



Influence of hay and animal feed exposure on respiratory status: a longitudinal study

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ABSTRACT: Our aim was to study respiratory symptoms and lung function decline in farmers, with particular attention to the influence of handling hay, straw and animal feed.

From a cohort recruited in 1993–1994, 219 (82.6%) dairy farmers, 130 (62.5%) nondairy agricultural workers and 99 (66.4%) controls were re-evaluated in 2006. They answered medical and occupational questionnaires, underwent spirometric tests at both evaluations and pulse oximetry in 2006.

Dairy and nondairy agricultural workers showed an increased risk for usual morning phlegm (adjusted OR 4.27 (95% CI 1.41–12.95) and 3.59 (95% CI 1.16–11.10), respectively). Animal feed handling was associated with increased risks of wheezing ($p=0.01$) and usual morning phlegm ($p=0.04$); hay or straw handling was associated with increased risk of wheezing ($p=0.008$). Adjusting for smoking, age, height, sex and altitude, dairy farmers had greater declines in forced expiratory volume in 1 s (FEV₁)/forced vital capacity ratio ($p=0.01$) than controls. An increased decline in FEV₁ for all agricultural workers was associated with animal feed handling, both measured as a categorical (currently *versus* never handling; $p=0.05$) or quantitative value (years of exposure during the survey period; $p=0.03$).

Hay, straw or animal feed handling represents a risk factor of bronchial symptoms and, for animal feed only, of accelerated decline in expiratory flows.

KEYWORDS: Asthma, chronic bronchitis, farming, longitudinal studies, respiratory function tests

An increased risk of chronic bronchitis has been demonstrated in various agricultural groups [1], notably in swine confinement workers [2, 3], poultry workers [4, 5] and dairy farmers [6–9]. Several cross-sectional studies have reported lung function impairment in agricultural workers [10, 11], including dairy farmers [8, 9]. An accelerated decline in lung function has been suggested in swine confinement workers [12, 13] and grain handlers [14]. The results of two controlled longitudinal studies we conducted in French dairy farmers in 1986 and 1994 were discordant. In the 1986 cohort, we found an accelerated decline in forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV₁) in dairy farmers at 5-yr follow-up [15], but these results were not confirmed at the second follow-up 12 yrs after inclusion [16]. This may be due to an improvement in working conditions leading to a decrease in agricultural exposure over time, as suggested by studies in grain elevator workers [17]. In the 1994 cohort, dairy farmers showed an accelerated decline in FEV₁/FVC at 6-yr follow-up compared with controls [18]. Hence, the present study aimed to compare lung function decline for a 12-yr follow-up period in the 1994 cohort between

dairy farmers, nondairy agricultural workers and controls, and to explore the influence of two situations that engender exposure to organic dust (hay or straw and animal feed handling) in dairy and nondairy agricultural workers.

METHODS

Population

The study population consisted of three groups of both sexes, aged 16–66 yrs (at baseline), living in the same rural area in the Doubs province of France. Subjects were selected from the Doubs Mutualité Sociale Agricole (MSA; Agricultural Health Insurance Mutual) medical files. Every 5 years, the MSA medical unit organises free medical examinations for all affiliated members. For the 1993–1994 examinations, we opened recruitment to 353 dairy farmers, 278 nondairy agricultural workers (poultry farmers, swine workers, fish farmers, beekeepers, herdsman, cattle inseminators, cheesemakers and forestry workers) and 189 controls (administrative employees from agricultural companies). From February 1993 to May 1994, 265 dairy farmers, 208 nondairy agricultural workers and 149 controls participated in the first investigations (T1). The T1 results, which compared dairy farmers

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and controls, were published in 1998 [9]. In 1999 (T2), identical investigations were conducted on the same farmers and controls [18].

In 2006 (T3), we decided to re-evaluate respiratory symptoms and lung function in this 1994 cohort including nondairy agricultural workers. An explanatory letter concerning the objectives and practical value of the study was sent to all surviving 1993–1994 participants (16 subjects had died). Those who agreed to participate were re-evaluated at the same time of year (winter or spring) as for the two previous analyses. Subjects who agreed to participate but could not come to the medical examination (having moved to another province, for example) were asked to answer the questionnaires and return them by post. The protocol comprised a medical and occupational questionnaire, spirometric tests in 1994 and 2006, and a noninvasive measure of blood oxygen saturation (arterial oxygen saturation measured by pulse oximetry; S_{p,O_2}) in 2006 only.

