Annual Decline in Forced Expiratory Volume is Steeper in Aluminum Potroom Workers Than in Workers Without Exposure to Potroom Fumes

Vidar Søyseth, MD, PhD,[1,2,3]* **Paul K. Henneberger,** MPH, ScD,[3] **Gunnar Einvik,** MD, PhD,[1] **Mohammed Abbas Virji,** MSc, ScD,[3] **Berit Bakke,** MSc, PhD,[4] **and Johny Kongerud,** MD, PhD[2,5]

Background *Aluminum potroom exposure is associated with increased mortality of COPD but the association between potroom exposure and annual decline in lung function is unknown. We have measured lung volumes annually using spirometry from 1986 to 1996. The objective was to compare annual decline in forced expiratory volume in 1 s (dFEV1) and forced vital capacity (dFVC).*
Methods *The number of aluminum potroom workers was 4,546 (81% males) and the number of workers in the reference group was 651 (76% males). The number of spirometries in the index group and the references were 24,060 and 2,243, respectively.*
Results *After adjustment for confounders, the difference in dFEV1 and dFVC between the index and reference groups were 13.5 ($P < 0.001$) and −8.0 ($P = 0.060$) ml/year.*
Conclusion *Aluminum potroom operators have increased annual decline in FEV1 relative to a comparable group with non-exposure to potroom fumes and gases.* Am. J. Ind. Med. 59:322–329, 2016. © 2016 The Authors. *American Journal of Industrial Medicine* Published by Wiley Periodicals, Inc.

KEY WORDS: lung function; longitudinal study; aluminum; smoking; potroom exposure; mixed model

INTRODUCTION

Aluminum is a lightweight metal with widespread use in a diversity of products from kitchen equipment to spacecraft. It is produced by electrolysis of alumina (Al_2O_3), which is dissolved in molten cryolite. Alumina normally has a melting point above 2000°C, but can be partly dissolved in molten cryolite at 960°C. Thereby, alumina may be reduced to Al-metal in electrolytic cells. Pollutants emitted to the workplace atmosphere during these processes include dust (alumina, coke, and other particles), fluorides (highly irritating and corrosive), sulfur dioxide and other fumes, and polycyclic aromatic hydrocarbons (PAH).

Already in the 1930s two Norwegian studies reported cases of asthma among workers in the electrolysis departments (potrooms), giving rise to the term potroom asthma [Frostad, 1936; Evang, 1938]. Later studies have indicated that the prevalence and incidence of airway symptoms, bronchial hyperresponsiveness and airways inflammation

[1]Medical Division, Akershus University Hospital, Lørenskog, Norway
[2]Faculty of Medicine, University of Oslo, Oslo, Norway
[3]Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Morgantown, West Virginia
[4]Department of Occupational Health Surveilance, National Institute of Occupational Health, Oslo, Norway
[5]Department of Respiratory Medicine, Rikshospitalet, Oslo University Hospital, Oslo, Norway
*Correspondence to: V. Søyseth, MD, PhD, Akershus University Hospital, Sykehusvn 25, 1478 Lørenskog, Norway. E-mail: vidar.soyseth@medisin.uio.no

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have been associated with exposure to potroom fumes [Kongerud et al., 1990; Kongerud and Samuelsen, 1991; Sorgdrager et al., 1995; Fritschi et al., 2003; Sjaheim et al., 2004; Abramson et al., 2010]. Additionally, some studies have indicated an increased mortality of chronic obstructive pulmonary disease (COPD) among potroom workers even after adjusting for smoking habits [Ronneberg, 1995; Romundstad et al., 2000; Gibbs and Sevigny, 2007; Gibbs et al., 2007]. COPD in these settings may be a direct effect of potroom pollutants on the airways, or the result of chronic asthma or smoking.

COPD is characterized by irreversible airflow limitation [Rabe et al., 2007]. Ever since the landmark study by Fletcher and co-workers it has been widely accepted that COPD is characterized by an accelerated decline in lung function [Fletcher and Peto, 1977; Agusti and Barnes, 2012]. Thereby, exposures that are associated with increased decline in pulmonary function have relevance for COPD causation [Eisner et al., 2010].

