# Wheezing in Tobacco Farm Workers in Southern Brazil

**Nadia Spada Fiori,** MD, MSc,[1,2*] **Anaclaudia Gastal Fassa,** MD, PhD,[1] **Neice Muller Xavier Faria,** MD, PhD,[3] **Rodrigo Dalke Meucci,** MSc,[1] **Vanessa Iribarrem Miranda,** MSc,[1] and **David C. Christiani,** MD, MPH, MS[4]

**Background** *Tobacco workers are exposed to several respiratory occupational sensitizers.*
**Methods** *A representative cross-sectional study was carried out on 2469 tobacco family farming growers. Gender-stratified multivariate analyses evaluated the association between wheezing and socio-demographic, behavioral, and occupational variables.*
**Results** *Wheezing prevalence was 11.0% with no difference between genders. Among men, age, smoking, strenuous work, pesticide use, contact with vegetable dust and dried tobacco dust, lifting sticks with tobacco leaves to the curing barns, and green tobacco sickness (GTS) were risk factors for wheezing. Among women, family history of asthma, tying hands of tobacco, strenuous work, contact with chemical disinfectants, and GTS were positively associated with wheezing. Harvesting lower tobacco leaves was a protective factor for the outcome in both genders.*
**Conclusions** *Pesticides, dusts exposure, and GTS were risk factors for wheezing. The synergic effect of these factors needs to be better evaluated to improve prevention.* Am. J. Ind. Med. 58:1217–1228, 2015. © 2015 Wiley Periodicals, Inc.

***KEY WORDS: wheezing; asthma; tobacco; occupational diseases; rural health; prevalence***

## INTRODUCTION

Tobacco production is estimated to involve more than 30 million farm workers in more than 100 countries worldwide. China, Brazil, India, the United States, Malawi, and Indonesia account for 2/3 of global production [Schmitt et al., 2007].

Work-related asthma has become one of the most common types of adult-onset asthma in industrialized countries, accounting for 25% or more of cases [Dykewicz, 2009]. It is classified into two types, sensitizer-induced asthma (whether measured or not by immunoglobulin E) and irritant-induced asthma [de Nijs et al., 2013]. Irritant agents can also exacerbate pre-existing asthma (work-exacerbated asthma). Occupational sensitizers are estimated to cause 1 in every 10 cases of asthma in adults of working age and more than 300 substances have already been associated with work-related asthma [GINA, 1993].

There are few studies evaluating the occurrence of respiratory diseases and symptoms among tobacco workers. Most studies are case–control conducted with workers in tobacco processing factories. Large studies of agricultural workers or studies of family farming in tobacco plantations have not been conducted. The literature shows a high concentration of dust and the presence of bacteria and fungus in tobacco processing environments [Reiman and Uitti, 2000; Mustajbegovic et al., 2003; Chloros et al., 2004; Zhang et al.,

[1]Social Medicine Department, Postgraduate Program in Epidemiology, Federal University of Pelotas, Pelotas, Brazil
[2]Takemi Program in International Health, Department of Global Health and Population, Harvard School of Public Health, Boston, Massachusetts
[3]Municipal Health Department of Bento Gonçalves, Rio Grande do Sul, Brazil
[4]Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts
*Correspondence to: Nadia Spada Fiori, MD, Social Medicine Department, Federal University of Pelotas, Avenida Duque de Caxias, 250-3° andar Pelotas, RS CEP: 96030-000, Brazil. E-mail: nsfiori@yahoo.com.br/nsfiori@gmail.com

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2005, 2009] as well as lung function deterioration as cumulative exposure to dust increases [Zhang et al., 2009], chronic bronchitis (20.6%), occupational asthma (6.2%), and respiratory symptoms (chronic cough 32.9% males and 28.3% females; chest tightness 20.0% males and 16.7% females) have been significantly reported by tobacco processing factory workers [Mustajbegovic et al., 2003; Chloros et al., 2004; Zhang et al., 2005].

The tobacco leaf processing working environment can be very humid owing to the use of curing barns. Together with the high concentration of tobacco dust arising from storing the leaves in closed barns, this is conducive to the development of microbes, gram-negative bacteria and diverse kinds of fungi (mesophilic, thermotolerant, thermophilic actinomycetic, among others) [Reiman and Uitti, 2000; Zhang et al., 2005].

Apart from the respiratory risk arising from contact with dust, microorganisms and pesticides, tobacco production gives rise to exposures that are peculiar to it, such as high nicotine absorption through the skin. The relationship between dermal absorption of nicotine and respiratory problems has not yet been described.

Brazil is currently the world's second largest tobacco producer. This activity is concentrated in the south of the country and is undertaken by more than 220,000 families. Despite the economic importance of tobacco growing and the involvement of a large number of family farmers, studies evaluating the occurrence of respiratory symptoms in this population were not found. The objective of this study is therefore to describe the prevalence of wheezing and to analyze associated factors among tobacco farmers in the municipality of São Lourenço do Sul, in the state of Rio Grande do Sul. This state accounts for more than 50% of Brazilian tobacco leaf production.

## METHODS

A cross-sectional study was performed on a random sample of tobacco growers in the municipality of São Lourenço do Sul, state of Rio Grande do Sul, Brazil, during the 2011 harvest period (January to March).

A total of 1,100 invoices issued by tobacco producers in 2009 were randomly selected. The issuing of invoices for tobacco sales is mandatory and this ensured that the sample of tobacco producers was representative. All individuals aged 18 or over working with tobacco for at least 15 hr a week and who had cultivated tobacco in 2010 were eligible to take part in the study. Invoices issued by individuals residing in other municipalities or in the urban area of São Lourenço do Sul, or who no longer cultivated tobacco were replaced by the next nearest tobacco producing property.

