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Sulfur Dioxide- and Fluoride-Associated Declines in Lung Function Over an 11-Year Observation Among Aluminum Smelter Workers

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ABSTRACT

Background: Work exposure-related declines in lung function among aluminum smelter workers are well documented, yet task-varying exposures are likely to contribute differently to respiratory outcomes. This study aimed to assess the association between potroom exposure and lung function changes over time among aluminum smelter workers.

Methods: A retrospective review of spirometric assessments of 265 potroom workers and their exposure to sulfur dioxide (SO_2) and fluoride was conducted. Cumulative exposure was described through job exposure matrices by job titles and exposure across the lifetime of employment. Associations between exposure and lung function were determined using mixed-effect models and a 1-year lag exposure.

Results: Exposures were within the prescribed occupational exposure limits. SO_2 was highest in the maintenance section (mean: 0.4 ppm [range 0.3–0.5 ppm]), while the process control section (mean: 1.1 mg/m^3 [range 0.04–2.6 mg/m^3]) had the highest level of fluoride. Among those workers who contributed lung function measures at each of the 10 years ($n = 98$), there was a decline in the percentpredicted forced expiratory volume in 1 second/forced vital capacity ratio (FEV_1/FVC) of 0.21% (95% CI: 0.35–0.07). Within the entire sample, there was an estimated decline of 2.9% (95% CI: −3.9 to −1.9) and 0.15% (95% CI: −0.23 to −0.07) in percentage-predicted FEV_1/FVC, associated with cumulative SO_2 and cumulative fluoride exposure, respectively. A 1-year lagged decline was also seen for the FEV_1/FVC ratio for both pollutants.

Conclusion: SO_2 and fluoride exposure in aluminum smelting is associated with statistically significant lung function declines over the years of exposure.

1 | Introduction

Aluminum smelter workers are exposed to hazards known to have substantial respiratory effects [1–5]. First described in the early 1980s, particularly in Swedish [6], Australian [7], and Canadian [8] smelters, these effects primarily include respiratory symptoms [4], asthma [9, 10], chronic obstructive pulmonary disease [2, 11], and bronchitis [12]. "Potroom Asthma" is the label given to the asthma associated with exposure in aluminum smelting [13]. Lung function changes, in the absence of asthma, are possible among these workers [14]. These health outcomes are associated with exposure to alumina [15], sulfur dioxide and gaseous fluoride [1], and other nonspecific gases produced at the potroom.

Investigation of exposure-related lung function changes in the aluminum industry has largely emerged through cross-sectional studies. A systematic review and meta-analysis, consisting of 15 cross-sectional studies, showed a small but statistically significant reduced percent-predicted forced expiratory volume (FEV_1) in 1 s of −7.53% (95% CI: −13.36 to −1.70), but a similar effect was absent for percent-predicted forced vital capacity (FVC) [16]. The range of reported cross-sectional exposure-related effects varies across these studies, from −0.3% predicted FEV_1 among bauxite-exposed workers [17] to 30% among aluminum-exposed workers [18] when compared to nonexposed, with several studies showing an absence of effect. These variations may result from the selected pollutant for study, levels and duration of exposure, or, as is common with cross-sectional studies, a healthy worker effect [19].

While cross-sectional studies may not characterize the impact of exposure on long-term decline in lung function, the limited cohort studies investigating the longitudinal changes in lung function among employees in the potroom area have suggested exposure-related effects. These cohort studies similarly show variation in the rates of decline. Within a Western Australia inception cohort, a statistically significant annual decline in adjusted FEV_1 (−52.8 [95% CI: −87.2 to −18.3]) was only seen in a sub-sample within the highest exposed group, when compared to nonexposed [20]. In the same cohort, when assessing the effect of caustic mist exposure, a smaller annual decline in FEV_1 was observed (−21.93 [95% CI: −37.04 to −6.83]) in the highest exposure group when compared to a reference group of workers [21]. Previously in the latter cohort, effects varying across exposure types were described: sulfur dioxide was associated with 0.4% (95% CI: 0.1–0.6) decline in FEV_1/FVC, and fluoride exposure was also associated with 0.2% (95% CI: 0.1%–0.6%) decline in FEV_1/FVC [17, 22]. The data from the Norwegian smelters were more convincing, with statistically significant declines in lung function reported across large cohorts followed up over a 6-year [23] and another over a 11-year period [24]. However, in a 6-year follow-up at a British Columbia aluminum smelter, no exposure-related decline in FEV_1 among potroom-exposed workers was found [25].

The aluminum industry is global, with the Asian continent being the largest producer. In Africa, the aluminum smelting industry started in Western Africa in 1960 in Cameroon and Ghana, and then commenced in Southern Africa. In 1971, an aluminum smelting plant was started on the west coast of South Africa, followed by a second plant in the same locality in 1996, driven by South Africa's cheap electricity costs. In 2000, a smelter was opened in Mozambique [19].

The main process of smelting aluminum occurs within the potroom department, where the chemical reaction of reduction using alumina, electricity, and a carbon-based anode takes place. Gaseous SO_2 and fluorides are generated during the process and, depending on the level and duration of exposure, result in adverse respiratory outcomes [4, 10, 26].

