

Asthma Associated With Pesticide Exposure Among Women in Rural Western Cape of South Africa

Vuyelwa Ndlovu, BSc (Hons), MPH,^{1,2*} Mohamed Aqiel Dalvie, BSc, BSc (Med) Hons, MSc, PhD,¹ and Mohamed F. Jeebhay, MB ChB, DOH, MPhil (Epi), MPH (Occ Med), PhD¹

Background Few studies have investigated asthma and pesticides among women farm workers in developing countries.

Methods A cross-sectional study was conducted to investigate the association between pesticides and asthma among rural women ($n = 211$). Outcome measurements included respiratory symptoms (European Community Respiratory Health Survey questionnaire), immunological status (Phadiatop, serum IgE to mite allergens) and lower airway inflammation (fractional exhaled nitric oxide (FeNO) levels). Exposure variables included self-reported pesticide exposure and whole blood cholinesterase (ChE).

Results The prevalence of ocular-nasal symptoms (ONS), doctor-diagnosed asthma and current asthma was 24%, 11%, and 6% respectively. ONS was positively associated with re-entering a sprayed field ($OR = 2.97$; $CI: 0.93–9.50$). Asthma symptom score was associated with low ChE ($OR = 1.93$; $CI: 1.09–3.44$). Participants with high FeNO (>50 ppb) also had an elevated odds of having low ChE ($OR = 4.8$; $CI: 0.80–28.00$).

Conclusion Pesticide exposure among women farm workers is associated with increased risk of ocular nasal symptoms and an elevated asthma symptom score. *Am. J. Ind. Med.* 57:1331–1343, 2014. © 2014 Wiley Periodicals, Inc.

KEY WORDS: pesticides; farm women; asthma; allergy; cholinesterase

INTRODUCTION

South Africa is the largest consumer of pesticides in Sub Saharan Africa as evidenced by the large volumes used in agriculture [Naidoo and Buckley, 2003]. Within the Western Cape Province where crop farming is important, pesticide use has been increasing and agricultural pesticide residues have been detected in the rural environment and in farm workers [London, 2003; Dalvie et al., 2009a,b, 2011].

Pesticide residues have been detected in South African crops as reported by Dalvie and London [2009c] in an analysis of local and imported wheat samples.

A large number of epidemiological studies have reported that farm workers are exposed to pesticides especially organophosphate and carbamate pesticides that may adversely affect their respiratory health [Ndlovu et al., 2011]. The respiratory health effects include upper respiratory tract disorders such as rhinitis and lower airway disorders such as wheeze and asthma [Chatzi et al., 2007; Fieten et al., 2009; Hoppin et al., 2002, 2006, 2009; Slager et al., 2009, 2010]. Recent studies have shown that different pesticides are associated with adult-onset allergic asthma and non-allergic asthma [Hoppin et al., 2009].

Most studies of the adverse respiratory health effects of pesticides have been conducted in developed countries and have mainly focused on men. However, it has become increasingly apparent that women are also a high-risk group [London et al., 2002; Zhang et al., 2002; Garcia, 2003; Faria et al., 2005; Hoppin et al., 2008; Fieten et al., 2009]. Two

¹Centre for Occupational and Environmental Health Research, School of Public Health and Family Medicine, University of Cape Town, Rondebosch, South Africa

²Department of Environmental Science and Health, Faculty of Applied Sciences, National University of Science and Technology, Ascot, Bulawayo, Zimbabwe

*Correspondence to: Vuyelwa Ndlovu, BSc (Hons), MPH, Department of Environmental Science and Health, Faculty of Applied Sciences, National University of Science and Technology, P.O. Box 939, Ascot, Bulawayo, Zimbabwe.

E-mail: vuyelwa.ndlovu@nust.ac.zw, vuyiendlovu@yahoo.com

Accepted 23 July 2014

DOI 10.1002/ajim.22384. Published online 27 October 2014 in Wiley Online Library (wileyonlinelibrary.com).

studies reported that respiratory symptoms or doctor-diagnosed asthma were more prevalent and strongly associated with pesticide exposure in women than in men [Zhang et al., 2002; Faria et al., 2005]. In the study by Faria et al. [2005], the higher prevalence of asthma symptoms in women was ascribed to the inadequate protection provided against pesticide exposure than men and they were also more likely to have been exposed in domestic settings.

Respiratory health problems have also been identified among women farm workers in the Western Cape Province of South Africa [Bowers et al., 2009]. However, few studies of the effect of pesticide exposure on respiratory health have been conducted in South Africa. Innes et al. [1990] reported that 17.5% of male rural workers engaged in crop spraying in Cape Town reported chronic organophosphate poisoning, asthma, and chronic bronchitis. No association between long-term exposure to paraquat and reported symptoms and lung function but a decrease in exercise oximetry was found in a study in the rural Western Cape [Dalvie et al., 1999]. A more recent study in South Africa demonstrated that the spider mite, *Tetranychus urticae*, is an important outdoor allergen among table-grape farm workers and an increased risk of spider mite allergy was related to high pesticide exposure among crop sprayers [Jeebhay et al., 2007].

The aim of this study was to investigate the effect of pesticide exposure on allergy and asthma among rural women in the Western Cape province of South Africa. The data presented in this paper is part of a larger study investigating various health effects of pesticide exposure among women on farms in the Western Cape of South Africa.

MATERIALS AND METHODS

Study Design, Population and Sampling

A cross-sectional study of women farm workers and residents and women living in towns neighboring the farms, in the Western Cape region of South Africa was conducted during the period 24 October to 3 December 2009. Recruitment of participants was achieved with the assistance of the Women on Farms Project (WFP), a rural women's rights Non-Governmental Organisation. A similar proportion of women were recruited from the five most accessible agricultural areas and neighboring towns that were about 5–10 km away from these agricultural areas. The Boland areas included Stellenbosch, Ceres, Paarl, Grabouw, and Worcester. Farm workers and residents were selected from these non-organic farms in each area and town dwellers from houses in each neighboring town. All selected farms and town areas reflected the varied non-organic commercially productive agricultural activities in the Western Cape since they produce wine, grapes, and deciduous fruit. One adult female participant per household was selected. WFP

recruited a total of 211 women into the study including 113 women currently living on a farm and 98 residents in towns. There were 8 women who lived in a town but worked on a farm and were included in the farm worker group. In total there were, therefore, 97 farm workers (89 women living in farms and 8 not living in farms). There were an additional 24 women residing but not working on farms. The farm workers and residents ($n = 121$) are, therefore, referred to as “farm dwellers”. The remaining 90 women who neither lived nor worked on a farm are referred to as “town dwellers”. The study was approved by the University of Cape Town's (UCT) Research Ethics Committee (Reference 393/2009). Written informed consent was obtained from participants prior to the study.

Questionnaire

The questionnaire had sections on socio-demographic aspects (age, schooling, home language, income, employment); residential history (place of residence on a farm or town, period of residence); environmental pesticide exposure (pesticide drift, distance of residence to spraying and other exposures to agricultural spraying), job history (farm worker, non-farm worker, number of years in a job, job title), household pesticide exposure, lifestyle factors (smoking and alcohol consumption) and respiratory health. The respiratory health section incorporated the abbreviated form of the standardized and validated European Community Respiratory Health Survey (ECRHS) questionnaire [Burney et al., 1994]. The pesticide exposure-related questions were based on those used in previous surveys [Dalvie et al., 1999, 2004]. Trained interviewers administered questionnaires (which were translated and back-translated) to participants in the language of their choice (Afrikaans and Xhosa).

Whole Blood Cholinesterase (ChE)

Whole blood ChE levels (the sum of serum butyl cholinesterase and erythrocyte acetylcholinesterase), a validated method for measuring cholinesterase, were determined for each subject [Haigh et al., 2008]. A whole blood sample (9 ml) was drawn from each participant by a qualified nurse using a tube containing sodium heparin or EDTA as anticoagulant. EDTA does not inhibit cholinesterase activity (Roche Diagnostics). The tubes were kept on ice and transported to the South African National Accreditation System (SANAS) accredited Pathcare laboratory at N1 City Hospital, Cape Town for ChE analyses. ChE activity was quantified using the Roche Diagnostics Cholinesterase method (Roche/Hitachi analyser, Cobas[®], Roche Diagnostics GmbH, D-68298 Mannheim), a photometric test based on the principles of a study by Ellman et al. [1961].

Phadiatop and Mite Specific Serum IgE

A blood sample (9 ml) was drawn from each participant using a Becton Dickinson Vacutainer SST tube (with gel medium and clot activator) by the nurse. The blood was allowed to clot for 1–2 hr at room temperature (20–24°C) and then centrifuged at 1350 rpm for 10 min at room temperature. The serum was then transferred to another tube and stored at –20°C in a field freezer. The stored serum sample was transported on dry ice to the Lung Institute, UCT where it was stored at –80°C. The samples were then couriered to the SANAS accredited (ISO 15189:2007), National Institute for Occupational Health (NIOH) Immunology laboratory for testing. Presence of sensitization to common aeroallergens (house dust mites, grass pollens, cat, dog, and cockroach) was determined by the Phadiatop[®] test (Phadia AB, Uppsala, Sweden). The Phadiatop[®] test has a binary outcome with a positive test indicative of the presence of sensitization to any one of these common aeroallergens. In this study, atopy was defined as a positive Phadiatop[®] test. The quantification of specific IgE antibodies to house dust mite and other specific mite occupational allergens (spider mite: *Tetranychus urticae* and storage mite, *Lepidoglyphus destructor*) was performed using the UniCAP[®] system (Phadia AB, Uppsala, Sweden).

