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Decline in FEV_1 and airflow limitation related to occupational exposures in men of an urban community

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ABSTRACT: The purpose of this survey was to evaluate the effects of smoking and occupational exposures on the decline in forced expiratory volume in one second (FEV_1), and the presence of airflow limitation (FEV_1 ×100/forced vital capacity (FVC) being <65) at follow-up.

A random sample of 1,933 men aged 22–54 years in Bergen, Norway, were invited into the survey. Smoking habits and measurements of FEV_1 were recorded at the initial survey in 1965–1970 (n=1,591) and at follow-up in 1988–1990 (n=951). Past or present self-reported occupational exposures to eleven airborne agents (dusts, gases, vapours and fumes) and measurements of FVC were recorded at follow-up only.

The decline in FEV_1 was associated ($p<0.001$) with age, body height and smoking. Smoking cessation reduced the decline to the level of lifetime nonsmokers. Accelerated decline in FEV_1 was observed in subjects exposed to sulphur dioxide gas and to metal fumes. The adjusted decline in FEV_1 increased progressively in subjects exposed to increasing numbers of occupational agents (test for trend: $p<0.01$). Airflow limitation was observed in 9.5% at follow-up, and increased with age and cigarette consumption.

In this community follow-up survey in men, smoking and occupational exposures to sulphur dioxide gas, metal fumes and the numbers of specific agents were found to be important predictors for accelerated decline in FEV_1.

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Observations from numerous cross-sectional studies have identified cigarette smoking as the most important determinant for the level of ventilatory function [1]. These observations have been confirmed in several longitudinal studies demonstrating accelerated decline in forced expiratory volume in one second (FEV_1) among smokers [2–6]. The role of occupational exposure to airborne irritants as independent predictors for accelerated decline in FEV_1 is still debated [7]. Although several longitudinal studies have been performed in selected occupational groups [7], only one longitudinal study in a general population has observed an association between accelerated decline in FEV_1 and self-reported occupational exposure to dusts in men [5]. Evidence of an association between accelerated decline in FEV_1 and occupational exposure to individual agents, such as gases, vapours and fumes, are unknown in general population studies.

Longitudinal studies from general populations of FEV_1 decline have, so far, mainly been performed over follow-up periods of 13 yrs or less [4–6, 8–11].

The aims of this 20–25 yr community follow-up survey in men were: 1) to estimate the decline in FEV_1 related to age, body height, smoking and self-reported occupational exposures to mineral-dusts, gases, vapours and fumes; and 2) to estimate the presence of airflow limitation (FEV_1×100/forced vital capacity (FVC) <65) at follow-up, as predicted by these variables.

Subjects and methods

Initial survey

The source population included all men living in the city of Bergen, Norway, on January 1, 1964, born between 1914 and 1943, and comprised 21,239 men from a total of 116,876 inhabitants. A random sample of 1,933 men was obtained from the Population Registry of Bergen by selecting all eligible subjects in the source population born on the 3rd, 13th or 23rd day of each month. From September 1965 to January 1970 the sample was invited to the Bergen Blood Pressure Survey and included 1,591 subjects after two reminder letters (attendance 82%). Information on smoking habits was obtained through a standardized interview by trained nurses using a modified British Medical Research Council questionnaire [12] translated into Norwegian.

Follow-up survey

From November 1988 to September 1990, a follow-up survey was performed among those of our sample living in Bergen and 33 surrounding municipalities (Hordaland county). All subjects were asked to complete postal self-administered questionnaires, and those living in Bergen were also invited to a follow-up examination including spirometry. The questionnaires elicited information on smoking habits and past or present exposures to eleven occupational airborne agents (asbestos, quartz, ammonia, chlorine, nitrous gas, ozone, sulphur dioxide, aldehydes, anhydrides, diisocyanates and the metals: chromium, nickel and platinum) potentially harmful to the airways. Completed questionnaires were obtained in 92% (n=1,063) of those invited to follow-up (n=1,154), representing 67% of the attendants at the initial survey (table 1). The subjects had a mean age of 61 yrs (range: 46–76 yrs), after a mean follow-up period of 23 yrs (range: 20–25 yrs).

Table 1. – Follow-up status in 1988–1990 among subjects attending an initial survey in 1965–1970 of a random sample of men initially aged 22–54 yrs

	Attendants to initial survey in 1965–1970: n=1591	
	n	%
Follow-up status in 1988–1990		
Participants with completed questionnaires	1063	67
Nonresponding residents in the study area	91	6
Not available for follow-up due to:		
Changed residence out of study area	134	8
Deceased by January 1, 1990	303	19

Loss of follow-up

All deaths and emigrations in the sample were identified from records at the Central Population Registry of Norway. Altogether, 27% of subjects attending the initial survey were unavailable for follow-up (table 1). Thirty percent of those attending the initial survey in the age group 40–54 yrs had died prior to follow-up compared to 9% of those aged 22–39 yrs. The crude mortality rate was inversely related to baseline level of FEV_1 and was 2.5 times higher in those with FEV_1 <70% of reference level [13], compared to those with FEV_1 ≥100%.

