 | 0.99-1.34 | >30.9-≤78.1 | 917 | 787 | 1.21 | 1.08-1.35 | 1.03-1.42 |
| | >99.5 | 1,140 | 971 | 1.35 | 1.21-1.49 | 1.16-1.56 | >78.1 | 883 | 804 | 1.29 | 1.15-1.44 | 1.09-1.53 |
| | Unexposed | 9,520 | 12,672 | 1.00 | Ref. | Ref. | Unexposed | 10,421 | 13,343 | 1.00 | Ref. | Ref. |
| | >0-≤15.3 | 959 | 933 | 1.12 | 1.00-1.25 | 0.96-1.30 | >0-≤11.9 | 667 | 760 | 0.92 | 0.82-1.05 | 0.78-1.10 |
| 10 years | >15.3-≤40.3 | 1,016 | 941 | 1.19 | 1.07-1.33 | 1.03-1.39 | >11.9-≤30.9 | 717 | 765 | 1.04 | 0.92-1.17 | 0.87-1.23 |
| | >40.3-≤99.5 | 977 | 945 | 1.16 | 1.04-1.29 | 0.99-1.35 | >30.9-≤78.1 | 930 | 786 | 1.23 | 1.10-1.38 | 1.05-1.44 |
| | >99.5 | 1,133 | 960 | 1.34 | 1.20-1.48 | 1.15-1.55 | >78.1 | 870 | 797 | 1.27 | 1.13-1.42 | 1.08-1.49 |
| | Unexposed | 9,674 | 12,809 | 1.00 | Ref. | Ref. | Unexposed | 10,556 | 13,464 | 1.00 | Ref. | Ref. |
| | >0-≤15.3 | 927 | 899 | 1.12 | 1.01-1.25 | 0.96-1.31 | >0-≤11.9 | 601 | 726 | 0.87 | 0.77-0.99 | 0.63-2.26 |
| 20 years | >15.3-≤40.3 | 966 | 910 | 1.16 | 1.04-1.29 | 0.99-1.35 | >11.9-≤30.9 | 702 | 745 | 1.04 | 0.92-1.17 | 0.53-2.14 |
| | >40.3-≤99.5 | 970 | 906 | 1.19 | 1.06-1.32 | 1.02-1.38 | >30.9-≤78.1 | 914 | 753 | 1.24 | 1.11-1.39 | 0.60-3.18 |
| | >99.5 | 1,068 | 927 | 1.29 | 1.16-1.44 | 1.11-1.50 | >78.1 | 832 | 763 | 1.26 | 1.12-1.41 | 0.42-4.01 |
| | **Women** | | | | | | **Women** | | | | | |
| | Unexposed | 3,142 | 4,369 | 1.00 | Ref. | Ref. | Unexposed | 3,149 | 4,383 | 1.00 | Ref. | Ref. |
| | >0-≤15.3 | 51 | 48 | 1.05 | 0.67-1.67 | 0.55-2.01 | >0-≤11.9 | 53 | 49 | 1.19 | 0.76-1.87 | 0.63-2.26 |
| | >15.3-≤40.3 | 47 | 40 | 1.40 | 0.86-2.30 | 0.70-2.81 | >11.9-≤30.9 | 40 | 42 | 1.06 | 0.65-1.75 | 0.53-2.14 |
| 5 years | >40.3-≤99.5 | 40 | 39 | 0.99 | 0.60-1.63 | 0.48-2.01 | >30.9-≤78.1 | 34 | 27 | 1.38 | 0.77-2.51 | 0.60-3.18 |
| | >99.5 | 16 | 18 | 1.02 | 0.47-2.21 | 0.34-3.05 | >78.1 | 20 | 13 | 1.30 | 0.59-2.94 | 0.42-4.01 |
| | Unexposed | 3,145 | 4,372 | 1.00 | Ref. | Ref. | Unexposed | 3,151 | 4,385 | 1.00 | Ref. | Ref. |
| 10 years | >0-≤15.3 | 48 | 47 | 1.11 | 0.70-1.77 | 0.57-2.15 | >0-≤11.9 | 50 | 49 | 1.14 | 0.72-1.80 | 0.59-2.17 |
| | >15.3-≤40.3 | 45 | 39 | 1.23 | 0.75-2.03 | 0.61-2.50 | >11.9-≤30.9 | 41 | 44 | 1.04 | 0.64-1.71 | 0.52-2.09 |

