



Construction of a Job Exposure Matrix to Dust, Fluoride, and Polycyclic Aromatic Hydrocarbons in the Norwegian Aluminum Industry using Prediction Models

Vidar Søyseth^{1,2,3*}, Paul Henneberger³, Mohammed Abbas Virji³,
Berit Bakke⁴ and Johny Kongerud^{2,5}

1. Medical Division, Akershus University Hospital, Lørenskog 1478, Norway;

2. Faculty of Medicine, University of Oslo, Oslo 0318, Norway;

3. Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, MS 2800, 1095 Willowdale Road, Morgantown, WV 26505, USA;

4. Department of Chemical and Biological Work Environment, National Institute of Occupational Health, Oslo 0363, Norway;

5. Department of Respiratory Medicine, Rikshospitalet, Oslo University Hospital, Oslo 0372, Norway

*Author to whom correspondence should be addressed. Tel: 4767968860; e-mail: Vidar.soyseth@medisin.uio.no

Submitted 9 December 2014; revised 16 July 2015; revised version accepted 16 July 2015.

ABSTRACT

Background: The Norwegian aluminum industry developed and implemented a protocol for prospective monitoring of employees' exposure using personal samplers. We analyzed these data to develop prediction lines to construct a job exposure matrix (JEM) for the period 1986–1995.

Methods: The protocol for personal monitoring of exposure was implemented in all seven Norwegian aluminum plants in 1986 and continued until 1995. Personal samplers were used to collect total dust, fluorides, and total polycyclic aromatic hydrocarbons (PAH). In addition, exposure could be categorized according to process, i.e. prebake, Søderberg, and 'other'. We constructed four-dimensional JEMs characterized by: Plant, Job descriptor, Process, and Year. Totally 8074, 6734, and 3524 measurements were available for dust, fluorides, and PAH, respectively. The data were analyzed using linear mixed models with two-way interactions. The models were assessed using the Akaike criterion (AIC) and unadjusted R^2 . The significance level was set to 10% (two-sided) for retaining variables in the model.

Results: In 1986, the geometric mean (95% confidence interval in parentheses) for total dust, total fluorides, and PAH were 3.18 (0.46–22.2) mg m^{-3} , 0.58 (0.085–4.00) mg m^{-3} , and 33.9 (2.3–504) $\mu\text{g m}^{-3}$, respectively. During 10 years of follow-up, the exposure to total dust, fluorides, and PAH decreased by 9.2, 11.7, and 14.9% per year, respectively. Each model encompassed from 49 to 72 significant components of the interaction terms. The interaction components were at least as important as the main effects, and 65 to 91% of the significant components of the interaction terms were time-dependent.

Conclusion: Our prediction models indicated that exposures were highly time-dependent. We expect that the time-dependent changes in exposure are of major importance for longitudinal studies of health effects in the aluminum industry.

KEYWORDS: aluminium; epidemiology; exposure assessment-mixed models; exposure estimation; measurement strategy; polycyclic aromatic hydrocarbons

INTRODUCTION

Aluminum is a lightweight metal that has widespread applications in most industrial sectors ranging from its use in the aerospace industry to food packaging, usually alloyed with other metals. It is produced by the electrolytic reduction of alumina (Al_2O_3) in smelting cells (pots) into molten aluminum. During the process, a complex mixture of particulates and gases are emitted into workplace environment including particulates (e.g. inorganic fluoride F^-), and gases (hydrogen fluoride and sulfur dioxide), particularly fluorides. Polycyclic aromatic hydrocarbons (PAH) are also emitted from the pots, especially at the Söderberg anode. Aluminum production, especially smelting in the potrooms is associated with adverse respiratory outcomes. As early as the 1930s, [Frostad \(1936\)](#) reported new asthma cases (potroom asthma) among potroom workers. Several subsequent studies have shown an association between exposure to potroom fumes and asthma-like symptoms as well as bronchial responsiveness ([Kongerud and Samuelsen, 1991](#); [Søyseth et al., 1994](#); [Abramson et al., 2010](#)). Moreover, some studies have shown an increased mortality from chronic obstructive disease among potroom workers ([Rønneberg, 1995](#); [Romundstad et al., 2000a,b](#); [Gibbs et al., 2007](#); [Gibbs and Sevigny, 2007](#)). However, the results of lung cancer studies in the aluminum industry have been inconclusive ([Armstrong et al., 1994](#); [Romundstad et al., 2000a,b](#); [Gibbs et al., 2007](#)). The association between bladder cancer and exposure to benzo(a)pyrene in primary aluminum plants is well accepted ([Gibbs and Labrèche, 2014](#)).

In the Electrolysis Department, the production of aluminum begins with the electrolytic reduction of alumina in cells (pots) to molten aluminum by the Hall-Héroult process. Since alumina has a high melting point ($>2000^\circ\text{C}$), cryolite (Na_3AlF_6), a fluoride containing compound, is added to reduce the melting temperature to 950°C and aluminum can be extracted by the electrolysis process. The electrolytic cells have an anode top (fused coke) and a cathode bottom (graphite). Carbon from the anode reduces alumina, thereby producing carbon dioxide that escapes into the environment and molten aluminum that sinks to the bottom. There are two types of anodes: the Söderberg anode and the prebake anode. The Söderberg anode contains a mixture of pitch and coke that is added to the top of the anode, and is continuously baked by

the heat generated from the reduction process. The prebake anodes are produced by molding and sintering coke and pitch into blocks in large gas-fired ovens in separate buildings or plants; before they are used for aluminum electrolysis conducting rods are inserted. Both kinds of anodes are consumed during electrolysis. The prebake anodes have to be replaced as they are consumed, whereas the top of the Söderberg electrode has to be refilled with coke and pitch. Moreover, the Söderberg electrode consists of iron studs that have to be pulled toward the top as the anode is consumed.

In most studies conducted in this industry, exposure assessment represents a major limitation for the interpretation of the results. In order to improve the assessment of exposure to particulates (dust), fluorides, and PAH, the Nordic Aluminum Industry Environmental Secretariat (AMS) developed a protocol for systematically monitoring these pollutants. The AMS's committee for industrial hygiene completed this protocol in 1986, which included recommendations for personal sampling and analytical methods for monitoring dust, fluorides, and PAH as well as a system for job classification in the Norwegian aluminum industry. The recommendations were implemented at all Norwegian aluminum plants during spring 1986. Neither the protocol nor the results of the air sampling in the seven Norwegian primary aluminum plants have been published. Furthermore, we have data from annual follow-up of respiratory disorders in the Norwegian aluminum industry from 1986 to 1996. Hence, analyses of these exposure data could improve exposure assessment in the respiratory study in order to make exposure estimates to the employees during this period.

The objective of this study was to describe the system for job classification, how the measurements were collected and how this information was utilized to develop a job exposure matrix (JEM) using prediction equations for exposures to workers in the Norwegian aluminum industry.

