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# Obstructive Lung Disease Linked to Occupational Exposures in Malawian Tobacco Farmers

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**ABSTRACT**

Nicotine and pesticide exposure in agricultural settings have been linked to the development of chronic respiratory disease in workers. However, this has not been extensively studied in Africa. The aim of this study was therefore to determine the prevalence of obstructive lung disease and its relationship to concurrent nicotine and pesticide exposure among small-scale tobacco farmers in Malawi. For this purpose, sociodemographic characteristics, occupational and environmental exposures were evaluated in relation to work-related respiratory symptoms and lung function impairment. A cross-sectional study was conducted enrolling 279 workers in flue-cured tobacco farms in Zomba, Malawi. The study instruments used for assessing the health outcomes were a standardised European Community Respiratory Health Survey II (ECRHS) questionnaire and Spirometry testing. The questionnaires were aimed at collecting relevant data on sociodemographic factors and self-reported respiratory health outcomes. Data were also collected on potential pesticide and nicotine exposures. Spirometry was done to evaluate objective respiratory impairment in accordance with American Thoracic Society guidelines. The mean age of participants was 38 years with 68% being male. The prevalence of work-related ocular nasal symptoms, chronic bronchitis, and work-related chest symptoms was 20%, 17%, and 29%, respectively. Airflow limitation (FEV1/FVC <70%) was found in 8% of workers. Self-reported exposure to pesticides varied from 72%- to 83%, whilst the prevalence of recent green tobacco sickness was 26%. Tasks linked to nicotine exposure, such as sowing (OR: 2.5; CI 1.1–5.7) and harvesting (OR: 2.6; CI 1.4–5.1), were significantly associated with work-related chest symptoms. Pesticide application (OR:1.96; CI 1.0–3.7) was associated with an increased risk of work-related oculonasal symptoms. Duration of pesticide exposure was also associated with obstructive impairment FEV1/FVC<LLN (OR: 5.11; CI 1.6–16.7) and FEV1/FVC <70% (OR: 4.68; CI 1.2–18.0). This study demonstrated that tobacco farmers in Malawi had a high prevalence of respiratory symptoms and airflow limitation due to obstructive lung disease. This could be attributed to nicotine or pesticide exposure in small-scale tobacco farming. The implementation of occupational health and safety measures to mitigate these exposures may play an important role in modifying the risk of obstructive lung disease in this population.

**KEYWORDS**
Obstructive lung disease; tobacco farming; pesticides; nicotine

## Introduction

Malawi's economy is reliant on agriculture for subsistence and commercial reasons. Tobacco is the main cash crop[1] and Malawi is ranked among the five largest tobacco producers globally.[2] About 20% of the national labour force is involved in mainly small-scale tobacco farming. Tobacco farming involves processes such as tilling, sterilizing the nursery, planting and transplanting, weeding, topping, chemical spraying, harvesting, stacking, curing and packing for transportation. In each of these work processes, workers are exposed to various hazards such as organic and inorganic dusts, biomass smoke, pesticides and nicotine, all of which have the potential to adversely affect respiratory health.[2–4]

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Tobacco farming involves the utilization of a large amount of diverse pesticides. The commonly used chemicals are organophosphates, pyrethroids, synthetic pyrethroids, and neonicotinoids, among others.[5] A study among Pakistani tobacco farmers reported a high concentration of neonicotinoid, carbamate, pyrethroid and organochlorine pesticide residues above the acceptable daily intake (ADI) for humans in the blood of tobacco farmers.[6] Health effects among pesticide handlers are associated with the type of pesticide, number of chemicals handled, use of protective equipment, duration of exposure/tasks, age, and gender.[7] Studies on pesticide handlers in tobacco farming have shown an increased risk of allergic and nonallergic wheezes among this group of workers.[4,8,9] In agricultural settings, exposure to pesticides such as organophosphates, pyrethroids, neonicotinoids, and herbicides have been associated with respiratory effects such as wheeze, rhinitis, as well as atopic and nonatopic asthma.[10–13]

A study by Yoo et al.[14] demonstrated that various sections of tobacco farms have very high levels of environmental nicotine reaching 610.3 mg/m$^3$ against the threshold limit value[15] time weighted average of 0.5 mg/m$^3$. Such high exposures were noted in the barns and were generally higher than in the fields. Tobacco farm exposures are associated with Green Tobacco Sickness (GTS) as a result of nicotine exposure in a dose-dependent manner.[3] GTS occurs due to inhalation of environmental nicotine and dermal absorption of nicotine from wet tobacco leaves during tobacco farming. It was first described in the 1970s as a neurotoxic syndrome characterized by headache, nausea, vomiting, and headache. Other symptoms may also be present such as abdominal cramps, diarrhea, and palpitations. It occurs as a result of stimulation of cholinergic receptors in the nervous system.[4,16] A Brazilian study of tobacco farmers found a greater risk of wheezing and GTS associated with barn storage of tobacco leaves. The findings showed an increased risk of wheezing in men involved with strenuous work and lifting sticks with tobacco leaves to the curing barns.[17] Among the females in that study, strenuous work and tying hands of tobacco were associated with wheezing.[17] In vitro, nicotine has been shown to affect the mucin formation in the airways as well as disrupting the surfactant levels in the lungs.[18] It has been postulated through these mechanisms that nicotine may increase airway resistance and predispose to obstructive pulmonary disease. These findings suggest that increased nicotine exposure resulting in GTS may also potentially increase the risk of adverse respiratory health outcomes.

