Nicotine & Tobacco Research, 2016, 1517–1525
doi:10.1093/ntr/ntv187
Original investigation
Advance Access publication September 16, 2015

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Urinary Cotinine Levels Among Latino Tobacco Farmworkers in North Carolina Compared to Latinos Not Employed in Agriculture

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Abstract

Introduction: This analysis describes urinary cotinine levels of North Carolina Latino farmworkers, compares cotinine levels of farmworkers to those of Latinos non-farmworkers, determines factors associated with farmworker cotinine levels, and determines if differences in farmworker and non-farmworker cotinine levels are associated with smoking.

Methods: Data are from 63 farmworkers and 44 non-farmworkers who participated in a larger study of occupational exposures. Questionnaire data and urine samples collected in 2012 and 2013 are analyzed.

Results: Farmworkers had urinary cotinine levels that were far greater than the non-farmworker group. Geometric mean (GM) urinary cotinine levels for farmworkers were 1808.22 ng/ml in 2012, and 396.03 ng/ml in 2013; corresponding GM levels for non-farmworkers were 4.68 ng/ml and 9.03 ng/ml. Farmworker GM cotinine levels were associated with harvesting tobacco (1242.77 ng/ml vs. 471.26 ng/ml; P = .0048), and working in wet shoes (1356.41 ng/ml vs. 596.93 ng/ml; P = .0148). Smoking did not account for cotinine level differences; the GM cotinine level for farmworkers who did not smoke was 541.31 ng/ml; it was 199.40 ng/ml for non-farmworkers who did smoke.

Conclusion: North Carolina farmworkers experience large nicotine doses. The long-term health effects of these doses are not known. Although procedures to reduce occupational nicotine exposure are known, no changes in work practices or in policies to protect workers have been implemented. Research on the health effects of occupational nicotine exposure must become a priority. Current knowledge of occupational transdermal nicotine exposure must be used to improve occupational safety practice and policy for tobacco workers.

Implications: This study documents the heavy burden of nicotine exposure and dose experienced by tobacco workers in North Carolina. Hundreds of thousands of farmworkers and farmers in the United States and Canada, as well as agricultural workers around the world, share this burden of nicotine exposure and dose. These results support the need to change work practices and regulations to protect workers. They also document the need to delineate the health effects of long-term exposure to high transdermal nicotine doses.

Introduction

Latino farmworkers in North Carolina are often employed in the cultivation and harvesting of tobacco.[1–4] Latinos comprise the majority of farmworkers in the United States, and the majority of those employed in tobacco production.[5] Work in tobacco production is associated with a number of occupational health risks, with nicotine exposure being an important risk in tobacco production.[6] Nicotine is a naturally occurring alkaloid that is produced by the tobacco plant. Nicotine is both water and lipid soluble; contact with green tobacco plants or water on green tobacco plants leads to dermal absorption of nicotine. Sufficiently high levels of absorbed nicotine have been associated with acute symptoms, including headache, dizziness, nausea and vomiting, anorexia, and insomnia. Together, these symptoms reflect an occupational illness referred to as green tobacco sickness (GTS).[7–9] GTS is self-limiting; its symptoms will dissipate in 1 or 2 days if no further contact with tobacco occurs. The most severe effects of GTS are dehydration and heat stress that results from vomiting while working in the heat.[10,11]

Long term health effects of repeated dermal nicotine exposure or GTS have not been investigated. Nicotine is a potent stimulant, raising heart rate and blood pressure. In younger workers, impacts on brain development, cognition, and mood disorders are known.[12,13]