This study respects the European Respiratory Society (ERS) principles for research involving humans and was approved by the local ethics committee (Comité consultatif de protection des personnes dans la recherche biomédicale de Franche-Comté, Besançon, France).

Questionnaires

Occupational and medical questionnaires were sent by post 10 days before the scheduled medical examination and were collected during the check-up examination. The medical questionnaire was based on the American Thoracic Society (ATS) questionnaire [19] and on the long version of the European Community Respiratory Health Survey questionnaire [20]. Chronic bronchitis was defined as cough and expectoration for ≥ 3 months of the year for at least two consecutive years. Questions on smoking habits, respiratory symptoms, and history of allergy have been defined previously [9].

The occupational questionnaire was designed by the authors in collaboration with engineers and technicians from the local Department of Agriculture and the MSA. Some questions have been added to the version used in previous studies [9, 16, 18]. Working status in 2006 was designated as: “still working” (at the same or another job), “retired”, and “unemployed or having stopped working for personal reasons”. Dairy and nondairy agricultural workers were asked if they handled hay or straw, and animal feed (including grain and flour but not hay) “never”, “currently” (in 2006) or “formerly” (stopped before 2006).

Respiratory function tests

Respiratory function tests were performed according to ATS recommendations [21] with a portable pneumotachograph (SpiroPro; SensorMedics, Voisins le Bretonneux, France). A minimum of three adequate measures of FVC, FEV₁, forced expiratory flow at 25–75% of FVC (FEF_{25-75%}) and forced peak expiratory flow (PEF) were taken, and the best blow was selected. The spirometer was calibrated daily for atmospheric pressure, hygrometry and temperature. Values were expressed as absolute values and as percentages of European Community for Steel and Coal (ECSC) reference values, calculated in relation to sex, age and height [22].

Oximetry data

For each subject, S_{p,O_2} and pulse rate were evaluated with a finger pulse oximeter Onyx® model 9500 (Nonin Medical Inc., Minneapolis, MN, USA). Three measurements were performed at 30-s intervals after subjects had spent ≥ 30 min in a heated room, seated for ≥ 15 min. The highest S_{p,O_2} value and corresponding pulse rate were retained.

Data analysis

A first series of analyses was carried out on the 2006 cross-sectional data. Each respiratory symptom was cross-tabulated by farming (dairy farmers, nondairy farmers and controls), age, sex, smoking status (current smokers, ex-smokers and never-smokers), altitude (<400, 400–800 and >800 m) and employment status. Associations between farming groups (reference controls) and respiratory symptoms were evaluated by multiple logistic regressions adjusted for age and smoking. Respiratory symptoms were compared with the same models in dairy and nondairy agricultural workers for subjects having handled hay or straw (first: currently and/or formerly; secondly and separately: currently or formerly) and for those never having handled hay or straw. The same factors were compared for the animal feed handling.

Secondly, the relationship between lung function in 2006, S_{p,O_2} and exposure was analysed with multiple linear regression models adjusted for age, smoking, sex, height, altitude and, for S_{p,O_2} only, pulse rate and FEV₁ % predicted.

Finally, longitudinal analyses of respiratory function were performed. The effect of farming (dairy and nondairy agricultural workers *versus* controls) on the annual change in lung function parameters between T1 and T3 (2006 value – 1994 value/number of years between the T1 and T3 examinations) was tested by multiple linear regressions adjusted for age, smoking, sex, height, altitude and initial value of the parameter in 1994. Then, multiple linear regression models were used to analyse the relationship between annual change in respiratory parameters and hay or straw handling, or animal feed handling coded as a categorical (currently or formerly *versus* never) and quantitative (years of exposure between T1 and T3) value. The level of significance was set at $p < 0.05$, but all p -values < 0.10 are reported. Statistical analyses were carried out using the SAS 9.1.3 package (SAS Institute Inc., Cary, NC, USA).