In occupational settings, the majority of employees usually are healthier than the general population [Lea et al., 1999; Radon et al., 2006; Dumas et al., 2011]. Hence, the association between occupational exposure and COPD development is likely to be underestimated due to selection bias [Radon et al. 2002]. In order to take these considerations into account we conducted a prospective longitudinal study among aluminum potroom workers using a control group consisting of workers without exposure to potroom fumes. The participants were followed up annually for 10 years. The aim of the present study was to compare the annual decline in lung function between aluminum potroom workers and a control group.

MATERIALS AND METHODS

Study Population

The study was a prospective cohort study among full-time workers from 1986 to 1995. The potroom workers consisted of potroom workers in seven Norwegian aluminum plants (n = 4,646). We selected a control group of active workers with work tasks comparable to the potroom workers and non-exposure to aluminum potroom fumes [Miettinen, 1982]. The control group consisted of employees in a factory producing aluminum wheel rims for cars (n = 277), a road construction company (n = 109), and a factory producing rolled aluminum products (n = 265). The rim factory and road construction company followed the study protocol for 4 years, whereas the roller factory followed the protocol for the entire 10 years.

All employees were invited to participate. After enrollment the employees were examined annually, preferably in the time period between September 1st and October 31st. The foremen determined the date and time for health examination on workdays between 08 and 12 am. In case of absence the employee was offered a new examination date that was no later than December 31st of the same year. The participants were registered using the unique national personal identification (ID) number. After the study was completed (Dec 31, 1995), the data from all plants were pooled in a central project database. The national personal ID number was then replaced by a unique random study ID number. The database was then anonymized by deleting the key that connected the national and study ID numbers.

The study was started before the current legislation for medical research was implemented in Norway. As the participants completed a self-administered questionnaire an informed consent was given by each participant. The current protocol was approved by the Regional Committee for Medical Research Ethics, Eastern Norway (no **2013/861**).

Annual Examinations

At each examination, the study participants completed a questionnaire that included questions regarding smoking habits (e.g., dates for starting and quitting smoking) and work history (e.g., current job title and previous occupations) [Kongerud et al., 1989].

At the start of the study a mandatory spirometry course was arranged for all the technicians by one of the authors (JK). During the follow-up period there were annual meetings between JK and the technicians regarding spirometry as well as the questionnaires.

The performance of spirometry and calibration procedures followed the recommendations of the American Thoracic Society (ATS) [Statement of the American Thoracic Society, 1987], that is, similar to the updated recommendations from ATS/ERS [Miller et al., 2005]. Prediction equations for FEV_1 and FVC were taken from Quanjer et al. [1993].

Statistical Analyzes

The statistical analyzes were performed in three steps. First, we analyzed the association between relevant covariates and exposure status, that is, potroom workers and controls. In these analyzes *t*-tests were used for continuous variables and categorical variables were analyzed using chi-square tests. For covariates that had a P-value <0.2 we estimated the annual decline in FEV_1 ($dFEV_1$) and FVC (dFVC) using univariate linear mixed models [Fitzmaurice, 2004]. Age and gender were kept in the analyzes regardless of the P-values.

For covariates that were associated with $dFEV_1$ or dFVC having a P-value <0.2, we performed stratified analyzes of

$dFEV_1$ (dFVC) between the potroom workers and the controls by subgroups, for example, males/females, age groups, and other relevant covariates (for details, see online supplement). The differences within each stratum were assessed using *t*-test. Confounding by any of the covariates was assessed by comparing the product-term between follow-up time and exposure (i.e., potroom workers or controls) and the crude difference in $dFEV_1$ or dFVC between the potroom workers and the controls. We also investigated effect modification of the product-term between follow-up time and exposure status (index/controls) by the covariate. Effect modification was considered to be present if the *P*-value of the product-term between the follow-up time and a covariate and the exposure status (index/controls) was 0.01 or lower.

