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Respiratory conditions and pesticide exposure in British pesticide applicators

D. Fishwick[1], A. H. Harding[1], Y. Chen[1], C. M. Barber[1], N. Pearce[2] and G. Nicholls[1]

[1]HSE Science and Research Centre, Health and Safety Executive (HSE), Buxton, Derbyshire SK17 9JN, UK
[2]London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK

Correspondence to: David Fishwick, HSE Science and Research Centre, Health and Safety Executive (HSE), Harpur Hill, Buxton, Derbyshire SK17 9JN, UK. E-mail: david.fishwick@hse.gov.uk; d.fishwick@sheffield.ac.uk

ABSTRACT

Background: The relationship between pesticide exposure and respiratory ill-health remains under researched.
Aims: We set out to define the prevalence of respiratory complaints, excluding asthma, and estimates of exposure in a cohort of pesticide applicators based in Great Britain (GB).

Methods: A baseline cross-sectional study (n = 5817), with follow-up at up to 5 years (n = 2578), was conducted in GB pesticide workers. Demographic and personal factors, details of working hours and practices, exposures to specific pesticide types, self-reported respiratory ill-health and doctor-diagnosed health conditions were recorded. Multivariable logistic regression models were used to assess the association between exposures to pesticides and respiratory health.

Results: The mean age was 54.1 years; 98% were male. At baseline, 70 (1.2%) had doctor-diagnosed chronic bronchitis, and 60 (1%) had chronic obstructive pulmonary disease (COPD). Twenty-six (0.4%) reported farmer's lung. In contrast, reported respiratory symptoms were common at follow-up; nasal allergies reported by 541 participants (21%), regular cough by 351 (14%), chest tightness ever by 329 (13%) and work-related chest tightness by 45 (1.8%). Nasal allergies were more common in those not using pesticides in the last 12 months [odds ratio (OR) 1.54 (95% CI 1.14–2.06)], chest tightness was more common in retired workers [OR 1.87 (1.25–2.81)], and work-related chest tightness more common in the current high exposure category [OR 2.68 (1.28–5.60)].

Conclusions: This study has confirmed low levels of self-reported doctor-diagnosed conditions, but high levels of reported respiratory symptoms. This suggests potential under diagnosis of respiratory ill-health in this sector.

INTRODUCTION

Exposure to pesticides is linked to increased levels of reported respiratory symptoms [1, 2], adverse changes in pulmonary function [3–6] and respiratory conditions including asthma. Whilst most literature deals with asthma, including our own [7], fewer studies have considered the links between pesticide exposures and other respiratory diagnoses.

De Matteis [8] has identified exposure to pesticides, in addition to cleaning products, as a potential cause of chronic obstructive pulmonary disease (COPD). A subsequent review identified a similar association between exposure to both generally defined pesticides, certain herbicides, specifically organophosphate and carbamate insecticides, and the development of COPD [9]. Recent data [10] from the Lifelines Cohort Study have also suggested this specific link.

Associations between pesticide exposures and the development of hypersensitivity pneumonitis (HP) are less commonly described, perhaps given that organic dust exposures, often co-exposures with pesticides, are a well-established cause of HP [3, 5, 6]. Thus, differential attribution of likely causation in this context may be more difficult, although individual cases of HP [11, 12] are described, with limited support for this association found from population-based studies. The Agricultural Health Study [13] identified that those who had high pesticide exposure events, and ever used organochlorine and carbamate pesticides had higher levels of self-reported doctor-diagnosed farmer's lung, a type of HP. Handling silage and fermented agricultural by-products was specifically associated with HP. In addition, working in poultry houses and raising dairy cattle had elevated, but non-significant, HP risks.

We have previously reported in relation to asthma and pesticide exposures in this group of workers from the Prospective Investigation of Pesticide Applicators' Health (PIPAH) study in GB. We report here relevant findings from the British PIPAH

- Pesticide exposure has been linked to an excess of respiratory symptoms, adverse changes in pulmonary function and respiratory conditions including asthma.
- Fewer studies have considered the links between pesticide exposures and other respiratory diagnoses, and differences between levels of self-reported symptoms and diagnosed respiratory conditions.