Cotinine is a nicotine metabolite, used as a biomarker of nicotine exposure.[14–16] Research on cotinine levels among agricultural workers has been conducted in several tobacco producing countries, including Brazil,[17–20] Malaysia,[21] Thailand,[22] Italy,[23] Poland,[23]and the United States.[25–27] These analyses show that cotinine levels are associated with the symptoms of GTS, and that these levels are much higher among tobacco workers compared to controls, after adjusting for tobacco consumption. Cotinine levels vary among tobacco workers based on the type of tobacco in which they work (eg, flue-cured tobacco vs. shade tobacco). They also vary in terms of the tasks which workers perform (those harvesting tobacco have higher cotinine levels than those planting or loading tobacco), the conditions in which they work (those working in wet tobacco have higher cotinine levels than those working in dry tobacco), and the use of personal protective equipment (those wearing wet clothes and shoes have higher cotinine levels than those wearing dry clothes and shoes, or wearing a rain-suit).[27]

Research on cotinine levels of tobacco workers has focused on those with diagnosed GTS, and it has used data collected in a single season. Further research on the general nicotine exposure of tobacco workers, irrespective of the presence of GTS symptoms, is needed to begin documenting their long-term exposure and the health consequences of this exposure. This analysis uses data collected from Latino farmworkers and a comparison group of Latino non-farmworkers in two agricultural seasons. The aims of this analysis are to: (1) describe urinary cotinine levels of Latino farmworkers in North Carolina, based on urine samples collected in two separate agricultural seasons; (2) compare the urinary cotinine levels of Latino farmworkers to the levels of Latinos in North Carolina who are not employed in farm work; (3) determine whether variation in farmworker cotinine levels are associated with work tasks, the use of personal protective equipment, and working in wet clothing; and (4) determine if differences in cotinine levels between farmworkers and non-farmworkers are accounted for by smoking.

Methods

Data were collected as part of the PACE4 project, a community-based participatory research project comparing occupational exposures, particularly pesticide exposure, among immigrant Latino farmworkers and immigrant Latino non-farmworker manual workers. Community partners for this research were the North Carolina Farmworkers Project (Benson, NC), and El Buen Pastor Latino Community Services (Winston-Salem, NC). The research protocol was approved by the Wake Forest School of Medicine IRB; all participants gave signed informed consent. Participants were recruited from three agricultural counties in east central North Carolina (Harnett, Johnston, Sampson), and an urban county in Piedmont, North Carolina (Forsyth).

Participants

PACE4 participants were men aged 30 to 70 years. Workers younger than 30 years were excluded from the sample due to the larger study's focus on cognitive and neurological outcomes. All participants self-identified as Latino or Hispanic. Farmworkers were currently employed in agriculture and worked in agriculture for at least 3 years. Non-farmworkers could not be employed for the past 3 years in jobs that exposed them to pesticides, including farm work, forestry, landscaping, grounds keeping, lawn maintenance, and pest control. Potential farmworker and non-farmworker participants were excluded if they reported being told by a healthcare provider that they had diabetes.

Community partners assisted with recruitment. North Carolina Farmworkers Project staff approached farmworker camps that they served. They explained the project to the camp residents, including inclusion and exclusion criteria, time commitments and incentives, and asked for volunteers. Winston-Salem staff worked with El Buen Pastor Latino Community Services to identify potential participants. Project staff contacted potential participants, explained the project, and asked if the individual wanted to volunteer. All volunteers were screened to ensure that they met the inclusion criteria.

A total of 235 farmworkers and 212 non-farmworkers completed the baseline interviews. As groups of farmworkers were asked to volunteer, only the number who agreed to volunteer is available; generally, all of the farmworkers in a camp who met the inclusion criteria volunteered. However, individual farmworkers who did not want to participate could have avoided contact with project staff or may have indicated that they did not meet the inclusion criteria to avoid refusal. Among the non-farmworkers, 101 individuals were contacted who did not meet the inclusion criteria. Of those contacted and meeting the inclusion criteria, 87 individuals refused, for a participation rate of 70.9% (212/[87+212]). Reasons given for refusing included time commitment and study length (51), blood draws (27), need to come to a clinic for data collection (31), and providing contact information (30) (individuals could give more than one reason for refusing).

Participants completed a baseline interview in May and June (farmworkers), and June and July (non-farmworkers), 2012, with up to four follow-up contacts in 2012 completed at monthly intervals, up to four monthly follow-up contacts in 2013 beginning in June for farmworkers and July for non-farmworkers, and one follow-up in 2014. Urine samples were collected from participants for each follow-up contact in 2012 and 2013.

