

# Characteristics and Magnitude of Acute Pesticide-Related Illnesses and Injuries Associated With Pyrethrin and Pyrethroid Exposures—11 States, 2000–2008

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**Background** Excluding disinfectants, pyrethrins and pyrethroids are the pesticides used most commonly in and around homes. Respiratory effects and paresthesia are among the concerns about pyrethrin/pyrethroid exposures.

**Methods** Acute pesticide-related illness/injury cases were identified from the Sentinel Event Notification System for Occupational Risks-Pesticides Program and the California Department of Pesticide Regulation from 2000–2008. Characteristics and incidence rates were determined for acute pyrethrin/pyrethroid-related illness/injury cases. Logistic regression analyses were performed to determine odds of respiratory and dermal symptoms in persons with illness/injury following pyrethrin/pyrethroid exposure compared to persons with illness/injury following exposure to other pesticides.

**Results** A total of 4,974 cases of acute pyrethrin/pyrethroid-related illness were identified. Incidence rates increased over time, reaching 8 cases/million population in 2008. The majority of cases were low severity (85%) and 34% were work-related. Respiratory effects were the most common symptoms reported (48%). Risk of acute respiratory effects were significantly elevated among persons exposed only to pyrethrins (adjusted odds ratio [aOR] 1.79; 95% confidence interval [95% CI]: 1.49–2.16), only to pyrethroids (aOR 1.99 95% CI: 1.77–2.24), to a mixture of pyrethroids (aOR 2.36; 95% CI: 1.99–2.81) or to a

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Abbreviations: CPS, Current Population Survey; FTE, full-time equivalent; IRR, incidence rate; IR, incidence rate ratio; CI, confidence interval; PPE, Personal Protective Equipment; NIOSH, National Institute for Occupational Safety and Health; SENSOR, Sentinel Event Notification System for Occupational Risks; CDPH, California Department for Public Health; PISP, Pesticide Illness Surveillance Program; US EPA, US Environmental Protection Agency; FQPA, Food Quality and Protection Act; IPM, Integrated Pest Management; TESS, Toxic Exposure Surveillance System.

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*mixture containing both pyrethrins and pyrethroids (aOR 2.99; 95% CI: 2.33–3.84) compared to those with illness arising from exposure to other pesticides. The most common factors contributing to pyrethrin/pyrethroid-related illness included exposure from spills/splashes, improper storage, and failure to evacuate during pesticide application.*

**Conclusions** *The magnitude of acute pyrethrin/pyrethroid-related illness/injury is relatively low but is increasing. As such, additional measures to prevent them are needed.* Am. J. Ind. Med. 57:15–30, 2014. © 2013 Wiley Periodicals, Inc.

**KEY WORDS:** *pyrethrin; pyrethroid; surveillance; pesticide; illness*

## INTRODUCTION

Pyrethroids are one of the most commonly used pesticides in the home and garden market sector, and are insecticides of choice in public health and residential settings due to their high toxicity to insects and low toxicity to humans [Walters et al., 2009]. Use of pyrethroids in the home and garden sector increased dramatically in the last decade (from less than 1 million pounds used in 2001 to 2–4 million pounds used in 2007) [US Environmental Protection Agency (US EPA), 2011]. This increased use is thought to be a response to the cancellation for residential use of several organophosphate pesticides (cancelled because residential organophosphate use posed unreasonable risks to children) [US EPA, 2012a]. The numbers of acute illnesses and injuries arising from exposure to pyrethrins and pyrethroids are also increasing, likely concomitant with their increased use [Power and Sudakin, 2007; Walters et al., 2009].

Pyrethrins were first developed in 1949 from extract of the flower *Chrysanthemum cinerariaefolium*, which is in the Compositae family [Bradberry et al., 2005]. Since pyrethrins degrade rapidly in sunlight and moisture, more stable synthetic analogues (i.e., pyrethroids) were developed [He, 1994]. There are two categories of pyrethroids: Type II pyrethroids (such as cyfluthrin, cypermethrin, deltamethrin, and esfenvalerate) have the addition of an  $\alpha$ -cyano-3-phenoxybenzyl moiety, whereas Type I pyrethroids (such as bifenthrin, permethrin, phenothrin, and resmethrin) lack such a moiety [He, 1994; Lessenger, 1992; Bradberry et al., 2005; Spencer and O'Malley, 2006]. Both types of pyrethroids delay the closure of sodium ion channels [Bradberry et al., 2005; Ahdab et al., 2011], but when compared to Type I pyrethroids, Type II pyrethroids hold sodium ion channels open longer, have increased insecticidal activity, and are more toxic to mammals [Bradberry et al., 2005]. Pyrethrins and pyrethroids are quickly metabolized in the human body. In addition to concerns about pulmonary effects arising from exposure to pyrethrins and pyrethroids [Osimitz et al., 2009; US EPA, 2009], distressing paresthesias have also been reported [Dorman and Beasley, 1991]. Paresthesias have been reported to be more commonly caused by dermal exposure to Type II pyrethroids, but can occur from exposure to Type I pyrethroids [US EPA, 1999; Ray and

Forshaw, 2000]. To enhance the insecticidal properties of pyrethrin/pyrethroid products, pesticide formulators added piperonyl butoxide or MGK-264, which are synergists that inhibit pyrethroid metabolism in insects so as to increase the “knock down” effect (i.e., paralysis before death) [Wickman et al., 1974]. While human data are lacking, animal data suggest that the addition of synergists can also cause greater toxicity in humans due to pesticide concentrations persisting longer in the body [Bradberry et al., 2005].

The purpose of this study was to identify the frequency, magnitude, and characteristics of acute pesticide-related illnesses associated with pyrethrin and pyrethroid exposures between 2000, when EPA announced the phase-out of organophosphates for residential use [Power and Sudakin, 2007], and continuing through 2008, which was the most recent year of data availability. Given the concern about pulmonary toxicity and paresthesias, this study also examined the risk of these effects among persons who became ill after exposure to pyrethrins and pyrethroids.

## MATERIALS AND METHODS

Data systems that were used for this analysis include the Sentinel Event Notification System for Occupational Risks (SENSOR)-Pesticides program and California's Pesticide Illness Surveillance Program (PISP). The SENSOR-Pesticides program is comprised of eleven states (California, Florida, Iowa, Louisiana, Michigan, New Mexico, New York, North Carolina, Oregon, Texas, and Washington) whose state health departments conduct routine surveillance for pesticide related illness/injury. These state health departments identified acute pesticide-related illness/injury associated with pyrethrins and pyrethroids for the following years: California, 2000–2008; Florida, 2000–2008; Iowa, 2006–2008; Louisiana, 2000–2008; Michigan, 2000–2008; North Carolina, 2007–2008; New Mexico, 2005–2008; New York, 2000–2008; Oregon, 2000–2008; Texas, 2000–2008; and Washington, 2000–2008. In California, there are two programs that identify cases of acute pesticide-related illness/injury: one program is located at the California Department for Public Health (CDPH) and participates in the SENSOR-Pesticides program, and the other program is PISP,

which is administered by the California Department of Pesticide Regulation (CDPR). PISP operates similarly to, but does not participate in the SENSOR-Pesticides program [Calvert et al., 2010]. CDPH collects only work-related cases of acute pesticide-related illness/injury, while PISP collects data for both work-related and non-work-related acute pesticide-related illness/injury. An illness is considered work-related if the pesticide exposure occurred at the case's place of work. To ensure California cases were counted only once, CDPH cross-referenced its cases with those from PISP using social security numbers, names, dates of illness or injury, and dates of birth. A total of 263 California cases were identified by both programs and counted only once. For matches that were identified, information provided by both CDPH and PISP was used to populate the variables used in the analyses. All other SENSOR-Pesticides states collect data on both work-related and non-work-related acute pesticide-related illness/injury. Because each state removes any personal identifiers from the data prior to submission to NIOSH, this study was exempt from consideration by the federal Human Subjects Review Board.

