Farming, pesticide exposure and respiratory health: a cross-sectional study in Thailand

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ABSTRACT
Objective To assess the association of lung function and respiratory symptoms with farming, particularly pesticide use, in an agricultural province in Thailand.

Methods We undertook a cross-sectional survey of adults aged 40–65 in Nan province, Thailand, between May and August 2019. We randomly recruited 345 villagers and enriched the sample with 82 government employees. All participants performed post-bronchodilator spirometry and completed a questionnaire covering information on respiratory symptoms, farming activities, pesticide use and known risk factors for respiratory disease. Associations of respiratory outcomes with farming and pesticide exposures were examined by multivariable regression analysis.

Results The response rate was 94%. The prevalence of chronic airflow obstruction among villagers was 5.5%. Villagers had, on average, a lower percent predicted post-bronchodilator forced expiratory volume in one second/forced vital capacity (FEV1/FVC) than government employees (98.3% vs 100.3%; p=0.04). There was no evidence of association of lung function with farming activities, the use of specific herbicides (glyphosate and parquat), insecticides (organophosphates and pyrethroids) or fungicides. The exceptions were poultry farming, associated with chronic cough and an increase of FEV1/FVC, and atrazine, for which duration (p-trend <0.01), intensity (p-trend <0.01) and cumulative hours (p-trend=0.01) of use were all associated with higher FEV1/FVC in an exposure–response manner. Cumulative hours (~280 mL/hour), low duration (~270 mL/year) and intensity (~270 mL/hour/year) of atrazine use were associated with lower FVC.

Conclusions Chronic airflow obstruction is uncommon among villagers of an agricultural province in Nan, Thailand. Farming and pesticide use are unlikely to be major causes of respiratory problems there.

INTRODUCTION
Worldwide, more than a billion people—about a third of the global workforce—work on farms. Farmers are frequently exposed to organic and inorganic dusts and fumes, as well as pesticides, which may lead to respiratory tract inflammation and respiratory disease. Two systematic reviews of the literature on chronic respiratory disease in farmers have been published recently. Guillien et al reported that both chronic obstructive pulmonary disease (COPD) and airflow limitation associated with several farming activities (eg, livestock, crop and mixed farming). Similarly, Fontana et al reported that COPD is associated with several farm categories (ie, greenhouse, pesticides, dairy and multiple exposures). Both reviews suggested further epidemiological studies of different farm types and practices, specific agents and factors, particularly in crop farmers. Farming is a common occupation in low-income and middle-income countries (LMICs) and any adverse effects are likely to have a high impact on public health and economic growth. Yet in these reviews there were only six studies from LMICs (three in North Macedonia, one in China, one in Nigeria and one in India). Whether farming has a role in COPD remains unclear in developing countries. Thailand is one of the largest rice exporters in the world and 31% (11.6 of 37.9 million) of its working population is in the agricultural sector, accounting for 11% of gross domestic product. The poorer, lower 40% of the population, are more likely to work in agriculture. Due to the rapid development of intensive agriculture for commercialisation, Thailand is among the highest users of

Key messages

What is already known about this subject?
► Farm work, including the use of pesticides, has been associated with adverse respiratory health effects. Few studies, however, have used spirometry to examine the risks of chronic airflow obstruction in the context of agricultural work in low-income or middle-income countries.

What are the new findings?
► In a rural community in Thailand, chronic airflow obstruction was uncommon; as with other studies in developing countries, villagers had a low prevalence of smoking. Most farmers applied pesticides regularly but neither this nor other farming practices are likely to be a major cause of chronic respiratory problems in this setting.

How might this impact on policy or clinical practice in the foreseeable future?
► Agriculture plays a fundamental economic role in developing countries and the use of pesticides is crucial in modern farming practice. While the findings of this work are reassuring, health education and training in self-protection training for farming villagers remain important.
Occupational pesticide exposure is associated with chronic respiratory symptoms, chronic bronchitis and asthma, but data on the relationships between pesticide exposures and COPD and lung function impairment are limited. A recent systematic review reported tentative evidence that exposure to cholinesterase-inhibiting pesticides is associated with reduced forced expiratory volume in one second/forced vital capacity (FEV₁/FVC), perhaps reflecting their activity on the muscarinic cholinergic receptors, resulting in increased respiratory tract bronchial secretions and bronchoconstriction.