The sample size was calculated to allow wheezing prevalence of 11% to be estimated, with a margin of error of 1.5% points. Estimated wheezing prevalence was 11%. The sample size was also calculated to estimate associations with risk ratios over 1.5 considering a 95% confidence level, 80% statistical power, 10% wheezing prevalence in the unexposed and an unexposed–exposed ratio of 1:4.

Two questionnaires were used in the study. The first questionnaire was administered to the person in charge of the farm property and collected information about the property, such as economic indicators, tobacco production, agricultural production, mechanization, vehicles, and pesticides used on the property. The second questionnaire was administered to all the workers and sought to obtain information about sociodemographic factors (gender, age, and schooling), family history of asthma, smoking, occupational exposures, and comorbidities. A family history of asthma was determined by the occurrence of asthma in one or both parents, reported by the respondent. Smoking was categorized as non-smoker, smoker (one cigarette or more per day) and former smoker (stopped smoking a month or more ago).

Workers performed more than one activity during tobacco growing, as follows:

– Harvesting the leaves next to the ground (lower tobacco leaves).
– Lifting sticks with tobacco leaves to the curing barns was executed concomitantly with the organization of the sticks inside these barns. While some of the workers raise the sticks from the ground, others climb the scaffolding to take hold of the sticks and position them from the highest part of the curing barns.
– During tobacco classification, the leaves were separated in accordance with their size, color, and texture that determine their commercial value.
– After classification, workers tied hands of tobacco leaves into small bundles. This is a repetitive activity that does not require physical effort and takes place inside sheds.

To characterize dust exposure, the respondents reported if they had contact, in the year prior to the survey, with:

– Dried tobacco leave dust.
– Other vegetables dust, except tobacco dust (e.g., flowers pollen, corn straw, grain dust as cotton, soy, and bean).
– Chemical dust, except pesticides (e.g., fertilizers dust, and urea).
– Animal feed dust.
– Mineral dust (e.g., ground/land dust, stone or rock powder, limestone, and ashes).
– Animal dust (e.g., pens, animal hair, and dry manure).
– Domestic dust (e.g., old things and moldy).

Cumulative exposure to pesticides was determined by the number of years of pesticide exposure in life and the monthly frequency of contact with these products.

Workers also reported whether they worked in smoky conditions, performed strenuous work (jobs that require great physical effort) and the number of months of intensive work during the year. Green tobacco sickness (GTS) was assessed as comorbidity and characterized by the number of episodes of sickness in the previous year (headache or dizziness together with nausea or vomiting, following contact with green tobacco leaves).

The outcome was wheezing in the year prior to the survey. This variable is a good predictor of active asthma and has been widely used by other studies [GINA, 1993; Gomez et al., 2004; Hoppin et al., 2006; Douwes et al., 2007; Smit et al., 2008]. The questions about respiratory symptoms were designed based on the questionnaire used in the Platino study [PLATINO, 2002].

The group of interviewers was trained and was comprised of people who lived in the region. The majority were community health agents and interviewers for the Brazilian Census, undertaken by the Brazilian Institute of Geography and Statistics. The interviews took place at the farm properties, using Personal Digital Assistants (PDA). An abridged version of the questionnaire was administered to 10% of the respondents for the purposes of quality control.

The data were analyzed by describing the variables using the Wald test for heterogeneity and linear trend with regard to the categorical variables, with stratification by gender. The crude and adjusted analyses were performed using Poisson regression with robust estimation of variance and backward selection. The multivariate analysis followed an hierarchical model, which included sociodemographic, economic, and family history of asthma variables on the first level; smoking on the second level; occupational variables (tasks performed in the last year) on the third level; workloads on the fourth level; and GTS on the fifth level. Variables having a $P$-value of $\leq$0.2 were maintained in the model and those with a $P$-value of $<$0.05 were considered to be associated.

This study was reviewed and approved by the Federal University of Pelotas Research Ethics Committee. The participants voluntarily signed a consent form and cases with health problems were referred for medical assessment free of charge.

## RESULTS

Total sample size was 2,626 tobacco growers from 912 farm properties. 5.9% of those selected were not located or refused to take part in the study, thus the final sample comprised 2,469 workers.

Family members comprised the workforce predominantly, fewer than 5% of the sample were tenants or employees and 59.3% were male. The average number of workers per property was 2.7.

Forty-four percent of the workers lived on properties producing between 5 and 10 tons of tobacco in the previous year, more than a third had been working with tobacco for at least 20 years and about 90.0% of males and 80.0% of females worked more than 8 hr a day during the harvest season (Table I).

The majority of the tobacco workers, around 50% from both genders, were aged between 25 and 44. Males and females had a similar level of schooling of between 5 and 8 years (50.0% and 47.1%, respectively). Family history of asthma was reported by 7.6% of males and 8.8% of females. More than 30% of males were smokers, compared to 3.1% of females (Table I).

Tobacco leaf harvesting was undertaken by more than 90.0% of the workers of both genders. The majority of males (75.5%) undertook tasks requiring strenuous work, while the majority of females tied hands of tobacco leaves, classified the tobacco and lifted the sticks with tobacco leaves to be hung in the curing barns (86.6%, 86.3%, and 73.1%, respectively) (Table I).

Activities involving contact with pesticides were significantly different between the genders ($P < 0.001$), with greater male exposure. Some 85.0% of males reported contact with pesticides in the previous year and 12.6% of them had had contact more than 10 days a month in the period when pesticides are used intensively. 43.1% of males and 20.5% of females reported having been exposed to pesticides for more than 20 years (Table I).