State case ascertainment sources include: poison control centers, other government agencies (such as a state's Department of Agriculture), workers' compensation documents, and physician reports. In some states, there are other sources that infrequently identify cases, such as medical record reviews, news reports, and reports from worker representatives [Centers for Disease Control and Prevention (CDC), 2005]. Staff from state surveillance programs attempt to interview cases to obtain more details about the event and use standardized variables to systematically code all information about a case [CDC, 2005]. Information collected by states include demographic variables, occupation and industry, exposure descriptions, information on the pesticide (e.g., product name, active ingredients, functional and chemical class, and toxicity category), health effects, case classification category, and factors contributing to exposure/illness [CDC, 2005]. The toxicity of a pesticide is determined by EPA under guidance available from the Code of Federal Regulations 40 CFR 156.208(c)(2)(iii) [US EPA, 1975]. Pesticides in category I are the most acutely toxic and pesticides in category IV are the least toxic [US EPA, 1975]. A pyrethrin/pyrethroid handler was defined as any person (e.g., homeowner or worker) who mixed, loaded, transferred, disposed of and/or applied pyrethrins/pyrethroids, or who repaired or maintained pesticide application equipment at the time of pyrethrin/pyrethroid exposure.

## Case Definition

Persons were considered cases in this analysis if they became ill or injured after exposure to pyrethrins, pyrethroids, or pesticide mixtures that included pyrethrins and/or pyrethroids. The SENSOR-Pesticides case definition, de-

scribed in detail elsewhere [CDC, 2005], requires information about pesticide exposure and health effects, and this information is compared to the known toxicology of the pesticide exposure. Cases in the SENSOR-Pesticides program are categorized as definite, probable, possible, and suspicious. Definite cases are based exclusively on objective data about exposure and health effects, probable cases are based on a mix of objective and subjective data, and possible cases are based on subjective exposure and health effects data. Suspicious cases arise when there is insufficient toxicological information to determine a causal relationship between pesticide exposure and illness, often because the given pesticide is relatively new and little toxicological data involving humans exists. The PISP case definition differs only slightly from that of the SENSOR-Pesticides program. In PISP, cases are categorized as definite, probable, or possible. There is not a "suspicious" category in PISP; cases classified as "suspicious" and "possible" by SENSOR-Pesticides would most likely be classified as "possible" by PISP. In addition, SENSOR-Pesticides programs require cases to have at least two signs/symptoms caused by the pesticide exposure, whereas PISP requires only one sign/symptom. Definite, probable, possible, and suspicious cases associated with pyrethrin, and/or pyrethroid exposures were included as cases in this analysis.

Illness/injury severity was categorized into four groups using standardized criteria for state-based surveillance programs [CDC, 2005]. In low severity cases, the illness/injury usually resolves without treatment and there are fewer than 3 days lost from work. In moderate severity cases, the illness/injury is non-life threatening, but requires medical treatment. No residual impairment is expected, and time lost from work is 5 days or fewer. In high severity cases, illness/injury is life threatening, requires hospitalization, often has greater than 5 days lost from work, and may result in permanent impairment. Fatal cases of pesticide poisoning were placed in a separate category.

Factors contributing to the pesticide exposure that produced illness/injury were obtained from several sources. Some contributing factors were systematically gathered by SENSOR-Pesticides state partners (e.g., drift and Personal Protective Equipment—PPE use). All cases captured by PISP are investigated by the relevant county agriculture commissioner. The commissioner's investigation reports were reviewed by PISP staff to identify some contributing factors (i.e., drift, early re-entry, failure to use required PPE, and equipment failure). Contributing factors (e.g., label requirements, transport for care, improper storage, etc.) were also identified using narrative descriptions, documentation of violations identified during investigation, and reviewing usage requirements on pesticide labels. Contributing factors were coded independently by two National Institute for Occupational Safety and Health (NIOSH) researchers (NLH and EJK). Coding disagreements occurred for approximately

10% of cases, many of which involved one NIOSH researcher coding the contributing factor as “unknown.” Coding disagreements were resolved by discussion with a third NIOSH researcher (GMC).

## Data Analysis

Basic descriptive statistics were calculated using SAS 9.2<sup>®</sup>. Chi-square tests were performed to test whether factors contributing to exposure were more likely associated with work-related or non-work-related illnesses/injuries.

Incidence rates (IRs), incident rate ratios (IRRs), and 95% confidence intervals (CIs) were calculated by year of exposure, geographic region, sex, and age for work-related and non-work-related illness/injury. The IR numerators represent the number of cases involving pyrethroids/pyrethrins captured by SENSOR-Pesticides and PISP from 2000 through 2008. To calculate IRs of work-related acute illness/injury, denominator data (i.e., estimates of employment counts and hours worked) were obtained from the Current Population Survey (CPS) [US Bureau of Labor Statistics, 2010]. The hours worked data were used to derive full-time equivalents (FTEs) estimates, with one FTE equal to 2,000 hr worked. Denominator data correspond to the states and time periods of numerator availability. Because the work-related rates calculated with the two denominator estimates (employment counts and FTE estimates) produced similar results, only rates calculated with FTEs as the denominator were provided, as they have been demonstrated to be conceptually preferable to the use of raw employment counts [Ruser, 1998].

To calculate rates of non-work-related acute illness/injury, the denominator was the mid-interval population estimate per year for participating states, obtained from the U.S. Census [2011]. Combined rates (including both work-related and non-work-related cases) were calculated using the total number of relevant cases captured by SENSOR-Pesticides and PISP as the numerator and the U.S. Census mid-interval population estimates as the denominator. To compare IRs, IRRs were calculated by dividing one IR by another IR. A ratio greater than one suggests an increased risk in the group represented in the numerator and a ratio below one suggests an increased risk in the group represented in the denominator. CIs were also calculated for each IRR [Rothman, 1986]. All IRRs reported in the results section are statistically significant at the  $P < 0.05$  level using the z-test statistic, which assumed normal distribution of the logarithm of the rate ratio; however, not all IR comparisons were evaluated nor are all statistically significant findings reported in the Results section. Trend analyses were conducted on IRs using the Kendall trend test in SAS 9.2<sup>®</sup>.

Multivariable logistic regressions were performed to determine whether pyrethrin and/or pyrethroid exposures were more likely to be associated with a priori outcomes of interest (i.e., cough, dyspnea, wheeze, lower respiratory

irritation, and paresthesias). Several variables were considered for inclusion in the models including work relatedness, toxicity category, agricultural application site, private residence application site, drift exposure, exposure from indoor air, and exposures from being directly sprayed during application. A single parsimonious model with no evidence of lack of fit, as measured by the Hosmer and Lemeshow test [Lemeshow and Hosmer, 1982], was produced to examine each health effect and active ingredient. The only variables that produced a greater than 10% change in the regression coefficient for active ingredient and had no evidence of lack of fit in the model were: being directly sprayed versus other type of exposure, and agricultural application site versus other application site location. The single multivariable logistic regression model is provided below:

$$\text{Logit}(P) = \alpha + \beta_1 \text{ Active Ingredient} + \beta_2 \text{ Directly Sprayed} + \beta_3 \text{ Agricultural Application Site}$$

where  $\text{logit}(P)$  is the probability of developing the health outcome of interest (i.e., cough, wheeze, dyspnea, lower respiratory tract pain and irritation, and paresthesia),  $\alpha$  is the constant of the equation, and  $\beta$  is the coefficient of the predictor variables. The predictor variables for  $\beta_1$  include exposure to: pyrethrins only, pyrethroids only, selected pyrethroid active ingredients only, 2+ pyrethroids only, pyrethrins plus one or more pyrethroids only. The comparison group for  $\beta_1$  was all acute pesticide related illness/injury, excluding those exposed to pyrethrins, pyrethroids, and disinfectants.