PACE4 was a multi-component study in which some participants were included in an analysis of epigenetics or brain structure with data collected through Magnetic Resonance Imaging. Selection of participants for the genetic and Magnetic Resonance Imaging components was not related to their tobacco exposure or use. Initial selection was based on changes in cholinesterase levels, an indicator of exposure to organophosphorus and carbamate pesticides; farmworkers with the greatest change in cholinesterase levels were selected, and non-farmworkers with the least change in cholinesterase levels were selected. However, to meet the needs of the community-based participatory research program other interested participants were allowed to enroll. Urine samples used in this analysis were selected from those collected in July through September in 2012, and July and August in 2013, on a day that the participant worked. Urine samples were available for 63 different farmworkers, 62 in 2012 and 56 in 2013; for non-farmworkers, urine samples were available for 44 participants in 2012 and 34 in 2013.

Date Collection

Data for this analysis are from two sources. Interview data are taken from interviewer-administered questionnaires completed at the baseline contact with the participant, and on the day that urine samples used in this analysis were collected. The baseline interview included personal and employment characteristics. Follow-up contacts provided information on any changes in employment status and tasks. Questionnaires were developed in English and translated into Spanish. When possible, existing Spanish items and scales were used. The Spanish and English versions were checked for comparable meaning for each item, and item wording was adjusted as needed. The Spanish versions of the questionnaires were pre-tested, and final corrections were made. Interviews were conducted by native Spanish speakers who were trained and supervised by the investigators.

Participants provided a spot urine sample at each of the follow-up contacts. A primary 10 ml aliquot was prepared from each sample for analysis of pesticide urinary metabolites. A back-up 10 ml aliquot was also prepared from each urine sample, if sufficient volume was provided by the participant. Many participants provided urine samples at the end of a work day when they were very dehydrated, and could not provide more than the initial 10 ml of urine. All aliquots were frozen at −80°C. The primary aliquots were delivered to the laboratory for pesticide urinary metabolite analysis. The back-up aliquots were used for the analysis of cotinine.

Participants were provided with a $30 incentive for completing the baseline contact, and a $20 or $30 incentive for completing follow-up contacts, depending on the data collected (questionnaire, cognitive test, urine sample, blood sample). Study data were collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at Wake Forest School of Medicine.[28] REDCap is a secure, web-based application designed to support data capture for research studies.

Measures

The outcome measure is cotinine, which is reported in ng/ml of urine. Samples were tested in duplicate using a highly-sensitive enzyme immunoassay (Salimetrics LLC, State College, PA). The individual cotinine measures are not adjusted for creatinine. Creatinine was measured for composites of up to four individual samples collected for each year. Most of the non-farmworkers, as well as the farmworkers, worked in physically demanding jobs that could result in dehydration. A comparison of composite creatinine measures for Year 1 (farmworker geometric mean (GM) = 98.69, non-farmworker GM = 77.35; P = .0975), and for Year 2 (farmworker GM = 155.02, non-farmworker GM = 145.73; P = .5882) indicates little difference between the two populations.

Personal characteristic measures included age, country of origin, educational attainment, and occupation. Age is reported in the categories of 30–34 years, 35–44 years, and 45 years or older. Country of origin had the values of Mexico or other. Educational attainment has the values of 0–6 years, 7–11 years, 12 or more years. Occupation had the values of farmworker, construction, manufacturing, food preparation, maintenance, truck driver, mechanic, other, and unemployed.

Three measures of smoking status are included. Pack years is based on data collected in the baseline interview (May–July, 2012) and has the values of 0, less than 1 year, 1 to 4 years, and 9 to 25 years. Number of cigarettes smoked in the last month is also based on the baseline interview and has the values of none or any. Finally, ever smoked during data collection is based on a baseline question that asked participants if they smoked in the last month, and questions at four of the eight follow-up contacts which asked if they had smoked that day; it has the values of never or ever reported smoking during data collection.

