Occupational Medicine, 2024, **74**, 632–638
https://doi.org/10.1093/occmed/kqae089

OXFORD

Original Papers

Strong inorganic acid mists and respiratory tract cancers: a meta-analysis

M. S. Seyyedsalehi[1,2], A. Di Lorenzo[3], L. Vimercati[3] and P. Boffetta[1,4,5]

[1]Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy
[2]Cancer Research Center, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran
[3]Interdisciplinary Department of Medicine, University of Bari, 70124 Bari, Italy
[4]Stony Brook Cancer Center, Stony Brook University, Stony Brook, NY, USA
[5]Department of Family, Population and Preventive Medicine, Renaissance School of Medicine, Stony Brook University, Stony Brook, NY, USA

Correspondence to: P. Boffetta, Department of Medical and Surgical Sciences, University of Bologna, Via Massarenti 9, 40138 Bologna, Italy.
E-mail: paolo.boffetta@unibo.it

Background: Exposure to strong inorganic acid mists (SIAMs) in the workplace has been linked to respiratory tract cancers.
Aims: We conducted a meta-analysis of cohort and case–control studies examining the association between occupational SIAMs and respiratory tract cancers other than laryngeal cancer, which is already established.

Methods: Studies mentioned in the 1992 IARC Monograph on carcinogenicity of SIAMs were combined with later studies identified from a systematic search of Scopus, PubMed and Embase. Forest plots of relative risks (RR) and odds ratios were constructed for the 34 identified studies. A random-effects model was used to address heterogeneity.

Results: An association between the roles associated with occupational SIAMs exposure and risk of lung (RR = 1.17; 95% confidence interval [CI] = 1.05–1.32), and nasal cancers (RR = 3.30, 95% CI = 1.16–9.41) was found. The risk of oral and pharyngeal cancer was also associated with SIAMs exposure-related roles (RR = 1.59, 95% CI = 0.98–2.57). Results did not differ by study design, gender or outcome for all three cancers. A positive association for lung cancer was found with chemical (RR = 1.25, 95% CI = 1.13–1.38), and metal and steel industries (RR = 1.19, 95% CI = 1.04–1.37), as well as for oral and pharyngeal cancer with chemical industry (RR = 1.72, 95% CI = 1.57–1.89). We checked publication bias for lung (p = 0.35), oral and pharyngeal (p = 0.02) and nasal cancer (p = 0.40).

Conclusions: Our study showed an association between occupational SIAM exposure and risk of lung, nasal, and possibly oral and pharyngeal cancers. However, weaknesses in the recording of confounding and exposure data in the currently available literature were found.

INTRODUCTION

Respiratory tract cancers are the leading cause of death due to cancer worldwide, and the rate in males is more than twice that in females [1]. Risk factors identified for respiratory cancers include smoking for lung, oral cavity and pharynx cancers; alcohol for oral cavity and pharynx cancers; as well as occupational and environmental carcinogens, such as wood dust for sinonasal cancers. Occupational exposure to sulphuric acid and other strong inorganic acid mists (SIAMs) such as hydrochloric, nitric, hydrofluoric and phosphoric acids have also been identified as risk factors [2,3].

Sulphuric acid is the most used strong inorganic acid in industrial processes globally. This group of agents is most commonly absorbed through the respiratory tract, but also through the skin and by oral ingestion. However, it is important to note that the toxicity is largely due to effects at the site of initial contact, though systemic effects may be observed such as metabolic acidosis, hypoxia, respiratory failure and acute renal failure [4,5].

There are many industrial processes that can generate strong acids, including pickling and other acid treatments of steel and other metals, copper smelting, lead batteries, phosphate fertilizer production and the synthesis of various chemicals, including strong acids [6,7]. In 1991, the International Agency for Research on Cancer (IARC) released a report indicating that exposure to SIAM is carcinogenic for laryngeal cancer. The IARC subsequently updated their evaluation in 2012, categorizing Mists from Strong Inorganic Acids as a Group 1 carcinogen for humans for laryngeal cancer, and with a positive association with lung cancer [6]. While there exists a positive correlation between SIAM exposure and cancer in other respiratory organs, this had not yet been definitively established. Limited information on the possible mechanism of carcinogenicity of inorganic acid mists is available, especially in experimental animals [8,9]. However, previous reports indicate that acid mist, depending on its droplet size and other characteristics, can infiltrate

Key learning points

What is already known about this subject:

- Strong inorganic acid mists may be produced during various industrial processes, including pickling, copper smelting, lead batteries and phosphate fertilizers manufacturing.
- Sulphuric acid is, however, the most pervasive of the strong inorganic acids used in industrial processes globally.
- According to the International Agency for Research on Cancer, sufficient evidence exists that strong inorganic acid mists are carcinogenic to humans, in particular laryngeal cancer.

