Prevalence and risk factors for COPD in farmers: a cross-sectional controlled study

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ABSTRACT There are conflicting data regarding the magnitude and determinants of chronic obstructive pulmonary disease (COPD) risk in farmers.

In a cross-sectional study of 917 nonfarming working controls and 3787 farmers aged 40–75 years, we assessed respiratory symptoms, tobacco exposure, job history (without direct exposure measurement) and lung function. COPD was defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criterion (post-bronchodilator forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) <0.70) and by the Quanjer reference equation (post-bronchodilator FEV_1/FVC <lower limit of normal (LLN)).

The prevalence (95% CI) of COPD according to the GOLD criterion was 5.1% (4.4–5.8%) and 2.9% (1.8–4.0%) in farmers and controls, respectively (p=0.005), and 3.1% (2.5–3.6%) and 1.5% (0.7–2.3%), respectively, for the LLN criterion (p<0.01). For both COPD criteria after adjustment for age, sex and smoking status, COPD prevalence was similar in controls and crop farmers. Compared to controls, four job categories had a higher prevalence of COPD according to the GOLD criterion, namely, cattle breeders, swine breeders, poultry breeders and breeders of two or more livestock types. Among cattle breeders, only those from Franche-Comté had higher prevalence of COPD according to both GOLD and LLN criteria.

The prevalence of COPD in farmers is higher than in nonfarming working controls, and depends on the farming activity, the region and the criterion used to define COPD.

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Introduction

Chronic obstructive pulmonary disease (COPD) is an increasingly widespread cause of morbidity and mortality worldwide [1]. In most cases, COPD is caused by chronic irritation of the airways by inhaled substances [2]. The current therapies for COPD are poorly effective and the mainstay of management is therefore to avoid exposure to substances known to contribute to COPD development [3]. Although cigarette smoke is the most frequent single causal factor for developing COPD, causal relationships between occupational respirable exposures and development of COPD have been demonstrated [1, 2, 4]. A low prevalence of asthma and atopy has been shown in farmers and agricultural workers, but a high prevalence of respiratory symptoms related to chronic bronchitis and COPD has been established [5, 6]. Although farmers tend to smoke less often than the general population [7, 8], a higher prevalence of COPD has been suggested in subjects exposed to farm animals, especially swine, poultry and cattle [5, 9–11]. However, a cross-sectional study of the risk of COPD in farmers using nonfarming working subjects as controls is still lacking, and there are conflicting data regarding the magnitude and determinants of COPD risk in farmers [5, 9, 10]. Discrepancies in findings between studies from various countries may be due to differences in climate, working conditions and/or tobacco smoking history, but may also be secondary to differences in the definition used to define COPD. In the literature, COPD cases are defined either by spirometry-based criteria or by self-reported diagnosis of chronic bronchitis, emphysema and/or COPD [4]. When spirometry is performed, some investigators use the 5th percentile lower limit of normal (LLN) of the forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) ratio to define COPD [5], while others use a fixed ratio of 70% [9, 10]. In addition, some investigators use pre-bronchodilator values of FEV_1 and FVC [5, 10] to define COPD while others use post-bronchodilator measurements, in accordance with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [9].

According to the French Ministry of Agriculture, there are ~1 million persons working in farms in France. However, the burden of COPD among French farmers is currently unknown. Therefore, we performed a controlled cross-sectional study in order to determine the prevalence of and risk factors for COPD in

