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Twelve-year longitudinal study of respiratory status in French dairy farmers

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Short title: Respiratory status in farmers

SUMMARY

Objectives: To evaluate respiratory risk in dairy farmers, a longitudinal study was conducted in the Doubs (France).

Methods: From a cohort constituted in 1986 (T1), 157 (62.8%) dairy farmers and 159 (63.6%) controls were re-evaluated in 1998 (T3). The study protocol comprised a medical and occupational questionnaire, spirometric tests at both evaluations and non-invasive measure of blood oxygen saturation (Spo2) at T3.

Results: In 1998, the prevalence of chronic bronchitis was higher in dairy farmers ($p<0.025$). In cross-sectional analyses, all respiratory function parameters and Spo2 were significantly lower in dairy farmers. In a multiple linear regression model, farming, age, gender (male) and smoking were significantly and negatively correlated with Spo2. However the mean annual decline in respiratory function parameters did not differ significantly between groups. After adjustment on co-variables, accelerated decline in VC and FEV_1 was associated with age ($p<0.001$), smoking ($p<0.01$) and male gender ($p<0.001$). Decline in VC was accelerated in dairy farmers working in traditional farms ($p<0.05$) and currently foddering ($p<0.001$).

Conclusions: This study shows that dairy farming is associated with an increase in risk of lung disorders and a decrease in Spo2, and suggests that respiratory function impairment is correlated with cumulated exposure to organic dusts.

Key words: farming – longitudinal studies – respiratory function tests

INTRODUCTION

Many epidemiological studies listed in recent reviews [1, 2] have shown significant and consistent associations between agricultural occupational exposure and an increase in respiratory symptoms, especially chronic bronchitis. The effects of exposure on respiratory function are less clear. Cross-sectional studies generally show a moderate alteration in respiratory flows in farmers. Very few longitudinal studies with control groups have been conducted to date [3, 4] and in most cases, the follow-up is short and the interpretation of the results is difficult [5]. Nevertheless, accelerated decline of forced expiratory volume in one second (FEV_1) and of forced vital capacity (FVC) has been suggested in grain handlers [6], swine confinement workers [7] and dairy farmers [4, 8]. The causes and mechanisms of this respiratory involvement, probably multifactorial and complex, have not yet been clearly elucidated [1]. Exposure to organic dust may have a determinant role [9]. Farmers are exposed to many organic particles which induce inflammatory or allergic reactions of the respiratory tract [10]. These lung disorders may theoretically have repercussions on gas exchanges. As far as we know, only one study conducted in dairy farmers [4] has shown blood oxygenation disorders.

In our region, two controlled longitudinal studies were conducted in two different geographic zones [4, 8]. A cross-sectional analysis of these studies showed a significant excess in respiratory symptoms and, to a lesser degree, in bronchial obstruction among farmers compared to non-farming controls [11, 12]. These two cohorts were re-evaluated at five [4] and six years [8], respectively, and the analysis revealed an excess of respiratory symptoms (particularly in chronic bronchitis) and bronchial obstruction among exposed subjects. These studies did not clearly reveal an accelerated decline in respiratory function among dairy farmers. This might be due to an improvement in working conditions leading to a decrease in agricultural exposure over time, as suggested by studies in grain elevator handlers [13].

The present study concerns the earlier of the two cohorts. In 1986 (T1), 250 dairy farmers were compared to 250 non-exposed control subjects living in the same rural area [11]. The study protocol comprised a medical and occupational questionnaire and a spirometry. Identical investigations were conducted on both groups (194 farmers and 155 control subjects) six years later (T2) [8].

All 500 subjects were re-evaluated in 1998 (T3) with the following objectives:

- to re-evaluate the excess of lung disorders in dairy farmers twelve years after the initial evaluation, and to confirm their consequences on blood oxygenation in another cohort.
- to compare changes in respiratory function parameters between groups and, to analyse the role of agricultural exposure in these changes in the exposed group.