What this study adds:

- This is the first meta-analysis conducted to investigate the association between strong inorganic acid mist exposure and the risk of respiratory cancers other than the larynx.
- Our results showed an association between occupational strong inorganic acid mist exposure and cancers of the respiratory tract other than laryngeal cancer, particularly cancers of the lung and of the nasal cavity, sinuses and nasopharynx.
- An association was observed between employment in the chemical and the metal and steel industries and the risk of lung and oral and pharyngeal cancer.

What impact this may have on practice, policy or procedure:

- Using these results will help prepare protective guidelines and equipment better and be more attentive to their use.
- Furthermore, this study recommends paying attention to countries other than North America and Europe where information is limited.

various parts of the respiratory system, and compromise the defence mechanisms of the respiratory tract potentially leading to harmful effects [4,6].

To our knowledge, no meta-analysis has been conducted to investigate the association between SIAM exposure and the risk of respiratory cancers other than the larynx. Conducting a meta-analysis can provide a comprehensive assessment, identify sources of heterogeneity, detect small but significant effects, and offer a quantitative summary of the evidence. These results can contribute to a better understanding of the need for protective measures in the workplace. Thus, the current study aims to address the current state of scientific evidence regarding the association between SIAM exposure and incidence and mortality of respiratory cancers other than laryngeal cancer.

METHODS

The reference lists in the IARC Monograph on carcinogenicity of SIAMs [6] were supplemented with searches of English, Spanish, French, Italian, and German languages peer-reviewed publications with no limit to year of publication on three databases: MEDLINE (PubMed), SCOPUS and EMBASE (Ovid) up to 10 April 2023. The studies identified reported results on incidence or mortality from cancers of the lung and upper respiratory tract cancers (nasal cavity and sinuses, pharynx) and occupational exposure to SIAMs. As most reports relating to pharyngeal cancer also include the oral cavity, these were included in the analysis. We excluded laryngeal cancer because an association with SIAM exposure has been established [6]. The search strategy was designed using MeSH terms (neoplasms OR carcinoma OR cancer OR malignant [Title/Abstract]) AND (acid mist OR nitric acid OR hydrochloric acid OR sulphuric acid [Title/Abstract]).

We included cohort studies, including nested case–control analyses and case–control studies of workers employed in industries and occupations in which SIAMs represent a major source of exposure and the exposure assessment approach was defined. Manufacturing of phosphate fertilizers, batteries, steel pickling, cellophane, titanium dioxide, petroleum refinery, electrochemical drilling, uranium ore processing, and isopropyl alcohol, surface-active agents, ammonium sulfate, methyl methacrylate, hydrofluoric acid and aluminium sulphate are examples. Community-based case–control studies were included if they reported results on occupational exposure to SIAMs accessed via job-exposure matrices or expert evaluation of questionnaires or other records. We excluded studies of workers mainly exposed to other respiratory carcinogens, including mixtures of polycyclic aromatic hydrocarbons (PAHs), including diesel exhaust, asbestos, crystalline silica and heavy metals. Studies involving animals, biomarkers in blood and tissue samples, intervention studies, studies restricted to laryngeal cancer and environmental studies were excluded. Duplicate and irrelevant references were eliminated. Moreover, the reference lists of each study were reviewed for possible additional relevant studies. If a report included pooled data from multiple studies, we excluded the primary studies to avoid double counting. The most informative report was included if multiple reports were based on the same population. A study protocol was registered in the PROSPERO database (Registration No. CRD42023415107), and the meta-analysis was performed and reported according to the PRISMA statement [10].

The extraction file included information about the original studies, such as the author's name, publication year, country, study design (case–control or cohort), subject characteristics (gender, age, ethnicity), sample size (number of cases and controls), sampling method, type of cancer, type of acid, period of exposure, duration and level of exposure, as well as follow-up periods (cohort studies) or recruitment periods (case–control studies). In addition, effect size measures such as relative risk (RR), odds ratio (OR), risk ratio, rate ratio, standardized mortality ratio (SMR) and standardized incidence ratio (SIR) were extracted, as well as their 95% confidence intervals (CI).

Results for subgroups of subjects (e.g. by gender, type of job or level or duration of exposure) were also abstracted. If only the results for subgroups were reported, we combined them using a fixed-effects meta-analysis. In cases where RR or CI were not reported, we calculated them from the raw data. During all phases of the review process, including reviewing titles and abstracts, selecting articles based on their full texts, and abstracting data, two reviewers (M.S.S. and A.D.L.) worked independently. In cases of disagreement or doubt, results were discussed with a

third reviewer (P.B.) until consensus was reached. In addition, two independent reviewers (M.S.S. and A.D.L.) critically appraised eligible studies using a modified version of Newcastle–Ottawa Scale (NOS) for case–control (10 items) and cohort (9 items) studies [11] (Table 1, available as Supplementary data at *Occupational Medicine* online). Any disagreements that arose were resolved through discussion, or with a third reviewer (P.B.). Those studies with a score of <7.5 corresponded to low quality and those with a score of ≥7.5 reflected high quality.