Measures of work tasks and exposure risk factors for 2012 and 2013 were collected for farmworkers. The first measure is whether the participant worked in tobacco in the 3 days before providing the urine sample. Tasks included planting tobacco, topping (removing the plant's flower), harvesting, and barning (putting the tobacco in the curing barn) in the 3 days before providing the urine sample. Exposure risk factors included wearing gloves, wearing a rain-suit, working in wet shoes, or working in wet clothes in the 3 days before providing the urine sample. Farmworkers often wear rain-suits to reduce exposure to water on tobacco plants.

Analysis

Frequencies and percentages were calculated by farmworker status for participant baseline personal characteristics. Chi-square tests were conducted to test for differences in participant characteristics and farmworker status. Cotinine concentrations were measured in duplicates for each participant at each time point (ie, each year) and the average of the two replicates was used for all analyses. Summary measures (mean, standard deviation, minimum, median, maximum) were calculated for the cotinine levels of farmworkers and non-farmworkers within each year of data collection. For farmworkers, frequencies and percentages were calculated for the tasks and exposure risk factors of interest across both years. A linear mixed effects model which accounted for repeated measures across both years with random intercepts was used to evaluate the overall differences in the natural-log of the cotinine levels for the farmworkers who did perform a task versus those who did not, and those who did protect themselves from exposure versus those who did not. Least square means and standard errors were calculated based on the natural-log cotinine outcome and then back-transformed for each task and protection from exposure level, both overall and within each year. Standard errors for the GMs were calculated using Delta method.[29] The interaction between task/protection from exposure level and year was also examined. For all variables of interest the interaction with year was not significant, thus we examined the main effect of each variable across both years. We also examined the interaction between farmworker status and the smoking variable on cotinine levels using the linear mixed effects model accounting for repeated measures over time. Since the interaction is significant, we conducted a stratified analysis by smoking status to compare cotinine levels between farmworkers and non-farmworkers across 2 years. Least square means and standard errors were calculated and then back-transformed for each level of farmworker and smoking status. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC) and *P* values of less than .05 were considered statistically significant.

Results

Participant Characteristics

Farmworkers and non-farmworkers had similar age distributions (Table 1). All of the farmworkers were from Mexico, but 29.5% of the non-farmworkers were from other countries (most from Central America). Farmworkers had less education than non-farmworkers, with 38.1% of farmworkers compared to 27.3% of non-farmworkers having 6 or fewer years of education. Non-farmworkers were employed in a number of manual occupations, with the most common being in construction, manufacturing, and food preparation.

Half of farmworkers but 68.2% of non-farmworkers had zero pack years of cigarette consumption at baseline. Almost one-third (30.6%) of the farmworkers, but 9.1% of the non-farmworkers reported smoking any cigarettes in the previous month at baseline. One-third of the farmworkers, but 9.1% of non-farmworkers, reported smoking cigarettes at any time during data collection.

Farmworker and Non-Farmworker Cotinine Levels

Farmworkers had substantially greater levels of urinary cotinine than non-farmworkers (Table 2). The GM cotinine levels for farmworkers were 1808.22 ng/ml in 2012, and 396.03 ng/ml in 2013. The corresponding levels for non-farmworkers were 4.68 ng/ml and 9.03 ng/ml. The cotinine level for farmworkers was significantly lower in 2013 compared to 2012 ($P < .0001$); non-farmworkers did not have a statistically significant change in cotinine levels from 2012 to 2013. Although cotinine levels for farmworkers were significantly lower in 2013, their cotinine levels remained substantially greater than non-farmworkers.