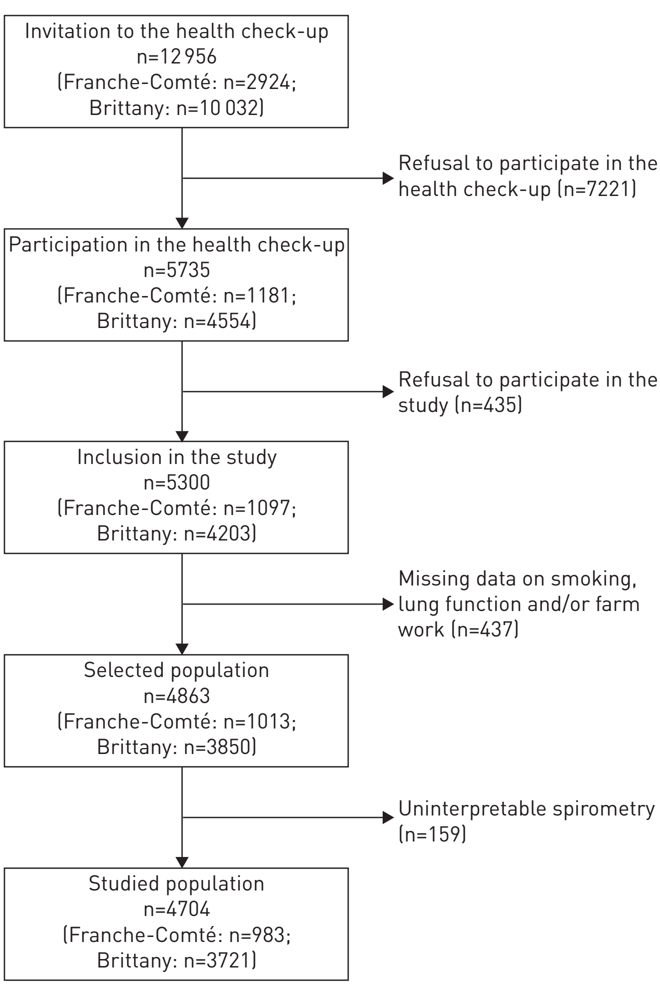

FIGURE 1 Flow chart of participants included in the study.

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agricultural workers covering several farming activities in two regions of France. To this end, we analysed data collected through a real-life systematic COPD detection programme performed in consecutive subjects (farmers or nonfarming working controls) who attended a health check-up organised by the French national social security system for agricultural workers (Mutualité Sociale Agricole (MSA)).

Materials and methods

Study population

Data were collected between October 2012 and May 2013 in two French regions (Brittany and Franche-Comté) among affiliated members (farmers and administrative workers of both sexes) of the MSA. Brittany is located in the west of France, and is mainly flat and rainy with an oceanic climate. The region of Franche-Comté is a hilly and rainy region with a continental climate, located in the eastern part of France. During the study period, 12 956 subjects aged 40–75 years were invited to attend a free health check-up performed at a location close to the subjects' homes. ∼44% of the invited subjects participated in the check-up. Among those, 7.6% refused to participate in the COPD screening study (fig. 1).

Ethical approval was received from the local ethics committee (Comité de Protection des Personnes (CPP) Est; 13–682) and written consent was obtained from all subjects.

Spirometry testing

Spirometry was performed using a pneumotachograph (MedGraphics; MSE Medical, Strasbourg, France). The spirometer was calibrated at least once daily using a 3-L syringe. Nurses who performed spirometry were trained through a specific training course in a pulmonary function laboratory. According to the organisation of the health check-ups, all lung function tests were performed between 07:30 h and 12:00 h. A minimum of three adequate measurements was required for each patient and the best value was selected for the analysis [12]. Spirometry outcomes included FEV_1 and FVC. A bronchodilation test was applied when the FEV_1/FVC ratio was <0.70 and/or below the LLN. Bronchodilation was performed by administering 400 μg of the short-acting β_2-agonist salbutamol (Ventoline; GlaxoSmithKline, Marly-le-Roi, France). Four separate puffs of 100 μg each were given through a spacer device (Vortex; PARI PulmoMed, Nanterre, France) and the spirometry was repeated after a 10- to 15-min delay, as recommended [12]. Predicted values were based on the European Community for Steel and Coal (ECSC) equations [13]. Spirometry data were anonymised and interpreted according to the American Thoracic Society/European Respiratory Society recommendations [12] by two respiratory medicine specialists (B. Degano, S. Guillot, F. Rannou or D. Marquette) via a web-based platform within 48 h.

COPD definition and severity

COPD was defined according to the GOLD cut-off criterion (FEV_1/FVC <0.70) and according to the 5th percentile of the FEV_1/FVC ratio distribution (FEV_1/FVC <LLN) based on the ECSC equations [13]. COPD cases were categorised according to severity as stage I (FEV_1 ⩾80% predicted) *versus* stage II or higher (stage II+: FEV_1 <80% pred).

Anthropometric data and symptom questionnaire

Height and weight measured by a nurse on the same day as the health check-up were used for the current analysis.