The aim of this study was to determine the presence of long-term sulfur dioxide and fluoride exposure-related lung function decline among potroom workers, using well-defined exposure matrices.

2 | Materials and Methods

2.1 | Study Site and Production Process

The study was conducted in the potroom department within an aluminum smelter located in Southern Africa, with an annual production of 575,000 tons of primary aluminum per annum. The smelter consists of five sections in the reduction process: maintenance, where the equipment is repaired, cleaned, and maintained; early life and start up, where the pots are initiated; line services, where the molten aluminum is poured into ingot form; and process control and production, where the actual smelting occurs in pots to form molten aluminum. The plant started recruiting workers in 2001, and production started in 2003.

A total of 388 workers were employed in the reduction area. The production and process control section consisted of 200 workers across four teams working in four shifts in each of four potrooms. The early life and start up sections consisted of 76 workers, also working in four teams across four shifts in each potroom. The maintenance and line sections had 64 workers respectively, working in a single team. Job titles across all sections included the superintendent, shift supervisors, and section-specific operators.

2.2 | Sample Selection

A retrospective cohort study design was used with available data from 2004 to 2014. All workers were assessed each year between 2004 and 2014 at the factory health service as part of their annual medical assessments. These assessments consisted of a standardized respiratory surveillance questionnaire, clinical examination, and a formal lung function test. All potroom workers employed at this aluminum smelter over this 10-year period were eligible to participate in the study. The entry criteria for inclusion into the study required at least 2 years of observation across this 10-year period.

2.3 | Clinical Data

Each worker underwent a clinical assessment annually as part of the medical surveillance program of the company. This assessment was performed by a trained nurse and, if necessary, a more in-depth clinical assessment by the occupational medical doctor at the company. During this assessment, each worker completed a standardized interview, which enquired about their respiratory health and smoking histories, as well as demographic information. Based on the question during the annual surveillance, "What is your smoking status?" with the options: current, never, and former, which were provided as possible responses, smoking was described as former, current, and never smoking. These variables were used to adjust for smoking in the regression models. Data on pack-year tobacco history were not available.

Spirometry was performed as part of this medical surveillance by a trained nurse at the health service. Over the 10-year period, the equipment used was Schiller Spirovit SP-1 and Schiller Spirovit SP-250. The tests were performed according to the American

Thoracic Society (ATS) guidelines [27, 28] with a minimum of three acceptable maneuvers performed. The lung function data were saved in hardcopy in the files of the employee.

Clinical data (interview and spirometry) were extracted from the medical records of each worker for the years of interest (2004–2014) anonymously by giving a number to each record in the presence of the active occupational nurse. These data were captured onto a spreadsheet which allowed for analysis using a repeated measures analysis. Of the 300 eligible workers who commenced during the period, data were available for 88.3% ($n = 265$).

2.4 | Exposure Data

Historical occupational hygiene data collected by the company hygienist were analyzed for this study. Data were available for the years 2007, 2013–2019 for fluoride ($n = 561$), and 2013–2019 for sulfur dioxide ($n = 255$). Sampling for sulfur dioxide and fluorides was performed according to the National Institute of Occupational Safety and Health (NIOSH) Occupational Exposure Sampling Strategy Manual system for each pollutant. Before conducting air monitoring, exposed workers were divided into homogenous exposure groups, which involved job task analysis in relation to exposure profile, and all similarly exposed workers were grouped together, irrespective of their job title. The worker or task with the potential for the highest exposure in a group was then selected for monitoring. If any of the exposure measurements taken on the maximum risk employee/task or subgroups were at or exceeded an action level ($0.475\ mg/m^3$ for fluoride and 2 ppm for sulfur dioxide), then this subgroup was subjected to a more frequent exposure assessment. In certain sections where, following a systematic risk assessment by the hygienist, exposures were likely to be non-existent or very low, further monitoring was not conducted. Levels recorded as less than the detection limit are "normalized" by adjusting them to half of the occupational exposure limit (OEL). A geometric and arithmetic mean from each job for each year was obtained by calculating the mean of all observations obtained for that particular year, for that job.

The company's hygiene records included information on the risk assessments conducted on-site, as well as historical job placement data. The datasets were available as spreadsheets, reporting the concentration of sulfur dioxide and fluoride, the personal sampling method, with full dates of sampling and sampling duration. Data before 2007 were not available and for the other missing years could not be retrieved due to software issues. The hygiene monitoring data were further strengthened through key personnel interviews with the company hygienist and human resources personnel as well as several guided walkthroughs of the potroom during operations.

2.5 | Exposure Characterization

Using the available data for the specific years, data imputation was performed to achieve a more comprehensive exposure data set. Linear regression equations were used to generate exposure estimates for the missing years based on the available data, using job titles, sections, and year.