Smoking habits

Smoking habits at the initial survey were recorded using the definition of FLETCHER *et al.* [12], and at follow-up as defined by BJARTVEIT *et al.* [14]. The prevalence of smokers and nonsmokers differed within 1% using the two criteria [15]. Good agreement was found at follow-up between self-reported smoking habits and venous carboxyhaemoglobin-levels [16].

Body height

In both surveys, body height was measured to the nearest cm, with heels and neck nearest the measure, without shoes. Measurements from the initial survey were used in the analysis. The mean (SEM) body height was 176.2 cm (0.2 cm) at the initial survey. At follow-up those attending had a mean (SEM) body height 0.7 cm (0.1 cm) lower than at the initial survey.

Spirometry

Forced expirations at the initial survey and at follow-up were recorded using dry-wedge bellow spirometers (Vitalograph P-model and S-model, respectively). During the initial survey, the instrument was calibrated at regular intervals using a 1 *l* syringe, and the technician measured his own FEV_1 and FVC daily to assure that the spirometer did not drift. Forced expiration manoeuvres were performed with the subject standing, without using a noseclip. Highest values of FEV_1 were recorded from at least two acceptable attempts, and values used in the analysis were corrected to 37°C and pressure saturated (BTPS) conditions.

During follow-up, the spirometer was calibrated to 7 *l* twice daily using a 1 *l* syringe, with maximum readings varying from 6.95 to 7.05 *l* (median 7.04 *l*). Room temperature and barometric pressure were recorded twice daily with mean (SD) values of 21(1)°C and 753(13) mmHg, respectively. Forced expiration manoeuvres were performed with the subject sitting, using a noseclip, with a minimum exhalation time of 6 s, unless there was an obvious plateau on the chart. A minimum of three acceptable attempts was performed and the two highest FVC values should not differ by more than 300 ml [17]. Highest BTPS values of each FEV_1 and FVC were used in the analysis.

The criteria from the American Thoracic Society for acceptable forced expiration manoeuvres [18] was applied, and identical acceptability criteria at both examinations was ensured as the initial technician was interviewed by the follow-up technician prior to start of the follow-up examination. Acceptable spirometric measurements were obtained in 1,588 subjects, from a total of 1,591 subjects at the initial survey, and 951 subjects, from a total of 972 subjects at follow-up. At follow-up, 15 men were not willing to do the test and six subjects failed to produce satisfactory measurements.

In a sample of 46 subjects, where the spirometric method from the initial survey was compared in a random order with the method from follow-up, FEV_1 was on average 2 ml (SEM 14 ml) lower using the former method than the latter method.

The rate of change in FEV_1 (decline in FEV_1), expressed in $ml \cdot yr^{-1}$, was estimated for each subject by: annual decline in FEV_1=(FEV_1 (ml) at initial survey - FEV_1 (ml) at follow-up) × 12/(months between the two examinations). Airflow limitation was defined as $FEV_1 \times 100/FVC$ <65 at follow-up and similar ratios have been applied in previous follow-up studies [2, 8, 19].

Age- and height-standardized residuals of FEV_1 ($SFEV_1$) from the initial survey were calculated by dividing the absolute residual (recorded FEV_1 minus predicted) by the residual standard deviation taken from the regression equation from the reference population [13].

Mean baseline levels of FEV_1 from initial survey in all those attending (n=1,588), and subjects with complete data for follow-up analysis (n=951) were 99.7 and 100.3% in percentage of the reference values, respectively.

Statistical methods

All analyses were performed using the BMDP package [20]. Unpaired t-tests were used to compare mean values. Differences between prevalences were tested by chi-squared tests. Comparison of mean values adjusted for co-variables was performed by one-way analysis of covariance. Test for trend was performed by linear regression analysis. A significance level of p=0.05 (two-tailed) was used for all the analyses, unless otherwise stated.

Multiple linear regression analysis and multiple logistic regression analysis were used in selecting the factors important for prediction of annual decline in FEV_1 and presence of airflow limitation at follow-up, respectively. Ordinal variables were introduced to the equations using dummy variable technique.

