

**Table 2.2 Case-control studies of inorganic acid mists and cancer**

| Reference, study location and period | Characteristics of cases   | Characteristics of controls   | Exposure assessment   | Organ site (ICD code)    | Exposure categories   | No. of exposed cases | Relative risk (95% CI)*   | Adjustment for potential confounders                                    | Comments  |
|--------------------------------------|--|---|---|--------------------------|---|----------------------|---|---|---|
|                                      |  |   |   | <i>Upper Respiratory</i> |   |                      |   |   |   |
| d'Errico et al. (2009) Italy         | 113 sino-nasal cancer incident cases (53 adenocarcinomas, 37 squamous cell carcinomas, 23 other histologies) among 153 diagnosed during study period | 336 hospital controls (ear nose and throat, orthopaedics), frequency matched to cases by 10-year age groups, sex, and province of residence | Interviewer-administered questionnaire /job history (company size, type, job title, tasks, colleagues, machinery, substances, etc.). Probability and intensity of exposure rated by epidemiologist & physician; discordant ratings reviewed by industrial hygienist | Sinonasal (160)          | All histologies: Ever acid mists<br><br>Basocellular, mucoepidermoid, neuroendocrine, undifferentiated, or unspecified: Ever acid mists<br>1-10 years<br>>10 years<br>Low intensity<br>High intensity | 6<br><br>4           | <b>OR</b><br>1.7 (0.61-4.90)<br><br>7.5 (2.0-28)<br>6.0 (1.32-27)<br>15.6 (1.3-187)<br>5.6 (1.25-25.1)<br>17.1 (1.42-207) | Age and sex<br><br>Age, sex, co-exposure to wood dust or solvent vapors | Unclear if adjustment for co-exposures is just for those significant in histology group or all evaluated occupational exposures (arsenic, wood dust, leather dust, nickel, chromium, PAHs, welding fumes, oil mists, formaldehyde, flour dust, cocoa powder, silica, coal dust, textile dusts, paint mists, organic solvents) |
| Brown, et al. (1988) USA             | 183 white men age 30-79 with squamous cell carcinoma of the larynx   | 250 white men frequency matched by 5-year age group, vital status, ethnicity, county of residence   | Work histories since 1939, categorized by industry and occupation, job titles classified for potential exposure by industrial hygienist   | Larynx (161)             | Sulfuric acid   | 22                   | 0.76 (0.42-1.35)  | Smoking and alcohol consumption   |   |

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| Cookfair, et al. (1985) USA          | 352 white men admitted to Roswell Park Memorial Institute with laryngeal cancer | 1050 age-matched white male hospital controls   | Life time occupational histories assessed for sulfuric acid exposure                                      | Larynx (161)          | <i>Sulfuric acid exposure:</i><br><20 years<br>>20 years                       |                      | 2.05<br>2.43   | Smoking  | Heavy smokers with sulfuric acid exposure had increased risk over heavy smokers without sulfuric acid exposure, suggesting an interaction.  |
| De Stefani, et al. (1998) Uruguay    | 112 men age 30-75, histologically confirmed, admitted to 5 major hospitals      | 509 men with other cancer (except oral, pharyngeal, oesophageal, stomach, bladder, or lung) | Work histories, supplemental questions for select substances, including mists from strong inorganic acids | Larynx (161)          | <i>Strong inorganic Acid mists:</i><br>Ever exposed<br>1-20 years<br>21+ years | 46<br>12<br>34       | <b>OR</b><br>1.6 (0.9-2.6)<br>1.2 (0.6-2.5)<br>1.8 (1.1-3.1) | Age, residence, education, cigarettes, and alcohol<br>Ever & ≤35 packyears 1.1 (0.4-3.1)<br>Ever & >35 packyears 11.6 (5.5-24.2) | Unexposed (to acid mists) are the referent group  |
| Eisen, et al. (1994) USA             | 108 cases (99% male) within cohort of 45,000 auto workers                       | 538 controls matched by year of birth, plant, race, and gender                              | Work histories + measurements + exposure tables   | Larynx (161)          | <i>Acid mists:</i><br>1 exposure year  | (not reported)       | <b>OR</b><br>0.90 (0.66-1.22)                                | Metalworking fluids  | No employment data past 1985; focus is metalworking fluids, not acid mists. Acid mists only at 2 of the 3 plants and “only a small number of jobs were linked with acid mist exposure”. |