Long term of follow-up (12 years) and non invasive measurement of oxygen saturation are the main originalities of this study.

METHODS

Population

The cohort was formed in 1986 and was composed of 250 dairy farmers of both genders and 250 administrative employees from various agricultural companies matched on basis of their gender, age, smoking status and altitude [11]. The 500 subjects were selected from Mutualite Sociale Agricole (MSA) medical files by a method described previously [11]. They came from six distinct districts (three located on plains at an altitude of 250 to 400 meters and three others located on tablelands at 400 to 700 meters). The symptoms and lung function of both groups were compared; the characteristics of the initial population and the results of the cross-sectional comparisons were described in our previous study [11].

In 1998 (T3), 87 subjects from the initial cohort were lost to follow-up and 7 had died. Among the 220 dairy farmers and the 186 control subjects remaining, each subject - and not only those investigated 6 years earlier - was contacted individually and invited to participate in the third identical investigation. Subjects who agreed were re-evaluated at the same time of year as for the two previous analyses. They were examined between 8:30 a.m. and 11:30 a.m. near their home. The medical questionnaire and spirometric tests were the same as those used in T1 and T2; they were completed with an occupational questionnaire, and oxygen blood saturation and pulse rate measures.

This study respects the ERS principles for research involving humans and has received approval from the local ethics committee.

Questionnaires

Medical questionnaires were sent by mail 10 days before the scheduled medical examination and were collected during check-up examinations. They were read and completed, when necessary (in the case of missing data), by the same investigator as in 1986 (T1) and 1992 (T2). The questionnaire was based on the American Thoracic Society questionnaire [14] and on the long version of the European Community Respiratory Health Survey questionnaire [15]. Questions concerning smoking habits, respiratory symptoms, and allergy as well as the definition of chronic bronchitis, dyspnoea, and asthma have been given previously [11]. The occupational questionnaire, used in previous studies [16, 17], was filled out during the examination. It was performed by the authors in collaboration with engineers and technicians from the local Department of Agriculture and with MSA technicians. The main professional exposure indicators concerned the size of the farm, the size of the herd, and the method of storing and drying fodder. Exposure to fodder was assessed in terms of fodder handling, the farm's modernisation and the average time spent in the barn. Fodder handling was measured two ways, first in terms of actual handling and second, in terms of bale years. There were 3 handling categories: 1) never having handled fodder, 2) having stopped handling fodder at least one year before filling in the questionnaire and 3) currently handling fodder. Bale years were defined by the number of average density bales of hay (or equivalent when farmers used other methods of storage) fed to cattle per day, multiplied by the number of years of foddering. The modernisation of farms: was classified as 1) traditional (fodder in bulk or packed in average density bales, no drying method for the fodder and no electric ventilation of the barn), 2) modernised (fodder packed in round bales, no drying method and no electric ventilation), and 3) modern (drying method of fodder and electric ventilation of the barn). These exposure indicators concerned the winter of 1997 and the 12 years of the follow-up (T1 to T3).

Respiratory function tests

They were performed by the same investigator as 6 and 12 years earlier, according to American Thoracic Society recommendations [18], with a portable pneumotachograph (Autospiro Minato, AS 500, Medical Science Company, Ltd, Osaka, Japan). Three measures of slow vital capacity (VC), forced expiratory volume in one second (FEV_1), forced mid-expiratory flow ($FEF_{25-75\%}$) and peak flow (PEF) were performed and the best values were selected. The spirometer was calibrated daily for atmospheric pressure, hygrometry and temperature, and periodically with a 1.5L syringe. The values were expressed as absolute values and as percentages of European Community for Steel and Coal (ECSC) reference values, calculated in relation to gender, age and height [19].