| | Cumulative chromium (VI) exposure | | | | | | Cumulative nickel exposure | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Lag period** | **[µg/m$^3$-years]** | **Cases** | **Controls** | **OR2** | **95%CI** | **99.4%CI°** | **[µg/m$^3$-years]** | **Cases** | **Controls** | **OR2** | **95%CI** | **99.4%CI°** |
| | >40.3-≤99.5 | 42 | 35 | 1.24 | 0.75-2.07 | 0.60-2.55 | >30.9-≤78.1 | 35 | 23 | 1.69 | 0.93-3.13 | 0.72-3.98 |
| | >99.5 | 16 | 21 | 0.79 | 0.37-1.66 | 0.28-2.28 | >78.1 | 19 | 13 | 1.14 | 0.52-2.59 | 0.37-3.53 |
| | Unexposed | 3,156 | 4,385 | 1.00 | Ref. | Ref. | Unexposed | 3,161 | 4,397 | 1.00 | Ref. | Ref. |
| | >0-≤15.3 | 42 | 44 | 1.01 | 0.67-1.65 | 0.51-2.02 | >0-≤11.9 | 47 | 47 | 1.06 | 0.66-1.70 | 0.54-2.06 |
| 20 years | >15.3-≤40.3 | 46 | 32 | 1.34 | 0.79-2.29 | 0.63-2.84 | >11.9-≤30.9 | 37 | 33 | 1.22 | 0.71-2.09 | 0.57-2.61 |
| | >40.3-≤99.5 | 37 | 37 | 1.10 | 0.65-1.85 | 0.53-2.29 | >30.9-≤78.1 | 31 | 24 | 1.46 | 0.79-2.74 | 0.61-3.52 |
| | >99.5 | 15 | 16 | 1.00 | 0.45-2.23 | 0.32-3.09 | >78.1 | 20 | 13 | 1.19 | 0.56-2.62 | 0.40-3.53 |

OR2 is adjusted for study, age group, smoking (log(cigarette pack-years+1), time-since-quitting smoking (current smokers, stopping smoking 2-7 years, 8-15 years, 16-25, 26+ years before interview/diagnosis, never smokers)), and list A jobs

° 99.4%CI Bonferroni-corrected for 9 subtests

**Table S5.** Lung cancer odds ratios and 95% CI in relation to cumulative hexavalent chromium exposure stratified by lung-cancer cell type and smoking status in men in the SYNERGY Study