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| Olsen & Sabroe (1984) Denmark                             | 326 cases (50 women, 276 men)   | 1134 (971 men, 163 women) matched by sex, birthdate, residence              | Questions about exposure to specific agents, latest job, longest job                     | Larynx (161)          | Battery chemicals<br>Acids/lye   | 16 men<br>43 (36 men, 7 women) | 1.3 (0.7-2.4)<br>1.3 (0.9-1.9)   | Age, tobacco, alcohol, and sex where relevant                                | “Battery chemicals” not enumerated.<br>“Acids/lye” not enumerated, and no indication of percentage exposed only to acids.                                    |
| Shangina, et al. (2006) Poland, Romania, Russia, Slovakia | 316 men, age 15-79, histologically or cytologically confirmed                       | 728 hospital controls, frequency-matched by age ±5 years                    | Occupational histories evaluated by industrial hygienists blinded to case/control status | Larynx (161)          | Inorganic acid mist  | 37                             | <b>OR</b><br>0.94 (0.6-1.5)  | Age, country, tobacco, and alcohol   | “Inorganic acids” not enumerated<br>For 34 hypopharyngeal cases, results for acid mist were not presented  |
| Soskolne, et al. (1992) Canada                            | 204 cases histologically confirmed, including 183 men with sulfuric acid assessment | 204 neighbourhood referents including 183 men with sulfuric acid assessment | Retrospective assessment sulfuric acid exposure for each job                             | Larynx (161)          | <i>Sulfuric acid</i><br>≤10 years, probable exposure<br>≤10 years, substantial exposure<br>>10 years, probable exposure<br>>10 years, substantial exposure | 23<br>6<br>34<br>19            | <b>OR</b><br>1.97 (0.63-6.1)<br>3.57 (1.19-10.7)<br>4.3 (1.69-10.9)<br>5.57 (2.0-15.5) | Includes a 5-year lag period, adjusted for cigarette and alcohol consumption | Substantial exposure = medium or high concentration, frequency ≥5% of workday, certainty probable or certain; probable exposure = all other lesser exposures |

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| Zemła, et al. (1987) Poland          | 328 men presenting to Institute of Oncology in Gliwice           | 656 men without cancer   | "History of professional hazards"  | Larynx (161)          | Constant exposure to vapors of sulfuric, hydrochloric, or nitric acid                                | 11                   | <b>RR</b><br>4.27 (p<0.001)   | Unadjusted; 92% of patients and 83% of controls were smokers; 97% of patients and 96% of controls drank alcohol. | No information as to whether work histories were recorded & then classified by researchers or participants were asked about specific exposures                                |
| Petrauskaitė et al. (2002) Lithuania | 277 men of Lithuanian nationality who lived in Kėdainiai ≥1 year | 1108 men : deceased (not lung cancer) of Lithuanian nationality who lived in Kėdainiai ≥1 year, frequency matched by 5-year age groups and year of death | Questionnaire with residential & occupational history completed by next of kin | Lung                  | Residence within 5 km of sulfuric acid factory (ambient sulfuric acid level ~100 µg/m <sup>3</sup> ) | 96                   | <b>OR</b><br>1.03 (0.76-1.39) | Age, year of death, smoking, and occupation  | 92 controls worked at the factory, 304 controls lived in the exposed area, and 915 controls worked in chemical plants; these exposures might have contributed to their deaths |
|                                      |  |  |  |                       | Employment at the factory  | 14                   | 0.56 (0.3-1.0)                |  |   |
|                                      |  |  |  |                       | Residence within 5 km, excluding chemical plant workers  | 82                   | 1.08 (0.79-1.48)              |  |   |

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| Rachtan (2002) Poland                | 242 women with primary carcinoma, histologically verified, admitted to M. Skłodowska-Curie Memorial Institute | 352 women, next-of-kin of other patients (without tobacco related cancer) hospitalized at the same time  | Interview with occupational history, questions about occupational exposure to certain dusts, fumes, chemicals | Lung                  | Ever exposed to sulfuric and/or hydrochloric acid fumes | 13                   | 24 (2.85-201)<br>43 (3.85-480) | Age, pack-years<br>Pack-years, second-hand tobacco smoke, sibling cancer, coal dust, rubber, vodka, margarine, carrots, other vegetables | Matching criteria, if any, other than being at the hospital at the same time not stated. Bias because cases three times as likely as controls to have had occupational exposure. (Perhaps nonemployed next-of-kin preferentially are at the hospital?) |
| Yamaguchi, et al. (1992) Japan       | 144 (117 male, 27 female) hospitalized histologically confirmed cases   | 676 patients (479 male, 197 female) hospitalized 1989-1990 in same ward without lung cancer, matched on hospital, sex, and 5-year age category | Questionnaire on smoking and history of occupations, exposure to chemicals)                                   | Lung                  | Any inorganic acid/base exposure                        | 5                    | <b>RR</b><br>4.03 (1.1-15.5)   | Smoking status, any exposure to asbestos, dust, organic chemicals, metals, or "other" selected substances                                | Inorganic acid/base sulfuric, hydrochloric, or phosphoric acid, ammonia, ammonium sulfate, or lime   |