The association between level and FEV_1 decline was assessed using mean FEV_1 level ((baseline FEV_1 level + follow-up FEV_1 level)×0.5) by body height^3, age and smoking as independent variables, with FEV_1 decline as the dependent variable in a multiple linear regression analysis [2, 3, 21]. Separate analyses were performed in different smoking groups to assess the effect of smoking on the relationship between level and decline in FEV_1.

Results

Subjects with completed questionnaires and three acceptable spirometric measurements at follow-up (n=951) were younger (p<0.001) than those who died prior to follow-up (n=303), but older (p<0.001) than nonresponders in the study area at follow-up (n=91) and subjects who had left the area prior to follow-up (n=134) (table 2). Those who died prior to follow-up included a larger proportion of smokers than those still alive. $SFEV_1$ in the group deceased at follow-up was lower (p<0.001) than in those still alive.

Among those attending both surveys, the percentage of smokers decreased from 66% at the initial survey to 39% at follow-up. However, among cigarette smokers at both surveys the mean (SD) number of cigarettes smoked·day^{-1} increased from 11 (6) at initial survey to 15 (7) at follow-up.

The annual decline in FEV_1 was slowest (p<0.001) in those aged 22–24 yrs at initial survey, whereas no clear age-related difference in FEV_1 decline was observed in those aged ≥25 yrs (table 3). The decline in FEV_1 was slowest in lifetime nonsmokers and increased with number of cigarettes smoked·day^{-1}. Pipe or cigar smokers, as well as those who started to smoke between the surveys, were associated with an FEV_1 decline similar to that in cigarette-smokers. On the other hand, smoking cessation prior to the initial survey was associated with an FEV_1 decline similar to that in lifetime nonsmokers.

Airflow limitation at follow-up was present in 9.5% of the subjects, and increased with age and cigarette consumption (table 3).

The prevalence of self-reported occupational airborne exposures (table 4) varied between 22% (asbestos dust) and 2% (ozone gas). Those who did not report any occupational exposure to the eleven agents, included 57% (n=518) of all the subjects (table 4 and fig. 1). Exposure to one, two, three, four, five and six or more of the agents was reported by 20, 11, 4, 4, 3, and 2% of all attendants at follow-up, respectively.

No statistical differences were observed in baseline levels of FEV_1 between exposed and nonexposed individuals for each occupational agent listed in table 4 after adjusting for age, height and smoking (in six groups).

Compared to subjects without any known exposure, the age-, height- and smoking-adjusted FEV_1 decline was 13(SEM 5)% faster in subjects exposed to sulphur dioxide gas (p<0.05), 10(4)% faster in subjects exposed to metal fumes (p<0.05) and 9(5)%, 7(4)%, 7(4)% and 6(2)% faster (0.05<p<0.10) in those exposed to nitrous gas, quartz dust, ammonia gas and anhydride vapours, respectively (table 4). Similar results were observed in subjects below (n=492) and above 40 yrs of age (n=419), although only exposure to metal fumes in subjects below 40 yrs of age reached the 5% level of statistical significance.

Airflow limitation was three times more prevalent (p<0.05) in subjects with high exposure to asbestos dust, compared to subjects without any known exposure (table 4). Furthermore, accelerated decline in FEV_1 was observed in those reporting asbestos exposure, compared to those without any known exposure, and a borderline significant trend test (p=0.08) was observed between FEV_1 decline and three levels of asbestos exposure (high/medium, low and no exposure).

The adjusted annual decline in FEV_1 increased progressively in subjects exposed to increasing numbers of occupational agents, from 52 ml·yr^{-1} in subjects without any known exposure to 61 ml·yr^{-1} among those exposed to six or more different agents (test for trend: p<0.01, fig. 1). Similar effects were observed within each smoking group (fig. 2). Although the age- and body height-adjusted regression coefficient per agent (from 0–6 or more) was higher in persistent cigarette smokers (regression coefficient: 1.9 ml·yr^{-1}; SE: 0.9 ml·yr^{-1}; p<0.05) than in nonsmokers (lifetime nonsmokers and ex-smokers) (regression coefficient: 1.2 ml·yr^{-1}; SE: 0.7 ml·yr^{-1}; p<0.05), no interaction effect was observed between occupational exposure and smoking (no departure from an additive model).