RESULTS

Of the 622 subjects who had participated in 1994, 174 were not available for the 2006 study: 11 dairy farmers, two nondairy agricultural workers and three controls died before 2006, 20 dairy farmers, 20 nondairy agricultural workers and seven controls refused to participate, and 15 dairy farmers, 56 nondairy agricultural workers and 40 controls were lost to follow-up. Therefore, 219 (82.6%) dairy farmers, 130 (62.5%) nondairy agricultural workers and 99 (66.4%) controls participated in the 2006 follow-up. 33 (7.4%) out of the 448 participants only returned their occupational and medical questionnaires. The subjects lost to follow-up or who refused to participate were: more often male (69.5 *versus* 60.3%; $p = 0.03$) and more often current smokers in 1994 (34.8 *versus* 19.2%; $p < 0.001$) than those who participated. They were also younger (mean age at baseline 38.5 *versus* 42.2 yrs; $p = 0.0007$).

There was no difference in respiratory symptoms or lung function parameters at baseline between subjects who did or did not participate in the follow-up.

The main characteristics and comparison of the three exposure groups for the 12-yr follow-up participants are reported in table 1. Dairy farmers were more often never-smokers than controls and nondairy agricultural workers were more often current smokers than controls. However, at baseline, dairy farmers were older (mean age 45.8 yrs) and more often never-smokers (75.3%) than nondairy agricultural workers (mean age 38.4 yrs; never-smokers 52.3%) and controls (mean age 37.9 yrs; never-smokers 57.8%). In 2006, 166 (37.5%) subjects had already stopped working and 280 were still working; however, lung function parameters at baseline did not differ between the two groups.

Respiratory symptoms in 2006

Six dairy farmers with hypersensitivity pneumonitis were excluded from the following analyses. Respiratory diseases

(asthma, chronic bronchitis, emphysema and pulmonary infections) were more frequent in dairy farmers (OR 2.85, 95% CI 1.20–6.80) than in controls. The prevalence of respiratory symptoms in the three exposure groups is presented in table 2. After adjustment for age and smoking, usual morning phlegm was more frequent both in dairy farmers (OR 4.27, 95% CI 1.41–12.95) and in nondairy agricultural workers (OR 3.59, 95% CI 1.16–11.10) than in controls. In the same model, usual morning phlegm was also more frequent in current and former smokers than in never-smokers (OR 4.88 (95% CI 2.10–11.34) and OR 2.29 (95% CI 1.15–4.57), respectively).

Farmers handling or having handled hay or straw seemed to be at an increased risk of wheezing and personal history of allergy. The age- and smoking-adjusted OR was 3.49 (95% CI 1.43–8.54) for wheezing at any time in their life and 1.55 (95% CI 1.16–2.07) for personal history of allergy. They also reported waking up more during the night due to coughing (adjusted OR 2.73, 95% CI 1.02–7.31).

TABLE 1 Main characteristics of the participants in 2006 in the three exposure groups

	All	Dairy farmers	Nondairy agricultural workers [#]	Controls	p-value
Subjects	448 (100.0)	219 (48.9)	130 (29.0)	99 (22.1)	
Age yrs	54.8 ± 11.4	58.0 ± 11.1	52.0 ± 11.2	51.2 ± 10.0	<0.0001
Sex					
Male	270 (60.3)	123 (56.2)	99 (76.2)	48 (48.5)	<0.0001
Female	178 (39.7)	96 (43.8)	31 (23.8)	51 (51.5)	
Smoking status in 2006					
Never	273 (61.0)	159 (72.6)	62 (47.7)	52 (52.5)	<0.0001
Currently	49 (10.9)	15 (6.8)	22 (16.9)	12 (12.1)	
Formerly	126 (28.1)	45 (20.6)	46 (35.4)	35 (35.4)	
Exposure [†] pack-yrs	25.5 ± 20.8	28.3 ± 25.8	23.9 ± 16.0	24.1 (20.0)	<0.0001
Altitude					
Plain <400 m	218 (48.7)	118 (53.9)	49 (37.7)	51 (51.6)	
Tableland 400–800 m	134 (29.9)	50 (22.8)	60 (46.2)	24 (24.4)	0.0001
Mountain ≥800 m	96 (21.4)	51 (23.4)	21 (16.1)	24 (24.4)	
Working status in 2006					
Working in the same or another job	280 (62.5)	118 (53.9)	90 (69.2)	72 (72.7)	<0.0001
Retired	151 (33.3)	97 ⁺ (44.3)	35 (26.9)	19 (20.0)	
Unemployed or stopped working for other reasons	17 (4.2)	4 [§] (1.8)	5 [‡] (3.9)	8 [‡] (8.1)	
Hay or straw handling					
Never	93 (27.3)	39 (18.2)	54 (42.5)		
Formerly	128 (37.5)	80 (37.4)	48 (37.8)		
Currently	120 (35.2)	95 (44.4)	25 (19.7)		
Animal feed handling i.e. grains					
Never	109 (32.1)	43 (20.1)	66 (52.4)		
Formerly	141 (41.5)	101 (47.2)	40 (31.7)		
Currently	90 (26.5)	70 (32.7)	20 (15.9)		