The self-administered questionnaire was an adapted French version of the European Community Respiratory Health Survey questionnaire, as described previously by our group [14]. The main items regarding respiratory status were personal and family history of respiratory disease, atopy, asthma (self-reported and confirmed by a doctor), asthma attack, wheezing or whistling in the chest, being woken by attacks of shortness of breath or coughing, morning cough or morning sputum in the winter, chronic bronchitis and breathlessness (questions related to the modified Medical Research Council (mMRC) stages). Self-reported asthma was defined by a positive answer to the question "Have you ever had asthma?" Chronic bronchitis was defined as cough and expectoration for ⩾3 months of the year for at least two consecutive years. The presence of atopy was based on a history of hay fever, allergies, asthma, nasal symptoms not related to a cold or a flu, itchy rash and/or eczema.

Smoking history included the number of cigarettes/pipe/cigars smoked per day and dates upon which smoking was taken up/given up. From these data, the number of pack-years was calculated and the "smoking status" was defined: nonsmokers were defined as those having smoked on average less than one cigarette, one cigar or one pipe a day for a year. Current smokers smoked this amount or more and ex-smokers had stopped smoking at >1 month before the time at which they completed the questionnaire [14].

TABLE 1 Population characteristics

	Controls	Farmers (all)	Farmers (by category)					
			Crop	Cattle	Swine	Poultry	⩾2 types of livestock	Other farm production
Subjects	917	3787	411	1638	233	192	333	980
Males	423 (46)	2371 (63)*	272 (66)*	998 (61)*	153 (66)*	102 (53)	209 (63)*	637 (65)*
Age years								
40–49	307 (34)	1200 (32)	164 (40)*	450 (27)*	73 (31)	72 (38)*	98 (29)	343 (35)
50–59	288 (31)	1181 (31)	134 (33)*	501 (31)*	86 (37)	72 (38)*	102 (31)	286 (29)
⩾60	322 (35)	1406 (37)	113 (27)*	687 (42)*	74 (32)	48 (24)*	133 (40)	351 (36)
BMI kg·m^{-2}	25.7±4.4	26.8±4.5*	26.5±4.4*	27.1±4.7*	26.1±3.8	26.0±4.2	26.4±3.7*	27.1±4.7*
Smoking status								
Never	540 (59)	2571 (68)*	237 (58)	1227 (75)*	169 (73)*	127 (66)	239 (72)*	572 (58)
Former	250 (27)	736 (19)*	94 (23)*	261 (16)*	49 (21)*	36 (19)	61 (18)*	235 (24)
Current	127 (14)	480 (13)*	80 (19)*	150 (9)*	15 (6)*	29 (15)	33 (10)*	173 (18)
Smoking intensity								
<1 pack-year	549 (60)	2599 (69)*	238 (58)	1240 (76)*	172 (74)*	128 (67)	241 (72)*	580 (59)
1–15 pack-years	189 (21)	542(14)*	70 (17)	194 (12)*	35 (15)*	25 (13)	42 (13)*	176 (18)
>15 pack-years	179 (19)	646(17)*	103 (25)	204 (12)*	26 (11)*	39 (20)	50 (15)*	224 (23)
Pack-years	7.14±14.4	5.70±12.6*	7.78±14.6	4.09±10.1*	3.86±9.3*	6.76±14.0	4.98±11.5*	8.11±15.4
Region								
Brittany	796 (87)	2925 (77)*	327 (80)*	1091 (67)*	231 (99)*	187 (97)*	320 (96)*	769 (78)*
Franche-Comté	121 (13)	862 (23)*	84 (20)*	547 (33)*	2 (1)*	5 (3)*	13 (4)*	211 (22)*
mMRC dyspnoea >0	165 (19)	816 (22)*	92 (23)	352 (22)*	34 (15)	44 (24)	50 (16)	244 (26)*
Chronic cough	106 (12)	687 (19)*	77 (19)*	296 (19)*	33 (15)	31 (17)	66 (21)*	184 (19)*
Chronic sputum	81 (9)	538 (15)*	52 (13)*	247 (16)*	22 (10)	24 (13)	48 (15)*	145 (15)*
Atopy	242 (27)	954 (26)	115 (29)	366 (23)*	58 (26)	44 (24)	93 (29)	278 (29)
Pre-bronchodilator spirometry								
FEV_1 L	3.09±0.77	3.11±0.84	3.27±0.81*	3.05±0.83	3.23±0.88*	3.09±0.85	3.14±0.85	3.13±0.84
z-score	0.69±1.03	0.52±1.10*	0.61±1.07	0.51±1.06*	0.63±1.15	0.55±1.13	0.55±1.02*	0.45±1.19*
FVC L	3.87±0.97	3.94±1.02	4.11±0.98*	3.84±1.01	4.05±1.04*	3.91±0.97	3.99±1.06*	3.98±1.00*
z-score	0.92±1.04	0.74±1.07*	0.83±1.04	0.71±1.05*	0.81±1.11	0.85±1.09	0.79±1.03	0.70±1.13*
FEV_1/FVC %	80.2±6.6	79.2±7.3*	79.5±7.0	79.4±7.0*	79.6±7.6	79.0±7.0*	79.0±6.6*	78.7±7.9*
z-score	0.36±0.95	0.25±1.04*	0.25±0.99	0.31±1.00	0.32±1.09	0.16±0.97*	0.24±1.07	0.18±1.11*
PEF L·s^{-1}	7.60±2.05	7.64±2.18	7.97±2.19*	7.49±2.13	7.91±2.09*	7.60±2.05	7.67±2.28	7.71±2.22
z-score	0.46±1.33	0.21±1.41*	0.35±1.41	0.17±1.35*	0.35±1.28	0.22±1.45*	0.20±1.47*	0.19±1.49*
FEF_{25-75} L·s^{-1}	3.08±1.10	3.03±1.18	3.20±1.21	2.98±1.16*	3.18±1.30	2.98±1.10	3.01±1.16	3.02±1.20
z-score	−0.24±1.00	−0.35±1.02*	−0.29±1.06	−0.35±0.99*	−0.24±1.11	−0.43±0.94*	−0.37±0.98*	−0.39±1.05*