In order to assess the association of lung function and respiratory symptoms with farming, particularly pesticide use, we conducted a survey in Nan—one of the largest agricultural provinces in Thailand—which recently reported the highest number of chronic bronchitis, emphysema and COPD deaths (52.7 per 100 000) and hospital admission rates in the country. The published literature on farming and adverse respiratory health effects in Thailand is very limited and there has been no study in Nan province before.

METHODS

Study setting and population

We undertook a survey in Nan province, Thailand, between May and August 2019. This district was selected as, according to a recent census, 47% of its population were farmers. Based on Pothirat et al, a previous survey in Chiangmai province in which 34% of rural villagers aged over 40 were farmers, we calculated a sample size of 345 potential participants. We sampled using a cluster random method in three villages (villages no. 3, 11 and 13 in the Tha Wang Pha district, Nan province) from a pool of adults aged 40–65 years old in the provincial Public Health database and invited them to the study. Having surveyed the first two villages, we made a preliminary check of the data collected and found that the large majority of villagers (183 of 218 who participated in the study; 84.9%) reported ‘farming’ as their longest held jobs. To increase exposure contrast for the association analysis, we additionally sampled local government employees in Tha Wang Pha district (including school teachers, association analysis, we additionally sampled local government employees using the Student’s t-test for continuous variables and chi-square test or Fisher’s exact test (for n<5) for categorical variables, as appropriate. To assess the association of lung function (i.e., FEV₁/FVC and FEV₁/FVC) with farming and pesticide exposure, we used multivariable linear regression; when the dependent variable was respiratory symptoms, we used multivariable forms (https://opendatokit.org). In addition, participants had their height, weight, pulse rate, blood pressure and lung function measured.

Assessment of respiratory symptoms

We collected data on respiratory symptoms including chronic cough, chronic phlegm, dyspnoea and wheeze. Chronic cough was defined by cough on most days for at least 3 months per year. Similarly, chronic phlegm was defined by the production of sputum on most days for at least 3 months per year. Dyspnoea was defined as breathlessness at least when walking more slowly than people of the same age or having to stop walking due to shortness of breath, according to the modified Medical Research Council dyspnoea scale. Wheeze was defined as having had any whistling in the chest at any time in the last 12 months.

Assessment of lung function

We conducted spirometry on all participants using the ndd EasyOne spirometer (ndd Medizintechnik; Zurich, Switzerland). Participants were tested before and 20 min after 200 μg of salbutamol administered via a spacer. Each spirogram was reviewed and scored using the American Thoracic Society and European Respiratory Society criteria. Usable spirometry was defined as two or more acceptable trials, with FEV₁ and FVC repeatability within 200 mL. At the beginning of each day, the spirometer was calibrated using a 3 L syringe.

A post-bronchodilator FEV₁ to FVC ratio below the lower limit of normal (LLN) was considered chronic airflow obstruction, and an FVC less than the LLN was considered spirometric restriction. The LLNs were calculated using the Global Lung Initiative (GLI) 2012 equations for South East Asia, which were based on data from the region, including Thailand. Reversibility was defined as an increase of >12% (and 200 mL) of the pre-bronchodilator FEV₁.

Data analysis

Age, sex, socioeconomic status (household assets, education), body mass index (BMI) using a classification for Asian populations (underweight (<18.5 kg/m²); normal (18.5 to <23.0 kg/m²); overweight (23.0 to <25.0 kg/m²); obese level 1 (25.0 to <30.0 kg/m²) and obese level 2 (≥30.0 kg/m²)), smoking status, farming and pesticide exposure data were described. Farming exposure variables including years of living on a farm, farm size and types of crops were included in the analyses; farming practices comprised crop farming, livestock farming and pesticide spraying. Farming activities such as ploughing, harvesting, chemical protection of crops, fertiliser use and crop burning were analysed as potential risk factors. Pesticide exposure variables included mixing pesticides, and time of the last exposure to pesticide. Pesticide exposures were also classified by specific types of pesticide. An assessment of the level of pesticide exposure was estimated by (1) cumulative hours of exposure in a lifetime; (2) duration, as years of exposure; and (3) intensity, as estimated hours of exposure per year. Respiratory symptoms, spirometry data, both raw and percent predicted values were analysed.