Data are presented as n (%) or mean ± SD, unless otherwise stated. Chi-squared tests were used for qualitative variables; unpaired t-tests were used for quantitative variables. [#]: including 40 farmers (23 poultry workers, two pig farmers, two fish farmers, two agricultural labourers, one beekeeper and nine flower cultivators), 11 people with regular contact with cattle (three herdsmen, seven cattle inseminators, two cattle-lorry drivers and a slaughterhouse worker), two subjects in regular contact with grain (one grain silo worker and one miller), 42 forestry or sawmill workers, 24 cheesemakers and nine subjects who frequently went to the dairy farms (six milk quality control technicians or collectors and three agricultural machine mechanics); [†]: for current and ex-smokers; ⁺: two retired farmers had stopped work before retirement age due to respiratory diseases (asthma or farmer's lung disease); [§]: only one farmer stopped working due to asthma; [‡]: no subject stopped working due to respiratory diseases.

TABLE 2 Prevalence of respiratory symptoms in 2006 in the three exposure groups, and adjusted odds ratios for dairy farmers and nondairy agricultural workers

	Dairy farmers	Nondairy agricultural workers	Controls	Adjusted OR [#] (95% CI)	
				Dairy farmers	Nondairy agricultural workers
Subjects n	213 [†]	130	99		
Respiratory antecedents including asthma	33 (15.5)	14 (10.8)	7 (7.1)	2.42 (1.002–5.83)	1.55 (0.60–4.00)
History of allergy[‡]					
Personal	92 (44.0)	61 (47.3)	42 (43.3)	1.21 (0.73–2.02)	1.19 (0.70–2.03)
Familial	64 (34.0)	32 (30.8)	40 (46.5)	0.73 (0.42–1.26)	0.53 (0.29–0.97)
Asthma at any time in their life					
Self-reported	16 (7.5)	6 (4.6)	5 (5.1)	1.60 (0.56–4.56)	0.92 (0.27–3.11)
Doctor-diagnosed	15 (7.0)	5 (3.9)	5 (5.1)	1.54 (0.53–4.45)	0.76 (0.21–2.71)
Asthma attack in the previous year	4 (1.9)	2 (1.5)	0 (0.0)		
Attack of shortness of breath at rest in the previous year	4 (1.9)	4 (3.1)	1 (1.0)	1.59 (0.17–15.25)	3.20 (0.35–29.32)
Woken by shortness of breath, in the previous year	7 (3.3)	2 (1.5)	1 (1.0)	3.81 (0.43–33.36)	1.35 (0.12–15.27)
Woken by cough in the previous year	25 (11.8)	12 (9.2)	15 (15.5)	0.83 (0.40–1.73)	0.54 (0.24–1.21)
Wheezing					
Wheezing at any time in their life	35 (16.5)	18 (13.9)	12 (12.1)	1.63 (0.78–3.42)	1.10 (0.50–2.43)
Wheezing in the previous year	18 (8.5)	10 (7.7)	6 (6.1)	1.25 (0.45–3.43)	1.16 (0.40–3.36)
Wheezing apart from a cold in the previous year	12 (5.6)	5 (3.9)	4 (4.0)	0.97 (0.28–3.35)	0.76 (0.20–3.04)
Wheezing with breathlessness in the previous year	7 (3.3)	5 (3.9)	5 (5.1)	0.54 (0.15–1.86)	0.70 (0.19–2.53)
Usual morning cough	23 (10.8)	12 (9.2)	5 (5.1)	2.46 (0.83–7.32)	1.65 (0.53–5.16)
Usual morning phlegm	29 (13.6)	18 (13.8)	4 (4.0)	4.27 (1.41–12.95)	3.59 (1.16–11.10)
Chronic bronchitis	8 (3.8)	3 (2.3)	1 (1.0)	4.66 (0.53–40.78)	2.00 (0.20–20.06)
Dyspnoea	43 (22.8)	17 (14.2)	12 (12.8)	1.26 (0.61–2.58)	1.01 (0.46–2.25)