| Lung cancer cell type | Cr(VI) exposure [µg/m$^3$-years] | Never smokers* | | | | | Former smokers** | | | | | Current smokers*** | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Cases | Contr. | OR | 95%CI | 99.4%CI° | Cases | Contr. | OR | 95%CI | 99.4%CI° | Cases | Contr. | OR | 95%CI | 99.4%CI° |
| All | Unexposed | 374 | 3,592 | 1.00 | Ref. | Ref. | 3,390 | 5,540 | 1.00 | Ref. | Ref. | 5,710 | 3,499 | 1.00 | Ref. | Ref. |
| | <40.23 | 55 | 397 | 1.42 | 1.03-1.92 | 0.91-2.20 | 660 | 921 | 1.06 | 0.94-1.19 | 0.89-1.25 | 1,278 | 575 | 1.23 | 1.09-1.38 | 1.04-1.44 |
| | ≥40.23 | 61 | 448 | 1.33 | 0.98-1.79 | 0.87-2.04 | 737 | 867 | 1.28 | 1.13-1.43 | 1.08-1.51 | 1,340 | 612 | 1.23 | 1.10-1.38 | 1.05-1.44 |
| *Test for trend, p-value* | | | | *0.07* | | | | | *<0.01* | | | | | *0.02* | | |
| *Excl. never exposed* | | | | *0.36* | | | | | *0.02* | | | | | *0.74* | | |
| Adenocarcinoma | Unexposed | 141 | 3,592 | 1.00 | Ref. | Ref. | 926 | 5,540 | 1.00 | Ref. | Ref. | 1,360 | 3,499 | 1.00 | Ref. | Ref. |
| | <40.23 | 20 | 397 | 1.19 | 0.71-1.91 | 0.59-2.39 | 174 | 921 | 1.05 | 0.87-1.27 | 0.81-1.37 | 269 | 575 | 1.15 | 0.96-1.37 | 0.90-1.47 |
| | ≥40.23 | 16 | 448 | 0.83 | 0.46-1.39 | 0.38-1.79 | 172 | 867 | 1.12 | 0.92-1.35 | 0.85-1.46 | 245 | 612 | 1.04 | 0.87-1.25 | 0.81-1.34 |
| *Test for trend, p-value* | | | | *0.81* | | | | | *0.48* | | | | | *0.39* | | |
| *Excl. never exposed* | | | | *0.62* | | | | | *0.62* | | | | | *0.12* | | |
| Squamous cell carcinoma | Unexposed | 108 | 3,592 | 1.00 | Ref. | Ref. | 1,446 | 5,540 | 1.0 | Ref. | Ref. | 2,391 | 3,499 | 1.00 | Ref. | Ref. |
| | <40.23 | 14 | 397 | 1.30 | 0.69-2.25 | 0.57-2.97 | 302 | 921 | 1.18 | 1.01-1.38 | 0.95-1.48 | 556 | 575 | 1.23 | 1.07-1.41 | 1.01-1.49 |
| | ≥40.23 | 19 | 448 | 1.42 | 0.82-2.33 | 0.68-2.95 | 348 | 867 | 1.42 | 1.21-1.65 | 1.14-1.76 | 644 | 612 | 1.36 | 1.19-1.56 | 1.13-1.64 |
| *Test for trend, p-value* | | | | *0.11* | | | | | *<0.01* | | | | | *<0.01* | | |
| *Excl. never exposed* | | | | *0.23* | | | | | *0.02* | | | | | *0.13* | | |
| Small-cell lung cancer | Unexposed | 33 | 3,592 | 1.00 | Ref. | Ref. | 434 | 5,540 | 1.0 | Ref. | Ref. | 1,032 | 3,499 | 1.00 | Ref. | Ref. |
| | <40.23 | 9 | 397 | 2.65 | 1.16-5.48 | 0.89-7.85 | 96 | 921 | 1.15 | 0.89-1.47 | 0.81-1.64 | 238 | 575 | 1.28 | 1.07-1.54 | 0.99-1.66 |
| | ≥40.23 | 14 | 448 | 3.39 | 1.70-6.42 | 1.33-8.61 | 97 | 867 | 1.32 | 1.03-1.69 | 0.93-1.88 | 247 | 612 | 1.28 | 1.07-1.54 | 1.00-1.65 |
| *Test for trend, p-value* | | | | *<0.01* | | | | | *0.05* | | | | | *0.04* | | |
| *Excl. never exposed* | | | | *0.68* | | | | | *0.30* | | | | | *0.49* | | |

* OR in never smokers adjusted for study, age group, and List A jobs

** OR in former smokers adjusted for study, age group, List A jobs, cigarette pack-years, and time-since-quitting smoking

*** OR in current smokers adjusted for study, age group, List A jobs, and cigarette pack-years

° 99.4%CI Bonferroni-corrected for 9 subtests

**Table S6.** Lung cancer odds ratios and 95% CI in relation to cumulative nickel exposure stratified by lung-cancer cell type and smoking status in men in the SYNERGY Study