Data are presented as n, n (%) or mean±SD, unless otherwise stated. BMI: body mass index; mMRC: modified Medical Research Council; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; PEF: peak expiratory flow; FEF_{25-75}: forced expiratory flow at 25–75% of FVC. *: p<0.05 *versus* controls.

Professional history questionnaires

Data regarding professional history included the last five jobs held by the subjects, with the start and finish dates for each job. Six specific groups were identified. Subjects who declared having worked in only nonagricultural jobs without any known exposure were used as controls. The five other specific groups were exclusive crop farmers (growing cereals, fruits, potatoes, *etc.*), cattle breeders (either dairy farmers or meat producers), swine breeders, poultry breeders and livestock farmers breeding two or more types of livestock. To be classified in one of these five groups, subjects must have worked at the specified job for ⩾10 years. To be classified in one of the four groups of breeders, subjects must have raised only the specified livestock, but could also work or have worked as crop farmers and/or worked in a job without any known exposure. All subjects who did not meet the criteria for classification in one of the six specific groups defined above were classified as “others”.

Statistical analysis

For subjects who did not undergo post-bronchodilator spirometry despite a pre-bronchodilator result showing FEV_1/FVC <0.70 and/or FEV_1/FVC <LLN, we used the fully conditional specification method to impute missing values for post-bronchodilator FVC and FEV_1 from pre-bronchodilator FVC and FEV_1 values, sex, age and tobacco history [15].

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Comparisons between controls and agricultural workers for data collected in the questionnaires (age, body mass index, smoking habits, region and job types) were performed using the Chi-squared test and the t-test for qualitative and quantitative data, respectively. Moreover, we assessed the prevalence of COPD for each job category and for each smoking status (nonsmokers and ever-smokers).

Odds ratios were computed using logistic regression and adjusted for covariates that are known to be independent risk factors for COPD [16], namely age (as a continuous variable), smoking status (1–15 pack-years, >15 pack-years and <1 pack-year (reference)) [17] and sex (female as reference).

All analyses were repeated according to COPD definition (GOLD or LLN) and were performed using SAS (version 9.3; SAS Institute, Inc., Cary, NC, USA).

Results

5300 subjects were included in the study. Among them, 596 were not analysed further either because of missing data on smoking and/or lung function and/or farm work (n=437) or because they were unable to perform appropriate spirometry (n=159) (fig. 1). The main characteristics of the 4704 remaining participants are shown in table 1. All subjects in the control group reported that they had undertaken a maximum of five jobs in their life and none of these jobs was in the farming sector. The 10 most common jobs in the control group were accountants, teachers, secretaries, computer scientists, office managers, bank clerks, sales engineers, engineers, commercial counsellors and management consultants.