Data are presented as n (%), unless otherwise stated. Unexposed controls were used as the reference group.[#]: adjusted for age and smoking (never-smokers were used as the reference group for this adjustment); [†]: nasal allergies including hay fever, eczema or any kind of skin allergy, or allergy to insect stings or bites; [‡]: six farmers with hypersensitivity pneumonitis were excluded.

Farmers handling or having handled animal feed seemed to present increased risks of wheezing at any moment in their life (adjusted OR 2.40, 95% CI 1.14–5.04). They also reported waking up more during the night due to coughing (adjusted OR 2.95, 95% CI 1.17–7.39) and more usual morning cough (adjusted OR 2.75, 95% CI 1.03–7.29).

Subjects who had stopped handling hay or straw, or animal feed had higher risks of respiratory symptoms (table 3).

Lung function in 2006

In 2006, dairy farmers had lower PEF (mean 101.7 *versus* 109.0% pred; $p=0.007$), FEV₁/FVC (100.1 *versus* 102.6% pred; $p=0.07$) and FEF_{25–75%} (81.3 *versus* 87.7% pred; $p=0.08$) than controls. Current smokers had lower FEV₁ ($p=0.05$) and FEV₁/FVC ($p=0.05$) than never-smokers. Dairy farmers also had lower Sp,O₂ than controls (96.06 *versus* 96.68%; $p=0.02$ after adjustment for age, smoking, height, sex, altitude, pulse rate and FEV₁).

Lung function decline during follow-up

Lung function parameter decline during follow-up in the three exposure groups is presented in table 4. Dairy farmers had greater declines in FEV₁ and FEV₁/FVC than controls ($p=0.04$ and $p=0.007$, respectively). After adjustment for smoking, age, height, sex and altitude (table 5), dairy farmers still had a greater decline in FEV₁/FVC ($p=0.01$) than controls. Nondairy agricultural workers also showed an increased decline in FEV₁/FVC and in FEF_{25–75%} but these differences did not reach the level of significance. Current handling of animal feed was associated with an increased decline in FEV₁ ($p=0.05$; table 5). Moreover, decline in FEV₁ increased with years spent handling animal feed during the survey period T1 to T3 ($p=0.03$; table 5). Current smoking was also associated with an accelerated decline in FEV₁ ($p=0.02$), FEV₁/FVC ($p=0.02$) and FEF_{25–75%} ($p=0.0003$).

DISCUSSION

An increased risk of respiratory symptoms related to chronic bronchitis (usual morning phlegm and, to a lesser degree,

TABLE 3 Influence of farming exposure on respiratory symptoms in farmers[#]