Oximetry data

Arterial oxygen saturation and pulse rate were evaluated for each subject with a finger pulse oximeter Onyx® model 9500 (Nonin Medical Inc, Plymouth, MN, USA). Three measurements at 30-second intervals were taken on the left index finger for each subject, seated for at least 15 minutes. The highest value of blood oxygen saturation (Spo2) was retained with the corresponding pulse rate. The right index finger was used in left-handed subjects. In case of an injured nail, we used another finger on the same hand. We also ensured that subjects were not wearing nail polish; if they were, it was removed. Measures were taken for both farmers and controls after they had spent at least 30 minutes in heated rooms. The pulse oximeter was tested for accuracy weekly by comparing Spo2 with the oxygen saturation of arterial blood gases.

Data analysis

Firstly, a cross-sectional analysis of 1998 data was performed to compare dairy farmers with control subjects. A multiple logistic regression was used to compare the odds ratios for respiratory symptoms in order to correct for imbalances in age, sex and smoking. Relationships between lung function, Spo2 and pulse rate, and farming were assessed by using multiple linear regression models. Adjustments were made for smoking (current smoker, ex-smoker, non-smoker) in the respiratory function model, and for age (as a continuous variable), gender (female=0, male=1), smoking (pack-years), FEV_1/VC ratio (as a continuous variable) and altitude (plain=0, tableland=1) in the Spo2 models. Farming was added in a model analysing Spo2. Secondly, a longitudinal analysis of respiratory function was performed. The effect of farming on the annual change in respiratory parameters between T1 and T3 (1998 value–1986 value/number of years between the T1 and T3 examinations) was tested by using a multiple linear regression model adjusted for the 1998 value of farming, age, gender, smoking, altitude and the fact of being re-evaluated in 1992 (not re-evaluated=0, re-evaluated=1). Thirdly, a cross-sectional analysis was performed on T3 data to compare the annual change in respiratory parameters and the blood oxygen saturation with occupational exposure indicators in 1998 and their evolution between T1 and T3. Univariate analyses were used: Student's t test and analysis of variance for discrete variables and simple linear regression for continuous variables. Statistical analyses were carried out using the BMDP statistical software package (BMDP, Los Angeles, CA, USA). All tests were two-sided and p-values less than or equal to 0.05 were considered as statistically significant.

RESULTS

Population characteristics

In 1986 (T1), the initial cohort included 500 subjects. In 1998 (T3), 87 subjects were lost to follow-up and 7 had died. Among the 220 dairy farmers and the 186 control subjects remaining, 316 (77.8%) accepted to participate in the present study and were re-evaluated. Among 90 non re-evaluated subjects, 66 (37 dairy farmers and 29 controls) were contacted by telephone and answered a questionnaire. Reasons for refusal included lack of time, lack of interest for this kind of study and not being able to attend the medical evaluation for occupational reasons. Only 7 cases refused for medical reasons (5 dairy farmers and 2 controls). Individual characteristics, respiratory symptoms and function at T1 were compared between re-evaluated and non re-evaluated subjects. Except for a decrease in women re-evaluated in the control population in 1998 ($p<0.05$), no significant difference was found for age, respiratory symptoms and function. Among the population re-evaluated in 1998, 246 subjects (133 farmers and 113 controls) had been re-evaluated in 1992. The individual characteristics of the study population at T3 are presented in Table 1. Statistically significant differences between both groups were observed for smoking ($p<0.05$) and altitude ($p<0.001$). The occupational characteristics in dairy farmers at T3 are detailed in Table 2.

Cross-sectional analyses

The prevalence of asthma, asthma-related symptoms and dyspnoea were the same in both groups. The prevalence of atopy was lower in farmers after adjustment on age, gender, and smoking (36.9% versus 50.3%, odds ratio: 0.57, 95% IC [0.36-0.91]). Conversely, the prevalence of chronic bronchitis was significantly higher in dairy farmers after adjustment on the same co variables (17.2% versus 5.7%, odds ratio: 2.22, 95 % IC [1.09-4.53]). The results of respiratory function and Spo2 at T3 are shown in Table 3. All respiratory function parameters were significantly lower in dairy farmers. The Spo2 was lower ($p<0.001$) among dairy farmers too, with a mean difference of 0.7%. In a linear multiple regression model, farming, age, and smoking were inversely correlated with Spo2 ($p<0.025$) (table 4). A positive correlation was found between FEV_1/VC ratio and Spo2 ($p<0.001$). Blood oxygen saturation was significantly lower among males ($p<0.001$).