Occupational exposure to SIAMs and incidence and mortality from respiratory tract cancers other than laryngeal cancer (cancer of nasal cavity, nasal sinuses, pharynx including oral cavity, and lung) was assessed, based on the effect size measures and the corresponding 95% CIs of each study. Because of the rare disease assumption, the different risk assessments are assumed to approximate the RRs [12]. Studies were evaluated for heterogeneity (het.) using the *Q* test, which compares variations across studies rather than within studies, and the I^2 statistic (the percentage of variance attributable to study heterogeneity in a meta-analysis) [13]. A random-effects model was used to account for heterogeneity in design characteristics between the cohort and case–control studies included in the meta-analysis [14]. A meta-analysis including all non-overlapping studies was followed by stratified analyses by anatomical sites: (i) lung, (ii) oral cavity, oropharynx and hypopharynx (abbreviated as pharynx), (iii) nasal cavity, nasal sinuses and nasopharynx (abbreviated as nose); pharyngeal cancer not otherwise specified was included in group (ii). The studies were also stratified by geographic region (North American, European, Asian countries), study design (cohort, case–control), quality score (low, high), outcome (incidence, mortality), year of publication (<2000, ≥2000), year of first employment (<1965, ≥1965), industry type (chemical industry, inorganic acid production, metal and steel industry, other), control of potential confounders (only adjusted for gender, age and calendar period; adjusted for additional factors, particularly tobacco smoking), exposure level (low, high, based on study-specific categories) and gender (both genders, predominantly [>75%] males). We also conducted a sensitivity analysis in which the meta-analysis was repeated after leaving out one study at a time. In addition, publication bias was examined by creating a funnel plot and applying a regression asymmetry test [15]. STATA version 14.0 (Stata, College Station, TX) was used for all analyses.

RESULTS

Based on literature searches and selection criteria, 33 [7,16–48] independent studies were identified in the review and meta-analysis, of which 7 were case–control [16–22,48] and 26 a cohort design [7,23–47]. Figure 1 shows the flow diagram of the literature searches and the study selection process.

Details on these studies are provided in Table 2 (available as Supplementary data at *Occupational Medicine* online). These studies reported a total of 28 risk estimates for lung cancer [7,16–18,20,23–27,29–41,44–48], 9 for pharyngeal cancer [7,25,31,36–39,41,46] and 6 for nasal cancer [7,17,19,22,39,42].

