

Table S1: Effects of pesticides on the respiratory health of agricultural workers: cross-sectional and case / control studies

References ; Country ; Study type	Population	Pesticide	Indicators of exposure	Health outcomes	Result	Adjustment factors
Respiratory diseases (asthma and bronchitis)						
Senthilselva n [25], 1992, Canada	1939 farmers Men : only , Mean age : 45.2 years	Insecticides : organophosphates, organochlorines, carbamates.	Face to face questionnaire: use of pesticides and fertilizers during the last 5 years.	Face to face questionnaire based on ATS-DLD (respiratory symptoms – determine self-report) Pulmonary function (spirometry): FVC, FEV1, FEF ₂₅₋₇₅ following ATS guidelines	significant association with carbamate insecticide use and asthma (OR=1.8; 95% CI 1.1-3.1) In Asthmatics significant lower mean values of pulmonary function: FEV1 (p=0.01) and FEF ₂₅₋₇₅ (p=0.001) than in non asthmatics.	Age, smoking habit
Kang [26], 2006, USA	1,499 Vietnam veterans (exposure to Agent Orange) (mean age: 53 years) and a group of 1,428 non-Vietnam veterans (mean age: 51 years)	Sprayed herbicides (Agent Orange) with contaminant 2,3,7, 8-tetrachlorodibenzo- p-dioxin (TCDD or dioxin) for military purposes.	serum dioxin levels.	Self-reported data : computer-assisted telephone interview (CATI); chronic medical condition diagnosed by physician	Prevalence of chronic bronchitis, asthma, emphysema, pleurisy, or tuberculosis (OR=1.62; 95%CI 1.28-2.05) significantly elevated among Vietnam veteran who sprayed herbicides vs non Vietnam veterans. Prevalence of “respiratory problems” was similar in low TCDD group (<2.5ppt) and in high TCDD group (≥2.5 group).	Age, race, body mass index, rank, and regular smoking.
Bener [27] 1999, United Arab Emirates	Men: only 98 farmers exposed to pesticide (mean age: 33.02) and 98 controls (non-farmers) (mean age: 34.02). Men : only	pesticides (not specified)	Face to face questionnaire to collected information on using fertilizer or exposed to pesticide.	Face to face questionnaire based on BMRC (respiratory symptoms - covering the life history of the subject’s). Pulmonary function (spirometry: FVC, FEV ₁ , FEV ₁ /FVC, FEF ₂₅₋₇₅) following ATS guidelines	Higher prevalence of chronic cough (OR=2.96 ; 95% CI 1.44-6.19), CB (OR=1.38 ; 95% CI 1.09-1.78) and asthma (OR=1.8 ; 95% CI 1.01-3.01) in farmers than in controls. All spirometry parameters reduced in farmers compared to the reference group.	
Salameh* [28], 2006, Lebanon Case-control	245 cases of asthma (Men: 52.9%, mean age: 36.2 years) and 262 controls (Men: 44.3%, mean age: 37.6 years) recruited from hospital centre	Pesticides (not specified)	Self-report questionnaire :occupational, regional, local and domestic pesticide exposures. A détailler	Self-report questionnaire based on ATS-DLD (respiratory symptoms asthma- during life) confirmation by pulmonologist during the study	Any exposure to pesticides associated to asthma (OR=2.11; 95% CI 1.47-3.02), occupational use having the highest association (OR=4.98; 95% CI 1.07-23.28). Results confirmed by multivariate analysis, particularly for regional exposure (OR=2.78 ; 95% CI 1.18-6.67) and household exposure (OR=2.17; 95% CI 1.37-3.50).	Age, education, nationality, working in dust or toxic fumes
Salameh* [56], 2006, Lebanon	110 cases of CB(Men: 65.5%, mean age: 50.7 years) and 262 controls	Pesticides (not specified)	Self-report questionnaire: occupational, regional, local and domestic pesticide	Self-report questionnaire based on ATS-DLD (respiratory symptoms	Any exposure to pesticides associated to chronic bronchitis (OR=2.46; 95% CI 1.53- 3.94),occupational having the highest	Age, sex, smoker, education