Longitudinal analyses

The longitudinal analysis of respiratory function tests was performed on 289 subjects (145 dairy farmers and 144 controls) whose explorations were concordant with the American Thoracic Society criteria [18] both at T1 and T3. Mean annual changes in respiratory function parameters between 1986 and 1998 are presented in Table 5. The mean annual decline in VC and FEV_1 was 23.7 ml per year and 15.09 ml per year respectively for the whole cohort. The decline in lung function was similar in both groups (Table 6). The factors associated with an accelerated decline in VC and in FEV_1 were age ($p<0.001$), smoking ($p<0.001$ for FEV_1 and $p<0.01$ for VC) and male sex ($p<0.001$). The subjects re-evaluated in 1992 (133 dairy farmers re-evaluated at T1, T2 and T3) had a lower decline in VC ($p<0.001$) than those re-evaluated in 1998 only.

Relationship between occupational exposure and respiratory parameters (lung function decline and oxygen blood saturation)

Results are detailed in Table 7. Dairy farmers who were officially retired showed a significant decline in VC ($p<0.001$) and FEV_1 ($p<0.025$) and a decrease in blood oxygen saturation ($p<0.001$). Decline in lung function accelerated significantly in dairy farmers working on traditional farms (for CV $p<0.05$), and in those already having handled fodder ($p<0.001$). Foddering was deleterious on Spo2. The mean duration of exposure was significantly associated with the decline in FEV_1 ($p<0.05$) and with a decrease in Spo2 ($p<0.025$). In a multiple regression model, after adjustment on these same co-variables, the decline in VC was accelerated ($p<0.001$) in dairy farmers who had stopped handling fodder and who were currently foddering versus those who had never handled fodder.

DISCUSSION

The results of this study are consistent with those of the 1986 and 1992 cross-sectional analyses [8, 11], and with those of other studies conducted in the same region [4,12]. Dairy farmers present a persistent excess of chronic bronchitis with bronchial obstruction. These lung disorders have a significant impact on blood oxygenation. Conversely, an accelerated decline of respiratory function parameters was not observed in this cohort, possibly due to a decrease in exposure with over time.

In our study, the prevalence of chronic bronchitis was higher in dairy farmers, but the prevalence of asthma was not. In addition, the prevalence of atopy was lower in exposed subjects. These results concur with studies recently reviewed [20]. In cross-sectional analyses, all respiratory function parameters were significantly lower among farmers, particularly FEV_1 and FEV_1/CV ratio, with the same difference between the two groups as 12 years earlier at T1 [11].

