REVIEW ARTICLE

A Systematic Review of Association between Pesticide Exposure and Respiratory Outcomes among Farmers and Farmworkers

Ratana Sapbamrer, Mathuramat Seesen

Department of Community Medicine, Faculty of Medicine, Chiang Mai University, 110, Inthavaroros Road, Sri Phum Subdistrict, Muang District, Chiang Mai, 50200 Thailand

ABSTRACT

This review paper aimed to analyze scientific evidence and provide an overview of the relationship of pesticide exposure with respiratory outcomes among farmers and farmworkers. It also synthesized the association of exposure to specific pesticides and other factors with respiratory outcomes. Articles published in PubMed, Scopus, and ScienceDirect databases from 1991 to 2018 were reviewed and the scientific evidence was evaluated. Forty-five articles were selected for synthesis. Twenty-nine pesticides revealed an association with respiratory diseases and 49 pesticides with respiratory symptoms. In addition, 14 pesticides had an association with both respiratory diseases and symptoms (seven for herbicides, six for insecticides, and one for fungicide). Although the evidence from these reviewed studies suggested an association between pesticide exposure and respiratory outcomes among farmers and farmworkers, several limitations from the studies were found. Toward a better quality for further research, prospective study, standardized tools for exposure and outcome assessment, appropriate sample size and sampling method, and controlled confounding factors, should be thoroughly considered.

Keywords: Pesticide; Insecticide; Herbicide; Respiratory; Farmer

Corresponding Author:
Ratana Sapbamrer, PhD
Email: lekratana56@yahoo.com, lekratana56@gmail.com
Tel: +6653935472

INTRODUCTION

Pesticides, including herbicides, insecticides, fungicides, and others, are commonly used worldwide to control pests in agriculture. Although pesticides provide many benefits to farmers, such as an increasing productivity and protection of crop yields, they can pose a potential risk to human health both in acute and chronic effects. Exposure to pesticides may contribute to several organ disorders, including respiratory disorders (1). Farmers and farmworkers have been known as high risk groups exposed to pesticides because they encounter pesticides from both occupational and environmental exposure. In addition, some studies suggested that an increased prevalence of respiratory disorders have been found in specific work tasks, such as spraying and mixing of pesticides (2).

Many epidemiological studies have shown that respiratory diseases, including asthma and chronic bronchitis, were associated with pesticide exposure (3-8). Asthma is the most common respiratory disorder, and studies suggest that pesticide exposure contributes to allergic asthma more than non-allergic asthma (3-5). Available studies on the effects on lung function measured by spirometry test were also found to have a reduction in forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC, forced expiratory flow 25-75% ($FEF_{25-75\%}$), and PEFR (peak expiratory flow rate) as a result of pesticide exposure (6-8). Several studies investigated respiratory symptoms caused by pesticide exposure (8-11). The relevant respiratory symptoms were wheezing, coughing, phlegm, breathlessness, chest pain, dyspnea, irritation to throat, and nasal irritation. In addition, types of pesticides used, types of farming, tasks, time of exposure, living area, and gender were the contributory factors affecting pesticide exposure and respiratory outcomes (2,9,12). Although available studies have shown the factors contributing to respiratory health, the scientific data available are limited and inconsistent. Thus, the aim of this review was to analyze scientific evidence and provide an overview of the relationships of pesticide exposure with respiratory outcomes among farmers and farmworkers. This review also synthesizes the association of exposure to specific pesticides and other confounding factors with respiratory outcomes.

MATERIALS AND METHODS

Search strategy

The objective of this review was to collect all articles published regarding effects of pesticide exposure on respiratory outcomes among farmers and farmworkers. This paper was divided into three sections. Section 1: Comparison of respiratory outcomes between an exposed pesticide population and an unexposed pesticide population aimed to review respiratory diseases, lung function, and respiratory symptoms between the exposed pesticide population and unexposed pesticide population. Section 2: Association of exposure to specific pesticides with respiratory outcomes aimed to review scientific evidence for exposure to specific pesticides contributing to respiratory outcomes. Section 3: Association of other factors with respiratory outcomes aimed to review scientific evidence for other factors contributing to respiratory outcomes. All published articles were searched by using PubMed, Scopus, and ScienceDirect Databases. The following keywords: (“pesticide” OR “herbicide” OR “insecticide” OR “fungicide”), AND (“respiratory symptom” OR “respiratory disease” OR “lung function” OR “pulmonary” OR “asthma” OR “bronchitis” OR “wheeze” OR “dyspnea”), AND (“farmer” OR “farmworker”) were searched from 1991-2018. A systematic review of Mamane et al. (2015) and a review of Ye et al.(2013) was also considered for completeness (13,14).

Inclusion criteria

The inclusion criteria were as follows: (a) original and full-text article; (b) written in English; (c) published from 1991-2018; (d) published in PubMed, Scopus, or ScienceDirect Databases; (e) assessed respiratory outcomes such as respiratory diseases, lung function (spirometry); or respiratory symptoms; (f) conducted with cross-sectional study, cohort study, or case-control study; and (g) conducted in farmers or farmworkers. First, the articles were searched through databases by the determined keywords (n = 4,123). Second, the title and abstract were reviewed (n = 166). Third, a full-text of each article was thoroughly reviewed (n = 73). Fourth, eligible articles were selected and summarized in this review (n = 45). The 45 selected articles were presented and summarized into three sections, including Section 1: Comparison of respiratory outcomes between an exposed pesticide population and an unexposed pesticide population (n = 16); Section 2: Association of exposure to pesticides with respiratory outcomes (n = 14); and Section 3: Association of other factors with respiratory outcomes (n = 19) (Figure 1).

Respiratory outcomes were defined as respiratory diseases, lung function, and respiratory symptoms. Respiratory diseases were defined as asthma and chronic bronchitis. Lung function was defined as spirometry testing, consisting of forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC, forced expiratory flow 25-75% ($FEF_{25-75\%}$), and peak expiratory flow rate (PEFR). Respiratory symptoms were defined as wheezing, coughing, breathlessness, chest pain/tightness, phlegm, dyspnea, and irritation to throat. Finally, the selected articles were independently evaluated by three reviewers for the quality of articles by using the STROBE Statement checklist. We assessed only the methodology section which had nine items for a full-text article. The quality of article was categorized as low (L, 0-3 scores), moderate (M, 4-6 scores), and high (H, 7-9 scores). Each article was summarized and the outcomes, study site, study design, study population, main findings, and adjusted /confounding variables were presented.

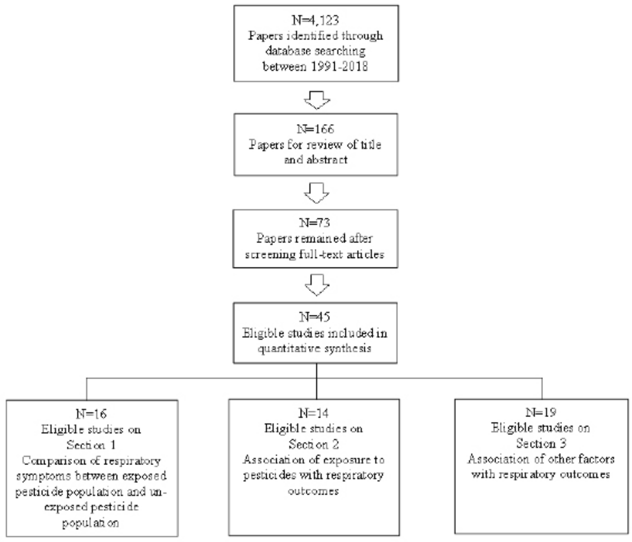

Figure 1: Flow chart of study selection

RESULTS AND DISCUSSIONS

Section 1: Comparison of Respiratory Outcomes Between Exposed Pesticide Population and Unexposed Pesticide Population

Sixteen articles compared respiratory outcomes between exposed pesticide population and unexposed pesticide population, three on respiratory diseases, twelve on lung function, and six on respiratory symptoms.

Respiratory diseases

A comparison of respiratory diseases between exposed pesticide population and unexposed pesticide population was presented in Table 1. The study designs of all articles were cross-sectional (n=3).

Asthma: A study by Eduard et al. (2004) found that farmers had asthma less often than the general population both in atopic asthma (OR=0.33, 95%CI=015-0.69) and non-atopic asthma (OR=0.60, 95%CI=0.39-0.93) (15). In contrast, two studies found no difference between the exposed pesticide and unexposed pesticides group (16,17).

Chronic bronchitis: A study by Dalphin et al. (1998) found that dairy farmers had a significantly higher prevalence of chronic bronchitis than the unexposed group (OR=11.8, 95%CI=1.4-97.1) (16).

Lung function

Comparison of spirometry testing between exposed pesticide population and unexposed pesticide

Table I: Comparison of respiratory diseases between exposed pesticide population and un-exposed pesticide population

Outcomes	Country	Design	Study population	Main findings	Adjusted / Confounding variables	Reference
Asthma	Norway	CS[a,c]	- Farming population (2,106) - General population (1,078)	Farming population < General population -Atopic asthma (OR=0.33, 95%CI=0.15-0.69) -Non-atopic asthma (OR=0.60, 95%CI=0.39-0.93)	Age, Gender, Smoking status	15
	France	CS[a,c]	- Dairy farmers (265) - Un-exposed group (149)	Dairy farmers ≈ Un-exposed group -Asthma (self-reported)-ever (OR=2, 95%CI=0.6-6.4) -Asthma (confirmed by a doctor)-ever (OR=2.3, 95%CI=0.7-7.8) -Attack of asthma (last year) (OR=0.7, 95%CI=0.1-4.7)	Age, Gender, Smoking status	16
	Europe region	CS[a,b,c]	- Exposed pesticides workers (248) - Un-exposed workers (231)	Exposed pesticides workers ≈ Un-exposed workers -Asthma diagnosis (OR=0.41, 95%CI=0.15-1.11) -Asthma attack (OR=0.52, 95%CI=0.12-2.25) -Asthma medication (OR=0.79, 95%CI=0.25-2.53)	Age, Gender, Residence, Education level, Smoking status	17
Chronic bronchitis	France	CS[a,c]	- Dairy farmers (265) - Un-exposed group (149)	Dairy farmers > Un-exposed group (OR=11.8, 95%CI=1.4-97.1)	Age, Gender, Smoking status	16

[a] = Exposure assessment by using questionnaire; [b] = Exposure assessment by using laboratory; [c] = Outcome assessment by using questionnaire, or interview, or self-reported of history of doctor diagnosis; CS = Cross-sectional study; OR=odds ratio; 95%CI=95% confidence interval; > Statistically higher than;
< Statistically lower than; ≈ Non-difference

population was presented in Table II. The study designs of most articles were cross-sectional studies (n=11) and only one study was cohort study (n=1).