| Lung cancer cell type | Nickel Exposure [µg/m$^3$-years] | Never smokers* | | | | | Former smokers** | | | | | Current smokers*** | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Cases | Contr. | OR | 95%CI | 99.4%CI° | Cases | Contr. | OR | 95%CI | 99.4%CI° | Cases | Contr. | OR | 95%CI | 99.4%CI° |
| All | Unexposed | 402 | 3,735 | 1.00 | Ref. | Ref. | 3,691 | 5,867 | 1.00 | Ref. | Ref. | 6,296 | 3,709 | 1.00 | Ref. | Ref. |
| | <30.75 | 41 | 334 | 1.24 | 0.86-1.76 | 0.75-2.05 | 462 | 740 | 0.91 | 0.79-1.04 | 0.75-1.10 | 914 | 472 | 1.03 | 0.91-1.17 | 0.86-1.23 |
| | ≥30.75 | 47 | 368 | 1.21 | 0.86-1.67 | 0.75-1.93 | 634 | 721 | 1.31 | 1.15-1.49 | 1.09-1.57 | 1,114 | 505 | 1.20 | 1.07-1.36 | 1.01-1.42 |
| *Test for trend, p-value* | | | | *0.85* | | | | | *<0.001* | | | | | *0.02* | | |
| *Excl. never exposed* | | | | *0.59* | | | | | *0.012* | | | | | *0.15* | | |
| Adenocarcinoma | Unexposed | 154 | 3,735 | 1.00 | Ref. | Ref. | 1,004 | 5,867 | 1.00 | Ref. | Ref. | 1,464 | 3,709 | 1.00 | Ref. | Ref. |
| | <30.75 | 11 | 334 | 0.74 | 0.37-1.37 | 0.30-1.82 | 115 | 740 | 0.88 | 0.70-1.10 | 0.65-1.21 | 206 | 472 | 1.12 | 0.92-1.35 | 0.85-1.47 |
| | ≥30.75 | 14 | 368 | 0.83 | 0.45-1.43 | 0.37-1.87 | 153 | 721 | 1.16 | 0.94-1.41 | 0.87-1.54 | 204 | 505 | 1.03 | 0.85-1.25 | 0.79-1.35 |
| *Test for trend, p-value* | | | | *0.56* | | | | | *0.55* | | | | | *0.83* | | |
| *Excl. never exposed* | | | | *0.21* | | | | | *0.63* | | | | | *0.47* | | |
| Squamous cell carcinoma | Unexposed | 116 | 3,735 | 1.00 | Ref. | Ref. | 1,585 | 5,867 | 1.00 | Ref. | Ref. | 2,645 | 3,709 | 1.00 | Ref. | Ref. |
| | <30.75 | 12 | 334 | 1.37 | 0.69-2.48 | 0.56-3.34 | 217 | 740 | 1.01 | 0.84-1.21 | 0.78-1.30 | 407 | 472 | 0.99 | 0.84-1.15 | 0.79-1.23 |
| | ≥30.75 | 13 | 368 | 1.18 | 0.62-2.08 | 0.51-2.77 | 293 | 721 | 1.42 | 1.20-1.69 | 1.13-1.79 | 539 | 505 | 1.35 | 1.17-1.55 | 1.10-1.65 |
| *Test for trend, p-value* | | | | *0.87* | | | | | *<0.01* | | | | | *<0.01* | | |
| *Excl. never exposed* | | | | *0.44* | | | | | *0.01* | | | | | *0.05* | | |
| Small-cell lung cancer | Unexposed | 38 | 3,735 | 1.00 | Ref. | Ref. | 486 | 5,867 | 1.00 | Ref. | Ref. | 1,166 | 3,709 | 1.00 | Ref. | Ref. |
| | <30.75 | 6 | 334 | 2.12 | 0.78-4.89 | 0.60-7.61 | 56 | 740 | 0.86 | 0.63-1.17 | 0.56-1.34 | 149 | 472 | 0.98 | 0.79-1.22 | 0.72-1.34 |
| | ≥30.75 | 12 | 368 | 3.19 | 1.55-6.15 | 1.21-8.40 | 85 | 721 | 1.29 | 0.99-1.67 | 0.89-1.87 | 202 | 505 | 1.18 | 0.98-1.43 | 0.90-1.55 |
| *Test for trend, p-value* | | | | *0.03* | | | | | *0.13* | | | | | *0.04* | | |
| *Excl. never exposed* | | | | *0.91* | | | | | *0.18* | | | | | *0.04* | | |

* OR in never smokers adjusted for study, age group, and List A jobs

** OR in former smokers adjusted for study, age group, List A jobs, cigarette pack-years, and time-since-quitting smoking

*** OR in current smokers adjusted for study, age group, List A jobs, and cigarette pack-years

° 99.4% CI Bonferroni-corrected for 9 subtests

**Table S7.** Lung-cancer odds ratios and 95% CI in relation to cumulative chromium (VI) and nickel exposure stratified by smoking status in women in the SYNERGY Study