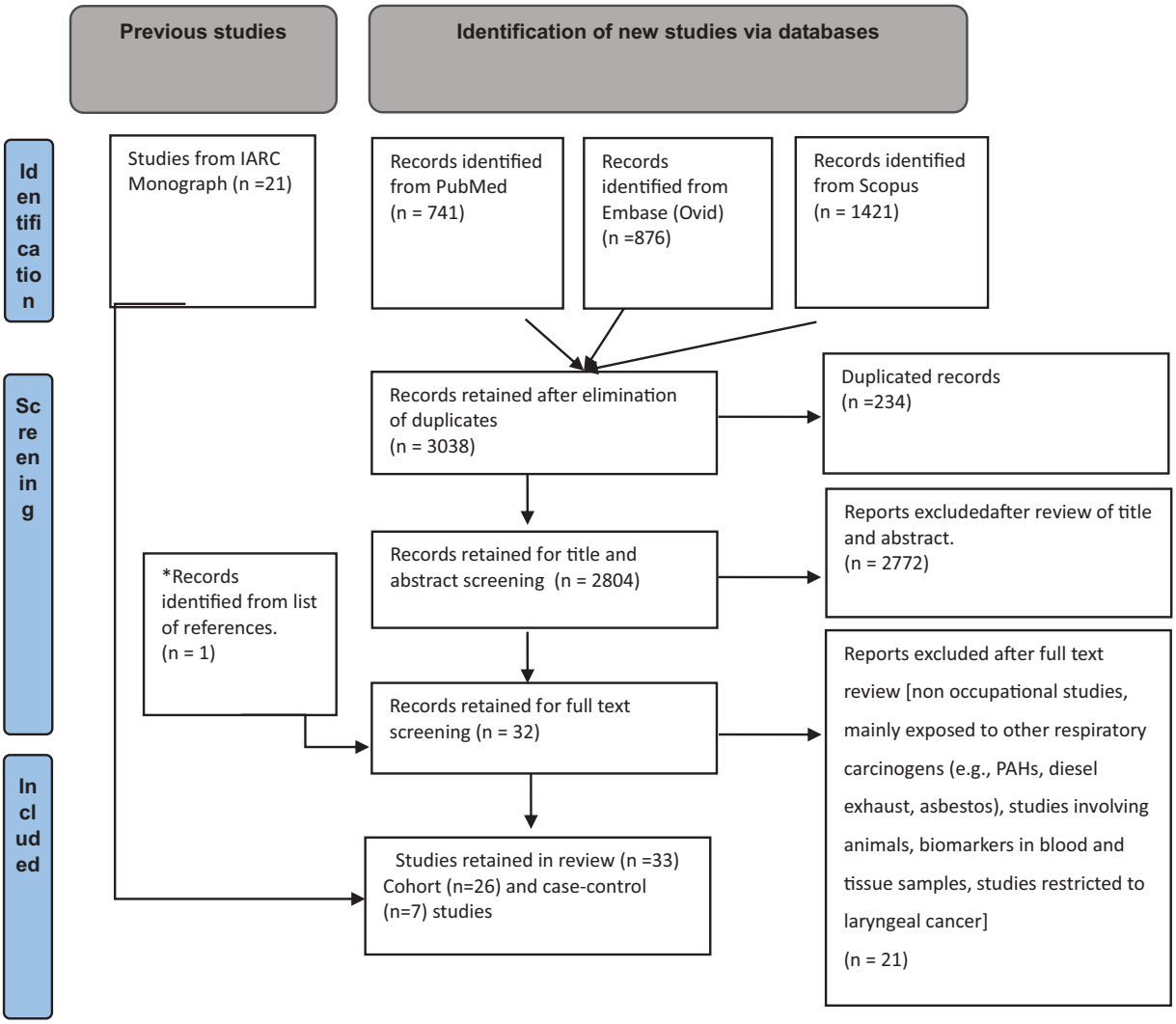
We detected an association between ever-occupational exposure to SIAMs and lung cancer (RR = 1.18, 95% CI = 1.05–1.33; I^2 = 64%, *P*-het = <0.001), and nasal cancer (RR = 3.30, 95% CI = 1.16–9.41; I^2 = 87%, *P*-het = <0.001), whereas the RR for pharyngeal cancer was 1.59 (95% CI = 0.98–2.57; I^2 = 87%, *P*-het = <0.001) (Figures 2–4, available as Supplementary data at *Occupational Medicine* online). Publication bias was checked through the Egger test and the examination of the funnel plot for lung cancer (P = 0.35), oral and pharyngeal cancers, (P = 0.02), nasal cavity, sinuses and nasopharynx cancers (P = 0.40) (Figure 5, available as Supplementary data at *Occupational Medicine* online).

Results of stratified analyses for different subsites of respiratory cancer according to selected characteristics are reported in Table 4 (available as Supplementary data at *Occupational Medicine* online). These results showed that the risk of lung (RR = 1.27, 95% CI = 1.11–1.46, P = 0.05) and nasal cancers (RR = 24.29, 95% CI = 9.86–59.84, P < 0.001) was higher for studies published before 2000 year. According to years of first employment, we found a higher RR before 1965 for oral and pharyngeal cancer (RR = 1.97, 95% CI = 1.11–3.50, *P*-het = 0.43), and for nasal cavity, sinonasal and nasopharyngeal cancer (RR = 50, 95% CI = 5.03–497, *P*-het = 0.003). Also, we identified heterogeneity in results for pharyngeal (p = 0.024) and nasal cancers (P < 0.001) by geographic region. The focus of most studies was on exposure to sulphuric acid; stratification based on the type of acid was not informative. The stratification analysis according to control for potential confounding, showed a difference for oral and pharyngeal cancer (p-het = 0.004), and nasal cavity, sinonasal and nasopharyngeal cancer (*P*-het < 0.001), but not for lung cancer (p-het = 0.52). There was no difference in results between geographic region (p-het = 0.63) for lung cancer, study design, outcome and gender. Results were also consistent in the leave-one-out meta-analysis (Figure 1, available as Supplementary data at *Occupational Medicine* online) .

Stratified analyses according to industry type showed an association between employment in the chemical (RR = 1.25, 95% CI = 1.13–1.38) and metal and steel industries (RR = 1.19, 95% CI = 1.04–1.37) and lung cancer (*P*-het = 0.08), as well as between employment in the chemical industry and oral and pharyngeal cancer (RR = 1.72, 95% CI = 1.57–1.89, *P*-het = 0.008), and between employment in inorganic acid production (RR = 24.29, 95% CI = 9.86–59.84, *P*-het < 0.001) and sinonasal cancer (Table 4, available as Supplementary data at *Occupational Medicine* online). The number of studies of non-laryngeal respiratory cancer, which reported results on exposure level was limited (n = 6; details on dose categories are reported in Table 3, available as Supplementary data at *Occupational Medicine* online); however, we did not find a difference between the meta-analyses of results on low and high exposure (*P*-het = 0.77). Because of the limited number of studies, we were unable to repeat this analysis separately for different subsites (results not shown in detail).