MATERIALS AND METHODS

The exposure measurements used in this study were provided by the laboratories at each of the seven Norwegian aluminum plants over a period of 10 years from 1986 to 1996. The sampling strategy and sampling and analytical methods were standardized across all the facilities and were based on the AMS recommendations.

In addition to the Electrolysis Department processes described above, other production-related departments/jobs include up to 14 other departments that mostly support the electrolysis. Departments like Rodding, Relining, and Scrubbing are tightly linked to the Electrolysis Department, and thus, present in all plants. Likewise, all the plants had a casting house, transportation, mechanical and electrical repair, and maintenance. However, not all the plants had departments for production of prebake anodes or Söderberg paste. These nonelectrolysis departments have gained less attention in health perspectives. Thus, the exposure surveillance of these departments is more sparsely performed. Production lines (Söderberg/prebake/other) and departments within the plants include electrolysis, scrubber, pot relining, casting house, rodding, paste plant, anode plant, mechanical workshop, transport department/quay, warehouse, and laboratory. Only three plants had paste plant and two plants had anode plant.

During the process, complex mixtures of pollutants are emitted to the environment, foremost being dust. The dust consists predominately of alumina, carbon, and fluoride containing compounds. Fluorides are emitted partly as gaseous hydrogen fluoride (HF) and partly bound to particles. Moreover, the anodes are contaminated with sulfur which is oxidized to SO₂ during the consumption of the anodes and the vehicles emit exhaust to the work place atmosphere. During the baking process, a minor amount of pitch in the Söderberg anodes is transformed to PAH. During the last decades, the amount of PAH in Söderberg potrooms has, however, decreased dramatically (Romundstad *et al.*, 1999).

Collection and description of exposure measurements in the aluminum industry development of an exposure database

The AMS protocol specified a sampling strategy which called for conducting sampling campaigns every spring and autumn. It recommended collecting eight or more full-shift samples per year for each job category during the day-time shift, for a sampling duration of at least 420 min. The measurements were to be taken during daily job routines, and not during the investigation of high exposures or irregular operations. Workers were selected for sampling in coordination with a foreman and a union representative. The sampling and analysis

was performed by a staff member from each plant's industrial hygiene laboratory. Workers could participate in multiple sampling campaigns over the years, thus generating repeated measurements collected on individual workers. Such repeated measurements were tracked by a randomly assigned worker id number; however, if the worker moved to a different plant, a new id was assigned.

In three of the plants the results of the measurements were digitalized on spread sheets (MS Excel®, $n = 4120$ records). In the remaining plants the results were stored as hardcopies ($n = 4823$ records). One of the authors (V.S.) visited each of these plants and digitalized the records in a relational database (MS Access®). This database had tables for the codes that were linked to the measurement table, such as job categories, plant, and technology.

Air sampling and analyses of the personal samples

Personal dust samples were collected using air sampling pumps calibrated to a flow rate of 2 l minute⁻¹, and were checked after termination of sampling. A 37 mm diameter, 0.8 µm pore size Gelman Vasapore or Millipore AAWP filter was used in closed-face cassettes placed in the breathing zone of the worker.

The samples were analyzed at the laboratories at each plant. The Gelman Versapore or Millipore AAWP filters were analyzed gravimetrically using internal standard equivalent to the present NS (Norwegian Standard) 4860: Measurement of total concentration of dust and fume in workplace atmosphere. Detection limit for micro-scales was 0.1 mg. Particulate on filters and gaseous fluoride on absorption pads were measured according to the internal procedures using ion selective electrodes, with a detection limit of 0.1 mg.

The PAH is analyzed according to NS 9813 (NS 9813 is developed by the Norwegian Standardization organization and describes a method for sample preparation, analysis and quantification of PAH samples), i.e. using gas chromatography with a detection limit of 10 ng. In this report only total PAH was available.

Structure of JEM and job classification

The AMS protocol introduced a hierarchical system for job classification. Within each department jobs with shared features, such as pot and vehicle operators were grouped in job groups. Each job group was divided into job categories according to their job

tasks: e.g. metal tappers, anode shifters, and beam raisers had responsibility for certain pots and were classified as pot operators. Similarly, vehicle operators were divided into job categories according to their respective vehicle type. During this period, there was some rotation of operators within each group but negligible rotation of workers between the groups, and almost no rotation between Söderberg and prebake cells. The majority of personal exposure samples were taken from specified job categories as recommended in the protocol. If an operator changed job category during the sampling period, the measurement was allocated to the corresponding group or department. The job classification system was categorized using a 6 digit code: digits 1–2 determined the department; digits 3–4 determined the groups within each department, whereas digits 5–6 determined the job categories within the groups. If a worker during a switched within different job categories he/she was allocated to the corresponding group, and if he/she performed jobs within different groups he/she was allocated to the corresponding Electrolysis Department. The structure of the hierarchical job structure and a short description of the job categories in the Electrolysis Department is shown in Table 2. In the concurrent epidemiological study, same system for job classification was used for each participating employee.

In addition to the job descriptors (department/group/job category) the exposure level was categorized by plant, process (Söderberg/prebake/'other'), and calendar time. Hence, the JEM was constructed as a combination of job descriptor (department/group/job category), plant (1–7), process (Söderberg/prebake/'other'), and calendar year (dummy variables).

For the period 1986–1995, all the Norwegian plants followed the AMS recommendations for exposure assessment, and 8423 dust, 7215 fluoride, and 4255 PAH measurements were available for data analyses. However, dust measurements of 50 mg m^{-3} or higher were excluded because they were considered invalid due to sampling errors (0.77% of the measurements) (Johnsen *et al.*, 2008), as were measurements with sampling durations of <2 h (3.7% of the measurements). Nonetheless, levels $>50 \text{ mg m}^{-3}$ had minimal influence on the estimates of the geometric mean. Most likely, these high measurements resulted from contamination of the filters with particles before,

during, or even after the sampling period. This exclusion resulted in a total number of 8109 dust, 6734 fluoride, and 3524 PAH measurements available for data analyses, of which 0.5, 2.9, and 11.4% were below their respective detection limits for dust, total fluorides, and PAH. These measurements were allocated to 50% of the detection limit, i.e. total dust, total fluorides, and PAH were replaced by 0.005 mg m^{-3} , 0.005 mg m^{-3} , and 0.5 mg , respectively.

Statistical analyses

The exposure measurements were log-normally distributed; therefore, the crude results were expressed as geometric means, and the multiple regression analyses were performed using log-transformed data as outcome variables.

The individual workers who wore the samplers were accounted for in one of two ways. First, 7038 (82%) of the measurements could be assigned the plant's employee number [2670 employees (62%)] which permitted the identification of repeated measurements. The remaining 18% of the measurements were assigned a random employee number, which precluded the identification of repeated measurements on the same worker. These measurements were included in the analyses. Statistical analyses were performed using linear mixed model to account for multiple measurements from the same worker (available for the majority of the workers) (Symanski *et al.*, 2001).