Case-control	(Men: 44.3%, mean age: 37.6 years) recruited from hospital centre		exposures.	chronic bronchitis- during life) - confirmation by pulmonologist during the study	association (OR=15.92; 95% CI 3.50-72.41). Significant increase in the risk of chronic bronchitis according to increase in intensity and/or duration of different levels of exposure to pesticides.	
Respiratory symptoms						
Zuskin [30], 1993, Croatia	174 exposed (135 female, mean age 36 years; 32 male, mean age 33 years) workers in greenhouses and 115 unexposed workers (51 female, mean age 33 years; 30 male, mean age 29 years) employed as office workers	pesticides (not specified)	Face to face questionnaire	Face to face questionnaire based on the BMRC : lifelong respiratory symptoms Pulmonary function (spirometry: FVC, FEV1, FEF ₂₅ , FEF ₇₅) following ATS guidelines	higher prevalence of chronic cough, dyspnea, chest tightness in exposed women / controls(p<0.01) Workers: significant lower mean ventilation capacity measurements (except in the case of FVC) compared to standard predicted values	Age, sex, smoking habit and duration of employment
Zuskin [31], 1997, Croatia	174 exposed (vineyard and orchard workers) and 115 unexposed workers (employed in the food industry) Men only Age: 18-59 years	pesticides (not specified)	Face to face questionnaire	Face to face questionnaire based on the BMRC Pulmonary function measures (spirometry: FVC, FEV ₁ , FEF ₂₅ , FEF ₇₅) following ATS guidelines	Significant differences for dyspnea and chest tightness (p< 0.01), chronic cough and chronic phlegm (p<0.05). Higher significant prevalence of cough in smokers (p< 0.05) in workers employed for more than 10 years. Significant differences between measured and predicted FEV ₁ , FEF ₅₀ , and FEF ₂₅ in workers employed for more than 10 years.	Age, smoking habit and duration of employment
Castro-Gutiérrez [32], 1997, Nicaragua	134 (Men : 100, Women : 34) workers paraquat exposed and 152 (Men : 88, Women : 34) unexposed workers.	Herbicide: paraquat	Face to face questionnaire: cumulative exposure of paraquat knapsack sprayers for 24 months.	Face to face questionnaire based on the BMRC (respiratory symptoms - during the last 24 months). Pulmonary function measures (spirometry: FVC, FEV ₁) following ATS guidelines	Consistent dose-response relationship according to intensity of exposure, relationship more marked for more severe dyspnea (OR=4.6; 95% CI 2.4-9.0). Increase in episodic wheezing accompanied by shortness of breath (OR=2.9 ; 95% CI 1.4-6.3) among the more intensely exposed workers .	Age, sex, smoking history
Wilkins [33], 1999, USA	1793 farmers in the Ohio Farm Family Health and Hazard Surveillance Project (FFHHSP) Men :only Mean age : 54 years	pesticides (not specified)	Self-report questionnaire by mail and telephone follow-up: farm characteristics and farming practices during the past 12 months.	Self-report questionnaire based on ATS-DLD (respiratory symptoms - during the last 12 months) by mail.	Association of lifetime cab tractor operations (1 to 3,599 hours) with chronic cough: OR=3.34; 95% CI 1.03-0.83.	Age, smoking