Multiple linear regression analysis, that included occupational exposure to agents with significant effects (p<0.05) in table 4 (sulphur dioxide gas and metal fumes), showed that the decline in FEV_1 was dependent on age, body height and smoking (p<0.01). Unfavourable associations were found between annual decline in FEV_1 and exposure to sulphur dioxide gas (regression coefficient: 5.6 ml·yr^{-1}; SE:

Table 2. – Age, smoking habits and standardized residuals of FEV_1 ($SFEV_1$) in subjects attending the initial survey in 1965–1970 by their follow-up status in 1988–1990

Follow-up status in 1988–1990:	Total	Alive at follow-up			Deceased by January 1, 1990
	Attendants at initial survey	Attendants at follow-up with questionnaire and spirometry	Responders at follow-up with questionnaire only	Lost to follow-up†	
	n=1591	n=951	n=112	n=225	n=303
Variables from the initial survey in 1965–1970					
Age* yrs (SD)	38 (8.8)	38 (8.5)	34 (8.3)	34 (8.2)	44 (7.0)
Smoking habit %					
Lifetime nonsmokers	18	18	21	25	9
Ex-smokers	15	16	13	17	13
Smokers	67	66	66	58	78
$SFEV_1$ *	-0.00[A] (1.14)	0.04 (1.09)	0.12[B] (1.19)	0.23 (1.07)	-0.36[C] (1.23)

See text for calculations of $SFEV_1$. *: Mean(±SD). †: Nonresponders in study area (n=91) and subjects who had left the area (n=134). Spirometry was missing in three (A), one (B) and two (C) subjects. FEV_1: forced expiratory volume in one second.

Table 3. – FEV_1 from initial survey, subsequent decline in FEV_1 and presence of $FEV_1 \times 100/FVC$ <65 at follow-up by age, body height and smoking habits

	Subjects	FEV_1 from initial survey*	Decline of FEV_1*	$FEV_1 \times 100/FVC$ <65 at follow-up
	n	*l*	ml·yr^{-1}	%
Total series	951	4.40±0.03	52.8±0.6	10
Age at initial survey				
22–24 yrs	58	5.02±0.08	44.6±1.9	2
25–34 yrs	294	4.88±0.04	54.5±1.0	4
35–44 yrs	347	4.27±0.04	52.1±1.0	8
45–54 yrs	252	3.90±0.05	53.5±1.2	19
Body height at initial survey				
≤169 cm	120	3.74±0.06	46.5±1.6	10
170–174 cm	253	4.06±0.04	51.1±1.1	13
175–179 cm	285	4.47±0.04	52.9±1.0	7
180–184 cm	194	4.72±0.05	55.9±1.3	8
≥185 cm	99	5.29±0.07	58.2±2.2	5
Smoking groups†				
Lifetime nonsmokers	156	4.62±0.06	46.6±1.4	0
Ex-smokers prior to initial survey	128	4.35±0.07	47.0±1.3	7
Stopped smoking between initial survey and follow-up	252	4.33±0.05	51.5±1.1	9
Cigarette smokers at initial survey and at follow-up				
< 10 cigarettes·day^{-1} at initial survey	154	4.39±0.08	56.5±1.6	8
≥ 10 cigarettes·day^{-1} at initial survey	151	4.35±0.07	60.4±1.5	21
Others that had ever smoked#	70	4.48±0.09	58.1±2.4	10
Inconsistent information +	31	4.34±0.18	46.3±3.1	3

*: data are presented as mean±SEM; †: information on smoking habits were missing in nine subjects; #:this group included pipe or cigar smokers at initial survey who still smoked at follow-up (n=35) and subjects who had started to smoke between the two surveys (n=35); +: inconsistent information included smokers and ex-smokers from initial survey who reported never having smoked at follow-up. FEV_1: forced expiratory volume in one second; FVC: forced vital capacity.

Table 4. – Mean decline in FEV_1 and presence of $FEV_1 \times 100/FVC$ <65 at follow-up by various airborne occupational exposures after adjusting for age, body height and smoking*

	Subjects	Decline in FEV_1+	$FEV_1 \times 100/FVC$ <65 at follow-up
	n=911	ml·yr^{-1}	%
Subjects without any known exposure	518	51.9±0.8	10
Subjects exposed to†:			
Mineral dusts			
Asbestos	197	53.0±1.2	11
High	10	54.4±5.5	28**
Medium	41	55.1±2.7	12
Low	146	52.4±1.4	10
Quartz	86	55.4±1.9*	11
Gases			
Ammonia	100	55.6±1.8*	10
Chlorine	48	55.3±2.5	9
Nitrous	46	56.6±2.6*	7
Ozone	16	58.4±4.5	14
Sulphur dioxide	44	58.7±2.7**	11
Vapours and fumes			
Aldehydes	88	54.2±1.9	7
Anhydrides	122	55.2±1.6*	10
Diisocyanates	33	54.7±3.1	9
Metals (chromium/nickel/platinum)	90	56.8±1.9**	7

+: data presented as mean±SEM; #: adjusted for age, body height and smoking (in six groups as in table 3) using one-way analysis of covariance after excluding subjects with missing information on smoking habits (n=9) and those with inconsistent information (n=31); †: the sum of exposed subjects is higher than the number of subjects because each subject may be exposed to more than one agent. Probability values for each exposure comparing subjects exposed to those without any known exposure: *: 0.05<p<0.10; **: p<0.05. For abbreviations see legend to table 3.