Fractional Exhaled Nitric Oxide (FeNO)

Fractional exhaled nitric oxide measurement is a recognised non-invasive method for assessing allergic airway inflammation [Quirce et al., 2010]. Although the inflammation can be controlled using medication in asthmatics, previous research done in the Western Cape [Jeebhay et al., 2007] has shown that this is not widespread in these communities. The fractional exhaled NO (FeNO) testing was conducted by a trained nurse. A hand-held portable nitric oxide sampling device (NIOX MINO[®] Airway Inflammation Monitor (NIOX MINO; Aerocrine AB, Solna, Sweden)) was used. Three technically adequate measurements were performed in line with the American Thoracic Society/European Respiratory Society recommendations [ATS/ERS, 2005a]. The average value of the three measurements was used in the analysis. Exhaled nitric oxide (NO) test was done after hours during the working week. Special instructions were provided to workers to ensure that tested individuals do not smoke tobacco, eat nor drink (at least 1 hr before) prior to the test. The participants' height and weight were measured and this information was used to calculate BMI. Ambient NO and temperature was also recorded.

Exposure Ascertainment

There were several self-reported exposure variables encompassing domestic, occupational, and environmental

exposure to pesticides that were obtained from the questionnaire. These included household pesticide use; history of living or working on farms; currently living or working on farms; pesticide drift; re-entry into sprayed fields (immediate – same day, delayed); and permanency of farm work (permanent, seasonal) which were classified as dichotomous variables and job duration a continuous variable. ChE measurements, as described previously, were used as an objective marker for exposure to cholinesterase-inhibiting carbamates and organophosphates. The values were dichotomised using a cut-off value of 6021 IU which represented the low end of the expected laboratory range (data on file at Roche Diagnostics[®]).

Outcome Characterization

Outcome variables were predominantly dichotomous. Ocular-nasal symptoms (ONS) were defined as answering “yes” to “Have you had any nasal allergies including hay fever or itchy and watery eyes/nose in the last 12 months?” Current asthma (CA) was defined as “yes” to at least one of the following two questions: “Have you had an attack of asthma in the last 12 months?” or “Are you currently taking any medicines including inhalers, aerosols or tablets for asthma?” Adult-onset asthma (AOA) was defined as the presence of doctor-diagnosed asthma and having had the first asthma attack at the age of 16 years or later. Furthermore, asthma symptom score (ASS) was computed as a continuous outcome from the sum of positive responses to four questions related to asthma-related symptoms in the last 12 months. These included the presence of wheeze with breathlessness; woken up with chest tightness; attack of shortness of breath at rest; and woken by an attack of coughing. The asthma symptom score was a simplified version of an asthma score proposed by Pekkanen et al. [2005] and used by Sunyer et al. [2007] and Vizcaya et al. [2011].

Other dichotomous outcomes included the presence of allergic sensitization (specific IgE levels to house dust mite, storage mite and spider mite greater than 0.35 ku/l) (UniCAP[®] system Phadia AB, Uppsala, Sweden); FeNO = 25–50 ppm and FeNO > 50 ppb suggestive of allergic airway inflammation. FeNO levels were also analyzed as a continuous variable.

Statistical Analysis

The selected software for analysis was Stata: Release 11 (Stata Corp. 2009. Statistical Software. College Station, TX: StataCorp LP). Since all continuous variables were not normally distributed, median and interquartile ranges were used to summarize these variables. After conducting univariate and bivariate analysis, multiple logistic regression analyses were used to test for associations between

dichotomous outcomes and exposure variables while controlling for confounding. Confounders were selected on an a priori basis, according to biological plausibility, or using bivariate testing if $P < 0.10$ or showing at least a 10% change in the β coefficient of the crude OR between exposure and outcome. Atopy and current smoking were selected a priori for all outcomes. Other potential confounders included in bivariate testing were age, BMI, years of schooling, employment, household income, born on a farm, and drinking alcohol. The covariates selected for inclusion in the final models in addition to smoking and atopy were years of schooling, born on a farm as they had consistently strong associations ($P < 0.05$) with most outcomes in bivariate analysis (refer to section 3.8). Exposure variables were then added separately to all the different outcomes adjusting for these covariates.

To test for effect modification, interaction variables were created between exposure variables and potential effect modifiers (atopy, smoking, years of schooling, and being born on a farm). These were the products between each exposure variable and a suspected effect modifier. For all the outcomes, an interaction term between the variable and the exposure variable of interest was included in the model. If this interaction term was significant ($P < 0.05$), the variable would be an effect modifier. None of the interaction terms were significant so all were not retained in the models.

For the continuous outcome, asthma symptom score, the underlying distribution was not normal. Since the asthma symptom score was a count, this suggested a Poisson regression model be used. However, since the mean score (0.9) was lower than the standard deviation (1.5), a Negative Binomial Regression Analysis was used. Model building and checking procedures were similar to that used for Logistic Regression Analysis. The estimated negative binomial regression coefficient is the difference in the logs of expected counts in the exposed group compared to the unexposed group, while holding the other variables constant in the model. The exponentiated coefficients of negative binomial regression can therefore be interpreted as incidence rate ratios.

RESULTS

Participation

Two hundred and eleven women from the Boland were recruited into the study with 20% ($n = 42$) coming from Ceres, 18% ($n = 38$) from Grabouw, 19% ($n = 39$) from Paarl, 22% ($n = 47$) from Stellenbosch and 21% ($n = 45$) from Worcester.

Table I summarizes the distribution of farm dwellers and town dwellers (as already been defined earlier) that participated in the study.

TABLE I. Demographic and Socioeconomic Characteristics of Rural Women in the Boland of the Western Cape ($n = 211$)

Characteristics	Farm dwellers ($n = 121$)	Town dwellers ($n = 90$)	Total ($n = 211$)
Participation by area (n,%)			
Ceres	23 (19)	19 (21)	42 (20)
Grabouw	35 (29)	3 (3)	38 (18)
Paarl	16 (13)	23 (26)	39 (18)
Stellenbosch	25 (21)	22 (24)	47 (22)
Worcester	22 (18)	23 (26)	45 (21)
Demographics (median, IQR ^a)			
Age (years)	33 (27–40)***	40.5 (31–49)	37 (28–45)
BMI ^b (kg/m ²) ($n = 207$)	25.2 (21.6–30.8)**	28.6 (23.8–35.7)	26.44 (22.5–32.9)
Education (years of schooling)	9 (7–10)	9 (7–11)	9 (7–10)
Household income/month (\$US) ^c ($n = 189$)	270 (188–500)**	379 (221–744)	324 (199–600)
Length of stay in current residence (years)	15 (8–24)*	21.5 (12–41)	17 (9–29)
Other socio-economic indicators, n (%)			
Currently employed	101 (83)***	25 (28)	126 (60)
Born on a farm	83 (69)***	13 (14)	96 (46)
Drinks alcohol	79 (65)**	39 (43)	118 (56)
Current smoker	69 (57)*	36 (40)	105 (50)

* $P < 0.05$.

** $P < 0.01$.

*** $P < 0.001$.

^aInter quartile range.

^bBody Mass Index = body mass divided by the square of height.

^cHousehold income converted to \$US from Rands at a rate of 1 \$US to 8 Rands.

The 24 farm residents were included in the farm dweller group because sub-analysis treating them as a different exposure group showed that they had similar outcomes as farm workers (data not shown).

Demographic and Socioeconomic Characteristics

The farm dwellers were significantly younger than the town dwellers having median ages of 33 years and 40.5 years respectively (Table I). BMI was also significantly lower amongst farm dwellers. Household monthly income was below US\$ 600 in both groups and slightly but significantly less in the farm dwellers group. A significantly higher proportion (83%) of farm dwellers was currently employed compared to town dwellers (27%). Educational status was similarly low in both groups with more than half not having matriculated and none with tertiary education.

There was a small proportion of town dwellers that were born on a farm (14%) but substantially less than in the farm dweller group (69%) ($P < 0.01$). Smoking and drinking alcohol was also significantly more common among the farm dwellers.

Environmental and Occupational Exposure to Agricultural Pesticide Spraying Among Farm Dwellers (n = 121)

The crops grown on farms on which farm dwellers lived and worked were predominantly popular fruit such as grapes, apples, berries, pears, prunes, and oranges. Among the participants currently living on a farm (n = 113), the average distance from the nearest vineyard was 10 m (Inter-quartile Range (IQR) = 5–20 m) and 73% of the women indicated that they had come into contact with pesticide contaminated surfaces or were exposed to pesticide drift when doing chores outside the house such as hanging the washing. The use of unprotected sources of water such as rivers or farm dams for drinking and household use was reported by 83% of the farm dwellers.