We assumed that the data followed a normal distribution and analysed differences between villagers and government employees using the Student’s t-test for continuous variables and the χ² test or Fisher’s exact test (for n<5) for categorical variables, as appropriate. To assess the association of lung function (i.e., FEV₁/FVC and FEV₁/FVC) with farming and pesticide exposure, we used multivariable linear regression; when the dependent variable was respiratory symptoms, we used multivariable

Patient and public involvement

No patient involved.

Data collection

We used a structured questionnaire from the Burden of Obstructive Lung Disease (BOLD) study to obtain information on socioeconomic variables and respiratory health and symptoms. The BOLD questionnaire has been widely used across several countries, including LMICs in Asia. To assess farming and pesticide activities, practices and exposures, we developed a questionnaire appropriate for developing countries such as Thailand. This questionnaire covered (1) the farming environment and activities; (2) crops grown and animals raised; (3) pesticide use; and (4) crop burning (see details in the online supplemental material 1). This questionnaire contained photos of all pesticides available in the local marketplaces. All questionnaires were translated into Thai, piloted among 19 villagers in another subdistrict and applied using Open Data Kit (ODK) electronic

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logistic regression. All regression models were adjusted for age, sex and smoking status based on a priori knowledge. We additionally adjusted for subject group (villagers or government employees) to account for unmeasured confounders that may be characteristic of each group. Models with FVC and FEV1 as outcomes were further adjusted for height, and models with dyspnoea and wheeze were further adjusted for BMI.

Pesticide exposure–response relations were examined after categorisation of the distributions of lifetime cumulative hours, duration and intensity of exposure. The median number of each measure of exposure was used as the cut-off value. We analysed exposure–response effects comparing high and low levels of exposure by testing for trend (p-trend). Statistical significance was set at p<0.05. We performed all analyses using Stata V.16 (Stata, College Station, Texas, USA).

RESULTS

Demographic characteristics
Four hundred men and women (94% of those eligible) took part in the study and completed all questionnaires. Table 1 summarises some characteristics of the study population. Almost two-thirds had never smoked. Compared with the group of government employees, villagers were 3.4 years older (p<0.001), 3.3 cm shorter in men (p<0.001) and 2.3 cm shorter in women (p=0.03). Most villagers had only primary school education (68.5%), while most government employees had a university degree. Based on household assets ownership, villagers were worse off than government employees (p<0.001). Among the villagers, 86.6% reported farming as their longest-held occupation. There were significant differences in measures of pesticide exposure (ie, cumulative hours, duration (year) and intensity (hours/year)) between the two subject groups.

Respiratory symptoms and farming practice
After adjustment for age, sex, smoking and study subject, chronic cough was positively associated with poultry farming (OR=2.07, 95%CI 1.08 to 3.96). There were no associations between respiratory symptoms and other farming practices or pesticide use (table 2).

Lung function and farming
Among villagers, the prevalence of chronic airflow obstruction was 5.5% and the prevalence of restriction was 10.3% (table 3). We found no evidence of association of lung function with any of the considered farming exposure variables (ie, harvesting, threshing, ploughing, the application of fertilisers and the burning of crop-residues), except for rearing poultry, which was associated with a small increase in FEV1/FVC (table 4).

Lung function and pesticides
Lung function was not associated with the way farmers applied pesticides (online supplemental table S1). There were 304 regular pesticide sprayers (76% of all participants). Pesticides were classified into three main types: herbicides, insecticides and fungicides. Specifically, pesticide sprayers used glyphosate (91%), paraquat (69%), atrazine (13%), organophosphates (34%), pyrethroids (69%), mancozeb (17%) or pyraclostrobin (23%).

Table 5 is a summary of the associations between lifetime cumulative hours of use for each pesticide and spirometric parameters. Online supplemental tables S2 and S3 show the relationships between all spirometric parameters and duration (year) and intensity (hours/year) of pesticide exposure. There were no significant associations between the use of specific herbicides (glyphosate and paraquat), insecticides (organophosphates and pyrethroids) or fungicides (mancozeb and pyraclostrobin) and lung function. The exception was atrazine, for which cumulative hours (p-trend <0.01) of use were all associated with higher FEV1/FVC in an exposure–response relationship. Low duration, low cumulative hours (p-trend=0.01), duration (p-trend <0.01) and intensity (p-trend <0.01) of use were all associated with higher FEV1/FVC in an exposure–response relationship. Low duration, low intensity and low cumulative hours of atrazine use were associated with lower FVC.
spirographic restriction were higher compared with the results from post-bronchodilator spirometry (online supplemental table S4). However, after adjustment for confounding factors, multi-variability analyses showed that the relationships between farming and pesticide variables and pre-bronchodilator spirometry were similar to those using post-bronchodilator values (online supplemental tables S5 to S9).