Sprince [34], 2000, USA	385 farmers in the Iowa Farm Family Health and Hazard Surveillance Project (FFHHSP) Men :only Mean age : 54 years	Agricultural pesticides (insecticide to crops and livestock, herbicides)	Self-report questionnaire by mail and telephone follow-up : pesticide applications /exposure to crops, to livestock and hand/arms contact with pesticides during the past 12 months.	Self-report questionnaire based on ATS-DLD (respiratory symptoms - during the last 12 months) by mail.	Applying pesticides to livestock associated with: phlegm (OR=1.91, 95% CI 1.02-3.57), chest ever wheezy (OR=3.92, 95% CI 1.76-8.72), flu-like symptoms (OR=2.93, 95% CI 1.69-5.12)	Age, smoking
Beseler [35], 2009 USA	761 farm operators and their spouses farm residents enrolled in the Colorado Farm Family Health and Hazard Survey (CFFHHS). Men : 60.4 % Mean age: 50.5 years	Agricultural pesticides (not specified)	Face to face questionnaire: - pesticide poisoning diagnosed by physician - detailed information on work tasks during spraying season June, July, August; - use of personal protective equipment	Face to face questionnaire to report history of respiratory disorders and symptoms Pulmonary function (spirometry: FVC, FEV1/FVC)	Pesticide poisoning - in current smokers : significantly associated with wheeze (n=79, OR=8.21; IC95% 1.28-52.6) and reduced FVC (n=17, p = 0.01). - in non-smokers: significantly associated with cough (OR=2,18 ; IC95% 1,03-4,64).	Age, sex
Masley [29], 2000, Canada	511 men, 499 women, and 393 children (<18 years of age) residing in 549 households in the rural study area of the families living in the Prairie Echo Study (PECOS) mean age adult : 49,4 years	Pesticides and fertilizers : herbicides, insecticides, fungicides, granular fertilizer, liquid fertilizer and manure	Self-report questionnaire by mail : contact with pesticides and fertilizers through home or garden use	Self-report questionnaire based on ATS-DLD (respiratory symptoms - during life)	Pesticide exposure associated with the presence of one or more respiratory symptoms (cough, phlegm, wheeze or shortness of breath) (OR=2.4, 95% CI 1.1-5.2) and with bronchitis (OR=4.3, 95% CI 2.0-9.4) in women. Children from non-farming households: higher frequency of bronchitis (35.1%) than children from farming households (16.5%) (OR=2.6, 95% CI 1.1-5.8).	Age, sex, current residence and smoking
Schenker [37], 2004, Costa Rica	219 farm workers (paraquat handlers) and 110 controls (nonhandlers) working from banana, coffee and palm oil farms in the Study of agricultural lung disease (SALUD) Men: only Mean age: 37 years	Herbicide: paraquat	Face to face questionnaire : work history (handling of paraquat in each job, length of employment, type of crop, use of personal protective equipment) cumulative paraquat exposure index based on work history.	Face to face questionnaire based on ATS-DLD (respiratory symptoms – determine self-report) Pulmonary function measures (spirometry: TLC, DLCO, FVC, FEV ₁ /FVC, VO ₂ , and VE/VCO ₂) following ATS guidelines	Each unit increase in the total cumulative paraquat index associated with a 1.8 increase in the odds of chronic cough (95% CI 1.0–3.1) and a 2.3 increased odds of shortness of breath with wheeze (95% CI 1.2–5.1), but not significantly associated with CB persistent wheeze, or ever having a diagnosis of asthma.	Age and current smoking.
Fieten [38], 2009, Costa Rica	69 exposed worked (on plantain plantations where pesticides were used) and 58 unexposed participants.	Agricultural OPs insecticides (terbufos and chlorpyrifos) and bipyridylum herbicide (paraquat)	Face to face questionnaire: pesticide use = frequency (average days a week during the period of use) and duration (number of years).	Face to face questionnaire based on ECRHS (respiratory symptoms – self-report covering the last year).	Among nonsmokers: wheeze associated with exposure to the OP insecticides chlorpyrifos (OR=6.7; 95%CI 1.6-28.0) and terbufos (OR=5.9, 95%CI 1.4-25.6). No difference in prevalence of chronic cough, asthma, according	Age and atopic symptoms,

	Women: only Aged: 24-58 years		Cumulative exposure (frequency of exposure per year, and number of lifetime days of pesticide application).	Pulmonary function (spirometry: FVC and FEV ₁) following MIR guidelines.	to the cumulative exposure estimate	
Faria [39], 2005, Brasil	1379 farms from 2 municipalities of southern Brazil with at least 15 hours of weekly agricultural activity	Agricultural pesticides : OPs, pyrethroids, triazines, dithiocarbamates, paraquat ...	Face to face questionnaire based the self-reported of pesticide use at their place of the subject's work.	Face to face questionnaire based on ATS-DLD (respiratory symptoms – determine self-report of asthma and chronic respiratory disease)	Pesticide poisoning associated with higher prevalence of asthma symptoms (OR=1.64; 95% CI: 1.04-2.58) and chronic respiratory disease symptoms (OR=1.57; 95% CI: 1.08-2.28).	Age, sex, schooling, marital status, smoking, socioeconomic indicators, years of chemical exposure.
Ejigu [40], 2005, Ethiopia	Men : 55 % Mean age: 42 years 82 farm workers (pesticide sprayers) and 47 controls (unexposed) working on 2 farms	Agricultural pesticides (not specified)	Face to face questionnaire based the self-reported of pesticide use - use of personal protective equipment	Face to face questionnaire based on BMRC (respiratory symptoms - covering the life history of the subject's)	Prevalence of respiratory symptoms, including cough, phlegm, and wheeze significantly higher in farm workers than in controls (p < 0.05).	
Pathak [41], 2011, India	Men: only Mean age: 34 years 108 Pesticide sprayers (42 knapsack sprayers and 66 tractor-mounted sprayers) et 30 control subjects	Types of pesticide used: chlorpyrifos, monocrotophos, dichlorvos, malathion, endosulfan, methyl parathion and cypermethrin	Face to face questionnaire: blood AChE activity levels - Use of personal protective equipment	Face to face questionnaire to report of respiratory symptoms without any precision	Tractor-mounted sprayers compared to controls: OR significantly raised for respiratory symptoms (OR= 5.14 ; 95% CI 1–29). Activity of AChE significantly (p= 0.001) lower in exposed groups (tractor-mounted and knapsack sprayers) than in controls AChE depletion greater in tractor-mounted sprayers than in knapsack sprayers (p=0.001).	
Ngowi [42], 2001, Tanzania	Men : only, Aged : 18-55 years 133 subjects on coffee farmworkers in 1991-1992	Agricultural pesticides: fungicide, insecticide and herbicide.	Face to face questionnaire: - short term exposure were conducted similarly during spraying and nonspraying seasons - Use of personal protective equipment	Face to face questionnaire to report of symptoms during spraying and nonspraying seasons	No significant difference for prevalence of cough between spraying and nonspraying periods (p=0.69). No significant difference in AChE activity during spraying and nonspraying periods.	
Jones [43], 2003, USA	Men : only, Mean age m : 41 years 100 exposed pesticide aviators (Men : 85 % ; mean age : 43 years) and 100 controls (unexposed Men : 91 % ; mean age : 42 years)	Agricultural pesticides: methyl parathion, lambda-cyhalothrin, profenofos, acephate, cyfluthrin, azinphos-methyl, oxamyl, methomyl, and thiodicarb.	Self-report questionnaire: -Short term exposure : during the study days (7 to 14 days)	Self-report questionnaire based on ATS-DLD (respiratory symptoms - during life). Pulmonary function (spirometry during same study days) following ATS recommendation.	Prevalence of reported asthma symptoms and lung function measures similar between exposed aviators and controls.	