Participants reported that there were women who were employed as pesticide applicators in nearly 20% of farms but only 4 (3%) participants were applicators. There were 28 (23%) farm dwellers who reported that personal protective equipment (PPE) was not provided on farms and 69 (57%) reported that there are no showers on the farm. Tractor with a mist blower was the most common spraying method used on farms and was reported by almost all the farm dwellers (97%). Other application methods such as using a tractor without a mist blower, backpack spraying and using a quad bike were reported by 28%, 37%, and 20% of farm dwellers respectively. The median time since the last spray applied was 1 day (IQR = 0–4 days).

Self-reported Household and Agricultural Pesticide Exposure Indicators and Measured ChE Levels

Over half of the participants in both exposure groups reported that pesticides were used at home (Table II). Almost a third of the farm dwellers reported living with a pesticide applicator and some (11%) reported using empty pesticide containers for domestic purposes. Over half of the farm dwellers (57%) reported that pesticide drift reached their home. There were 26 (29%) town dwellers that had previously lived or worked on a farm. Pesticide spraying was highly prevalent on farms that participants had currently lived or worked in since they reported a median number of spraying days in a year of 96 days (IQR = 72–144 days).

On spraying days, about two thirds (67%) of the farm dwellers reported that they re-entered the field on the same day after pesticide spraying. Workers were employed for an average of 5 years on the farms and about a third of farm dwellers were seasonal farm workers.

ChE levels below the laboratory reference value of 6021 IU (Data on file at Roche Diagnostics®) were significantly more prevalent amongst farm dwellers. There were 18 (9%) participants with low ChE (below laboratory reference standard) among whom 78% were farm dwellers.

Prevalence of Asthma and Allergic Outcomes

Upper airway symptoms (ocular-nasal symptoms) were reported by 24% of the participants (Table III). The prevalence of lower airway symptoms was higher and significantly more prevalent amongst the farm dwellers (12–46%) than town dwellers (8–24%) for various individual symptom outcomes.

Doctor-diagnosed asthma, current asthma and adult-onset asthma were not significantly different in the two exposure groups although a higher prevalence was observed in the town dwellers (Table III). Among those who reported doctor-diagnosed asthma, a large proportion (83%) had adult-onset asthma. The prevalence of adult-onset asthma among farm dwellers was 7% which was lower than among town dwellers (11%). The median age at asthma diagnosis was 25 years (IQR = 17–35 years). However, only 1% reported having an asthma attack in the past 12 months and 6% were currently on medication. Current asthma with and without ocular-nasal symptoms had a prevalence of 3% each with both phenotypes being more prevalent among the town dwellers. The asthma symptom score was significantly higher among the farm dwellers ($P < 0.01$). Half of the participants reported no asthma-like symptoms with an asthma score of 0 which was significantly more prevalent among town

TABLE II. Self-Reported Household and Agricultural Pesticide Exposure and Measured Cholinesterase Enzyme Levels of Rural Women in the Boland of the Western Cape (n = 211)

Exposure variables	Farm dwellers (n = 121)	Town dwellers (n = 90)	Total (n = 211)
Household pesticide use indicators, n (%)			
Use pesticides at home	67 (55)	56 (62)	123 (58)
Living with a pesticide applicator	36 (30)*	1 (1)	37 (18)
Domestic use of pesticide containers	13 (11)*	0 (0)	13 (6)
Pesticide exposure indicators, n (%)			
History of living or working on farms	121 (100)	26 (29)	147 (70)
Pesticide drift into home	69 (57)	n/a	n/a
Farm worker status (n = 208)			
Permanent	53 (45)*	0 (0)	53 (25)
Seasonal	40 (34)*	4 (4)	44 (21)
Re-entry into sprayed fields			
Delayed re-entry ^a	33 (27)*	1 (1)	34 (16)
Immediate re-entry ^b	81 (67)*	0 (0)	81 (38)
Job duration (years)	5 (1–13)	n/a	n/a
Pesticide spraying days/year in current farm (n = 196) median, IQR	96 (72–144)	n/a	n/a
Cholinesterase < 6021 IU (n = 206) ^c	14 (12)**	4 (5)	18 (9)

n/a, not applicable.

^are-entry into field 1–7 days after pesticide spraying.^bre-entry into field on the same day after pesticide spraying.^ccholinesterase level below 6021 IU (low end of the laboratory range) indicating enzyme inhibition and exposure to carbamate and organophosphate pesticides.* $P < 0.001$.** $P = 0.08$.

dwellers. There were significantly more participants with 1–3 symptoms among the farm dwellers (13–23%) than the town women (3–13%).

The median FeNO level was significantly lower among the farm dwellers (Table III). There was also a greater proportion of town dwellers with elevated FeNO, compared to farm dwellers.

About half (52%) of those with doctor-diagnosed asthma had current asthma ($P < 0.01$). Only 26% (n = 6) of those with doctor-diagnosed asthma and 33% (n = 4) of those with current asthma ($P = 0.03$) had elevated FeNO between 25 ppb and 50 ppb ($P = 0.03$). Only one participant with FeNO > 50 ppb had doctor-diagnosed asthma and current asthma. The median asthma symptom score for those with doctor-diagnosed asthma was 2 (IQR = 1–3) compared to 0 (IQR = 0–2) for those without ($P < 0.001$). The median asthma symptom score for those with current asthma was 2 (IQR = 0.5–3) compared to 0 (IQR = 0–2) for those without ($P = 0.01$).

There was a significant positive association between asthma symptom score and two asthma phenotypes which were doctor-diagnosed asthma and current asthma and also a positive and near significant association with FeNO between 25 ppb and 50 ppb.

The overall prevalence of atopy was 44% and the town dwellers had a higher proportion (51%) compared with farm dwellers (38%) ($P = 0.07$). The proportion of women sensitized to the domestic allergen (house dust mite) and other mite allergens (storage mite and spider mite) was higher among the town dwellers compared to the farm dwellers.

The prevalence of allergic asthma phenotype defined as the presence of current asthma and sensitization were found in 1–5% of the participants, with a relatively higher prevalence of all allergic asthma phenotypes, especially atopic asthma, in the town dweller group. Further detailed analysis of these phenotypes could not be conducted because of the low overall prevalence (Supplementary Material, Table SI).

Host Factors Associated With Asthma and Allergic Outcomes

Unadjusted logistic regression models revealed that age, BMI, and house hold income were not predictors of asthma outcomes (Supplementary Material, Table SIII). Atopy, on the other hand, was strongly and positively associated with all outcomes. Higher education level and employment were generally protective for asthma outcomes. Being born on a farm was associated with increased odds of ocular-nasal

TABLE III. Prevalence of Asthma and Allergic Outcomes Among Women Farm Workers in the Boland of the Western Cape (n = 211)

Outcome	Prevalence, n (%)		
	Farm dwellers (n = 121)	Town dwellers (n = 90)	Total (n = 211)
Upper airway symptoms (n = 211)			
Ocular-nasal symptoms	31 (26)	19 (21)	50 (24)
Lower airway symptoms (n = 211)			
Wheeze	45 (37)*	20 (22)	65 (31)
Shortness of breath with wheeze	34 (28)*	15 (17)	49 (23)
Wheeze without cold	21 (17)	14 (16)	35 (17)
Woken up by chest tightness	42 (35)**	9 (10)	51 (24)
Attack of shortness of breath at rest	14 (12)	7 (8)	21 (10)
Woken by cough	56 (46)**	22 (24)	78 (37)
Asthma phenotype characteristics			
Doctor-diagnosed asthma	11 (9)	12 (13)	23 (11)
Adult-onset asthma	9 (7)	10 (11)	19 (9)
Current asthma	4 (3)	8 (9)	12 (6)
Asthma with ocular-nasal symptoms	2 (2)	4 (4)	6 (3)
Asthma without ocular-nasal symptoms	2 (2)	4 (4)	6 (3)
Asthma score (Median (IQR))	1 (0–2)**	0 (0–1)	0 (0–2)
Asthma symptom score categories:			
0	48 (40)**	63 (70)	111 (53)
1	28 (23) [†]	12 (13)	40 (19)
2	23 (19)*	8 (9)	31 (15)
3	16 (13)*	3 (3)	19 (9)
4	6 (5)	4 (4)	10 (5)
Fractional exhaled nitric oxide levels (n = 207)			
FeNO ppb (median, IQR)	9.2 (5.67–14)**	12.3 (8.3–22.3)	10.3 (6–17.3)
FeNO 25–50 ppb	11 (9)	12 (14)	23 (11)
FeNO > 50 ppb	7 (6)	8 (9)	15 (7)
Immunological profile (n = 206)			
Atopy (Positive Phadiatop)	46 (38) [†]	44 (51)	90 (44)
Storage mite sensitization (>0.35 kU/l)	23 (19)	21 (24)	44 (21)
Spider mite sensitization (>0.35 kU/l)	18 (15)	17 (20)	35 (17)
Allergic asthma phenotypes			
Atopic asthma	3 (2) [†]	7 (8)	10 (5)
Non-atopic asthma	1 (1)	1 (1)	2 (1)
House dust mite allergic asthma	3 (2)	4 (4)	7 (3)
Storage mite allergic asthma	3 (2)	4 (4)	7 (3)
Spider mite allergic asthma	2 (2)	5 (6)	7 (3)

Data presented as n (%) except where indicated otherwise in parenthesis as median (IQR).