Each participant was allocated an exposure level based on their job title within a section in any given year of participation in the study. Using these measures, two exposure metrics were employed for the exposure–outcome relationships: (1) exposure measures using the imputed data for all the years that the participant had health outcome measures ("imputed exposure") and (2) a lifetime cumulative exposure. To characterize cumulative exposure for each participant for all years of participation in the study in each job in the different work sections, a cumulative exposure index was constructed for each participant, for each contaminant. The estimates of arithmetic mean exposures for each job were combined with the work history for each study subject, i, to calculate the cumulative exposure for all the years worked at the smelter as provided by the formula:

$$\mathrm{CE}_i = \sum \mathrm{AM}_{ijy}$$

where AM is the arithmetic mean exposure for job of subject i in work section and j in year y.

2.6 | Statistical Analysis

Extracted clinical and exposure data were captured in a Microsoft Excel spreadsheet and imported into STATA 15 [29]. Percent predicted values of the lung function parameters were calculated using the global lung initiative equations, without any race or ethnicity correction [30]. The key outcome variables of interest were percent-predicted FEV_1, percent-predicted FVC, and the predicted ratio of these parameters. Exposure metrics outlined above were included in the analysis both as the current year of the measure and as a 1-year lag measure, to investigate whether the previous exposure year explained variability in lung function.

Descriptive statistics were performed. Skewed data are presented using medians and ranges, and SO_2 and fluoride exposure are presented using geometric means. A subset of the participants for whom data were available for the full 10 years ($n = 98$) was used to analyze the trend of lung function parameters over the 10 years of observation. Mixed-effect models were used to analyze the effect of exposure on lung function, accounting for the correlation of repeated measurements among participants during follow-up. Single pollutant models examined the relationship between lung function and pollutant concentration, using the different exposure metrics and their 1-year lags (relationship between the current year lung function and the previous year level of exposure). Effect estimates derived from the models using sampled exposure data were compared to those derived from the imputed exposure measures models as a sensitivity analysis. All models were adjusted for smoking history (current, never, and past smoker), weight, age, height, and history of tuberculosis.

2.7 | Ethics

The study was approved by the Biomedical Research Ethics Committee at the University of KwaZulu-Natal (BE446/19). The research team was provided with anonymized data from the Company records. Company consent to assess the historical data was obtained. Individual consent of participants was not necessary as only anonymized data were accessed.

3 | Results

There were 545 measurements of fluoride exposure and 255 for SO_2 exposure for potroom department, with 93% in the production section. After imputation, there were 2029 estimated values for fluoride and 1420 for sulfur dioxide. Of the 300 eligible workers who commenced work at potroom during the period, data were available for 88.3% ($n = 265$).

The process control and production sections had the highest mean levels of fluoride while maintenance and early life had the highest levels of sulfur dioxide (Table 1). There was a statistically significant trend with pollutants over time, increasing for SO_2 in the production section and fluoride in the line services section but decreasing over time for all the other sections.

Only four (1.5%) women participated in the study. Most participants were under the age of 29 years at the beginning of study. The average years worked at potroom at the beginning of study was 1.6 years (SD = 1.09) (Table 2).

Prevalence of known allergy and asthma was very low at the first interview (3.77% and 2.64%, respectively) as well as chest tightness at work (0.5%). Lung function of the sample at beginning of study was within normal ranges (Table 3).

At the point of entry into the study, mean percent predicted lung function was within normal limits across the entire sample.

Among those workers who contributed lung function measures at each of the 10 years ($n = 98$), there was a decline in the percent predicted FEV_1/FVC ratio (Figure 1) of 0.21% (p value < 0.01, 95% CI: 0.35–0.07) compared to the increase in 0.1% (p value < 0.01, 95% CI: 0.15–0.03) and 0.32% (p value < 0.01, 95% CI: 0.4–0.23) for the percent predicted FEV_1 and FVC, respectively.

There was an estimated decline of 2.9% (95% CI: −3.9 to −1.9) and 0.15% (95% CI: −0.23 to −0.07) in percentage-predicted FEV_1/FVC, associated with cumulative SO_2 and cumulative fluoride exposure, respectively (Table 4). This effect was not seen for the imputed exposure model. A 1-year lagged decline was also seen for the FEV_1/FVC ratio for both pollutants. The effect was statistically significantly higher at the process control section compared to line services in association with fluoride exposure and higher at maintenance compared to production in association with SO_2 exposure, but not statistically significant (Table S1). The unadjusted estimates are presented in Table S2. Statistically significant cumulative exposure-related associations in the counter-intuitive direction were observed for FEV_1 and FVC, respectively.

4 | Discussion

Our study found a statistically significant exposure-related decline in FEV_1/FVC ratio over a 10-year period in this sample of potroom workers. The study is the first to document a lagged decline in lung function among a cohort of aluminum smelter workers. The decline in the percent predicted FEV_1/FVC ratio with lagged cumulative fluoride exposure suggests a complex exposure–outcome relationship in the aluminum smelting working environment.

Cumulative exposures to both pollutants were associated with significant dose-related declines in the percent-predicted FEV_1/FVC ratio, with a greater effect for SO_2 than fluorides. This finding is consistent with an inception cohort [22] that looked at the cumulative effect of potroom exposures on lung function. In this latter study, a decline of 0.40% (95% CI: 0.72 to −0.17) of FEV_1/FVC ratio and 0.55% (95% CI: 0.79 to −0.31) for unit increase in cumulative exposure to fluoride and SO_2, respectively, was reported. We report a 0.15% (95% CI: 0.23 to −0.07) and 2.9% (95% CI: −3.97 to −1.83) decline in the percentage predicted of the FEV_1/FVC ratio for cumulative exposure to fluoride and cumulative exposure to sulfur dioxide, respectively. The differences across the studies may be due to several reasons, including differences in the predictive equations used to calculate lung function parameters [31, 32], as well as varying cumulative exposure across cohorts.