Abu Sham'a [44], 2010, Palestine	N : 250 farmers, Men : only, Aged: 22-77 years.	Agricultural pesticides list not specified not except for OPs	Face to face questionnaire: - Short term exposure: « Spraying pesticides now? » (yes/no) - Index of exposure « hours spray pesticide per year » - Use of personal protective equipment	Face to face questionnaire based on ATS-DLD (respiratory symptoms - during the last 12 months). Pulmonary function (spirometry) following ERS recommendation.	No association between present spraying pesticides and cough with phlegm (OR=1.14 ; 95% CI 0.98-1.33) and wheezy chest (OR=0.95 ; 95% CI 0.88-1.01). No association between organophosphate use with cough with phlegm (OR=1.17; 95% CI 0.84-1.61) and wheezy chest (OR=1.13; 95% CI 0.75-1.70).	Age, BMI, duration of farming, education, PPE, Have animals, Smoking
Respiratory function						
Mekonnen [45], 2004, Ethiopia	102 pesticide sprayers in state farms and 69 non sprayers. No smokers, Men : only, Aged : 15-44 years	Pesticide applied on the farms : chlorpyrifos, diazinon and malathion	Face to face questionnaire: to report spraying pesticide (season) of the plantations during 1999/2000.	Face to face questionnaire based on BMRC (respiratory symptoms - during the last 12 months). Pulmonary function (spirometry) following ATS recommendation.	decreased or abnormal respiratory function (FVC, FEV1) was found in the 15-24 years age group of pesticide sprayers as compared to that of similar age group non-sprayers	
Hernandez [46], 2008, Spain	89 exposed (pesticide sprayers) and 25 unexposed farm workers in intensive agricultural area of plastic greenhouses Men : 57,1 % Mean age: 37,1 years	10 agricultural individual or groups of pesticides: neonicotino ids, abamectin, OPs, carbamates, dithiocarbamates, endosulfan, oxadixyl, xythioquinox, phenylureas and bipyridiliums	Face to face questionnaire : - use of pesticide during the current crop season serum measurement of PChE and AChE level - short term exposure : based on depression of cholinesterase (PChE, AChE) - long-term exposure: lifelong cumulative index for each worker - use of personal protective equipment	Face to face questionnaire To report symptoms attributable to pesticide exposure in the last 2 years and physical examination during the peak spraying season. - chest radiographs - Pulmonary function measures (spirometry: TLC, RV, and FRC) following ERS guidelines	Lifelong cumulative exposure to pesticides (sprayers only): reduction in FEF 25-75 Recent exposure to bipyridiliums: associated with a fall in the diffusing capacity of the lungs (alveolar function) Recent exposure to neonicotinoids: associated with lower lung volumes (restrictive disease). Endosulfan use associated with respiratory symptoms (OR=3,68 ; IC95% 1,16-11,68).	Age, sex, smoking, body mass index (BMI), alcohol consumption, PON1 polymorphism, ChE depression and sprayer status
Chakraborty [47], 2009, India	376 exposed agricultural (mean age: 41 years) and 348 controls group (mean age: 40 years) unexposed agricultural workers residing the rural villages. Men : only, Non-smokers,	Agricultural pesticides (eastern India) Organophosphate (methyl-parathion, phosphamidon, dichlorvos monocrotophos, carbaryl, chlorpyrifos, dimethoate) and carbamate (carbofuran) insecticides	Face to face questionnaire : frequency and duration of spraying - regular exposure : « Sprayed for at least an hour a day, 5 days a month for the past 5 years » - occasional exposure : « Sprayed less regular exposure ». blood AChE activity levels	Face to face questionnaire based on BMRC and ATS-DLD (respiratory symptoms - covering the last 12 months). Pulmonary function measures (spirometry during) following ATS guidelines	Higher prevalence of upper and lower respiratory symptoms (wheeze, cough, dyspnea) and higher reduction of lung function in exposed workers than in controls (p < 0.001). Diagnosis of COPD made in 10.9% of workers versus in 3.4% of controls (p < 0.05).	