What this study adds:

- Levels of common self-reported respiratory symptoms, both work-related and overall, were generally high in this group; certain symptoms were associated with higher pesticide exposure assessment categories.
- By contrast, levels of doctor-diagnosed COPD, hypersensitivity pneumonitis and chronic bronchitis were very low; this suggests that a significant proportion of the respiratory ill-health within this group may be underdiagnosed.

What impact this may have on practice or policy:

- Workers that use pesticides and related chemicals may have a diverse set of job roles.
- Occupational enquiry about the nature and extent of exposure to such agents is key to fully assessing patients with respiratory ill-health.

study of a baseline and first respiratory follow-up questionnaire survey of pesticide users, designed to assess the link between exposures to pesticides and both reported respiratory symptoms and doctor-diagnosed conditions other than asthma.

METHODS

The details of recruitment have been published in detail elsewhere [7, 14]. Pesticide workers in GB were recruited for this study using the National Register of Sprayer Operators (NRoSO, https://www.nroso.org.uk/) and the National Amenity Sprayer Operators' Register (NAsOR). Previous participants from the Pesticide Users' Health Study (PUHS [15]) were also invited to participate. In 2013, ~21 000 members of NRoSO and NAsOR were sent a survey pack inviting them to participate. In 2014, around 7500 participants from the existing PUHS were invited to join the study. From 2014, new members of NRoSO have been invited to join the study in an on-going recruitment program. Each consenting participant was also invited to complete a follow-up respiratory questionnaire in 2018. Participants were provided with a unique study identification number at recruitment, which appears on all study documents and enables linkage of baseline and follow-up data.

The *baseline questionnaire* recorded demographic factors, smoking and other lifestyle information, diet, general occupational information, specific self-reported occupational exposures and a comprehensive set of questions relating to health end points, including the presence of the lung conditions COPD and farmer's lung (subsequently termed hypersensitivity pneumonitis for the purposes of this analysis (HP)). Smoking data (ever versus never tobacco smoker) were specifically used to adjust subsequent regression models.

The follow-up respiratory questionnaire [16] enquired about self-reported respiratory symptoms (where possible, conformed to those used in the European Community Respiratory Health Survey [17]), doctor-diagnosed respiratory complaints including asthma, chronic bronchitis, COPD and HP, and their use of pesticides over the past year.

An estimate of hours worked with pesticides in the past year was calculated by multiplying the typical number of hours worked per day with pesticides by the number of days worked with pesticides in the past year as reported at follow-up. This variable was then categorized into four groups; zero exposure in the past year (not retired), zero exposure in the past year (retired), low and high. The low and high groups were split by the median of the values greater than zero (median = 120 h). In addition, duration of lifetime exposure was estimated from the number of years working with pesticides as reported at baseline, plus additional years reported at follow-up.

Data from both the baseline and the respiratory questionnaires were used in this analysis, conducted using Stata version 17 (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC). Following data cleaning, descriptive statistics were generated for the main demographic and measured variables between different health outcomes.

Logistic regression analyses were conducted to assess factors associated with self-reported doctors' diagnoses and separately also self-reported symptoms at follow-up. The diagnoses of interest were chronic bronchitis, COPD and HP, and symptoms of interest were nasal allergy, morning cough, chest tightness and work-related chest tightness. Work-related chest tightness was defined as self-reported chest tightness that got better on days off work. Separate pre-specified multivariable models were used for each of the diagnoses/symptoms of interest. The potential predictor variables were the categorical variable estimating the hours spent working with pesticides in the past year, and the continuous duration of lifetime exposure variable. All models were adjusted for age, sex and smoking status. Models including ever use of specific pesticide types as reported at baseline (fungicides, insecticides, etc.) were considered; however, due to concerns about adding eight variables to models based on small numbers of cases and their addition making little difference to the results, these models are not presented. Participants with missing data in any of the analysis variables were excluded. Odds ratios (ORs), 95% confidence intervals (95% CIs) and *P*-values were estimated. The joint Wald test was used to provide the overall *P*-value of variables with more than two categories. Statistical significance was taken at the 5% level.

The PIPAH study was granted ethical clearance by the National Research Ethics Service Committee of North West-Greater Manchester (reference 12/NW/0654).