TABLE 1 | SO_2 and fluoride measurements by section (2004–2014).

	Production	Line services	Process control	Early life and start up	Maintenance
Sulfur dioxide (ppm) (mean SD, range)	0.02 (0.03) (0.009–0.1) ($n = 1246$)	No measurements taken	0.05 (0.02) (0.02–0.09) ($n = 105$)	0.2 (0.1) (0.03–0.4) ($n = 49$)	0.4 (0.1) (0.3–0.5) ($n = 20$)
SO_2 trend over years (rho**)	0.69		−0.93	−0.95	−0.86
Fluoride (mg/m^3) (mean SD, range)	0.3 (0.1) (0.1–0.5) ($n = 1246$)	0.04 (0.03) (0.03–0.05) ($n = 54$)	1.1 (0.8) (0.04–2.6) ($n = 204$)	0.3 (0.1) (0.2–0.7) ($n = 66$)	0.08 (0.04) (0.02–0.1) ($n = 49$)
Fluoride trend over the years (rho**)	−0.86	0.91	−0.52	−0.83	0.01

**$p < 0.05$, $p < 0.01$.

TABLE 2 | Participants at entry into the study by section.

Year of study entry	Production ($n = 171$) Number (%)	Line services ($n = 51$) Number (%)	Early life and start up ($n = 4$) Number (%)	Process control ($n = 29$) Number (%)	Maintenance ($n = 10$) Number (%)
2004	74 (43.27)	24 (47.05)	2 (50)	10 (34.48)	0
2005	3 (1.75)	3 (5.88)	0	0	2 (20)
2006	6 (3.50)	2 (3.92)	0	2 (6.89)	1 (10)
2007	16 (9.35)	11 (21.56)	1 (25)	1 (3.44)	1 (10)
2008	4 (2.33)	1 (1.96)	0	1 (3.44)	1 (10)
2009	28 (16.37)	3 (5.88)	0	4 (13.79)	0
2010	16 (9.35)	4 (7.84)	0	3 (10.34)	2 (20)
2011	7 (4.09)	1 (1.96)	0	4 (13.79)	1 (10)
2012	2 (1.17)	2 (3.92)	0	1 (3.44)	0
2013	15 (8.77)	0	1 (25)	3 (10.34)	2 (20)
2014	0	0	0	0	0
Sex					
Male	168 (98.24)	51 (100)	4 (100)	28 (96.55)	10 (100)
Female	3 (1.75)	0	0	1 (3.44)	0
Age (years)					
< 25	62 (36.25)	13 (25.49)	1 (25)	6 (20.68)	5 (50)
25–29	57 (33.33)	25 (49.01)	1 (25)	11 (37.93)	0
30–34	38 (22.22)	7 (13.72)	2 (50)	8 (27.58)	2 (20)
> 35	14 (8.18)	6 (11.76)	0	4 (13.79)	3 (30)
Median age (years [range])[a]	27 (19–44)	27 (20–43)	29 (23–33)	28 (23–43)	24.5 (21–48)
Current smoker[a]	12 (7.01)	4 (7.84)	1 (25)	1 (3.45)	0
Ex-smoker[a]	1 (0.58)	1 (1.96)	0	0	0
Never smoker[a]	158 (92.41)	46 (90.20)	3 (75)	28 (96.54)	100

[a]At the time of entry into study.

TABLE 3 | Mean lung function at entry to the study by section.

	Production	Line services	Early life	Process control	Maintenance
Mean FEV_1 % pred[a] (SD) (range)	93.41 (11.34) (67.72–133.60)	95.21 (11.33) (70.49–131.40)	91.72 (14.76) (75.61–104.68)	94.66 (8.85) (76.78–111.23)	96.41 (12.20) (74.5–111.62)
Mean FVC % pred[a] (SD) (range)	92.85 (11.50) (64.62–124.23)	95.37 (11.68) (69.29–123.68)	95.95 (4.62) (90.64–100.28)	95.23 (9.36) (75.86–111)	98.89 (12.32) (81.26–17.47)
Mean FEV_1/FVC %pred[a] (SD) (range)	100.49 (6.90) (73.27–118.07)	99.66 (5.70) (88.68–110.62)	94.80 (10.83) (82.87–104)	99.26 (7.13) (85.82–115.02)	97.25 (9.27) (86.05–114.60)

[a]Calculated using GLI2012 equations.

The counterintuitive findings of statistically significant increase in FEV_1 and FVC with cumulative exposure could have been due to several uninvestigated reasons, including a healthy worker bias or missing covariate data, particularly smoking or past respiratory health history. However, this may imply that the FEV_1/FVC ratio is a more sensitive marker of exposure-related adverse respiratory effects.