FEV1: Two studies concluded that the exposed pesticide population had a higher FEV1 than the unexposed population, whereas five studies found that the exposed pesticide population had a lower FEV1 than the unexposed population (18,19,6,20-23). However, four studies found no difference of FEV1 between the exposed pesticide and the unexposed pesticides group (16,24-26).

FVC: Four studies concluded that the exposed pesticide population had a lower FVC than the unexposed population (6,22-24). In contrast, six studies found no difference of FVC between the exposed pesticide and the unexposed pesticides group (16,19-21, 25,26).

FEV1/FVC: Four studies concluded that the exposed pesticide population had a lower FEV1/FVC than the unexposed population (6,16,20,21). In contrast, five studies found no difference of FEV1/FVC between the exposed pesticide and the unexposed pesticides group (19,23-26).

$FEF_{25-75\%}$: Two studies concluded that the exposed pesticide population had a lower $FEF_{25-75\%}$ than the unexposed population, whereas a study by Hernandez et al.(2008) found a higher $FEF_{25-75\%}$ in the exposed pesticide population(6,19,20). However, four studies found no difference of $FEF_{25-75\%}$ between the exposed pesticide and the unexposed pesticides group (16,23,25,26).

PEFR: Three studies concluded that the exposed pesticide population had a lower PEFR than the unexposed population (6,21,27), whereas a study by Jones et al.(2003) found a higher PEFR in the exposed pesticide population (18). However, a study by Sutoluk et al.(2011) found no difference of PEFR between the exposed pesticide and the unexposed pesticides group (26).

Respiratory symptoms

Comparison of respiratory symptoms between the exposed pesticide population and unexposed pesticide population was presented in Table III. The study designs of most articles were cross-sectional studies (n=5) and only one study was cohort study (n=1).

Wheezing: A study by Dalphin et al.(1998) found that increased prevalence of wheezing was higher in dairy farmers compared with the unexposed pesticide group (OR=2.7, 95%CI=1.1-7.1 for wheezing (ever) and OR=5.2, 95%CI=1.1-24.4 for wheezing (last year)) (16). In contrast, a study by Boers et al.(2008) found a higher risk of wheezing in unexposed pesticide workers (OR=0.56, 95%CI=0.32-0.98) (17). However, two studies found no difference of wheezing symptom between the exposed pesticide population and the unexposed pesticide population (21,28).

Coughing: Two studies concluded that the exposed pesticide population had a significantly higher prevalence of coughing than the unexposed population (OR=5.0 and 10.41, 95% CI=1.9-13.6 and 1.59-437.09, respectively) (16,21). However, a study by Sapbamrer and Nata (2014) found no difference of coughing between the exposed pesticide population and the unexposed pesticide population (10).

Breathlessness: Two studies concluded that breathlessness in the exposed pesticide population was significantly higher than in the unexposed population (OR=2.80 and 6.67, 95%CI = 1.3-6.0 and 2.60-17.58, respectively) (10,20). However, a study by Dalphin et al.(1998) found no difference of breathlessness between the exposed pesticide population and the unexposed pesticide population (16).

Chest pain/tightness: A study by Sapbamrer and Nata (2014) found that chest pain in the exposed pesticide population was significantly higher than in the unexposed population (OR=2.5, 95%CI = 1.2-5.1)(10). However, a study by Boers et al.(2008) found no difference between

Table II: Comparison of lung function between exposed pesticide population and un-exposed pesticide population

Outcomes	Country	Design	Study population	Main findings	Adjusted / Confounding variables	Reference
FEV_1	USA	CS[a,b]	- Arial pesticide applicators (135) - Un-exposed population (118)	Arial applicators > Un-exposed population (Mean±SD.= 545±21. L for aerial applicators and 2467±21.4 L for un-exposed population, P=0.012)	None	18
	Spain	CS[a,b]	- Spraying farmers (89) - Non-spraying farmers(25)	Sprayers > Non-sprayers (B=18.77, P<0.001)	Age, Gender, Smoking status, BMI, Height, Alcohol consumption, PON_1, PChE, AChE	19
	India	CS[a,b]	- Agricultural workers who sprayed OP and carbamates (376) - Non-agricultural workers (348)	Agricultural workers < Non-agricultural workers (Mean±SD.=1.94±0.8 L for agricultural workers and 2.36±0.9 L for non-agricultural workers, P<0.0001)	None	6
	Ethiopia	CS[a,b]	- Farm workers (205) - Un-exposed population (177)	Farm workers < Un-exposed population (B=-0.14, 95%CI= -0.25- -0.03)	Age, Gender, BMI, Smoking status, Ever pneumonia, Income, Marital status, Chewing status	20
	India	CS[a,b]	- Pesticide sprayers (166) - Non-sprayers (77)	Sprayers < Non-sprayers (Mean±SD.= 1.76±0.63 L for sprayers and 2.26±0.59 L for non-sprayers, P<0.01)	None	21
	Ethiopia	CS[a,b]	Farm workers (231) - Sprayers (103) - Supervisors (15) - Technicians (14) - Pest assessors (19) - Office workers on farm (80)	Non-smokers: Sprayers < other groups (Mean±SD.= 94.59±6.95 % for sprayers, 95.01±2.19% for supervisors, 94.93±2.49% for technicians, 95.26±1.09% for pest assessors, and 95.16±1.53% for office workers on farm, F=4.77, P=0.03)	None	22
	Sri Lanka	CS[a,b]	- Farmers (25) - Fishermen (22) - Control group (40)	Farmers < Controls (P<0.001) (Mean±SD.=84.04±17.08 L for farmers and 102.49±33.42 L for controls)	None	23
	France	CS[a,b]	- Dairy farmers (265) - Un-exposed group (149)	Dairy farmers ≈ Un-exposed group (Mean±SD.= 98.4±14.5% for dairy farmers and 98±14.1% for un-exposed group)	None	16
	South Korea	CS[a,b]	- Pesticide applying farmers (n=2,508) - Non-pesticides applying farmers (374)	Non-smokers: Pesticide applying farmers ≈ Non- pesticide applying farmers (Mean±SE.=100.7±0.8% for applying farmers and 100.6±2.4% for non-pesticide applying farmers)	Age, Gender, Height, Distance from oil spill site, Smoking status, Alcohol consumption, Education level, Pesticide exposure	24
	Costa Rica	CS[a,b]	Farm workers (338) - Handler (219) - Non-handler (110)	Handlers ≈ Non-handlers (Mean±SE.=106.0±0.8% for handlers and 105.3±1.1% for non-handlers, P=0.61)	None	25
	Turkey	CS[a,b]	- Farm workers (50) - Non-farm workers (50)	Farm workers ≈ Non-farm workers (Mean±SD.=92.7±14.0% for farm workers and 94.8±13.8% for non-farm workers, P=0.440)	None	26
FVC	India	CS[a,b]	- Agricultural workers who sprayed OP and carbamates (376) - Non-agricultural workers (348)	Agricultural workers < Non-agricultural workers (Mean±SD.=2.23±0.9 L for agricultural workers and 2.58±0.83 L for non-agricultural workers, P<0.0001)	None	6
	Sri Lanka	CS[a,b]	- Farmers (25) - Fishermen (22) - Control group (40)	Farmers < Controls (Mean±SD.=71.09±13.21 L for farmers and 87.02±7.34 L for controls, P<0.001)	None	23
	Ethiopia	CS[a,b]	Farm workers (231) - Sprayers (103) - Supervisors (15) - Technicians (14) - Pest assessors (19) - Office workers on farm (80)	Non-smokers: Sprayers < other groups (Mean±SD.= 3.05±0.50 L for sprayers, 3.14±0.47 L for technicians, 3.08±0.36 L for pest assessors, and 3.22±0.52 L for office workers on farm, P=0.03)	None	22
	South Korea	CS[a,b]	- Pesticide applying farmers (n=2,508) - Non-pesticides applying farmers (374)	Male farmers: Pesticide applying farmers < Non- pesticide applying farmers (Mean±SE.=95.7±0.5% for applying farmers and 102.5±1.7% for non-pesticide applying farmers, P<0.05) Non-smokers: Pesticide applying farmers ≈ Non- pesticide applying farmers (Mean±SE.=97.2±3.7% for applying farmers and 96.6±0.9% for non-pesticide applying farmers)	Age, Gender, Height, Distance from oil spill site, Smoking status, Alcohol consumption, Education level, Pesticide exposure	24
	France	CS[a,b]	- Dairy farmers (265) - Un-exposed group (149)	Dairy farmers ≈ Un-exposed group (Mean±SD.= 98.4±14.5% for dairy farmers and 98±14.1% for un-exposed group)	None	16
	Ethiopia	CS[a,b]	- Farm workers (205) - Un-exposed population (177)	Farm workers ≈ Un-exposed population (B=-0.05, 95%CI=-0.18-0.07)	Age, Gender, BMI, Smoking status, Ever pneumonia, Income, Marital status, Chewing status	20
	Spain	CS[a,b]	- Spraying farmers(89) - Non-spraying farmers(25)	Sprayers ≈ Non-sprayers	Age, Gender, Smoking status, BMI Height, Alcohol consumption, PON1, PChE, AChE	19
	India	CS[a,b]	- Pesticide sprayers (166) - Non-sprayers (77)	Sprayers ≈ Non-sprayers (Mean±SD.= 2.20±0.77 L for sprayers and 2.23±0.74 L for non-sprayers)	None	21

continue.........