Three multiple regression models were developed for each of the outcomes (total dust, fluorides, and PAH). In Model 1, department was used as the job descriptor, i.e. all the available measurements from the plants were included. Models 2 and 3 were restricted to the Electrolysis Department only. Group was used as the job descriptor in Model 2, whereas job category was used in Model 3. Thereby, we omitted to develop nested models. Hence, we developed 9 models altogether, i.e. if information on job category was available, job category, technology, year, and plant were used to predict exposure. Likewise, if information on job category was not available or the subject changed job category within the same group, then group, technology, year, and plant were used to predict exposure, whereas if a subject changed between different groups, the combination of department, technology, year, and plant was used to predict exposure. We considered using one nested model for each

Table 1. Geometric mean (geometric standard deviation—GSD) of total dust, total fluorides (Tot-F), and polycyclic aromatic hydrocarbons (PAH) with number of measurements in parentheses by plant and process.

Plant	Geometric mean (GSD)					
	Dust, mg m ⁻³	<i>n</i>	Tot-F, mg m ⁻³	<i>n</i>	PAH, µg m ⁻³	<i>n</i>
Plant 1						
Søderberg	1.77 (2.83)	543	0.29 (2.32)	478	9.8 (3.7)	386
Prebake	1.83 (2.67)	576	0.44 (2.26)	514	7.2 (2.6)	78
Other	1.69 (3.66)	21	0.14 (3.23)	18	23.8 (39.9)	4
Plant 2						
Søderberg	1.70 (2.51)	546	0.35 (2.51)	473	34.0 (2.3)	99
Prebake	2.27 (2.88)	460	0.55 (2.60)	437	7.0 (3.1)	51
Other	1.70 (2.91)	22	0.50 (1.78)	8	9.5 (2.9)	8
Plant 3						
Søderberg	1.97 (2.30)	582	0.38 (2.78)	478	12.3 (2.1)	274
Prebake	1.74 (2.01)	510	0.55 (3.14)	280	19.0 (na)	1
Other	1.72 (2.28)	85	0.17 (2.89)	75	6.4 (2.1)	10
Plant 4						
Søderberg	1.53 (2.61)	531	0.35 (2.58)	531	17.5 (2.3)	531
Other	1.42 (3.40)	411	0.10 (3.76)	386	10.3 (2.8)	281
Plant 5						
Søderberg	1.14 (3.60)	1,138	0.46 (2.25)	1134	37.5 (3.4)	632
Prebake	1.57 (2.91)	192	0.26 (3.02)	189	na	0
Plant 6						
Prebake	4.13 (2.47)	821	0.42 (3.10)	795	2.0 (1.0)	2
Plant 7						
Søderberg	1.37 (3.85)	885	0.21 (2.95)	504	9.6 (3.9)	783
Prebake	0.75 (4.07)	504	0.19 (2.66)	319	4.2 (3.3)	306
Other	0.68 (4.85)	282	0.02 (4.71)	115	7.3 (5.3)	78
Process						
Søderberg	1.52 (3.15)	4,258	0.29 (2.80)	3,400	16.0 (3.6)	2,705
Prebake	2.01 (3.21)	3,030	0.41 (1.06)	2,732	4.9 (1.1)	438
Other	1.16 (3.95)	821	0.07 (4.96)	602	9.5 (3.4)	381

na, not available.

Table 2. The geometric mean (GM) of total dust and total fluorides (F) and polycyclic aromatic hydrocarbons (PAH) and the number of measurements (N) by job descriptor expressed as department, group, and job category during 1986–1995.

Department	Group	Job category	Description	Geometric mean—GM (geometric standard deviation—GSD)			
				Total dust, mg m ⁻³		Total F, mg m ⁻³	
				GM (GSD)	N	GM (GSD)	N
01	Electrolysis			1.69 (4.53)	7050	0.36 (2.64)	5,986
0101	Pot operators			1.61 (3.18)	4407	0.36 (2.56)	3,851
010101	General	Monitoring of the pots		1.93 (2.63)	774	0.39 (2.21)	731
010102	Anode	Anode shift (P) Stud puller (S)		1.30 (3.58)	1401	0.31 (3.04)	1,217
010103	Beam raiser	Adjust the anode level		1.34 (3.68)	523	0.24 (2.72)	464
010104	Metal tapper	Moving metal to foundry		1.78 (2.56)	1016	0.47 (2.05)	917
010105	Day shift	Diversity of jobs		1.43 (3.46)	105	0.29 (2.47)	96
010109	Unspecified	Combinations within the group		2.15 (3.13)	588	0.41 (2.16)	426
0102	Vehicle operators			1.40 (3.37)	774	0.25 (3.00)	646
010201	Oxide	Filling oxide into the pots		1.15 (3.67)	165	0.18 (2.47)	136
010202	Briquette	Filling Soderberg anodes		0.87 (3.13)	88	0.14 (2.42)	53
010203	Fluoride	Filling fluorides to the pots		1.58 (3.41)	31	0.35 (2.76)	19
010204	Truck driver	Different tasks		1.03 (3.38)	104	0.18 (3.28)	80
010205	Sweeper	Vehicles for cleaning		2.05 (3.09)	223	0.27 (3.31)	201
010209	Unspecified	Combinations within the group		1.52 (3.03)	163	0.40 (2.53)	157
0103	Foremen			1.25 (2.61)	492	0.30 (2.41)	432
0104	Service, general			2.74 (3.15)	598	0.55 (2.63)	520
010401	Measurement	Metal sampling from the pots		1.80 (2.95)	229	0.39 (2.41)	195
010402	Ladle cleaner	Cleaning, metal ladles		4.53 (2.79)	97	1.05 (2.54)	96