RESULTS

Altogether, 5817 individuals responded at baseline, giving a response rate of 20% for the two recruitment waves. The 4818 remaining participants, at 5 years post baseline of the original 5817, were invited to complete the respiratory questionnaire. Of these 4818, 2578 (54%) responded. Table 1 shows baseline characteristics for all participants, with a mean age of 54.1 years; 98% male. The majority were never (63%) or ex-smokers (27%).

Table 2 illustrates the work characteristics of the *baseline population*, stratified by self-reported diagnosis. Participants had a long duration of farm residence (mean 36.7 years) and started living on a farm at an early age (median of 1 year of age, IQR 0–4). The majority still lived on a farm at baseline; 78% overall. Most respondents reported working with pesticides at some time (99%). In terms of self-reported (ever) exposures to a variety of pesticide types, the three commonest categories were herbicides (94%), fungicides (89%) and insecticides (89%).

The respiratory questionnaire *follow-up population* of 2578 participants were similar to the baseline population. Their mean age was 60.0 years (median 60.2 years, range 24–90) and 807 (34%) had ever smoked. The majority (2493, 97%) were male. In comparison to the previously reported [7] prevalence of asthma in this group (11%), levels of doctor-diagnosed chronic bronchitis (*n* = 23, 0.9%, 95% CI 0.6–1.3), COPD (*n* = 33, 1.3%, 95% CI 0.9–1.8) and HP (*n* = 9, 0.3%, 95% CI 0.2–0.7) were very low. The median age at diagnosis for chronic bronchitis was 35 years (range 4–76 years), COPD 61 years (5–77) and HP 42 years (30–70).

In contrast, self-reported respiratory symptoms were common. Nasal allergies were reported by 541 participants (21%, 95% CI 19–23), regular cough by 351 (14%, 95% CI 12–15), chest tightness ever by 329 (13%, 95% CI 11–14) and work-related chest tightness by 45 (1.7%, 95% CI 1.3–2.3).

Table 3 shows the multivariable logistic regression models for the binary presence or absence of doctor-diagnosed (i) chronic bronchitis, (ii) COPD and (iii) HP at follow-up. The analysis regarding chronic bronchitis needs to be interpreted with caution due to the small number of events, and the results may not be reliable. Adjusted for age, sex, smoking status and years spent working with pesticides, there was evidence that the odds of retired participants having chronic bronchitis were more than four times higher than those participants who had relatively low exposure to pesticides in the past year (OR 4.25, 95% CI 1.23–16.0).

Table 1. Personal characteristics at the baseline (2013–2017) of all participants, and those with chronic bronchitis, chronic obstructive pulmonary diseases and hypersensitivity pneumonitis

Characteristic	All	Chronic bronchitis	Chronic bronchitis only[a]	COPD[b]	COPD only[a,b]	HP
	N = 5817	*N* = 70	*N* = 34	*N* = 60	*N* = 37	*N* = 26
Age						
Mean (SD)	54.1 (12.4)	57.6 (9.8)	56.9 (10.2)	65.6 (9.0)	65.1 (7.7)	61.1 (12.2)
Missing, *n*	58	0	0	2	1	1
Gender						
Male, *n* (%)	5629 (98)	69 (99)	34 (100)	56 (98)	34 (97)	26 (100)
Missing, *n*	59	0	0	3	2	0
Smoking status						
Current, *n* (%)	480 (9)	5 (8)	3 (9)	19 (33)	12 (33)	1 (4)
Ex, *n* (%)	1458 (27)	26 (40)	15 (45)	32 (56)	20 (56)	7 (28)
Never, *n* (%)	3364 (63)	34 (52)	15 (45)	6 (11)	4 (11)	17 (68)
Missing, *n*	515	5	1	3	1	0
Pack years[c]						
Mean (SD)	16.0 (18.3)	23.9 (30.1)	23.4 (31.2)	39.1 (29.5)	38.3 (23.0)	29.9 (27.5)
Median (IQR)	10.0 (3.75–22.5)	14.5 (5–20)	15 (8–20)	30 (20–52.5)	35 (20–50)	18.75 (15–37.5)
Missing, *n*	563	6	2	4	2	3
N/A: Never-smoker, *n*	3364	34	15	6	4	17
Family history of asthma						
Yes, *n* (%)	914 (16)	20 (29)	7 (21)	10 (17)	5 (14)	3 (12)
Not reported, *n* (%)	4903 (84)	50 (71)	27 (79)	50 (83)	32 (86)	23 (88)
Age at diagnosis						
Mean (SD)	N/A	31.0 (18.7)	33.3 (16.5)	57.4 (14.6)	57.8 (12.5)	35.9 (13.2)
Median (IQR)		31 (12–45)	32 (25–45)	60 (55–63)	60 (55–63.5)	35 (25–43)
Missing, *n*		7	3	3	1	1