Globally, there is limited information about the role of tobacco farm exposures in obstructive lung diseases such as Chronic Obstructive Pulmonary Disease (COPD) and asthma.[2,17,19] There is paucity of documented studies in this population to our knowledge, which focused on the adverse respiratory effects associated with tobacco cultivation. Studies that have investigated obstructive lung disease prevalence have not extensively evaluated the potential association with workplace exposures.[5,6]

Nicotine and pesticide exposure in agricultural settings have been linked to the development of chronic respiratory disease in workers. However, this has not been extensively studied in Africa. The aim of this study was therefore to determine the prevalence of obstructive lung disease and its relationship to concurrent nicotine and pesticide exposure among small-scale flue cured tobacco farmers in Malawi. For this purpose, sociodemographic characteristics, occupational and environmental exposures were evaluated in relation to work-related respiratory symptoms and lung function impairment.

## Methods

### *Study design, population and sampling*

This was a cross-sectional study of 279 small-scale flue-cured tobacco farm workers employed in four tobacco estates in Zomba, Malawi. A tobacco farm worker was considered to be an individual of 18 years or older involved in cultivating or handling tobacco in the fields, barns or offices as part of their job.

Participants were selected from the largest estates of the district based on the Tobacco Control Commission employment statistics. The four neighbouring largest estates that include flue curing as part of the tobacco process were chosen. After considerations of the total number of employees per farm, all available workers within these tobacco estates aged 18 years and above, were invited to participate in the study. Invitations were made in order to have representation from all departments. The study was conducted at the end of the work shift during the spraying and topping season, which was between December 2017 and January 2018.

The minimum sample size computed, based on a population size of 5,000 tobacco farmers and an estimated population COPD prevalence of 10%[20] (with 5% margin of error, power of 80% and 95% confidence level) was 136 participants. As this was the minimum sample size needed and given that we were interested in multiple outcomes some for which the prevalence is unknown, we oversampled by approximately doubling the sample size (279). This would also enable the investigation of multiple associations and biologically plausible risk factors with the outcomes of interest and strengthen the estimates generated.

### Data collection

Data were collected electronically by trained interviewers. A modified European Community Respiratory Health Survey II questionnaire[21] (ECHRS) stranslated into Chichewa was used and data was collected electronically using Open Data Kit (ODK) software on computer tablets. The questionnaire was modified for local conditions and was also translated into Chichewa and back translated to assess validity and reproducibility. The questionnaire was administered to consenting participants and included participants' demographic characteristics and questions about respiratory symptoms with specific reference to GTS, asthma and chronic bronchitis. Additional questions on demographic, occupational and environmental risk factors with particular reference to nicotine and pesticide exposures were included.

Data related to nicotine exposure was qualitatively assessed using proxy indicators such as performing work tasks that regularly involved contact with tobacco and the presence of GTS symptoms within the past 12 months. Involvement in tasks with tobacco contact included transplanting, topping, harvesting or curing. In this study GTS symptom was considered to be present if any one of the four common symptoms of headache, dizziness, nausea or vomiting was present.[22]

Pesticide exposure was qualitatively assessed using proxy indicators such as tasks involving regular pesticide use resulting in environmental exposure. These included working with pesticides, cleaning the spraying equipment, working near pesticide applicators, entering the field soon after spraying, pesticide drift into the home, use of pesticides in the home and other related tasks.[23].

Lung function data was collected through spirometry tests that were conducted according to guidelines of the American Thoracic Society/European Respiratory Society (ATS/ERS)[24] using EasyOne PC Spirometer[25] (NDD Medical Technologies, Zurich, Switzerland) according to the manufacturer's instructions. Field staff were trained to ensure the quality of spirograms using ATS/ERS Guidelines for interpretation of spirometry.[24] Spirometers were computer based and were calibrated by a 3 L syringe before each session. Special instructions were given to workers to abstain from smoking tobacco (at least 2 hours before), taking any anti-asthmatic inhalers (12 hours before) or oral asthma medications (48 hours before) prior to the test. Both the National Health and Nutrition examination survey (NHANES) and the Global Lung Function Initiative (GLI) 2012 reference values using "other" ethnic group were used for grading impairment of lung function.[26,27]

HIV status was determined by self-reporting and verification with consent to view the health passport. Counselling and testing was offered using HIV rapid test kits to consenting participants with unknown HIV status.

### Operational definitions

The dependent variables were symptom-based definitions of obstructive lung disease (based on respiratory questionnaire) as well as spirometry-based definitions of lung function limitation (based on standardized spirometry testing). These were the main outcomes of interest:

*Current asthma* was defined as an attack of shortness of breath (SOB) in the last 12 months or asthma attack in the last 12 months or current use of asthma medication (ECRHS definition).[28]

*Asthma symptom score* was computed based on the sum of answers (0=no, 1=yes) to five questions of asthma-related symptoms in the past 12 months. These were shortness of breath while wheezing, woken up with chest tightness, attack of shortness of breath (SOB) at rest, attack of shortness of breath after exercise, and woken up by an attack of shortness of breath.[29] An asthma symptom score ≥2 was used a cut-off for identifying more symptomatic asthma.

*Chronic bronchitis* was defined as cough and sputum on most days lasting at least 3 months for two consecutive years.