Illnesses/injuries arising from disinfectant exposure were excluded from the logistic regression analysis because five SENSOR-Pesticides states do not systematically capture them. Cases exposed to pyrethrins only, Type I and Type II pyrethroids only, two or more pyrethroids only, a mixture of pyrethrins and/or pyrethroids only, and specific active ingredients (i.e., when there were greater than 50 cases) were analyzed. Although fewer than 50 cases were exposed only to tetramethrin, this pyrethroid was also analyzed using logistic regression since it is considered an asthmagen [AOEC, 2009]. Exposures to the synergists piperonyl butoxide or MGK-264 did not exclude individuals from being considered as exposed to pyrethrins only, Type I and Type II pyrethroids only, two or more pyrethroids only, a mixture of pyrethrins and/or pyrethroids only. Adjusted odds ratios and CIs were calculated using SAS 9.2<sup>®</sup>.

## RESULTS

### Counts and Incidence Rates of Acute Illness/Injury Associated With Exposure to Pyrethrins and/or Pyrethroids

From 2000 through 2008, 4,974 acute illnesses/injuries due to exposure to pyrethrins and/or pyrethroids were

identified (Tables I, IIa, and IIb). Pyrethrins and/or pyrethroids accounted for 32% of all acute non-disinfectant pesticide-related illness/injury cases (24% of all work-related cases and 39% of all non-work-related cases). Of the 4,974 cases, 3,207 (65%) cases were only exposed to pyrethrins and/or pyrethroids and no other pesticides (Table IIb). Pyrethrins and pyrethroids accounted for an increasing proportion of acute non-disinfectant pesticide-related illness/injury, reaching 42% in 2008 (Table I). Thirty-four percent of acute pyrethrin/pyrethroid-related illness/injury cases were work-related (Table IIa). From 2000 to 2008, the overall IR for work-related illness/injury due to exposure to pyrethrins and pyrethroids was 3 cases/million FTEs, and the overall rate for non-work-related illness/injury was 4 cases/million persons (Table IIa). In the early part of the decade, work-related incidence rates were higher than non-work-related rates (Tables IIa and IIb). Incidence rates for non-work-related cases (and the rate that combined both work-related and non-work-related cases) increased over time ( $P = < 0.01$ ), but the incidence rates for work-related cases appeared stable (Tables IIa and IIb). Among non-work-related cases, children under 5 had the highest incidence of acute pyrethrin/pyrethroid-related illness/injury. The western region (comprised of California, New Mexico, Oregon, and Washington) had the highest IR for work-related cases and the southern region (comprised of Florida, North Carolina, Louisiana, and Texas) had the highest IR for non-work-related cases (Tables IIa and IIb).

## Location of Pyrethrin/Pyrethroid Exposure Events and Activity at Time of Exposure

Eighty-four percent of non-work-related cases occurred at private residences (Table III). Work-related cases most commonly occurred in agricultural settings (29%) and in non-manufacturing facilities (29%). Among cases with information on activity at time of exposure, 59% were not pyrethrin/pyrethroid handlers. Handlers accounted for a total of 28% of work-related illnesses/injuries and 41% of non-work-related illnesses/injuries. The most common types of exposure for both work-related and non-work-related illness/injury were exposure to contaminated indoor air (32% work-related and 28% non-work-related) and direct spray exposure to the pesticide during application (21% work-related and 37% non-work-related) (Table III). Most pyrethrin/pyrethroid exposure events involved a single case (75% of total cases); however, 41% of work-related cases involved events with two or more cases. At least 867 (17%) of the acute pyrethrin/pyrethroid-related illnesses/injuries occurred after exposure to total release foggers (i.e., bug bombs) and 121 (14%) of these were work-related.

## Illness/Injury Severity With a Focus on Fatal Cases

Most cases of illness/injury associated with exposure to pyrethrins, and/or pyrethroids were low severity (85%). Work-related cases were significantly more likely to be

**TABLE I.** Illnesses/Injuries Caused by Pyrethrin/Pyrethroid Exposures, and Non-Disinfectant Pesticides in the US, Counts and Proportions 2000—2008\*

Year	All pesticide-related illness/injury cases			Work-related pesticide-related illness/injury cases			Non-work-related pesticide-related illness/injury cases		
	Total	Related to pyrethrin/pyrethroid pesticides	Related to other pesticides	Total	Related to pyrethrin/pyrethroid pesticides	Related to other pesticides	Total	Related to pyrethrin/pyrethroid pesticides	Related to other pesticides
2000	1,398	337 (24)	1,061 (76)	799	190 (24)	609 (76)	599	147 (25)	452 (75)
2001	1,099	313 (28)	786 (72)	650	194 (30)	456 (70)	449	119 (27)	330 (74)
2002	1,797	399 (22)	1,398 (78)	944	181 (19)	763 (81)	853	218 (26)	635 (74)
2003	1,609	441 (27)	1,168 (73)	719	152 (21)	567 (79)	890	289 (32)	601 (68)
2004	1,530	494 (32)	1,036 (68)	824	189 (23)	635 (77)	706	305 (43)	401 (57)
2005	1,877	579 (31)	1,298 (69)	763	200 (26)	563 (74)	1,114	379 (34)	735 (66)
2006	1,620	600 (37)	1,020 (63)	656	153 (23)	503 (77)	964	447 (46)	517 (54)
2007	2,281	884 (39)	1,397 (61)	830	204 (25)	626 (75)	1,451	680 (47)	771 (53)
2008	2,231	927 (42)	1,304 (58)	739	229 (31)	510 (69)	1,492	698 (47)	794 (53)
Total	15,442	4,974 (32)	10,468 (68)	6,924	1,692 (24)	5,232 (76)	8,518	3,282 (39)	5,236 (61)

\*There were 4,974 cases exposed to pyrethrins, pyrethroids, or a combination of any pesticides including pyrethrins or pyrethroid. Persons exposed to disinfectants, and mixtures that included disinfectants were excluded, which leaves 15,442 non-disinfectant related cases.

**TABLE IIa.** Number and Rate of Acute Illness/Injury Cases Due To Pyrethrin and Pyrethroid Exposures by Year, Region, Sex, Age, and Work Relatedness in the US, 2000—2008\*

Characteristics	Total exposed to pyrethrins and pyrethroids								
	Work related			Non-work related			Overall rate <sup>a</sup>	IRR <sup>b</sup>	95% CI
	Count	FTE estimate <sup>c</sup>	Rate per 1,000,000	Count	Population estimate <sup>d</sup>	Rate per 1,000,000			
Total	1,692	497,390,363	3.4	3,282	880,052,505	3.7	5.67	0.9	(0.86–0.97)
Year of exposure									
2000	190	52,152,854	3.7	147	89,844,115	1.6	3.8	2.3	(1.80–2.76)
2001	194	51,469,216	3.8	119	91,134,627	1.3	3.4	2.9	(2.30–3.63)
2002	181	51,117,258	3.5	218	92,350,768	2.4	4.3	1.5	(1.23–1.83)
2003	152	52,234,877	2.9	289	93,504,429	3.1	4.8	0.9	(0.77–1.15)
2004	189	53,182,558	3.6	305	94,716,595	3.2	5.2	1.1	(0.92–1.32)
2005	200	55,351,246	3.7	379	97,494,753	3.9	6.0	0.9	(0.78–1.10)
2006	153	57,701,157	2.7	447	100,923,220	4.4	6.0	0.6	(0.50–0.72)
2007	204	62,429,631	3.3	680	109,367,575	6.2	8.1	0.5	(0.45–0.61)
2008	229	61,751,566	3.8	698	110,716,423	6.3	8.4	0.6	(0.51–0.68)
Region <sup>e</sup>									
East/central	205	120,506,569	1.7	386	216,941,593	1.8	2.7	1.0	(0.81–1.13)
South	578	189,396,471	3.1	1,948	334,074,163	5.8	7.6	0.5	(0.48–0.57)
West	909	187,487,323	4.9	948	329,036,749	2.9	5.7	1.7	(1.54–1.84)
Sex									
Male	967	288,382,582	3.4	1,436	429,352,454	3.3	5.6	1.0	(0.92–1.09)
Female	711	209,007,781	3.5	1,825	450,700,051	4.0	5.7	0.9	(0.77–0.92)
Unknown	14	—	—	21	—	—	—	—	—
Age									
0–5	—	—	—	350	75,890,584	4.6	4.6	—	—
6–14	1	—	—	285	156,364,839	1.8	1.8	—	—
15–24	298	58,432,325	5.1	386	157,412,725	2.5	4.4	2.1	(1.79–2.42)
25–44	816	246,678,487	3.3	920	319,272,271	2.9	5.5	1.2	(1.04–1.26)
45+	449	192,279,551	2.4	1,133	403,367,509	2.8	3.9	0.8	(0.75–0.93)
Missing	128	—	—	208	—	—	—	—	—