Abbreviations: COPD = chronic obstructive pulmonary disease; HP = hypersensitivity pneumonitis (formerly extrinsic allergic alveolitis, EAA); SD = standard deviation; IQR = interquartile range; N/A = not applicable.
[a]Only the stipulated diagnosis, excluding all other self-reported respiratory diagnoses within the group of asthma, COPD, CB and hypersensitivity pneumonitis (HP).
[b]COPD at baseline represents COPD and/or emphysema.
[c]Pack years = (number of cigarettes smoked a day/20) multiplied by the number of years smoked.

Table 2. Farming exposure characteristics at the baseline (2013–2017) of all participants and those with doctor-diagnosed chronic bronchitis, chronic obstructive pulmonary diseases and hypersensitivity pneumonitis

Characteristic	All	Chronic bronchitis	Chronic bronchitis only[a]	COPD[b]	COPD only[a,b]	HP
	N = 5817	*N* = 70	*N* = 34	*N* = 60	*N* = 37	*N* = 26
Years worked or lived on a farm						
Mean (SD)	36.7 (22.0)	30.6 (23.7)	31.1 (23.1)	36.9 (28.6)	42.1 (28.6)	49.5 (17.7)
Median (IQR)	40 (20–54)	34 (1–51)	38 (1–48)	48 (0–64)	54 (8–65)	47 (36–65)
Missing, *n*	183	4	1	10	8	2
Have you ever lived on a farm?						
Yes, *n* (%)	4455 (77)	45 (64)	23 (68)	34 (59)	21 (58)	25 (96)
Missing	63	0	0	2	1	0
How old were you when you first lived on a farm?[c]						
Mean (SD)	4.8 (9.0)	6.1 (10.5)	5.9 (8.6)	6.4 (8.7)	3.9 (5.7)	5.5 (9.6)
Median (IQR)	1 (0–4)	1 (0–9)	1 (0–12)	1 (1–11)	1 (1–5)	1 (0–10)
Missing, *n*	107	0	0	2	1	2
Are you still living on a farm?[c]						
Yes, *n* (%)	3463 (78)	35 (78)	20 (87)	25 (74)	16 (76)	20 (83)
Missing, *n*	83	0	0	2	1	1
Reported ever working with:[d]						
Pesticides, *n* (%)	5760 (99)	69 (99)	34 (100)	60 (100)	37 (100)	25 (96)
Fungicides, *n* (%)	5182 (89)	60 (86)	30 (88)	47 (78)	29 (78)	21 (81)
Insecticides, *n* (%)	5191 (89)	61 (87)	30 (88)	48 (80)	29 (78)	23 (88)
Animal insecticides, *n* (%)	1689 (39)	20 (29)	10 (29)	19 (32)	11 (29)	13 (50)
Plant growth regulators, *n* (%)	4597 (79)	55 (79)	29 (85)	39 (65)	25 (68)	20 (77)
Herbicides, *n* (%)	5493 (94)	65 (93)	34 (100)	52 (87)	33 (89)	24 (92)
Fumigants, *n* (%)	1899 (33%)	36 (51)	17 (50)	22 (37)	13 (35)	10 (38)
Wood preservers, *n* (%)	3076 (53)	25 (36)	15 (44)	25 (42)	16 (43)	12 (46)
Treated seed, *n* (%)	4671 (80)	53 (76)	28 (82)	35 (58)	23 (62)	21 (81)

Abbreviations: COPD = chronic obstructive pulmonary disease; HP = hypersensitivity pneumonitis (formerly extrinsic allergic alveolitis, EAA); SD = standard deviation; IQR = interquartile range; N/A = not applicable.
[a]Only the stipulated diagnosis, excluding all other self-reported respiratory diagnoses within the group of asthma, COPD, CB and Hypersensitivity pneumonitis (HP).
[b]COPD at baseline represents COPD and/or emphysema.
[c]N/A for those who never lived on a farm.
[d]Categories are not mutually exclusive.