* $P < 0.05$.

** $P < 0.01$.

*** $P < 0.001$.

[†] $P = 0.07$.

symptoms (2.41, 95% CI: 1.26–4.63) but decreased odds for current asthma, adult-onset asthma, doctor-diagnosed asthma and elevated FeNO. Smoking was negatively associated with FeNO. Similar associations were found for the asthma symptom score and host factors in the unadjusted negative binomial regression models (Supplementary Material, Table SII).

Asthma Symptom Score and Pesticide Exposure

Table IV summarizes the results of the associations between asthma symptom score and pesticide exposure indicators using negative binomial regression models adjusted for atopy, born on a farm, smoking, and education. The mean

TABLE IV. Adjusted Negative Binomial Regression Models of Pesticide Exposure Indicators Associated with Continuous Asthma Symptom Score Among Rural Women in the Boland of the Western Cape

Pesticide exposure variable	Asthma symptom score
	IRR (95% CI) ^a
Use pesticides at home	1.17 (0.82–1.69)
History of living or working on farms	2.22 (1.30–3.80)**
Currently living and working on farms	2.25 (1.45–3.48)**
Pesticide drift into the home	2.03 (1.38–2.98)**
Permanent versus seasonal farm worker	1.06 (0.70–1.70)
Immediate versus delayed re-entry	1.21 (0.75–1.90)
Number of years in current farm job	1.02 (1.00–1.04)
Number of days of pesticide spraying/year in current farm	1.01 (1.00–1.01)**
Cholinesterase levels < laboratory reference standard	1.93 (1.09–3.44)*

Each IRR represents a separate model adjusted for atopy, smoking, born on a farm and years of schooling.

^aNegative binomial regression models IRR (Incidence Rate Ratio), the ratio of the mean score among exposed and unexposed.

* $P < 0.05$.

** $P < 0.01$.

*** $P < 0.001$.

asthma symptom scores were consistently higher among those that reported either household or agricultural pesticide exposure, the latter demonstrating stronger associations. Women who were either currently or previously living or working on a farm had a two-fold higher mean score than their town counterparts. These associations remained unchanged even after adjusting for household pesticide use (Supplementary Material, Table SIV). Furthermore, a borderline significant association was also observed with the number of days of pesticide spraying per year on a farm reported among those currently residing and/or working on the farm.

Exposure to pesticide drift in the home was also strongly associated with the asthma score as the exposed had double the mean score compared to the unexposed (95% CI: 1.38–2.98). A sub-analysis of farm dwellers revealed that there was a 57% higher mean score among those exposed to pesticide drift compared to the unexposed (95% CI: 1.06–2.32) (Supplementary Material, Table SIV).

Also presented in Table IV are the results of the associations between ChE measurements and the asthma symptom score. Those with ChE levels less than the laboratory reference value (6021 IU, Roche Diagnostics®) had a significant twofold higher mean asthma symptom score (95% CI: 1.09–3.44) than women with ChE levels higher than the laboratory reference value.

Associations Between Pesticide Exposure and Asthma and Allergic Outcomes

Table V summarizes the results of the associations between asthma outcomes and pesticide exposure indicators using multiple logistic regression models adjusted for atopy, born on a farm, smoking, and years of schooling. Multiple linear regression results using FeNO measurement as a continuous variable did not show statistically significant associations with the pesticide exposure indicators (Supplementary Material, Table SV). Using pesticides at home was weakly but positively associated with ocular-nasal symptoms, adult-onset asthma and elevated FeNO. There were non-significant positive associations between FeNO outcomes and currently living or working on a farm whereas the effects were negative for the remaining asthma outcomes. The measure and direction of the effects between all outcomes and currently or having a history of living or working on farms did not change even after adjusting for household pesticide use (Supplementary Material, Table SIV). A sub-analysis of farm dwellers only revealed weak positive associations between doctor-diagnosed asthma (OR = 1.04, 95% CI: 0.26–4.15), ocular-nasal symptoms (OR = 1.66, 95% CI: 0.65–4.24), adult-onset asthma (1.11, 95% CI: 0.25–4.94) and those exposed to pesticide drift (Supplementary Material, Table SIV).

There were also weak non-significant positive associations for ocular-nasal symptoms and almost all asthma outcomes among women who reported that they re-entered the fields on the same day after pesticide spraying compared to those who re-entered the field 1–7 days after spraying.

Also presented in Table V are the results of the associations between ChE measurements and the asthma outcomes. Positive associations were found between women with ChE levels below the laboratory reference standard and ocular-nasal symptoms or FeNO outcomes. Those with ChE levels below the laboratory reference standard had, with borderline significance, an almost five-fold increased odds of having highly probable allergic airway inflammation based on the FeNO measurements when compared with the women with ChE levels above this reference value. Including variables for sensitization to house dust mite, storage mite, and spider mite into all the multivariate models in Tables SIV and SV did not change the findings (data not shown).

Additional analysis between multi-level asthma outcomes generated from current asthma, doctor-diagnosed asthma and FeNO outcomes did not add further insight to the findings of this study. Some of these results are presented in Supplementary Material Tables and SVII.

There was generally no consistent or significant association between pesticide exposure indicators and sensitization outcomes (atopy, house dust mite sensitization, storage mite sensitization; Supplementary Material, Tables SVIII and SIX).

TABLE V. Adjusted Multiple Logistic Regression Models of Pesticide Exposure Indicators Associated with Upper Airway and Asthma Outcomes Among Rural Women in the Boland of the Western Cape

Prevalence, (%) (n = 211)	Upper airway symptoms and asthma outcomes. Odds ratio (95% confidence interval)					
	Ocular-nasal symptoms 24%	Doctor-diagnosed asthma 11%	Adult-onset asthma 9%	Current asthma 6%	FeNO = 25–50 ppb 11%	FeNO >50 ppb 7%
Use pesticides at home	1.40 (0.70–2.90)	0.97 (0.40–2.50)	1.30 (0.50–3.50)	0.40 (0.10–1.70)	3.10 (1.02–9.30)*	1.10 (0.30–4.20)
History of living or working on farms	1.65 (0.57–4.76)	0.68 (0.20–2.25)	0.53 (0.14–2.02)	0.69 (0.15–3.16)	1.17 (0.40–3.41)	1.19 (0.30–4.77)
Currently Living and working on farms	0.87 (0.40–2.10)	0.80 (0.30–2.30)	0.76 (0.25–2.30)	0.70 (0.20–3.00)	1.30 (0.50–3.60)	1.90 (0.50–7.50)
Pesticide drift into the home	1.30 (0.60–2.80)	0.90 (0.30–2.70)	0.90 (0.30–2.80)	—	0.60 (0.20–2.10)	0.70 (0.20–3.30)
Permanent vs seasonal farm worker	2.24 (0.80–6.30)	0.19 (0.04–1.05)**	0.23 (0.04–1.30)	0.30 (0.02–4.30)	0.36 (0.08–1.73)	2.54 (0.20–30.00)
Immediate vs delayed re-entry	2.97 (0.93–9.50)**	4.81 (0.55–42.20)	3.49 (0.40–31.00)	—	1.24 (0.30–5.30)	0.82 (0.10–6.05)
Number of years in current farm job	1.00 (0.97–1.06)	1.01 (0.95–1.10)	1.01 (0.96–1.08)	1.00 (0.90–1.10)	0.96 (0.90–1.05)	1.02 (0.90–1.10)
Number of days of pesticide spraying/year in current farm	1.00 (0.99–1.01)	1.00 (0.99–1.00)	1.00 (0.99–1.01)	1.00 (0.99–1.01)	1.00 (0.99–1.01)	1.00 (0.99–1.01)
Cholinesterase levels < laboratory reference standard	1.10 (0.30–3.80)	—	—	—	1.14 (0.20–5.70)	4.80 (0.80–28.00)

Each OR represents a separate regression model adjusted for atopy, smoking, born on a farm and years of schooling.

—Odds Ratios not determinable.

* $P < 0.05$.

** $P < 0.1$.

Multiple logistic regression models of allergic asthma phenotypes (atopic asthma, non-atopic asthma, house dust mite allergic asthma, storage mite allergic asthma and spider mite allergic asthma) which were generated from a combination of current asthma and allergic sensitization outcomes did not reveal any meaningful information because of the low prevalence of the outcomes (Supplementary Material, Table SI).

DISCUSSION

The findings of this study demonstrated that pesticide exposure especially to organophosphates and carbamates are associated with upper and lower airway symptoms including asthma in this group of women workers working and living in nearby farms.

Consistently, positive associations were observed between the pesticide exposure variables; farm job, farm residence, household pesticide use, and low ChE levels (a marker of organophosphate or carbamate pesticide exposures) with asthma symptom scores. That the association between asthma symptoms and farm exposure or ChE persisted after controlling for household use, and that the majority (78%) of those with low ChE levels were farm workers or residents,

suggests that occupational and environmental exposures on farms were independently associated with these outcomes. These results are consistent with the results of previous studies in other settings that have shown a high prevalence of these symptoms among farm workers [Innes et al., 1990; Senthil-selvan et al., 1992; Zuskin et al., 1997; Dalvie et al., 1999; Hoppin et al., 2002; Mekonnen and Agonafrir, 2002; Zhang et al., 2002; Beseler and Stallones, 2009; Chakraborty et al., 2009; Hoppin et al., 2009].