DISCUSSION

Our meta-analysis identified an association between occupational SIAM exposure and cancers of the respiratory tract other than laryngeal cancer, particularly cancers of the lung and of the nasal cavity, sinuses and nasopharynx. While statistically



*Soskolne CL. Ph.D. dissertation, University of Pennsylvania. "Upper respiratory cancer among refinery and chemical plant workers: a case-control study in Baton Rouge, Louisiana" (1982, 327 pp.). Published by University Microfilms International. (Order No. DA 8217180). This study didn't report results for non-laryngeal cancer.

Figure 1. Selection of studies for inclusion in the review and meta-analysis. *Soskolne CL. PhD dissertation, University of Pennsylvania. 'Upper respiratory cancer among refinery and chemical plant workers: a case-control study in Baton Rouge, Louisiana' (1982, 327 pp.). Published by University Microfilms International. (Order No. DA 8217180). This study did not report results for non-laryngeal cancer.

significant, the risk estimates for these cancers are, however, lower than those for laryngeal cancer.

SIAMs are generated in multiple industrial processes. Although in most cases the mists contain sulphuric acid, exposure to other strong acids, such as hydrochloric, nitric, hydrofluoric and phosphoric acid may occur [49,50]. SIAMs are highly reactive agents that can lead to acute, chronic and severe complications, including inflammation of the mouth, and airway damage [5,51–53]. In 1991, occupational exposure to inorganic acid mists containing sulphuric acid was classified by IARC as carcinogenic to humans, based on an association with laryngeal and lung cancer [6,21]. We note that the epidemiological evidence upon which this designation was reached was from studies noting long-term, high-level exposures being at the highest risk for carcinogenicity.

The foundational study for the IARC evaluation was published in 1984 [54]. This article also reflects on mechanisms of action, several of which can be proposed for the association between exposure to SIAMs and respiratory cancer more broadly. First, these agents can cause sensitivity of epithelial cells in conjunction with cigarette smoking and change inflammatory mediators' activities [51]. Inflammation is a critical component of cancer progression. Cancer is often triggered by infections, chronic irritations and inflammation. An essential part of the neoplastic process is the cancer microenvironment, which is largely orchestrated by inflammatory cells [55]. In addition, SIAMs can exert a direct genotoxic effect due to pH modification. These agents are irritants, and small aerosol particles may reach the respiratory mucosa and cause genetic damage by locally lowering pH [9,56,57]. A low pH can lead to chromosomal

aberrations, sister chromatid exchanges, micronuclei and gene mutations. Also, highly hydrophilic molecules may deposit in the nose and mouth, having similar effects via acute and chronic irritation of the mucosa, leading to soft tissue damage, such as mucosal ulcers. Considering previous studies, poor oral hygiene and chronic ulcers may contribute to cancer development [58–60]. However, no studies of localized pH or *in vivo* chromosomal effects on upper respiratory epithelium have been reported. Furthermore, A few factors, including droplet size, atmospheric concentration and relative humidity, can influence how acid mist droplets are deposited in the respiratory system as well as their reactions in different parts of the respiratory system [4,6,51].

Finally, it must be considered that chemicals in mixtures, like SIAMs, may also interact with one another and modify the magnitude or the nature of their toxic effect [61]. Also, it is possible to hypothesize a synergistic effect of interaction between SIAMs and cigarette smoke in respiratory cancer development.

Several confounding factors can influence the risk of the cancers we included in our meta-analysis. These factors include tobacco smoking and chewing, alcohol drinking, genetic susceptibility, occupational exposures including asbestos, PAHs, wood and leather dust, nickel and chromium, air pollution and viral infections. Because most of the studies included in the analysis, in particular those of cohort design, did not adjust for these factors, residual confounding cannot be ruled out [2,22,62]. We compared results between two groups of studies: those that adjusted only for age, gender and calendar period, mostly cohort studies, and those that adjusted for additional potential confounders such as tobacco smoking, and other occupational exposures. The associations were stronger in the former group of studies; this result is compatible with the hypothesis that a variety of important factors can confound the effect of strong acid mists, so consideration of these factors is important during study design. However, we should pay attention to other sources of bias, because the studies in the two groups have different designs.