The findings for COPD largely confirmed the expected association with increasing age (OR 1.06, 95% CI 1.01–1.11) and tobacco smoking (OR 5.61, 95% CI 2.39–13.2) when corrected for the exposure to pesticides. The odds of having COPD amongst retired members of the study was about three times higher than for those members of the study who had relatively low exposure to pesticides in the past year in the model adjusted for age, smoking status and years spent working with pesticides (OR 3.15, 95% CI 1.11–8.92).

Only nine participants reported a doctor's diagnosis of HP at follow-up, and the percentage of those who had ever smoked at baseline was relatively small (32%). The presence of HP was primarily influenced by increasing age (OR 1.15, 95% CI 1.06–1.25), and there was no evidence of an association with smoking status ($P > 0.10$). Although including unity, the estimate of odds of having HP for participants who had high exposure to pesticides in the past year was greater than for retired participants with no exposure to pesticides in the past year (OR 6.11, 95% CI 0.91–41.0, $P = 0.063$).

Table 4 illustrates a similar set of analyses for reported symptoms suggestive of nasal and respiratory problems. There were relatively limited effects of increasing age and sex or from the pesticide exposure variables. Nasal allergies were statistically significantly associated with workers who did not use pesticides in the past year compared to those with low use (OR 1.54, 95% CI 1.14–2.06). Work-related chest tightness, in contrast, was statistically significantly associated with high as opposed to low pesticide exposure in the past year (OR 2.68, 95% CI 1.28–5.60).

DISCUSSION

This study was able to collect further health data from a population of pesticide workers that had a significant exposure history. Whilst previous work on this cohort identified generally expected levels of doctor-diagnosed asthma [7], this paper identified generally very low levels of other doctor-diagnosed respiratory conditions.

Only 0.9% of the follow-up participants reported doctor-diagnosed chronic bronchitis, and the regression model was thus based on small numbers of events. It was interesting to note that retired participants were much more likely to report this condition than participants with low exposures to these agents in the

Table 3. Separate multivariable logistic regression models for doctor-diagnosed chronic bronchitis, COPD and hypersensitivity pneumonitis at follow-up in 2018, adjusted for age, sex, smoking status, hours and years worked with pesticides[a]

Model—chronic bronchitis *N* = 2354[b]	**Non-cases[c,d] *N* = 2333**	**Cases[d] *N* = 21**	**Odds ratio**	**95% CI**	***P*-value**
Age	59.9 (11.2)[e]	60.7 (10.7)[e]	0.97	0.92–1.03	0.324
Sex					
Male (reference)	2278	20	1.00		
Female	55	1	1.77	0.21–14.6	0.597
Smoking status					
Never smoked (ref)	1550	10	1.00		
Ever smoked	783	11	2.06	0.86–4.95	0.107
Total hours worked with pesticides in the last year					0.158[f]
Low (≤120 h; reference)	836	5	1.00		
High (>120 h)	802	6	1.14	0.34–3.84	0.828
Not used in past year (= 0)	357	3	1.36	0.31–5.89	0.684
Retired (= 0)	338	7	4.25	1.23–16.0	0.033
Years spent working with pesticides	27.6 (11.3)[e]	27.7 (10.3)[e]	1.01	0.96–1.05	0.790
Model—COPD *N* = 2365[b,g]	**Non-cases[c,d] *N* = 2333**	**Cases[d] *N* = 32**	**Odds ratio**	**95% CI**	***P*-value**
Age	59.9 (11.2)[e]	68.4 (7.66)[e]	1.06	1.01 –1.11	0.019
Smoking status					
Never smoked (ref)	1560	7	1.00		
Ever smoked	773	25	5.61	2.39–13.2	<0.001
Total hours worked with pesticides in the last year					0.126[f]
Low (≤120 h; reference)	837	6	1.00		
High (>120 h)	803	6	1.29	0.41–4.08	0.665
Not used in past year (= 0)	360	4	1.28	0.35–4.66	0.703
Retired (= 0)	333	16	3.15	1.11–8.92	0.031
Years spent working with pesticides	27.6 (11.3)[e]	28.2 (11.2)[e]	0.98	0.95–1.01	0.153
Model—Hypersensitivity Pneumonitis *N* = 1522[b,g]	**Non-cases[c,d] *N* = 1513**	**Cases[d] *N* = 9**	**Odds ratio**	**95% CI**	***P*-value**
Age	60.4 (11.8)[e]	70.0 (8.1)[e]	1.15	1.06–1.25	0.001
Smoking status					
Never smoked (ref)	983	7	1.00		
Ever smoked	530	2	0.40	0.08–1.97	0.260
Total hours worked with pesticides in the last year[h]					0.160[f]
Retired (reference)	347	2	1.00		
Not used in past year	362	2	2.05	0.28–15.2	0.481
High (>120 h)	804	5	6.11	0.91–41.0	0.063
Years spent working with pesticides	27.6 (11.3)[e]	29.4 (11.3)[e]	0.97	0.91–1.03	0.306