*Work-related chest symptoms* were defined as episode of high exposure at work causing tight chest, shortness of breath, wheeze or cough

*Work-related ocular-nasal symptoms* (WRONS) were defined as an episode of high exposure at work causing irritation of the eyes or nose.

Spirometry-based airway obstruction was defined as an $FEV_1$<Lower Limit of Normal (LLN) or $FEV_1/FVC$<LLN using the Global Lung Initiative (GLI) reference equations; $FEV_1$ <80% or $FEV_1/FVC$ <70% using the NHANES III reference values.

Independent variables were those linked to nicotine and pesticide exposure with relevant host and demographic factors considered as potential confounders as outlined below.

The main exposure variables for nicotine exposure were GTS symptoms, tasks involving contact with tobacco, e.g., weeding, topping, harvesting, hanging tobacco, sorting, grading, stacking and related tasks.

For Pesticide exposure assessment variables included working with pesticides, cleaning spraying equipment, working near pesticide applicators, getting into the field soon after spraying, pesticide drift into the home, use of tobacco pesticides at home, and related tasks. Confounding factors and covariates:

Potential occupational covariates that were considered were host factors such as age, gender, smoking status, family history of asthma, use of biomass fuel, HIV status, and previous TB episode.

### *Statistical analysis*

In this study, both continuous and categorical analyses were conducted using statistical package STATA version 14. Frequencies and percentages were used to summarize categorical variables, whilst the mean and standard deviation (and where appropriate median and interquartile range) were used for numerical variables. Bivariate analysis was conducted to investigate the association between occupational or environmental risk factors and adverse respiratory health outcomes. Unadjusted logistic regression was used to investigate the association between occupational/environmental risk factors and health outcomes. Finally, multivariate logistic regression was conducted to investigate the association between significant exposures adjusted for potential confounders and potential covariates that were considered included host factors such as age, gender, smoking status, family history of asthma, home use of biomass fuel, HIV status and a previous TB episode. For logistic regression models, results were reported as odds ratio (OR) with 95% confidence intervals.

The study received ethics approval from the University of Cape Town Health Sciences Faculty Research Ethics Committee (HREC) as well as the Research Ethics Committee of the College of Medicine in Malawi (COMREC)[30,31] and its study approval number was P.09/17/2288.

## Results

### *Demographic and occupational characteristics*

A total of 279 tobacco farmers participated in the study. Their average age was 37.7 years and a larger proportion (68%) were male. Only 20% of workers were current smokers. Most workers (73%) had attained at least a primary education but a significantly larger proportion of women reported no schooling history. Overall, 16% of workers were HIV positive with women having a higher prevalence than men (Table 1). Farmers were employed for a median duration of 5 years. Only 22% reportedly had access to personal protective equipment (PPE) at work. PPE

Table 1. Demographic, health and occupational characteristics of Malawian tobacco farmers.

| Demographic characteristics | Prevalence $n = 279\%$) | Men n = 189 | Women n = 90 | p-value** |
|---|---|---|---|---|
| **Age (years)*** | 37.7 ± 12.6 | 37.8 (35.9–39.7) | 37.4 (35.1–39.6) | 0.787 |
| **Home Language** | | | | 0.637 |
| Lhomwe | 123 (44) | 87 (46) | 36 (40) | |
| Yao | 40 (14) | 28 (14) | 12 (13) | |
| Sena | 1 (0.3) | 1 (1) | 0 | |
| Other | 115 (41) | 73 (39) | 42 (47) | |
| **Education** | | | | **<0.001** |
| None | 30 (11) | 9 (5) | 21 (23) | |
| Lower primary | 86 (31) | 49 (26) | 37 (41) | |
| Upper primary | 117 (42) | 87 (46) | 30 (33) | |
| Secondary | 46 (16) | 44 (23) | 2 (2) | |
| **Smoking status:** | | | | |
| Current smokers | 57 (20) | 39 (21) | 18 (20) | 0.902 |
| Ex-smokers | 19 (7) | 15 (8) | 4 (4) | 0.279 |
| Never smokers | 203 (73) | 135 (71) | 68 (76) | 0.469 |
| **Cannabis use** | 14 (5) | 10 (5) | 4 (4) | 0.762 |
| **Past medical history** | | | | |
| Repeated childhood chest infections | 29 (10) | 23(12) | 6 (7) | 0.159 |
| Previous TB | 10 (4) | 7(4) | 3 (3) | 1.000 |
| Chronic bronchitis | 9 (3) | 7(4) | 2 (2) | 0.723 |
| **HIV status** | | | | 0.115 |
| Positive (reported or tested) | 44 (16) | 25 (13) | 19 (21) | |
| Negative (reported or tested) | 184 (66) | 132 (70) | 52 (58) | |
| Unknown | 51 (18) | 32 (17) | 19 (21) | |

*Presented as mean and standard deviation. ** based on chi-squared test.
A p-value of <0.05 denotes significance.

consisted of masks, apron, gloves or goggles. The main task for which PPE was worn was for spraying of chemicals.

### Occupational and environmental exposures

Most farmers (87%) had regular exposure to biomass fuel burning for an average of 3 hours per day (Table 2). A larger proportion of workers were exposed in the home setting. Over a third (35%) of workers reported ever having had an episode of GTS with annual GTS prevalence of 26%, reporting on average three episodes per year. A much higher proportion of farmers (57%) reported exposure to pesticides in their job for approximately 1 hour per day for 14 days per season. Many farmers (72%) reported pesticide exposure during spraying. The most common pesticides that were used included organophosphates (18%) for home grain storage as well as copper (15%) and pyrethroids (8%).