Table 2. Continued

Department Group	Job category	Description	Geometric mean—GM (geometric standard deviation—GSD)				PAH, $\mu\text{g m}^{-3}$	
			Total dust, mg m^{-3}		Total F, mg m^{-3}		GM (GSD)	
			GM (GSD)	N	GM (GSD)	N	GM (GSD)	N
010404	Maintenance	Mostly small repair on the pots	4.12 (3.05)	115	0.58 (2.53)	88	14.1 (3.4)	66
010405	Cleaning	Cleaning apart from 010205	3.22 (2.67)	73	0.61 (1.95)	71	9.0 (2.5)	56
010409	Unspecified	Combinations within the group	2.38 (3.12)	84	0.48 (2.55)	70	26.7 (3.7)	28
0105	Service Söderberg		2.08 (3.18)	441	0.37 (2.48)	370	22.2 (4.0)	305
010501	Burner cleaner	Cleaning gas burners & tubes	2.29 (3.07)	76	0.38 (1.99)	66	13.0 (4.8)	37
010502	Gas shirt	Changing gas shirt	2.29 (2.88)	277	0.44 (2.49)	224	23.5 (3.8)	230
010503	Stud cleaner	Cleaning removed studs	1.74 (2.35)	72	0.22 (2.05)	68	30.6 (3.3)	26
010509	Unspecified	Combinations within the group	0.51 (15.5)	16	0.20 (3.87)	12	19.3 (4.8)	12
010909	Unspecified	Electrolysis, unspecified	2.56 (2.09)	338	0.49 (2.04)	167	13.4 (1.9)	144
02	Scrubber	Cleaning emissions	2.51 (4.08)	132	0.36 (2.98)	119	16.4 (3.1)	106
03	Pot relining	Rebuilding cathodes	1.36 (3.81)	283	0.12 (2.90)	185	8.7 (4.0)	244
05	Casting house	Preparing aluminum for sale	0.77 (3.39)	248	0.07 (2.08)	130	4.2 (1.5)	33
06	Rodding	Reconstructing anodes (P)	1.59 (3.02)	122	0.18 (2.88)	103	5.1 (3.5)	91
07	Paste plant	Production of anode paste (S)	0.71 (4.44)	99	0.04 (1.97)	83	11.9 (4.7)	91
08	Anode plant	Production of anodes (P)	0.62 (3.93)	42	0.05 (2.16)	28	4.0 (2.9)	24
09	Mechanics	Support for production units	1.11 (4.12)	80	0.17 (2.49)	79	13.8 (2.8)	67
12	Transportation	Support for production units	2.68 (4.34)	20	0.20 (2.63)	7	17.4 (1.9)	6
13	Warehouse	Store equipment	0.57 (1.63)	2	na	0	9.2 (4.9)	2
14	Laboratory	Metal and environ.control	0.29 (3.25)	31	0.04 (2.33)	13	na	0
Total			1.61 (3.07)	8109	0.32 (2.85)	6,734	13.1 (3.8)	3524

P, prebake; S, Söderberg; na, not available.

of the outcomes but we chose to use separate models for each level of job classification (i.e. department, group, and job category), in part to yield a better fit at each level. For each of these models the initial model had no covariates. Then, the covariates were entered in the following order: plant, job descriptor, process, and year. In addition product terms between these covariates were included to test for interaction. #The following models were assessed for each outcome variable and each dimension of job descriptor (department, group and job category), i.e. nine models with the following 6 interactions: [plant]*[job descriptor], [plant]*[process], [plant]*[year], [job descriptor]*[process], [job descriptor]*[year] and [process]*[plant]. Product terms having P -values <0.1 were retained in the final model. # All the main effects were in the model, whereas the product terms with P -values ≥ 0.1 were removed.

The fit of the model was assessed using the Akaike criterion (AIC) and R^2 , i.e. $1 - [\text{Residual variance}(\text{full model})]/[\text{Residual variance}(\text{no covariates})]$ to compare and select the model with the best fit. First we compared the model fit using different covariance matrices in the repeated statement. It turned out that autoregressive moving average model, ARMA(1,1) and Toeplitz(8) matrix were comparable when the models converged. ARMA(1,1) was preferred because Toeplitz(8) frequently caused problems with convergence. Second, we investigated a model with random intercept without covariance matrix as well

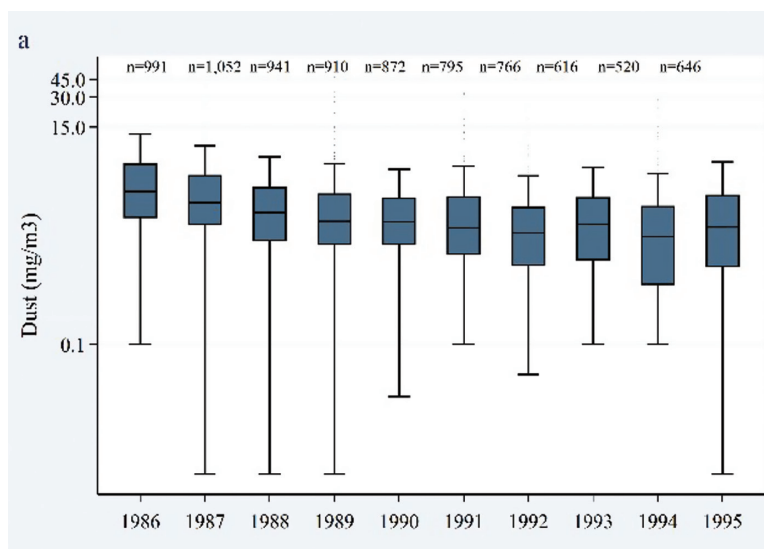
as models with covariance matrix without a random intercept. Inclusion of plant as a random covariate was also investigated. The data were analyzed using SAS version 9.3 (proc mixed SAS Institute Inc., Cary, NC, USA) and Stata version 13.1 (StataCorp, TX, USA).

Ethical considerations

The study was approved by the Regional Committee of Medical Ethics and verbal consent was obtained from the worker before sampling.

RESULTS

A summary of the number of measurements and geometric mean levels of the three types of exposure are presented by plant and technology (i.e. Söderberg, prebake, other) in Table 1 and by job classification (i.e. department, group, and job category) in Table 2. Over the observation period 1986–1996, the overall geometric mean of dust, total fluorides, and PAH were 1.61 mg m^{-3} , 0.32 mg m^{-3} , and $13.1 \text{ } \mu\text{g m}^{-3}$, respectively. Figure 1a–c indicates approximately a linear annual decline in the log-transformed measurements of dust, total fluorides as well as PAH during the follow-up. The figure shows the 95% confidence intervals, the quartiles, and range of each exposure variable during the follow-up. Similarly, a wide variation of the exposure estimates was found in each of the other JEM dimensions. Generally the standard deviation and variance were larger between individuals than within individuals, whereas the opposite was