The association between SIAM exposure and respiratory cancer was restricted to studies published before 2000. Also, our results according to the year of first employment showed an association before 1965 particularly regarding oral and pharyngeal cancers as well as nasal cavity, sinonasal and nasopharyngeal cancer. This may be explained by the fact that more recent studies investigated circumstances of lower exposure compared to older studies, because of technological developments, improved hygienic conditions, and the enhanced use of workplace protective equipment [63]. Since 1965 until 2011, the prevalence of smoking among adults in the USA has declined by around 20%. The decreasing trend may therefore help reduce the incidence and mortality of respiratory cancers, which are primarily caused by tobacco use [2,64]. To our knowledge, this study is the first systematic review and meta-analysis on the association between occupational SIAM exposure and cancer of the lung, pharynx and nose. An important limitation of our review is the relatively small number of available studies on cancers other than lung cancer and on female workers. For example, only six studies reported risk estimates for nasal cancer. Because of the rarity of such tumours, it is possible that risk estimates were only presented where cases were observed. This could produce a form of publication bias. Furthermore, we found publication bias regarding oral and pharyngeal cancers. In addition, the dose–response analysis was based on a limited number of studies ($n = 6$). Moreover, there is a possibility of exposure misclassification because different studies used different data collection methods, such as environmental measurements, job-exposure matrices, personal interviews and self-reported exposure information, which is a limitation in community-based studies.

Due to potential differences in occupational exposure circumstances between men and women, future studies on the carcinogenicity of SIAMs should consider gender differences. Additionally, each inorganic acid might have specific toxicological properties leading to a different impact on the body, which should be taken into consideration in future studies. Since there were few studies outside North America and Europe, it could be important to reflect on what difference, if any, additional well-designed studies would add if they were to be conducted in other countries. While biological mechanisms of action are unlikely to differ between populations, other important confounders may be different. This review and meta-analysis indicated that occupational SIAM exposure might be associated with lung and nasal cancers, including nasopharynx, as well as, albeit less convincingly, pharyngeal and oral cancer. However, methodological limitations, including residual confounding, prevent a conclusion on the causal nature of the observed association.

ACKNOWLEDGEMENTS

The authors appreciate the help of Germana Giupponi in identifying the articles included in the review.

FUNDING

Internal resources were used by the participating institutions to conduct the study.

COMPETING INTERESTS

None declared.

REFERENCES

1. Sung H, Ferlay J, Siegel RL *et al.* Global Cancer Statistics 2020: GLOBOCAN estimates incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;**71**:209–249.
2. Malhotra J, Malvezzi M, Negri E, La Vecchia C, Boffetta P. Risk factors for lung cancer worldwide. *Eur Respir J* 2016;**48**:889–902.
3. Barsouk A, Aluru JS, Rawla P, Saginala K, Barsouk A. Epidemiology, risk factors, and prevention of head and neck squamous cell carcinoma. *Med Sci* 2023;**11**:42.
4. Hinds WC, Zhu Y. *Aerosol Technology. Properties, Behavior and Measurement of Airborne Particles*. New York: John Wiley & Sons, 2022, Vol. **1**; 3.
5. Chen WL, Chen YY, Wu WT, Lai C-H, Sun Y-S, Wang C-C. Examining relationship between occupational acid exposure and oral health in workplace. *BMC Public Health* 2020;**20**:1371.
6. International Agency for Research on Cancer (IARC). *Occupational exposures to mists and vapours from strong inorganic acids and other industrial chemicals*. Working Group Views and Expert Opinions, Lyon, 1991. Lyon, France: IARC Monographs on the Evaluation of the Carcinogenic Risks of Chemicals to Humans, 1992, Vol. **54**; 1–310.
7. Ker YF, Tsai PJ, Guo HR. Application of standardized proportional mortality ratio to the assessment of health risk in relatively healthy populations: using a study of cancer risk in telecommunication