Cha [48], 2012, South Korea	2508 paraquat applying farmers (Men : 69,7 % ; aged older than 60 years 72%) and 374 non-paraquat-applying farmers (Men : 52,9 % ; aged older than 60 years 68%)	Herbicide: paraquat	Face to face questionnaire: ever/never application, number of years of application, number of annual days of application lifetime days of application. - Use of personal protective equipment	Face to face questionnaire to report of doctor diagnosed symptoms / diseases: COPD, asthma - during life. Pulmonary function measures (spirometry during) following ATS guidelines	Significant exposure-response relationships between restrictive ventilatory defect and: - paraquat application years (OR=1.89 ; IC95% 1.11-3.24) - lifetime paraquat application days (OR=1.76 ; IC95% 1.04-2.98).	Age, gender, distance from the oil spill site, smoking status, alcohol consumption, level of education and the cumulative exposure of paraquat.
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*case-control study

ERS: European Respiratory Society

ATS-DLD : American Thoracic Society and the Division of Lung Diseases

BMRC: British Medical Research Council

ECRHS: European Community Respiratory Health Survey

MIR Medical International Research –Rome, Italy

Respiratory function measures :(FVC, FEV₁, FEV₁ to FVC ratio, FEF_{25-75%}, TLC, and RV)

Table S2: respiratory health of agricultural workers: longitudinal studies

References ; Country ; Study type	Population	Pesticide	Indicators of exposure	Health outcomes	Result	Adjustment factors
Asthma and wheeze						
Hoppin [50], 2002, USA : Iowa and North Carolina.	20,468 pesticide applicators (farmers) including 3,838 farmer having reported wheezing in the past year and 16,630 farmers who did not - Men : 98% - Aged : 16-88 years	40 pesticides selected among the most heavily used in Iowa and North Carolina: herbicides (n=16), insecticides (n=16), fungicides (n=6), fumigants (n=2).	Self-administered first questionnaire by mail: - specific chemicals used in the year before enrollment, - pesticide application methods, - current agricultural activities,	Second questionnaire: self-report of wheeze in the previous year based on the question “How many episodes of wheezing in your chest have you had in the past 12 months?”	Wheezing: highest odds ratios with paraquat, parathion, malathion, chlorpyrifos, and <i>S</i> -ethyl-dipropylthiocarbamate (EPTC) highest OR for Parathion (OR=1.5; 95% CI 1.0- 2.2). Wheezing: significant dose–response trends for atrazine, chlorpyrifos and parathion applying atrazine more than 20 days/year : OR = 1.5 (95% CI 1.2-1.9)	Age, state, smoking and asthma.