Although not directly comparable with our study design, cross-sectional studies have reported substantial, but not statistically

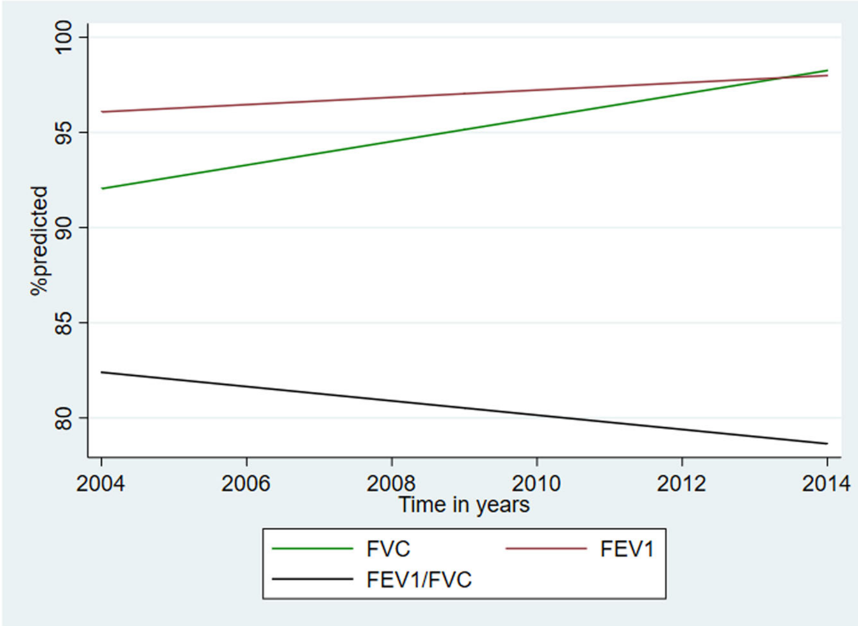

FIGURE 1 | Lung function (as % predicted) trend over 10 years of observation ($n = 98$). [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 4 | Adjusted[a] effect of exposure on lung function parameters.

	% Predicted FEV_1/FVC ratio coefficient p value (95% CI)	% Predicted FVC coefficient p value (95% CI)	% Predicted FEV_1 coefficient p value (95% CI)
Sulfur dioxide			
Cumulative SO_2	**−2.9** **< 0.01 (−3.9 to −1.9)**	5.1 < 0.01 (3.5–6.6)	2.2 < 0.01 (0.8–3.6)
Lag cumulative SO_2	**−2.1** **< 0.01 (−3.2 to −0.9)**	4.8 < 0.01 (3.1–6.6)	2.7 < 0.01 (1.3–4.4)
Imputed SO_2	1.4 0.63 (−4.57 to 7.55)	−2.8 0.52 (−11.71 to 5.93)	−1.6 0.67 (9.45–6.11)
Lag imputed SO_2	−0.1 0.92 (−0.07 to 0.64)	−0.1 0.51 (−0.13 to 0.06)	−0.1 0.43 (−0.12 to 0.05)
Fluoride			
Cumulative fluoride	**−0.15** **< 0.01 (−0.23 to −0.07)**	0.26 < 0.01 (0.13–0.39)	0.09 0.12 (−0.02 to 0.20)
Lag cumulative fluoride	**−0.09** **0.02 (−0.17 to −0.01)**	0.21 0.02 (0.08–0.35)	0.12 0.04 (0.01–0.25)
Imputed fluoride	0.63 0.15 (−0.23 to 1.49)	−0.60 0.36 (−1.90 to 0.70)	0.02 0.97 (−1.11 to 1.15)
Lag imputed fluoride	0.12 0.77 (−0.71 to 0.95)	−0.44 0.50 (−1.76 to 0.86)	−0.38 0.50 (−1.52 to 0.75)

Bold text indicates a statistically significant effect in the expected direction.
[a] Adjusted for smoking and history of tuberculosis.

significant, differences between FEV_1 and FVC in workers exposed to fluorides and sulfur dioxide compared to nonexposed: $FEV_1 = 54$ mL difference (95% CI: −21 to 129) and FVC = 51 mL difference (95% CI: 6−184), for fluoride exposure (levels less than 0.16 mg/m^3); and $FEV_1 = 96$ mL (95% CI: 18–173) and FVC = 95 mL (95% CI: 6–184) to sulfur dioxide (levels below 1.17 mg/m^3 [0.44 ppm]) [4, 33, 34].

While our findings of associations with aluminum smelter-related exposures are consistent with other studies, the lag effect has not been previously reported for occupational exposures. Lagged effects for acute outcomes are biologically plausible, and as the precise mechanisms of action by pollutant at the target organ are generally not clear, exploring a range of exposure–response relationships is important. This is less clear when studying the effects on chronic outcomes. This is particularly so with aluminum smelter exposures, where a range of respiratory outcomes have been documented, from the acute, as in asthma, to chronic outcomes, such as COPD, but also with subclinical declines in pulmonary function [35]. In our study design, using a repeated measures approach, the assumption that each annual exposure measure will be associated with the lung function measure of that year is plausible. However, if our hypothesis that there is a gradual exposure-related decline in lung function holds, then an annual measures analysis will not fully explain the exposure–outcome relationship. Among these workers, with ongoing exposure to respiratory irritants (or allergens) over their lifetime of employment and presumed ongoing deterioration in lung function, lagged analyses with exposure may provide further understanding of the relationships.