Table 1. Participant Personal Characteristics in 2012 for PACE4 Study of Cotinine, Farmworkers Compared to Non-Farmworkers

	Farmworkers *n* = 63		Non-farmworkers *n* = 44		
Personal characteristics	*n*	%	*n*	%	*P*
Age (in years)					.3326
30 to 34	25	39.7	13	29.5	
35 to 44	23	36.5	15	34.1	
45 or more	15	23.8	16	36.4	
Country of birth					<.0001
Mexico	63	100	31	70.5	
Other	0		13	29.5	
Education (in years)					.0154
0 to 6	24	38.1	12	27.3	
7 to 11	31	49.2	16	36.4	
12 or more	8	12.7	16	36.4	
Occupation					NA
Farm work	63	100			
Construction			15	34.1	
Manufacturing			8	18.2	
Food preparation			6	13.6	
Maintenance			4	9.1	
Truck driver			2	4.5	
Mechanic			3	6.8	
Other			3	6.8	
Unemployed			3	6.8	
Pack years at baseline[a]					.2076
0 years	31	50.0	30	68.2	
Less than 1 year	19	30.6	7	15.9	
1 to 4 years	9	14.5	4	9.1	
9 to 25 years	3	4.8	3	6.8	
Number of cigarettes smoked in the last month at baseline[a]					.0080
None	43	69.4	40	90.9	
Any	19	30.6	4	9.1	
Smoked during data collection					.0035
Never	42	66.7	40	90.9	
Ever	21	33.3	4	9.1	

[a]One missing observation.

Table 2. Cotinine Levels in ng/ml of Urine in Each Project Year for Farmworkers and Non-Farmworkers, PACE4 Project

	N	Mean	*SD*	Minimum	Median	Maximum	Geometric Mean (GM)
Farmworkers							
2012	62	4054.98	4376.85	4.56	2527.86	20866.95	1808.22
2013	56	1527.45	2318.05	1.09	477.27	13718.29	396.03
Non-farmworkers							
2012	44	70.76	238.43	0.49	2.70	1401.48	4.68
2013	34	373.51	1159.88	0.45	2.90	4997.20	9.03

Table 3. Farmworker Work Characteristics for the Day Urine Samples Were Collected, and the Associations of Work Characteristics With Least Square Mean Cotinine Levels, 2012 (n = 62), 2013 (n = 56), and Overall

Work characteristics	*n*	%	Geometric mean (standard error) cotinine levels		*P**
Worked in tobacco in the last 3 days			Yes	No	
2012	57	91.9	2426.73 (517.14)	74.51 (39.95)	
2013	51	91.1	549.88 (121.25)	16.88 (9.07)	
Overall			1155.17 (223.06)	35.47 (18.71)	<.0001
Tobacco work in last 3 days			Performed task	Did not perform task	
Planting					
2012	13	21.0	1384.09 (514.88)	1978.91 (502.44)	
2013	15	26.8	316.05 (114.69)	451.87 (121.15)	
Overall			661.43 (230.77)	945.58 (221.46)	.3189
Topping					
2012	5	8.1	1988.43 (850.45)	1824.57 (445.20)	
2013	22	39.3	433.11 (148.56)	397.42 (115.73)	
Overall			927.97 (338.62)	851.59 (199.70)	.8228
Harvesting					
2012	41	66.1	2562.40 (660.07)	971.65 (307.43)	
2013	33	58.9	602.75 (164.67)	228.56 (71.17)	
Overall			1242.77 (297.15)	471.26 (137.56)	.0048
Barning					
2012	27	43.5	1956.48 (576.77)	1748.13 (482.48)	
2013	30	53.6	434.11 (125.94)	387.84 (114.22)	
Overall			921.59 (247.08)	823.37 (214.32)	.7082
In last 3 days, worked wearing			Wore	Did not wear	
Gloves					
2012	46	74.2	1876.19 (499.07)	1727.45 (689.25)	
2013	45	80.4	417.38 (109.98)	384.33 (164.22)	
Overall			884.92 (209.90)	814.77 (322.89)	.8471
Rain-suit					
2012	41	66.1	2050.63 (545.67)	1488.02 (481.52)	
2013	33	58.9	469.42 (133.64)	340.67 (107.28)	
Overall			981.13 (244.40)	712.02 (211.33)	.3353
Wet shoes					
2012	36	58.1	2597.75 (708.41)	1143.10 (344.53)	
2013	20	35.7	708.25 (230.82)	311.69 (83.31)	
Overall			1356.41 (373.15)	596.93 (154.01)	.0148
Wet clothes					
2012	44	71.0	2138.80 (556.09)	1276.27 (428.19)	
2013	24	42.9	555.18 (174.83)	331.29 (94.48)	
Overall			1089.75 (284.10)	650.21 (185.70)	.1245