| | Cr(VI) exposure [µg/m³-years] | Never smokers* | | | | | Former smokers** | | | | | Current smokers*** | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Cases | Ctrls. | OR | 95%CI | 99.4%CI° | Cases | Ctrls. | OR | 95%CI | 99.4%CI° | Cases | Ctlrs. | OR | 95%CI | 99.4%CI° |
| All | Unexposed | 844 | 2,640 | 1.00 | Ref. | Ref. | 621 | 857 | 1.00 | Ref. | Ref. | 1672 | 871 | 1.00 | Ref. | Ref. |
| | <40.23 | 23 | 45 | 1.29 | 0.75-2.17 | 0.61-2.73 | 13 | 26 | 0.61 | 0.28-1.27 | 0.21-1.76 | 66 | 19 | 1.63 | 0.94-2.93 | 0.73-3.61 |
| | ≥40.23 | 12 | 31 | 0.79 | 0.36-1.60 | 0.28-2.23 | 11 | 9 | 1.67 | 0.60-4.80 | 0.39-7.17 | 34 | 16 | 1.04 | 0.55-2.03 | 0.42-2.60 |
| *Test for trend, p-value* | | | | *0.29* | | | | | *0.15* | | | | | *0.70* | | |
| *Excl. never exposed* | | | | *0.73* | | | | | *0.03* | | | | | *0.78* | | |
| | **Nickel exposure [µg/m³-years]** | **Never smokers*** | | | | | **Former smokers**** | | | | | **Current smokers***** | | | | |
| | | **Cases** | **Ctrls.** | **OR** | **95%CI** | **99.4%CI°** | **Cases** | **Contr.** | **OR** | **95%CI** | **99.4%CI°** | **Cases** | **Contr.** | **OR** | **95%CI** | **99.4%CI°** |
| All | Unexposed | 847 | 2,650 | 1.00 | Ref. | Ref. | 623 | 859 | 1.00 | Ref. | Ref. | 1675 | 874 | 1.00 | Ref. | Ref. |
| | <30.75 | 24 | 43 | 1.54 | 0.89-2.58 | 0.73-3.24 | 14 | 25 | 0.77 | 0.37-1.56 | 0.28-2.13 | 62 | 21 | 1.54 | 0.90-2.73 | 0.70-3.36 |
| | ≥30.75 | 8 | 23 | 0.67 | 0.26-1.56 | 0.19-2.36 | 8 | 8 | 1.03 | 0.31-3.39 | 0.19-5.45 | 35 | 11 | 1.38 | 0.68-3.00 | 0.49-3.90 |
| *Test for trend, p-value* | | | | *0.64* | | | | | *0.67* | | | | | *0.66* | | |
| *Excl. never exposed* | | | | *0.76* | | | | | *0.65* | | | | | *0.70* | | |

* OR in never smokers adjusted for study, age group, and list A jobs

** OR in former smokers adjusted for study, age group, list A jobs, cigarette pack-years, and time-since-quitting smoking

*** OR in current smokers adjusted for study, age group, list A jobs, and cigarette pack-years

° 99.4% CI Bonferroni-corrected for 9 subtests

**Table S8.** Lung cancer odds ratios and 95% CI, p-value for multiplicative interaction and relative excess risk due to interaction (RERI) and 95% CI in relation to occupational chromium (VI) and nickel exposure and smoking among men and women**:** Lung cancer subtype-specific results