Agricultural workers were more frequently male and never-smokers than unexposed control subjects. In addition, agricultural workers reported dyspnoea (mMRC score >0) and symptoms of chronic bronchitis (*i.e.* chronic cough and chronic sputum) more frequently than control subjects. The prevalence of atopy was similar in controls and in agricultural workers.

In total, 8.4% of the analysed population had a pre-bronchodilator FEV_1/FVC <0.70 and 5.2% had a pre-bronchodilator FEV_1/FVC <LLN. 80 subjects with a pre-bronchodilator FEV_1/FVC <0.70 and/or FEV_1/FVC <LLN did not undergo post-bronchodilator spirometry and their post-bronchodilator values were imputed. 221 cases of GOLD-COPD (137 (62%) in stage I and 84 (38%) in stage II+) were detected, and 131 cases (60 (46%) in stage I and 71 (54%) in stage II+) according to the LLN definition. All subjects who had COPD according to the LLN definition also had COPD according to the GOLD definition.

The prevalence of COPD was higher in agricultural workers (farmers) than in control subjects who had never had any identified occupational exposure (table 2). After adjustment for age, sex and tobacco exposure, the prevalence of COPD was approximately two-fold higher in agricultural workers than in nonfarming working control subjects, suggesting that agricultural exposure by itself was associated with an increased risk for COPD (table 2). Mean durations of exposure of the six predefined agricultural categories of jobs are shown in table 3. Subanalysis of these predefined categories of jobs demonstrated that all categories except exclusive crop farming had higher prevalence of COPD compared to controls (table 2).

The adjusted prevalence of COPD was similar in nonfarming working controls in both the regions studied (table 4). In three agricultural job categories (swine breeders, poultry breeders and livestock farmers breeding two or more types of animals), very few subjects were from the Franche-Comté region (1.1%, 2.6% and 3.7%, respectively; see table 1). Therefore, the association between agricultural job categories, COPD prevalence and regions was studied only in the three other categories, *i.e.* exclusive crop farmers, cattle breeders and "other" agricultural job categories (as defined in the methods section). After adjustment for age, sex and tobacco exposure, only cattle breeders from Franche-Comté had a higher prevalence of COPD than cattle breeders from Brittany.

The adjusted odds ratios of GOLD- and LLN-COPD for each job category after stratification by smoking status are summarised in table 5. The risk of COPD attributable to occupational exposure was much higher in nonsmokers than in ever-smokers in three job categories (cattle breeders from Franche-Comté, swine breeders, breeders ⩾2 types of livestock). In addition, in cattle breeders from Franche-Comté with a smoking history, there was a two-fold increase in the risk of COPD compared with control smokers. Tobacco smoking and job exposure had an additive effect on COPD prevalence in four job categories (cattle breeders from Franche-Comté, swine breeders, breeders of more than two types of livestock and other farm production).

Discussion

By using robust and recommended spirometric criteria, we found that the prevalence of COPD was higher in farmers than in nonfarming working control subjects. However, the prevalence of COPD was much lower than rates previously reported in farmers or nonfarming working controls from other countries.

In addition, our analysis demonstrates that the prevalence of COPD depends not only on the farming activity but also on the region in which farmers work.

Although farming is often considered a risk factor for COPD, there are few and conflicting data regarding prevalence and the magnitude of the risk [18]. In a study performed in Norway in 4735 farmers, Eduard *et al.* [5] reported a COPD prevalence of 16.1%, ranging from 13.5% in exclusive plant producers to 17.0% in livestock producers. In a population-based study performed in Austria including a subgroup of 288 farmers, Lamprecht *et al.* [9] reported a prevalence of COPD ranging from 9.6% to 29.9% in farmers aged 40–70 years. In a sample of 105 nonsmoking farmers from the European Farmers' Project, Monsó *et al.* [10] reported a COPD prevalence of 17%. In our study, we observed a prevalence of COPD among farmers that is two- to six-fold lower than in these studies. This much lower COPD rate may have several explanations. One possible explanation is the use of post-bronchodilator spirometry in our study. The use of pre-bronchodilator spirometric measurements may lead to misclassifications of COPD and to an apparent increase of COPD prevalence. It is regularly claimed that the exclusion of subjects who report ever having asthma from studies in which only pre-bronchodilator spirometry is used for COPD diagnosis makes it possible to avoid any bias [5, 19, 20]. Nevertheless, even in healthy subjects, a bronchodilation test allows for an increase in FEV_1/FVC of ∼3%, which can allow subjects with pre-bronchodilator FEV_1/FVC ratio just below 70% to be misclassified as COPD cases [21]. In line with this, we found in our series that 44% of the subjects with a pre-bronchodilator FEV_1/FVC ratio <70% would have been misclassified as having COPD if a bronchodilation test had not been performed.