**P* value for overall difference between groups.

Variation in Cotinine Levels Among Farmworkers

Urinary cotinine levels were significantly greater among farmworkers who worked in tobacco in the 3 days prior to the collection of urine sample compared to those who had not worked in tobacco (Table 3). Those who reported harvesting tobacco in the last 3 days had significantly greater cotinine levels than those not harvesting tobacco; cotinine levels did not vary between those who did or did not report other tasks (planting, topping, or barning) in the last 3 days. Wearing gloves or rain-suits in the last 3 days was not associated with cotinine levels. Those who reported working in wet shoes in the last 3 days had significantly greater cotinine levels than those not working in wet shoes; cotinine levels did not differ for those who reported wearing or not wearing wet clothes.

Cotinine Level by Smoking Status

Farmworkers and non-farmworkers who smoked during data collection have significantly greater cotinine levels across both years versus

Table 4. Comparison of Cotinine Levels Between Never/Ever-Smokers Within Farmworkers and Non-Farmworkers, and Comparison of Cotinine Levels by Farmworkers and Smoking Status

	Geometric mean (standard error)[a]		
	Smoked during data collection		
	Never	Ever	*P*
Farmworkers			
2012	1117.56 (296.49)	5056.35 (1836.47)	
2013	246.46 (67.65)	1114.99 (408.09)	
Overall	524.84 (128.11)	2374.40 (821.30)	.0008*
Non-farmworkers			
2012	3.30 (0.99)	153.53 (128.69)	
2013	5.57 (1.87)	258.99 (217.09)	
Overall	4.29 (1.16)	199.40 (163.77)	<.0001*
	Cotinine levels by farmworkers and smoking status		
	Never	Ever	
Farmworkers	541.31 (137.06)	2393.71 (859.58)	.0113**
Non-farmworkers	3.81 (1.01)	199.40 (160.61)	

[a]Back-transformed.

**P* value for overall difference between groups.

***P* value for interaction between smoking groups and farmworker status.

those who did not (Table 4). Interactions between year and smoking status (smoked during data collection) were not significant for either farmworkers or non-farmworkers (the cotinine levels in relation to smoking status and year remained consistent). However, farmworkers who smoked during data collection showed a significant decrease comparing 2012 to 2013 in cotinine levels; whereas non-farmworkers who smoked during data collection did not have a significant difference. Although farmworkers and non-farmworkers show significantly higher cotinine levels for smokers, farmworkers who smoked have higher cotinine levels compared to non-farmworkers who smoke. Farmworkers who did not smoke also have higher cotinine levels compared to non-farmworkers who did smoke.

Discussion

Farmworkers engaged in tobacco production have far greater cotinine levels than the comparison group of Latinos not employed in agriculture. The high urinary cotinine levels of farmworkers did not result from tobacco consumption. Farmworkers who "did not" smoke during the data collection period had higher cotinine levels (GM 541.31 ng/ml) than did non-farmworkers who "did" smoke during the data collection period (GM 199.40 ng/ml).

Urinary cotinine levels are higher for North Carolina farmworkers than are those reported for tobacco workers in other studies (Table 5). A difference between the current study and other analyses is that several of the previous analyses compared cotinine levels of workers reporting GTS with workers not reporting GTS. Differences in cotinine levels may result from differences in time of year when samples were collected, laboratory methods, and biological matrix.