Abbreviations: COPD = chronic obstructive pulmonary disease; CI = confidence interval.
[a]Each variable is adjusted for all the other variables in the model.
[b]Number of individuals included in each model differ due to differences in the variables/categories included.
[c]Non-cases are all other participants without the specific diagnosis.
[d]Data are number of participants unless otherwise stated.
[e]Mean (standard deviation).
[f]Joint Wald test across all categories.
[g]There were no female cases, so sex was not included in the model because of collinearity.
[h]There were no cases in the 'Low' category so the 'Retired' category was the reference category and participants with 'low' total hours were excluded from the model.
Number of individuals reporting chronic bronchitis (*n* = 23), COPD (*n* = 33) and HP (*n* = 9) at follow-up. Smaller numbers in the models due to missing values in the predictors.

Table 4. Separate multivariable logistic regression models for various self-reported respiratory symptoms at follow-up in 2018, adjusted for age, sex, smoking status, hours and years worked with pesticides[a]

Model—Nasal allergies *N* = 2305[b]	**Non-cases**[c,d] *N* = 1804	**Cases**[d] *N* = 501	**Odds ratio**	**95% CI**	***P*-value**
Age	60.2 (11.3)[e]	58.4 (10.7)[e]	0.98	0.97–0.99	<0.001
Sex					
Male (reference)	1769	482	1.00		
Female	35	19	1.54	0.85–2.77	0.151
Smoking status					
Never smoked (ref)	1193	341	1.00		
Ever smoked	611	160	0.95	0.77–1.18	0.650
Total hours worked with pesticides in the last year					0.005
Low (≤120 h; reference)	655	171	1.00		
High (>120 h)	631	163	0.91	0.71–1.16	0.451
Not used in past year (= 0)	255	100	1.54	1.14–2.06	0.005
Retired (= 0)	263	67	1.27	0.90–1.80	0.179
Years spent working with pesticides	27.6 (11.3)[e]	27.1 (11.0)[e]	1.01	0.99–1.02	0.111

Morning cough *N* = 2313[b]	**Non-cases**[c,d] *N* = 1990	**Cases**[d] *N* = 323	**Odds ratio**	**95% CI**	***P*-value**
Age	59.8 (11.3)[e]	60.8 (10.3)[e]	1.00	0.98–1.01	0.525
Sex					
Male (reference)	1943	315	1.00		
Female	47	8	1.02	0.46–2.22	0.968
Smoking status					
Never smoked (ref)	1361	176	1.00		
Ever smoked	629	147	1.78	1.40–2.26	<0.001
Total hours worked with pesticides in the last year					0.328
Low (≤120 h; reference)	720	107	1.00		
High (>120 h)	694	103	1.00	0.74–1.34	0.983
Not used in past year (= 0)	295	58	1.33	0.94–1.90	0.110
Retired (= 0)	281	55	1.23	0.83–1.81	0.299
Years spent working with pesticides	27.4 (11.3)[e]	28.8 (11.4)[e]	1.01	1.00–1.02	0.064