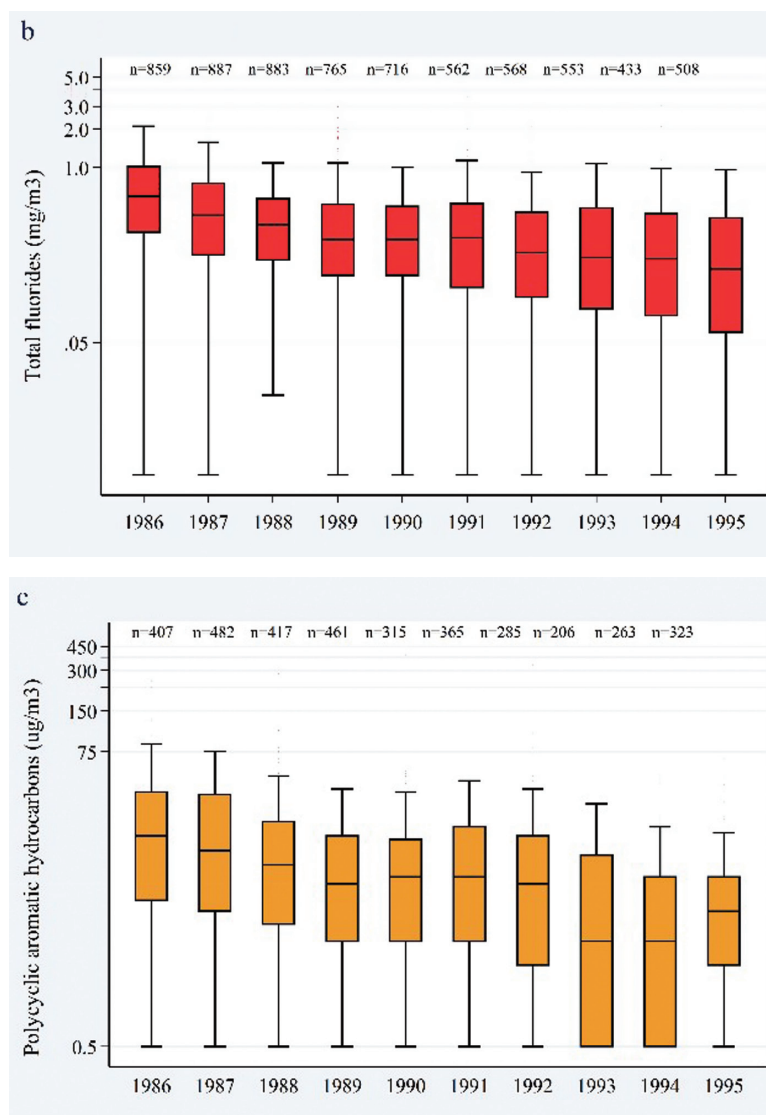


Figure 1 Box plots of (a) total dust (mg m^{-3}), (b) total fluorides (mg m^{-3}), and (c) polycyclic aromatic hydrocarbons (PAH in $\mu\text{g m}^{-3}$) during the follow-up.

found regarding the four JEM dimensions. Using univariate linear mixed models, this trend was estimated as a decline of 9.2% ($P < 0.0001$), 11.7% ($P < 0.0001$), and 14.9 % per year ($P < 0.0001$) for total dust, fluorides, and PAH, respectively. Overall, the crude estimates indicated that the exposure levels of dust and fluorides were highest in the prebake potrooms, whereas the level of PAH was highest in the Söderberg potrooms (Table 1). The exposure group 'other' had lowest exposure levels of dust and fluorides but not PAH, which was mostly due to paste production,

exposure in scrubbers, relining, or supporting tasks for other departments, including Söderberg potrooms (Table 2). The majority of measurements (82–89%) were performed in the potrooms (Table 2), reflecting that health concerns were mostly focused on this part of production. Except from the individuals who carried the samplers the variation was larger within the units than between them (Supplementary Tables 1.1–1.7). Generally, it appeared that in the potrooms maintenance workers were exposed to higher concentrations than regular pot operators and that vehicle

Table 3. Natural logarithm of dust, total fluorides, and polycyclic aromatic hydrocarbons (PAH) expressed by main effects using linear mixed model by plant, department, technology, and year (Model 1). Significant interaction terms are shown in [Supplementary Tables 3.1–3.3, a+b](#).

Plant	Dust (mg m ⁻³)		Total fluorides (mg m ⁻³)		PAH (µg m ⁻³)	
	Coef.	SE (P-value)	Coef.	SE (P-value)	Coef.	SE (P-value)
Intercept	1.02	0.06 (<0.001)	−0.63	0.05 (<0.001)	3.64	0.08 (<0.001)
Plant						
1	0.00	—	0.00	—	0.00	—
2	1.02	0.07 (<0.001)	0.30	0.07 (<0.001)	1.51	0.18 (<0.001)
3	−0.26	0.09 (0.003)	0.14	0.08 (0.079)	−1.46	0.19 (<0.001)
4	−0.21	0.07 (0.004)	0.07	0.07 (0.339)	−0.42	0.11 (<0.001)
5	−0.27	0.06 (<0.001)	0.01	0.05 (0.803)	1.02	0.10 (<0.001)
6	0.88	0.07 (<0.001)	−0.29	0.07 (<0.001)	−0.97	0.70 (0.165)
7	0.14	0.07 (0.040)	−4.64	0.44 (<0.001)	0.18	0.07 (0.007)
Department						
Electrolysis	0.00	—	0.00	—	0.00	—
Scrubber	0.16	0.31 (0.607)	−0.09	0.19 (0.626)	0.57	0.17 (<0.001)
Relining	0.41	0.11 (<0.001)	−0.25	0.12 (0.045)	−0.63	0.10 (<0.001)
Casting house	0.45	0.45 (0.010)	0.95	0.21 (<0.001)	−1.11	0.23 (<0.01)
Rodding	2.07	0.42 (<0.001)	3.30	0.30 (<0.001)	−0.19	0.26 (0.464)
Paste	0.28	0.25 (0.260)	0.95	0.25 (<0.001)	8.16	1.00 (<0.001)
Anode	−0.03	0.25 (0.908)	−1.31	0.86 (0.127)	0.05	0.27 (0.838)
Mechanics	−0.64	0.30 (0.034)	−0.19	0.27 (0.477)	0.32	0.18 (0.078)
Transport	2.41	0.32 (<0.001)	−1.21	0.67 (0.072)	0.21	0.46 (0.639)
Process						
Søderberg	0.00	—	0.00	—	0.00	—
Prebake	−0.01	0.05 (0.973)	0.37	0.04 (<0.001)	−1.16	0.08 (<0.001)
Other	−0.72	0.14 (<0.001)	−2.25	0.18 (<0.001)	−0.59	0.16 (<0.001)
Year						
1986	0.00	—	0.00	—	0.00	—
1987	−0.17	0.05 (<0.001)	−0.24	0.05 (<0.001)	−0.81	0.09 (<0.001)
1988	−0.28	0.05 (<0.001)	−0.49	0.05 (<0.001)	−1.19	0.10 (<0.001)
1989	−0.67	0.06 (<0.001)	−0.68	0.05 (<0.001)	−1.10	0.12 (<0.001)
1990	−0.87	0.06 (<0.001)	−0.87	0.06 (<0.001)	−2.73	0.16 (<0.001)
1991	−1.26	0.07 (<0.001)	−1.33	0.10 (<0.001)	−2.19	0.11 (<0.001)

Table 3. Continued

Plant	Dust (mg m ⁻³)		Total fluorides (mg m ⁻³)		PAH (μg m ⁻³)	
	Coef.	SE (P-value)	Coef.	SE (P-value)	Coef.	SE (P-value)
1992	-0.70	0.07 (<0.001)	-0.83	0.06 (<0.001)	-2.51	0.13 (<0.001)
1993	-0.34	0.08 (<0.001)	-0.66	0.07 (<0.001)	-2.66	0.14 (<0.001)
1994	-0.43	0.09 (<0.001)	-0.52	0.07 (<0.001)	-2.02	0.13 (<0.001)
1995	-0.63	0.08 (<0.001)	-0.43	0.11 (<0.001)	-1.54	0.08 (<0.001)
Model	R ² (%)	ΔAIC	R ² (%)	ΔAIC	R ² (%)	ΔAIC
No covariates	0.0	0.0	0.0	0.0	0.0	0.0
Main effects	18.1	-517.3 ^a	20.7	-565.6 ^a	38.3	-517.6 ^a
With interaction	46.4	-661.6 ^b	45.7	-831.8 ^b	53.3	-511.8 ^b

Coef., coefficient; SE, standard error; AIC, Akaike criterion.