Smaller statistically significant lag effects were noted for the cumulative exposure for both pollutants for the FEV_1/FVC ratio, and these were not substantially different from the non-lagged estimates. Although not substantially significant, lagged declines of the ratio were noted for both pollutants using the cumulative exposure metric, compared to an absence of statistically significant effect among the imputed models.

The effect of cumulative exposure of both pollutants, fluoride and sulfur dioxide, shows a significant association with a decline in FEV_1/FVC ratio, suggesting an increased risk of airflow limitation. This finding is consistent with the other cohort study findings [22].

Previous studies at aluminum smelters looked at the potroom as a single department and made comparisons with non-potroom departments. This approach ignores the different sections within the potroom, each of which may have different risk profiles for respiratory outcomes. Maintenance, early life, and start up had the highest mean levels of sulfur dioxide over the 10 years of observation, suggesting there is a heterogeneity of exposure within the potroom.

Controlling for lagged fluoride exposure, workers involved in process control activities presented with a significant difference in the FEV_1 and FVC percentage predicted values compared to line services, which was the section with the lowest mean level of fluoride across the years. When controlling for cumulative exposure to SO_2, there was no statistically significant difference on percentage-predicted FEV_1/FVC ratio among the sections. This could be due to the fact that these sections are the key source of exposure at potroom [36]. The evidence that adverse spirometric effects varied across sections seems to support the view that exposures are not uniform. Lagged exposures have been modeled for different respiratory outcomes in occupational epidemiology because of the inherent latency between occupational exposure and disease outcomes [5].

At this smelter the mean levels of exposure for both pollutants were below the recommended exposure limit of NIOSH of 2.5 mg/m^3 and 5 ppm for fluorides and sulfur dioxide, respectively. The overall mean of SO_2 across all sections was 0.18 ppm (0.47 mg/m^3) and 0.3 mg/m^3 for fluoride.

In general, in the aluminum smelter industry, exposure to coal dust, silica, particulate matter (PM 2.5), fluoride compounds, and other fumes and gases may contribute to lung function decline. From the site assessment and the information reported by the company, silica was not of concern. Coal dust was observed at the anode maintenance area, but the hygiene data did not indicate that this was a risk.

The strengths of our study are the exposure and lung function data, which were available for 3 and 10 years, respectively. We had over 500 and 250 actual observations of fluoride and SO_2 measures respectively (which increased to 2029 and 1420 when imputed), together with 2043 lung function observations. The majority of the previous studies in potroom workers are cross-sectional studies and prone to healthy worker bias. We believe that we may have reduced potential healthy worker bias to some extent and any participation bias, as we accessed all available data over this period, irrespective of health status. The exposure characterization in our study also represents a strength, as we integrated several years of exposure measures, using different approaches. Previous studies compared potroom and non-potroom workers, whereas we compared the potroom workers amongst themselves based on an exposure matrix and different sections inside the potroom. This more in-depth approach gives the possibility to target specific interventions for the prevention of respiratory effect of exposures inside the potroom.

A key limitation in using retrospectively collected data not collected primarily for research purposes is a possible lack of consistency, particularly for the interview data, the use of different operators and machines for the spirometry, and the missing exposure data. To mitigate these limitations, we used imputation methods to estimate the missing exposure values. We carefully evaluated the spirometry data to ensure that only those tests in which ATS criteria for quality and reproducibility were included in the analysis. Because using estimation values for exposure may bias results, we conducted sensitivity analysis comparing the measured and imputed data, which revealed little change in estimates. Because of the lack of consistency on the interview data regarding the history of asthma, chest infection, shortness of breath, cough, and allergy, we decided to exclude them from the analysis. The degree of cumulative smoke exposure would be more accurate if we could have the exposure history in smoke pack years instead of current, former, and never smoker as it was presented, given a known relationship between smoking and lung function decline.

Despite the repeated measures design of the study, it is likely that the sample was still affected by a healthy worker bias. The exit of workers after entry into the workforce, soon after employment, before the completion of the second lung function assessment, is possible. This may account for some of the inconsistencies seen in our findings, particularly with the counterintuitive lung function responses.

In conclusion, our study found important associations between exposures in a smelter potroom and declines in lung function. A particularly interesting finding was the 1-year lagged effect of exposure on the lung function parameters. Although effects were not consistently seen across all exposure metrics, lifetime cumulative exposure was consistent across both fluorides and SO_2. These effects were seen despite mean pollution levels being below international OELs, suggesting that these standards may not be protective of workers' health.

Author Contributions

Edite Macaringue Raja: proposal development, data collection, data cleaning, data analysis, primary drafting of manuscript. **Rajen Naidoo:** conceptualization of the project, development and review of field instruments, data analysis and review of manuscript drafts, final approval of submitted manuscript. **Sujatha Hariparsad:** data analysis and review of manuscript drafts, final approval of submitted manuscript.