The prevalence of ocular-nasal symptoms among farm dwellers (24%), was within the range (20–74%) of the prevalence of rhinitis reported in other countries among farm workers and the general population [Chatzi et al., 2007; Nathan, 2007; Radon et al., 2008; Slager et al., 2009, 2010]. The wide range reported could be due to the difference in the definition of upper respiratory symptoms used in these studies. The pesticides commonly associated with current rhinitis in these studies were cholinesterase-depressing pesticides such as the organophosphates (chlorpyrifos, diazinon, dichlorvos, and malathion) and carbaryl, a carbamate. However, non-cholinesterase inhibiting pesticides, such as permethrin, 2,4-D, glyphosate, paraquat, captan, and benomyl, have also been implicated [Chatzi et al., 2007; Slager et al., 2009, 2010].

The positive association between low ChE and FeNO > 50 ppb could suggest that exposure to one or more ChE inhibiting organophosphate and/or carbamate pesticides may contribute to probable allergic airway inflammation. Pesticide exposure not associated with sensitization to any of the mite allergens measured in this study could suggest that the pesticides may themselves be respiratory sensitizers causing allergic airway inflammation or alternatively, this association may be due to un-identified allergens associated with pesticide exposure. Cholinesterase-inhibiting pesticides, such as carbaryl and zineb, as well as non-cholinesterase-inhibiting pesticides, such as alachlor and nitrofen, have been shown to directly affect the immune system through a Th2 dependent mechanism leading to the development of allergy and asthma [Chalubinski and Kowalski, 2006]. Pesticides may also be irritants and can induce work-exacerbated asthma in workers with previous asthma [Hernandez et al., 2011]. To our knowledge, this is the first study that has investigated the association between depressed cholinesterase levels and elevated FeNO. This relationship should be explored further in a longitudinal study with a larger sample size.

An unexpected finding was that most of those with elevated FeNO did not have either doctor-diagnosed asthma or current asthma. An explanation for the latter could be that those with elevated FeNO may be in the pre-clinical phase of allergic asthma. It is possible that the participants may have had irritant induced or work-exacerbated asthma [Hernandez et al., 2011]. Elevated FeNO could also be due to other associated respiratory problems.

While this current study did not identify specific pesticides associated with specific atopic and non-atopic asthma outcomes, the study by Hoppin et al. [2008] among American farm women, demonstrated that the use of organophosphate pesticides, such as parathion and malathion, was associated with atopic asthma (OR = 1.46; 95% CI: 1.14–1.87). However, in a later study by Hoppin et al. [2009], it was found that use of the organophosphates coumaphos and parathion as well as heptachlor, 80/20 mix (carbon tetrachloride/carbon disulfide) and ethylene dibromide was significantly associated with atopic asthma while DDT (dichloro-diphenyltrichloroethane), an organochlorine, was significantly associated with non-atopic asthma.

In this study, spider mite sensitization was more common among farm dwellers who reported exposure to pesticide drift in homes. However, the lack of an association between low ChE levels and allergic sensitization to spider mite in this study is in contrast to findings from a previous study among table grape farm workers in the Western Cape. The latter study demonstrated an association between pesticide exposure (crop sprayers) and those workers with low acetylcholinesterase levels and allergic respiratory disease outcomes due to spider mite, *Tetranychus urticae* [Jeebhay et al., 2007].

Asthma (using different definitions for doctor-diagnosed asthma, adult-onset asthma and current asthma) was more prevalent among town dwellers despite asthma-like symptoms being higher amongst farm dwellers. This could be due to the well known protective effect of being born on a farm for atopic asthma and this has also been reported in other studies [Hoppin et al., 2008]. Another possible explanation for the lower prevalence of self-reported asthma among the farm dwellers than the town dwellers could be due to the healthy worker effect, commonly observed in cross-sectional studies, in that women that worked on farms in the past who had developed asthma may have left the farm to work in the town. Furthermore, the relatively higher prevalence of sensitization to the various mite allergens in the town dweller group suggests that these allergens were mainly responsible for the asthma when compared to the pesticide exposures in the farm dwellers group. This is supported by the results of analyses excluding non-farm women that showed a higher prevalence of doctor-diagnosed asthma, adult-onset asthma and current asthma among those reporting pesticide drift into homes as well as those workers who reported immediate re-entry into spraying fields.

The higher prevalence of asthma-like symptoms among those with a current or past history of living and/or working on farms with relatively similar allergen sensitization rates suggests a local irritant effect on the airways may also be responsible for their symptoms. Inhaled pesticides may cause damage to the airways either directly or through neurogenic inflammation which, when sustained over time may lead to non-specific bronchial hyper-reactivity and the subsequent development of asthmatic symptoms [Hernandez et al., 2011]. The latter is supported by the data indicating that farm job and residence and low ChE were associated with asthma. Furthermore, studies of animal models have reported that organophosphate pesticides can also cause asthma through inhibition of acetylcholinesterase or causing parasympathetic prejunctional muscarinic M2 receptor dysfunction leading to bronchial hyper-responsiveness [Hernandez et al., 2011]. These mechanisms may also be applicable to asthma in human subjects.

The self-reported exposures and ChE levels in this study and also evidence from other studies conducted previously among similar communities show that farm workers and residents are exposed to pesticides in the environment in a number of ways [Dalvie et al., 2003, 2004, 2009a,b; Dalvie and London, 2001, 2009c; English et al., 2012]. Up to 83% of farm dwellers reported using unprotected sources of water for drinking and household use which might be an additional source of exposure to pesticides. Data on the proportion of participants that use unprotected water sources from other studies in developed countries could not be found. However, available data on the proportion of contaminated water sources indicate that in the United States, 10.4% of community wells and 4.2% of rural wells were found to

contain detectable levels of one or more pesticides [US-EPA, 1992] and in south-western Ontario (Canada), 35% of the groundwater wells tested positive for pesticides on at least one occasion [Lampman, 1995].

Although the number of sprayers was low in this study, the percentage of farm workers (11%) that reported the use of empty containers for drinking purposes is higher than that found in previous studies amongst these communities [Dalvie et al., 2001, 2003, 2004]. The mean number of pesticide spraying days/year (96, range 72–144) is substantially higher than that reported in the Agricultural Health Study in the United States with the median number of days per year applying pesticides being in the range of 10–19 days, and only 7% applied pesticides 40 or more days per year [Hoppin et al., 2009] indicating extensive exposure to pesticides. Additionally, 67% of farm dwellers reported that workers re-entered the field on the same day after pesticide spraying. Furthermore, nearly a quarter of farm workers reported that PPE was not provided. There were at least three times as many women with low ChE levels in the farm dwellers compared to the town dwellers ($P=0.08$). These results demonstrate that these women from the farms are exposed to high levels of pesticides and were at increased risk of developing adverse respiratory health effects associated with pesticide exposure.

In this study only about 200 participants were targeted due to financial constraints. One of the limitations, therefore, in the study is the potential for selection bias in that the sampling of participants was not random and the population represented mostly export farms. However, the participants were recruited from five major agricultural areas in the Western Cape that produced a wide variety of crops, thereby representing an array of potential exposures. It is possible that since the number of applicators was relatively low, (lower than the 20% reported by the farm dwellers when asked how many women applicators there are on the farm they live or work) the true extent of exposure in this population may have been underestimated. While bio-monitoring for specific pesticides is a more sensitive method for measuring specific pesticide exposure, this could not be pursued in this study due to resource constraints. Therefore, the exposure assessment methods that were used were unable to identify specific pesticides implicated.

The use of whole blood cholinesterase as a biomarker for organophosphate also has its limitations. Whole blood ChE is regarded as a non-specific marker of OP and carbamate exposure and is only responsive when an individual is highly exposed [McCauley et al., 2006]. Since a small proportion (9%) of participants were identified as having low ChE in this study, suggests that the study may have underestimated the pesticide effect. Furthermore, whole blood ChE is also affected by individual variability and since individual seasonal monitoring was not possible in this study and this may have impacted on the findings.

CONCLUSIONS AND RECOMMENDATIONS

This study provided evidence suggesting that occupational and environmental exposure to pesticides among women working and/or living on farms in the Western Cape is associated with increased risk of ocular-nasal symptoms and asthma. The study was however limited by a small sample size, lack of information on specific pesticides and the cross sectional design. The findings need further exploration in a larger longitudinal study.

ACKNOWLEDGMENTS

This study was supported by the Women on Farms Project and the University of Cape Town as well as a grant from the National Research Foundation of South Africa [Grant no. IFR 2011041400063] and the Medical Research Council of South Africa. Vuyelwa Ndlovu was sponsored by the Centre for International Health of the Ludwig-Maximilian-University, Munich, Germany (CIHLMU) to complete her studies at the University of Cape Town. The assistance of Prof Francesca Little with regard to statistical advice is hereby acknowledged.