	Hay or straw handling		Animal food handling	
	Current [†] versus never ⁺	Former [‡] versus never ⁺	Current [†] versus never ^{##}	Former ^{††} versus never ^{##}
Personal history of allergy	1.51 (0.84–2.71)	2.31 (1.29–4.14)	1.26 (0.70–2.25)	1.79 (1.03–3.09)
Asthma at any time in their life				
Self-reported	1.20 (0.21–6.82)	8.37 (1.78–39.25)	0.50 (0.09–2.84)	5.69 (1.53–17.04)
Doctor-diagnosed	0.93 (0.15–5.81)	7.51 (1.59–35.41)	0.26 (0.03–2.39)	4.56 (1.36–15.33)
Woken by cough in the previous year	1.88 (0.61–5.78)	3.57 (1.26–10.10)	2.47 (0.84–7.23)	3.31 (1.24–8.86)
Wheezing at any time in their life	2.21 (0.81–6.01)	4.99 (1.93–12.88)	1.25 (0.48–3.20)	3.58 (1.60–8.00)
Wheezing in the previous year	1.26 (0.31–5.01)	3.31 (1.06–10.36)	1.61 (0.38–6.85)	3.55 (1.13–11.15)
Wheezing apart from a cold in the previous year	1.10 (0.14–8.40)	4.67 (0.99–21.95)	2.99 (0.45–19.80)	3.65 (0.77–17.35)
Usual morning cough	1.34 (0.44–4.09)	2.11 (0.78–5.68)	2.21 (0.64–7.49)	3.04 (1.09–8.50)
Usual morning phlegm	1.91 (0.76–4.88)	2.26 (0.94–5.45)	1.14 (0.48–2.74)	1.21 (0.57–2.59)
Chronic bronchitis⁺⁺			2.63 (0.23–30.44)	7.39 (0.85–64.16)

Data are presented as OR (95% CI). Odds ratio adjusted for age and smoking status in 2006 (never-smokers were used as the reference group). [#]: six farmers with hypersensitivity pneumonitis were excluded; [†]: n=118; ⁺: n=92; [‡]: n=125; [†]: n=90; ^{##}: n=109; ^{††}: n=135; ⁺⁺: no cases of chronic bronchitis in subjects never having handled hay or straw.

usual morning cough) was found in dairy farmers and nondairy agricultural workers. Dairy farmers also presented an increased decline in FEV₁/FVC and lower S_pO₂ than controls. Animal feed and hay or straw handling were associated with increased risks of respiratory symptoms and animal feed handling was associated with an increased decline in FEV₁. Finally, we found a healthy worker effect indicated by the stronger effect of animal feed, hay and straw handling observed in former than in the current handlers.

This longitudinal study has limitations. We have no measurements of exposure associated with hay, straw or animal feed handling. These parameters were evaluated by self-report questionnaires previously used in dairy farmer studies conducted in the same province [16, 18, 23], one of which included measurements of hay and fodder contamination by microorganisms [23]. We observed high levels of hay contamination

by microorganisms, especially in relation to low modernity of farms [23–25] and to bad climatic conditions during haymaking season. In particular, we highlighted a large variability in results, in that the concentration of microorganisms differed considerably between farms as well as within the same farm, depending on the time of day and where measurements were taken with respect to work patterns and the time of year [26]. The conditions inherent to this type of longitudinal study, with a 12-yr follow-up, made it extremely difficult to reach an accurate estimate of the level of professional exposure. In our study, animal feed, hay and straw handling were strongly related: only 24.4% had discordant exposures to animal feed and hay or straw. Similarly, in a cross-sectional study recently published on farmers lung function and including personal measurements of exposures to dust, microorganisms and gas, many agents were strongly correlated [27]. In our study, these correlations of exposures limit the possibility of forming

TABLE 4 Annual changes in respiratory function parameters between 1994 and 2006

	Dairy farmers	Nondairy agricultural workers	Controls
Time between the two surveys yrs	12.7 ± 0.29	12.4 ± 0.40	12.5 ± 0.41
Respiratory function			
Available data n	157 [#]	105	72
ΔFVC mL·yr ⁻¹	-10.7 ± 29.6	-12.6 ± 37.1	-11.0 ± 42.7
ΔFEV ₁ mL·yr ⁻¹	-16.4 ± 30.0 [†]	-14.0 ± 27.9	-8.2 ± 23.0
ΔFEV ₁ /FVC %·yr ⁻¹	-0.21 ± 0.64 ⁺	-0.11 ± 0.41	0.005 ± 0.57
ΔPEF mL·s ⁻¹ ·yr ⁻¹	33.2 ± 112.1 [‡]	65.4 ± 125.4	64.0 ± 118.9
ΔFEF _{25–75%} mL·s ⁻¹ ·yr ⁻¹	-41.5 ± 57.4 [†]	-41.4 ± 60.0 ^{**}	-20.7 ± 58.2