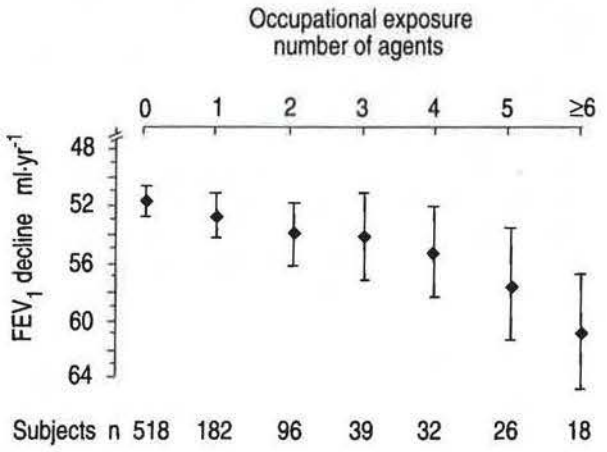

Fig. 1. – Decline in FEV_1 in subjects exposed to increasing number of occupational agents adjusted for age, body height and smoking (in six groups as in table 4) (test for trend: p<0.01). Data are presented as mean±SEM. FEV_1: forced expiratory volume in one second.

2.7 ml·yr^{-1}; p<0.05) and to metal fumes (regression coefficient: 4.3 ml·yr^{-1}; SE: 1.9 ml·yr^{-1}; p<0.05). These effects were similar in subjects aged below and above 40 yrs. No interaction effect was observed between sulphur dioxide gas and metal fumes (no departure from an additive model). Occupational exposure defined as a categorical variable (from 0 (no exposure) to 6 (exposure to six or more different agents)) was found to be an important predictor for decline in FEV_1 (table 5). The regression coefficients were of similar size in subjects aged below (1.05 ml·yr^{-1}) and above 40 years (1.14 ml·yr^{-1}). No interaction effect was seen between age and occupational exposure.

Mean FEV_1 level divided by body height^3 was not a significant predictor (regression coefficient: -2.8 ml·yr^{-1}·m^3; SE: 5.8 ml·yr^{-1}·m^3; p=0.63) of FEV_1 decline. Regression coefficients for mean FEV_1 by body height^3 varied significantly (p<0.001) between different smoking groups from +26.2 ml·yr^{-1}·m^3 in lifetime nonsmokers to -22.4 ml·yr^{-1}·m^3 in persistent heavy smokers (≥10 cigarettes·day^{-1}). However, none of these regression coefficients were significantly different from zero.

In a multiple logistic regression analysis, the adjusted odds ratios for airflow limitation at follow-up was 3.1 (95% confidence interval: 2.1–4.6) for 10 yrs increase in age and 6.9 (3.2–14.8) for persistent cigarette smokers compared to nonsmokers (lifetime nonsmokers and exsmokers from 1965–1970). An exposure-response relationship was found between airflow limitation and number of cigarettes smoked·day^{-1} with the adjusted odds ratios in persistent light smokers (<10 cigarettes·day^{-1}) and persistent heavy smokers being 3.5 (1.5–8.6) and 12.2 (5.4–27.7), respectively, compared to nonsmokers. Exposure to one or more occupational agents compared to nonexposure was not a significant risk factor for airflow limitation (adjusted odds ratio: 1.3 (0.8–2.2)).