There were significant differences between the genders ($P < 0.001$) with regard to several types of dust. Females were more exposed to dry tobacco dust (57.8%) and mold dust (6.8%), whereas males were mostly exposed to vegetable dust (19.1%), chemical dust (36.3%), mineral dust (19.7%), and pesticides (17.7%). A higher number of females reported not working in smoky environments (81.4%). Reports of more than five episodes of GTS in the previous year were significantly more prevalent in females (5.5%) than in males (2.5%).

There was no significant difference between the genders in the prevalence of wheezing in the previous year; it was reported by 11.0% of the population studied (Table II). However, the crude and adjusted analyses stratified by gender showed important differences with regard to factors associated with wheezing in the last year. Schooling and income (the amount of tobacco produced in the previous year) were not associated with the outcome in either gender. Adjusted analysis in males showed that age was associated with wheezing in the last year and males aged 55 or above had the greatest risk (1.71 RR, $P$-trend = 0.022). Smokers showed greater risk of wheezing (1.53 RR, 95% CI 1.10–2.13). Among activities involving tobacco, harvesting lower leaves was found to be inversely associated with wheezing

**TABLE I.** Demographic, Socioeconomic, Behavioral, and Occupational Description of Tobacco Farmers, Stratified by Gender (Brazil, 2011)

| | Male (N = 1,464) | | Female (N = 1,005) | | |
|---|---|---|---|---|---|
| **Variables** | **N** | **% (95% CI)** | **N** | **% (95% CI)** | ***P*-value**[a] |
| Age (years) | | | | | 0.015 |
| 18–24 | 205 | 14.0 (12.2–15.8) | 151 | 15.0 (12.8–17.2) | |
| 25–34 | 383 | 26.2 (23.9–28.4) | 275 | 27.4 (24.6–30.1) | |
| 35–44 | 319 | 21.8 (19.7–23.9) | 216 | 21.5 (18.9–24.0) | |
| 45–54 | 317 | 21.6 (19.5–23.8) | 246 | 24.5 (21.8–27.1) | |
| ≥55 | 240 | 16.4 (14.5–18.3) | 117 | 11.6 (9.6–13.6) | |
| Schooling (years) | | | | | 0.020 |
| 0–4 | 644 | 44.0 (41.4–46.5) | 442 | 44.0 (40.9–47.1) | |
| 5–8 | 732 | 50.0 (47.4–52.6) | 473 | 47.1 (44.0–50.2) | |
| ≥9 | 88 | 6.0 (4.8–7.2) | 90 | 8.9 (7.2–10.7) | |
| Family history of asthma | | | | | 0.293 |
| No | 1,353 | 92.4 (91.1–93.8) | 917 | 91.2 (89.5–93.0) | |
| Yes | 111 | 7.6 (6.2–8.9) | 88 | 8.8 (7.0–10.5) | |
| Amount of tobacco produced (kg) | | | | | 0.200 |
| 1–2,500 | 91 | 6.3 (5.0–7.5) | 69 | 6.9 (5.3–8.5) | |
| 2,501–5,000 | 396 | 27.2 (24.9–29.5) | 290 | 29.1 (26.2–31.9) | |
| 5,001–10,000 | 368 | 43.8 (41.3–46.4) | 438 | 43.9 (40.8–47.0) | |
| 10,001–36,000 | 330 | 22.7 (20.5–24.8) | 201 | 20.1 (17.7–22.6) | |
| Employment status | | | | | 0.339 |
| Family owned | 1,385 | 94.8 (93.6–95.9) | 960 | 95.7 (94.4–97.0) | |
| Tenants/employees | 76 | 5.2 (4.1–6.3) | 43 | 4.3 (3.0–5.5) | |
| Smoking | | | | | 0.000 |
| No | 729 | 49.8 (47.2–52.3) | 930 | 92.5 (90.0–94.2) | |
| Former | 278 | 19.0 (17.0–21.0) | 44 | 4.4 (3.11–5.6) | |
| Smoker | 457 | 31.2 (28.8–33.6) | 31 | 3.1 (2.0–4.1) | |
| Time working with tobacco (years) | | | | | 0.136 |
| ≤9 | 457 | 31.2 (28.8–33.6) | 311 | 31.0 (28.1–33.9) | |
| 10–19 | 455 | 31.1 (28.7–33.5) | 347 | 34.6 (31.6–37.5) | |
| ≤20 | 551 | 37.7 (35.5–40.1) | 345 | 34.4 (31.4–37.3) | |
| Days/month of pesticides use | | | | | 0.000 |
| No | 242 | 16.5 (14.6–18.4) | 604 | 60.7 (57.7–63.7) | |
| 1–10 | 1,038 | 70.9 (68.6–73.2) | 354 | 35.6 (32.6–38.5) | |
| ≥11 | 184 | 12.6 (10.9–14.3) | 37 | 3.7 (2.5–4.9) | |
| Time of exposure to pesticides in life (years) | | | | | 0.000 |
| None | 100 | 6.9 (5.6–8.2) | 377 | 38.0 (35.0–41.1) | |
| 1–10 | 362 | 24.8 (22.6–27.1) | 226 | 22.8 (20.2–25.4) | |
| 11–20 | 367 | 25.2 (22.9–27.4) | 185 | 18.7 (16.2–21.1) | |
| 21–30 | 355 | 24.4 (22.2–26.6) | 120 | 12.1 (10.1–14.1) | |
| ≥31 | 273 | 18.7 (16.7–21.0) | 83 | 8.4 (6.7–10.1) | |
| Working hours during agricultural season | | | | | 0.000 |
| ≤8 | 124 | 8.5 (7.1–9.9) | 195 | 19.5 (17.0–21.9) | |
| 9–12 | 805 | 55.2 (52.6–57.7) | 556 | 55.4 (52.3–58.5) | |
| 13–18 | 530 | 36.3 (33.9–38.8) | 252 | 25.1 (22.4–27.8) | |
| Lifting sticks with tobacco leaves to the barns | | | | | 0.000 |
| No | 528 | 36.1 (33.6–38.6) | 179 | 17.8 (15.4–20.2) | |
| Sometimes | 415 | 28.4 (26.0–30.7) | 91 | 9.1 (7.3–10.8) | |
| Always | 520 | 35.5 (33.1–38.0) | 735 | 73.1 (70.4–75.9) | |