**DISCUSSION**

In this community-based survey in Nan, an agricultural province in northern Thailand, we found that chronic airflow obstruction was uncommon, suggesting that farming and pesticide use are unlikely to be a major cause of respiratory problems there.

In this study, villagers (86.6% of whom defined themselves as farmers) had a low prevalence of chronic respiratory symptoms and chronic airflow obstruction, which was no higher than would be expected in a healthy population. This figure is at the lower end of those reported from previous studies of the association between farming and COPD, where the prevalence of airflow obstruction varied between 3% and 68%. A similar study in Thailand reported a similar prevalence of COPD (5.5%) among adult farmers. The prevalence of COPD is generally low (4.5%–9.4%) in South East Asians, perhaps reflecting the low smoking prevalence in these populations. Moreover, farming in Nan province is mainly crop farming conducted in open fields. A cross-sectional survey in France found that only 2.9% of crop farmers had COPD, a figure much lower than those from other studies in European farmers mainly working on livestock farms where the reported COPD prevalence ranged between 10.7% and 30.2%. It is also interesting that our findings suggest a relatively high prevalence of a restrictive spirometric pattern (10.3%) among villagers. Currently, the determinants of restrictive spirometry pattern remain poorly understood; explanations might include genetic

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**Table 2** Respiratory symptoms and farming practices

| Farming practice (n=400) | Chronic cough (n=43) | Chronic phlegm (n=28) | Dyspnoea (n=9) | Wheeze (n=24) |
|--------------------------|----------------------|-----------------------|---------------|---------------|
|                          | n OR 95% CI          | n OR 95% CI           | n OR 95% CI   | n OR 95% CI   |
| Crop farming             |                      |                       |               |               |
| No (n=111)               | 11 ref               | 6 ref                 | 1 ref         | 7 ref         |
| Yes (n=289)              | 32 0.93 0.42 to 2.09 | 22 1.11 0.4 to 3.1    | 8 3.44 0.24 to 48.92 | 17 0.83 0.3 to 2.3 |
| Poultry farming          |                      |                       |               |               |
| No (n=240)               | 19 ref               | 16 ref                | 4 ref         | 13 ref        |
| Yes (n=160)              | 24 2.07* 1.08 to 3.96 | 12 1.11 0.51 to 2.43  | 5 2.72 0.53 to 14.05 | 11 1.3 0.56 to 3.01 |
| Pesticide spraying       |                      |                       |               |               |
| No (n=96)                | 8 ref                | 5 ref                 | 0 ref         | 4 ref         |
| Yes (n=304)              | 35 1.22 0.45 to 3.32 | 23 0.9 0.27 to 3.04   | 9 – –         | 20 1.77 0.44 to 7.22 |
| Herbicide                |                      |                       |               |               |
| No (n=103)               | 8 ref                | 5 ref                 | 0 ref         | 5 ref         |
| Yes (n=297)              | 35 1.43 0.53 to 3.81 | 23 1.1 0.34 to 3.63   | 9 – –         | 19 1.3 0.37 to 4.61 |
| Insecticide              |                      |                       |               |               |
| No (n=123)               | 11 ref               | 6 ref                 | 2 ref         | 4 ref         |
| Yes (n=277)              | 32 1.16 0.48 to 2.79 | 22 1.17 0.39 to 3.53  | 7 1.13 0.16 to 8.1 | 20 3.14 0.78 to 12.65 |
| Fungicide                |                      |                       |               |               |
| No (n=242)               | 21 ref               | 11 ref                | 5 ref         | 9 ref         |
| Yes (n=158)              | 22 1.53 0.77 to 3.05 | 17 2.27 0.99 to 5.23  | 4 1.8 0.36 to 8.87 | 15 3.02 1.18 to 7.74 |

Chronic cough and chronic phlegm odd ratios (OR) and 95% CIs were calculated by using a multivariable regression model adjusted for age, sex, smoking status and study subject (villagers vs government employees).