Table II: Comparison of lung function between exposed pesticide population and un-exposed pesticide population

Outcomes	Country	Design	Study population	Main findings	Adjusted / Confounding variables	Reference
	Costa Rica	CS[a,b]	Farm workers (338) - Handler (219) - Non-handler (110)	Handlers ≈ Non-handlers (Mean±SE.=101.3±0.8% for handlers and 101.6±1.1% for non-handlers, P=0.83)	None	25
	Turkey	CS[a,b]	- Farm workers (50) - Non-farm workers (50)	Farm workers ≈ Non-farm workers (Mean±SD.=82.8±15.2% for farm workers and 84.4±13.4% for non-farm workers, P=0.574)	None	26
FEV_1/FVC	India	CS[a,b]	- Agricultural workers who sprayed OP and carbamates (376) - Non-agricultural workers (348)	Agricultural workers < Non-agricultural workers (Mean±SD.=87.0±15.5% for agricultural workers and 91.5±14.1% for non-agricultural workers, P<0.0001)	None	6
	France	CS[a,b]	- Dairy farmers (265) - Un-exposed group (149)	Dairy farmers < Un-exposed group (Mean±SD.= 102.8±15.2% for dairy farmers and 100.4±13% for un-exposed group, P=0.025)	None	16
	Ethiopia	CS[a,b]	- Farm workers (205) - Un-exposed population (177)	FEV1/FVC<0.8: Farm workers > Un-exposed population (OR=4.31, 95%CI=-2.11-8.81)	Age, Gender, BMI, Smoking status, Ever pneumonia, Income, Marital status, Chewing status	20
	India	CS[a,b]	- Pesticide sprayers (166) - Non-sprayers (77)	Sprayers < Non-sprayers (Mean±SD.= 0.79±0.01 L for sprayers and 0.84±0.01 L for non-sprayers, P<0.01)	None	21
	Sri Lanka	CS[a,b]	- Farmers (25) - Fishermen (22) - Control group (40)	Farmers ≈ Controls (P=0.159) (Mean±SD.=0.973±0.06 L for farmers and 0.941±0.67 L for controls)	None	23
	Spain	CS[a,b]	- Spraying farmers(89) - Non-spraying farmers(25)	Sprayers ≈ Non-sprayers	Age, Gender, Smoking status, BMI Height, Alcohol consumption, PON1, PChE, AChE	19
	South Korea	CS[a,b]	- Pesticide applying farmers (n=2,508) - Non-pesticides applying farmers (374)	Non-smokers: Pesticide applying farmers ≈ Non- pesticide applying farmers (Mean±SE.=75.0±0.4% for applying farmers and 74.4±1.2% for non-pesticide applying farmers)	Age, Gender, Height , Distance from oil spill site, Smoking status, Alcohol consumption, Education level, Pesticide exposure	24
	Costa Rica	CS[a,b]	Farm workers (338) - Handler (219) - Non-handler (110)	Handlers ≈ Non-handlers (Mean±SE.=81.8±0.4% for handlers and 81.4±0.6% for non-handlers, P=0.54)	None	25
	Turkey	CS[a,b]	- Farm workers (50) - Non-farm workers (50)	Farm workers ≈ Non-farm workers (Mean±SD.=116.8±9.1% for farm workers and 117.1±5.6% for non-farm workers, P=0.312)	None	26
$FEF_{25-75\%}$	India	CS[a,b]	- Agricultural workers who sprayed OP and carbamates (376) - Non-agricultural workers (348)	Agricultural workers < non-agricultural workers (Mean±SD.=2.25±1.2 L for agricultural workers and 2.81±1.4 L for non-agricultural workers, P<0.0001)	None	6
	Ethiopia	CS[a,b]	- Farm workers (205) - Un-exposed population (177)	Farm workers < Un-exposed population (B=-0.55, 95%CI=-0.80- -0.31)	Age, Gender, BMI, Smoking status, Ever pneumonia, Income, Marital status, Chewing status	20
	Spain	CS[a,b]	- Spraying farmers(89) - Non-spraying farmers(25)	Sprayers > Non-sprayers (B=23.17, P=0.001)	Age, Gender, Smoking status, BMI Height, Alcohol consumption, PON1, PChE, AChE	19
	France	CS[a,b]	- Dairy farmers (265) - Un-exposed group (149)	Dairy farmers ≈ Un-exposed group (Mean±SD.= 84.6±23.5% for dairy farmers and 85.9±27.1% for un-exposed group)	None	16
	Sri Lanka	CS[a,b]	- Farmers (25) - Fishermen (22) - Control group (40)	Farmers ≈ Controls (P=0.209) (Mean±SD.=111.45±37.24 L for farmers and 123.36±33.42 L for controls)	None	23
	Costa Rica	CS[a,b]	Farm workers (338) - Handler (219) - Non-handler (110)	Handlers ≈ Non-handlers (Mean±SE.=106.8±2% for handlers and 105.3±1.1% for non-handlers,P=0.35)	None	25
	Turkey	CS[a,b]	- Farm workers (50) - Non-farm workers (50)	Farm workers ≈ Non-farm workers (Mean±SD.=105.7±23% for farm workers and 108.4±23.8% for non-farm workers, P=0.571)	None	26
PEFR	India	CS[a,b]	- Agricultural workers who sprayed OP and carbamates (376) - Non-agricultural workers (348)	Agricultural workers < non-agricultural workers (Mean±SD.=2.04±1.4 L for agricultural workers and 2.73±0.3 L for non-agricultural workers, P<0.0001)	None	6
	India	CS[a,b]	- Pesticide sprayers (166) - Non-sprayers (77)	Sprayers < Non-sprayers (Mean±SD.= 60.03±20.74 % for sprayers and 81.09±20.34 % for non-sprayers, P<0.01)	None	21
	India	CS[a,c]	- Farmers (35) - Non-farmers (35)	Farmers < Non-farmers (Mean±SD.=340.9±68.44 L/min for farmers and 405.6±65.90 L/min, P<0.001)	None	27
	USA	C[a,b]	- Arial pesticide applicators (135) - Un-exposed population (118)	Arial applicators > Un-exposed population Arial applicators > Un-exposed population (Mean+SD.= 698±20.0 L for aerial applicators and 640±20.3 L for un-exposed population, P=0.046)	None	18
	Turkey	CS[a,b]	- Farm workers (50) - Non-farm workers (50)	Farm workers ≈ Non-farm workers (Mean±SD.=84.3±19.6% for farm workers and 87.7±20.0% for non-farm workers, P=0.359)	None	26

[a] = Exposure assessment by using questionnaire; [b] = Outcome assessment by using spirometry test; [c] = Outcome assessment by using peak flow meter; CS = Cross-sectional study; C = Cohort study; FEV_1 = Forced expiratory volume in 1 second; FVC = Forced vital capacity; PEFR = Peak expiratory flow rate; FEF = Forced expiratory flow; AChE=Acetylcholinesterase; PChE=plasma-cholinesterase; B=Beta; SD.=Standard deviation; SE.=Standard error; > Statistically higher than; < Statistically lower than; ≈ Non-difference

the exposed pesticide population and the unexposed pesticide population (17).

Phlegm: A study by Dalphin et al.(1998) found that phlegm in dairy farmers was significantly higher than in un-exposed group (OR=11.3, 95%CI =3.1-40.5)(16).

Dyspnea: Two studies concluded that found no difference of dyspnea between the exposed pesticide population and the unexposed pesticide population (16,21).

Irritation to throat: a study by Fareed et al.(2013) found that irritation to throat in sprayers was significantly higher than in non-sprayers (21). Nevertheless, a study by Sapbamrer and Nata (2014) found no difference of sore throat between farmers and non-farmers (10).

Section 2: Association of Exposure to Pesticides with Respiratory Outcomes among Farmers and Farmworkers

Table IV summarized the association of exposure to specific pesticides with respiratory diseases and symptoms. The evidence showed that 29 pesticides found an association with respiratory diseases and 49 pesticides with respiratory symptoms. Out of the 29 pesticides which were found to have an association with respiratory diseases, elven were classified as herbicides, fourteen as insecticides, and four as fungicides. Out of the 49 pesticides which showed an association with respiratory symptoms, 24 were classified as herbicides, 20 as insecticides, and five as fungicides. In addition, 14 pesticides found an association with both respiratory diseases and symptoms (seven for herbicides, six for insecticides, and one for fungicides). The seven herbicides were as follows: 2,4-D, chlorimuron-ethyl, EPTC, glyphosate, paraquat, pendimethalin, and petroleum oil. The six insecticides were as follows: dichorvos, malathion, parathion, phorate, carbaryl, and permethrin. One fungicide was metalaxyl.

Asthma: Three studies suggested that pesticide exposure contributed to asthma (3-5). For allergic asthma, the association with exposure to specific herbicide was found with a range of OR between 1.31 and 2.1. The following specific herbicides were as follows: glyphosate (OR=1.31, 95%CI=1.02-1.67), 2,4-D (OR=1.53, 95%CI=1.12-2.10), EPTC (OR=1.61,95%CI=1.06-2.43), paraquat (OR=1.67,95%CI=1.05-2.65), 2,4,5-TP (OR=1.91, 95%CI=1.06-3.44), and pendimethalin (OR=2.1,95%CI=1.1-4.1), respectively (3-5). Exposure to specific insecticides was also found to be associated with a range of OR between 1.41 and 10.2. The following specific insecticides were as follows: carbaryl (OR=1.41, 95%CI=1.10-1.80), diazinon (OR=1.57, 95%CI=1.05-2.35), lindane (OR=1.57, 95%CI=1.01-2.41), malathion(OR=1.60, 95%CI=1.22-2.10), permethrin (OR=1.71, 95%CI=1.01-2.91), chordane (OR=1.77, 95%CI=1.19-2.63), DDT (OR=1.79, 95%CI=1.06-3.03), heptachlor (OR=2.01, 95%CI=1.30-3.11), phorate (OR=2.04, 95%CI=1.07-3.88), parathion (OR= 2.05 and 2.88, 95%CI=1.21-3.46 and 1.34-6.20, respectively), coumaphos (OR=2.19 and 2.34, 95%CI=1.02-4.69 and 1.49-3.70, respectively), and aldicarb (OR=10.2, 95%CI=1.9-55), respectively (3-5). Exposure to specific fungicide was also found to be associated with a range of OR between 1.83 and 2.61. The following specific fungicides were as follows: captan (OR=1.83, 95%CI=1.15-2.94), ethylene dibromide (OR=2.07, 95%CI=1.02-4.20), 80/20mix (OR=2.15, 95%CI=1.23-3.76), and metalaxyl (OR=2.61, 95%CI=1.35-5.04), respectively (3-5).