The choice of the threshold for FEV_1/FVC also has a clear impact on the prevalence of COPD. A fixed threshold of 70% for FEV_1/FVC regardless of age increases the prevalence of COPD in older subjects [16]. By contrast, a statistically determined LLN cut-off (*i.e.* the 5th percentile of the distribution of age-specific FEV_1/FVC values from a healthy, lifelong nonsmoking population) increases the prevalence of COPD in younger subjects. In the study by Eduard *et al.* [5] the percentage of subjects with a pre-bronchodilator FEV_1/FVC <0.70 was almost half (6.9%) that obtained using the LLN definition (13.5%). In contrast, in our study, the percentage of subjects with a pre-bronchodilator FEV_1/FVC <LNN (5.2%) was not only much lower than that reported by Eduard *et al.* [5], but was also lower than the percentage of subjects with pre-bronchodilator FEV_1/FVC <0.70 (8.4%). These differences are partly due to the fact that the mean age of our study population (57±9 years) was greater than that in the study by Eduard *et al.* [5] (49±11 years).

The prevalence of COPD in farmers compared to control subjects without any identified occupational exposure has rarely been examined. Grain elevator workers and grain handlers have been shown to have accelerated decline in lung function [22]. Conversely, farm workers who grow citrus fruit, grapes or tomatoes have been reported to have better pulmonary function than controls, suggesting a "healthy worker effect" [23] or, perhaps, an effect related to a different diet in these workers. Eduard *et al.* [5] reported that farmers who cultivated crops only had less COPD than farmers who had both crops and livestock. To the best of our knowledge, our study is the first to report that exclusive crop farmers have a prevalence of COPD that is not different to that of subjects without any identified occupational exposure, after adjustment for smoking, age and sex. In our study, the odds ratios of COPD in farmers compared

TABLE 2 Prevalence and odds ratios for chronic obstructive pulmonary disease (COPD) adjusted# for age, smoking status and sex, according to the definition used to identify COPD

	GOLD			LLN		
	Cases	**Prevalence**	**Adjusted OR (95% CI)**	**Cases**	**Prevalence**	**Adjusted OR (95% CI)**
All subjects	221/4704	4.70 (4.08–5.30)		131/4704	2.78 (2.31–3.26)	
Controls	27/917	2.94 (1.85–4.04)	1.00	14/917	1.53 (0.73–2.32)	1.00
Farmers	194/3787	5.12 (4.42–5.82)	**1.94 (1.23–3.06)**	117/3787	3.09 (2.54–3.64)	**2.28 (1.24–4.20)**
Crop	12/411	2.92 (1.29–4.55)	1.02 (0.48–2.20)	13/502	2.19 (0.77–3.60)	1.43 (0.56–3.66)
Cattle	79/1638	4.82 (3.79–5.86)	**1.84 (1.12–3.02)**	46/1822	2.50 (1.75–3.26)	1.86 (0.95–3.66)
Swine	13/233	5.58 (2.63–8.53)	**2.28 (1.06–4.87)**	9/266	3.86 (1.39–6.34)	**3.02 (1.16–7.83)**
Poultry	11/192	5.73 (2.44–9.02)	**2.60 (1.11–6.08)**	10/226	3.65 (0.99–6.30)	**3.04 (1.05–8.79)**
⩾2 types of livestock	19/333	5.71 (3.21–8.20)	**2.02 (1.00–4.06)**	11/354	3.30 (1.38–5.22)	2.13 (0.83–5.47)
Other farm production	60/980	6.12 (4.62–7.62)	**2.01 (1.20–3.35)**	28/617	4.08 (2.84–5.32)	**2.47 (1.26–4.84)**

Data are presented as n/N or % (95% CI), unless otherwise stated. Data presented in bold are statistically significant. GOLD: Global Initiative for Chronic Obstructive Lung Disease; LLN: lower limit of normal. #: odds ratio for COPD adjusted for age (as a continuous variable), smoking status (1–15 pack-years, >15 pack-years or <1 pack-year (as reference)) and sex (female as reference).