Dyspnoea and wheeze odd ratios (OR) and 95% CIs were calculated by using a multivariable regression model adjusted for age, sex, BMI, smoking status and study subject (villagers vs government employees).

*p<0.05.

BMI, body mass index; ref, reference.

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**Table 3** Percent predicted values of post-bronchodilator spirometric parameters and prevalence of abnormal spirometric patterns among study participants

| Spirometric parameter | Villagers (n=290) | Government employees (n=68) | P value* |
|-----------------------|-------------------|-----------------------------|----------|
|                       | Mean SD           | Mean SD                     |          |
| FEV1/FVC (% predicted) | 98.34 7.51        | 100.32 3.99                 | 0.04     |
| FVC (% predicted)     | 92.88 13.28       | 90.93 11.83                 | 0.26     |
| FEV1 (% predicted)    | 91.41 14.04       | 90.93 11.91                 | 0.80     |
| Spirometric patterns  |                   |                             |          |
| n Percent             |                   |                             |          |
| Chronic airflow obstruction | 16 5.5% | 0 0.0% | 0.05 |
| Spirometric restriction | 30 10.3%       | 9 13.0%                     | 0.51     |

Chronic airflow obstruction: FEV1/FVC<LLN; spirometric restriction: FVC<LLN.

*Analysing differences between subject groups by Student’s t-test.

†Analysing differences between subject groups by χ² test or Fisher’s exact test (for n<5).

FEV1, forced expiratory volume in one second; FVC, forced vital capacity; LLN, lower limit of normal based on GLI2012 reference equations.
Workplace factors or some adverse early life exposures impacting on childhood development.\textsuperscript{25}

We found no association of organic dust exposure variables, including harvesting and threshing cereals, with significant changes in spirometry, although we found an association between poultry farming and chronic cough. Our findings are in agreement with a recent nationwide study in Denmark which indicated no association of cumulative occupational organic dust exposure and an increased risk of COPD.\textsuperscript{26} However, we did find an association between rearing poultry and a small increase in FEV\textsubscript{1}/FVC with no significant change of FVC, whereas another recent study in the USA concluded that there was no association between raising animals, including poultry, and COPD.\textsuperscript{27} The apparently contradictory finding from our study might have occurred by chance or in reflection of a ‘healthy worker’ effect.\textsuperscript{28} For inorganic soil dust exposure, we found no association between ploughing and lung function. One explanation might be due to open air farmland with high humidity, which is typical in the study region and results in relatively low exposure intensities.\textsuperscript{29}