Urinary cotinine levels among the farmworkers in this analysis reflected their work in tobacco. Farmworkers who had not worked in tobacco during the 3 days before the collection of the urine sample had significantly lower cotinine levels compared to those who had worked in tobacco in the previous 3 days. Specific work tasks and conditions are risk factors associated with the cotinine levels of these farmworkers. Harvesting tobacco, which involves the greatest worker contact with the green tobacco plant, was associated with higher cotinine levels. Working in wet shoes was also associated with higher cotinine levels. These risk factors are similar to those reported by Quandt and colleagues[27] among North Carolina farmworkers in which salivary cotinine levels were positively associated with harvesting tobacco, working when the tobacco was wet, and working in wet clothes, and inversely associated with changing out of wet cloths and wearing a rain-suit. Arcury and colleagues[9] demonstrate that the cotinine levels associated with these occupational risk factors significantly increase the odds for the occurrence of GTS. However, Onuki and colleagues[21] found no association of cotinine levels with wearing gloves or boots, or working in wet conditions, but did find that those not wearing protective equipment reported GTS symptoms more frequently than those who did. Bartholomay and colleagues[18] did not find associations of working in wet tobacco with reporting GTS; they did not report association with cotinine levels, but did find that hired workers were more likely to have symptoms than farm owners.

This analysis is novel in that it measured urinary cotinine levels among the same tobacco workers and comparison group in two successive growing seasons (2012 and 2013). It shows that the cotinine levels differed significantly for farmworkers, but not for non-farmworkers. We should expect fluctuation in cotinine levels among farmworkers as their nicotine exposure largely results from dermal contact with tobacco. The amount of dermal contact with tobacco, especially wet tobacco, experienced by farmworkers on a given day will be affected by the weather, the number of hours they work, the number of hours they are wet, and the number of hours they wear protective equipment. For example, D'Alessandro et al.[23] note that variation in nicotine and cotinine levels across a day could reflect a pattern in which residual nicotine on waterproof suits results in initially high nicotine and cotinine levels, that these levels subside when the water-proofs suits are removed,

Table 5. Summary of Publications Reporting Cotinine and Nicotine Levels in Agricultural Workers Exposed to Tobacco

Citation	Country	Research population	Biological matrix	Cotinine and nicotine levels reported
Oliveria et al.[17]	Brazil	Farmworkers, GTS, smokers	Urine	Cotinine: median 811 ng/ml
		Farmworkers, GTS, nonsmokers	Urine	Cotinine: median 288 ng/ml
Bartholomay et al.[18]	Brazil	Tobacco workers, GTS	Urine	Cotinine: mean 432ng/ml (*SD* 476)
		Tobacco workers, no GTS	Urine	Cotinine: mean 353 ng/ml (*SD* 549)
Onkui et al.[21]	Malaysia	Tobacco workers, smoking >10 cigarettes/d[a]	Urine	Cotinine: median 1846.7 ng/ml[a]
		Tobacco workers, smoking 1–10 cigarettes/d[a]	Urine	Cotinine: median 1564.7 ng/ml[a]
		Tobacco workers, nonsmokers	Urine	Cotinine: median 29.2 ng/ml[a]
Kongtip et al.[22]	Thailand	Tobacco processing workers, nonsmokers	Urine	Cotinine: median 3030 ng/ml, range 200 to 5180 ng/ml[b]
D'Alessandro et al.[23]	Italy	Female tobacco workers, nonsmokers	Blood	Nicotine: mean 0.79 (*SE* 0.12) ng/ml to 3.45 (*SE* 0.84) ng/ml
			Urine	Nicotine: mean 69.5 (*SE* 14.3) ng/ml to 158.3(*SE* 42.5) ng/ml
			Blood	Cotinine: mean 8.74 (*SE* 1.7) ng/ml to 20.54 (*SE* 9.55) ng/ml
			Urine	Cotinine: mean 81.90 (*SE* 34.82) ng/ml to 108.84 (*SE* 47.02) ng/ml
		Female hospital workers, nonsmokers	Blood, Urine	Negligible
Satora et al.[24]	Poland	Tobacco farmer, GTS	Urine	Cotinine: 869 ng/ml
Trapé-Cardoso et al.[25]	USA (Connecticut)	Farmworkers (shade tobacco), smokers	Saliva	Cotinine: range 16 ng/ml to 194 ng/ml
		Farmworkers (shade tobacco), nonsmokers	Saliva	Cotinine: not measurable
Quandt et al.[27]	USA (North Carolina)	Farmworkers, current smokers	Saliva	Cotinine: mean 145 (*SE* 20) ng/ml
		Farmworkers, current occasional smokers	Saliva	Cotinine: mean 75 (*SE* 11) ng/ml
		Farmworkers, not current but occasional smokers	Saliva	Cotinine: mean 57 (*SE* 9) ng/ml
		Farmworkers, nonsmokers	Saliva	Cotinine: mean 46 (*SE* 7) ng/ml