REFERENCES

- American Thoracic Society and the European Respiratory Society (ATS/ERS). 2005a. Recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide. *Am J Respir Crit Care Med* 171: 912–930.
- American Thoracic Society and the European Respiratory Society (ATS/ERS). 2005b. Standardisation of lung function testing: Standardisation of spirometry. *Eur Respir J* 26:319–338.
- Beseler CL, Stallones L. 2009. Pesticide poisoning and respiratory disorders in Colorado farm residents. *J Agric Saf Health* 15(4): 327–334.
- Bowers Y, London L, Holtman Z, Messina S, Arendse B, Lindoor E, Rhodes G. 2009. Obstacles to the rights of access to health care for farm worker women in the Western Cape. *Crit Health Perspect People's Health Mov S Afr* 1.
- Burney PG, Luczynska P, Chinn S, Jarvis D. 1994. The European community respiratory health survey. *Eur Respir J* 7:954–960.
- Chakraborty S, Mukherjee S, Roychoudhury S, Siddique S, Lahiri T, Ray MR. 2009. Chronic exposures to cholinesterase-inhibiting pesticides adversely affect respiratory health of agricultural workers in India. *J Occup Health* 51(6):488–497.
- Chalubinski M, Kowalski ML. 2006. Endocrine disruptors – potential modulators of the immune system and allergic response. *Allergy* 61:1326–1335.
- Chatzi L, Alegakis A, Tzanakis N, Siafakas N, Kogevinas M, Lionis C. 2007. Association of allergic rhinitis with pesticide use among grape farmers in Crete, Greece. *Occup Environ Med* 64(6):417–421.
- Dalvie MA, White N, Raine R, Myers JE, London L, Thompson M, Christiani DC. 1999. Long-term respiratory health effects of the

- herbicide, paraquat, among workers in the Western Cape. *Occup Environ Med* 56(6):391–396.
- Dalvie MA, London L. 2001. Unwanted agricultural chemicals in Stellenbosch: A need for public health intervention. *S Afr J Sci* 97(7&8):309–312. *S Afr J Sci* 95(8):316–320.
- Dalvie MA, Cairncross E, Solomon A, London L. 2003. Contamination of rural surface and ground water by endo-sulfan in farming areas of the Western Cape, South Africa. *Environ Health* 2:1.
- Dalvie MA, Myers JE, Lou Thompson M, Dyer S, Robins TG, Omar S, Riebow J, Molekwa J, Kruger P, Millar R. 2004. The hormonal effects of long term DDT exposure on malaria vector control workers in Limpopo Province, South Africa. *Environ Res* 96(1):9–19.
- Dalvie MA, Africa A, Solomons A, London L, Brouwer D, Kromhout H. 2009a. Pesticide exposure and blood endosulfan levels after first season spray amongst farm workers in the Western Cape, South Africa. *J Environ Sci Health B* 44(3):271–277.
- Dalvie MA, Africa A, London L. 2009b. Change in the quantity and acute toxicity of pesticides sold in South African crop sectors. 1994–1999. *Environ Int* 35(4):683–687.
- Dalvie MA, London L. 2009c. Risk assessment of pesticide residues in South African raw wheat. *Crop protection* 28(10):864–869.
- Dalvie MA, Naik I, Channa K, London L. 2011. Urinary dialkyl phosphate levels before and after first season chlorpyrifos spraying amongst farm workers in the Western Cape, South Africa. *J Environ Sci Health B* 46(2):163–172.
- Ellman GL, Courtney KD, Andres V, Featherstone RM. 1961. A new and rapid colorimetric determination of acetylcholinesterase activity. *Biochem Pharmacol* 7:88–95.
- English RG, Perry M, Lee MM, Hoffman E, Delpont S, Dalvie MA. 2012. Farm residence and reproductive health among boys in rural South Africa. *Environ Int* 47C:73–79.
- Faria NM, Facchini LA, Fassa AG, Tomasi E. 2005. Pesticides and respiratory symptoms among farmers. *Rev Saude Publica* 39(6):973–981.
- Fieten KB, Kromhout H, Heederik D, van Wendel de Joode B. 2009. Pesticide exposure and respiratory health of indigenous women in Costa Rica. *Am J Epidemiol* 169(12):1500–1506.
- Garcia AM. 2003. Pesticide exposure and women's health. *Am J Ind Med* 44(6):584–594.
- Haigh JR, Lefkowitz LJ, Capacioc BR, Doctora BP, Gordon RK. 2008. Advantages of the WRAIR whole blood cholinesterase assay: Comparative analysis to the micro-Ellman, Test-mate ChETM, and Michel (delta pH) assays. *Chem Biol Interact* 175:417–420.
- Hernandez AF, Parron T, Alarcon R. 2011. Pesticides and asthma. *Curr Opin Allergy Clin Immunol* 11(2):90–96.
- Hoppin JA, Umbach DM, London SJ, Alavanja MC, Sandler DP. 2002. Chemical predictors of wheeze among farmer pesticide applicators in the agricultural health study. *Am J Respir Crit Care Med* 165(5):683–689.
- Hoppin JA, Umbach DM, London SJ, Lynch CF, Alavanja MC, Sandler DP. 2006. Pesticides associated with wheeze among commercial pesticide applicators in the agricultural health study. *Am J Epidemiol* 163(12):1129–1137.
- Hoppin JA, Umbach DM, London SJ, Henneberger PK, Kullman GJ, Alavanja MC, Sandler DP. 2008. Pesticides and atopic and nonatopic asthma among farm women in the agricultural health study. *Am J Respir Crit Care Med* 177(1):11–18.
- Hoppin JA, Umbach DM, London SJ, Henneberger PK, Kullman GJ, Coble J, Alavanja MC, Beane Freeman LE, Sandler DP. 2009. Pesticide use and adult-onset asthma among male farmers in the agricultural health study. *Eur Respir J* 34(6):1296–1303.
- Innes DF, Fuller BH, Berger GM. 1990. Low serum cholinesterase levels in rural workers exposed to organophosphate pesticide sprays. *S Afr Med J* 78(10):581–583.
- Jeebhay MF, Baatjies R, Chang YS, Kim YK, Kim YY, Major V, Lopata AL. 2007. Risk factors for allergy due to the two-spotted spider mite (*Tetranychus urticae*) among table grape farm workers. *Int Arch Allergy Immunol* 144(2):143–149.
- Lampman W. 1995. Susceptibility of groundwater to pesticide and nitrate contamination in predisposed areas of south-western Ontario. *Water Qual Res J Canada* 30:443–468.
- London L. 2003. Human rights, environmental justice and the health of farm workers in South Africa. *Int J Occup Environ Health* 9:59–68.
- London L, de Grosbois S, Wesseling C, Kisting S, Rother H, Mergler D. 2002. Pesticide usage and health consequences for women in developing countries: Out of sight, out of mind? *Int J Occup Environ Health* 8(1):46–59.
- McCauley LA, Anger WK, Keifer M, Langley R, Robson MG, Rohlman D. 2006. Studying health outcomes in farm worker populations exposed to pesticides. *Environ Health Perspect* 114:953–960.
- Mekonnen Y, Agonafir T. 2002. Effects of pesticide applications on respiratory health of Ethiopian farm workers. *Int J Occup Environ Health* 8(1):35–40.
- Naidoo V, Buckley CA. 2003. Survey of pesticide wastes in South Africa and review of treatment options. *Water Research Commission (WRC) Pretoria* 1128/1/03.
- Nathan RA. 2007. The burden of allergic rhinitis. *Allergy Asthma Proc* 28:3–9.
- Ndlovu V, Dalvie MA, Jeebhay MF. 2011. Pesticides and the airways - A review of the literature. *Curr Allergy Clin Immunol* 24(4):212–217.
- Pekkanen J, Sunyer J, Anto JM, Burney P on behalf of the European Community Respiratory Health Study (ECRHS). 2005. Operational definitions of asthma in studies on its aetiology. *Eur Respir J* 26:28–35.
- Quirce S, Lemiere C, de Blay F, del Pozo V, Gerth Van Wijk R, Maestrelli P, Pauli G, Pignatti P, Raulf-Heimsoth M, Sastre J, et al. 2010. Noninvasive methods for assessment of airway inflammation in occupational settings. *Allergy* 65(4):445–458.
- Radon K, Gerhardinger U, Schulze A, Zock JP, Norback D, Toren K, Jarvis D, Held L, Heinrich J, Leynaert B, et al. 2008. Occupation and adult-onset of rhinitis in the general population. *Occup Environ Med* 65(1):38–43.
- Senthilselvan A, McDuffie HH, Dosman JA. 1992. Association of asthma with use of pesticides. Results of a cross-sectional survey of farmers. *Am Rev Respir Dis* 146(4):884–887.
- Slager RE, Poole JA, LeVan TD, Sandler DP, Alavanja MC, Hoppin JA. 2009. Rhinitis associated with pesticide exposure among commercial pesticide applicators in the agricultural health study. *Occup Environ Med* 66(11):718–724.
- Slager RE, Simpson SL, Levan TD, Poole JA, Sandler DP, Hoppin JA. 2010. Rhinitis associated with pesticide use among private pesticide applicators in the agricultural health study. *J Toxicol Environ Health A* 73(20):1382–1393.
- Sunyer J, Pekkanen J, Garcia-Esteban R, Svanes C, Künzli N, Janson C, de Marco R, Anto JM, Burney P. 2007. Asthma score: Predictive ability and risk factors. *Allergy* 62:142–148.
- US-EPA. 1992. National pesticide survey: Update and summary of phase II results. Office of Water & Office of Pesticides and Toxic

Substances, United States Environmental Protection Agency Report # EPA570/9-91-021, Washington, DC.