^aDifference in AIC between a model with main effects and a model without covariates.

^bDifference in AIC between a model with and without interaction terms.

operators were least exposed. However, there was considerable overlap between the exposure categories.

Among the covariates, plant and year had the greatest impact on AIC as well as R^2 in the multivariate analyses. The only exception to this rule was found in Model 1 with total fluorides as the outcome, in which inclusion of department caused a larger decrease in AIC and increase in R^2 than plant and year. However, inclusion of process as a covariate caused a moderate decrease in AIC and increase in R^2 but less than plant and year. Nevertheless, process did not decrease AIC in any of the models with total dust as the dependent variable. Inclusion of a random intercept did not decrease the AIC but was associated with a considerable increase in R^2 , approximately from 20–25% to 45–55% or even more (highest for PAH). Models containing both a random statement and repeated statement did not have a noteworthy difference in AIC or R^2 compared with models having only the random intercept. Thus, we decided to use a model with random intercept.

Finally, we included the interaction components. The interaction components decreased the AIC with the same magnitude as the main effects, and R-squared increased approximately 20% (Tables 3–5). The number of interaction components decreased by 2–5 variables if the significance level was increased from 0.1 to 0.05 and by 5–20 variables if the significance level was increased from 0.1 to 0.01. We decided to use 0.1

as the significance level for all the models in order to get differentiated prediction values. Coefficients for the main effects in the final models are found in Tables 3–5, and the results for interaction terms are shown in Supplementary Tables 3.1a–5.3b. The final models had 41–75 components of the interactions, and 65–91% of these components were time-dependent.

For the interpretation of the results it is in generally important to take the interaction terms into account, e.g. in Table 3 the coefficient for fluorides in plant 7 is -4.64 indicating a dramatically lower fluoride exposure than in plant 1. However, if one takes the results in Supplementary Table 3.2a into account one must add +1.99 to +4.56 depending on the year in order to compare fluoride exposure in plant 7 with plant 1. One can find many similar results regarding several other covariates. Moreover, 94–100% components of the interactions involved plant or year as one of the product-terms. Hence, the results are predominantly useful for prediction of exposure to with the total dust, fluorides, and PAH in these plants during 1986 to 1996 only. Some of the interaction terms should, however, have some external validity. For example, stud pullers in Söderberg potrooms are more exposed to PAH than their counterparts (anode shift) in the prebake potrooms (job category 010102), whereas the latter group is more exposed to fluorides than the former group (Supplementary Tables 5.3b and 5.2b).

Table 4. Natural logarithm of dust, total fluorides, and polycyclic aromatic hydrocarbons (PAH) expressed by main effects using linear mixed model by plant, group, technology and year (Model 2, see methods). Significant interaction terms are shown in [Supplementary Tables 4.1–4.3, a+b](#).

Plant	Dust (mg m ⁻³)		Total fluorides (mg m ⁻³)		PAH (µg m ⁻³)	
	Coef.	SE (P-value)	Coef.	SE (P-value)	Coef.	SE (P-value)
Intercept	0.73	0.06 (<0.001)	-0.71	0.06 (<0.001)	3.60	0.08 (<0.001)
Plant						
1	0.00	—	0.00	—	0.00	—
2	0.84	0.09 (<0.001)	0.43	0.08 (<0.001)	2.37	0.27 (<0.001)
3	-0.10	0.07 (0.147)	-0.25	0.15 (0.104)	-1.68	0.21 (<0.001)
4	-0.17	0.08 (0.040)	0.11	0.08 (0.154)	-0.19	0.12 (0.122)
5	-0.10	0.07 (0.158)	0.01	0.06 (0.799)	1.24	0.09 (<0.001)
6	0.85	0.07 (<0.001)	-0.41	0.08 (<0.001)	-0.92	0.69 (0.178)
7	0.54	0.08 (<0.001)	-4.09	0.36 (<0.001)	0.44	0.07 (<0.001)
Group, electrolysis only						
Pot operators	0.00	—	0.00	—	0.00	—
Vehicle opr.	0.37	0.10 (<0.001)	-0.25	0.05 (<0.001)	-0.16	0.10 (0.107)
Foremen	-0.51	0.06 (<0.001)	-0.11	0.09 (0.221)	-0.39	0.10 (<0.001)
Service, general	0.69	0.07 (<0.001)	0.16	0.08 (0.048)	-0.10	0.07 (0.190)
Service Søderb.	0.65	0.07 (<0.001)	0.38	0.07 (<0.001)	-0.17	0.09 (0.067)
Technology						
Søderberg	0.00	—	0.00	—	0.00	—
Prebake	0.33	0.06 (<0.001)	0.61	0.05 (<0.001)	-1.18	0.07 (<0.001)
Year						
1986	0.00	—	0.00	—	0.00	—
1987	-0.11	0.05 (0.028)	-0.30	0.05 (<0.001)	-0.81	0.09 (<0.001)
1988	-0.31	0.06 (<0.001)	-0.53	0.06 (<0.001)	-1.04	0.11 (<0.001)
1989	-0.68	0.06 (<0.001)	-0.68	0.06 (<0.001)	-1.15	0.12 (<0.001)
1990	-0.87	0.06 (<0.001)	-0.82	0.06 (<0.001)	-2.48	0.12 (<0.001)
1991	-1.21	0.07 (<0.001)	-1.37	0.10 (<0.001)	-2.02	0.10 (<0.001)
1992	-0.46	0.07 (<0.001)	-1.05	0.07 (<0.001)	2.50	0.13 (<0.001)
1993	-0.28	0.08 (0.001)	-0.74	0.09 (<0.001)	-2.88	0.15 (<0.001)
1994	-0.45	0.10 (<0.001)	-0.71	0.08 (<0.001)	-2.06	0.15 (<0.001)
1995	-0.61	0.07 (0.001)	-0.62	0.11 (<0.001)	-1.68	0.10 (<0.001)

Table 4. Continued

Plant	Dust (mg m ⁻³)		Total fluorides (mg m ⁻³)		PAH (μg m ⁻³)	
	Coef.	SE (P-value)	Coef.	SE (P-value)	Coef.	SE (P-value)
Model assessment	R² (%)	ΔAIC	R² (%)	ΔAIC	R² (%)	ΔAIC
No covariates	0.0	0.0	0.0	0.0	0.0	0.0
Main effects only	20.7	-547.0 ^a	17.0	-565.6 ^a	41.0	-384.5 ^a
With interaction	45.7	-533.3 ^b	43.5	-831.8 ^b	58.8	-411.0 ^b

Coef., coefficient; SE, standard error; AIC, Akaike criterion.