Data are presented as mean ± SD, unless otherwise stated. Change: (2006 value – 1994 value)/(number of years between the T1 and T3 examinations). Δ: change in; FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 s; PEF: peak expiratory flow; FEF_{25–75%}: forced expiratory flow at 25–75% of FVC. [#]: six farmers with hypersensitivity pneumonitis were excluded (only four had valid respiratory function tests); [†]: p=0.04; ⁺: p=0.007; [‡]: p=0.07; [†]: p=0.02; ^{**}: p=0.01.

TABLE 5 Influence of farming and farming exposure on mean annual change in respiratory function parameters: multiple regression models adjusted for age, sex, altitude and parameter value in 1994

	Δ FVC mL·yr ⁻¹		Δ FEV ₁ mL·yr ⁻¹		Δ FEV ₁ /FVC %·yr ⁻¹		Δ PEF mL·s ⁻¹ ·yr ⁻¹		Δ FEF _{25-75%} mL·s ⁻¹ ·yr ⁻¹	
	Coefficient±SD	p-value	Coefficient±SD	p-value	Coefficient±SD	p-value	Coefficient±SD	p-value	Coefficient±SD	p-value
Model 1: farming[#]										
Dairy farmers	6.67±4.65	≥0.10	-3.20±3.86	≥0.10	-0.21±0.08	0.01	-26.25±14.52	0.07	-14.22±8.02	0.08
Nondairy agricultural workers	2.22±5.00	≥0.10	-2.51±4.15	≥0.10	-0.10±0.09	≥0.10	-4.64±15.60	≥0.10	-12.77±8.64	≥0.10
Model 2: hay or straw handling[†]										
Formerly	-10.33±4.71	0.03	-3.45±4.24	≥0.10	0.12±0.08	≥0.10	-15.87±15.80	≥0.10	10.17±8.40	≥0.10
Currently	-8.78±5.19	0.09	-7.96±4.68	0.09	0.01±0.09	≥0.10	-12.26±17.51	≥0.10	1.88±9.24	≥0.10
Model 3: animal feed handling[†]										
Formerly	2.80±4.59	≥0.10	3.30±4.65	≥0.10	0.03±0.08	≥0.10	-19.60±15.33	≥0.10	7.94±8.18	≥0.10
Currently	-7.78±5.22	≥0.10	-9.12±4.65	0.05	-0.07±0.10	≥0.10	-14.01±17.43	≥0.10	-2.59±9.27	≥0.10
Model 4: animal feed handling[†]										
Time spent handling between T1 and T3 yrs	-0.38±0.36	≥0.10	-0.71±0.32	0.03	-0.009±0.006	≥0.10	-1.08±1.20	≥0.10	-0.61±0.64	≥0.10

Δ : change in; FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 s; PEF: peak expiratory flow; FEF_{25-75%}: forced expiratory flow at 25–75% of FVC. [#]: multiple linear regressions performed in the whole cohort with adjustment for smoking status (current smokers and ex-smokers versus never-smokers), age (yrs), height (cm), sex, altitude (mountain and tableland versus plain) and analysis of the initial value of the lung function parameter; [†]: multiple linear regressions performed in dairy farmers and other agricultural workers with adjustment for smoking status (current smokers and ex-smokers versus never-smokers), age (yrs), height (cm), sex, altitude (mountain and tableland versus plain) and analysis of the initial value of the lung function parameter.

conclusions about the specific role of each exposure on respiratory impairment.

A second limitation concerns the differences in participation rates between the three groups. These differences were not related to increased mortality or more refusals to participate in the nondairy agricultural workers or controls than in dairy farmers. They can be explained by an excess of loss to follow-up in nondairy agricultural workers and controls, in that dairy farmers in our area are less likely to move than nondairy agricultural workers and administrative employees, particularly to find a new job. Subjects lost to follow-up were younger than those who participated. However it is important to note that there was no difference in respiratory symptoms or lung function parameters at baseline between subjects who participated or did not participate in the follow-up. Moreover, the differences observed at T3 in age and smoking rates between dairy farmers and nondairy agricultural workers, and controls, can be related to similar differences observed at baseline. The same differences in smoking rates have been observed in all studies conducted in the same province. However the inclusion of fewer smokers in the dairy farmer group than in the control group would only have lead to a lack of power, as smoking is related to an increased risk of lung function impairment. However, the inclusion of more older farmers than controls would have induced a selection bias, but all multiple analyses were adjusted for age.