For non-allergic asthma, the specific herbicide which had association was petroleum oil (OR=1.35, 95%CI=1.04-1.74). Three specific insecticides which were found to have the association were phorate (OR=1.29, 95%CI=1.01-1.65), malathion (OR=1.04, 95%CI=1.04-1.75), and DDT (OR=1.41, 95%CI=1.09-1.84)(4).

Chronic bronchitis: Two studies have shown that exposure to herbicides were associated with an increased prevalence of chronic bronchitis with a range of OR between 1.20 and 1.91. The specific herbicides were as follows: chlorimuron-ethyl (OR=1.20, 95%CI=1.00-1.42), petroleum oil (OR=1.25, 95%CI=1.03-1.52), 2,4,5-T (OR=1.31, 95%CI=1.06-1.62), 2,4,5-TP (OR=1.41, 95%CI=1.15-1.73), methyl bromide (OR=1.82, 95%CI=1.02-3.24), cynazine (OR=1.88, 95%CI=1.00-3.54), and paraquat (OR=1.91, 95%CI=1.02-3.55), respectively (29,30). Exposure to insecticides was also found to have a positive association with a range of OR between 1.22 between 1.68. The specific insecticides were as follows: carbaryl (OR=1.22, 95%CI=1.01-1.48), diazinon (OR=1.25, 95%CI=1.02-1.53), permethrin (OR=1.26, 95%CI=1.00-1.59), DDT (OR=1.27 and 1.67, 95%CI=1.04-1.56 and 1.13-2.47, respectively), malathion (OR=1.44, 95%CI=1.19-1.76), heptachlor (OR=1.50, 95%CI=1.19-1.89), dichorvos (OR=1.6, 95%CI=1.01-2.61), and carbosulfan (OR=1.40 and 1.68, 95%CI=1.18-1.66 and 1.03-2.74, respectively), respectively (29,30).

Wheezing: Available studies suggested that exposure to herbicides were linked to an increased prevalence of wheezing. For allergic wheezing, the association with exposure to specific herbicides was found with a range of OR between 1.28 and 2.45 The following specific herbicides were as follows: dicamba (OR=1.28, 95%CI=1.04-1.58), picloram (OR=1.28, 95%CI=1.06-1.56), atrazine (OR=1.33, 95%CI=1.09-1.62), tricopyr (OR=1.40, 95%CI=1.11-1.76), 2,4-D (OR=1.46, 95%CI=1.19-1.79), trifluralin (OR=1.54, 95%CI=1.22-1.94), bentazon (OR=1.56, 95%CI=1.06-2.30), glyphosate (OR=1.56, 95%CI=1.19-2.03), simazine (OR=1.71, 95%CI=1.17-2.50), and petroleum oil (OR=2.45, 95%CI=1.50-4.03), respectively (9). Exposure to insecticides was also found to have a

Table III: Comparison of respiratory symptoms between exposed pesticide population and un-exposed pesticide population

Outcomes	Country	Design	Study population	Main findings	Adjusted / Confounding variables	Reference
Wheezing	France	CS[a,c,d]	- Dairy farmers (265) - Un-exposed group (149)	Dairy farmers > Un-exposed group -Wheeze (ever)(OR=2.7, 95%CI=1.1-7.1) -Wheeze (last year)(OR=5.2, 95%CI=1.1-24.4) Dairy farmers ≈ Un-exposed group -wheeze apart from a cold (OR=4.1, 95%CI=0.8-20.8)	Age, Gender , Smoking status	16
	Europe region	CS[a,b,c]	- Exposed pesticides workers (248) - Un-exposed workers (231)	Exposed pesticides workers < Un-exposed workers (OR=0.56, 95%CI=0.32-0.98)	Age, Gender, Residence, Education level, Smoking status	17
	India	CS[a,c]	- Pesticide sprayers (166) - Non-sprayers (77)	Sprayer ≈ Non-sprayers (OR=cannot compute)	Smoking status	21
	Egypt	C[b,c]	- Male applicators (57) - Non-applicators (38)	- Applicators ≈ Non-applicators (Age-adjusted OR=3.27, 95%CI=0.97-11.08)	Age	28
Coughing	France	CS[a,c,d]	- Dairy farmers (265) - Un-exposed group (149)	Dairy farmers > Un-exposed group (Morning cough) (OR=5.0, 95%CI=1.9-13.6)	Age, Gender, Smoking status	16
	India	CS[a,c]	- Pesticide sprayers (166) - Non-sprayers (77)	Sprayers > Non-sprayers -Dry cough (OR=10.41, 95%CI=1.59-437.09) -Productive cough: (OR= -, P<0.01)	Smoking status	21
	Thailand	CS[a,c]	- Farmers (182) - Non-farmers (122)	Farmers ≈ Non-famers (OR=1.2, 95%CI=0.7-2.1)	None	10
Breathless-ness	Thailand	CS[a,c]	- Farmers (182) - Non-farmers (122)	Farmers > Non-famers (OR=2.8, 95%CI=1.3-6.0)	None	10
	Ethiopia	CS[a,c]	- Farm workers (205) - Un-exposed population (177)	Farm workers > Un-exposed population (OR=6.67, 95%CI=2.60-17.58)	Age, Gender, BMI, Smoking, status, Ever pneumonia, Income, Marital status, Chewing status	20
	France	CS[a,c]	- Dairy farmers (265) - Un-exposed group (149)	Dairy farmers ≈ Un-exposed group -Attack of breathlessness at rest (last year)(OR=1.9, 95%CI=0.4-10) -Woken by breathlessness (last year) (OR=4.6, 95%CI=0.5-41)	Age, Gender, Smoking status	16
Chest pain/ tightness	Thailand	CS[a,c]	- Farmers (182) - Non-farmers (122)	Farmers > Non-famers (OR=2.5, 95%CI=1.2-5.1)	None	10
	Europe region	CS[a,b,c]	- Exposed pesticides workers (248) - Un-exposed workers (231)	Exposed pesticides workers ≈ Un-exposed workers (OR=0.60, 95%CI=0.36-1.02)	Age, Gender, Residence, Education level, Smoking status	17
Phlegm	France	CS[a,c]	Farmers (414) - Dairy farmers (265) - Un-exposed group (149)	Dairy farmers > Un-exposed group (OR=11.3, 95%CI=3.1-40.5)	Age, Gender, Smoking status	16
Dyspnea	France	CS[a,c]	- Dairy farmers (265) - Un-exposed group (149)	Dairy farmers ≈ Un-exposed group (OR=1.2, 95%CI=0.6-2.3)	Age, Gender, Smoking status	16
	India	CS[a,c]	- Pesticide sprayers (166) - Non-sprayers (77)	Sprayer ≈ Non-sprayers (OR=2.15, 95%CI=0.43-20.87)	Smoking status	21
Irritation to throat	India	CS[a,c]	- Pesticide sprayers (166) - Non-sprayers (77)	Sprayers > Non-sprayers (OR= cannot compute, P<0.01)	Smoking status	21
	Thailand	CS[a,c]	- Farmers (182) - Non-farmers (122)	Farmers ≈ Non-famers (OR=0.9, 95%CI=0.6-1.6)	None	10

[a] = Exposure assessment by using questionnaire; [b] = Exposure assessment by using laboratory; [c] = Outcome assessment by using questionnaire, or interview, or self-reported of history of doctor diagnosis; [d] = Outcome assessment by using physician diagnosis; CS = Cross-sectional study; C = Cohort study; OR = Odds ratio; > Statistically higher than; < Statistically lower than; ≈ Non-difference

positive association with a range of OR between 1.23 between 2.02. The specific insecticides were as follows: chlorpyrifos (OR=1.23, 95%CI=1.00-1.52), permethrin (OR=1.38, 95%CI=1.09-1.75), malathion (OR=1.48, 95%CI=1.19-1.86), dimethoate (OR=1.67, 95%CI=1.03-2.73), carbaryl (OR=1.70, 95%CI=1.32-2.19), pyrethrin (OR=1.70, 95%CI=1.13-2.56), and zeta cypermethrin (OR=2.02, 95%CI=1.24-3.30), respectively (9). One specific fungicide was also found to have the association which was warfarin (OR=1.55, 95%CI=1.0-7.0) (9).

For non-allergic wheezing, the association with exposure to specific herbicides was found with a range of OR between 1.14 and 1.61. The following specific herbicides were as follows: matolachlor (OR=1.14, 95%CI=1.01-1.28), nicosulfuron (OR=1.14, 95%CI=1.00-1.30), mesotrione (OR=1.16, 95%CI=1.03-1.31), tricopyr (OR=1.16, 95%CI=1.00-1.35), picloram (OR=1.21, 95%CI=1.09-1.36), acetochlor (OR=1.24, 95%CI=1.11-1.39), glyphosate (OR=1.24, 95%CI=1.07-1.44), trifluralin (OR=1.24, 95%CI=1.08-1.43), fluazifop-butyl/fenoxaprop-p-ethyl (OR=1.25, 95%CI=1.03-1.53), dicamba (OR=1.29, 95%CI=1.14-1.45), clopyralid/flumetasulam (OR=1.33, 95%CI=1.16-1.54), imazaquin (OR=1.37, 95%CI=1.09-1.71), atrazine (OR=1.42, 95%CI=1.26-1.59), and petroleum oil (OR=1.61, 95%CI=1.15-2.25), respectively (9). Exposure to insecticides was also found to have a positive association with a range of OR between 1.13 between 1.43. The specific insecticides were as follows: cyfluthrin (OR=1.13, 95%CI=1.00-1.29), malathion (OR=1.29, 95%CI=1.13-1.46), permethrin (OR=1.35, 95%CI=1.17-1.55), and pyrethrin (OR=1.43, 95%CI=1.10-1.85), respectively (9).