One of originalities of this study was the Spo2 measure. To date, there have been no published recommendations for the use of pulse oximeter in epidemiological studies. A recent study evaluating the potential relationship between air pollution and blood oxygen saturation in elderly adults suggested that the accuracy and reproducibility of Spo2 measures allowed the use of a pulse oximeter for epidemiological studies [21]. In our study, we used a recent pulse oximeter, in accordance with the 1995 European regulation. The best of three measures was retained. We ensured that subjects were not wearing nail polish [22]; if they were, it was removed. Our results demonstrated that Spo2 was lower in dairy farmers ($p<0.001$). Fodder handling and a longer time spent in the barn were associated negatively with Spo2. In a recent study, the first to measure Spo2 in farmers, we observed the same difference of Spo2 between farmers and non-exposed subjects groups (0.7%), but with a lower level of significance [4]. In our study the fact that Spo2 was, as expected, negatively correlated to smoking and age, and positively correlated to all respiratory function parameters argues for both the accuracy and the relevance of the tool. After adjustment for FEV_1/VC ratio, farming remained associated with a decreased Spo2; this suggests that mechanisms other than bronchial obstruction are involved. Desaturation can be due to alveolitis (possibly infra-clinical) as in hypersensitivity pneumonitis. Indeed, this affection is frequent in this part of France [23]. Dairy farmers are usually exposed to a great quantity of organic particles, including endotoxins, which may induce inflammatory reactions of alveoli and small airways, and therefore alter the alveolo-capillar diffusion [8, 24–26]. This may partially explain the decrease in Spo2. Yet, it cannot be totally excluded that more callous hands in farmers play a role in the observed results. As our study was conducted in winter and in spring, pulse oximetry readings may also been affected by physiologic processes such as vasoconstriction reaction to cold. However, in our study, people first completed the questionnaires with the physician, and then the Spo2 measures were performed after at least 30 minutes spent in a heated room. Furthermore, both farmers and controls were investigated in the same heated rooms. People accustomed to working outdoors also present cold acclimatization in the hands. Among these outdoor workers, cold vasodilatation occurred earlier than in non-acclimatized subjects working indoors [27, 28]. Hence, in a cold room, we should have observed higher Sp02 measures in farmers than in controls, given earlier vasodilatation due to cold acclimatization in farmers.

The longitudinal analysis of lung function showed no significant difference between the two groups for the mean annual decline in respiratory function parameters.

Cross-sectional results at T1 (1986), which showed a significant bronchial obstruction in dairy farmers might predict an accelerated decline in lung function in exposed subjects. But we did not observe such accelerated decline in farmers that is consistent with previous results reported in the European Community Respiratory Health Survey [31]. In the ECRHS, subjects exposed to dust, gases and fumes during the follow-up did not have accelerated decline in FEV_1, although they have an excess of chronic phlegm like our subjects. Various hypotheses have been stated to explain these discrepancies between longitudinal and cross-sectional results [29, 30, 32]. In our study, ill subjects were not lost in follow-up. Respiratory function parameters at T1 in re-evaluated and non re-evaluated subjects, in dairy farmers and controls, were similar. Therefore, we can exclude a selective follow-up, but we cannot exclude a selection effect in farmers at inclusion. In our study, the mean annual decline was higher between T1 and T2 than between T1 and T3 [8]. The deceleration in decline might be explained by a learning effect [29, 30] or by systematic errors in measurements of lung function at T2 or T3. In our current study, mean annual changes were positively correlated with smoking and age. This shows the relevance of our measures and therefore of our results. Glindmeyer et al. also suggested that past noxious exposures may influence sectional analyses, whereas longitudinal analyses are sensitive only to influence that continue to affect annual decline during the study period [30]. The decrease in respiratory risk exposure over time might explain this absence of accelerated decline. In our study, occupational characteristics in farmers showed that, between 1986 and 1998, 40% of the farmers claim to have reduced their occupational exposure, 41.4% developed prevention and in 1998 approximately 40% worked on a modern farm. Moreover subjects with bronchial obstruction at T0 (1986) might have been more likely to decrease their exposure and to develop prevention. The respiratory function in farmers had probably decreased significantly before 1986, when occupational exposure was greater. And during the first six years [8], the decline of respiratory function parameters in dairy farmers accelerated slightly, whereas it slowed down over the next 6 years. We speculate that this type of course over the follow-up period may result from a decrease in the offending exposure. Decline in respiratory function parameters seemed to decrease in dairy farmers foddering in modern farms, especially those with a barn drying system (table 7). Previous studies have suggested that the barn drying fodder system is an important criterion of modernisation, known to lower exposure aero-contaminants by reducing microorganisms' proliferation [16, 33]. Another recent study has shown working on a modern farm to be associated with a decrease in risk of lung impairment [34]. In addition, accelerated decline in respiratory function was correlated with fodder handling and average time spent in barn (decline in FEV_1 ($p < 0.001$) and decline in $FEF_{25-75\%}$ ($p<0.05$)). All these relationships between exposure and lung function impairment fit with our speculation that the observed "improvement" of lung function in farmers is related to a significant improvement in working condition over time.