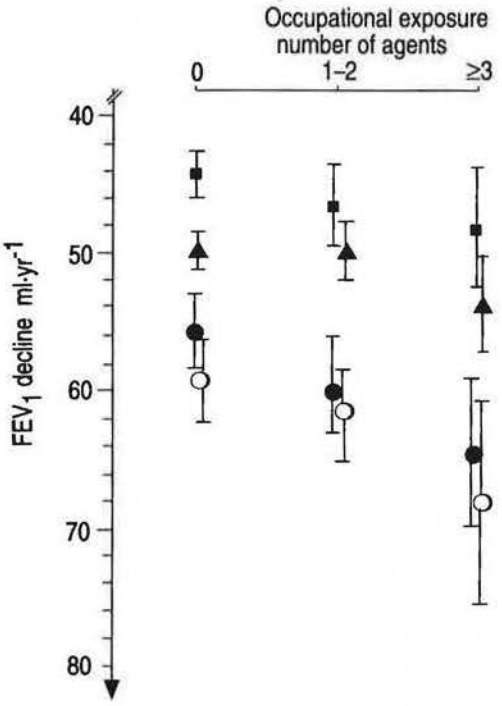

Fig. 2. – Age- and body height-adjusted decline in FEV_1 by number of occupational agents in different smoking groups: lifetime nonsmokers (■) (n=113); ex-smokers (▲) (n=225); smokers of 1–9 cigarettes·day^{-1} (●) (n=92); and smokers of ≥10 cigarettes·day^{-1} (○) (n=88). Subjects with "don't know" answers or missing values on any of the agents are not included. Data are presented as mean ±SEM. FEV_1: forced expiratory volume in one second.

Table 5. – Regression coeficients with standard errors (SE), F-ratios and p-values of the multiple linear regression equation for decline in FEV_1 (ml·yr^{-1}) between initial survey in 1965–1970 and at follow-up in 1988–1990 (n=911), multiple R^2=0.14

Factor	Regression coefficient ml·yr^{-1}	SE	Partial F-ratio	p
Constant	-79.66			
Age yrs	0.26	0.07	13.6	<0.01
Body height cm	0.66	0.09	51.5	<0.01
Smoking groups#:			16.1	<0.01
Ex-smokers (prior to initial survey)	-1.92	2.08		
Stopped smoking (between surveys)	3.41	1.77		
Cigarette smokers at both surveys				
<10 cigs·day^{-1} (at initial survey)	8.72	1.96		
≥10 cigs·day^{-1} (at initial survey)	12.89	1.96		
Other that had ever smoked	9.82	2.47		
Occupational exposure per agent†	1.09	0.40	7.6	0.01

#: reference category - lifetime nonsmokers; †: from 0 (no exposure) to 6 (exposure to 6 or more agents). FEV_1: forced expiratory volume in one second.

Discussion

Detrimental effects of smoking and beneficial effects of smoking cessation were observed on decline in FEV_1 and presence of airflow limitation at follow-up in male adults. After adjusting for age, body height and smoking, an accelerated decline in FEV_1 was observed in subjects exposed to sulphur dioxide gas and to metal fumes. The adjusted decline in FEV_1 increased progressively in subjects exposed to increasing numbers of occupational airborne agents.

The application of the two slightly different spirometry methods in this follow-up survey could have a minor effect on the observed absolute decline in FEV_1. However, both dry wedge-shaped bellow spirometers had identical dimensions of breathing tubes and mouthpieces, recording styluses and chart carriers with timing devices. Quality control of the spirometers and identical acceptability criteria were applied in both examinations, and only minimal differences in FEV_1 recordings were observed, when comparing the two different spirometry methods in this follow-up survey. This is in agreement with previous observations, where measurements of FEV_1 were about 1% higher in standing position than in sitting position [22], and within 1% lower using best of two recordings instead of three [23], as well as negligible influence of using a noseclip [18].

Selection bias may affect the results in a community-based follow-up survey. However, the subjects were selected randomly from the community regardless of occuptional exposures. The age-compositions of attendants and non-attendants to the initial survey were identical to all male residents of similar age-range in the same city on July 1, 1963 [24]. Those attending the initial survey had a mean FEV_1 of 100% in percentage predicted. Those attending at follow-up had similar initial age, body height, smoking habits, occupational status and lung function to those attending the initial survey. A 23 yr follow-up survey poses problems due to loss of follow-up. However, the attendance rate after 23 yrs follow-up in our survey was higher than that obtained in similar longitudinal community studies in Cracow (60% attendance after 13 yrs follow-up) [5], and in Copenhagen (55% attendance after 5 yrs follow-up) [6]. In our survey, death was the most important reason for loss of follow-up, and increased with age. Hence, observed associations with FEV_1 decline would be more representative in younger than in older subjects.

Although the outcome variable in this survey was based on objective spirometric measurements, any recall bias could produce a positive association between exposure and decline in FEV_1, if subjects with accelerated decline in FEV_1 reported exposure more frequently than those with a slower decline in FEV_1. In order to minimize this possible bias, each subject answered the self-administered questionnaires prior to spirometric measurements, with the spirometric technician unaware of answers given.