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TABLE 3 Summary of the number of years worked in each group of farmers

	Years worked
Crop	27.5±9.6 (10–50)
Cattle (all)	28.8±9.7 (10–51)
Brittany	28.6±9.6 (10–51)
Franche-Comté	29.2±10.0 (10–49)
Swine	27.2±9.0 (10–47)
Poultry	26.1±9.1 (10–46)
⩾2 types of livestock	30.5±8.7 (10–50)
Other farm production	17.2±14.7 (0–52)

Data are presented as mean±SD (range).

with controls were higher than in most previous reports [5, 9, 10]. It is plausible that a lower prevalence in our control group explained at least in part these higher odds ratios. Nevertheless, as our control group declared they are not currently, and have not regularly been in contact with a farm, it is very unlikely that any agricultural environment could have had a significant effect on their pulmonary function tests. In addition, as controls and farmers were recruited during the same health check-up sessions and had a similar screening process, a selection bias in the control group is very unlikely.

Our finding that farmers working in swine or poultry confinement buildings are at higher risk of COPD has previously been suggested by some authors [18, 24], but was not confirmed by others [5]. Our cross-sectional population-based study allows us to conclude that occupation as a swine or poultry breeder is associated with a higher prevalence of COPD compared with subjects without any identified occupational exposure.

There have also been previous reports suggesting a higher risk of COPD in dairy farmers compared to unexposed subjects [5, 25, 26]. In a 12-year longitudinal study, we previously reported that dairy farmers presented a more accelerated decline in FEV_1/FVC than controls [25]. In a study performed in Norwegian farmers, a higher risk of COPD in dairy farmers compared to exclusive crop farmers was observed [5]. Our study demonstrated that cattle farmers had higher prevalence of COPD than controls. The fact that this higher prevalence was restricted to cattle farmers from Franche-Comté is intriguing. This could be due to greater exposure to organic dusts in the Franche-Comté region. Indeed, animal feed and hay handling has been reported to be associated with an increased decline in FEV_1 in farmers [26]. Wetter hay due to meteorological factors and more frequent traditional work in smaller farms due to regional habits, combined with the fact that cattle breeders from Franche-Comté are most often dairy farmers, while those from Brittany are mainly meat producers, could at least partially explain these differences.

We acknowledge that our study suffers from some limitations. First, the estimation of COPD prevalence in our study could have been biased by the fact that only a fraction of subjects invited to the health check-up actually participated in the COPD screening programme. Nevertheless, the characteristics of the subjects

TABLE 4 Adjusted odds ratios# for chronic obstructive pulmonary disease (COPD) according to region and definition used to identify COPD

	GOLD				LLN			
	Brittany		Franche-Comté		Brittany		Franche-Comté	
	Cases	OR	Cases	OR	Cases	OR	Cases	OR
Controls	24/796	1.00	3/121	0.62 (0.17–2.25)	13/796	1.00	1/121	0.40 (0.05–3.26)
Farmers (all)	129/2925	1.00	65/862	**1.55 (1.11–2.16)**	81/2925	1.00	36/862	1.41 (0.92–2.15)
Cattle	34/1091	1.00	45/547	**2.46 (1.49–4.06)**	18/1091	1.00	23/547	**2.54 (1.29–5.01)**
Crop	8/327	1.00	4/84	1.22 (0.28–5.25)	7/327	1.00	2/84	0.67 (0.11–4.20)
Other farm production	44/769	1.00	16/211	1.34 (0.71–2.52)	29/769	1.00	11/211	1.45 (0.68–3.05)

Data are presented as n/N or OR (95% CI). Data presented in bold are statistically significant. GOLD: Global Initiative for Chronic Obstructive Lung Disease; LLN: lower limit of normal. #: odds ratio for COPD adjusted for age (as a continuous variable), smoking status (1–15 pack-years, >15 pack-years or <1 pack-year (as reference)) and sex (female as reference).