(*Continued*)

**TABLE I.** (*Continued*)

| Variables | Male (N = 1,464) | | Female (N = 1,005) | | P-value[a] |
|---|---|---|---|---|---|
| | N | % (95% CI) | N | % (95% CI) | |
| Tobacco classification | | | | | 0.000 |
| No | 198 | 13.5 (11.8–15.3) | 87 | 8.6 (6.9–10.4) | |
| Sometimes | 94 | 6.4 (5.2–7.7) | 49 | 4.9 (3.5–6.2) | |
| Always | 1,171 | 80.1 (78.0–82.1) | 869 | 86.5 (84.3–88.6) | |
| Tying hands of tobacco | | | | | 0.289 |
| No | 68 | 4.6 (3.6–5.7) | 54 | 5.3 (4.0–6.8) | |
| Sometimes | 142 | 9.7 (8.2–11.2) | 81 | 8.1 (6.4–9.7) | |
| Always | 1,253 | 85.7 (83.8–87.4) | 870 | 86.6 (84.4–88.7) | |
| Harvesting lower tobacco leaves | | | | | 0.019 |
| No | 37 | 2.5 (1.7–3.3) | 42 | 4.2 (2.9–5.4) | |
| Sometimes | 28 | 1.9 (1.2–2.6) | 29 | 2.9 (1.8–3.9) | |
| Always | 1,399 | 95.6 (94.5–96.6) | 934 | 92.9 (91.3–94.5) | |
| Strenuous work | | | | | 0.000 |
| No | 359 | 24.5 (22.3–26.7) | 533 | 53.1 (50.0–56.2) | |
| Yes | 1,105 | 75.5 (73.3–77.7) | 471 | 46.9 (43.8–50.0) | |

Ninety-five percent CI, confidence interval.
[a]Fisher exact test of heterogeneity for the difference between genders.

(0.35 RR, $P$-trend = 0.000), while lifting sticks with tobacco leaves to be hung in the curing barns was directly associated (1.48 RR, $P$-trend = 0.024). Pesticide use was found to be associated with the occurrence of wheezing between males and those using pesticides for more than 10 days a month were at the higher risk (2.71 RR, 95% CI 1.56–4.71). After adjustment, chemical dust and the number of days per year of intensive work lost statistical significance, while association remained in relation to vegetable dust (1.54 RR, $P$-trend 0.053), dried tobacco dust (1.59 RR, $P$-trend 0.039), and strenuous work (1.72 RR, 95% CI 1.14–2.61). The number of GTS episodes showed a direct association with wheezing and high relative risk for those who had more than five episodes in the last year (3.12 RR, $P$-trend = 0.000) (Table III).

The adjusted analysis in females maintained the majority of the results obtained in the crude analysis. Family history of asthma (2.02 RR, 95% CI 1.3–3.15) and sporadically tying hands of tobacco (3.89 RR, 95% CI 1.17–12.94) were positively associated with wheezing, while harvesting lower tobacco leaves was a protection factor (0.46 RR, $P$-trend = 0.018). The longer the exposure time to pesticides, the greater the risk of wheezing, and those females with more than 30 years of exposure were at greater risk (RR2.32, $P$-trend = 0.002). With regard to workloads, strenuous work (1.76 RR, 95% CI 1.22–2.54), working in smoky environments (1.86 RR, $P$-trend = 0.061) and having contact with chemical disinfectants (1.54 RR, 95% CI 1.00–2.35) remained associated after adjustment. The number of GTS episodes in the last year was directly associated with wheezing and females with more than five episodes in the previous year had twice the risk of those who had not had any episodes. (2.29 RR, $P$-trend = 0.005) (Table IV).

## DISCUSSION

The prevalence of wheezing in the last year was similar between males and females (11%). Among males, age was directly associated with wheezing in the last year. Being a smoker, lifting sticks with tobacco leaves to be hung in the curing barns, monthly frequency of pesticide use and contact with dry tobacco leaf dust were risk factors for wheezing in the last year. Among females, family history of asthma, tying hands of tobacco, length of exposure to pesticides, working in smoky environments and having had contact with disinfectants in the last month were found to be positively associated with wheezing in the last year. In both genders, the number of GTS episodes in the last year was directly associated with wheezing and strenuous work showed positive association, while harvesting lower tobacco leaves showed inverse association.