### The prevalence of obstructive lung disease (based on symptom-based definitions of asthma and COPD) and work-related symptoms

The prevalence of current asthma was 20% (Table 3), and 7% of the workers reported childhood-onset asthma, mainly among men. A higher proportion of workers (23%) had an asthma symptom score ≥2. Women were more likely to have upper airway symptoms and chronic bronchitis, for which the overall prevalence for the latter was 17% for the entire group. The overall prevalence of work-related chest symptoms was 29%, and higher in men as opposed to ocular-nasal symptoms which was higher in women.

While exposure to pesticides (8%), soil dust (5%) and dried tobacco (4%) were mainly reported to cause work-related upper airway symptoms, reported causes of the work related chest symptoms were exposure to dried tobacco (12%), smoke from fires (5%), soil dust (5%), pesticides (4%), and farming in the field (4%).

Table 2. Occupational and environmental exposures reported by Malawian tobacco farmers.

| Exposures | Prevalence (%) n = 279 |
|---|---|
| **Biomass fuel-related exposures** | |
| Exposed to biomass fuels | 242 (87) |
| – home only | 118 (42) |
| – work only | 48 (17) |
| – both home and work | 76 (27) |
| Frequency of exposure to biomass* | |
| - hours per day (IQR) | 3 (2–6) |
| **Nicotine-related exposures** | |
| GTS symptoms ever | 98 (35) |
| GTS Symptoms in the past 12 months | 73 (26) |
| GTS spectrum | |
| – headache | 81 (29) |
| – nausea | 47 (17) |
| – dizziness | 29 (10) |
| – vomiting | 16 (6) |
| Episodes of GTS in the last 12 months‡ | 3.2 ± 1 |
| Farm activities associated with GTS symptoms | |
| – harvesting | 50 (18) |
| – curing | 31 (11) |
| – sowing | 28 (10) |
| – transplanting | 23 (8) |
| - other: uprooting, planting, grading | 30 (11) |
| **Workplace pesticide exposures** | |
| Pesticide application | 158 (57) |
| Working near pesticide sprayers | 200 (72) |
| No. of days per season working near sprayers in the field[#] | 14.0 ± 22 |
| Exposure during spraying activities | 45 (16) |
| Field re-entry soon after spraying | 232 (83) |
| **Environmental pesticides exposure** | |
| Pesticide drift | 22 (8) |
| Home use of pesticides | 142 (51) |

*median and interquartile range.
‡mean and standard deviation.

### The prevalence of obstructive lung disease based on airflow limitations reflected in pulmonary function indices

Among the workers, 258 successfully performed spirometry. There were 8% of workers with evidence if airway obstruction ($FEV_1$/FVC <70%), while 31% had $FEV_1$<LLN according to GLI reference equations (Table 4). Using NHANES lung function reference values, a lower proportion of workers (20%) had an $FEV_1$ below 80% of the predicted value.

### The association between pesticide and nicotine exposures and respiratory symptoms and obstructive lung function indices in multivariate models

The following host characteristics and potential confounders (gender, and a history of childhood chest infections) had shown an association with the outcomes of interest and were therefore included in the multivariate models (Tables 5 and 6). Age and smoking were also adjusted for as smoking is a known risk factor for obstructive lung disease and increasing age is associated with decline in lung function (Suplementary Table S1a and S1b in appendix).

Two tasks (sowing and transplanting) showed significant associations with all symptom-based respiratory outcomes (OR 1.78–7.26) (Table 5). Harvesting was significantly associated with increased odds of all symptom-based outcomes (OR 1.93–8.81) except for current asthma. Curing of tobacco was associated with increased odds of current asthma (OR 2.40, CI 1.01–5.71) and work-related ocular-nasal symptoms (WRONS) (OR 22.45, CI 8.74–57.68).

Pesticide application was positively associated with all symptom-based respiratory outcomes (OR 1.96–2.62) except for work-related chest

Table 3. General and work-related respiratory symptoms reported by Malawian tobacco farmers.