^aDifference in AIC between a model with main effects and a model without covariates.^bDifference in AIC between a model with and without interaction terms.Table 5. Natural logarithm of dust, total fluorides and polycyclic aromatic hydrocarbons (PAH) expressed by main effects using linear mixed model by plant, job category, technology, and year (Model 3, see methods). Significant interaction terms are shown in [Supplementary Tables S.1–S.3, a+b](#).

Plant	Dust (mg m ⁻³)		Total fluorides		PAH (μg m ⁻³)	
	Coef.	SE (P-value)	Coef.	SE (P-value)	Coef.	SE (P-value)
Intercept	1.03	0.06 (<0.001)	-0.47	0.05 (<0.001)	3.40	0.08 (<0.001)
Plant						
1	0.00	—	0.00	—	0.00	—
2	0.66	0.08 (0.078)	0.35	0.06 (<0.001)	1.86	0.17 (<0.001)
3	0.26	0.08 (0.002)	-0.12	0.06 (0.063)	-1.54	0.20 (<0.001)
4	-0.11	0.07 (0.116)	0.05	0.06 (0.383)	-0.17	0.12 (0.186)
5	-0.01	0.07 (0.873)	0.01	0.06 (0.775)	1.53	0.09 (<0.001)
6	0.80	0.07 (<0.001)	-0.29	0.07 (<0.001)	-1.14	0.67 (0.093)
7	0.36	0.07 (<0.001)	-4.54	0.33 (<0.001)	0.38	0.08 (<0.001)
Job category						
Pot operators	0.00	—	0.00	—	0.00	—
Anode opr.	-1.04	0.06 (<0.001)	-1.03	0.10 (<0.001)	0.66	0.11 (<0.001)
Beam raiser	-0.57	0.08 (<0.001)	-0.10	0.10 (0.319)	-0.26	0.11 (0.014)
Metal tapper	-0.30	0.05 (<0.001)	-0.10	0.06 (0.075)	-0.19	0.08 (0.014)
Day shift	0.06	0.10 (0.539)	-0.10	0.10 (0.303)	-0.26	0.15 (0.075)
Oxide refill	0.00	—	0.00	—	0.00	—
Briquette refill	-0.03	0.25 (0.903)	-0.83	0.16 (<0.001)	0.24	0.24 (0.333)
Fluoride refill	-3.60	1.09 (0.001)	0.06	0.22 (0.790)	-0.33	0.26 (0.204)
Truck driver	0.17	0.16 (0.263)	0.31	0.17 (0.057)	-0.06	0.17 (0.707)

Table 5. Continued

Plant	Dust (mg m ⁻³)		Total fluorides		PAH (µg m ⁻³)	
	Coef.	SE (P-value)	Coef.	SE (P-value)	Coef.	SE (P-value)
Sweeper	0.21	0.18 (0.231)	-0.18	0.08 (0.033)	-0.48	0.17 (0.005)
Measurement	0.00	—	0.00	—	0.00	—
Ladle cleaner	0.47	0.13 (0.002)	0.75	0.11 (<0.001)	0.74	0.23 (0.001)
Maintenance	0.61	0.41 (0.136)	1.10	0.36 (0.002)	na	na
Cleaning	0.16	0.11 (0.160)	0.01	0.12 (0.902)	0.69	0.18 (<0.001)
Service Søderb.	0.00	—	0.00	—	0.00	—
Burner cleaner	-0.16	0.11 (0.153)	0.18	0.07 (0.012)	-0.23	0.10 (0.017)
Gas shirt	1.51	0.66 (0.022)	-0.62	0.11 (<0.001)	0.10	0.20 (0.618)
Technology						
Søderberg	0.00	—	0.00	—	0.00	—
Prebake	0.01	0.06 (0.825)	0.10	0.04 (0.008)	-0.80	0.14 (<0.001)
Year						
1986	0.00	—	0.00	—	0.00	—
1987	-0.11	0.05 (0.032)	-0.21	0.05 (<0.001)	-0.71	0.09 (<0.001)
1988	-0.17	0.06 (0.003)	-0.50	0.05 (<0.001)	-1.06	0.09 (<0.001)
1989	-0.64	0.05 (<0.001)	-0.63	0.05 (<0.001)	-1.08	0.12 (<0.001)
1990	-0.70	0.05 (<0.001)	-0.69	0.05 (<0.001)	-2.02	0.11 (<0.001)
1991	-0.81	0.06 (<0.001)	-1.27	0.10 (<0.001)	-1.88	0.13 (<0.001)
1992	-0.59	0.08 (<0.001)	-0.84	0.05 (<0.001)	-2.29	0.12 (<0.001)
1993	-0.47	0.08 (<0.001)	-0.56	0.06 (<0.001)	-2.72	0.15 (<0.001)
1994	-0.51	0.10 (<0.001)	-0.63	0.06 (<0.001)	-2.13	0.13 (<0.001)
1995	-0.85	0.07 (<0.001)	-0.75	0.08 (<0.001)	-1.53	0.09 (<0.001)
Model assessment						
	R ² (%)	ΔAIC	R ² (%)	ΔAIC	R ² (%)	ΔAIC
No covariates	0.0	0.0	0.0	0.0	0.0	0.0
Main effects only	23.4	-492.4 ^a	20.7	-497.8 ^a	42.5	-533.4 ^a
With interaction	44.3	-1063.1 ^b	46.6	-1261.5 ^b	61.2	-555.7 ^b

Coef., coefficient; SE, standard error; AIC, Akaike criterion.

^aDifference in AIC between a model with main effects and a model without covariates.^bDifference in AIC between a model with and without interaction terms.

DISCUSSION

In this study we found a highly significant time-related decrease in exposure to total dust, fluorides, and PAH among employees in the Norwegian aluminum

industry. Moreover, we found that the effect of several covariates on exposure was modified by time.

The strength of our study is the prospective design and that all the seven Norwegian plants followed the

same protocol for personal exposure sampling and used a common nested system for job classification. As such, the present results are well suited for implementation in a longitudinal study of obstructive lung diseases at the same plants during 1986–1995. Previous studies of occupational exposures in the aluminum industry have mainly relied on historical records of measurements that were not collected prospectively using a protocol (Romundstad *et al.*, 2000a,b; Gibbs *et al.*, 2007; Gibbs and Seignyn, 2007). In a study from the American aluminum industry the authors standardized job titles into distinct exposure groups (Noth *et al.*, 2014), that had some similarities with the present definitions of department, group, and job categories. Using their system they could explain about 26–36% of the variance of the data. Benke and coworkers developed a system for job classification at two Australian aluminum smelters that was similar to the current one, with a nested system based on department, job titles, and job tasks (Benke *et al.*, 2000). Their system, however, relied on historical characterization of the job tasks. Nonetheless, they claimed they could differentiate better between cumulative exposure levels among employees and reduce misclassification of exposure by introducing information on job tasks into the JEM [a task exposure matrix (TEM)]. Their TEM corresponds to a large extent to our job categories.