| Histological subtype | Exposure status | Men | | | | | Women | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Cases | Ctrls. | OR* | 95%CI | 99.4%CI° | Cases | Ctrls. | OR* | 95%CI | 99.4% CI° |
| Squamous cell carcinoma | **Chromium (VI)** | | | | | | | | | | |
| | Never smoker and never Cr(VI) | 108 | 3,592 | 1.00 | Ref. | Ref. | 112 | 2,640 | 1.00 | Ref. | Ref. |
| | Never smoker and Cr(VI) | 33 | 845 | 1.17 | 0.79-1.74 | 0.67-2.06 | 4 | 76 | 0.82 | 0.29-2.37 | 0.18-3.67 |
| | Ever smoker and never Cr(VI) | 3,837 | 9,039 | 13.0 | 10.7-15.9 | 9.88-17.2 | 527 | 1,728 | 9.32 | 7.44-11.7 | 6.77-12.8 |
| | Ever smoker and ever Cr(VI) | 1,850 | 2,975 | 17.4 | 14.2-21.3 | 13.1-23.2 | 32 | 70 | 11.7 | 7.11-19.1 | 5.79-23.5 |
| | *p-value multiplicative interaction* | | | *0.52* | | | | | *0.44* | | |
| | RERI with linear model** | | | 4.19 | 2.80-5.58 | | | | 2.52 | -2.91-7.95 | |
| | **Nickel** | | | | | | | | | | |
| | Never smoker and never Ni | 116 | 3,735 | 1.00 | Ref. | Ref. | 112 | 2,650 | 1.00 | Ref. | Ref. |
| | Never smoker and Ni | 25 | 702 | 1.03 | 0.66-1.60 | 0.55-1.92 | 4 | 66 | 1.06 | 0.37-3.03 | 0.24-4.70 |
| | Ever smoker and never Ni | 4,231 | 9,576 | 13.2 | 10.9-15.9 | 10.1-17.2 | 526 | 1,733 | 9.34 | 7.45-11.7 | 6.79-12.9 |
| | Ever smoker and ever Ni | 1,456 | 2,438 | 15.9 | 13.0-19.1 | 12.0-21.0 | 33 | 65 | 13.3 | 8.07-21.8 | 6.57-26.8 |
| | *p-value multiplicative interaction* | | | *0.48* | | | | | *0.58* | | |
| | RERI with linear model** | | | 2.67 | 1.37-3.98 | | | | 3.86 | -2.34-10.1 | |
| Adeno-carcinoma | **Chromium (VI)** | | | | | | | | | | |
| | Never smoker and never Cr(VI) | 143 | 3,592 | 1.00 | Ref. | Ref. | 504 | 2,640 | 1.00 | Ref. | Ref. |
| | Never smoker and Cr(VI) | 36 | 845 | 1.01 | 0.70-1.47 | 0.60-1.72 | 17 | 76 | 1.06 | 0.60-1.90 | 0.42-2.06 |
| | Ever smoker and never Cr(VI) | 2,286 | 9,039 | 6.31 | 5.30-7.51 | 4.93-8.08 | 868 | 1,728 | 2.87 | 2.51-3.28 | 2.37-3.46 |
| | Ever smoker and ever Cr(VI) | 860 | 2,975 | 7.06 | 5.86-8.51 | 5.42-9.20 | 38 | 70 | 3.25 | 2.08-5.07 | 1.76-5.87 |
| | *p-value multiplicative interaction* | | | *0.25* | | | | | 0.59 | | |
| | RERI with linear model** | | | 0.74 | -0.02-1.46 | | | | 0.31 | -1.23-1.85 | |

| Histological subtype | Exposure status | Men | | | | | Women | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Cases | Ctrls. | OR* | 95%CI | 99.4%CI° | Cases | Ctrls. | OR* | 95%CI | 99.4% CI° |
| Small cell lung cancer | **Nickel** | | | | | | | | | | |
| | Never smoker and never Ni | 154 | 3,735 | 1.00 | Ref. | Ref. | 505 | 2,650 | 1.00 | Ref. | Ref. |
| | Never smoker and Ni | 25 | 702 | 0.82 | 0.53-1.26 | 0.44-1.51 | 16 | 66 | 0.93 | 0.53-1.63 | 0.47-2.42 |
| | Ever smoker and never Ni | 2,468 | 9,576 | 6.21 | 5.24-7.34 | 4.89-7.88 | 872 | 1,733 | 2.86 | 2.50-3.27 | 2.38-3.47 |
| | Ever smoker and ever Ni | 678 | 2,438 | 6.55 | 5.43-7.89 | 5.03-8.53 | 34 | 65 | 3.21 | 2.10-4.92 | 1.73-6.09 |
| | *p-value multiplicative interaction* | | | *0.60* | | | | | *0.59* | | |
| | RERI with linear model** | | | 0.53 | -0.21-1.26 | | | | 0.42 | -1.01-1.86 | |
| | **Chromium (VI)** | | | | | | | | | | |
| | Never smoker and never Cr(VI) | 33 | 3,592 | 1.00 | Ref. | Ref. | 51 | 2,640 | 1.00 | Ref. | Ref. |
| | Never smoker and Cr(VI) | 23 | 845 | 2.81 | 1.64-4.82 | 1.31-6.03 | 4 | 76 | 2.48 | 0.84-7.32 | 0.54-11.5 |
| | Ever smoker and never Cr(VI) | 1,466 | 9,039 | 17.4 | 12.3-24.7 | 10.6-28.5 | 442 | 1,728 | 14.8 | 10.9-20.0 | 9.58-22.7 |
| | Ever smoker and ever Cr(VI) | 678 | 2,975 | 22.8 | 16.0-32.8 | 13.8-37.7 | 33 | 70 | 28.9 | 16.6-50.3 | 13.2-63.3 |
| | *p-value multiplicative interaction* | | | *0.006* | | | | | *0.62* | | |
| | RERI with linear model** | | | 3.61 | 0.93-6.30 | | | | 12.70 | -1.64-27.1 | |
| | **Nickel** | | | | | | | | | | |
| | Never smoker and never Ni | 38 | 3,735 | 1.00 | Ref. | Ref. | 53 | 2,650 | 1.00 | Ref. | Ref. |
| | Never smoker and Ni | 18 | 702 | 2.46 | 1.39-4.35 | 1.10-5.50 | 2 | 66 | 1.50 | 0.35-6.44 | 0.19-11.8 |
| | Ever smoker and never Ni | 1,652 | 9,576 | 16.7 | 12.0-23.1 | 10.5-26.4 | 444 | 1,733 | 14.3 | 10.6-19.4 | 9.36-21.9 |
| | Ever smoker and ever Ni | 492 | 2,438 | 18.6 | 13.3-26.1 | 11.6-30.0 | 31 | 65 | 28.8 | 16.4-50.6 | 13.0-63.9 |
| | *p-value multiplicative interaction* | | | *0.008* | | | | | *0.77* | | |
| | RERI with linear model** | | | 0.52 | -1.88-2.93 | | | | 13.99 | -0.74-28.7 | |