In step 3, multivariate analyzes were performed using linear mixed models. Covariates were included in the initial model provided that the bivariate analyzes showed that they were associated with $dFEV_1$ or dFVC and exposure (i.e., potroom vs. controls) having $P < 0.2$. The models were then reduced by backward elimination provided that the product term between the covariate and time was ≥ 0.05 and the association between exposure (i.e., potroom vs. controls) and $dFEV_1$ or dFVC changed with less than 20%.

We used hierarchical models with random intercepts for the participants nested within each plant. The analyzes were performed using SAS 9.4 proc.mixed (SAS Institute Inc., Cary, NC). For details, see online supplement.

RESULTS

At baseline the controls were older, more likely to currently smoke, and more likely to have doctor-diagnosed asthma (Table I). Also, controls had lower lung function than the potroom workers. Although lung volumes were in the normal range, an obstructive pattern was suggested in both groups. The majority of both the controls and the index participants were male.

During the follow-up the decline in FVC was similar in the two groups, whereas FEV_1 declined more rapidly in the potroom workers than the controls (Fig. 1a,b).

Table II shows dFVC and $dFEV_1$ by covariates that were associated with exposure status (i.e., potroom workers or controls) having a *P*-value <0.2. The table shows that $dFEV_1$ as well as dFVC increased with increasing age, height, and lung function at baseline. Also, males had steeper dFVC and $dFEV_1$ than females, whereas doctor diagnosed asthma was not associated with increased decline in FEV_1 or FVC.

The stratified analyzes showed that the adjusted $dFEV_1$ in the potroom workers was significantly ($P < 0.001$) steeper than the controls (Table III). In contrast, the difference in dFVC between the index and control groups was statistically significant after adjusting for age but not after adjusting for any of the other covariates (online Table IIIb). However, the adjusted estimates did not deviate markedly from the crude estimates of $dFEV_1$ or dFVC except from baseline lung function (Table III and online Table IIIb. Thus, after adjustment for baseline lung function the difference in $dFEV_1$ as well as dFVC between the groups attenuated. It appeared that the differences in $dFEV_1$ between the potroom workers and the controls were larger in current smokers than never smokers. The *P*-value of the corresponding interaction term was, however, 0.068, that is, not significant (model not shown).

From multivariate analyzes, $dFEV_1$ was 13.5 ml/year ($P < 0.001$) steeper among potroom workers than the controls (Table IV), whereas the dFVC was 8.0 ml/year higher in the control group than the potroom workers and this difference was not statistically significant ($P = 0.060$). Moreover, $dFEV_1$ as well as dFVC increased with follow-up time, age at baseline, baseline lung function, and male versus female gender. Also, current smokers, but not former

TABLE I. Baseline Characteristics of Aluminum Potroom Workers and References

Characteristic	Potroom	References	
Baseline	N = 4,546	N = 651	*P*-value
Male, n (%)	3,679 (81)	495 (76)	0.0027
Age groups in years, n (%)			<0.0001
<25	2,285 (50)	151 (23)	
25–34	1,134 (25)	200 (31)	
35–44	552 (12)	139 (21)	
≥45	575 (13)	161 (25)	
Age in years, mean (sd)	29.0 (11.4)	35.5 (12.5)	<0.0001
Height in cm, mean (sd)	1.78 (0.08)	1.77 (0.08)	0.003
Smoking habits, n (%)			<0.0001
Never smokers	1,363 (30)	156 (24)	
Former smokers	72 (2)	40 (6)	
Current smokers	2,482 (55)	411 (63)	
Unknown	629 (14)	44 (7)	
Allergy and asthma, n (%)			
Asthma	203 (4)	88 (14)	<0.0001
Allergy	371 (8)	53 (8)	0.969
Familial asthma	657 (14)	102 (16)	0.945
Previous exposure			
Potrooms (mo.), mean (sd)	59 (95)	0 (0)	
Other, n (%)	732 (16)	195 (30)	<0.0001
Spirometry, mean (sd)			
FVC in liters	5.30 (0.96)	5.08 (0.98)	<0.0001
FEV_1 in liters	4.28 (0.80)	3.92 (0.82)	<0.0001
FEV_1/FVC-ratio	0.81 (0.078)	0.77 (0.082)	<0.0001
FVC as % of predicted	107 (16)	108 (16)	0.036
FEV_1 as % of predicted	102 (14)	100 (15)	<0.0001

mo., months.