<sup>a</sup>The numerators are the total count (work related and non-work related) of acute illnesses and the denominators are the population estimates. Denominator data correspond to the states and time periods of numerator availability. The rates are expressed per 1,000,000 population.

<sup>b</sup>The numerator for the incident ratios (IRR) are the work-related IRs and the denominators are the non-work-related IRs. The IRR compares the work-related rate with the non-work-related rate. If the IRR is above 1 then the work-related rate is higher than the non-work-related rate, and if the IRR is below 1, then the non-work-related rate is higher.

<sup>c</sup>The full-time equivalent (FTE) estimates were derived from the hours worked data obtained from the Current Population Survey (CPS) [US Bureau of Labor Statistics, 2010]. One FTE equals 2,000 hr worked. Denominator data correspond to the states and time periods of numerator availability.

<sup>d</sup>The denominator was mid-interval population estimates per year for participating states, and was obtained from the U.S. Census. Denominator data correspond to the states and time periods of numerator availability.

<sup>e</sup>States in the eastern/central region included Iowa, Michigan, and New York. States in the southern region included Florida, Louisiana, Texas, and North Carolina. States in the western region included California, New Mexico, Oregon, and Washington.

\*There were 4,974 cases exposed to pyrethrins, pyrethroids, or a combination of any pesticides including pyrethrins or pyrethroid. Persons exposed to a combination of pesticides that included pyrethrins and/or pyrethroids might also include pesticides that are not pyrethrins or pyrethroids. There were 3,207 cases exposed only to pyrethrins, pyrethroids, or a combination of pyrethrins and/or pyrethroids. These cases might also be exposed to the synergists piperonylbutoxide (PBO) or MGK-264.

moderate severity (19%) compared to non-work-related cases (12%) ( $P < 0.01$ ). A total of five fatalities were identified. One fatality occurred in Louisiana in 2005 when an 18 month old drank an unknown amount of a pesticide containing the pyrethroid allethrin. The child developed cough, upper respiratory pain and irritation, nausea, vomiting, tachycardia, and malaise before culminating in death. This case was

classified as definite. The second fatality occurred in 2005 in Oregon when a 76-year-old female experienced sudden cardiac arrhythmia and respiratory symptoms upon entering her home that had been treated 3½ hr earlier with esfenvalerate and pyrethrins by a licensed pesticide applicator. Resuscitation attempted by emergency medical technicians (EMTs) was unsuccessful and the woman died at her

**TABLE IIb.** Number and Rate of Acute Illness/Injury Cases Due To Pyrethrin and Pyrethroid Exposures by Year, Region, Sex, Age, and Work Relatedness in the US, 2000—2008\*

Characteristics	Only exposed to pyrethrins and pyrethroids								
	Work related			Non-work related			Overall rate <sup>a</sup>	IRR <sup>b</sup>	95% CI
	Count	FTE estimate <sup>c</sup>	Rate per 1,000,000	Count	Population estimate <sup>d</sup>	Rate per 1,000,000			
Total	918	497,390,363	1.9	2,289	880,052,505	2.6	3.7	0.7	(0.67–0.77)
Year of exposure									
2000	125	2,152,854	2.5	99	89,844,115	1.1	2.5	2.2	(1.67–2.83)
2001	76	51,469,216	1.5	72	91,134,627	0.8	1.6	1.9	(1.35–2.58)
2002	105	51,117,258	2.2	147	92,350,768	1.6	2.8	1.4	(1.00–1.66)
2003	86	52,234,877	1.6	194	93,504,429	2.1	3.0	0.8	(0.62–1.02)
2004	92	53,182,558	1.7	206	94,716,595	2.2	3.1	0.8	(0.62–1.02)
2005	91	55,351,246	1.7	240	97,494,753	2.5	3.4	0.7	(0.52–0.85)
2006	103	57,701,157	1.8	332	100,923,220	3.3	4.3	0.6	(0.44–0.68)
2007	137	62,429,631	2.2	515	109,367,575	4.7	6.0	0.5	(0.39–0.56)
2008	103	61,751,566	1.7	484	110,716,423	4.4	5.3	0.4	(0.31–0.47)
Region <sup>e</sup>									
East/central	138	120,506,569	1.2	304	216,941,593	1.4	2.3	0.8	(0.67–1.00)
South	332	189,396,471	1.8	1,351	334,074,163	4.0	2.8	0.4	(0.38–0.49)
West	448	187,487,323	2.4	634	329,036,749	1.9	3.3	1.3	(1.10–1.40)
Sex									
Male	536	288,382,582	1.9	995	429,352,454	2.3	3.6	0.8	(0.72–0.89)
Female	376	209,007,781	1.8	1,275	450,700,051	2.8	3.7	0.7	(0.57–0.71)
Unknown	6			19					
Age									
0–5				254	75,890,584	3.4	3.4		
6–14				199	156,364,839	1.3	1.3		
15–24	145	58,432,325	2.5	276	157,412,725	1.8	2.7	1.4	(1.16–1.73)
25–44	455	246,678,487	1.9	663	319,272,271	2.1	3.5	0.9	(0.79–1.00)
45+	270	192,279,551	1.4	787	403,367,509	1.9	2.6	0.7	(0.63–0.83)
Missing	48			110					

<sup>a</sup>The numerators are the total count (work related and non-work related) of acute illnesses and the denominators are the population estimates. Denominator data correspond to the states and time periods of numerator availability. The rates are expressed per 1,000,000 population.

<sup>b</sup>The numerator for the incident rate ratios (IRR) are the work-related IRs and the denominators are the non-work-related IRs. The IRR compares the work-related rate with the non-work-related rate. If the IRR is above 1 then the work-related rate is higher than the non-work-related rate, and if the IRR is below 1, then the non-work-related rate is higher.

<sup>c</sup>The full-time equivalent (FTE) estimates were derived from the hours worked data obtained from the Current Population Survey (CPS) [US Bureau of Labor Statistics, 2010]. One FTE equals 2,000 hr worked. Denominator data correspond to the states and time periods of numerator availability.

<sup>d</sup>The denominator was mid-interval population estimates per year for participating states, and was obtained from the U.S. Census. Denominator data correspond to the states and time periods of numerator availability.

<sup>e</sup>States in the eastern/central region included Iowa, Michigan, and New York. States in the southern region included Florida, Louisiana, Texas, and North Carolina. States in the western region included California, New Mexico, Oregon, and Washington.