| Table 4  | Post-bronchodilator spirometric parameters and farming variables |
|----------|---------------------------------------------------------------|
| **Farming variables (n=358)** | **FEV\textsubscript{1}/FVC (%)** | **FVC (L)** | **FEV\textsubscript{1} (L)** |
| n | β | 95% CI | β | 95% CI | β | 95% CI |
| Years of living on a farm | | | | | | | |
| Never | 32 | ref | ref | ref | |
| <33 years | 162 | −0.48 | −2.88 to 1.93 | 0.05 | −0.12 to 0.22 | 0.03 | −0.12 to 0.18 |
| ≥33 years | 164 | −0.21 | −2.75 to 2.33 | 0.04 | −0.14 to 0.22 | 0.02 | −0.13 to 0.18 |
| Farmland size | | | | | | | |
| <18.5 rai (7.3 acre) | 199 | ref | ref | ref | |
| ≥18.5 rai (7.3 acre) | 159 | 0.57 | −0.79 to 1.93 | 0.02 | −0.07 to 0.12 | 0.04 | −0.05 to 0.12 |
| Growing rice | | | | | | | |
| No | 148 | ref | ref | ref | |
| Yes | 210 | 0.64 | −0.62 to 1.91 | 0.02 | −0.07 to 0.11 | 0.04 | −0.03 to 0.12 |
| Growing maize/corn | | | | | | | |
| No | 175 | ref | ref | ref | |
| Yes | 183 | 0 | −1.3 to 1.3 | −0.05 | −0.15 to 0.04 | −0.05 | −0.13 to 0.03 |
| Growing longan | | | | | | | |
| No | 90 | ref | ref | ref | |
| Yes | 268 | 1.07 | −0.46 to 2.59 | 0.03 | −0.08 to 0.14 | 0.06 | −0.03 to 0.15 |
| Keeping poultry | | | | | | | |
| No | 216 | ref | ref | ref | |
| Yes | 142 | 1.38* | 0.17 to 2.59 | −0.02 | −0.11 to 0.06 | 0.01 | −0.06 to 0.09 |
| Harvesting cereal | | | | | | | |
| No | 167 | ref | ref | ref | |
| Yes | 191 | 1.15 | −0.43 to 2.73 | 0 | −0.12 to 0.11 | 0.03 | −0.06 to 0.13 |
| Threshing cereal | | | | | | | |
| No | 284 | ref | ref | ref | |
| Yes | 74 | 1.77 | −0.16 to 3.69 | −0.02 | −0.15 to 0.12 | 0.03 | −0.08 to 0.15 |
| Ploughing | | | | | | | |
| No | 189 | ref | ref | ref | |
| Yes | 169 | 0.36 | −0.96 to 1.67 | −0.05 | −0.14 to 0.05 | −0.02 | −0.1 to 0.06 |
| Applying natural fertiliser | | | | | | | |
| No | 130 | ref | ref | ref | |
| Yes | 228 | 0.4 | −0.89 to 1.68 | 0.06 | −0.03 to 0.15 | 0.07 | −0.01 to 0.14 |
| Applying chemical fertiliser | | | | | | | |
| No | 94 | ref | ref | ref | |
| Yes | 264 | 0.11 | −1.41 to 1.63 | 0.03 | −0.07 to 0.14 | 0.05 | −0.04 to 0.14 |
| Burning crop-residue smoke exposure | | | | | | | |
| No | 282 | ref | ref | ref | |
| Yes | 76 | 0.73 | −0.78 to 2.23 | 0.02 | −0.09 to 0.13 | 0.03 | −0.06 to 0.12 |
| Converting an arable land by burning | | | | | | | |
| No | 228 | ref | ref | ref | |
| Yes | 130 | 1.2 | −0.05 to 2.44 | 0 | −0.09 to 0.09 | 0.03 | −0.04 to 0.11 |

FEV\textsubscript{1}/FVC ratio coefficients (β) and 95% CIs were calculated by using a multivariable regression model adjusted for age, sex, smoking status and study subject (villagers vs government employees).

FVC and FEV\textsubscript{1} coefficients (β) and 95% CIs were calculated by using a multivariable regression model adjusted for age, height, sex, smoking status and study subject (villagers vs government employees).

*p<0.05.

FEV\textsubscript{1}, forced expiratory volume in one second; FVC, forced vital capacity; ref, reference representing an unexposed group of each variable.
a result of crop-residue burning, has given rise to widespread concern over its health consequences. Studies in India found a decline in local subjects’ lung function parameters during the period of intense agricultural burning\(^30\)\(^31\); in contrast, we found no such association among villagers in Nan. These differences might be explained by our focus on the long-term exposure effect of burning exposures, while others focused on short-term changes. We found no significant associations between the use of fertilisers and lung function.

We found no associations between respiratory symptoms and spraying pesticides. These findings are in contrast with the Lifelines Cohort study in the Netherlands, which reported that high occupational exposure to pesticides increases the odds of all respiratory symptoms.\(^10\) Further, a study similar to ours of Ethiopian farmers found a significant association between applying pesticides and reductions in both FEV\(_1\) and FEV\(_1\)/FVC.\(^33\) Around half of the participants in that study were employed in greenhouse farming with daily and high intensities of pesticide exposure, while all villagers in our study worked on open farms.

As in a previous meta-analysis,\(^10\) we found no significant association of paraquat exposure with FEV\(_1\)/FVC. An explanation is the low volatility of paraquat whereby the risk of damage, mainly via an inhalation route, is low.\(^34\) Nor did we find an association between glyphosate exposure and reduction in lung function. There were significant associations of atrazine exposure (duration, intensity and cumulative lifetime hours) and a higher FEV\(_1\)/FVC consistent with a lower FVC; these associations could reflect early lung restriction. To the best of our knowledge, there are no previous reports of such an association. In the USA, a study of male sprayers reported significant relationships between wheezing (no measurement of lung function) and both glyphosate and atrazine exposures.\(^35\) Organophosphate and pyrethroid were common insecticides used by farmers in Nan. While we found that participants with higher cumulative exposures to