TABLE 5 Adjusted odds ratios# for chronic obstructive pulmonary disease (COPD) in agricultural workers according to occupation and region after stratification by smoking status in separate models by COPD definition

	GOLD				LLN			
	⩾1 pack-year		<1 pack-year		⩾1 pack-year		<1 pack-year	
	Cases	OR	Cases	OR	Cases	OR	Cases	OR
Controls	21/368	1.00	6/549	1.00	11/368	1.00	3/368	1.00
Crop	12/173	1.11 (0.52–2.38)	0/238		9/173	1.59 (0.63–4.02)	0/238	
Cattle								
Franche-Comté	20/162	1.47 (0.75–2.89)	25/385	**5.06 (2.04–12.57)**	9/162	1.40 (0.55–3.56)	14/385	**5.59 (1.58–19.77)**
Brittany	16/236	1.09 (0.54–2.19)	18/855	1.63 (0.64–4.17)	9/236	1.22 (0.48–3.09)	9/855	1.79 (0.48–6.72)
Swine	5/61	1.21 (0.42–3.45)	8/172	**3.67 (1.23–10.90)**	4/61	1.93 (0.58–6.45)	5/172	**4.79 (1.11–20.65)**
Poultry	9/64	**3.48 (1.39–8.70)**	2/128	1.44 (0.28–7.29)	7/64	**4.50 (1.58–12.84)**	0/128	
⩾2 types of livestock	10/92	1.62 (0.71–3.71)	9/241	**2.92 (1.01–8.42)**	7/92	2.10 (0.76–5.74)	4/241	2.59 (0.56–12.00)
Other farm production	43/400	1.68 (0.96–2.94)	17/580	2.16 (0.84–5.56)	33/400	**2.54 (1.24–5.19)**	7/580	1.67 (0.43–6.58)

Data are presented as n/N or OR (95% CI). Unexposed controls were used as reference. Data presented in bold are statistically significant. GOLD: Global Initiative for Chronic Obstructive Lung Disease; LLN: lower limit of normal. #: odds ratios were adjusted for age (as a continuous variable) and sex (female as reference).

who did not participate in our study are not known. The participation rate in a previous round of health check-ups organised by the MSA in 2011, as well as the characteristics of participants and nonparticipants, has recently been studied [27]. In an analysis of 27 848 invited subjects (mean age 60.7 years), the participation rate was 39.4%, a value that is very close to the participation rate in our study. A hierarchical cluster analysis of all invited subjects identified two groups of nonparticipants (men in good health who are low users of healthcare (42% of all invited subjects); and men and women in poor health who are high users of healthcare (22% of all invited subjects)) and two main groups of participants (men in good health who are low users of healthcare except for health check-ups (16% of all invited subjects); and women in good health who are high users of healthcare (20% of all invited subjects)). Given that 22% of all invited subjects who do generally not participate in check-ups are in poor health, they may have a higher prevalence of COPD than groups who do participate. Therefore, the prevalence in the participating subjects could underestimate the actual prevalence in the overall population, and this limits the generalisability of our finding to the overall population. Second, only subjects with a FEV_1/FVC ratio <70% and/or LNN were subjected to bronchodilator testing. It has been reported that some subjects with a pre-bronchodilator FEV_1/FVC ratio >70% and/or LNN may have a post-bronchodilator criterion of COPD due to an increase in FVC without any further change in FEV_1 with bronchodilators [28]. Third, the cross-sectional design of our study only allowed estimation of the prevalence of COPD, and not its incidence. In addition, contrary to longitudinal studies, no firm conclusions regarding a causal relationship can be drawn from a cross-sectional study. Constitution of cohorts with longitudinal follow-up could help to refine the effect of exposure on the development of COPD in farmers. Fourth, there is currently no job-exposure matrix for the agricultural environment that associates a job title and exposure agents through cross-tabulation within each cell with one or several indices for exposure. Groups were therefore constituted according to job titles and not according to exposure levels to specified agents. High exposure to organic dusts, endotoxins, mites, ammonia and hydrogen sulfide in farmers has been associated with a higher prevalence of COPD [5]. However, we are unable to say whether or not such an exposure was present in our subjects, and at what level. This should be further examined, because management of COPD includes avoidance of exposure to substances known to contribute to COPD development.

In conclusion, this controlled study demonstrates that farmers have a higher prevalence of COPD than unexposed subjects, supporting existing evidence of a causal relationship between occupational exposure in agriculture and development of COPD. Any estimation of the burden of COPD attributable to agricultural exposures is sensitive to the choice of COPD definition. The data reported here should guide public health efforts in terms of prevention and cessation of exposure to occupational risk factors in farmers with a view to preventing and reducing COPD-related disability and mortality. Nevertheless, more research is needed to identify either environmental or biological agents that cause development of COPD in each subgroup of farmers.

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