Although wheezing may be related to colds and other obstructive pulmonary diseases, authors mention that wheezing has a high diagnostic value, good sensitivity and specificity, excellent positive predictive value, and Youden Index for identifying asthma, whereas bronchial hyper-responsiveness (BHR) has low sensitivity in population-based studies [Jenkins et al., 1996; Pekkanen and Pearce,

**TABLE II.** Occupational Description of Tobacco Farmers, Stratified by Gender (Brazil, 2011)

| | Male (N = 1,464) | | Female (N = 1,005) | | |
|---|---|---|---|---|---|
| **Variables** | **N** | **% (95% CI)** | **N** | **% (95% CI)** | ***P*-value[a]** |
| Contact with dried tobacco dust | | | | | 0.000 |
| No | 90 | 6.1 (4.9–7.4) | 69 | 6.9 (5.3–8.4) | |
| Little | 635 | 43.4 (40.8–45.9) | 355 | 35.4 (32.4–38.3) | |
| Too much | 739 | 50.5 (47.9–53.0) | 580 | 57.8 (54.7–60.8) | |
| Contact with vegetable dust | | | | | 0.000 |
| No | 465 | 31.8 (29.4–34.1) | 402 | 40.0 (37.0–43.1) | |
| Little | 720 | 49.2 (46.6–51.7) | 482 | 48.0 (45.0–51.1) | |
| Too much | 279 | 19.1 (17.0–21.1) | 120 | 11.9 (9.9–14.0) | |
| Contact with chemical dust | | | | | 0.000 |
| No | 207 | 14.1 (12.3–16.0) | 249 | 24.8 (22.1–27.5) | |
| Little | 725 | 49.5 (46.9–52.1) | 408 | 40.6 (37.6–43.7) | |
| Too much | 532 | 36.3 (33.9–38.8) | 347 | 34.6 (31.6–37.5) | |
| Contact with pesticides or other toxic gases | | | | | 0.000 |
| No | 754 | 51.5 (48.9–54.1) | 757 | 75.4 (72.7–78.1) | |
| Little | 452 | 30.9 (28.5–33.2) | 181 | 18.0 (15.6–20.4) | |
| Too much | 258 | 17.7 (15.7–19.6) | 66 | 6.6 (5.0–8.1) | |
| Contact with mold dust | | | | | 0.000 |
| No | 1,096 | 74.9 (72.6–77.1) | 546 | 54.4 (51.3–57.5) | |
| Little | 323 | 22.1 (20.0–24.2) | 390 | 38.8 (35.8–41.9) | |
| Too much | 45 | 3.1 (2.2–3.9) | 68 | 6.8 (5.2–8.3) | |
| Contact with animal dust | | | | | 0.041 |
| No | 573 | 39.1 (36.6–41.6) | 411 | 41.0 (37.9–44.0) | |
| Little | 789 | 53.9 (51.3–56.4) | 500 | 49.8 (46.7–52.9) | |
| Too much | 102 | 7.0 (5.7–8.3) | 93 | 9.3 (7.5–11.0) | |
| Contact with animal feed dust | | | | | 0.772 |
| No | 1,057 | 72.2 (69.9–74.5) | 717 | 71.4 (68.6–74.2) | |
| Little | 336 | 22.9 (20.8–25.1) | 232 | 23.1 (20.5–25.7) | |
| Too much | 71 | 4.8 (3.7–5.9) | 55 | 5.5 (4.1–6.9) | |
| Contact with mineral dust | | | | | 0.000 |
| No | 385 | 26.3 (24.0–28.5) | 488 | 48.6 (45.5–51.7) | |
| Little | 791 | 54.0 (51.5–56.6) | 386 | 38.5 (35.4–41.5) | |
| Too much | 288 | 19.7 (17.6–21.7) | 130 | 12.9 (10.9–15.0) | |
| Working in smoky conditions | | | | | 0.002 |
| No | 1,108 | 75.7 (73.5–77.9) | 817 | 81.4 (79.0–83.8) | |
| Little | 310 | 21.2 (19.1–23.3) | 157 | 15.6 (13.4–17.9) | |
| Too much | 46 | 3.1 (2.2–4.0) | 30 | 3.0 (1.9–4.0) | |
| Contact with chemical disinfectant | | | | | 0.000 |
| No | 1,306 | 89.2 (87.6–90.8) | 314 | 31.3 (28.4–34.1) | |
| Yes | 158 | 10.8 (9.2–12.4) | 690 | 68.7 (65.8–71.6) | |
| Month/year intensive work | | | | | 0.445 |
| None | 181 | 12.4 (10.7–14.1) | 131 | 13.1 (11.0–15.2) | |
| 1–6 | 941 | 64.6 (62.1–67.0) | 662 | 66.1 (63.1–69.0) | |
| 7–12 | 335 | 23.0 (20.8–25.1) | 209 | 20.9 (18.3–23.4) | |
| Number of GTS episodes in the previous year | | | | | |
| None | 1,324 | 91.2 (89.9–92.6) | 846 | 85.0 (82.8–87.2) | 0.000 |
| 1–5 | 92 | 6.3 (5.1–7.6) | 95 | 9.5 (7.7–11.4) | |
| ≥6 | 36 | 2.5 (1.7–3.3) | 54 | 5.5 (4.0–6.8) | |

(*Continued*)

**TABLE II.** (*Continued*)

| Variables | Male (N = 1,464) | | Female (N = 1,005) | | *P*-value[a] |
|---|---|---|---|---|---|
| | N | % (95% CI) | N | % (95% CI) | |
| Wheeze in the previous year | | | | | 0.617 |
| No | 1,302 | 89.0 (87.8–90.6) | 887 | 88.3 (86.3–90.3) | |
| Yes | 161 | 11.0 (9.4–12.6) | 117 | 11.7 (9.6–13.6) | |

Ninety-five percent CI: confidence interval.
[a]Fisher exact test of heterogeneity for the difference between genders.

1999; Sistek et al., 2001]. Several studies have used wheezing as an outcome in rural areas and this expands the analysis of the consistency of findings [GINA, 1993; Gomez et al., 2004; Hoppin et al., 2006; Douwes et al., 2007; Smit et al., 2008].