\*There were 4,974 cases exposed to pyrethrins, pyrethroids, or a combination of any pesticides including pyrethrins or pyrethroid. Persons exposed to a combination of pesticides that included pyrethrins and/or pyrethroids might also include pesticides that are not pyrethrins or pyrethroids. There were 3,207 cases exposed only to pyrethrins, pyrethroids, or a combination of pyrethrins and/or pyrethroids. These cases might also be exposed to the synergists piperonylbutoxide (PBO) or MGK-264.

home. This case was classified as definite. The third fatality occurred in Washington State in 2003 and involved a 10-month-old child who slept on a carpeted floor after 14 foggers containing tralomethrin were set off in a quadriplex. This child developed edema, eye pain, upper respiratory pain/irritation, and pulmonary edema culminating in death. This case was classified as suspicious. The fourth fatality occurred

in 2006 also in Washington State and involved a 64-year-old female with a history of asthma who sprayed a product containing permethrin and tetramethrin over her head, and material from the can dripped down her arm. She did not change her clothes after this occurred. The next morning she awoke with dyspnea and wheezing and called 911. She was unresponsive when the EMTs arrived and was hospitalized

**TABLE III.** Number and Percentage of Acute Illness/Injury Cases Due To Exposure to Pyrethrins, Pyrethroids, or Mixtures of Pesticides That Included Pyrethrins and/or Pyrethroids\* by Selected Characteristics and Work Relatedness in the US—2000–2008 (n = 4,974)

Characteristic	Total, no. (%)	Work related, no. (%)	Non-work related, no. (%)
Total	4,974	1,692 (34)	3,282 (66)
Illness severity <sup>a</sup>			
Fatal	5 (<1)	1 (<1)	4 (<1)
High	49 (1)	14 (1)	35 (1)
Moderate	715 (14)	325 (19)	390 (12)
Low	4,205 (85)	1,352 (80)	2,853 (87)
Lost time from work or regular activities <sup>b</sup>			
Yes	681 (14)	408 (24)	273 (8)
Event location			
Agriculture	562 (11)	489 (29)	73 (2)
Private residence	2,935 (59)	163 (10)	2,772 (84)
Institutions	97 (2)	83 (5)	14 (<1)
Schools	80 (2)	37 (2)	43 (1)
Non-manufacturing facility	532 (11)	490 (29)	42 (1)
Other	302 (6)	195 (12)	107 (3)
Unknown/missing	466 (9)	235 (14)	231 (7)
Activity at time of exposure			
Applying/mixing/loading/transporting/dispersing of pesticides	1,819 (37)	482 (28)	1,337 (41)
Routine indoor/outdoor living (no application)	1,449 (29)	—	1,449 (44)
Routine work (no application)	1,079 (22)	1,079 (64)	—
Other	87 (2)	33 (2)	54 (2)
Missing/unknown	540 (11)	98 (6)	442 (13)
Type of exposure <sup>c</sup>			
Drift from application site	412 (8)	221 (13)	191 (6)
Indoor air	1,473 (30)	548 (32)	925 (28)
Contact with treated surface	603 (12)	265 (16)	338 (10)
Directly sprayed during application	1,583 (32)	361 (21)	1,222 (37)
Leak/spill	561 (11)	228 (13)	333 (10)
Other	271 (5)	46 (3)	225 (7)
Unknown	411 (8)	122 (7)	289 (9)
Toxicity <sup>d</sup>			
I-Danger	178 (4)	132 (8)	46 (1)
II-Warning	449 (9)	224 (13)	225 (7)
III-Caution	4,122 (83)	1,242 (73)	2,880 (88)
Missing/unknown	225 (5)	94 (6)	131 (4)
Hospitalization <sup>e</sup>			
Yes	238 (5)	60 (4)	178 (5)
Event size			
One person	3,709 (75)	1,001 (59)	2,708 (83)
Two or more persons	1,265 (25)	691 (41)	574 (17)
Case status			
Definite	313 (6)	98 (6)	215 (7)
Probable	1,013 (20)	408 (24)	605 (18)
Possible	3,646 (73)	1,186 (70)	2,460 (75)
Suspicious	2 (<1)	—	2 (<1)

<sup>a</sup>Illness severity is classified using standardized criteria based on signs and symptoms. Low severity illness and injury often resolve without medical treatment and have minimal time lost from work. Moderate severity health illness and injury are non-life threatening, require medical treatment, and time lost from work is less than 6 days. High severity illness is life threatening, usually require hospitalization, and has time lost from work that is greater than 5 days. High severity health effects may also result in permanent disability.

<sup>b</sup>Cases were included if they lost one or more days from work or regular activities due to exposure to pyrethrins, pyrethroids, or mixtures of pesticides that included pyrethrins and/or pyrethroids. A total of 545 cases lost time from work and 136 cases lost time from regular activities.

<sup>c</sup>Because some cases had more than one type of exposure, the sum of the percentages exceeds 100%.

<sup>d</sup>Toxicity categories are classified by the US Environmental Protection Agency based on established criteria, with I being the most toxic and IV the least.

<sup>e</sup>Cases were considered hospitalized if their hospitalization was for one or more days due to exposure to pyrethrins, pyrethroids, or mixtures of pesticides that included pyrethrins and/or pyrethroids.

\*Of the 4,974 cases of acute illnesses, 3,207 cases were only exposed to pyrethrins and/or pyrethroids, and of these 2,248 cases were only exposed to 1 pyrethrin or pyrethroid. These cases might also be exposed to the synergists piperonylbutoxide (PBO) or MGK-264. Cases exposed to a combination of pesticides that included pyrethrins and/or pyrethroids also include pesticides that are not pyrethrins or pyrethroids.

9 days with an asthma attack, respiratory depression coma, and cardiac arrest resulting in death. This case was classified as probable. The fifth fatality occurred in 2001 in Florida and involved a 35-year-old white male with a history of asthma. When he arrived at his office one morning and turned on the air-conditioning, dust blew into his face from a nearby exhaust vent. The dust was thought to contain pyrethrins and diphacinone, a rodenticide, used by a pest control company the night before to treat the office attic. Within 15 minutes he was in severe distress with coughing, erythema, and lacrimation. The patient was temporarily hospitalized with a severe asthma attack and pneumonia, and treated with heavy steroid doses. After discharge he continued to have respiratory distress. Six weeks later, he died from a bleeding duodenal ulcer deemed to have been precipitated by a combination of the steroids used for asthma control and aspirin used for headache. This case was classified as probable.

## Health Effects

Only 5% ( $n = 238$ ) of cases were hospitalized for one or more days (Table III). A total of 14% of cases lost one or more days from work or regular activities.

Among cases exposed to pyrethrins and/or pyrethroids only ( $n = 3,207$ ), respiratory (48%), neurological (40%), and gastrointestinal symptoms (35%) were the most frequently reported health effects followed by skin (30%) and eye effects (28%) (Table IV). Furthermore, among cases exposed to a single pyrethrin or pyrethroid, Type II pyrethroids accounted for the largest number of illnesses/injuries (950 or 42% of cases exposed to a single pyrethrin or pyrethroid only) (Table V). The most common Type II pyrethroids associated with acute illness were cypermethrin ( $n = 369$ , 16% of cases exposed to a single pyrethrin or pyrethroid only), cyfluthrin, ( $n = 216$ , 10%), and deltamethrin ( $n = 136$ , 6%) (Table V). The most common Type I pyrethroids associated with acute illness/injury were permethrin ( $n = 350$ , 16% of cases exposed to a single pyrethrin or pyrethroid only) and bifenthrin ( $n = 175$ , 8%).