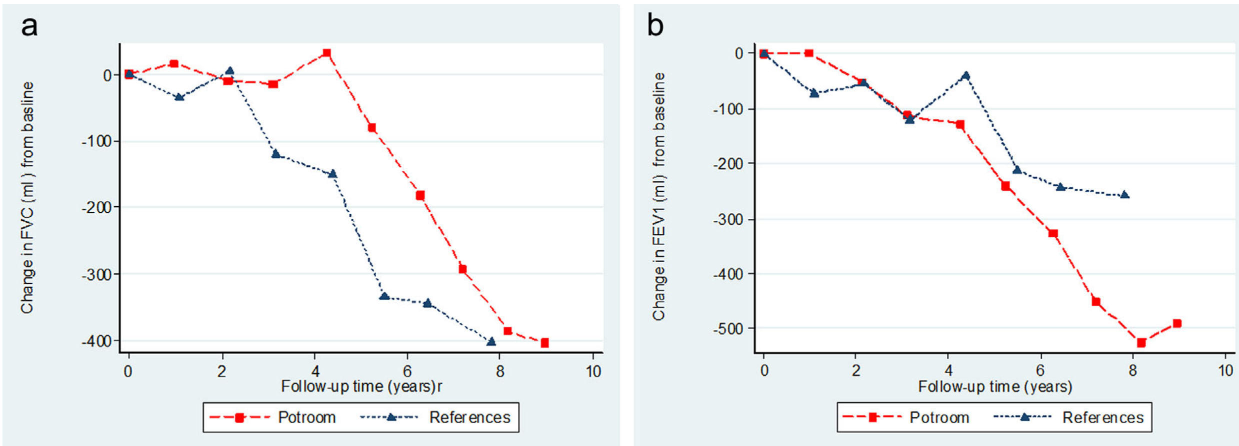

FIGURE 1. (**a**,**b**) Change in spirometry results during the follow-up.

smokers, had steeper annual declines in both FEV_1 ($P < 0.001$) and FVC ($P = 0.023$) than never smokers. Although height was a highly significant determinant of the level of FEV_1 as well as FVC, there was no significant association between height and $dFEV_1$ or dFVC in the multivariate models. Increasing body weight was associated with increasing dFVC but not dFEV1. The association between exposure status and dFEV1 or dFVC did not change after inclusion of body weight as a covariate. Regarding model fit, see online supplement (Figs. S1 and S2).

DISCUSSION

In this study, we have found that aluminum potroom workers had highly significant increased annual decline in FEV_1 but not in FVC compared with a control group of individuals who worked in similar settings as the potroom workers but without exposure to potroom fumes and gases.

This study has at least three strengths. First, it was a prospective longitudinal study with a large number of participants who were followed annually over a long period (up to 10 years). Second, smoking status of each participant was updated annually using a validated questionnaire [Kongerud et al., 1989]. Third, the spirometries were performed by well-trained technicians who participated in spirometry courses based on guidelines similar to those subsequently recommended by the ATS [Redlich et al., 2014].

The most striking finding was that $dFEV_1$ in the potroom workers was remarkably high even in the lowest age groups. As the technicians underwent common training courses in spirometry it is less likely that the high $dFEV_1$ could be explained by failure to perform the test correctly. Moreover, the $dFEV_1$ in never smokers in the control group was about the same as $dFEV_1$ among never smokers in other studies of subjects in the same age-group as our study and dFVC did not deviate substantially from dFVC in other studies [Dalphin et al., 1998; Downs et al., 2007]. As the smoking prevalence was higher in the control group than the potroom workers, the accelerated $dFEV_1$ in the potroom workers can probably not be explained by smoking. Since the controls also worked in similar settings as the potroom workers it is less likely that the difference can be explained by selection bias between the groups [Radon et al., 2006]. Hence, the difference in $dFEV_1$ is most likely explained by exposure in the potrooms that is not shared with controls. Actually, the difference in $dFEV_1$ between potroom workers and the controls was only marginally higher than the difference in $dFEV_1$ between welders and controls [Szram et al., 2013], that is, exposure to potroom pollutants appears to have a similar effect on lung function as welding fumes.