CONCLUSION

Our results show an excess of chronic bronchitis with obstructive airway disorders and decrease in blood oxygen saturation in farmers. No significant accelerated decline in respiratory function parameters was found in dairy farmers, possibly due to a decrease in the risk of occupational exposure over time. However, in farmers an accelerated decline in respiratory function was correlated with fodder handling and the average time spent in the barn.

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Table 1

DESCRIPTION OF THE STUDY POPULATION IN 1998

	Dairy farmers	Control subjects	p value
Number (%)	157 (49.7)	159 (50.3)	
Age in, years			
Mean (SD)	50.8 (9.3)	50.8 (8.6)	NS
25-34, n (%)	5 (3.2)	0	NS
35-44, n (%)	32 (20.4)	38 (23.9)	NS
45-54, n (%)	69 (43.9)	79 (49.7)	NS
55-64, n (%)	35 (22.3)	25 (15.7)	NS
>64, n (%)	16 (10.2)	17 (10.7)	NS
Gender			
Male, n (%)	88 (56.1)	94 (59.1)	NS
Female, n (%)	69 (43.9)	65 (40.9)	NS
Smoking			
Smokers, n (%)	23 (14.6)	34 (21.4)	<0.05
Ex-smokers, n (%)	42 (26.8)	59 (37.1)	<0.05
Non-smokers, n (%)	92 (58.6)	66 (41.5)	<0.05
Mean pack-years* (SD)	15.6 (12)	13.5 (11.7)	NS
Geography			
Plain, n (%)			

Tableland, n (%)	89 (56.7)	144 (90.6)	<0.001
	68 (43.3)	15 (9.4)	<0.001

SD = Standard deviation. * smokers and ex-smokers.

Chi-square tests for qualitative variables; Student’s t test for quantitative variables.

Table 2

OCCUPATIONAL CHARACTERISTICS IN DAIRY FARMERS IN 1998

(n=155)

Activity, n (%)	
Active	120 (77.4)
Retired but still working on a farm	13 (8.4)
Retired and no longer working on a farm	22 (14.2)
Farm characteristics	
Modernisation, n (%) :	
Traditional farm	14 (9)
Modernised farm	61 (39.4)
Modern farm	80 (51.6)
Size of the farm in hectares, mean (SD)	60.5 (27.1)
Size of the fodder lands in hectares, mean (SD)	31.5 (16.7)
Size of the herd, mean (SD)	67.2 (32.9)
Storage method, n (%)	
Fodder in bulk	14 (9)
Fodder pack in average density bale	66 (42.6)
Fodder pack in round bales	61 (39.4)
Barn drying fodder	67.2 (32.9)
Fodder handling	
Never	37 (23.9)
Stopped for at least one year	30 (19.4)
Currently	88 (56.8)
Bale-year, mean (SD)	
Between 1986 and 1998	265.8 (282.4)
Cumulated	584.7 (590.4)
Average time spent in the barn (in hours per year) between 1986 and 1998	897.4 (385.9)
Prevention system against exposure to microorganisms between 1986 and 1998	
Yes	63 (41.4)
No	89 (58.6)
Evolution of exposure between 1986 and 1998	
Unchanged	62 (40.3)
Increased	32 (20.8)
Decreased	60 (39)

Table 3

RESPIRATORY FUNCTION, SPO2 AND PULSE RATE IN DAIRY FARMERS AND CONTROLS IN 1998

	Dairy farmers	Controls	p value
Respiratory function, mean (SD)			
Available data, n	*155*	*153*	
%VC (SD)	96.1 (14.7)	99.3 (13.1)	<0.025*
$\%FEV_1$ (SD)	94.7 (16.5)	100.7 (14.8)	<0.001*
$\%FEV_1$ /VC (SD)	98.3 (7.9)	101.2 (7.1)	<0.001*
$\%FEF_{25-75\%}$ (SD)	81.3 (25.4)	93.2 (25.2)	<0.001*
Spo2			
Available data, n	*155*	*156*	
Mean (SD)	96.7 (1.7)	97.3 (1.2)	<0.001**
Pulse rate			
Available data, n	*155*	*156*	
Mean (SD)	73.9 (11)	72.5 (11.7)	NS**