Limited information is available on the quality of occupational exposure assessments. For a given exposure with a low prevalence, an increased specificity would have much greater effect on the estimated outcome variable

than the increased sensitivity [25]. Information on occupational exposures has been based on retrospective occupational histories and/or self-reported exposures recorded in a questionnaire (mostly used in community studies), estimates made by hygienists or physicians [3], or the use of job exposure matrices [26]. Exposure can be characterized according to occupational title (or status), work processes, type of industry or exposure to specific agents. In selected occupational groups, good agreement have been found between self-reported recall of occupational titles and company records [27]. Although measurement error and misclassification are inevitable in any occupational exposure assessment, the misclassification was found to be nondifferential, making it more difficult to detect any relations. An identical question on previous asbestos exposure to that used in our survey was validated in a cross-sectional community study of 21,453 men in another area of Norway [28]. It showed a high specificity (97%) and a low sensitivity (45%) against answers given in an interview with an occupational physician. The subject's age at interview was almost identical with the age at follow-up of our population, and recall was over a similar period. Both studies observed similar age-adjusted prevalence of self-reported previous occupational asbestos exposure (in men aged 50–69 yrs: 19% and 22%, respectively). These high prevalences are probably reflected by similar type of industries in the two areas. The prevalence of subjects exposed from one to six or more agents in our survey is in accordance with observations from a cross-sectional survey in 1987–1988 of the male population aged 18–73 yrs in the same area [29]. Good agreements were observed between self-reported specific occupational exposures and exposure-groups based on occupational titles.

Subjects exposed in our survey could also be exposed to other occupational contaminants. Thus, the agents used may be indicators of an unhealthy working environment. Subjects exposed to large numbers of agents could be more heavily exposed or exposed for a longer period than subjects exposed to few irritants. Consistent with this, we observed that the initial age of the subjects were inversely related to the number of irritants. This could suggest that subjects exposed to a large number of irritants commenced exposure earlier than those exposed to only a few irritants. The independent effects from sulphur dioxide gas and metal fumes on FEV_1 decline could also be due to the effects from other correlated exposures, since subjects exposed to sulphur dioxide gas and metal fumes reported past or present welding, grinding and soldering three to four times more frequently ($p<0.001$) than subjects without any occupational exposure. Adjustment of the simultaneous effects from sulphur dioxide and metal fumes to each of the other nine exposure-agents in our survey was performed using multiple linear regression analyses adjusted for age, height and smoking. This adjustment reduced the effects from sulphur dioxide and metal fumes by a maximum of 11 and 9%, respectively, when adjusting for anhydride exposure (regression coefficient for sulphur dioxide: 5.0 $ml \cdot yr^{-1}$; SE: 2.8 $ml \cdot yr^{-1}$; $p=0.07$: and regression coefficient for metal fumes: 3.9 $ml \cdot yr^{-1}$; SE: 2.0 $ml \cdot year^{-1}$; $p=0.05$). However, these adjustments could result in overcorrection of the co-variables, since most of the eleven exposure-agents were associated with each other. Despite possible overadjustments, metal fumes remained independently associated with accelerated decline in FEV_1.

Residual confounding by smoking could have affected the relationship between occupational exposures and decline in FEV_1. This could occur if smoking habits of an individual were imprecisely characterized or if the tobacco consumption was reported differently in subjects exposed and nonexposed. However, we also observed an exposure-response relationship between the number of occupational agents and decline in FEV_1 within lifetime nonsmokers, which indicates that residual confounding by smoking cannot explain this relationship.

It is generally accepted that FEV_1 reaches a peak around the age of 30 yrs in men [30]. This might explain why the observed decline in FEV_1 was slowest in those aged 22–24 yrs at the initial survey. In lifetime nonsmokers the absolute decline in FEV_1 observed in our study of men aged 22–54 yrs (47 $ml \cdot yr^{-1}$) was similar to that observed in male lifetime nonsmokers aged 19–50 yrs in the Cracow study (49 $ml \cdot yr^{-1}$) [5]. Measurements of FEV_1 in BTPS values were performed 13 yrs apart, using dry wedge spirometers (Vitalograph) similar to that used in our study. However, in the Copenhagen City Heart Study [6] a considerably slower decline was observed in men aged 20–55 yrs (21 $ml \cdot yr^{-1}$). Measurements of FEV_1 in ambient temperature and pressure, saturated (ATPS) values were recorded only 5 yrs apart, using electronic pneumotachograph spirometers (Monaghan N 403), and the subjects were considerably younger at follow-up (mean age about 42 yrs) than in our study (mean age 61 yrs).

In agreement with previous studies we found that the association between smoking and decline in FEV_1 was age- and exposure-dependent [5, 6]. Compared to lifetime nonsmokers, the decline in FEV_1 was 25% faster in persistent cigarette smokers, which is similar to 23 and 33% found in men of similar ages from the Cracow Study and the Copenhagen City Heart Study, respectively [5, 6]. Smoking cessation had a beneficial effect on the FEV_1 decline as shown in previous community studies from Denmark, Poland and the USA [4–6]. A 10 yr follow-up community study in Finland did not show this beneficial effect of smoking cessation in men [8]. Length of time between smoking cessation and follow-up might influence the observed decelerating effect of decline in FEV_1.