The effect of potroom exposure became apparent after about 6 years of follow-up. The most likely explanation for this is that one fourth of the pot operators were substitutes, that is, young people (<25 years, many students) who worked in the potrooms during the summer vacation, mostly 3–4 consecutive summers or less. It is likely that these individuals slowed down the decrease in annual decline in lung function.

The prevalence of doctor diagnosed asthma was lower in the potroom workers than the control group. This difference is mostly explained by selection based on health status as the Health Committee of International Primary Aluminum Association (currently: International Aluminium Institute—IAI) recommended that employees with asthma should not work in the potrooms. We found that asthma was not associated with increased $dFEV_1$ in this study suggesting that the exclusion of asthmatics from the potrooms is unnecessary. However, it is likely that there is health-based self-selection into and away from such industrial work among asthmatics. Therefore, our findings may not be valid for all asthmatics.

TABLE II. Mean Annual Decline (ml/year) in Forced Expiratory Volume in 1 s ($dFEV_1$) and Forced Vital Capacity (dFVC) by Selected Covariates (See Text, Statistical Analyzes), Both Groups

Characteristic	$dFEV_1$ (se)	*P*-value	dFVC (se)	*P*-value
Gender		<0.0001		<0.0001
Male	57.9 (1.0)		37.9 (1.4)	
Female	39.2 (4.1)		22.2 (5.5)	
Age groups, years		<0.0001*		<0.0001*
<25	40.3 (2.0)		0.35 (2.5)	
25–34	60.2 (1.6)		42.4 (2.1)	
35–44	57.1 (2.3)		51.3 (2.5)	
≥45	60.2 (2.5)		58.9 (2.8)	
Height, cm		<0.0001*		0.0175*
<170	35.8 (5.1)		18.9 (3.1)	
170–179	55.7 (1.3)		38.2 (1.6)	
≥180	60.9 (1.8)		35.0 (2.4)	
Smoking habits, n (%)		0.0009		0.0008
Never smokers	47.2 (1.9)		23.4 (2.5)	
Former smokers	57.0 (3.0)		48.6 (4.0)	
Current smokers	57.1 (1.4)		36.6 (1.6)	
Asthma		0.370		0.209
Yes	34.2 (6.4)		40.4 (15.3)	
No	54.9 (1.0)		34.8 (1.4)	
Previous exposure		0.292		0.536
Yes	57.7 (3.0)		44.2 (2.9)	
No	53.9 (1.1)		33.0 (1.5)	
FVC, ml		<0.0001*		<0.0001*
<4,500	35.1 (2.2)		14.0 (3.0)	
4,500–5,490	55.0 (1.6)		32.7 (2.0)	
≥5,500	67.5 (1.5)		45.9 (1.9)	
FEV1, ml		<0.0001*		0.616*
<3,500	35.6 (2.3)		29.8 (3.2)	
3,500–4,490	51.5 (1.3)		35.3 (1.8)	
≥4,500	66.0 (1.6)		32.6 (2.2)	

*Trend.

Furthermore, IPAA recommended that FEV_1 in new employees should be at least 80% of predicted. We found, however, that individuals with the highest lung function had steeper decline in lung volumes. This finding may appear like a paradox: that the subjects with largest lung volumes have increased risk of COPD. We believe that pre-employment FEV_1 is not a good selection criterion for assessment of the risk of future COPD.