For unspecified wheezing, the association with exposure to specific herbicides was found with a range of OR between 1.12 and 7.9. The following specific herbicides were as follows: trifluralin (OR=1.12 and 1.15, 95%CI=1.00-1.25 and 1.02-1.30, respectively), chlorimuron ethyl (OR=1.14, 1.62, and 1.62, 95%CI=1.02-1.29, 1.25-2.10, and 1.06-2.10, respectively), atrazine (OR=1.18, 1.20, and 1.38, 95%CI=1.05-1.32, 1.07-1.34, and 1.06-1.80, respectively), alachlor (OR=1.23 and 1.24, 95%CI=1.06-1.41 and 1.09-1.42, respectively), petroleum oil (OR=1.26, 1.28, and 1.47, 95%CI=1.09-1.47, 1.11-1.48, and 1.08-2.01, respectively), EPTC (OR=1.32 and 1.37, 95%CI=1.05-1.65 and 1.08-1.73, respectively), imazethapyr (OR=1.35,95%CI=1.05-1.75), matolachlor (OR=1.37,95%CI=1.05-1.78), glyphosate (OR=1.38,95%CI=1.03-1.86), pendimethalin (OR=1.38, 95%CI=1.07-1.79), metribuzin (OR=1.42,95%CI=1.05-1.92), paraquat (OR=1.27 and 7.9, 95%CI=1.04-1.56 and 1.5-41.9, respectively)(31-33). Exposure to insecticides was also found to have a positive association with a range of OR between 1.13 between 12.9. The specific insecticides were as follows: malathion (OR=1.13 and 1.14, 95%CI=1.00-1.27 and 1.02-1.28, respectively), permethrin (OR=1.26, 1.28, and 2.24, 95%CI=1.06-1.51, 1.06-1.55, and 1.37-3.68, respectively), parathion (OR=1.50, 95%CI=1.04-2.16), pyrethrin (OR=1.63, 95%CI=1.04-2.55), terbufos (OR=1.66 and 8.7, 95%CI=1.09-2.53 and 1.6-46.4, respectively), fonofos (OR=1.78, 95%CI=1.07-2.98), cypermethrin (OR=2.03, 95%CI=1.24-3.30), phorate (OR=2.35 and 2.87, 95%CI=1.36-4.06 and 1.70-4.84, respectively), dichlorvos (OR=2.48 and 2.48, 95%CI=1.08-5.66 and 1.09-5.64, respectively), tetramethrin (OR=3.88, 95%CI=1.17-12.91), phenothrin (OR=10.56, 95%CI=5.28-21.11), chlorpyrifos (OR=1.12, 1.47, and 12.9, 95%CI=1.01-1.25, 1.09-1.99, and 1.6-101.0, respectively)(31-35). One specific fungicide which was found to have the association was metalaxyl (OR=1.19, 95%CI=1.02-1.38)(31).

Dyspnea: Two studies have shown that exposure to pesticides was associated with an increased prevalence of dyspnea (35,36). One specific herbicide which was found to have the association was paraquat (OR=4.6, 95%CI=2.4-9.0) (36). Exposure to insecticides was also found to have a positive association with a range of OR between 1.52 between 5.50. The specific insecticides were as follows: pyrethrin ((OR=1.52, 95%CI=1.21-1.92), permethrin (OR=1.78, 95%CI=1.35-2.35), resmethrin (OR=1.86, 95%CI=1.10-3.15), cypermethrin (OR=2.64, 95%CI=2.08-3.36), esfenvalerate (OR=3.47, 95%CI=2.19-5.52),tetramethrin (OR=4.96, 95%CI=-2.41-10.22), and phenothrin (OR=5.50, 95%CI=3.15-9.60), respectively.

Allergic rhinitis: A study by Chatzi et al.(2007) suggested that two specific herbicides (glyphosate (OR=2.5,95%CI=1.0-6.5) and bipyridyls (OR=4.0,95%CI=1.4-11.2)) were associated with an increased prevalence of allergic rhinitis (37). They also suggested that exposure to fungicides was found to have an association with a range of OR between 2.7 between 3.5. The specific fungicides were as follows: triazole (OR=2.7, 95%CI=1.4-11.2), thiophithalimide (OR=3.3, 95%CI=1.2-8.7), and dithiocarbamate (OR=3.5, 95%CI=1.2-10.2), respectively.

Breathlessness: A study by Fieten et al.(2009) suggested that exposure to chlorpyrifos was associated with an increased prevalence of breathlessness (OR=4.0,95%CI=1.1-15.2)(34).

Coughing: Two studies have shown that exposure to insecticides was associated with an increased prevalence of coughing with a range of OR between 1.53 between 5.41. The specific insecticides were as follows: permethrin (OR=1.53, 95%CI=1.14-2.05), cyfluthrin (OR=1.59, 95%CI=1.10-2.29), endosulfan sulfate (OR=1.76,95%CI=1.07-2.91), pyrethrin (OR=2.06, 95%CI=1.67-2.57), tralomethrin (OR=2.23, 95%CI=1.34-3.73), tetramethrin (OR=3.35, 95%CI=1.56-7.18), esfenvalerate (OR=3.47, 95%CI=2.16-5.58), phenothrin (OR=4.22, 95%CI=2.37-7.54), and cypermethrin (OR=5.41, 95%CI=4.34-6.76), respectively (2,35).

Lower respiratory pain/irritation: A study by Hudson et al.(2014) suggested that exposure to resmethrin was associated with an increased prevalence of lower respiratory pain/irritation (OR=10.60, 95%CI=6.07-18.50)(35).

Phlegm: A study by Quansah et al.(2016) suggested that exposure to endosulfan sulfate was associated with an increased prevalence of phlegm (OR=1.96, 95%CI=1.15-3.34)(2).

Section 3: Association of Other Factors with Respiratory Outcomes

The factors associated with respiratory outcomes were as follows:

Demographic characteristics and behavioral habits

Demographic characteristics and behavioral habits, including gender, BMI, and smoking status, were the contributory factors associating with respiratory outcomes. A prospective study in an agricultural population found that men had more asthma than women (Risk ratio(RR)=2.12, 95%CI=1.99-2.26 for men and 1.84, 95%CI=1.76-1.92 for women)(12). The FVC in male greenhouse workers was also significantly lower than female greenhouse workers (7). Furthermore, FVC in pesticide applicators was significantly lower than non-applicators, and the significance was found only in men (24). In contrast, the cross-sectional study by Faria et al. (2005) found that women had more asthma than men (OR=1.34, 95%CI=1.00-1.81)(38). These results

Table IV: Association of exposure to pesticides with respiratory outcomes among farmers and farmworkers