| Symptoms | Prevalence (%) n = 279 | Prevalence Men (%) n = 189 | Prevalence Women (%) *n* = 90 | p-value |
|---|---|---|---|---|
| **Upper airway symptoms** | | | | |
| Ever ocular-nasal symptoms | 82 (29) | 50 (26) | 32 (36) | 0.119 |
| ≥2 episodes in the last 12 months | | | | |
| – Nasal | 36 (13) | 21 (11) | 15 (17) | 0.196 |
| – Ocular | 56 (20) | 31 (16) | 25 (28) | **0.027** |
| **Asthma history** | | | | |
| Ever asthma (self-reported) | 23 (8) | 19 (10) | 4 (4) | 0.111 |
| - onset ≤16 years | 19 (7) | 17 (9) | 2 (2) | **0.036** |
| - onset >16 years | 3 (1) | 1 (1) | 2 (2) | 0.200 |
| **Current Asthma (ECRHS definition)** # | 55 (20) | 40 (21) | 15 (17) | 0.377 |
| Doctor-diagnosed asthma | 4 (1) | 3 (2) | 1 (1) | 0.754 |
| Woken up by an attack of shortness of breath in the last 12 months | 50 (18) | 35 (19) | 15 (17) | 0.706 |
| Asthma attack in the past 12 months | 9 (3) | 8 (4) | 1 (1) | 0.168 |
| Current use of asthma medication | 3 (1) | 2 (1) | 1 (1) | 0.968 |
| **Asthma-related symptoms** | | | | |
| Wheezing in the past 12 months | 54 (19) | 38 (20) | 16 (18) | 0.645 |
| Wheezing or whistling without cold/flu symptoms | 40 (14) | 29 (15) | 11 (12) | 0.487 |
| Shortness of breath while wheezing in the last 12 months | 54 (19) | 38 (20) | 16 (18) | 0.645 |
| Woken up with chest tightness in the last 12 months | 23 (8) | 16 (8) | 7 (8) | 0.845 |
| Attack of shortness of breath at rest during daytime in the last 12 months | 50 (18) | 35 (19) | 15 (17) | 0.706 |
| Attack of shortness of breath following running or exercise in the last 12 months | 83 (30) | 54 (29) | 29 (32) | 0.533 |
| Asthma symptom score (ASS)* | | | | 0.754 |
| - ASS ≥2 | 65 (23) | 43 (23) | 22 (24) | |
| - ASS <2 | 214 (77) | 146 (77) | 68 (76) | |
| **COPD-related symptom** | | | | |
| Woken up by attack of cough or phlegm in the last 12 months | 91 (33) | 60 (32) | 31 (34) | 0.653 |
| Cough on most days or nights for 3 or more months a year in each of the last 2 years | 36 (13) | 22 (12) | 14 (16) | 0.362 |
| Phlegm on most days or nights for 3 or more months a year in each of the last 2 years | 28 (10) | 17 (9) | 11 (12) | 0.402 |
| **Chronic bronchitis**: Cough or phlegm on most days or nights for 3 or more months a year in each of the last 2 years | 48 (17) | 29 (15) | 19 (21) | 0.233 |
| **Work-related respiratory symptoms** | | | | |
| Work-related ocular-nasal symptoms | 57 (20) | 33 (17) | 24 (27) | 0.075 |
| Episode of high exposure at work causing tight chest, shortness of breath, wheeze or cough | 30 (11) | 19 (10) | 11(12) | 0.585 |
| Work-related chest symptoms | 80 (29) | 58 (31) | 22 (24) | 0.281 |
| Job change due to work-related chest symptoms | 10 (4) | 9 (5) | 1 (1) | 0.125 |

*Asthma symptom score: An asthma symptom score was computed based on the sum of answers (0=no, 1=yes) to five questions on asthma-associated symptoms in the past 12 months (short of breath while wheezing, woken up with chest tightness, attack of shortness of breath (SOB) at rest, attack of shortness of breath after exercise, woken up by attack of shortness of breath).
#Current asthma: attack of SOB in the last 12 months or asthma attack in the last 12 months or current use of asthma medication (ECRHS definition).
A p-value of <0.05 denotes significance

symptoms (WRCS). Exposure during spraying was associated with an increased odds of current asthma (OR 2.57, CI 1.22–5.40), ASS ≥2 (OR 2.09, CI 1.01–4.31), and WRONS (OR 2.43, CI 1.17–5.04). Exposure as a result of pesticide drift was associated with increased odds of current asthma (OR 2.62, CI 1.01–6.86). Whilst duration of exposure to pesticides was also associated with increased risk of WRONS (OR 9.50, CI 2.97–30.34).

Multivariate models for obstructive lung function indices did not show any significant associations with nicotine-related exposure. Only duration of daily exposure to pesticides was associated with an increased odds of airflow obstruction $FEV_1/FVC<LLN$ (OR 5.11, CI 1.57–16.66), $FEV_1/FVC$ <70% (OR 4.58, CI 1.17–17.98) and moderate-to-severe airway obstruction (OR 13.25, CI 1.69–103.93).

## Discussion

This study reveals that tobacco farmers in this setting are predominantly young adults most of whom are educated to the primary level with

**Table 4.** Pulmonary function indices of Malawian tobacco farmers.

| Pulmonary function index* | Prevalence (%) n = 258 | Prevalence (%) n = 258 |
|---|---|---|
| Prediction values | GLI | NHANES |
| $FEV_1$ L [median (IQR)] | 2.64 (2.15–3.13) | 2.64 (2.15–3.13) |
| FVC L [median (IQR)] | 3.29 (2.67–3.86) | 3.29 (2.67–3.86) |
| $FEV_1$ % pred. [median (IQR)] | 86(75–95) | 95 (82–105) |
| FVC % pred. [median (IQR)] | 89 (80–98) | 96 (85–108) |
| $FEV_1$< LLN | 80 (31) | - |
| $FEV_1$ <80% pred. | 91 (35) | 51 (20) |
| FVC < LLN | 72 (28) | - |
| FVC <80% pred. | 69 (27) | 47 (18) |
| $FEV_1$/FVC [median (IQR)] | 81 (76–85) | 81 (76–85) |
| $FEV_1$ /FVC < LLN | 35 (14) | - |
| $FEV_1$ /FVC <70% | 21 (8) | 21 (8) |

$FEV_1$: forced expiratory volume in 1 second; FVC: forced vital capacity; L: liters; LLN: Lower limit of normal; IQR: interquartile range; % pred: % predicted; *: pre-bronchodilator values, unless stated otherwise; GLI: Global Lung Function Initiative reference values; NHANES: National Health and Nutrition Examination Survey III reference values

a mean employment duration of 7.3 years. These farmers are more exposed to risky social behaviors such as current alcohol consumption (42%) and current smoking (20%) compared to the national average of 17.3% and 11%, respectively.[32] There was an observation of a very high prevalence of HIV infection (16%) in this population which is double the national average of 8%. The study revealed evidence of exposure to pesticides, nicotine and biomass fuel among these tobacco farmers. Both upper and lower airway obstructive conditions were prevalent in this study.