Finally, as we did not perform post-bronchodilator spirometry, we cannot affirm that the decrease in FEV₁/FVC observed in dairy farmers is related to chronic obstructive pulmonary disease, even if it is the most probably hypothesis, since dairy farmers also presented an excess risk of morning phlegm.

An excess of respiratory symptoms related to chronic bronchitis has been already found in dairy farmers from the same province [15, 16] and other agricultural settings (poultry workers [4, 5], pig farmers [2, 3], flower cultivators [28], grain silo workers [17] and sawmill or wood workers [29]). Conversely, the accelerated decline in FEV₁/FVC that we observed over a long follow-up period has rarely been reported, and then was not reproducible within other agricultural sectors [14]. Lung function parameters and mean annual changes were correlated with smoking and age. This shows the relevance of our measures and, therefore, of our results. The decrease in S_pO₂ in dairy farmers might not be clinically relevant, even if at this level of the haemoglobin dissociation curve, a small variation in S_pO₂ corresponds to a greater variation in arterial oxygen tension. However, this consistent finding [16, 18] probably indicates an alveolar involvement related to occupational exposure.

Our study originally found associations of hay, straw and animal feed (grains and flour) exposures with significant increased risks of asthma and wheezing. In the study by HOPPIN *et al.* [30], handling ground animal feed and stored hay was related with an increased risk of wheeze. In addition, animal feed handling and, in particular, the number of years of exposure to animal feed was also associated with an increased decline in FEV₁. In the study by EDUARD *et al.* [27], chronic bronchitis was significantly associated with exposure to all agents except glucans and hydrogen sulfide. In the same study there was an inverse association of FEV₁ with organic dust, bacteria, endotoxins, glucans, ammonia and hydrogen sulfide. Another study carried out in the same area (Eastern Franche-Comté, France and Switzerland) showed that working in a barn, particularly handling animal feed, was associated with

high peaks of air contamination for mold and actinomycetes, as well as for poaceae pollens [31]. Conversely, the concentration of airborne bacteria was not significantly influenced by animal feed handling. Therefore, it is likely that the exposure to molds and actinomycetes contributes to the deleterious effect of exposure to hay and animal feed on respiratory status in our study. Moreover, animal feed, straw and hay handling can also induce exposure to organic dust, bacteria, mites, endotoxins, muramic acid and even-numbered carbon chain length 3-hydroxy fatty acids. [1, 32] Working on a farm is associated with exposure to numerous inflammatory substances, which could contribute to the bronchial involvement observed in our study [32]. The risk for asthma and wheezing generated by this type of exposure might also be linked to a high concentration of pollen.

A final result worth noting was the stronger effect of former exposure to hay, straw or animal feed on respiratory symptoms than the effect of current exposure (table 3). This can probably be explained by the selection effect induced by respiratory diseases [33]. Farmers or agricultural workers who developed respiratory diseases are likely to have stopped performing dusty tasks. Similarly, CHENARD *et al.* [34] found that predicted FEV₁/FVC ratio and FEF_{25-75%} at baseline were lower in subjects who stopped swine farming compared to those who continued. In the study by EDUARD *et al.* [27], farmers who had left farming had more chronic bronchitis, and lower FEV₁ and FVC, and farmers who had changed farm production because of dust-related respiratory problems had an increased prevalence of chronic bronchitis and asthma [27].

Conclusion

Our study shows an excess of usual morning phlegm and an accelerated decline in FEV₁/FVC in dairy farmers. Handling hay, straw and animal feed is probably responsible for the excess of respiratory symptoms in dairy farmers and animal feed handling is associated with an accelerated decline in FEV₁. However, our data are insufficient to affirm a causal relationship and the exposure measurement needs to be refined.

STATEMENT OF INTEREST

None declared.

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