Model—Chest tightness *N* = 2310[b]	**Non-cases**[c,d] *N* = 2004	**Cases**[d] *N* = 306	**Odds ratio**	**95% CI**	***P*-value**
Age	60.1 (11.2)[e]	58.8 (11.2)[e]	0.98	0.97–0.99	0.005
Sex					
Male (reference)	1957	298	1.00		
Female	47	8	0.92	0.42–2.01	0.835
Smoking status					
Never smoked (ref)	1353	180	1.00		
Ever smoked	651	126	1.49	1.16–1.91	0.002
Total hours worked with pesticides in the last year					0.020[f]
Low (≤120 h; reference)	735	92	1.00		
High (>120 h)	686	109	1.17	0.87–1.58	0.307
Not used in past year (= 0)	301	51	1.40	0.96–2.04	0.079
Retired (= 0)	282	54	1.87	1.25–2.81	0.002
Years spent working with pesticides	27.6 (11.2)[e]	26.9 (11.7)[e]	1.00	0.99–1.01	0.792

Model—Work-related chest tightness *N* = 2301[b,g]	**Non-cases**[c,d] *N* = 2257	**Cases**[d] *N* = 44	**Odds ratio**	**95% CI**	***P*-value**
Age	59.9 (11.1)[e]	53.7 (11.6)[e]	0.96	0.93–1.00	0.053
Smoking status					

Table 4. Continued

Model—Work-related chest tightness *N* = 2301[b,g]	**Non-cases[c,d] *N* = 2257**	**Cases[d] *N* = 44**	**Odds ratio**	**95% CI**	***P*-value**
Never smoked (ref)	1498	33	1.00		
Ever smoked	759	11	0.77	0.38–1.55	0.462
Total hours worked with pesticides in the last year					0.018[f]
Low (≤120 h; reference)	815	10	1.00		
High (>120 h)	766	29	2.68	1.28–5.60	0.009
Not used in past year (= 0)	353	3	0.75	0.21–2.76	0.669
Retired (= 0)	323	2	0.83	0.17–4.05	0.818
Years spent working with pesticides	27.6 (11.2)[e]	25.5 (12.6)[e]	1.01	0.97–1.05	0.627

Abbreviations: CI = confidence interval.
[a]Each variable is adjusted for all the other variables in the model.
[b]Number of individuals included in each model differ due to differences in the variables/categories included and missing data.
[c]Non-cases are all other participants without the specific diagnosis.
[d]Data are number of participants unless otherwise stated.
[e]Mean (standard deviation).
[f]Joint Wald test across all categories.
[g]There were no female cases, so sex was not included in the model because of collinearity.
Number of individuals reporting nasal allergies (n = 541), cough (n = 351), chest tightness (n = 329), and work-related chest tightness (n = 45). Smaller number in the models due to missing values in the predictors.

last 12 months. By comparison, global data [18] have reported a pooled median prevalence of 5.3% (95% CI 3.9–7.1) for a patient-reported diagnosis of chronic bronchitis; more than the identified prevalence.

Similarly, only 1% of follow-up participants reported doctor-diagnosed COPD, with increasing age and tobacco smoking as statistically significant predictor variables. A similar effect was seen in retired participants as for chronic bronchitis. UK data, based on an aggregate reported category of COPD, chronic bronchitis or emphysema for doctor-diagnosed COPD [19], noted overall median levels of 2.8% (95% CI 2.3–3.2) from a population of 7879 participants of the UK Household Longitudinal Survey and the Health Survey for England 2010. The figure of 2.8% is remarkably consistent with more recent primary care estimates [20] of an overall population prevalence of 2.57% (95% CI 2.55–2.60). Furthermore, when definite and probable cases of COPD were combined, a prevalence of 3.02% (95% CI 3.0–3.05) was identified in the total population, with higher levels in those aged 35 or older (median 5.38%) and in current or ex-smokers (median 6.46%). Higher levels of both COPD and chronic bronchitis in recently retired participants suggest that retirement may have occurred consequentially. There is also the important consideration of likely health worker effects when interpreting the follow-up data, with those developing more serious health problems more likely to not participate in comparison to those with no ill-health problems.