workers with excess exposure to acid mists as an example. *Int J Environ Res Public Health* 2021;**18**:9870.
8. Swenberg JA, Beauchamp RO. A review of the chronic toxicity, carcinogenicity, and possible mechanisms of action of inorganic acid mists in animals. *Crit Rev Toxicol* 1997;**27**:253–259.
9. Martonen TB, Barnett AE, Miller FJ. Ambient sulfate aerosol deposition in man: modeling the influence of hygroscopicity. *Environ Health Perspect* 1985;**63**:11–24.
10. Moher D, Liberati A, Tetzlaff J *et al.*; The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009;**151**:264–269.
11. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;**25**:603–605.
12. Greenland S. Quantitative methods in the review of epidemiologic literature. *Epidemiol Rev* 1987;**9**:1–30.
13. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;**21**:1539–1558.
14. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;**7**:177–188.
15. Egger M, Davey Smith G, Schneider M, Minder CE. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**:629–634.
16. 't Mannetje A, Bencko V, Brennan P *et al.* Occupational exposure to metal compounds and lung cancer. Results from a multi-center case-control study in Central/Eastern Europe and UK. *Cancer Causes Control* 2011;**22**:1669–1680.
17. Soskolne CL, Jhangri GS, Pagano G *et al*; Acid Study Group P. Using established occupational respiratory cancer risk factors for assessing the internal validity in an unmatched case-control study in the Campania Region of Italy, 1988-1990. *Eur J Oncol.* 2007;**12**:23–29.
18. Grimsrud TK, Berge SR, Haldorsen T, Andersen A. Can lung cancer risk among nickel refinery workers be explained by occupational exposures other than nickel? *Epidemiology* 2005;**16**:146–154.
19. Chen Y, Chang ET, Liu Q *et al.* Occupational exposures and risk of nasopharyngeal carcinoma in a high-risk area: a population-based case-control study. *Cancer* 2021;**127**:2724–2735.
20. Soskolne CL, Jhangri GS, Scott HM *et al.* A population-based case-control study of occupational exposure to acids and the risk of lung cancer: evidence for specificity of association. *Int J Occup Environ Health* 2011;**17**:1–8.
21. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. *Chemical Agents and Related Occupations*. Lyon: International Agency for Research on Cancer, 2012. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 100F. Available from: https://www.ncbi.nlm.nih.gov/books/NBK304416/.
22. d'Errico A, Pasian S, Baratti A *et al.* A case-control study on occupational risk factors for sino-nasal cancer. *Occup Environ Med* 2009;**66**:448–455.
23. Checkoway H, Heyer NJ, Demers PA. An updated mortality follow-up study of Florida phosphate industry workers. *Am J Ind Med* 1996;**30**:452–460.
24. Park RM, Ahn YS, Stayner LT, Kang S-K, Jang J-K. Mortality of iron and steel workers in Korea. *Am J Ind Med* 2005;**48**:194–204.
25. Moulin JJ, Clavel T, Roy D *et al.* Risk of lung cancer in workers producing stainless steel and metallic alloys. *Int Arch Occup Environ Health* 2000;**73**:171–180.
26. Forastiere F, Valesini S, Salimei E, Magliola ME, Perucci CA. Respiratory cancer among soap production workers. *Scand J Work Environ Health* 1987;**13**:258–260.
27. Steenland K, Beaumont J. Further follow-up and adjustment for smoking in a study of lung cancer and acid mists. *Am J Ind Med* 1989;**16**:347–354.
28. Beaumont JJ, Leveton J, Knox K *et al.* Lung cancer mortality in workers exposed to sulfuric acid mist and other acid mists. *J Natl Cancer Inst* 1987;**79**:911–921.
29. Stayner LT, Meinhardt T, Lemen R *et al.* A retrospective cohort mortality study of a phosphate fertilizer production facility. *Arch Environ Health* 1985;**40**:133–138.
30. Al-Dabbagh S, Forman D, Bryson D, Stratton I, Doll R. Mortality of nitrate fertiliser workers. *Br J Ind Med* 1986;**43**:507–515.
31. Bulbulyan MA, Jourenkova NJ, Boffetta P, Astashevsky SV, Mukeria AF, Zaridze DG. Mortality in a cohort of Russian fertilizer workers. *Scand J Work Environ Health* 1996;**22**:27–33.
32. Fandrem SI, Kjuus H, Andersen A, Amlie E. Incidence of cancer among workers in a Norwegian nitrate fertilizer plant. *Br J Ind Med* 1993;**50**:647–652.
33. Hagmar L, Bellander T, Andersson C, Lindén K, Attewell R, Möller T. Cancer morbidity in nitrate fertilizer workers. *Int Arch Occup Environ Health* 1991;**63**:63–67.
34. Rafnsson V, Gunnarsdóttir H. Mortality study of fertiliser manufacturers in Iceland. *Br J Ind Med* 1990;**47**:721–725.
35. Cooper WC, Wong O, Kheifets L. Mortality among employees of lead battery plants and lead-producing plants, 1947–1980. *Scand J Work Environ Health* 1985;**11**:331–345.
36. Sorahan T, Esmen NA. Lung cancer mortality in UK nickel-cadmium battery workers, 1947–2000. *Occup Environ Med* 2004;**61**:108–116.
37. Enterline PE. Importance of sequential exposure in the production of epichlorohydrin and isopropanol. *Ann N Y Acad Sci* 1982;**381**:344–349.
38. Teta MJ, Perlman GD, Ott MG. Mortality study of ethanol and isopropanol production workers at two facilities. *Scand J Work Environ Health* 1992;**18**:90–96.
39. Alderson MR, Rattan NS. Mortality of workers on an isopropyl alcohol plant and two MEK dewaxing plants. *Occup Environ Med* 1980;**37**:85–89.
40. Rapiti E, Fantini F, Dell'Orco V *et al.* Cancer mortality among chemical workers in an Italian plant. *Eur J Epidemiol* 1997;**13**:281–285.
41. Block G, Matanoski GM, Seltser R, Mitchell T. Cancer morbidity and mortality in phosphate workers. *Cancer Res* 1988;**48**:7298–7303.
42. Hueper WC. Occupational and environmental cancers of the respiratory system. *Recent Results Cancer Res* 1966;**3**:1–214.
43. Weil CS, SmythNale HFTW. Quest for a suspected industrial carcinogen. *AMA Arch Ind Hyg Occup Med* 1952;**5**:535–547.
44. Hilt B, Langård S, Andersen A, Rosenberg J. Asbestos exposure, smoking habits, and cancer incidence among production and maintenance workers in an electrochemical plant. *Am J Ind Med* 1985;**8**:565–577.
45. Pesatori AC, Consonni D, Rubagotti M, Bonzini M, Catalano P, Bertazzi PA. Studio di mortalità in una coorte di lavoratori addetti alla produzione di acido solforico [Mortality study in a cohort of workers employed in a plant producing sulphuric acid]. *Med Lav* 2006;**97**:735–748.
46. Coggon D, Pannett B, Wield G. Upper aerodigestive cancer in battery manufacturers and steel workers exposed to mineral acid mists. *Occup Environ Med* 1996;**53**:445–449.
47. Bond GG, Flores GH, Shellenberger RJ, Cartmill JB, Fishbeck WA, Cook RR. Nested case-control study of lung cancer among chemical workers. *Am J Epidemiol* 1986;**124**:53–66.
48. Yamaguchi N, Kido M, Hoshuyama T *et al.* A case-control study on occupational lung cancer risks in an industrialized city of Japan. *Jpn J Cancer Res* 1992;**83**:134–140.
49. Rafieepour A, Dolatshahi NGT, Ghasemkhan AH, Asghari M, Sadeghian M, Asadi A. The effect of the use of NP305 masks in improving respiratory symptoms in workers exposed to sulfuric acid mists in plating and pickling units. *Electron Physician* 2013;**5**:616–622.
50. Hinds WC. Aerosol technology. *Properties, Behavior and Measurement of Airborne Particles*. New York: John Wiley & Sons, 1985; Vol. **6**.
51. Yang JH, Koedrith P, Kang DS *et al.* A putative adverse outcome pathway relevant to carcinogenicity induced by sulfuric acid in strong inorganic acid mists. *J Cancer Prev* 2019;**24**:139–145.
52. Gearhart JM, Schlesinger RB. Sulfuric acid-induced changes in the physiology and structure of the tracheobronchial airways. *Environ Health Perspect* 1989;**79**:127–136.
53. Tuominen M. Occurrence of periodontal pockets and oral soft tissue lesions in relation to sulfuric acid fumes in the working environment. *Acta Odontol Scand* 1991;**49**:261–266.