Adult-onset asthma was more prevalent among females. Authors suggest that female hormones could be involved in the pathogenesis of this disease, with greater incidence during puberty and lesser incidence during the menopause [de Nijs et al., 2013]. In this study, the prevalence of wheezing was similar in both genders and this may be related to the very low prevalence of smoking among women and their lower exposure to pesticides and dust than males.

The direct association between age and wheezing in male tobacco growers is in agreement with the literature [Rask-Andersen, 2011] and is reinforced by cumulative exposure to cigarette smoke [James et al., 2013]. Among females, no association was found, possibly owing to the low prevalence of smoking and less contact with pesticides.

Family history of asthma is a recognized risk factor for the development of atopic asthma in childhood, but is unclear in relation to adult-onset asthma [de Nijs et al., 2013]. Increased risk of wheezing in females with a family history of asthma may be related to the greater importance of atopic asthma in females while among males wheezing could be more related to the work environment and smoking.

The low prevalence of smoking among females resulted in low statistical power for evaluating this variable. Current smoking among males was associated with wheezing. Inhaling cigarette smoke for at least 15 years has been shown to be capable of inducing acute bronchoconstriction in both animals and humans [Hong et al., 1995; Hong and Lee, 1996; Matsumoto et al., 1996; Chiba et al., 2005]. Moreover, it has been suggested that simultaneous and persistent exposure to airborne allergens and to smoking may have an additional or synergetic effect on the occurrence of adult-onset asthma [de Nijs et al., 2013].

Strenuous work was associated with the occurrence of wheezing in both genders. Tobacco workers perform activities requiring physical effort in closed environments with high concentrations of dust, such as inside curing barns and sheds. People with and without asthma have presented prevalence of more than 20% of exercise-induced bronchoconstriction (EIB) syndrome [Parsons et al., 2013b]. Chronic exposure to airborne pollutants while exercising increases airway hyperreactivity and reduces lung function [Parsons et al., 2013a,b], and simultaneous exposure to smoking and organic dusts could contribute to EIB development and severity [Minov et al., 2006].

Lifting sticks with tobacco leaves to be hung in the curing barns was predominantly performed by females, however it was positively associated with wheezing only among males. Less healthy or less strong workers raise the sticks from the ground, while others, the healthier and stronger ones, climb the scaffolding to take hold of the sticks and position them in the curing barns, thus indicating a healthy workers effect. The lack of association among females might indicate that they are not selected for this activity according to their health status but rather because of their physical strength.

Another association biased by the healthy workers effect is harvesting the lower tobacco leaves, which showed inverse association with wheezing. Considering that this activity requires considerable physical effort, takes place in a hot and humid environment, demands leaf handling implying contact with pesticide residues and dermal absorption of nicotine, sick workers are unable to deal with these work conditions. This activity can both give rise to a wheezing attack and also prevent workers with active asthma from doing it.

Although both genders referred tying hands of dry tobacco leaves, females are usually responsible for monotonous and repetitive tasks and might spend more time doing this activity than males, thus being more exposed to the humid and closed environment of the sheds with high concentrations of dried tobacco dust and micro-organisms (fungi and bacteria) [Brito and D'Acri, 1991; Bee, 2000]. This might explain the positive association of tying hands of dry tobacco leaves and wheezing only among females. Studies of tobacco processing factory workers showed that the increase in cumulative doses of dust could reduce lung function [Mustajbegovic et al., 2003; Zhang et al., 2005, 2009].

The association between applying pesticides more than 10 days a month in males and contact with pesticides for more than 10 years in females with wheezing is in agreement with