### Table 5  Post-bronchodilator spirometric parameters by lifetime cumulative hours of pesticide exposure classified by pesticide type

| Cumulative exposure (total hours in lifetime) (n=358) | n  | FEV\(_1\)/FVC (%) | FVC (L) | FEV\(_1\) (L) |
|-----------------------------------------------|----|------------------|---------|--------------|
|                                               |    | β                | 95% CI  | β             | 95% CI        | β                  | 95% CI         |
| Herbicide                                     |    |                 |         |               |               |                   |                 |
| Glyphosate                                    |    |                 |         |               |               |                   |                 |
| Unexposed                                     | 108 | ref              | ref     | ref           | ref           | ref               | ref            |
| <240 hours                                    | 117 | −0.06            | −1.71 to 1.59 | 0.06          | −0.06 to 0.17 | 0.05             | −0.05 to 0.15  |
| ≥240 hours                                    | 133 | 0.44             | −1.23 to 2.12 | −0.05         | −0.17 to 0.07 | −0.01            | −0.11 to 0.09  |
| Paraquat                                      |    |                 |         |               |               |                   |                 |
| Unexposed                                     | 172 | ref              | ref     | ref           | ref           | ref               | ref            |
| <240 hours                                    | 83  | 0.3              | −1.27 to 1.86 | 0.01          | −0.1 to 0.12  | 0.01             | −0.08 to 0.11  |
| ≥240 hours                                    | 103 | −0.75            | −2.27 to 0.77 | 0             | −0.11 to 0.1  | 0                | −0.1 to 0.09   |
| Atrazine                                      |    |                 |         |               |               |                   |                 |
| Unexposed                                     | 319 | ref†             | ref‡    | ref           | ref           | ref               | ref            |
| <240 hours                                    | 19  | 2.91*            | 0.26 to 5.56 | −0.28†        | −0.46 to −0.09 | −0.15            | −0.32 to 0.01  |
| ≥240 hours                                    | 20  | 3.13*            | 0.49 to 5.78 | −0.02         | −0.21 to 0.17 | 0.08             | −0.09 to 0.24  |
| Insecticide                                    |    |                 |         |               |               |                   |                 |
| Organophosphate                               |    |                 |         |               |               |                   |                 |
| Unexposed                                     | 265 | ref              | ref     | ref           | ref           | ref               | ref            |
| <144 hours                                    | 44  | 0.7              | −1.15 to 2.56 | 0.01          | −0.12 to 0.14 | 0.06             | −0.06 to 0.17  |
| ≥144 hours                                    | 49  | −0.87            | −2.64 to 0.9  | −0.04         | −0.16 to 0.09  | −0.04            | −0.15 to 0.07  |
| Pyrethroid                                    |    |                 |         |               |               |                   |                 |
| Unexposed                                     | 165 | ref              | ref     | ref           | ref           | ref               | ref            |
| <128 hours                                    | 98  | −0.04            | −1.6 to 1.53 | −0.02         | −0.13 to 0.09  | −0.03            | −0.12 to 0.07  |
| ≥128 hours                                    | 95  | 1.17             | −0.42 to 2.76 | −0.07         | −0.18 to 0.05  | −0.03            | −0.13 to 0.07  |
| Fungicide                                     |    |                 |         |               |               |                   |                 |
| Mancozeb                                      |    |                 |         |               |               |                   |                 |
| Unexposed                                     | 313 | ref              | ref     | ref           | ref           | ref               | ref            |
| <120 hours                                    | 18  | −0.06            | −2.83 to 2.7  | −0.03         | −2.78 to 2.72  | 0.06             | −0.1 to 0.23   |
| ≥120 hours                                    | 27  | −1.14            | −3.41 to 1.14 | −1.23         | −3.5 to 1.03   | 0.06             | −0.08 to 0.19  |
| Pyraclostrobin                                |    |                 |         |               |               |                   |                 |
| Unexposed                                     | 299 | ref              | ref     | ref           | ref           | ref               | ref            |
| <24 hours                                     | 27  | −0.09            | −2.37 to 2.2  | 0.01          | −2.27 to 2.28  | 0.04             | −0.1 to 0.18   |
| ≥24 hours                                     | 32  | −0.02            | −2.12 to 2.08 | 0.08          | −2.01 to 2.17  | 0.07             | −0.06 to 0.2   |

FEV\(_1\)/FVC ratio coefficients (β) and 95% CIs were calculated by using a multivariable regression model adjusted for age, sex, smoking status and study subject (villagers vs government employees). FVC and FEV\(_1\) coefficients (β) and 95% CIs were calculated by using a multivariable regression model adjusted for age, height, sex, smoking status and study subject (villagers vs government employees).