54. Soskolne CL, Zeighami E, Hanis N *et al*. Laryngeal cancer and occupational exposure to sulfuric acid. *Am J Epidemiol* 1984;**120**:358–369.
55. Coussens LM, Werb Z. Inflammation and cancer. *Nature* 2002;**420**:860–867.
56. US Environmental Protection Agency. *An Acid Aerosols Issue Paper: Health Effects and Aerometrics (EPA Report No. EPA-600/8-88-005F)*. Washington, DC: Office of Health and Environmental Assessment, 1989.
57. Steenland K. Laryngeal cancer incidence among workers exposed to acid mists (United States). *Cancer Causes Control* 1997;**8**:34–38.
58. Ram H, Sarkar J, Kumar H, Konwar R, Bhatt MLB, Mohammad S. Oral cancer: risk factors and molecular pathogenesis. *J Maxillofac Oral Surg* 2011;**10**:132–137.
59. Chaudhuri S, Dey S, Bajpai RC. Prevalence of oral ulcers and its association with addictions in rural population of western Uttar Pradesh and eastern Rajasthan. *J Oral Biol Craniofac Res* 2016;**6**:179–186.
60. Wahi PN, Kehar U, Lahiri B. Factors influencing oral and oropharyngeal cancers in India. *Br J Cancer* 1965;**19**:642–660.
61. Elsa N, Grete O, Larsen JCh. *Toxicological Risk Assessment of Chemicals: A Practical Guide*. New York: Informa Healthcare: CRC Press, 2008.
62. Zheng W, McLaughlin JK, Chow WH, Chien HT, Blot WJ. Risk factors for cancers of the nasal cavity and paranasal sinuses among white men in the United States. *Am J Epidemiol* 1993;**138**:965–972.
63. National Research Council (US) Committee on Toxicology. *Emergency and Continuous Exposure Limits for Selected Airborne Contaminants*. Sulfuric acid. Vol. 1. Washington, DC: National Academies Press, 1984. https://www.ncbi.nlm.nih.gov/books/NBK208279/.
64. Cummings KM, Proctor RN. The changing public image of smoking in the United States: 1964-2014. *Cancer Epidemiol Biomarkers Prev* 2014;**23**:32–36.