Only nine (0.3%) follow-up participants reported a doctor's diagnosis of HP, its presence primarily predicted by increasing age. Although, as anticipated, this was mostly in non-smokers, the small number of cases severely limits further assessment of this effect. Population-based estimates are more difficult to identify in comparable populations for many contributing reasons [21, 22]. Notwithstanding this, HP is evidently relatively uncommon [23–26] even in populations exposed to relevant causative agents.

We did not observe any dose–response relationships between reported exposures and doctor-diagnosed respiratory conditions. Small numbers of cases will have influenced the ability of this study to comment on this relationship but, with perhaps the exception of HP, which was of borderline statistical significance, there was no suggestion of an increasing risk of health effects with increasing exposures. These data were unable to confirm the findings of a selected recent set of studies in relation to potential linkages with pesticide exposure and a diagnosis of chronic bronchitis, airflow obstruction [27, 28] or COPD [29], although consistent with other studies that have not identified a link [30].

In contrast, reported respiratory symptoms (cough, chest tightness and wheeze) were generally common. Noteworthy was the statistically significant relationship between nasal allergies and chest tightness with exposure categories that imply ceasing pesticide work, maybe directly because of those symptoms. Work-related chest tightness, potentially suggestive of asthma or occupational asthma, however, was significantly associated with high pesticide exposure. The positive association found with work-related chest tightness (OR 2.68, 95% CI 1.28–5.60), but not with general chest tightness (OR 1.17, 95% CI 0.87–1.58), strengthens the specificity of the potential causal link between work exposure to pesticides and chest tightness. This reduces the likelihood that the association is due to confounding variables that could be linked to general chest tightness but are unrelated to work. Others have similarly identified relationships between reported respiratory symptoms and pesticide exposure with similar findings, including the comprehensive Lifelines Cohort Study [10].

This suggests in part that low levels of doctor-diagnosed conditions may be due to under diagnosis in a group of workers typically known to be difficult to reach and with low levels of access to health care [31].

The strengths of this approach are related to the large numbers of participating workers in the predefined PIPAH study population, who are based in real-world pesticide exposure situations, coupled with the contextual information recorded about this population. The respiratory survey achieved a good response rate of 54% and previous analysis of the same survey found little evidence of non-response bias [7].

There are multiple weaknesses to this approach previously discussed in detail [7], including recruitment biases, uncertainty of the exact number of the population from which the participants were drawn, diagnostic onset dates, and differences between this and the general population. This study used information on self-reported respiratory conditions only, with a lack of physiology measures to define airway obstruction and stratify its severity or grade. Furthermore, case numbers of doctor-diagnosed diseases were low, limiting inference about exposure effects. Particularly, the question relating to farmer's lung may have limited utility in this context given the low numbers of positive responses. Self-reported health outcomes may well also be both under- and over-reported, and further estimation of this weakness is not possible given the limited clinical data available. Attribution of exposures to pesticides and related chemicals was based on detailed self-reported job tasks only; no workplace measurements were taken. It was not possible to easily comment on the use or otherwise of personal protective equipment from the data available. Additionally, the study design does not permit any comment on the potential mechanisms of pesticide-related respiratory ill-health.

This study has confirmed low levels of self-reported doctor-diagnosed conditions in this group of pesticide users, but high levels of reported respiratory symptoms, at least suggesting under diagnosis. Those with symptoms generally were found in the retired or lower-exposed categories, suggesting at least behavioural responses to these, but work-related chest tightness, a possible marker of occupational asthma, was related to high current pesticide exposure.

Given the conflicting conclusions derived from recent studies in this area, further health characterization of such populations would help to identify relationships between specific pesticide (or related) exposures and ill-health, and equally importantly to understand how organic and biologically active exposures contribute to, or modify, the health response reported.

Key learning points

What is already known about this subject:

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Competing interests

None declared.

DATA AVAILABILITY

All data relevant to the study are included in the article. No further data are available.

Disclaimer

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