This study demonstrates a higher prevalence of obstructive lung diseases (asthma and chronic bronchitis) among tobacco farmers in Malawi compared to other studies based on both symptomatology and lung function tests. This is higher than previously reported for the general population in Malawi. A community study by Banda et al. in Malawi reported a prevalence of 22.5% for chronic respiratory symptoms.[33] The findings in other studies measuring individual respiratory symptoms such as wheeze among tobacco farmers found lower prevalence of 11%[17] and 16%.[34] Other symptoms in this study, such as shortness of breath (30%), were comparable to findings by Gosh and others (20%)[35] and higher than a study by Van Minh (24.3%).[8] This current study also showed a much higher prevalence of spirometry-based airway obstruction (FEV1/FVC <0.70) among these rural-based tobacco farmers of 8% compared to urban dwellers (3.6%) in Malawi using similar reference values (NHANES III).[36] The prevalence of moderate-to-severe obstruction based on spirometry was also higher among the tobacco farmers than urban dwellers. This suggests tobacco farmers in this rural setting encounter more harmful occupational and environmental respiratory exposures or are exposed to higher levels of respiratory irritants than the general population.[33,36] The strength of this study is the use of the standardized symptoms definitions of asthma and chronic bronchitis. This strengthens the finding that obstructive lung diseases are more prevalent among tobacco farm workers than previously thought.

Our data suggest a potential association between the occurrence of chronic lung disease and proxies of both pesticide and nicotine exposure. Well-known host factors such as smoking and age did not show significant associations with the development of asthma or COPD symptoms. These findings suggest that asthma and COPD were probably more likely due to workplace exposures to pesticides and nicotine than other factors. This inference is plausible in this context for several reasons. Firstly, there was very low usage of mechanization in the farm processes making farmers excessively exposed to pesticides and nicotine.[37] Secondly, there was a serious lack of proper personal protective equipment among the farmers coming into contact with pesticides and

**Table 5.** Predictors of general and work-related respiratory symptoms suggestive of obstructive lung disease in multivariate models ($n = 279$)†.

| | ASS ≥2 | Current asthma | COPD symptoms | WRON symptoms | WRC symptoms |
|---|---|---|---|---|---|
| Prevalence (%) | 65%)$n = 55$ | $n = 48$ | $n = 57$ | $n = 80$ | |
| | | | **OR (95% CI)** | | |
| **Nicotine-related exposure** | | | | | |
| Previous GTS episode | **2.68 (1.48–4.83)**** | **2.89 (1.55–5.39)**** | **2.19 (1.12–4.26)*** | **5.94 (3.10–11.40)***** | **3.64(2.08–6.37)***** |
| GTS episode in past year | **3.28 (1.76–6.13)***** | **3.58 (1.87–6.85)***** | **3.03 (1.49–6.19)**** | **9.14 (4.51–18.51)***** | **3.02(1.68–5.45)***** |
| Activities related to GTS (All) | 1.57 (0.83–2.97) | **2.20 (1.14–4.25)*** | **2.10 (1.02–4.28)*** | **8.22(4.16–16.24)***** | **2.38 (1.31–4.30)**** |
| – sowing | **3.78 (1.62–8.85)**** | **4.93 (2.10–11.55)***** | **7.26 (2.86–18.41)***** | **5.74 (2.43–13.56)***** | **2.49 (1.09–5.70)*** |
| – transplanting | **3.80 (1.52–9.45)**** | **2.65 (1.04–6.76)*** | **5.43 (2.08–14.21)**** | **6.18 (2.49–15.35)***** | **2.23 (0.91–5.50)** |
| – harvesting | 1.93 (0.96–3.87) | 2.01 (0.98–4.13) | **2.40 (1.12–5.15)*** | **8.81 (4.33–17.91)***** | **2.65 (1.37–5.11)**** |
| – curing | 2.11 (0.91–4.88) | **2.40 (1.01–5.71)*** | **2.09 (0.81–5.40)** | **22.45 (8.74–57.68)***** | 1.78 (0.79–4.02) |
| **Pesticide-related exposure** | | | | | |
| Pesticide application | **2.35 (1.24–4.44)*** | **2.05 (1.05–3.99)*** | **2.62 (1.25–5.51)*** | **1.96 (1.03–3.71)*** | 1.50 (0.85–2.62) |
| Exposure during spraying | **2.09 (1.01–4.31)*** | **2.57 (1.22–5.40)*** | 1.05 (0.45–2.49) | **2.43 (1.17–5.04)*** | 1.54 (0.75–3.13) |
| Pesticide drift | 2.43 (0.96–6.17) | **2.62 (1.00–6.86)*** | 1.42 (0.47–4.28) | **3.00 (1.18–7.62)*** | 1.81 (0.72–4.58) |
| Field re-entry after spraying | 2.13 (0.85–5.35) | 1.31 (0.55–3.16) | **5.22 (1.20–22.75)** | **0.45 (0.22–0.92)*** | 1.09 (0.53–2.27) |
| Duration of exposure (hrs/day) | 1.06 (0.75–1.49) | 0.92 (0.54–1.58) | 1.20 (0.86–1.68) | **9.50 (2.97–30.34)***** | 1.02 (0.72–1.45) |

* $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$.