**TABLE III.** Multivariate Analysis: Asthma Symptoms—Prevalence and Associated Factors Among Men (Brazil, 2011)

| | | Crude | | | Adjusted | | |
|---|---|---|---|---|---|---|---|
| **Variables** | **Wheeze %** | **PR** | **95% CI** | ***P*-value** | **PR** | **95% CI** | ***P*-value** |
| 1st level | | | | | | | |
| Age (years) | | | | 0.022[a] | | | 0.022[a] |
| 18–24 | 7.8 | 1.00 | — | | 1.00 | — | |
| 25–34 | 8.9 | 1.14 | (0.65–1.98) | | 1.14 | (0.65–1.98) | |
| 35–44 | 13.2 | 1.69 | (0.98–2.91) | | 1.69 | (0.98–2.91) | |
| 45–54 | 11.7 | 1.50 | (0.86–2.61) | | 1.50 | (0.86–2.61) | |
| ≥55 | 13.3 | 1.71 | (0.97–3.02) | | 1.71 | (0.97–3.02) | |
| 2nd level | | | | | | | |
| Smoking | | | | 0.007[b] | | | 0.022[b] |
| No | 8.9 | 1.00 | — | | 1.00 | — | |
| Former | 10.1 | 1.13 | (0.75–1.70) | | 1.02 | (0.67–1.57) | |
| Smoker | 14.9 | 1.67 | (1.21–2.31) | | 1.53 | (1.10–2.13) | |
| 3rd level | | | | | | | |
| Harvesting lower tobacco leaves | | | | 0.002[a] | | | 0.001[a] |
| No | 24.3 | 1.00 | — | | 1.00 | — | |
| Sometimes | 17.9 | 0.73 | (0.28–1.94) | | 0.71 | (0.28–1.80) | |
| Always | 10.5 | 0.43 | (0.24–0.76) | | 0.35 | (0.19–0.66) | |
| Lifting sticks with tobacco leaves to the barns | | | | 0.035[a] | | | 0.024[a] |
| No | 9.3 | 1.00 | — | | 1.00 | — | |
| Sometimes | 10.1 | 1.09 | (0.73–1.63) | | 1.09 | (0.73–1.61) | |
| Always | 13.5 | 1.45 | (1.02–2.06) | | 1.48 | (1.05–2.10) | |
| Days/month of pesticides use | | | | 0.012[b] | | | 0.001[a] |
| None | 9.5 | 1.00 | — | | 1.00 | — | |
| 1–10 | 10.2 | 1.07 | (0.69–1.67) | | 1.49 | (0.92–2.41) | |
| ≥11 | 17.4 | 1.82 | (1.10–3.05) | | 2.71 | (1.56–4.71) | |
| 4th level | | | | | | | |
| Strenuous work | | | | 0.005[b] | | | 0.010[b] |
| No | 6.9 | 1.00 | — | | 1.00 | — | |
| Yes | 12.3 | 1.77 | (1.19–2.65) | | 1.72 | (1.14–2.61) | |
| Contact with dried tobacco dust | | | | 0.001[b] | | | 0.039[a] |
| No | 6.7 | 1.00 | — | | 1.00 | — | |
| Little | 8.3 | 1.25 | (0.56–2.78) | | 1.12 | (0.48–2.57) | |
| Too much | 13.8 | 2.07 | (0.96–4.48) | | 1.59 | (0.68–3.71) | |
| Contact with vegetable dust | | | | 0.002[a] | | | 0.053[a] |
| No | 8.0 | 1.00 | — | | 1.00 | — | |
| Little | 11.1 | 1.40 | (0.95–2.05) | | 1.31 | (0.88–1.93) | |
| Too much | 15.8 | 1.98 | (1.29–3.04) | | 1.54 | (0.99–2.39) | |
| Contact with chemical dust | | | | 0.001[a] | | | 0.078[a] |
| No | 5.8 | 1.00 | — | | 1.00 | — | |
| Little | 10.3 | 1.78 | (0.98–3.24) | | 1.56 | (0.89–2.76) | |
| Too much | 13.9 | 2.40 | (1.33–4.34) | | 1.76 | (1.00–3.08) | |
| Month/year of intensive work | | | | 0.059[b] | | | 0.077[b] |
| None | 12.1 | 1.00 | — | | 1.00 | — | |
| 1–6 | 9.6 | 0.79 | (0.51–1.22) | | 0.61 | (0.39–0.96) | |
| 7–12 | 14.3 | 1.18 | (0.74–1.88) | | 0.78 | (0.47–1.29) | |

(*Continued*)

**TABLE III.** (*Continued*)

| Variables | Wheeze % | Crude | | | Adjusted | | |
|---|---|---|---|---|---|---|---|
| | | PR | 95% CI | *P*-value | PR | 95% CI | *P*-value |
| 5th level | | | | | | | |
| Number of GTS episodes in the previous year | | | | 0.000[a] | | | 0.001[a] |
| None | 9.4 | 1.00 | — | | 1.00 | — | |
| 1–5 | 23.9 | 2.53 | (1.68–3.81) | | 2.41 | (1.62–3.60) | |
| ≥6 | 30.6 | 3.23 | (1.94–5.39) | | 3.12 | (1.98–4.94) | |

PR, prevalence rate; 95% CI, confidence interval.
[a]Wald test of linear trend.
[b]Wald test of heterogeneity.

the literature. A Brazilian study found an increased risk of asthma symptoms among farm workers as the number of days per month of pesticide application increased [Faria et al., 2005], while in the Agricultural Health Study, farmers and commercial pesticide appliers showed a positive dose–response effect between days of application per annum and wheezing in relation to chlorimuron-ethyl, chlorpyrifos, and phorate (only in commercial appliers) [Hoppin et al., 2006].

Males and females were exposed in different ways and intensities to the types of dust analyzed. Dry tobacco and vegetable dust were risk factors for wheezing only in men. Organic dust is known as a common risk factor as well as an aggravating factor for asthma [Sigsgaard and Schlunssen, 2004; Wang et al., 2005; Cummings et al., 2010]. Preliminary evidence has indicated that smoking could increase the sensitization to common occupational agents, increasing the risk of occupational asthma and allergies [Mustajbegovic et al., 2003; Vandenplas, 2011]. However, in this study there was no interaction between smoking and tobacco or other vegetable dust. These differences in the effect of dry tobacco and vegetable dust among genders needs further investigation.

The handling of chemical disinfectants was mostly done by females and was associated with wheezing only in them. Domestic and occupational exposure to cleaning agents is a risk factor both for occupational and non-occupational asthma [Jeebhay et al., 2014]. Recent studies have shown high risk of asthma attacks and new-onset asthma arising from exposure to bleaches, ammonia, degreasing sprays, and accidental inhalation of vapors and gases from cleaning products [Vandenplas, 2011].

The number of GTS episodes reported in the last year was linearly associated with wheezing in both genders. The action of nicotine inhaled through cigarette smoking on bronchoconstriction and increased mucous production have been widely described in the literature, either as direct action on the lungs or on the central nervous system [Hong et al., 1995; Hong and Lee, 1996; Matsumoto et al., 1996; Maouche et al., 2013]. However, respiratory risks when harvesting tobacco have not been investigated yet.

According to Physiologically Based Pharmacokinetic Modeling (PBPK model) [Smith and Kriebel, 2010], nicotine absorbed by skin reaches the lungs without the first-pass metabolism reducing its bioavailability. Nicotine high solubility and low molecular weigh (162.2 g/mol) [Zorin et al., 1999], added to the vasodilation, increase in heart rate and local blood flow, caused by heat and physical exercise, optimize its absorption through the skin [Lenz and Gillespie, 2011; Petersen et al., 2011]. The absorption of substances by the skin is lower than by inhaling [Smith and Kriebel, 2010], however skin exposure to nicotine when harvesting tobacco is believed to be high, enabling significant absorption by this route [Gehlbach et al., 1975; Arcury et al., 2003].