Hoppin [51], 2006, USA : Iowa and North Carolina.	17,920 pesticide applicators (Men : 97%) and 2.255 commercial pesticide applicators (Men : 95%) Aged : 16-88 years	40 pesticides selected among the most heavily used in Iowa and North Carolina: herbicides (n=16), insecticides (n=16), fungicides (n=6), fumigants (n=2).	Self-administered first questionnaire by mail: exposures during the year before enrollment. - lifetime use of the pesticides : ever use, use during the past year, frequency of use, and total number of years used. - current agricultural activities. - use of personal protective equipment.	Second questionnaire: self-report of wheeze in the previous year based on the question “How many episodes of wheezing in your chest have you had in the past 12 months?”	In farmers: 5 of 40 pesticides (alachlor, EPTC, atrazine, petroleum oil, trifluralin) used in the past year significantly associated with wheeze. In commercial applicators: 3 of 36 pesticides (chlorimuron-ethyl, dichlorvos, and phorate) associated with wheeze. applying chlorpyrifos more than 20 days /year: associated with wheeze in farmers (OR=1.48; 95% CI 1.00-2.19) and commercial applicators (OR=1.96 95% CI 1.05-3.66). 8 of 16 herbicides associated with wheeze in single-agent models; risk almost associated with chlorimuron-ethyl (OR=1.62; 95% CI 1.25- 2.10). Dose-response trends observed for chlorimuron-ethyl, chlorpyrifos, and phorate; the strongest odds ratio being for applying chlorpyrifos on more than 40 days per year (OR=2.40; 95% CI 1.24-4.65).	Age, BMI, smoking status, and asthma-atopy status.
Hoppin [52], 2006, USA : Iowa	2,255 commercial pesticide applicators Men : 95% Aged : 17-83 years	40 pesticides selected among the most heavily used in Iowa and North Carolina: herbicides (n=16), insecticides (n=16), fungicides (n=6), fumigants (n=2).	Self-administered first questionnaire by mail: exposures during the year before enrollment. - lifetime use of the pesticides : on ever use, use during the past year, frequency of use, and total number of years used. - current agricultural activities. - use personal protective equipment.	Second questionnaire: self-report of respiratory symptoms: wheeze, asthma (self-report of a doctor’s diagnosis).	8 of 16 herbicides associated with wheeze in single-agent models; risk almost associated with chlorimuron-ethyl (OR=1.62; 95% CI 1.25- 2.10). Dose-response trends observed for chlorimuron-ethyl, chlorpyrifos, and phorate; the strongest odds ratio being for applying chlorpyrifos on more than 40 days per year (OR=2.40; 95% CI 1.24-4.65).	Age, smoking status, asthma/atopy status, body mass index, and previous use of the pesticide.
Hoppin [53], 2008, USA : Iowa and North Carolina.	25,814 farm women, including 702 cases of asthma and 25,112 control subjects, Women: only Aged : 20-88 years	50 specific pesticides	Self-administered questionnaire by mail (81%) or telephone interview (19%): - lifetime use of the pesticides : on ever use, use during the past year, frequency of use, and total number of years used. - current agricultural activities. - use personal protective equipment.	Second questionnaire: self-reported doctor’s diagnosis of asthma after age 19 years.	7 of 16 insecticides, 2 of 11 herbicides, and 1 of 4 fungicides significantly associated with atopic asthma, parathion use having the highest odds ratio (OR=2.88 ; 95%CI 1.34-6.20) Only permethrin use on crops (OR=2.19 95% CI 1.33-1.92) associated with non atopic asthma. Growing up on a farm: protective for atopic asthma (OR=0.55 ; 95% CI 0.43-0.70).	Age, state, smoking status, body mass index, and “grew up on farm”
Hoppin [54], 2009, USA : Iowa and North Carolina.	19,704 farmers, including 441 cases of asthma and 19,263 control subjects, Men: only Aged : 20-88 years	50 specific pesticides	Self-administered first questionnaire by mail: -lifetime use of the pesticides: on ever use, use during the past year, frequency of use, and total number of years used. - use personal protective equipment.	Second questionnaire: self-reported doctor’s diagnosis of asthma after age 19 years.	Ever-use of 12 pesticides associated with allergic asthma and 4 associated with nonallergic asthma. For allergic asthma, strongest association with coumaphos (OR 2.34 ; 95%CI 1.49-3.70 for nonallergic asthma: strongest association with DDT (OR=1.41 ; 95% CI 1.09-1.84) . Exacerbation of allergic asthma associated with pendimethalin (OR=2.1; 95 % CI 1.1-4.1) and aldicarb (OR=10.2; 95 % CI 1.9-55).	Age, state, smoking, high pesticide and BMI
Henneberger [50], 2013, USA	926 adult pesticide applicators with active asthma (wheezing and	36 specific pesticides (omitted aldicarb, parathion, ziram,	Self-administered first questionnaire by mail: exposure during the year before enrollment:	Outcome of interest: exacerbation of asthma, self-reported visit		Age, state and ever smoked