When compared to persons exposed to non-pyrethrin/pyrethroid/disinfectant pesticides, cases were significantly more likely to present with one or more respiratory symptoms (i.e., cough, dyspnea, wheeze, and lower respiratory pain/irritation) after exposure to one of the following insecticide classes and active ingredients: pyrethrins only; Type I pyrethroids only; Type II pyrethroids only; permethrin only; phenothrin only; resmethrin only; tetramethrin only; cypermethrin only; esfenvalerate only; a mixture of two or more pyrethroids only; and, a mixture of pyrethrins and/or pyrethroids only (Table VI). When only wheeze was considered, the following insecticide classes and active ingredients were found to be significantly associated: Type I pyrethroids only; Type II pyrethroids only; a mixture of two

or more pyrethroids only; a mixture of pyrethrins and/or pyrethroids only; permethrin only; phenothrin only; tetramethrin only; and cypermethrin only. Cases were more likely to present with paresthesias after exposure to one of the following insecticide classes or active ingredients: Type I pyrethroids; a mixture of two or more pyrethroids only; bifenthrin only; permethrin only; resmethrin only; and esfenvalerate only (Table VII).

## Factors Contributing to Exposure

Information on factors that contributed to pyrethrin/pyrethroid exposure was available for 3,301 (66%) cases exposed to pyrethrins/pyrethroids, whether singly or combined with other pesticides, and for 2,160 (67%) cases exposed only to pyrethrins/pyrethroids (Table VIII). The most commonly reported contributing factors included a spill or splash of pyrethrin and/or pyrethroid (13%), exposure to off-target drift from the application site (12%), failure to evacuate the area during pesticide application (11%), and inadequate ventilation (10%). Among those exposed only to pyrethrins and/or pyrethroids, work-related cases were more likely to be exposed because of inadequate ventilation (23%) ( $P < 0.01$ ), inadequate PPE or PPE not worn as per label requirements (5%) ( $P < 0.01$ ), and off-target drift from the application site (5%) ( $P = 0.01$ ), compared to non-work-related cases. Of the 704 (21%) illnesses/injuries related to total release foggers that had information on contributing factors, 20% occurred because of early re-entry into the treated area ( $n = 140$ ), 17% occurred among non-handlers (i.e., persons not handling the pesticide) who failed to evacuate the area during the pyrethrin/pyrethroid application ( $n = 123$ ), and 16% occurred among handlers (i.e., homeowners or workers) who failed to leave the treated area post-application ( $n = 112$ ).

## DISCUSSION

To our knowledge, this is the most comprehensive report that is available on acute illness/injury associated with pyrethrins and pyrethroids. We identified 4,974 cases of acute pyrethrin/pyrethroid-related illness/injury, accounting for 32% of non-disinfectant pesticide-related illness/injury. Although the magnitude of acute pyrethrin/pyrethroid-related illness/injury is relatively low and the vast majority were low severity, our findings suggest that these illnesses/injuries are increasing, especially in the non-occupational setting. Other reports also observed an increase in illnesses/injuries [Power and Sudakin, 2007; Walters et al., 2009], which may be related to the increasing use of pyrethrins and pyrethroids [US EPA, 2011].

In contrast to our study, a study using American Association of Poison Control Centers (AAPCC) (i.e., poison

**TABLE IV.** Acute Illness/Injury Due To Exposure Only to Pyrethrins, Pyrethroids, or a Combination of Pyrethrins and/or Pyrethroids Signs and Symptoms, 2000–2008 (n = 3,207)\*

<b>Body part/ system affected</b>	<b>Total, no. (%)<sup>a</sup></b>	<b>Pyrethrins only, no. (%)<sup>a</sup></b>	<b>Pyrethroids only, no. (%)<sup>a</sup></b>	<b>2 or more pyrethroids only, no. (%)<sup>a</sup></b>	<b>Combination of pyrethrins and pyrethroids only, no. (%)<sup>a</sup></b>
Total	3,207	547 (17)	1,701 (53)	686 (21)	273 (9)
Respiratory	1,542 (48)	239 (44)	793 (47)	345 (50)	165 (60)
Cough	793 (25)	124 (23)	395 (23)	187 (27)	186 (68)
Upper respiratory pain/irritation	720 (22)	94 (17)	394 (23)	166 (24)	66 (24)
Dyspnea	671 (21)	101 (18)	356 (21)	143 (21)	71 (26)
Pain on deep breathing	95 (3)	10 (2)	54 (3)	19 (3)	12 (4)
Wheeze	145 (5)	23 (4)	79 (5)	28 (4)	15 (5)
Lower respiratory tract irritation	116 (4)	15 (3)	62 (4)	26 (4)	13 (5)
Other	47 (1)	7 (1)	20 (1)	12 (2)	8 (3)
Dermal	951 (30)	144 (26)	575 (34)	162 (24)	70 (26)
Edema	166 (5)	31 (6)	86 (5)	33 (5)	16 (6)
Erythema	379 (12)	60 (11)	227 (13)	67 (10)	25 (9)
Rash/irritation	266 (8)	52 (10)	159 (9)	42 (6)	13 (5)
Paresthesias	409 (13)	47 (9)	267 (16)	63 (9)	32 (12)
Pruritis	255 (8)	33 (6)	156 (9)	43 (6)	23 (8)
Other	114 (4)	12 (2)	72 (4)	16 (2)	14 (5)
Eye	901 (28)	213 (39)	456 (27)	166 (24)	66 (24)
Burn	52 (2)	25 (5)	20 (1)	4 (1)	3 (1)
Corneal abrasion	51 (2)	21 (4)	27 (2)	2 (<1)	1 (<1)
Lacrimation	234 (7)	68 (12)	111 (7)	40 (6)	15 (5)
Pain/irritation	768 (24)	179 (33)	390 (23)	149 (22)	50 (18)
Conjunctivitis	206 (6)	54 (10)	102 (6)	37 (5)	13 (5)
Other	8 (<1)	1 (<1)	3 (<1)	2 (<1)	2 (1)
Neurologic	1,269 (40)	228 (42)	653 (38)	279 (41)	109 (40)
Confusion	67 (2)	12 (2)	35 (2)	15 (2)	5 (2)
Headache	641 (20)	130 (24)	341 (20)	119 (17)	51 (19)
Muscle weakness	111 (3)	21 (4)	48 (3)	30 (4)	12 (4)
Blurred vision	82 (3)	13 (2)	47 (3)	18 (3)	4 (1)
Dizziness	461 (14)	70 (13)	222 (13)	125 (18)	44 (16)
Paresthesias	143 (4)	19 (3)	85 (5)	30 (4)	9 (3)
Other	131 (4)	26 (5)	66 (4)	26 (4)	13 (5)
Gastrointestinal	1,114 (35)	177 (32)	568 (33)	266 (39)	103 (38)
Abdominal pain/cramping	134 (4)	16 (3)	70 (4)	38 (6)	10 (4)
Diarrhea	151 (5)	19 (3)	78 (5)	40 (6)	14 (5)
Nausea	794 (25)	128 (23)	416 (24)	184 (27)	66 (24)
Vomiting	547 (17)	77 (14)	283 (17)	126 (18)	61 (22)
Other	37 (1)	13 (2)	13 (1)	6 (1)	5 (2)
Cardiovascular	241 (8)	52 (10)	110 (6)	57 (8)	22 (8)
Bradycardia	14 (<1)	2 (<1)	8 (<1)	4 (1)	
Tachycardia	67 (2)	9 (2)	28 (2)	23 (3)	7 (3)
Chest pain	105 (3)	27 (5)	48 (3)	21 (3)	9 (3)
Other	75 (2)	15 (3)	34 (2)	21 (3)	5 (2)
Other					
Renal/genitourinary symptoms	18 (1)	4 (1)	8 (<1)	4 (1)	2 (1)
Fever	85 (3)	15 (3)	51 (3)	13 (2)	6 (2)
Fatigue/malaise	159 (5)	21 (4)	85 (5)	41 (6)	12 (4)
Other	23 (1)	4 (1)	15 (1)	2 (<1)	2 (1)

<sup>a</sup>Cases may have experienced symptoms in multiple organ systems or multiple symptoms in the same organ system; therefore the sum of the percentages exceeds 100.