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| Cocco, et al. (1998) USA             | 1056 cases (1023 white men, 33 black men) age 20+: death certificates coded for occupation and industry | 5280 men who died of nonmalignant diseases, 5:1 matched to cases by region, race, and 5-year age group | Occupation and industry linked to job exposure matrix with estimated level and probability of 12 exposures | Gastric cardia (151.0) | <b>Sulfuric acid</b>         | 294                  | <b>OR</b><br>1.2 (1.0-1.4) |                                      | Referent group is those unexposed Occupation and industry on death certificate may be last but not longest-held employment; no data on lifestyle confounders. Analysis by probability and intensity of exposure only included white men |
|                                      |   |  |  |                        | Any exposure                 |                      |                            |                                      |   |
|                                      |   |  |  |                        | <i>Exposure probability:</i> |                      |                            |                                      |   |
|                                      |   |  |  |                        | Low                          | 229                  | 1.1 (0.9-1.3)              |                                      |   |
|                                      |   |  |  |                        | Medium                       | 35                   | 1.4 (0.9-2.1)              |                                      |   |
|                                      |   |  |  |                        | High                         | 30                   | 1.3 (0.8-2.1)              |                                      |   |
|                                      |   |  |  |                        |                              |                      | <i>P</i> -trend <0.05      |                                      |   |
| <i>Exposure intensity:</i>           |   |  |  |                        |                              |                      |                            |                                      |   |
| Low                                  | 209   | 1.1 (0.9-1.3)  |  |                        |                              |                      |                            |                                      |   |
| Medium                               | 74  | 1.5 (1.1-2.0)  |  |                        |                              |                      |                            |                                      |   |
| High                                 | 11  | 1.8 (0.9-3.8)  |  |                        |                              |                      |                            |                                      |   |
|                                      |   | <i>P</i> -trend <0.01  |  |                        |                              |                      |                            |                                      |   |

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| Cocco, et al. (1999) USA             | 41957 cases (20878 white men; 4125 white women; 4215 black men; 2739 black women) age 25+: death certificates coded for occupation and industry, homemakers excluded | Decedents of nonmalignant diseases, 2:1 matched to cases by region, race, sex, and 5-year age group | Occupation and industry linked to job exposure matrix with estimated level and probability of 12 exposure | Stomach               | <i>Sulfuric acid intensity</i> |                      | <b>OR</b>               |                                      |          | Referent group is those unexposed Occupation and industry on death certificate may be last but not longest-held employment; no data on lifestyle confounders |                       |
|                                      |  |   |   |                       | White men                      |                      |                         |                                      |          |  |                       |
|                                      |  |   |   |                       | Low                            | 4113                 |                         |                                      |          |  | 0.99 (0.95-1.03)      |
|                                      |  |   |   |                       | Medium                         | 1274                 |                         |                                      |          |  | 1.03 (0.96-1.11)      |
|                                      |  |   |   |                       | High                           | 263                  |                         |                                      |          |  | 1.23 (1.05-1.44)      |
|                                      |  |   |   |                       |                                |                      |                         |                                      |          |  | <i>P</i> -trend <0.01 |
|                                      |  |   |   |                       | Black men                      |                      |                         |                                      |          |  |                       |
|                                      |  |   |   |                       | Low                            | 1232                 |                         |                                      |          |  | 1.04 (0.96-1.14)      |
|                                      |  |   |   |                       | Medium                         | 228                  |                         |                                      |          |  | 1.05 (0.89-1.24)      |
|                                      |  |   |   |                       | High                           | 77                   |                         |                                      |          |  | 1.11 (0.83-1.47)      |
|                                      |  |   |   |                       | White women                    |                      |                         |                                      |          |  |                       |
|                                      |  |   |   |                       | Low                            | 565                  |                         |                                      |          |  | 0.88 (0.79-0.98)      |
|                                      |  |   |   |                       | Medium                         | 19                   |                         |                                      |          |  | 1.04 (0.91-1.19)      |
| High                                 | 13   | 0.78 (0.41-1.49)  |   |                       |                                |                      |                         |                                      |          |  |                       |
| Black women                          |  |   |   |                       |                                |                      |                         |                                      |          |  |                       |
| Low                                  | 212  | 1.09 (0.90-1.32)  |   |                       |                                |                      |                         |                                      |          |  |                       |
| Medium                               | 420  | 0.96 (0.79-1.16)  |   |                       |                                |                      |                         |                                      |          |  |                       |
| High                                 | 4  | 0.55 (0.18-1.68)  |   |                       |                                |                      |                         |                                      |          |  |                       |