: Iowa and North Carolina.	breathing problems in past 12 months) Aged: 16-83 years.	trichlorfon and aluminum phosphide)	use of pesticides in the past 12 months and various agricultural activities.	tohospital emergency room /doctor for an episode of wheezing or whistling during the past 12 months.		
Bread [51], 2003, Australia Cohort	1,999 outdoor staff working as part of an insecticide application program during 1935–1995 and 1,984 outdoor workers not occupationally exposed to insecticides. Men :only	Pesticides : arsenic, DDT and chemicals	Survey of surviving cohort members: self-administered questionnaire to obtain information on pesticide exposure history. Exposure assessment: - Use of arsenic (1935–1955), - use of DDT (1955–1962) - use of modern chemicals (1963–1996). Period of employment used to assess the type of chemicals and the duration of exposure.	Ascertainment of vital status by matching the cohort with national death registers and health insurance records. Surviving subjects completed a morbidity questionnaire : pesticide exposure story and non fatal outcomes potentially related to pesticides exposure	asthma mortality higher for applicators (SMR= 3.45; 95% CI 1.39-7.10, compared with the general Australian population) asthma mortality in subjects working with modern chemicals higher than in other subjects (SMR=6.44 ; 95% CI 1.33-18.8). Higher risk of asthma (OR=1.59 ; 95% CI 1.05–2.43) and of having a child diagnosed with asthma (OR=1.45 ; 95% CI 1.01–2.09) for pesticides applicators compared to others.	Age, period of follow-up and smoking
Baldi [57], 2013 France AGRICAN	15,494 farmers including 1,246 cases of asthma in the French agricultural cohort AGRICAN Men :55.5% Mean age: 62.9 years	Agricultural pesticides and farming activities.	Self-report questionnaire: farming activity, use of pesticide, history of pesticide poisoning.	Self-report of doctor-diagnosed asthma	Risks of allergic asthma increased in participants reporting a history of pesticide poisoning (OR=1.97; 95% CI 1.43-2.73). No association between non-allergic asthma and living during the first year of life on a farm	Age, sex, educational level and BMI
Boers [58], 2008, Europe (Netherlands , Italy, Finland, and Bulgaria) Multicenter study: EUROPIT	248 workers exposed (Men : 66.5 % ; mean age : 42.4 years) to pesticides and 231 non-exposed workers (Men : 62.4 % ; mean age : 42.2 years) of EUROPIT study	Ethylenebisdithiocarbamate (EBDCs) and/or other pesticides	Self-report questionnaire: job information, type of pesticide. Urinary ethylenethiourea (ETU) as biomarker of EBDC exposure	Self-report questionnaire based on IUATLD (respiratory symptoms - Asthma and asthmatic symptoms).	No significant associations between occupational exposure to pesticides and asthma diagnosis (OR=0.41; 95% CI 0.15-1.11) and asthma attack (OR=0.52; 95% CI 0.12-2.25). No significant association with urinary ETU as a continuous marker of exposure.	age, education, residence, smoking, gender and field study
Chronic bronchitis						
Hoppin [59], 2007, USA : Iowa and North Carolina.	20,908 farmers (20,400 male and 508 female) including 654 cases of chronic bronchitis and 16,630 farmers who did not Aged : 20-88 years	50 specific pesticides	Self-administered first questionnaire by mail: exposure during the year before enrollment. - lifetime use of the pesticides : on ever use, use during the past year, frequency of use, and total number of years used. - high pesticide exposure event.	Second questionnaire: self-reported doctor’s diagnosis of chronic bronchitis after age 19 years.	11 pesticides associated with prevalent chronic bronchitis, heptachlor use having the highest odds ratio (OR=1.50 ; 95% CI 1.19-1.89, in adjusted model). Significant association with chronic bronchitis for farmers having a high pesticide exposure event in their lifetime (OR=1.83 ; 95% CI 1.50-2.24) and pesticide	Age, state, gender and pack-years

Valcin [60], 2007, USA : Iowa and North Carolina.	21,541 non-smoking female spouses of farm workers, including 583 cases of chronic bronchitis and 20,958 controls, Women: only Aged : 20-88 years	50 specific pesticides	- use personal protective equipment. Self-administered first questionnaire by mail: exposure during the year before enrollment. - lifetime use of the pesticides : on ever use, use during the past year, frequency of use, and total number of years used. - current agricultural activities. - use personal protective equipment.	Second questionnaire: self-reported doctor's diagnosis of chronic bronchitis after age 19 years.	use off the farm (OR=1.40 ; 95% CI 1.04-1.88) Five pesticides associated with chronic bronchitis in non-smoking spouses of farmers, paraquat use having the highest odds ratio (OR=1.91 ; 95% CI 1.02-3.55). Risk of chronic bronchitis in women associated with application of pesticides 120 days or more in their lifetime (OR=1.50; 95% CI 1.17-1.91) and in those who used three or more agricultural pesticides (OR=1.58 ; 95% CI 1.19-2.09).	Age and state
Tual [61], 2013 France cohort AGRICAN	14,441 farmers including 1,207 cases of chronic bronchitis in the French agricultural cohort AGRICAN (AGRIculture and CANcer). Men :56.3% Mean age: 65.4 years	Agricultural pesticides and farming activities.	Self-report questionnaire: farming activity, use of pesticide, history of pesticide poisoning.	Self-report of doctor-diagnosed chronic bronchitis after age 20.	Significant associations between chronic bronchitis and two farming activities: cattle raising (OR=1.24; 95% CI 1.03-48) and potato production (OR=1.33; 95% CI 1.13-1.57). Significantly associated risk of chronic bronchitis exposed to pesticide poisoning (OR=1.64; 95% CI 1.11-2.41 and pesticide use potato farmers (OR=1.63; 95% CI 1.11-2.37).	Age, sex, educational level, smoking status, history of asthma, BMI and all agricultural exposures significant (p<0.05)

SMR: Standardized Mortality Ratio
ATS-DLD : American Thoracic Society and the Division of Lung Diseases
IUATLD: International Union Against Tuberculosis and Lung Disease
AHS : Agricultural Health Study