GTS = green tobacco sickness; *SE* = standard error.
[a]After adjustment for body surface area.
[b]Converted from µg/ml.

but then rise again with greater direct contact with tobacco plants. Cotinine levels for non-farmworkers are largely the result of smoking or exposure to environmental tobacco smoke, which have far less temporal variability (ie, smokers change their habits slowly, and exposure to environmental tobacco smoke is becoming more limited). Although cotinine levels were significantly lower among farmworkers in 2013 compared to 2012, the 2013 levels among participants in this analysis were higher than those reported in comparable studies.[17,18] The specific causes of the fluctuation in levels are not known, but this result suggests that future research should include a multi-year longitudinal component that documents variation in cotinine levels within and across growing seasons.

The long-term health effects of occupational nicotine exposure must be examined. No research on the long-term effects of occupational nicotine has been conducted, and research focused on long-term dermal nicotine absorption through nicotine patches is limited. Hundreds of thousands of Latino farmworkers, and thousands of farmers, are employed in the production of tobacco in the United States (especially the states of North Carolina, Kentucky, Virginia, and Tennessee) and Canada. In addition, tobacco production has expanded to nations in almost every continent.[6] Tobacco workers are often members of the most vulnerable communities in their countries, and all are exposed to high transdermal nicotine doses. Existing data sets, such as the Agricultural Health Study, may provide a mechanism for addressing the long-term health effects of occupational nicotine exposure, but new data on this topic may be required.

Farmworker nicotine exposure must be put in the context of other toxicants to which they are exposed. Research with Latino tobacco workers in North Carolina documents that these workers are exposed to large numbers of pesticides, often with large doses.[30–33] These include organophosphorus, carbamate, and pyrethroid pesticides, all of which are neurotoxic. Exposure to the organophosphorus and carbamate pesticides is reflected in depressed cholinesterase levels.[34] Latino tobacco workers in North Carolina have also been found to have high biological levels of the neurotoxicants lead and arsenic.[35] The nicotine to which they are exposed may interact with these other toxicants.

The results of this research must be interpreted in light of its limitations. Participants are drawn from a larger project which recruited a representative rather than a random sample. Participants were drawn from a single state. Therefore, generalizations of the results should be made with caution. Urinary samples were analyzed for only two points in successive years. Individual cotinine levels could not be adjusted for creatinine. Data on smoking behavior are limited.

Even in light of these limitations, this analysis continues to document the high nicotine exposure experienced by tobacco workers in the United States. Comparison with Latino immigrants who are not tobacco workers highlights the large doses of nicotine these workers receive daily across years. Although procedures to reduce nicotine exposure among tobacco workers have been documented for over a decade,[2,25] no changes in work practices or in policies to protect workers have been implemented. Efforts to delineate the health effects of long-term exposure to high transdermal nicotine doses also have not been implemented. Occupational nicotine exposure is an even greater concern when we realize that children as young as 10 years can legally work harvesting tobacco and research documents that children younger than ten are doing this work.[36–39] Research on the long term effects of occupational transdermal nicotine exposure must become a priority. More importantly, current knowledge of occupational transdermal nicotine exposure must be used to improve occupational safety practice and policy for adult and child tobacco workers.

Funding

This research was supported by grant R01-ES008739 from the National Institute of Environmental Health Sciences.

Declaration of Interests

None declared.

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