Respiratory diseases (n=29)	Respiratory symptoms (n=49)
Herbicides (n=11)	**(n=24)**
2,4-D (OR=1.53, 95%CI=1.12-2.10)[3a] 2,4,5-T (OR=1.31, 95%CI=1.06-1.62)[30c] 2,4,5-TP (OR=1.91, 95%CI=1.06-3.44)[4a]; (OR=1.41, 95%CI=1.15-1.73)[30c] Chlorimuron-ethyl (OR=1.20, 95%CI=1.00-1.42)[30c] Cynazine (OR=1.88, 95%CI=1.00-3.54)[29c] EPTC (OR=1.61, 95%CI=1.06-2.43)[4a] Glyphosate (OR=1.31, 95%CI=1.02-1.67)[3a] Methyl bromide (OR=1.82, 95%CI=1.02-3.24)[29c] Paraquat (OR=1.67, 95%CI=1.05-2.65)[4a]; (OR=1.91, 95%CI=1.02-3.55)[29c] Pendimethalin (OR=2.1, 95%CI=1.1-4.1)[5a] Petroleum oil (OR=1.35, 95%CI=1.04-1.74)[4b]; (OR=1.25, 95%CI=1.03-1.52)[30c]	2,4-D (OR=1.46, 95%CI=1.19-1.79)[9d] Acetochlor (OR=1.24, 95%CI=1.11-1.39)[9e] Alachlor (OR=1.24, 95%CI=1.09-1.42)[31f]; (OR=1.23, 95%CI=1.06-1.41)[32f] Atrazine (OR=1.33, 95%CI=1.09-1.62)[9d]; (OR=1.42, 95%CI=1.26-1.59)[9e]; (OR=1.20, 95%CI=1.07-1.34)[31f]; (OR=1.18, 95%CI=1.05-1.32)[32f]; (OR=1.38, 95%CI=1.06-1.80)[33f] Bipyridyls (OR=4.0, 95%CI=1.4-11.2)[37h] Bentazon (OR=1.56, 95%CI=1.06-2.30)[9d] Chlorimuron ethyl (OR=1.14, 95%CI=1.02-1.29)[31f]; (OR=1.62, 95%CI=1.25-2.10)[32f]; (OR=1.62, 95%CI=1.06-2.10)[33f] EPTC (OR=1.32, 95%CI=1.05-1.65)[31f]; (OR=1.37, 95%CI=1.08-1.73)[32f] Clopyralid/flumetasulam (OR=1.33, 95%CI=1.16-1.54)[9e] Dicamba (OR=1.28, 95%CI=1.04-1.58)[9d]; (OR=1.29, 95%CI=1.14-1.45)[9e] Fluazifop-butyl/fenoxaprop-p-ethyl (OR=1.25, 95%CI=1.03-1.53)[9e]; Glyphosate (OR=1.56, 95%CI=1.19-2.03)[9d]; (OR=1.24, 95%CI=1.07-1.44)[9e]; (OR=1.38, 95%CI=1.03-1.86)[33f]; (OR=2.5, 95%CI=1.0-6.5)[37h] Imazaquin (OR=1.37, 95%CI=1.09-1.71)[9e] Imazethapyr(OR=1.35, 95%CI=1.05-1.75)[33f] Matolachlor (OR=1.14, 95%CI=1.01-1.28)[9e]; (OR=1.37, 95%CI=1.05-1.78)[33f] Mesotrione (OR=1.16, 95%CI=1.03-1.31)[9e] Metribuzin (OR=1.42, 95%CI=1.05-1.92)[33f] Nicosulfuron (OR=1.14, 95%CI=1.00-1.30)[9e] Paraquat (OR=1.27, 95%CI=1.04-1.56)[31f]; (OR=7.9, 95%CI=1.5-41.9)[34f]; (OR=4.6, 95%CI=2.4-9.0)[36g] Pendimethalin (OR=1.38, 95%CI=1.07-1.79)[33f] Petroleum oil (OR=2.45, 95%CI=1.50-4.03)[9d]; (OR=1.61, 95%CI=1.15-2.25)[9e]; (OR=1.28, 95%CI=1.11-1.48)[31f]; (OR=1.26, 95%CI=1.09-1.47)[32f]; (OR=1.47, 95%CI=1.08-2.01)[33f] Picloram (OR=1.28, 95%CI=1.06-1.56)[9d]; (OR=1.21, 95%CI=1.09-1.36)[9e] Simazine (OR=1.71, 95%CI=1.17-2.50)[9d] Tricopyr (OR=1.40, 95%CI=1.11-1.76)[9d]; (OR=1.16, 95%CI=1.00-1.35)[9e] Trifluralin (OR=1.54, 95%CI=1.22-1.94)[9d]; (OR=1.24, 95%CI=1.08-1.43)[9e]; (OR=1.12, 95%CI=1.00-1.25)[31f]; (OR=1.15, 95%CI=1.02-1.30)[32f]
Insecticides (n=14)	**(n=20)**
Organophosphate group (n=6)	**(n=8)**
Coumaphos (OR=2.19, 95%CI=1.02-4.69)[3a]; (OR=2.34, 95%CI=1.49-3.70)[4a] Diazinon (OR=1.57, 95%CI=1.05-2.35)[4a]; (OR=1.25, 95%CI=1.02-1.53)[30c] Dichorvos (OR=1.6, 95%CI=1.01-2.61)[29c] Malathion(OR=1.60, 95%CI=1.22-2.10)[3a]; (OR=1.35, 95%CI=1.04-1.75)[4b]; (OR=1.44, 95%CI=1.19-1.76)[30c] Parathion (OR=2.88, 95%CI=1.34-6.20)[3a]; (OR=2.05, 95%CI=1.21-3.46)[4a] Phorate (OR=2.04, 95%CI=1.07-3.88)[3a]; (OR=1.29, 95%CI=1.01-1.65)[4b]	Chlorpyrifos (OR=1.23, 95%CI=1.00-1.52)[9d]; (OR=1.12, 95%CI=1.01-1.25)[31f]; (OR=1.47, 95%CI=1.09-1.99)[33f]; (OR=12.9, 95%CI=1.6-101.0)[34f]; (OR=4.0, 95%CI=1.1-15.2)[34i] Dichlorvos (OR=2.48, 95%CI=1.08-5.66)[32f]; (OR=2.48, 95%CI=1.09-5.64)[33f] Dimethoate (OR=1.67, 95%CI=1.03-2.73)[9d] Fonofos (OR=1.78, 95%CI=1.07-2.98)[33f] Malathion (OR=1.48, 95%CI=1.19-1.86)[9d]; (OR=1.29, 95%CI=1.13-1.46)[9e]; (OR=1.14, 95%CI=1.02-1.28)[31f]; (OR=1.13, 95%CI=1.00-1.27)[32f] Parathion (OR=1.50, 95%CI=1.04-2.16)[31f] Phorate (OR=2.35, 95%CI=1.36-4.06)[32f]; (OR=2.87, 95%CI=1.70-4.84)[33f] Terbufos (OR=1.66, 95%CI=1.09-2.53)[33f]; (OR=8.7, 95%CI=1.6-46.4)[34f]
Carbamate group (n=3)	**(n=1)**
Aldicarb (OR=10.2, 95%CI=1.9-55)[5a] Carbaryl (OR=1.41, 95%CI=1.10-1.80)[3a]; (OR=1.22, 95%CI=1.01-1.48)[30c] Carbosulfan (OR=1.68, 95%CI=1.03-2.74)[29c]; (OR=1.40, 95%CI=1.18-1.66)[30c]	Carbaryl (OR=1.70, 95%CI=1.32-2.19)[9d]
Pyrethroid group (n=1)	**(n=10)**
Permethrin (OR=1.71, 95%CI=1.01-2.91)[3a]; (OR=1.26, 95%CI=1.00-1.59)[30c]	Cyfluthrin (OR=1.13, 95%CI=1.00-1.29)[9e]; (OR=1.59, 95%CI=1.10-2.29)[35j] Cypermethrin (OR=2.03, 95%CI=1.24-3.30)[35f]; (OR=2.64, 95%CI=2.08-3.36)[35g]; (OR=5.41, 95%CI=4.34-6.76)[35j] Esfenvalerate (OR=3.47, 95%CI=2.19-5.52)[35g]; (OR=3.47, 95%CI=2.16-5.58)[35j] Permethrin (OR=1.38, 95%CI=1.09-1.75)[9d]; (OR=1.35, 95%CI=1.17-1.55)[9e]; (OR=1.26, 95%CI=1.06-1.51)[31f]; (OR=1.28, 95%CI=1.06-1.55)[32f]; (OR=2.24, 95%CI=1.37-3.68)[35f]; (OR=1.78, 95%CI=1.35-2.35)[35g]; (OR=1.53, 95%CI=1.14-2.05)[35j] Phenothrin (OR=10.56, 95%CI=5.28-21.11)[35f]; (OR=5.50, 95%CI=3.15-9.60)[35g]; (OR=4.22, 95%CI=2.37-7.54)[35j] Pyrethrin (OR=1.70, 95%CI=1.13-2.56)[9d]; (OR=1.43, 95%CI=1.10-1.85)[9e]; (OR=1.63, 95%CI=1.04-2.55)[35f]; (OR=1.52, 95%CI=1.21-1.92)[35g]; (OR=2.06, 95%CI=1.67-2.57)[35j] Resmethrin (OR=1.86, 95%CI=1.10-3.15)[35g]; (OR=10.60, 95%CI=6.07-18.50)[35k] Tetramethrin (OR=3.88, 95%CI=1.17-12.91)[35f]; (OR=4.96, 95%CI=-2.41-10.22)[35g]; (OR=3.35, 95%CI=1.56-7.18)[35j] Tralomethrin (OR=2.23, 95%CI=1.34-3.73)[35j] Zeta cypermethrin (OR=2.02, 95%CI=1.24-3.3[0)]9d
Organochlorine group (n=4)	**(n=1)**
Chordane (OR=1.77, 95%CI=1.19-2.63)[4a] DDT (OR=1.79, 95%CI=1.06-3.03)[3a]; (OR=1.41, 95%CI=1.09-1.84)[4b]; (OR=1.67, 95%CI=1.13-2.47)[29c]; (OR=1.27, 95%CI=1.04-1.56)[30c] Heptachlor (OR=2.01, 95%CI=1.30-3.11)[4a]; (OR=1.50, 95%CI=1.19-1.89)[30c]; Lindane (OR=1.57, 95%CI=1.01-2.41)[4a]	Endosulfan sulfate (OR=2.52, 95%CI=1.13-5.62)[2f]; (OR=1.76, 95%CI=1.07-2.91)[2j]; (OR=1.96, 95%CI=1.15-3.34[)2l]
Fungicides (n=4)	**(n=5)**
80/20mix (OR=2.15, 95%CI=1.23-3.76)[4a] Captan (OR=1.83, 95%CI=1.15-2.94)[4a] Ethylene dibromide (OR=2.07, 95%CI=1.02-4.20)[4a] Metalaxyl (OR=2.61, 95%CI=1.35-5.04)[3a]	Dithiocarbamate(OR=3.5, 95%CI=1.2-10.2)[37h] Metalaxyl (OR=1.19, 95%CI=1.02-1.38)[31f] Thiophithalimide (OR=3.3, 95%CI=1.2-8.7)[37h] Triazole (OR=2.7, 95%CI=1.4-11.2)[37h] Warfarin (OR=1.55, 95%CI=1.0-7.0[)9]d

[a] Allergic asthma; [b] Non-allergic asthma; [c] Chronic bronchitis; [d] Allergic wheezing; [e] Non-allergic wheezing; [f] Wheezing (unspecified); [g] Dyspnea; [h] Allergic rhinitis; [i] Breathlessness; [j] Coughing; [k] Lower respiratory pain/irritation; [l] Phlegm; OR=Odds ratio; 95%CI=95% confidence interval

were consistent with the study of Stoeklin-Marois et al. (2015) that also found the association between asthma and living 15 years or more in the United States only in women (OR=3.60, 95%CI=1.16-11.16)(39). The study by Hanssen et al. (2015) also suggested that women farmers had higher association of coughing with pesticide exposure (OR=2.7, 95%CI=1.2-6.0 for coughing in the morning, 2.20, 95%CI=1.0-5.1 for coughing the during day, and 2.5, 95%CI=1.0-6.5 for coughing with sputum) (43). In addition, age (OR=2.368, 95%CI=1.428-3.927), BMI (OR=0.388, 95%CI= 0.158-0.950) showed an association with the FEV1 (7). Smoking status was also a contributory factor to respiratory outcomes. A study by Hoppin et al. (2003) found that past smokers had higher odds of wheezing than current smokers and non-smokers (40). In addition, the study by Zhu et al. (2017) reported that FEV1 < 80% in the never smoking group was lower than ever the smoking group (P < 0.05)(7).

Types of crop production

The study conducted in France found that potato production had a higher prevalence of chronic bronchitis than all other productions (OR=1.33, 95%CI=1.13-1.57) (41). In addition, the study conducted in northern Thailand found an increased prevalence of coughing and dry coughing in rice cultivation (OR=6.2, 95%CI= 1.7, 23.1, and OR=3.5, 95%CI= 1.0, 11.7 compared with mixed rice and corn farmers, respectively (11).