Current asthma: shortness of breath in the past 12 months *or* an asthma attack in the past 12 months *or* current use of asthma medication.

ASS: Asthma symptom score – sum of positive responses to asthma-associated symptoms in the past 12 months (short of breath while wheezing, woken up with chest tightness, attack of shortness of breath at rest, attack of shortness of breath after exercise, woken up by attack of shortness of breath).

WRON symptoms: work related ocular-nasal symptoms; WRC symptoms: work related chest symptoms.

COPD: cough and sputum on most days lasting at least 3 months for two consecutive years.

† Each estimate based on individual regression models adjusted for age, gender, smoking and childhood chest infection.

**Table 6.** Predictors of obstructive lung function indices in multivariate models ($n = 279$)†.

| | $FEV_1$<LLN | $FEV_1$/FVC<LLN | $FEV_1$<80%‡ | $FEV_1$/FVC <70%‡ | Moderate/severe airway obstruction |
|---|---|---|---|---|---|
| Predictors $n = 258$ | $n = 80$ | $n = 35$ | $n = 51$ | $n = 21$ | $n = 11$ |
| | | | **OR (95% CI)** | | |
| **Nicotine-related exposure** | | | | | |
| Previous GTS episode | 0.95 (0.54–1.68) | 0.95 (0.44–2.04) | 0.55 (0.27–1.12) | 0.87 (0.32–2.33) | 0.58 (0.14–2.37) |
| GTS episode in past year | 0.89 (0.47–1.67) | 1.20 (0.53–2.72) | 0.64 (0.29–1.39) | 1.41 (0.52–3.88) | 0.95 (0.22–4.00) |
| Activities related to GTS (All) | 0.79 (0.42–1.49) | 0.74 (0.30–1.80) | 0.52 (0.26–1.27) | 0.75 (0.24–2.38) | 0.71 (0.15–3.47) |
| – transplanting | 0.45 (0.14–1.42) | 0.28 (0.04–2.22) | 0.34 (0.07–1.55) | 0.52 (0.06–4.32) | 0.96 (0.11–8.51) |
| – harvesting | 0.89 (0.43–1.83) | 0.59 (0.20–1.79) | 0.58 (0.23–1.49) | 0.80 (0.22–2.93) | 0.49 (0.06–4.02) |
| – curing | 1.34 (0.58–3.13) | 1.23 (0.39–3.82) | 1.00 (0.34–2.83) | 0.87 (0.18–4.13) | 0.91 (0.11–7.76) |
| – other | 1.19 (0.50–2.83) | 2.24 (0.85–5.91) | 0.61 (0.19–1.90) | 1.66 (0.48–5.74) | 0.49 (0.05–4.56) |
| **Pesticide-related exposure** | | | | | |
| Pesticide application | 0.74 (0.43–1.28) | 0.79 (0.38–1.66) | 0.92 (0.48–1.75) | 0.77 (0.30–1.97) | 0.56 (0.15–2.06) |
| Exposure during spraying | 0.96 (0.46–2.01) | 0.81 (0.28–2.34) | 0.72 (0.29–1.76) | 1.05 (0.28–4.00) | 1.12 (0.21–6.08) |
| Pesticide drift | 1.39 (0.54–3.60) | 1.91 (0.58–6.23) | 0.69 (0.19–2.52) | 2.84 (0.71–11.38) | 4.01 (0.74–21.86) |
| Field re-entry after spraying | 0.91 (0.43–1.89) | 0.71 (0.28–1.79) | 0.94 (0.40–2.21) | 0.65 (0.21–1.97) | 0.91 (0.18–4.60) |
| Duration of exposure (hrs/day) | 1.97 (0.80–4.84) | **5.11 (1.57–16.66)**** | 2.41 (0.95–6.11) | **4.58 (1.17–17.98)*** | **13.25 (1.69–103.93)*** |

*$p \le .05$; **$p \le .01$; ***$p \le .001$.

$FEV_1$: forced expiratory volume in 1 second; FVC: forced vital capacity; LLN: Lower limit of normal.

‡NHANES: National Health and Nutrition Examination Survey III reference values.

Moderate/severe obstruction: FEV1<Lower Limit of Normal (LLN) and FEV1/FVC<LLN.

†Each estimate based on individual regression models adjusted for age, gender, smoking and childhood chest infection.

nicotine.[38] Thirdly, there is excessive use of prohibited pesticides which were declared to be harmful by the authorities such as organophosphates and carbamates, which subject the farmers to further risk of toxicity.[5] One unique feature of this study is the characteristic higher prevalence of work-related chest symptoms compared to upper airway symptoms. Usually, airborne workplace respiratory hazards such as dust reach the upper airways first in higher concentrations. Due to immune mechanisms in the respiratory tract, the concentration is gradually reduced down the tract as more particles get trapped before they descend to the lower respiratory tract. Thus, one would expect more and early symptoms to be manifested in the upper respiratory tract. However, this is not the pattern of respiratory symptoms demonstrated in this study. There could be possible explanations for this particular pattern. Firstly, it could be that the hazard responsible for these respiratory effects reaches the respiratory system through some other route other than the respiratory system.[38,39] The possible route could be dermal, in case of both nicotine and pesticides. This makes it possible for the hazard to evade the natural airway protective mechanisms and reach any part of the body including the lungs in somewhat different concentrations and exert its effects there. This is likely to happen in this population especially considering the low prevalence of those using personal protective equipment. Another explanation could be that the characteristics of the upper airways make it more resilient to this particular hazard encountered by tobacco farmers than does the lower respiratory tract. Thirdly, a hazard with very small particle sizes in the respirable ranges or those in gaseous forms are likely to reach the lower parts of the respiratory system in rather higher concentrations.[40,41] In the context of the delicate nature of that part of the respiratory tract, an exposed individual may experience the adverse effects quicker than otherwise.