Spirometric values transformed into percentage of ECCS reference values, calculated in relation to gender, age and, height. Values take atmospheric pressure, hygrometry and temperature into account. VC: Vital Capacity; FEV_1: Forced Expiratory Volume in one second; $FEF_{25-75\%}$: Forced mid-Expiratory Flow.

* multiple linear regression adjusted for smoking.

** multiple linear regression adjusted for age, gender (female=0, male=1), smoking (pack-years), FEV_1/VC and altitude (plain = 0, tableland = 1).

Table 4

MULTIPLE REGRESSION MODEL FOR BLOOD OXYGEN SATURATION (Spo_2)

Independent variables	Spo_2		
	Coeff.	SE	P value
Farming	-0.54	0.16	< 0.001
Male	-0.75	0.16	< 0.001
Age	-0.02	0.01	< 0.001
Smoking	-0.01	0.01	< 0.025
FEV_1 / VC	0.05	0.01	< 0.001
Altitude (tableland)	-0.24	0.18	NS
Intercept	94.78		
r^2	0.26		

All variables listed were included simultaneously in the model ; each coefficient and p-value is controlled for all other covariates.

Age, smoking (pack-years) and FEV_1/VC are continuous variables. Farming: no = 0, yes= 1; Gender: female = 0, male = 1; Altitude: plain = 0, tableland = 1.

SE = Standard Error.

Table 5

MEAN ANNUAL CHANGES IN RESPIRATORY FUNCTION PARAMETERS BETWEEN 1986 AND 1998

	Farmers *n=145*	Controls *n=144*
Time between the two surveys, years (SD)	11.9 (0.2)	11.7 (0.2)
Δ VC $mL.yr^{-1}$ (SD)	-20.61 (37.7)	-26.97 (43.7)
Δ FEV_1 $mL.yr^{-1}$ (SD)	-13.2 (32.8)	-17.0 (31.5)
Δ FEV_1/VC $\%.yr^{-1}$ (SD)	0.08 (0.57)	0.00 (0.57)
Δ $FEF_{25-75\%}$ $mL.yr^{-1}$ (SD)	-19.5 (58.3)	-23.1 (67.4)

Results are expressed as mean (standard deviation).

Δ: change in spirometric parameters. Δ = (1998 value –1986 value)/ (number of years between the T1 and T3 examinations)

Table 6

REGRESSION MODELS FOR ANNUAL CHANGES IN LUNG FUNCTION

Independent variables	ΔVC		ΔFEV_1		$\Delta FEV_1/VC$		$\Delta FEF_{25-75\%}$	
	Coeff.	SE	Coeff.	SE	Coeff.	SE	Coeff.	SE
Farming	2.92	5.02	-1.75	4.08	-1.18§	0.07	-6.74	8.20
Age	-0.70§	0.25	-0.46§	0.20	0.01†	0.003	0.01	0.41
Smoking	-0.43‡	0.22	-0.39§	0.18	-0.0016	0.003	-0.32	0.36
Male	-15.04§	4.98	-9.54§	4.06	-0.04	0.07	-9.10	8.17
Altitude	13.58§	5.56	3.69	4.52	0.25	0.08	-2.28	9.10
Re-evaluated in 1992	16.64§	6.02	-0.20	4.90	-0.12§	0.08	-16.07*	9.85
Intercept	1.77		18.20		0.16		9.23	
r^2	0.13		0.07		0.05		0.02	

All listed variables were included simultaneously in the models; each coefficient and p-value is controlled for all other covariates.