Vizcaya D, Mirabelli MC, Anto JM, Orriols R, Burgos F, Arjona L, Zock JP. 2011. A workforce-based study of occupational exposures and asthma symptoms in cleaning workers. *Occup Environ Med* 68:914–919.

Zhang LX, Enarson DA, He GX, Li B, Chan-Yeung M. 2002. Occupational and environmental risk factors for respiratory symptoms in rural Beijing, China. *Eur Respir J* 20(6):1525–1531.

Zuskin E, Mustajbegovic J, Schachter EN, Kern J, Pavicic D. 1997. Respiratory function in vineyard and orchard workers. *Am J Ind Med* 31:250–255.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article at the publisher's web-site.

Disclosure Statement: The authors report no conflicts of interest.

Work performed at the Centre for Occupational and Environmental Health Research, School of Public Health and Family Medicine, University of Cape Town, Private bag X3, Rondebosch, 7701, South Africa.

Supplementary Material

Table I

Adjusted multiple logistic regression models of pesticide exposure indicators associated with asthma phenotypes among women farm workers in the Boland of the Western Cape

	Allergic Asthma phenotypes. Odds Ratio (95% Confidence Interval)				
	Atopic asthma	Non-atopic asthma	House dust mite allergic asthma	Storage mite allergic asthma	spider mite allergic asthma
Prevalence (%) (n=211)	5	1	3	3	3
Household pesticide use	0.60(0.16-2.30)	-	0.73(0.15-3.50)	0.73(0.15-3.50)	0.37(0.065-2.06)
History of living or working on farms	0.28(0.06-1.25)	0.34(0.02-6.53)	0.46(0.07-2.89)	0.46(0.07-2.89)	0.17(0.03-1.09)
Currently Living and working on farms	0.26(0.06-1.09)	0.72(0.04-12.13)	0.48(0.10-2.35)	0.48(0.10-2.35)	0.23(0.04-1.35)
Exposure to pesticide drift	-	-	-	-	-
Permanent vs seasonal farmworker	-	-	-	-	-
Immediate vs Delayed re-entry	-	-	-	-	-
Number of years in current farm job	0.79(0.56-1.12)	1.11(0.96-1.28)	0.84(0.62-1.13)	0.84(0.62-1.13)	0.60(0.16-2.15)
Number of days of pesticide spraying/year in current farm	0.99(0.98-1.00)	-	1.00(0.99-1.01)	1.00(0.99-1.01)	1.00(0.98-1.00)
Cholinesterase levels < laboratory reference standard	-	-	-	-	-

* p<0.05; ** p<0.01; *** p<0.001.

Each OR represents a separate regression model adjusted for smoking, and years of schooling.

-Odds Ratios not determinable

Table II.

Unadjusted negative binomial regression models of host factors and other potential confounders associated with asthma symptom score among women farm workers in the Boland of the Western Cape

	Asthma symptom score
	IRR(95% CI) ^a
Age (years)	1.00(0.99-1.02)
BMI (kg/m ²)	1.01(0.99-1.04)
Atopy (Positive Phadiatop)	1.22(0.84-1.78)
Education (years of schooling)	0.89(0.84-0.94)***
Currently employed	1.09(0.74-4.96)
Household income/month(\$US)	0.99(0.99-1.00)
Born on a farm	1.45(1.01-2.10)*
Drinks alcohol	1.30(0.89-1.90)
Current smoker	1.38(0.62-2.00) ^b

*p < 0.05; **p < 0.01; ***p < 0.001

^a Negative binomial regression models IRR (Incidence Rate Ratio), the ratio of the mean score among exposed and unexposed.

^bp=0.07

Table III.

Unadjusted logistic regression models of host and other potential confounders associated with upper airway symptoms and asthma outcomes among women farm workers in the Boland of the Western Cape

	Upper airway symptoms and Asthma outcomes. Odds Ratio (95% Confidence Interval)					
	Ocular nasal symptoms	Doctor diagnosed asthma	Adult onset asthma	Current asthma	FeNO=25ppb-50ppb	FeNO>50ppb
Prevalence, (%) (n=211)	24%	11%	9%	6%	11%	7%
Age (years)	1.00(0.96-1.02)	1.01(0.98-1.05)	1.02(0.99-1.06)	1.04(0.99-1.09)	1.00(0.95-1.03)	0.99(0.95-1.04)
BMI (kg/m ²)	1.02(0.98-1.07)	1.02(0.96-1.08)	1.03(0.97-1.10)	1.01(0.93-1.10)	1.05(0.98-1.11)	1.02(0.95-1.10)
Atopy (Positive Phadiatop)	3.79(1.93-7.48) ***	3.37(1.32-8.58) *	3.10(1.13-8.5)*	7.12(1.52-33.40) *	2.2(0.9-5.34)	21.28(2.74-165.23)***
Education (years of schooling)	0.96(0.87-1.06)	0.85(0.74-0.96) ***	0.85(0.74-0.97) *	0.78(0.66-0.92) **	0.95(0.83-1.09)	1.18(0.96-1.46)
Currently Employed	0.91(0.48-1.74)	0.86(0.36-2.07)	0.73(0.28-1.87)	0.46(0.14-1.5)	0.56(0.24-1.34)	0.55(0.19-1.58)
Household income/month (\$US)	1.00(0.99-1.00)	0.99(0.99-1.00)	1.00(0.99-1.00)	1.00(0.99-1.00)	1.00(0.99-1.00)	1.00(0.99-1.00)
Born on a farm	2.41(1.26-4.63) **	0.61(0.25-1.50)	0.67(0.25-1.79)	0.10(0.01-0.79)*	0.29(0.10-0.81)*	0.27(0.07-0.99) *
Drink alcohol	1.39(0.72-2.66)	0.69(0.29-1.65)	0.54(0.21-1.41)	0.37(0.11-1.28)	0.84(0.35-2.00)	0.67(0.23-1.91)
Current smoker	0.82(0.43-1.55)	1.66(0.68-4.02)	1.43(0.55-3.72)	1.44(0.44-4.70)	0.62(0.25-1.49)	0.23(0.06-0.84) *

*p < 0.05; **p < 0.01; ***p < 0.001.

Each OR represents a separate unadjusted logistic regression model

Table IV

Adjusted multiple logistic regression models of pesticide exposure indicators associated with asthma outcomes among women farm workers in the Boland of the Western Cape

	Asthma outcomes. Odds Ratio (95% Confidence Interval)						
	Ocular nasal	Current asthma	Doctor diagnosed	Adult onset asthma	FENO=25ppb-	FENO>50ppb	Asthma score ^a
	symptoms		asthma		50ppb		
History of living or working on farms	1.67(0.58-4.86)	0.70(0.15-3.23)	0.68(0.20-2.25)	0.53(0.14-2.02)	1.26(0.42-3.76)	1.20(0.30-4.85)	2.24(1.31-3.83)**
Currently Living and working on farms	0.89(0.37-2.14)	0.64(0.14-2.90)	0.81(0.28-2.30)	0.78(0.25-2.42)	1.48(0.53-4.15)	2.02(0.50-8.16)	2.28(1.47-3.53)***
Pesticide drift into the home ^b	1.66(0.65-4.24)	-	1.04(0.26-4.15)	1.11(0.25-4.94)	0.44(0.12-1.67)	0.20(0.02-1.92)	1.57(1.06-2.32)

* p< 0.05; ** p < 0.01; *** p < 0.001. Each OR represents a separate regression model adjusted for atopy, smoking, born on a farm, years of schooling and household pesticide use.

^a Negative binomial regression used for asthma score. It models IRR (Incidence Rate Ratio), the ratio of the mean score among exposed and unexposed.

^b sub analysis of farm dwellers only with each OR representing a separate regression model adjusted for atopy, smoking, born on a farm and years of schooling.

Table V

Unadjusted and adjusted linear regression models of pesticide exposure indicators associated with asthma outcomes among women farm workers in the Boland of the Western Cape

Pesticide exposure variable	Unadjusted log FENO	Adjusted log FENO ^a
	β coefficient (95% CI)	β coefficient (95% CI)
Use pesticides at home	0.08(-0.01-0.18)	0.03(-0.05-0.12)
History of living or working on farms	-0.18(-0.28- -0.08)**	-0.06(-0.18-0.06)
Currently living and working on farms	-0.12(-0.21- -0.02)*	0.01(-0.09-0.11)
Pesticide drift into the home	-0.12(-0.22- -0.02)*	-0.05(-0.15-0.05)
Permanent vs seasonal farmworker	0.12(-0.02-0.26)	0.05(-0.08-0.17)
Re-entry into sprayed fields		
Immediate vs Delayed re-entry	-0.02(-0.16-0.12)	-0.24(-0.16-0.10)
Number of years in current farm job	-0.01(-0.01- -0.02)**	-0.01(-0.01-0.01)
Number of days of pesticide spraying/year in current farm	-0.01(-0.01- -0.01)	-0.01(-0.01-0.01)
Cholinesterase levels < laboratory reference standard	0.13(-0.04-0.30)	0.09(-0.06-0.25)

* p< 0.05; ** p < 0.01; *** p < 0.001.