We did not observe an inverse relationship between mean FEV_1 level by body height^3 and decline in FEV_1 (the "horse-racing" effect) after adjusting for age and smoking. However, a "horse-racing effect" was indicated in persistent heavy smokers, as observed in male smokers of a North-American community [21].

This survey supports observations from several cross-sectional community studies [26, 31–34] of an association between occupational exposures and impaired ventilatory function. In agreement with the longitudinal Cracow study, we found that airborne occupational exposures in men was independently associated with accelerated decline in FEV_1 [5]. However, limited information is available from previous longitudinal studies on the effects from

occupational exposures to specific agents, such as sulphur dioxide gas or metal fumes, on FEV_1 decline [7]. In a cross-sectional community study in Sweden, an association was observed between occupational exposure to sulphur dioxide gas and the prevalence of chronic bronchitis defined according to British Medical Research Council [35]. Several workforce-based studies have reported occupational asthma among workers exposed to fumes from chromium, nickel or platinum [36].

Accidental industrial inhalation of irritants such as sulphur dioxide gas or metal fumes, may cause inflammation of peripheral airways, with reduction in FEV_1 and polymorphonuclear leucocytosis [36]. Since polymorphonuclear leucocytes are likely to be the major source of elastase in the lung, the raised leucocyte count could be a mechanism by which exposure to inhaled irritants induces pulmonary emphysema. This hypothesis is further supported by epidemiological observations of an association between accelerated decline in FEV_1 in subjects with raised leucocyte count [37].

Although no significant interaction effect was observed in our survey between smoking and occupational exposure per agent, persistent cigarette smokers appeared to be more susceptible to the effects of exposure on FEV_1 decline than lifetime nonsmokers and ex-smokers (fig. 2). This apparent increased susceptibility in smokers is consistent with observations from the cross-sectional, six cities community study in the USA [32]. They observed stronger associations between prevalences of respiratory symptoms and occupational exposure to gases or fumes in smokers than in lifetime nonsmokers. The apparent susceptibility to occupational airborne exposures in smokers might be due to increased airway reactivity to inhaled agents [7].

The observed prevalence of 9.5% with airflow limitation at follow-up is difficult to compare with other community studies, due to various spirometric criteria used and dissimilarities in age-composition of the study populations. The prevalences of airflow limitation among men over 45 yrs of age vary between 4–11% in Australian, Finnish, Norwegian and Polish studies [5, 8, 19, 33]. We did not observe any subjects with airflow limitation at follow-up in 156 lifetime nonsmokers. The same observation was made in 76 Finnish lifetime nonsmokers followed for 10 yrs [8]. A fixed FEV_1/FVC ratio as lower limit of normal has disadvantages because the ratio is inversely related to age and body height, as well as being lower in men than in women [13].

In agreement with the Cracow Study, we failed to observe an association between airflow limitation at follow-up and occupational airborne exposure. This is contrary to results from follow-up studies in Paris, (France) and Zutphen (the Netherlands) [3, 38]. In Paris area workers, the mean FEV_1/FVC ratio during follow-up (in % change·yr^{-1}) was independently associated with occupational exposure in men, using multiple linear regression analysis. Similarly, in the 20 yrs follow-up study from Zutphen, blue collar workers had significantly reduced initial adjusted FEV_1/FVC ratio compared with white collar workers. Lack of information on initial levels of FVC in our survey made it impossible to make further comparison with these studies. On the other hand, using FEV_1/FVC ratio at follow-up as a dependent variable in a multiple linear regression analysis did not change our results. Differences in exposure characterization might explain these discrepancies. However, both the Cracow study and our survey supports the hypothesis of corresponding effects on FVC as on FEV_1 from occupational airborne exposures [39]. This may account for a stable FEV_1/FVC ratio at the same time that an accelerated decline in FEV_1 is observed.

In conclusion, an exposure-response relationship was observed between exposure to increasing numbers of specific occupational airborne agents and accelerated decline in FEV_1 in men. Although random misclassification of the exposure variables might tend to obscure any true associations, our results strongly indicate that occupational airborne exposures may seriously reduce lung function independently of smoking. However, it is important to confirm the relationship between decline in FEV_1 and numbers of past or present occupational exposures to dusts, gases, vapours and fumes in longitudinal studies from other communities. Large sample sizes in general population studies are needed when assessing the relative importance of each specific exposure.

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