Tasks in farms

A study conducted in Ireland found a higher prevalence of airway diseases in mushroom growers when compared with other workers (OR=9.2, 95%CI=3.0-28.4)(42). These results were consistent with the study conducted in Ethiopia, reporting an increased prevalence of coughing in cutting and weeding workers compared with other workers (OR=2.7, 95%CI=1.2-6.0 for coughing in the morning, OR=2.2, 95%CI=1.0-5.1 for coughing during day or at night, OR=2.5, 95%CI=1.0-6.5 for coughing with sputum in the morning, and OR=2.1, 95%CI=1.0-4.4 for breathelessness)(43). The study conducted in northern Thailand also found an increased prevalence of dry throat in spraying pesticides (OR=2.5, 95%CI=1.2-5.0) and mixing pesticides (OR=2.6, 95%CI=1.3-5.4) (10).

Duration of farm experience

The study by Ndlovu et al. (2014) reported that asthma was positively associated with history of living or working on farms (OR=2.22, 95%CI=1.30-3.80), and current living and working on farms (OR=2.25, 95%CI=1.45-3.48)(44). The study by Stoecklin-Marois et al. (2015) also reported an association between asthma and number of years in agriculture (OR=1.04, 95%CI=1.00-1.09)(39). These results were consistent with the study reporting that farm workers who were exposed to pesticide equal or more than 31 years had the highest odds of asthma (OR=2.32, 95%CI=1.41-3.82)(45). The study by Burari et al.(2018) also found that years of rural work were associated with the decreases of FVC (beta=-0.01, 95%CI=-0.28--0.14), FEV1 (beta=-0.003, 95%CI=-0.005--0.002),, and $FEF_{25-75\%}$ (beta=-0.05, 95%CI=-0.07--0.03)(46).

Frequency and duration of pesticide application

The study by Ndlovu et al. (2014) found an association between asthma and the number of days of pesticide spraying per years in the current farm (OR=1.01, 95%CI=1.00-1.01)(44). These results were in agreement with the study by Fiori et al. (2015) who also found the association of wheezing with > 11 days/month of pesticide application (OR=2.71, 95%CI=1.56-4.71) and > 31 years of pesticide exposure (OR=2.32, 95%CI=1.41-3.82)(45). Quansah et al. (2016)2 also found the association of phlegm with frequency of pesticide application (Prevalence ratio (PR)=1.10, 95%CI=1.00-1.50 for 1-2 hours/day fungicide use, OR=1.20, 95%CI=1.11-1.72 for 3-5 hours/day fungicide use, and OR=1.32, 95%CI=1.09-2.53 for > 5 hours/ day fungicide use). In addition, the study by Thetkathuek et al. (2017) stated that the respiratory symptoms were positively associated with the spraying duration (OR=2.00, 95%CI=1.40-2.86 for 4-5 hrs. of spraying and OR=1.88, 95%CI=1.14-3.08 for 6-8 hrs. of spraying)(47). With regard to lung function, the FVC was negatively associated with the duration of pesticide application (P < 0.01), and restrictive defect was also positively associated with pesticide application of more than 30 years (24).

Pesticide poisoning and cholinesterase (ChE) levels

Asthma was also positively associated with ChE levels less than the laboratory standard (OR=1.93, 95%CI=1.09-3.44), and pesticide poisoning (OR=1.64, 95%CI=1.04-2.58) (38,44). Chronic bronchitis was also associated with pesticide poisoning with healthcare (OR = 1.64, 95%CI=1.11-2.41), pesticide poisoning without healthcare (OR=1.67, 95%CI=1.08-2.58)(41). In addition, the study by Chakraborty et al., (2009) reported that acetylcholinesterase (AChE) activity inhibition > 50% was associated with chronic bronchitis (OR=4.1, 95%CI=2.2-6.3), wheezing (OR=2.9, 95%CI=2.1-4.2), dyspnea (OR=3.7, 95%CI=2.7-4.8), chest pain (OR=3.1, 95%CI=2.1-5.4), sore throat (OR=2.6, 95%CI=1.5-4.7), breathlessness (OR=3.7, 95%CI=2.6-5.1), runny or stuffy nose (OR=4.8, 95%CI=2.3-6.9), and sinusitis (OR=3.6, 95%CI=2.7-7.0)(6). These results were consistent with the study by Sapbamrer et al. (2017) that also found that AChE inhibition was associated with breathlessness (P=0.015), chest pain (P=0.039), and dry throat (P=0.029)(11).

Exposure to dust, mold, other pollutants

The study by Kearney et al. (2014) stated that a significant association was shown between mold and coughed up phlegm when not having a cold (P=0.0262), mold and asthma (P=0.0084), and pesticides used in the home and tightness of chest (P=0.001)(48). In addition, the study by Faria et al. (2006) found that exposure to high concentrations of dust had a higher risk of asthma (OR=1.71, 95%CI=1.10-2.67) and chronic respiratory disease (OR=1.77, 95%CI=1.25-2.50)(49).

Limitations

There were some limitations from the reviewed studies. First, a large number of studies were cross-sectional studies. A cross-sectional study could not establish the causal relationship between pesticide exposure and respiratory outcomes, but it can only suggest the association (4, 28,34,37). Second, most studies assessed pesticide exposure by using a questionnaire, but few studies assessed by determining specific pesticides and their metabolites in biological fluids. Consequently, available evidence included a lack of information of specific pesticides influencing respiratory outcomes. Generally, respiratory outcomes may be caused by exposure to several pesticides or chemicals. However, some studies investigated only one or two specific pesticide exposures, resulting in misleading interpretations. In addition, recall bias may be possible because farmers or farmworkers may not recall the information regarding pesticide use or frequency of use in the past (6,50). Third, most studies assessed respiratory outcomes by using self-reported diseases or symptoms, but few studies assessed by physician diagnosis. A self-report without further diagnosis is a subjective measure that could have errors as well, leading to underestimation or overestimation of the prevalence. In addition, recall bias may have occurred. Some relationship between pesticide exposure and outcomes might be due to a bias in reporting (49,51). Fourth, a small sample size may not be representative of all study populations and reduce the power in statistical analysis (28,44,48). Fifth, the sampling method of some studies, convenience or purposive sampling method, was not selected at random, resulting in non-representation of all study populations (18,50,51). Finally, several co-factors and confounding factors contribute to respiratory outcomes. Smoking, age, gender, and others were identified as important determinations of respiratory health. Therefore, when the researchers aimed to assess respiratory outcomes as a result of pesticide exposure, co-factors and confounding factors should be considered, controlled, or adjusted for statistical analysis (52).

CONCLUSION

The evidence from these review studies suggested an association between pesticide exposure and respiratory outcomes among farmers and farmworkers. Twenty-nine specific pesticides were found to have an association with respiratory diseases and 49 specific pesticides with respiratory symptoms. In addition, 14 pesticides had an association with both respiratory diseases and symptoms (seven for herbicides, six for insecticides, and one for fungicide).

These 14 pesticides were: 2,4-D, chlorimuron-ethyl, EPTC, glyphosate, paraquat, pendimethalin, petroleum oil, dichorvos, malathion, parathion, phorate, carbaryl, permethrin, and metalaxyl. Therefore, it is reasonable to concern these effects in people who have been exposed to these pesticides. However, there were several limitations for the reviewed studies. Toward a better quality for future research, prospective study, standardized tools for exposure and outcome assessment, appropriate sample size and sampling method, and controlled confounding factors, should be thoroughly considered.

ACKNOWLEDGEMENTS

This study was supported by the Thailand Science Research and Innovation Grant (Grant no.RSA6280030), and Faculty of Medicine Research Fund, Chiang Mai University (Grant no.MT 02/62). We are grateful to Miss Sudthinee Sidthilaw for evaluating the research articles. We are also grateful to the Research Administration Section, Faculty of Medicine, Chiang Mai University for editing the manuscript.

REFERENCES

1. Mostafalou S, Abdollahi M. Pesticides: an update of human exposure and toxicity. Arch Toxicol. 2017; 91(2):549-599.
2. Quansah R, Bend JR, Abdul-Rahaman A, Armah FA, Luginaah I, Essumang D et al. Associations between pesticide use and respiratory symptoms: a cross-sectional study in Southern Ghana. Environ Res. 2016;150:245-254.
3. Hoppin JA, Umbach DM, London SJ, Henneberger PK, Kullman GJ, Alavanja MC, et al. Pesticides and atopic and nonatopic asthma among farm women in the Agricultural Health Study. Am.J.Respir.Crit. Care Med. 2008; 177(1):11-18.
4. Hoppin JA, Umbach DM, London SJ, Henneberger PK, Kullman GJ, Coble J, et al. Pesticide use and adult-onset asthma among male farmers in the Agricultural Health Study. Eur.Respir. J. 2009; 34(6):1296-1303.
5. Henneberger PK, Liang X, London SJ, Umbach DM, Sandler DP, Hoppin JA. Exacerbation of symptoms in agricultural pesticide applicators with asthma. International. Arch Environ Occup Health. 2014;87(4):423-432.
6. Chakraborty S, Mukherjee S, Roychoudhury S, Siddique S, Lahiri T, Ray MR. Chronic exposures to cholinesterase-inhibiting pesticides adversely affect respiratory health of agricultural workers in India. J.Occup.Health. 2009;51(6):488-497.
7. Zhu X, Gao P, Gu Y, Xiao P, Liu M, Chen J, et al. Positive rates and factors associated with abnormal lung function of greenhouse workers in China: a cross-sectional study. Int.J.Environ.Res.Public Health. 2017;14(9):pii: E956.
8. Sapbamrer R, Thongtip S, Khacha-Ananda S, Sittitoon N, Wunnapuk K. Changes in lung function and respiratory symptoms during pesticide spraying season among male sprayers. Arch Environ Occup Health. 2019; Epub 2019/03/21.
9. Hoppin JA, Umbach DM, Long S, London SJ, Henneberger PK, Blair A, et al. Pesticides are associated with allergic and non-allergic wheeze among male farmers. Environ.Health Perspect. 2017;125(4):535-543.
10. Sapbamrer R, Nata S. Health symptoms related to