* OR adjusted for study, age group and "List A" jobs
** Confidence intervals are based on 1,000 bootstrap samples.
° 99.4% CI Bonferroni-corrected for 9 subtests

**Supplementary Figures:**

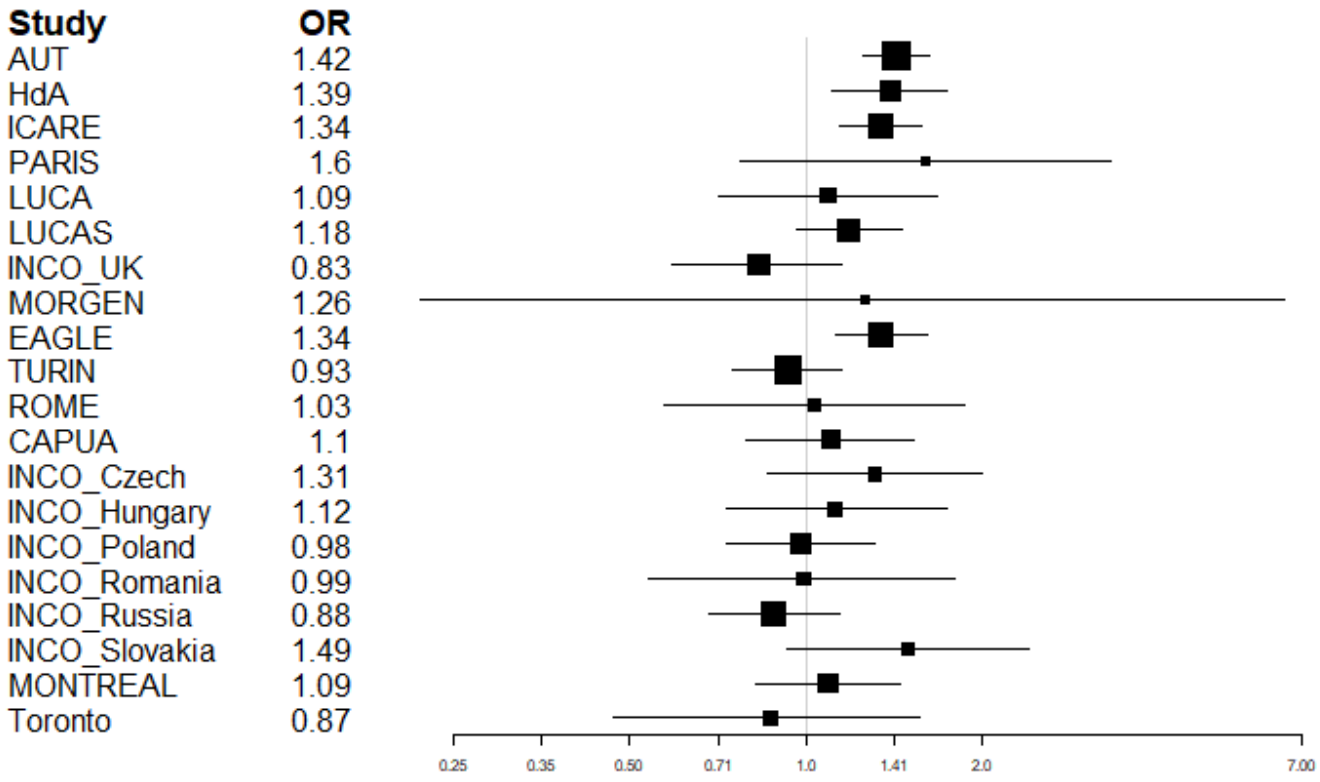


**Fig S1a:** Study-specific odds ratios (OR2) for ever exposure to chromium (VI) compared to subjects never exposed, adjusted for age, sex, cigarette pack-years, time-since-quitting smoking, and ever-employment in a 'list A' job.