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Disclosure

The authors have nothing to report.

Ethics Statement

Ethical approval was obtained from the University of KwaZulu-Natal's Biomedical Research Ethics Committee (BREC) ref. No: BE446/19. The protocol was reviewed by the participating company structures, who provided access to the data. No individual consent was obtained as the study was retrospective, and anonymised data was obtained from the company.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. O. A. Taiwo, K. D. Sircar, M. D. Slade, et al., "Incidence of Asthma Among Aluminum Workers," *Journal of Occupational and Environmental Medicine* 48, no. 3 (2006): 275–282, https://doi.org/10.1097/01.jom.0000197876.31901.f5.

2. M. J. Abramson, J. H. Wlodarczyk, N. A. Saunders, and M. J. Hensley, "Does Aluminum Smelting Cause Lung Disease?," *American Review of Respiratory Disease* 139, no. 4 (1989): 1042–1057.

3. M. Debia, S. Weichenthal, R. Tardif, et al., "Ultrafine Particle (UFP) Exposures in an Aluminium Smelter: Soderberg vs. Prebake Potrooms," *Environment and Pollution* 1, no. 1 (2012): 2.

4. L. Fritschi, M. R. Sim, A. Forbes, et al., "Respiratory Symptoms and Lung-Function Changes With Exposure to Five Substances in Aluminium Smelters," *International Archives of Occupational and Environmental Health* 76, no. 2 (2003): 103–110.

5. A. M. Neophytou, S. Costello, S. Picciotto, et al., "Accelerated Lung Function Decline in an Aluminium Manufacturing Industry Cohort Exposed to PM2.5: An Application of the Parametric g-Formula," *Occupational and Environmental Medicine* 76, no. 12 (2019): 888–894.

6. K. Larsson, A. Eklund, R. Arns, et al., "Lung Function and Bronchial Reactivity in Aluminum Potroom Workers," *Scandinavian Journal of Work, Environment & Health* 15, no. 4 (August 1989): 296–301, https://doi.org/10.5271/sjweh.1850.

7. G. B. Field, "Pulmonary Function in Aluminium Smelters," *Thorax* 39 (1984): 743–751.

8. M. Chan-Yeung, R. Wong, L. MacLean, et al., "Epidemiologic Health Study of Workers in an Aluminum Smelter in British Columbia," *American Review of Respiratory Disease* 127, no. 4 (April 1983): 465–469, https://doi.org/10.1164/arrd.1983.127.4.465.

9. H. Aboufaddan, H. Zayet, L. Shaaban, A. Ewis, and S. Elghazally, "Prevalence of Respiratory Disorders Among Primary Aluminum Workers, and Their Relation to the Duration of Exposure and Smoking Habits," *Journal of Current Medical Research and Practice* 1, no. 3 (2016): 61.

10. J. Kongerud and V. Søyseth, "Respiratory Disorders in Aluminum Smelter Workers," supplement, *Journal of Occupational & Environmental Medicine* 56, no. 5 Suppl (2014): S60–S70.

11. L. Fritschi, J. Beach, M. Sim, et al., "Respiratory Symptoms and Lung Function in Two Prebake Aluminum Smelters," *American Journal of Industrial Medicine* 35, no. 5 (1999): 491–498.

12. K. Larsson, A. Eklund, R. Arns, et al., "Lung Function and Bronchial Reactivity in Aluminum Potroom Workers," *Scandinavian Journal of Work, Environment & Health* 15 (1989): 296–301.

13. B. Sorgdrager, A. J. A. de Looff, T. M. Pal, F. J. H. van Dijk, and J. G. R. de Monchy, "Factors Affecting FEV1 in Workers With Potroom Asthma After Their Removal From Exposure," *International Archives of Occupational and Environmental Health* 74, no. 1 (2000): 55–58.

14. J. Kongerud and V. Søyseth, "Respiratory Disorders in Aluminum Smelter Workers," *Journal of Occupational & Environmental Medicine* 56 (2014): S60–S70, https://doi.org/10.1097/jom.0000000000000105.

15. X. Muñoz and P. V. d'Hebron, "Occupational Asthma Due to Alumina Exposure," *Journal of Investigational Allergology and Clinical Immunology* 34, no. 4 (2024): 270–272, https://doi.org/10.18176/jiaci.0974.

16. G. Ferguson, R. Hopkins, K. Poortinga, et al., *Systematic Review of Occupational Aluminium Exposure and Adverse Health Conditions* (Intrinsik Corp, 2017).

17. M. Dennekamp, N. H. de Klerk, A. Reid, et al., "Longitudinal Analysis of Respiratory Outcomes Among Bauxite Exposed Workers in Western Australia," *American Journal of Industrial Medicine* 58 (2015): 897–904, https://doi.org/10.1002/ajim.22492.

18. L. N. Şan, H. Uysal, H. Gökbel, C. Ş. Bediz, and A. Sayal, "Pulmonary Function of Workers in the Aluminum Industry," *American Journal of Industrial Medicine* 33 (1998): 305–307.