pesticide exposure and agricultural tasks among rice farmers from Northern Thailand. Environ. health Prev.Medicine. 2014;19(1):12-20
11. Sapbamrer R, Hongsibsong S, Kerdnoi T. Urinary dialkylphosphate metabolites and health symptoms among farmers in Thailand. Arch.Environ.Occup. Health. 2017;72(3):145-152.
12. Karjalainen A, Kurppa K, Martikainen R, Klaukka T, Karjalainen J. Work is related to a substantial portion of adult-onset asthma incidence in the Finnish population. Am.J.Respir.Crit.Care Med.2001;164(4):565-568.
13. Mamane A, Baldi I, Tessier JF, Raherison C, Bouvier G. Occupational exposure to pesticides and respiratory health. Eur.Respir. Rev.2015;24(136):306-319.
14. Ye M, Beach J, Martin JW, Senthilselvan A. Occupational pesticide exposures and respiratory health. Int.J.Environ.Res.Public Health. 2013;10(12):6442-6471.
15. Eduard W, Omenaas E, Bakke PS, Douwes J, Heederik D. Atopic and non-atopic asthma in a farming and a general population. Am.J.Ind.Med. 2004;46(4):396-399.
16. Dalphin JC, Dubiez A, Monnet E, Gora D, Westeel V, Pernet D, et al. Prevalence of asthma and respiratory symptoms in dairy farmers in the French province of the Doubs. Am.J.Respir.Crit.Care Med. 1998; 158:1493-1498.
17. Boers D, van Amelsvoort L, Colosio C, Corsini E, Fustinoni S, Campo L, et al. Asthmatic symptoms after exposure to ethylenebisdithiocarbamates and other pesticides in the Europit field studies. Hum. Exp.Toxicol.2008; 27(9):721-727.
18. Jones SM, Burks AW, Spencer HJ, Lensing S, Roberson PK, Gandy J, et al. Occupational asthma symptoms and respiratory function among aerial pesticide applicators. Am.J.Ind.Med. 2003; 43(4):407-417.
19. Hern6ndez AF, Casado I, Pena G, Gil F, Villanueva E, Pla A. Low level of exposure to pesticides leads to lung dysfunction in occupationally exposed subjects. Inhal.Toxicol. 2008;20(9):839-849.
20. Negatu B, Kromhout H, Mekonnen Y, Vermeulen R. Occupational pesticide exposure and respiratory health: a large-scale cross-sectional study in three commercial farming systems in Ethiopia. Thorax. 2017;72(6):498-499.
21. Fareed M, Pathak MK, Bihari V, Kamal R, Srivastava AK, Kesavachandran CN. Adverse respiratory health and hematological alterations among agricultural workers occupationally exposed to organophosphate pesticides: a cross-sectional study in North India. PLoS One. 2013;8(7):e69755.
22. Mekonnen Y, Agonafir T. Effects of pesticide applications on respiratory health of Ethiopian farm workers. Int.J.Occup.Environ.Health. 2002;8(1):35-40.
23. Peiris-John RJ, Ruberu DK, Wickremasinghe AR, van-der-Hoek W. Low-level exposure to organophosphate pesticides leads to restrictive lung dysfunction. Respir.Med. 2005;99(10):1319-1324.
24. Cha ES, Lee YK, Moon EK, Kim YB, Lee YJ, Jeong WC, et al. Paraquat application and respiratory health effects among South Korean farmers. Occup. Environ.Med. 2012;69(6):398-403.
25. Schenker MB, Stoecklin M, Lee K, Lupercio R, Zeballos RJ, Enright P, et al. Pulmonary function and exercise-associated changes with chronic low-level paraquat exposure. Am.J.Respir.Crit.Care Med. 2004;170(7):773-779.
26. Sutoluk Z, Kekec Z, Daglioglu N, Hant I. Association of chronic pesticide exposure with serum cholinesterase levels and pulmonary functions. Arch..Environ.Occup.Health.2011;66(2):95-99.
27. Priyadharshini UK, Latha R, Kavitha U, Nirmala N. Effects of Organophosphorus pesticides on cardiorespiratory parameters among the farmers. J.Clin.Diagn.Res.2017; 11(9):CC01-CC04.
28. Callahan CL, Al-Batanony M, Ismail AA, Abdel-Rasoul G, Hendy O, Olson JR, et al. Chlorpyrifos exposure and respiratory health among adolescent agricultural workers. Int.J.Environ.Res.Public Health.2014;11(12):13117-13129.
29. Valcin M, Henneberger PK, Kullman GJ, Umbach DM, London SJ, Alavanja MC, et al. Chronic bronchitis among nonsmoking farm women in the agricultural health study. J.Occup.Environ. Med.2007;49(5):574-583.
30. Hoppin JA, Valcin M, Henneberger PK, Kullman GJ, Umbach DM, London SJ, et al. Pesticide use and chronic bronchitis among farmers in the Agricultural Health Study. Am.J.Ind.Med. 2007;50(12):969-979.
31. Hoppin JA, Umbach, DM, London SJ, Alavanja MC, Sandler DP. Chemical predictors of wheeze among farmer pesticide applicators in the Agricultural Health Study. Am.J.Respir.Crit.Care Med.2002;165(5):683-639.
32. Hoppin JA, Umbach DM, London SJ, Lynch CF, Alavanja MC, Sandler DP. Pesticides and adult respiratory outcomes in the agricultural health study. Ann.NY Acad. Sci. 2006a;1076:343-354.
33. Hoppin JA, Umbach DM, London SJ, Lynch CF, Alavanja MC, Sandler DP. Pesticides associated with wheeze among commercial pesticide applicators in the Agricultural Health Study. Am.J.Epidemiol.2006b;163(12):1129-1137.
34. Fieten KB, Kromhout H, Heederik D, van Wendel de Joode B. Pesticide exposure and respiratory health of indigenous women in Costa Rica. Am.J.Epidemiol. 2009;169(12):1500-1506.
35. Hudson NL, Kasner EJ, Beckman J, Mehler L, Schwartz A, Higgins S, et al. Characteristics and magnitude of acute pesticide-related illnesses and injuries associated with pyrethrin and pyrethroid exposures--11 states, 2000-2008. Am.J.Ind.

Med.2014; 57(1):15-30.
36. Castro-Gutiйrrez N, McConnell R, Andersson K, Pacheco-Antyn F, Hogstedt C. Respiratory symptoms, spirometry and chronic occupational paraquat exposure. Scand.J.Work Environ. Health.1997; 23(6):421-427.
37. Chatzi L, Alegakis A, Tzanakis N, Siafakas N, Kogevinas M, Lionis C. Association of allergic rhinitis with pesticide use among grape farmers in Crete, Greece. Occup.Environ.Med.2007;64(6):417-421.
38. Faria NM, Facchini LA, Fassa AG, Tomasi E. Pesticides and respiratory symptoms among farmers. Rev. Saude Publica.2005;39(6):973-981.
39. Stoecklin-Marois MT, Bigham CW, Bennett D, Tancredi DJ, Schenker MB. Occupational exposures and migration factors associated with respiratory health in California Latino farm workers: the MICASA study. J.Occup.Environ.Med. 2015; 57(2):152-158.
40. Hoppin JA, Umbach DM, London SJ, Alavanja MC, Sandler DP. Animal production and wheeze in the Agricultural Health Study: interactions with atopy, asthma, and smoking. Occup.Environ. Med.2003;60(8):e3.
41. Tual S, Clin B, Levкque-Morlais N, Raherison C, Baldi I, Lebailly P. Agricultural exposures and chronic bronchitis: findings from the AGRICAN (Agriculture and Cancer) cohort. Ann.Epidemiol. 2013;23(9):539-545.
42. Hayes JP, Rooney J. The prevalence of respiratory symptoms among mushroom workers in Ireland. Occup.Med.(London).2014:64(7):533-538.
43. Hanssen VM, Nigatu AW, Zeleke ZK, Moen BE, Bretveit M. High prevalence of respiratory and dermal symptoms among Ethiopian flower farm workers. Arch.Environ.Occup. Health.2015;70(4):204-213.
44. Ndlovu V, Dalvie MA, Jeebhay MF. Asthma associated with pesticide exposure among women in rural Western Cape of South Africa. Am.J.Ind. Med. 2014;57(12):1331-1343.
45. Fiori NS, Fassa AG, Faria NM, Meucci RD, Miranda VI, Christiani DC. Wheezing in tobacco farm workers in southern Brazil. Am.J.Ind. Med.2015;58(11):1217-1228.
46. Buralli RJ, Ribeiro H, Mauad T, Amato-Lourenзo LF, Salge JM, Diaz-Quijano FA, et al. Respiratory condition of family farmers exposed to pesticides in the State of Rio de Janeiro, Brazil. Int.J.Environ. Res.Public Health.2018;15(6):pii: E1203.
47. Thetkathuek A, Jaidee W. Factors that contribute to insecticide poisoning among immigrant agricultural. Int.J.Occup.Environ.Health.2017;23:60-70.
48. Kearney GD, Chatterjee AB, Talton J, Chen H, Quandt SA, Summers P, et al. The association of respiratory symptoms and indoor housing conditions among migrant farmworkers in eastern North Carolina. J.Agromedicine.2014;19(4):395-405.
49. Faria NM, Facchini LA, Fassa AG, Tomasi E. Farm work, dust exposure and respiratory symptoms among farmers. Rev.Saude Publica.2006;40(5):827-836.
50. Desalu O, Busari O, Adeoti A. Respiratory symptoms among crop farmers exposed to agricultural pesticide in three rural communities in South Western Nigeria: a preliminary study. Ann. Med.Health Sci.Res.2014;4(4):662-666.
51. Kishi M, Hirschhorn N, Djajadisastra M, Satterlee LN, Strowman S, Dilts R. Relationship of pesticide spraying to signs and symptoms in Indonesian farmers. Scand.J.Work Environ. Health.1995;21(2):124-133.
52. Zhang LX, Enarson DA, He GX, Li B, Chan-Yeung M. Occupational and environmental risk factors for respiratory symptoms in rural Beijing, China. Eur.Respir.J.2002;20(6):1525-1531.