We found that high FEV_1 was an important determinant of $dFEV_1$ and that the potroom workers had higher FEV_1 than the controls. Thus, it is possible that the observed increase in $dFEV_1$ in the potroom workers only reflects a normal change in lung function in these individuals. However, a similar effect was not observed regarding dFVC. A similar effect was found among employees in the Norwegian Smelters [Søyseth et al., 2015]. We have, however, not been able to find any other studies where the association between the level of FEV_1 or FVC and their corresponding annual decline. Hence, it is likely that the accelerated $dFEV_1$ is beyond any expected change and instead represents a response in the airways to conditions in the potrooms. However, the mean level of spirometry was high in this young population. Therefore, the increased $dFEV_1$ should be regarded as a risk factor for development of COPD at a later stage [Svanes et al., 2010].

The association between $dFEV_1$ and exposure status was stronger among current smokers than never smokers, although this difference was not statistically significant. Nonetheless, this difference was close to the difference between current smokers and never smokers and therefore

TABLE III. Annual Decline in FEV_1 (ml/year) in Potroom Workers and References by Relevant Covariates and Their Differences Assessed Using Univariate and Bivariate Analyzes

Covariates	Potroom	Reference	Difference (95%CI)
None (univariate)	56.7 (1.0)	36.8 (2.7)	20.3 (15.2 to 26.3)
Gender			
Male	59.5 (1.1)	39.4 (2.7)	20.6 (15.0 to 26.2)
Female	42.4 (5.6)	26.6 (7.2)	18.7 (−3.0 to 40.3)
Adjusted for gender			20.3 (13.2 to 27.3)
Age at inclusion, years			
<25	40.9 (2.0)	23.2 (9.3)	18.9 (0.42 to 37.5)
25–34	62.4 (1.7)	36.8 (15.4)	26.3 (−4.1 to 56.6)
35–44	52.4 (2.7)	33.8 (13.3)	21.6 (−4.9 to48.0)
≥45	65.3 (2.7)	39.6 (13.3)	26.2 (−0.26 to 52.6)
Adjusted for age			22.8 (15.8 to 29.8)
Height, cm			
<170	39.0 (5.0)	17.0 (7.7)	22.0 (4.0 to 40.0)
170–179	57.5 (1.3)	39.5 (3.4)	18.0 (10.9 to 25.1)
≥180	62.2 (1.8)	44.3 (6.1)	17.9 (5.4 to 30.4)
Adjusted for height			22.6 (3.6 to 29.7)
Smoking habits			
Never smokers	48.2 (2.0)	34.7 (5.9)	14.3 (2.1 to 26.4)
Former smokers	58.2 (3.2)	52.3 (7.2)	6.2 (−9.2 to 21.6)
Current smokers	59.6 (1.4)	31.5 (4.0)	29.0 (20.8 to 37.2)
Adjusted for smoking			22.5 (15.5 to 29.5)
FVC, ml			
≥5500	68.9 (1.5)	48.3 (5.2)	20.6 (10.0 to 31.2)
4500–5490	55.6 (1.5)	40.1 (4.9)	15.5 (5.5 to 25.5)
<4500	37.7 (2.2)	22.5 (4.7)	15.2 (5.0 to 25.4)
Adjusted for baseline FVC			17.6 (10.7 to 24.5)
FEV_1, ml			
≥4500	66.4 (1.6)	54.1 (7.3)	12.3 (−2.3 to 26.9)
3500–4490	52.2 (1.3)	44.8 (3.5)	7.4 (0.1 to 14.7)
<3500	40.4 (2.5)	15.8 (10.7)	24.6 (3.1 to 46.9)
Adjusted for baseline FEV_1			16.5 (9.6 to 23.4)

CI, Confidence interval.