Importantly we found that follow-up time was a major determinant of exposure, and also the most important modifier of different risk factors for exposure. Moreover, the majority (up to 100%) of statistically the significant components of interaction terms involved plant or time. Thus, the abundant findings are apparently mostly applicable for the Norwegian Aluminum Industry in this period. However, it demonstrates that the large datasets enabled construction of complicated and detailed exposure assessments that can be used in epidemiological studies of health effects related to exposure. Associations between exposure and health may be overlooked if the exposure assessment was more restricted in space and time. However, the main effects and interactions involving job descriptors and technology may have interest beyond this cohort. For example, relining in the prebake potroom was associated with higher exposure to fluorides than relining in separate buildings or Söderberg potrooms.

The exposure levels in this study were in the same range as found in American ALCOA smelters from

1983 to 2011 [particulates GM 3.86 geometric standard deviation (GSD) 4.43 mg m⁻³] and in Australian smelters from 1995 to 2003 (inhalable dust 2.tertile: 0.62 to 3.15, fluoride 2.tertile: 0.027 to 0.44 mg m⁻³) (Abramson *et al.*, 2010; Noth *et al.*, 2014).

There are different explanations for the decrease of exposure during this period. Several technological improvements were incorporated during this period such as automatic alumina feeding, and more jobs were performed from cranes or vehicles with ventilated cabins. It also is likely that some of the improvements can be explained by a change in attitudes that took place during the 1980s. The industry may have responded to an increasing awareness of the potential detrimental health effects of such exposure to air pollutants at the work place and thus both management and the union paid more attention to safety and environment than in earlier periods.

A large number of measurements were collected from all the plants during the entire follow-up period indicating that the results should be valid for these plants over the study period. It is likely that the natural wide variation in exposure represents the most important limitation of exposure assessment in this environment. This problem could probably be solved by using a sufficiently large number of measurements for all the employees. This option is, however, impractical and economically unrealistic.

In conclusion, calendar year was the most important determinant of exposure in this study because it was an important effect modifier, and a large number of interactions had to be taken into account when modeling the data. Hence, we believe it is crucial for future longitudinal health studies to assess changes in exposure during the follow-up period.

SUPPLEMENTARY DATA

Supplementary data can be found at <http://annhyg.oxfordjournals.org/>.

ACKNOWLEDGEMENTS

The authors want to thank the Norwegian Aluminum Industry and AMS to give us the opportunity to analyze their exposure data. Special thanks to Manager AMS Eirik Nordheim, Laboratory Chief Rikard Karstensen, Laboratory Chief Sten Helland, and Union Representative Edgar Gundersen who worked out the protocol for personal measurements and monitoring of the workplace

exposure in the Norwegian Aluminum Industry. Eirik Nordheim also contributed with valuable comments on the manuscript. We want to thank Professor Gerry Hobbs, WV University, for statistical advice, Jean Cox-Ganser, PhD, NIOSH, for her comments on the manuscript and the employees in the Norwegian plants who have collected and analyzed the exposure samples as well as the employees who carried the air samplers.

DECLARATION

The Norwegian Aluminum covered travelling costs for V.S. B.B. and J.K. received 50 000 NOK each for their contribution in the advisory board. P.H. and M.A.V. have no conflict of interest to declare.

REFERENCES

- Abramson MJ, Benke GP, Cui J *et al.* (2010) Is potroom asthma due more to sulphur dioxide than fluoride? An inception cohort study in the Australian aluminium industry. *Occup Environ Med*; 67: 679–85.
- Armstrong B, Tremblay C, Baris D *et al.* (1994) Lung cancer mortality and polynuclear aromatic hydrocarbons: a case-cohort study of aluminum production workers in Arvida, Quebec, Canada. *Am J Epidemiol*; 139: 250–62.
- Benke G, Sim M, Fritschi L *et al.* (2000) Beyond the job exposure matrix (JEM): the task exposure matrix (TEM). *Ann Occup Hyg*; 44: 475–82.
- Frostad EW. (1936). Fluorine intoxication in Norwegian aluminium plant workers. *Tidsskr Nor Laegeforen*; 56: 179.
- Gibbs GW, Armstrong B, Sevigny M. (2007) Mortality and cancer experience of Quebec aluminum reduction plant workers. Part 2: mortality of three cohorts hired on or before January 1, 1951. *J Occup Environ Med*; 49: 1105–23.
- Gibbs GW, Labrèche F. (2014) Cancer risks in aluminum reduction plant workers: a review. *J Occup Environ Med*; 56: S40–S9.
- Gibbs GW, Sevigny M. (2007) Mortality and cancer experience of Quebec aluminum reduction plant workers. Part 3: monitoring the mortality of workers first employed after January 1, 1950. *J Occup Environ Med*; 49: 1269–87.
- Johnsen HL, Hetland SM, Saltyte Benth J *et al.* (2008) Quantitative and qualitative assessment of exposure among employees in Norwegian smelters. *Ann Occup Hyg*; 52: 623–33.
- Kongerud J, Samuelsen SO. (1991) A longitudinal study of respiratory symptoms in aluminum potroom workers. *Am Rev Respir Dis*; 144: 10–6.
- Noth EM, Dixon-Ernst C, Liu S *et al.* (2014) Development of a job-exposure matrix for exposure to total and fine particulate matter in the aluminum industry. *J Expo Sci Environ Epidemiol*; 24: 89–99.
- Romundstad P, Andersen A, Haldorsen T. (2000a) Cancer incidence among workers in six Norwegian aluminum plants. *Scand J Work Environ Health*; 26: 461–9.
- Romundstad P, Andersen A, Haldorsen T. (2000b) Nonmalignant mortality among workers in six Norwegian aluminum plants. *Scand J Work Environ Health*; 26: 470–5.
- Romundstad P, Haldorsen T, Rønneberg A. (1999) Exposure to PAH and fluoride in aluminum reduction plants in Norway: historical estimation of exposure using process parameters and industrial hygiene measurements. *Am J Ind Med*; 35: 164–74.
- Rønneberg A. (1995) Mortality and cancer morbidity in workers from an aluminium smelter with prebaked carbon anodes—Part III: Mortality from circulatory and respiratory diseases. *Occup Environ Med*; 52: 255–61.
- Søyseth V, Kongerud J, Ekstrand J *et al.* (1994) Relation between exposure to fluoride and bronchial responsiveness in aluminium potroom workers with work-related asthma-like symptoms. *Thorax*; 49: 984–9.
- Symanski E, Chan W, Chang CC. (2001) Mixed-effects models for the evaluation of long-term trends in exposure levels with an example from the nickel industry. *Ann Occup Hyg*; 45: 71–81.