Table S3 : Studies on the respiratory health of workers in the pesticide industry

References ; Country ; Study type	Population	Pesticide	Indicators of exposure	Health outcomes	Result	Adjustment factors
Salameh [62], 2005, Lebanon cross-sectional	19 pesticide factory workers (mean age: 39.8 years) and 43 control group (mean age: 28.0) other factory workers in Lebanon. Men: only	Pesticide: pyrethroid and carbamate insecticides (liquid pesticides)	Face to face questionnaire: employment history and exposure to pesticides.	face to face questionnaire based on ATS-DLD (respiratory symptoms) Pulmonary function (spirometry: FVC, FEV ₁ , FEV ₁ /FVC, FEF ₂₅₋₇₅) following ATS guidelines.	No significant differences between pesticide-exposed and non-exposed workers for respiratory symptoms and other diseases. Higher risk of abnormal FEV ₁ /FVC (OR=5.6 ; p<0.001) and FEF _{25-75%} (OR=16.5 ; p<0.001) in pesticide-exposed workers.	Age, smoking, BMI
Zuskin [63], 2008, Croatia cross-sectional	82 workers employed in processing pesticides (Men: 63.4%; mean age : 44 years) and in 60 control workers (Men : 58.3% ; mean age :41.5 years) not exposed to irritants and employed in a soft drink bottling plant.	Pesticides processed at the Herbos Plant in Sisak : insecticides, rodenticides, herbicides, and fungicides primarily for commercial farming and gardening.	Face to face questionnaire : detailed occupational History.	Face to face questionnaire filled in with physicians based on BMRC (respiratory symptoms - covering the life history of the subject's). Pulmonary function (spirometry: FVC, FEV ₁ , FEF ₂₅ , FEF ₅₀) following ECCS guidelines	Significant association between exposure and chronic cough (OR=1.29; IC95% 1.15-15.84) and dyspnea (OR=1.11 ; IC95% 1.06-1.97) in women. Significant association only with dyspnea (OR=2.35; IC95% 1.50-4.10) in men. For all exposed subjects: significant reductions in ventilation capacity for all tests compared to predicted.	Age, sex, exposure and smoking
Ruder [64], 2011,	2,122 US pentachlorophenol (PCP)	Pentachlorophenol (PCP), TCP	Exposure assessment of cohort members: followed in	Ascertainment of vital status from Social	Significant association of mortality risk higher in workers and COPD (SMR=1.38; 95% CI	

USA Cohort of PCP production from the NIOSH.	production workers including 1,402 PCP production only and 720 workers in PCP and TCP production from Michigan, Illinois, Washington and Kansas. Men : 97%		the NIOSH, Period of employment was used to estimate both the type of manufacturing plants as likely to have been exposed to and the duration of this exposure.	Security Administration and Internal Revenue Service records, from state divisions of motor vehicles, and from the National Death Index at December 2005.	1.06-1.77).	
Bruns [65], 1998, USA cross- sectional	496 exposed subjects (Men: 85.3%) employees of the Dow Chemical Company who worked in the manufacture or formulation of chlorpyrifos and 911 control subjects (Men: 87.3%)	chlorpyrifos	Exposure to chlorpyrifos : high, moderate, low, or negligible for each job.	Morbidity data from company medical records.	Significant association between exposure and acute respiratory infections (OR=1.49 ; 95% CI 1.08- 2.05) and other diseases of the respiratory system (OR=2.80 ; 95% CI 1.18-6.65).	Age, sex, pay status and race
Calver [66], 1991, USA cross- sectional	281 workers (Men : 95% ; mean age : 55.4 years) and 260 unexposed (Men : 93% ; mean age: 56.0 years)	- 2,4,5-trichlorophenol (TCP) - 2,3,7,8- tetrachlorodibenzo-p- dioxin (TCDD), contaminant of TCP production	Face to face questionnaire, medical documents and computerised records: lifetime occupational history. TCDD level in blood	Standardized interviews and medical examinations (chronic bronchitis and COPD defined by ATS). Pulmonary function measures (spirometry: FVC, FEV ₁ , FEV ₁ /FVC) following ATS guidelines	Risk of chronic bronchitis (OR=1.04 ; IC95% 0.43-2.48) and COPD (OR=1.58 ; IC95% 0.59- 4.25) not significantly associated with any measure of TCDD (worker vs control). No significant differences between workers and controls for any of the spirometric parameters.	

ATS-DLD : American Thoracic Society and the Division of Lung Diseases
Respiratory function measures :(FVC, FEV₁, FEV₁ to FVC ratio, FEF_{25-75%})
ECCS : European Committee for Coal and Steel.
NIOSH : National Institute for Occupational Safety and Health