TABLE IV. Results of Multivariate Analyzes of Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 s, Annual Decline in FVC (dFVC) and FEV_1 ($dFEV_1$) During the Follow-Up

	Main effects (ml)		Annual decline (ml/y)		Main effects (ml)		Annual decline (ml/y)	
Characteristic	**FVC (se)**	***P*-value**	**dFVC (se)**	***P*-value**	**FEV_1 (se)**	***P*-value**	**$dFEV_1$ (se)**	***P*-value**
Intercept	772 (55.2)	<0.001	—	—	938 (51.2)	<0.001	—	—
Follow-up time, years	181 (8.0)	<0.001	6.7* (0.34)	<0.001	133.2 (7.4)	<0.001	2.7* (0.28)	<0.001
Male versus female	209 (13.7)	<0.001	25.1 (3.7)	<0.001	188 (12.6)	<0.001	14.2 (3.0)	<0.001
Height, m	222 (30.2)	<0.001	—	—	162 (27.0)	<0.001	—	—
Age at baseline, years	−11.2 (0.42)	<0.001	2.6 (0.11)	<0.001	−12.3 (0.43)	<0.001	1.8 (0.10)	<0.001
Smoking status								
Current versus Never	−11.3 (10.0)	0.259	5.8 (2.6)	0.023	−43.6 (9.1)	<0.001	10.6 (2.2)	<0.001
Former versus Never	−25.7 (14.2)	0.070	−2.9 (3.8)	0.446	−41.3 (12.3)	<0.001	4.0 (3.2)	0.202
FVC at baseline, L	810 (5.42)	<0.001	26.0 (1.3)	<0.001	70.7 (9.4)	<0.001	2.8 (2.1)	0.181
FEV_1 at baseline, L	—	—	—	—	651 (11.3)	<0.001	27.2 (2.5)	<0.001
Potroom versus references	−4.6 (15.4)	0.767	−8.0 (4.2)	0.060	8.6 (14.1)	0.026	13.5 (3.5)	<0.001

Se, Standard error of the mean.
*Follow-up time-squared.

clinically meaningful. Therefore, we recommend that potroom workers should not smoke, and smoking was prohibited in four of the plants already in 1994.

The mechanism of the increased decline in FEV_1 remains unclear. It could be a direct effect of the exposure on the airways. In the Norwegian non-aluminum smelter industry we found that $dFEV_1$ was associated with dust exposure [Johnsen et al., 2010, 2013]. In a sub cohort of the current sample we previously found that FEV1 was associated with dust exposure but not fluorides [Soyseth et al., 1997]. Alternatively, the possibility that it was an indirect effect mediated by work-related asthma [Hendrick, 1996] was inconsistent with the observation that neither $dFEV_1$ nor dFVC was associated with asthma.

The main limitation is that 20 years have elapsed since the study was finished. The analyzes of the complete follow-up of the aluminum study was delayed because the authors who were involved in aluminum study (JK and VS) were invited by the Norwegian Smelter Industry to start a 5 year longitudinal study among 4,000 employees in 1996. The smelter study is recently completed [Søyseth et al., 2015]. Therefore, the final analyzes of the aluminum study postponed until we requested the Norwegian Aluminum Industry for completion of the aluminum study in 2012. Due to this delay, the levels of workplace air pollutants may have declined for both the index and control groups. Nonetheless, the findings are of considerable interest to past potroom workers and their health care providers. Therefore, we believe our results are important.

In conclusion, aluminum potroom workers have an increased annual decline in FEV_1 but not FVC compared with controls who work in comparable settings but without the airborne exposures. The work-related difference in annual decline in FEV1 was more pronounced in current smokers than never smokers although this difference was only of borderline significance.

AUTHORS' CONTRIBUTIONS

VS: Design, acquisition and analyses of data, drafting, and approval of the final version. PKH: Data analyses, critical revision of the text, and approval of the final version. GE: Data analyses, critical revision of the text, and approval of the final version. MAV: Data analyses, critical revision of the text, and approval of the final version. BB: Data analyses, critical revision of the text, and approval of the final version. JK: Design, acquisition and analyses of data, drafting, and approval of the final version. All the authors have agreed that all aspects of the work have been appropriately investigated and resolved.

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DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

CONFLICT OF INTEREST

V. Søyseth has received support for traveling from the Norwegian Aluminum Industry, otherwise non conflict of interest to declare for any of the authors. The remaining authors have conflict of interest to declare.

DISCLOSURE BY AJIM EDITOR OF RECORD

Steven Markowitz declares that he has no competing or conflicts of interest in the review and publication decision regarding this article.

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