^aEach β coefficient represents a separate linear regression model adjusted for atopy, born on a farm, smoking, and years of schooling.

Table VI

Adjusted multiple logistic regression models of pesticide exposure indicators associated with multilevel asthma outcomes among rural women in the Boland of the Western Cape

	Multilevel Asthma outcomes. Odds Ratio (95% Confidence Interval)			
	Doctor diagnosed asthma or FeNO > 50ppb 18%	Doctor diagnosed asthma or FeNO 25ppb-50ppb 19%	Current asthma or FeNO > 50ppb 12%	Current asthma or FeNO 25ppb-50ppb 15%
Prevalence, (%) (n=211)				
Use pesticides at home	1.11(0.49-2.51)	1.63(0.75-3.51)	0.72(0.27-1.98)	1.53(0.64-3.65)
History of living or working on farms	0.82(0.31-2.18)	0.71(0.28-1.80)	1.03(0.35-3.04)	0.86(0.33-2.23)
Currently Living and working on farms	1.19(0.49-2.89)	1.04(0.45-2.36)	1.43(0.50-4.07)	1.19(0.49-2.94)
Pesticide drift into the home	0.85(0.33-2.16)	0.83(0.35-1.98)	0.38(0.10-1.47)	0.41(0.13-1.32)
Permanent vs seasonal farmworker	0.48(0.14-1.64)	0.27(0.08-0.90)	1.19(0.23-6.12)	0.33(0.08-1.34)
Immediate vs Delayed re-entry	2.32(0.57-9.46)	1.88(0.55-6.38)	1.79(0.30-10.80)	1.64(0.40-6.87)
Number of years in current farm job	1.01(0.96-1.07)	1.00(0.95-1.05)	1.01(0.94-1.08)	0.98(0.92-1.05)
Number of days of pesticide spraying/year in current farm	1.00(0.99-1.01)	1.00(0.99-1.01)	1.00(0.99-1.01)	1.00(0.99-1.01)
Cholinesterase levels < laboratory reference standard	1.19(0.29-4.91)	0.59(0.12-2.83)	2.69(0.54-13.35)	0.90(0.18-4.47)

* p < 0.05; ** p < 0.01; *** p < 0.001. Each OR represents a separate regression model adjusted for atopy, smoking, born on a farm and years of schooling

Table VII

Adjusted multiple logistic regression models of pesticide exposure indicators associated with multilevel asthma outcomes among rural women in the Boland of the Western Cape

	Multilevel Asthma outcomes. Odds Ratio (95% Confidence Interval)					
	Doctor diagnosed asthma or score50	Doctor diagnosed asthma or score75	Current asthma or score50	Current asthma or score75	Score at 75 th percentile or FeNO>50ppb	Doctor diagnosed asthma or Score at 75 th percentile or FeNO>50ppb
Use pesticides at home	0.71(0.39-1.29)	1.56(0.82-2.97)	0.58(0.32-1.06)	1.49(0.77-2.86)	1.73(0.92-3.27)	1.60(0.85-3.00)
History of living or working on farms	0.16(0.06-0.39)***	1.96(0.82-4.66)	0.17(0.07-0.41)***	2.39(0.98-5.80)	2.18(0.94-5.04)	1.87(0.82-4.28)
Currently Living and working on farms	0.27(0.13-0.55)***	2.69(1.25-5.76)*	0.27(0.13-0.55)***	3.25(1.48-7.16)**	3.39(1.58-7.27)**	2.84(1.34-6.00)*
Pesticide drift into the home	0.28(0.14-0.54)***	0.27(0.09-0.82)	0.22(0.11-0.44)	2.55(1.23-5.29)*	2.49(1.23-5.05)*	2.51(1.23-5.10)
Permanent vs seasonal farm worker	0.76(0.34-1.71)	1.17(0.50-2.79)	1.05(0.46-2.40)	1.36(0.56-3.27)	2.02(0.84-4.83)	1.53(0.65-3.63)
Immediate vs Delayed re-entry	0.77(0.34-1.75)	1.33(0.56-3.17)	0.64(0.28-1.45)	1.37(0.56-3.31)	1.16(0.49-2.74)	1.22(0.51-2.90)
Number of years in current farm job	0.96(0.92-0.99)*	1.01(0.97-1.05)	0.95(0.91-0.99)*	1.01(0.97-1.05)	1.02(0.98-1.06)	1.02(0.98-1.06)
Number of days of pesticide spraying/year in current farm	0.99(0.98-0.99)	1.00(0.99-1.01)	1.00(0.99-1.01)	1.00(0.99-1.01)	1.00(0.99-1.01)	1.00(0.99-1.01)
Cholinesterase levels < laboratory reference standard	0.33(0.12-0.94)*	1.71(0.59-4.94)	0.39(0.14-1.12)	2.06(0.71-5.98)	2.51(0.89-7.09)	1.97(0.69-5.63)

* p< 0.05; ** p < 0.01; *** p < 0.001. Each OR represents a separate regression model adjusted for atopy, smoking, born on a farm and years of schooling

Table VIII

Unadjusted logistic regression models of host and other potential confounders associated with allergic sensitisation outcomes among women farm workers in the Boland of the Western Cape

	Allergic sensitisation outcomes Odds Ratio (95% Confidence Interval)			
	House dust mite sensitisation	Storage mite sensitisation	Spider mite sensitisation	Atopy (Positive Phadiatop)
Age (years)	0.99(0.97-1.02)	1.01(0.98-1.04)	1.01(0.98-1.04)	1.00(0.98-1.03)
BMI (kg/m ²)	1.02(0.97-1.06)	0.99(0.95-1.04)	0.97(0.91-1.02)	1.02(0.98-1.06)
Atopy (Positive Phadiatop)	81.65(18.97-351.47)***	-	11.00(4.06-29.83)***	-
education (years of schooling)	0.95(0.86-1.05)	0.93(0.84-1.03)	0.92(0.82-1.03)	0.97(0.89-1.06)
Currently Employed	0.71(0.38-1.32)	0.72(0.37-1.42)	0.47(0.23-0.98)*	0.58(0.33-1.02)
Household income /month(\$US)	1.00(1.00-1.01)	1.00(1.00-1.01)	1.00(1.00-1.01)	1.00(1.00-1.01)
Born on a farm	0.42(0.22-0.81)**	0.60(0.30-1.19)	0.73(0.35-1.54)	0.64(0.37-1.12)
Drink alcohol	1.33(0.71-2.49)	0.89(0.46-1.74)	2.12(0.96-4.68)	1.26(0.72-2.20)
Current smoker	1.38(0.74-2.57)	1.98(1.00-3.93)	1.57(0.75-3.30)	1.44(0.83-2.50)

*p < 0.05; **p < 0.01; ***p < 0.001.

Each OR represents a separate unadjusted logistic regression model

-OR not determinable

Table IX

Adjusted multiple logistic regression models of pesticide exposure indicators associated with allergic sensitisation outcomes among women farm workers in the Boland of the Western Cape

Prevalence (%) (n=211)	Allergic sensitisation outcomes Odds Ratio (95% Confidence Interval)			
	House dust mite sensitisation 27	Storage mite sensitisation 21	Spider mite sensitisation 17	Atopy (Positive Phadiatop) ^a 44
Use pesticides at home	1.38(0.56-3.38)	1.86(0.72-4.80)	0.76(0.33-1.75)	1.12(0.63-2.00)
History of living or working on farms	1.33(0.43-4.12)	0.72(0.23-2.28)	0.48(0.16-1.47)	0.98(0.45-2.12)
Currently Living and working on farms	2.26(0.80-6.40)	1.20(0.44-3.29)	0.90(0.35-2.28)	0.64(0.33-1.24)
Pesticide drift into the home	0.51(0.19-1.33)	1.07(0.39-2.90)	1.10(0.44-2.78)	0.91(0.47-1.75)
Pesticide drift in the farm dweller group only	0.14(0.03-0.61)	0.87(0.24-3.08)	1.12(0.36-3.51)	
Permanent vs seasonal farmworker	0.48(0.12-1.89)	1.49(0.37-5.92)	0.60(0.17-2.19)	1.77(0.76-4.13)
Immediate vs Delayed re-entry	0.99(0.26-3.69)	0.40(0.10-1.65)	1.06(0.31-3.66)	0.94(0.41-2.16)
Number of years in current farm job	1.02(0.96-1.08)	1.01(0.95-1.07)	0.96(0.90-1.02)	0.99(0.95-1.03)
Cholinesterase levels < laboratory reference standard	1.48(0.29-7.70)	1.38(0.25-7.60)	0.83(0.16-4.35)	0.75(0.26-2.16)

* p< 0.05; ** p < 0.01; *** p < 0.001. Each OR represents a separate regression model adjusted for atopy, smoking, born on a farm and years of schooling.

^aEach OR represents a separate regression model adjusted for smoking, born on a farm and years of schooling.