Age and smoking are continuous variables. Farming: controls=0, farmers=1; Altitude: plain = 0, tableland = 1; not re-evaluated in 1992 = 0, re-evaluated in 1992 = 1.

* p<0.05, † p<0.025, ‡ p<0.01, § p<0.001.

Table 7

ANNUAL DECLINE OF RESPIRATORY FUNCTION BETWEEN 1986 AND 1998 AND OCCUPATIONAL EXPOSURE, UNIVARIATE ANALYSIS

	SpO_2 (%)	ΔVC (ml/year)	ΔFEV_1 (ml/year)	$\Delta FEV_1/VC$ (ml/year)	$\Delta FEF_{25-75\%}$ (ml/year)
Activity					
Active	96.86(1.37) ‖	-14.71(35.31) §	-10.30(30.22) †	0.05(053)	22.52(57.35) *
Retired but still working on a farm**	94.84(2.03) ‖	-55.66(49.94) §	-42.82(36.55) †	-0.03(0.64)	40.71(52.28) *
Retired and no longer working on a farm	96.66(2.22) ‖	-29.65(30.88) §	-10.02(34.59) †	0.25(0.71)	8.32(54.16) *
Farm characteristics					
Modernisation:					
Traditional farm	96.84(1.82)	-26.88(27.42) *	-16.28(27.06)	0.81(6.12)	-17.64(62.45)
Modernised farm	96.63(1.47)	-22.91(32.25) *	-18.4(30.67)	0.86(6.29)	-24.72(54.64)
Modern farm	95.78(1.12)	-4.21(32.32) *	-5.33(30.1)	-1.00(4.74)	-13.57(64.99)
Size of the herd	0.03(1.65)	0.02(37.9)	0.08(32.6)	0.09(0.56)	0.18(57.49) *
Fodder handling					
Never	97.59(1.23) ‖	-19.20(24.81) §	-7.67(19.96) *	2.66(5.77)	-3.23(51.54)
Stopped for one year or more	96.63(1.47) ‖	-18.24(28.92) §	-15.94(27.66) *	-0.13(5.57)	-28.67(62.54)
Currently	96(2.29) ‖	-41.86(33.77) §	-27.29(37.21) *	1.03(7.28)	-13.57(57.57)
Time spent in the barn	-0.19(1.65) †	-0.04(30.34)	-0.16(28.73) *	-0.14(6.06)	-0.17(59.63) *
Prevention system					
Yes	96.52(1.81)	-16.36(35.48)	-13.11(31.29)	0.03(0.55)	-19.63(58.88)
No	96.73(1.55)	-23.55(39.71)	-13.57(33.95)	0.10(0.58)	-21.14(57.06)
Evolution of exposure					
Unchanged	96.83(1.40)	-20.37(26.92)	-16.27(23.83)	0.17(5.35)	-28.19(55.51)

Increased	†		15.94(27.66) *		-13.57(57.57)
Decreased		-19.20(24.81) §	-27.29(37.21) *	0.17(5.35)	
		-18.24(28.92) §		0.48(6.57)	-0.17(59.63) *
	96.52(1.81)	-41.86(33.77) §	-0.16(28.73) *	1.34(6.58)	
	96.73(1.55)				
		-0.04(30.34)			-19.63(58.88)
			-13.11(31.29)		-21.14(57.06)
	96.83(1.40)		-13.57(33.95)		
	96.75(1.36)	-16.36(35.48)			
	96.44(2.01)	-23.55(39.71)			-28.19(55.51)
			-16.27(23.83)		-24.85(65.85)
			-14.64(30.59)		-11.20(60.54)
		-20.37(26.92)	-16.76(32.94)		
		-18.44(30.34)			
		-28.78(33.51)			

* $p<0.05$, † $p<0.025$, ‡$p<0.01$, § $p<0.001$, || $p<0.0001$

Chi-square tests for qualitative variables, Student’s t tests for quantitative variables.

** Some farmers were officially retired in 1998 but continued to work by helping their spouse or children.