\*Cases were exposed only to pyrethrins and/or pyrethroids and not other pesticide. These cases might also be exposed to the synergists piperonylbutoxide (PBO) or MGK-264.

**TABLE V.** Acute Illness/Injury Due To Exposure Only to Pyrethrins, Pyrethroids, or a Combination of Pyrethrins and/or Pyrethroids—by Active Ingredient Associated With Illness, Severity, and Respiratory and Dermal Health Effects, 2000–2008 (n = 3,207)\*

Active ingredients	Total, no. (%) <sup>a</sup>	Low severity, no. (%) <sup>b</sup>	Moderate and	Respiratory symptoms, no. (%) <sup>b</sup>	Dermal symptoms, no. (%) <sup>b</sup>
			high severity, no. (%) <sup>b</sup>		
Exposed to only 1 pyrethrin or pyrethroid (total)	2,248 (70)	1,828 (80)	443 (20)	1,032 (46)	719 (32)
Pyrethrins	547 (24)	445 (81)	102 (19)	239 (44)	144 (26)
Type I pyrethroids	732 (32)	581 (79)	151 (20)	312 (43)	258 (35)
Allethrin	27 (1)	23 (85)	4 (15)	8 (30)	10 (37)
Bifenthrin	175 (8)	139 (79)	36 (21)	59 (34)	56 (32)
Permethrin	350 (16)	283 (81)	67 (19)	137 (39)	141 (40)
Phenothrin	57 (3)	36 (63)	21 (37)	37 (65)	22 (39)
Prallethrin	1 (<1)	1 (100)	—	1 (100)	—
Resmethrin	90 (4)	75 (83)	15 (17)	46 (51)	23 (26)
Tefluthrin	1 (<1)	1 (100)	—	—	1 (100)
Tetramethrin	31 (1)	23 (74)	8 (26)	24 (77)	5 (16)
Type II pyrethroids	950 (42)	767 (81)	183 (19)	472 (50)	313 (33)
Cyfluthrin	216 (10)	169 (78)	47 (22)	92 (43)	95 (44)
Cyhalothrin	20 (1)	15 (75)	5 (25)	4 (20)	6 (30)
Cypermethrin	369 (16)	287 (78)	82 (22)	239 (65)	89 (24)
Cyphenothrin	16 (1)	13 (81)	3 (19)	9 (56)	6 (38)
Deltamethrin	136 (6)	118 (87)	18 (13)	50 (37)	56 (41)
Esfenvalerate	87 (4)	78 (89)	9 (10)	39 (45)	22 (25)
Fenpropathrin	8 (<1)	8 (100)	—	2 (25)	5 (63)
Fenvalerate	5 (<1)	5 (100)	—	2 (40)	4 (80)
Fluvalinate	6 (<1)	5 (83)	1 (17)	1 (17)	2 (33)
Tralomethrin	87 (4)	69 (79)	18 (21)	34 (39)	28 (32)
Unknown type pyrethroid	19 (1)	15 (79)	4 (21)	9 (47)	4 (21)
Exposed to 2+ pyrethroids only	686 (21)	546 (80)	140 (20)	345 (50)	162 (24)
Exposed to pyrethrins and 1 or more pyrethroids only	273 (9)	213 (78)	60 (22)	165 (60)	70 (26)

<sup>a</sup>Denominators to calculate the percentages for pyrethrins, type I and type II pyrethroids and corresponding active ingredients are the total exposed to only 1 pyrethrin or pyrethroid (2,248). Denominators to calculate the percentages for the total exposed to only 1 pyrethrin or pyrethroid, cases exposed to 2+ pyrethroids only, and cases exposed to pyrethrins and 1 or more pyrethroids only are the total cases exposed to pyrethrins and/or pyrethroids and no other pesticide (3,207).

<sup>b</sup>Denominators to calculate the percentages are from the totals in the row corresponding to the active ingredient(s).

\* All cases in this table were exposed only to pyrethrins and/or pyrethroids and no other pesticide. These cases might also be exposed to the synergists piperonylbutoxide (PBO) or MGK-264.

control center data) from 2001 to 2003 found that the respiratory system was the fourth most commonly affected system (12% of cases had respiratory effects), preceded by effects on the gastrointestinal system (23%), ocular (15%), and miscellaneous effects (13%) among individuals exposed only to pyrethrins [Osimitz et al., 2009]. We found that the respiratory system was the most commonly affected organ system among persons exposed to pyrethrins only (44%). We are unaware of any reports using AAPCC data that examined the spectrum of health effects associated with pyrethroid exposures or exposures to mixtures of pyrethrins/pyrethroids.

There is currently little information about the effects of simultaneous exposure to mixtures of pyrethrins and pyrethroids. In vivo [Cao et al., 2011] and in vitro studies in rats [Wolansky et al., 2009] have shown that pyrethroids

have additive effects. We found that mixtures containing two or more pyrethroids only and mixtures containing pyrethrins and pyrethroids only were associated with an increased risk for all of the respiratory effects examined, compared to individuals whose acute pesticide-related illness did not involve pyrethrin or pyrethroid exposures. Mixtures containing two or more pyrethroids only were also associated with paresthesias.

## Respiratory Effects

We were unable to assess the association between asthma and exposure to pyrethrins and pyrethroids. This is because asthma was not systematically collected by pesticide poisoning surveillance programs prior to 2003, and only

**TABLE VI.** Risk of Selected Respiratory Symptoms Among Persons With Acute Illness/Injury Due To Exposure Only to Pyrethrins, Pyrethroids, or a Combination of Pyrethrins and/or Pyrethroids (n = 3,207)<sup>a</sup> Compared to Persons Exposed to All Other Pesticides (n = 10,422)<sup>b,c</sup>