19. C. Husband, G. McMahon, and P. Veen. The Aluminum Industry in West and Central Africa: Lessons Learned and Prospects for the Future, The World Bank, Extractive Industries and Development Series #13 (2009), https://openknowledge.worldbank.org/entities/publication/9f6670af-b851-5235-b245-406f70a27699.

20. A. Del Monaco, S. M. Gwini, S. Kelly, et al., "Respiratory Outcomes Among Refinery Workers Exposed to Inspirable Alumina Dust: A Longitudinal Study in Western Australia," *American Journal of Industrial Medicine* 63, no. 12 (December 2020): 1116–1123, https://doi.org/10.1002/ajim.23182.

21. G. Benke, A. Del Monaco, M. Dennekamp, et al., "Caustic Mist Exposure and Respiratory Outcomes in a Cohort Study of Alumina Refinery Workers," *Annals of Work Exposures and Health* 65, no. 6 (2021): 703–714.

22. M. J. Abramson, G. P. Benke, J. Cui, et al., "Is Potroom Asthma Due More to Sulphur Dioxide Than Fluoride? An Inception Cohort Study in the Australian Aluminium Industry," *Occupational and Environmental Medicine* 67, no. 10 (2010): 679–685.

23. V. Soyseth, J. Kongerud, H. Kjuus, and J. Boe, "Bronchial Responsiveness and Decline in FEV1 in Aluminium Potroom Workers," *European Respiratory Journal* 7, no. 5 (1994): 888–894.

24. V. Søyseth, P. K. Henneberger, G. Einvik, M. A. Virji, B. Bakke, and J. Kongerud, "Annual Decline in Forced Expiratory Volume Is Steeper in Aluminum Potroom Workers Than in Workers Without Exposure to Potroom Fumes," *American Journal of Industrial Medicine* 59 (2016): 322–329, https://doi.org/10.1002/ajim.22570.

25. M. Chan-Yeung, D. A. Enarson, L. Maclean, and D. Irving, "Longitudinal Study of Workers in an Aluminum Smelter," *Archives of*

Environmental Health: An International Journal 44, no. 3 (1989): 134–139.

26. J. Kongerud, J. K. Gronnesby, and P. Magnus, “Respiratory Symptoms and Lung Function of Aluminum Potroom Workers,” *Scandinavian Journal of Work, Environment & Health* 16 (1990): 270–277.

27. V. Brusasco, R. Crapo, and G. Viegi, “Coming Together: The ATS/ERS Consensus on Clinical Pulmonary Function Testing,” *European Respiratory Journal* 26, no. 1 (2005): 1–2.

28. M. R. Miller, R. Crapo, J. Hankinson, et al., “General Considerations for Lung Function Testing,” *European Respiratory Journal* 26, no. 1 (2005): 153–161.

29. Stata Corp., Stata 15 Base Reference Manual, (Stata Press, 2017).

30. P. H. Quanjer, S. Stanojevic, T. J. Cole, et al., “Multi-Ethnic Reference Values for Spirometry for the 3–95-yr Age Range: The Global Lung Function 2012 Equations,” *European Respiratory Society* 40, no. 6 (2012): 1324–1343, https://doi.org/10.1183/09031936.00080312.

31. American Thoracic Society Standardization of Spirometry, *American Journal of Respiratory and Critical Care Medicine* 152, no. 3 (1995): 1107–1136, https://doi.org/10.1164/ajrccm.152.3.7663792.

32. P. H. Quanjer and S. Stanojevic, “Do the Global Lung Function Initiative 2012 Equations Fit My Population?,” *European Respiratory Journal* 48, no. 6 (2016): 1782–1785.

33. K. Lund, J. Ekstrand, J. Boe, P. Søstrand, and J. Kongerud, “Exposure to Hydrogen Fluoride: An Experimental Study in Humans of Concentrations of Fluoride in Plasma, Symptoms, and Lung Function,” *Occupational and Environmental Medicine* 54, no. 1 (1997): 32–37.

34. K. Radon, D. Nowak, R. Heinrich-Ramm, and D. Szadkowski, “Respiratory Health and Fluoride Exposure in Different Parts of the Modern Primary Aluminum Industry,” *International Archives of Occupational and Environmental Health* 72, no. 5 (1999): 297–303.

35. P. D. Blanc, I. Annesi-Maesano, J. R. Balmes, et al., “The Occupational Burden of Nonmalignant Respiratory Diseases. An Official American Thoracic Society and European Respiratory Society Statement,” *American Journal of Respiratory and Critical Care Medicine* 199, no. 11 (2019): 1312–1334.

36. D. S. Wong, M. M. Hyland, N. I. Tjahyono, and D. Cotton, “Potroom Operations Contributing to Fugitive Roof Dust Emissions from Aluminium Smelters,” in *Light Metals 2019, The Minerals, Metals & Materials Series*, ed. C. Chesonis, (Springer, 2019), https://doi.org/10.1007/978-3-030-05864-7_110.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Supplementary Table 1: Adjusted* estimates effects of lag fluoride, cumulative SO_2 and cumulative fluoride on percentage predicted FEV_1, FVC and FEV_1/FVC ratio stratified by section. **Supplementary Table 2:** Unadjusted estimates effects of Sulphur dioxide and fluoride on percentage predicted lung function parameters.