\(*p<0.05.\)

\(†p<0.01.\)

\(‡p\)-trend<0.05.

FEV\(_1\), forced expiratory volume in one second; FVC, forced vital capacity; ref, reference.
organophosphates had lower values of FEV/FVC, FVC and FEV₁, these were not statistically different from those of non-exposed participants. This is in contrast with a study in Uganda farmers, which reported a significant association between lower FEV₁ and high exposure to organophosphate and carbamate. 36 That, however, was a 'panel' study with individual comparison across seasons and pesticide exposure data based on biological monitoring. We found weak exposure–response associations of pyrethroid exposure (intensity and cumulative hours) with an increase in FEV₁/FVC but a decrease in FVC, despite no statistical significance. A study in Canada reported an association between pyrethroid exposure and higher FEV₁/FVC and lower FVC. 37 Nan sprayers mainly used mancozeb and pyraclostrobin as fungicides of choice. A recent meta-analysis included articles reporting an association of unspecified fungicide exposures with obstructive lung disease 38; our study did not replicate these findings.

Our study has several strengths. First, the response rate was high compared with a range between 42% and 92% in previous similar cross-sectional studies included in recent systematic reviews. 39,40 This was achieved in part because in the study villages, the local public health volunteer system helped our research team to communicate with eligible participants before and during the fieldwork. Second, the study questionnaire focusing on farming and pesticide use considered the local context, including local crops and best-selling pesticides, so that the farming exposure data reflected local participants’ exposures. Although this questionnaire was not formally validated, it was piloted in similar villagers outside the sampling area before its use in this study. Moreover, this study has filled a gap in that most previous studies did not examine associations with specific farming activities and types of pesticides. Third, the study had very few missing data due to the use of an electronic data collection system. Fourth, we undertook high-quality post-bronchodilator spirometry; the majority of previous studies identified abnormalities of respiratory outcomes only from either self-reported questionnaires or pre-bronchodilator spirometry. 41-43

A limitation of this cross-sectional study is its inability to assess the direction of any potentially causal relationship. Furthermore, the self-reported information might be open to recall bias. Exposure misclassification might have occurred and, if at random, would bias the study findings towards the null. National data indicated that farmers in Tha Wang Pha, Nan province represented about half of the adult population. However, when collecting the data from the cluster randomly sampled villagers, we found that the true figure was much higher. To increase exposure contrast (ie, to avoid having only farmers), we enriched our sample with government employees. To limit the potential for selection bias due to this sampling approach, we adjusted our analyses for study subject. Also, we were unable to measure quantitatively individual exposures to pesticides, but we estimated cumulative metrics that allowed us to test for exposure–response trends. We calculated exposure–response relationships based on job titles and length and frequency of exposures, although these may not accurately reflect true ‘doses’ of each farming and pesticide variable. The lack of evidence of association between farming practices or pesticide exposures and spirometric parameters might be due to a healthy worker effect, as previously found in a recent large population-based study where only by analysing lifetime job-histories agriculture-related jobs emerged at increased COPD risk 39 whereby farmers affected by farming practices and/or pesticides would have quit farming and only healthier farmers would stay in the job, work longer and accept riskier farming tasks. In this study, having conducted around a hundred tests increased the probability of finding false positives, perhaps an explanation for the positive relationship between rearing poultry and FEV₁/FVC we report.

Although we found no evidence of increased risk of abnormal respiratory outcomes with farming, particularly pesticide exposures, it does not necessarily mean that such exposures have no serious effects on other aspects of health. There is growing evidence, for example, examining the associations of pesticide exposures and health effects such as cancer, reproductive and nervous system abnormalities. 40

In conclusion, chronic airflow obstruction was uncommon among villagers in Nan, Thailand. A high proportion of Nan farmers were pesticide applicators but farming and pesticide use seem unlikely to be a major cause of respiratory problems in this setting.

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