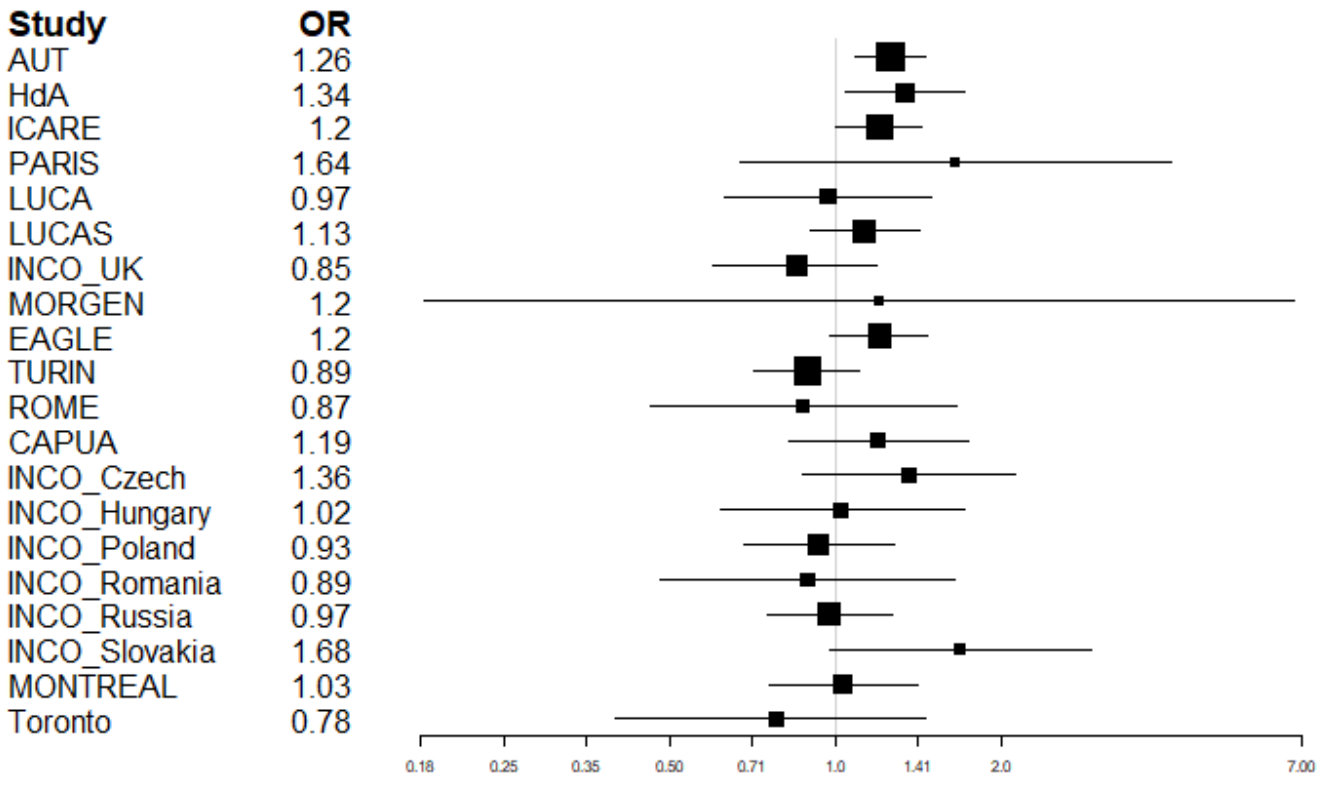


**Fig S1b:** Study-specific odds ratios (OR2) for ever exposure to nickel compared to subjects never exposed, adjusted for age, sex, cigarette pack-years, time-since-quitting smoking, and ever-employment in a 'list A' job.