This was the only identified study evaluating wheezing in a large sample of tobacco farm workers on family owned and operated farms. The strategy used to select the sample, as well as, the few losses and refusals guaranteed the representativeness of the studied population. The large number of studied variables increased the probability of associations by chance. Moreover, the lack of objective measures, such as biological markers of exposure to pesticides, nicotine, and dust is a limitation of this kind of study.

The findings highlight the importance of broadening perspectives about nicotine exposure considering its multiple source of absorption and variable intensity of exposure. GTS is an indicator of heavy exposure to nicotine [Fassa et al., 2014], however intense exposure might also course asymptomatic due to tolerance mechanisms.

These results provide an important support to draw actions to accomplish Article 18 of the Framework Convention on Tobacco Control regarding protection of the people and the environment. Mechanization of the harvesting and baling process could reduce tobacco farmers' exposure to nicotine. Often, farmers do not use personal protective equipment (PPE) or use PPE that has lost its effectiveness or is not certified to reduce nicotine exposure. Both developing efficient PPE and also ensuring its use in hot weather conditions in the harvesting season continue to be challenges. Article 17 of the same convention addresses the need of

**TABLE IV.** Multivariate Analysis: Asthma Symptoms—Prevalence and Associated Factors Among Women (Brazil, 2011)

| | | Crude | | | Adjusted | | |
|---|---|---|---|---|---|---|---|
| **Variables** | **Wheeze %** | **PR** | **95% CI** | ***P*-value** | **PR** | **95% CI** | ***P*-value** |
| 1st level | | | | | | | |
| Family history of asthma | | | | 0.002[a] | | | 0.002[a] |
| No | 10.7 | 1.00 | — | | 1.00 | — | |
| Yes | 21.6 | 2.02 | (1.30–3.15) | | 2.02 | (1.30–3.15) | |
| 2nd level | | | | | | | |
| Harvesting lower tobacco leaves | | | | 0.063[b] | | | 0.018[b] |
| No | 19.1 | 1.00 | — | | 1.00 | — | |
| Sometimes | 17.2 | 0.90 | (0.33–2.50) | | 0.57 | (0.20–1.64) | |
| Always | 11.1 | 0.58 | (0.30–1.12) | | 0.46 | (0.24–0.90) | |
| Tying hands of tobacco | | | | 0.0108[a] | | | 0.016[a] |
| No | 5.6 | 1.00 | — | | 1.00 | — | |
| Sometimes | 21.0 | 3.78 | (1.16–12.34) | | 3.89 | (1.17–12.94) | |
| Always | 11.2 | 2.01 | (0.65–6.18) | | 2.29 | (0.74–7.10) | |
| Time of exposure to pesticides in life (years) | | | | 0.003[b] | | | 0.002[b] |
| None | 9.8 | 1.00 | — | | 1.00 | — | |
| ≤10 | 8.4 | 0.86 | (0.50–1.45) | | 0.88 | (0.52–1.50) | |
| 11–20 | 14.1 | 1.43 | (0.90–2.30) | | 1.44 | (0.90–2.31) | |
| 21–30 | 12.5 | 1.27 | (0.72–2.24) | | 1.39 | (0.77–2.50) | |
| ≥31 | 22.9 | 2.33 | (1.41–3.87) | | 2.32 | (1.41–3.82) | |
| 3rd level | | | | | | | |
| Strenuous work | | | | 0.010[a] | | | 0.008[a] |
| No | 9.2 | 1.00 | — | | 1.00 | — | |
| Yes | 14.4 | 1.56 | (1.11–2.19) | | 1.76 | (1.22–2.54) | |
| Working in smoky conditions | | | | 0.018[b] | | | 0.061[b] |
| No | 10.6 | 1.00 | | | 1.00 | — | |
| Little | 15.3 | 1.43 | (0.96–2.15) | | 1.28 | (0.85–1.92) | |
| Too much | 20.0 | 1.88 | (0.89–3.94) | | 1.86 | (0.89–3.88) | |
| Contact with chemical disinfectants | | | | 0.055[a] | | | 0.046[a] |
| No | 8.6 | 1.00 | — | | 1.00 | — | |
| Yes | 13.0 | 1.51 | (0.99–2.30) | | 1.54 | (1.00–2.35) | |
| Month/year of intensive work | | | | 0.118[a] | | | 0.089[b] |
| None | 16.8 | 1.00 | — | | 1.00 | — | |
| 1–6 | 10.6 | 0.63 | (0.40–0.98) | | 0.61 | (0.36–1.03) | |
| 7–12 | 11.0 | 0.65 | (0.38–1.12) | | 0.56 | (0.31–1.00) | |
| 4th level | | | | | | | |
| Number of GTS episodes in the previous year | | | | 0.000[b] | | | 0.005[b] |
| None | 10.3 | 1.00 | — | | 1.00 | — | |
| 1–5 | 12.6 | 1.23 | (0.70–2.14) | | 1.13 | (0.66–1.93) | |
| ≥6 | 27.8 | 2.70 | (1.68–4.34) | | 2.29 | (1.37–3.82) | |

PR, prevalence rate; 95% CI, confidence interval.
[a]Wald test of heterogeneity.
[b]Wald test of linear trend.

governments to promote economically viable alternatives to tobacco plantation. However, promoting crop diversification is not enough to protect farmers' health, a sustainable agricultural production model with decreased pesticide use is also necessary.

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