In respect of nicotine-related exposures in this study, the prevalence of GTS was much higher (26%) than the 11% reported in Brazilian tobacco farmers.[17,42] Using a similar definition for GTS as the Brazilian study, it was still higher (14%), but other studies have documented much higher prevalences of up to 67%.[19,23] Furthermore, GTS was significantly associated with increased odds of both asthma and COPD-related outcomes. Fiori *et al.* [17] also demonstrated a relationship between number of GTS episodes and occurrence of wheeze in their study. A relationship was also observed between wheezing and lifting tobacco sticks to curing barns.[17,22] In the current study, GTS was associated with both asthma as well as COPD. Activities such as transplanting, harvesting and curing which are associated with manual handling of tobacco leaves were also found to have a strong association with symptoms of obstructive lung disease. These tasks are linked to high levels of dermal absorption of nicotine leading to potentially increased risk of nicotine toxicity. However, the mechanisms underlying this remains unclear and warrants further investigation.

Pesticide exposure in this study population was reportedly high compared to other studies of tobacco farmers,[17,43] with the exception of the study by Casaril *et al.*, which documented 97% of farm workers having contact with pesticides.[44] The study also revealed an association between pesticide exposure and asthma, chronic bronchitis, as well as work-related ocular nasal symptoms. These observations are consistent with findings from previous studies. Wheeze associated with exposure to pesticides has also been reported in the Agriculture Health Study among commercial pesticide applicators.[10] A Brazilian study of agricultural workers similarly showed an increased association between pesticide exposure and adult onset asthma (OR = 1.54, 95% CI: 1.04–2.58)[23] while a Canadian study of male farmers reported an association between self-reported asthma and exposure to carbamate (AChE inhibitor) pesticides (OR = 1.8, 95% CI: 1.1–3.1).[45] Hoppin *et al.* in a later study demonstrated that several pesticides were associated with both atopic and non-atopic wheeze.[10,46] In an earlier study of women farm workers working in fruit farms in South Africa, Ndlovu *et al.* [11] reported a positive association between pesticide exposure and ASS as well as ocular-nasal symptoms. The study also found that AChE suppression due to pesticide exposure was associated with possible allergic asthma (FeNO >25ppb). A further study by Mwanga *et al.* further demonstrated that exposure to organophosphates or pyrethroids may be associated with asthma-related cytokines, with non-Th2 cytokines demonstrating a consistently stronger relationship.[13]

The finding of the pesticides that were reported as being used by farmers being different from the list of recommended pesticides for use by the Tobacco Commission in Malawi[5] suggests that there is weak enforcement of the current legal instruments used to protect the health of workers and the environment. It is evident that having relevant policy documents in place does not necessarily translate to protection of workers' health unless there are measures in place to monitor their translation into practice on the ground, especially, in the absence of proper occupational safety and health regulations for the tobacco industry.

In this study, biomass fuel use was associated with work-related ocular-nasal symptoms and airflow limitation. Most farmers had regular exposure to biomass fuel with a larger proportion of them exposed in the home setting. Since biomass fuel use occurred at both home and during work, the study was unable to demonstrate differential effects across these two settings; hence, this variable was not included in the models. An earlier study of Malawian urban dwellers did not show any significant association between biomass fuel use in the home and airway obstruction.[36]

This is the first study to our knowledge to evaluate respiratory diseases related to workplace exposures among tobacco farmers in Malawi. The findings of this study expose huge vulnerabilities faced by farmers in this setting which are substantiated by the higher rates of occurrence of respiratory diseases compared to the general population and other previous studies. The study had some limitations. Firstly, the study design, being cross-sectional in nature could not establish a temporal relationship between environmental/occupational exposures and adverse obstructive lung disease outcomes. Furthermore, it is probable that the healthy worker effect may have resulted in under detection of workers with more advanced disease that are no longer active in tobacco farming. The contribution of other bioaerosol exposures common to agriculture was not ascertained and the influence on respiratory health is not known. Further and more detailed exposure assessment and characterization of both chemical and bioaerosol exposures in this setting would have contributed to deeper insights into exposure sources in order to develop exposure mitigation strategies. Finally, more objective testing for bronchial hyperresponsiveness could have added valuable information on the nature of airway obstruction detected that would have allowed for clearer discrimination between individuals with COPD and asthma.

## Conclusion

This study has demonstrated an increased risk of obstructive lung disease among Malawian tobacco farmers as evidenced by the excess prevalence of respiratory symptoms and airflow obstruction in this study population. These outcomes are strongly associated with occupational exposure to nicotine and pesticides. Stronger enforcement of current occupational health and safety legislation and policies for tobacco farms is recommended. This includes detailed listing of pesticide exposures, education and training of workers on safe work procedures, proper use of PPE, and longitudinal studies that accurately quantify these diverse exposures and adverse respiratory outcomes.

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