Active ingredients	Combined respiratory symptoms <sup>a</sup>		Cough		Dyspnea		Wheeze		Lower respiratory pain/irritation	
	No. (%) <sup>b</sup>	OR <sup>c</sup> (95% CI)	No. (%) <sup>b</sup>	OR <sup>c</sup> (95% CI)	No. (%) <sup>b</sup>	OR <sup>c</sup> (95% CI)	No. (%) <sup>b</sup>	OR <sup>c</sup> (95% CI)	No. (%) <sup>b</sup>	OR <sup>c</sup> (95% CI)
Pyrethrins	189 (35)	1.79 (1.49–2.16)	124 (23)	2.06 (1.67–2.57)	101 (18)	1.52 (1.21–1.92)	23 (4)	1.63 (1.04–2.55)	15 (3)	1.04 (0.61–1.78)
Pyrethroids	604 (36)	1.99 (1.77–2.24)	392 (23)	2.21 (1.93–2.54)	351 (21)	1.83 (1.59–2.11)	77 (5)	1.77 (1.34–2.35)	62 (4)	1.52 (1.14–2.04)
Type I pyrethroids	229 (31)	1.68 (1.42–2.00)	120 (16)	1.47 (1.19–1.83)	148 (20)	1.83 (1.50–2.25)	41 (6)	2.16 (1.50–3.11)	34 (5)	2.14 (1.47–3.13)
Bifenthrin	39 (22)	1.05 (0.73–1.51)	16 (9)	0.75 (0.45–1.28)	21 (12)	0.99 (0.62–1.59)	4 (2)	0.87 (0.32–2.40)	7 (4)	1.67 (0.77–3.64)
Permethrin	104 (30)	1.55 (1.21–1.97)	59 (17)	1.53 (1.14–2.05)	69 (20)	1.78 (1.35–2.35)	19 (5)	2.24 (1.37–3.68)	9 (3)	1.07 (0.54–2.12)
Phenothrin	31 (54)	5.03 (2.92–8.65)	19 (33)	4.22 (2.37–7.54)	23 (40)	5.50 (3.15–9.60)	13 (23)	10.56 (5.28–21.11)	—	—
Resmethrin	33 (37)	2.31 (1.49–3.58)	12 (13)	1.32 (0.71–2.45)	18 (20)	1.86 (1.10–3.15)	2 (2)	0.95 (0.23–3.94)	18 (20)	10.60 (6.07–18.50)
Tetramethrin	16 (52)	3.67 (1.80–7.48)	10 (32)	3.35 (1.56–7.18)	13 (42)	4.96 (2.41–10.22)	3 (10)	3.88 (1.17–12.91)	—	—
Type II pyrethroids	375 (39)	2.27 (1.96–2.62)	272 (29)	2.89 (2.46–3.40)	203 (21)	1.86 (1.56–2.21)	36 (4)	1.51 (1.04–2.19)	28 (3)	1.09 (0.73–1.64)
Cyfluthrin	59 (27)	1.37 (1.00–1.86)	37 (17)	1.59 (1.10–2.29)	32 (15)	1.07 (0.73–1.58)	7 (3)	1.31 (0.60–2.84)	9 (4)	1.70 (0.85–3.37)
Cypermethrin	206 (56)	4.30 (3.46–5.34)	161 (44)	5.41 (4.34–6.76)	104 (28)	2.64 (2.08–3.36)	19 (5)	2.03 (1.24–3.30)	10 (3)	1.00 (0.53–1.92)
Deltamethrin	31 (23)	1.02 (0.68–1.53)	17 (13)	1.04 (0.62–1.73)	16 (12)	0.91 (0.54–1.55)	4 (3)	1.15 (0.42–3.16)	2 (1)	0.54 (0.13–2.18)
Esfenvalerate	37 (43)	2.84 (1.84–4.40)	26 (30)	3.47 (2.16–5.58)	28 (32)	3.47 (2.19–5.52)	4 (5)	1.90 (0.68–5.28)	5 (6)	2.34 (0.93–5.89)
Tralomehrin	26 (30)	1.57 (0.98–2.52)	20 (23)	2.23 (1.34–3.73)	14 (16)	1.43 (0.80–2.56)	1 (1)	0.43 (0.06–3.12)	1 (1)	0.49 (0.07–3.59)
Exposed to 2+ pyrethroids only	268 (39)	2.36 (1.99–2.81)	187 (27)	2.81 (2.31–3.41)	143 (21)	1.95 (1.59–2.40)	28 (4)	1.76 (1.15–2.68)	26 (4)	1.66 (1.08–2.54)
Exposed to pyrethrins and 1 or more pyrethroids only	126 (46)	2.99 (2.33–3.84)	87 (32)	3.31 (2.53–4.34)	71 (26)	2.45 (1.85–3.26)	15 (5)	2.23 (1.29–3.86)	13 (5)	1.96 (1.10–3.50)
Non-pyrethrin/pyrethroid pesticides	2,427 (23)	1.00	1,254 (12)	1.00	1,412 (14)	1.00	257 (2)	1.00	332 (3)	1.00

<sup>a</sup>Combined respiratory symptoms include cough, dyspnea, wheeze, and lower respiratory tract irritation.

<sup>b</sup>Denominators to calculate the percentages for symptoms and corresponding active ingredients are taken from totals reported in Table V.

<sup>c</sup>Adjusted for type of exposure = "exposed during targeted application," and application site = "agricultural site."

\* All cases in this table were exposed only to pyrethrins and/or pyrethroids and no other pesticide. These cases might also be exposed to the synergist piperonylbutoxide (PBO) or MGK-264.

\*\* Persons exposed to disinfectants, pyrethrins, pyrethroids, or mixtures that included these pesticides were excluded from the control group.

**TABLE VII.** Risk of Paresthesias Among Persons With Acute Illness/Injury Due To Exposure Only to Pyrethrins, Pyrethroids, or a Combination of Pyrethrins and/or Pyrethroids (n = 3,207)\* Compared to Persons Exposed to All Other Pesticides (n = 10,422)\*\*

Active ingredients <sup>a</sup>	No. (%)	aOR (95% CI)
Pyrethrins	19 (3)	1.20 (0.74–1.93)
Pyrethroids	85 (5)	1.90 (1.47–2.47)
Type I pyrethroids	51 (7)	2.61 (1.88–3.62)
Bifenthrin	15 (9)	3.34 (1.91–5.84)
Permethrin	23 (7)	2.64 (1.68–4.17)
Phenothrin	1 (2)	0.64 (0.09–4.69)
Resmethrin	8 (9)	2.68 (1.27–5.65)
Tetramethrin	1 (3)	1.27 (0.17–9.39)
Type II pyrethroids	34 (4)	1.34 (0.92–1.94)
Cyfluthrin	6 (3)	0.94 (0.41–2.15)
Cypermethrin	10 (3)	1.04 (0.54–1.98)
Deltamethrin	7 (5)	1.81 (0.83–3.92)
Esfenvalerate	8 (9)	3.11 (1.47–6.58)
Tralomethrin	1 (1)	0.52 (0.07–3.75)
Exposed to 2+ pyrethroids only	30 (4)	1.81 (1.20–2.73)
Exposed to pyrethrins and 1 or more pyrethroids only	9 (3)	1.24 (0.62–2.45)
Non-pyrethrin/pyrethroid pesticides	354 (3)	1.00

<sup>a</sup>Adjusted for type of exposure = “exposed during targeted application” and application site = “private residence.”

\*All cases in this table were exposed only to pyrethrins and/or pyrethroids and no other pesticide. These cases might also be exposed to the synergist piperonylbutoxide (PBO) or MGK-264.

\*\*Persons exposed to disinfectants, pyrethrins, pyrethroids, or mixtures that included these pesticides were excluded from the control group.

by some programs after 2003. Although pyrethrins and tetramethrin are considered known asthmagens [AOEC, 2009], EPA reviewed animal studies and human incident data using a weight of evidence analysis and concluded that the evidence for an association between pyrethrin/pyrethroid exposure and asthma is equivocal [US EPA 2009]. However, we found that symptoms which are suggestive for the presence of asthma (i.e., wheeze, dyspnea and cough) [British Thoracic Society, Scottish Intercollegiate Guidelines Network, 2012], were significantly more likely to be present in individuals with acute pyrethrin and pyrethroid-related illness compared to individuals with acute pesticide-related illness not involving pyrethrin/pyrethroid/disinfectant exposures.

## Paresthesias

Several previous reports of paresthesias in persons exposed to pyrethroids focused on Type II pyrethroids [Tucker and Flannigan, 1983; He et al., 1988; Chester

et al., 1992; Weinberg et al., 2009] and only two assessed a Type I pyrethroid (i.e., permethrin) [Kolmodin Hedman et al., 1982; Flannigan et al., 1985]. As a result, some investigators concluded that Type II pyrethroids were more likely to produce paresthesias [US EPA, 1999; Wilks, 2000]. In contrast to these reports, we found that as a group, Type I pyrethroids were associated with paresthesias, but not Type II pyrethroids. Our study found that paresthesias were more likely to be found in those exposed to three Type I pyrethroids: bifenthrin, permethrin, and resmethrin. The only Type II pyrethroid found to be associated with paresthesias was esfenvalerate. Another Type II pyrethroid, fenpropathrin, also appeared to be associated with paresthesias (observed in two of eight cases), but we did not perform logistic regression on this chemical due to small sample size. In contrast to earlier studies, ours had a larger number of cases exposed to specific pyrethroids only; therefore our study may be better powered to detect paresthesias compared to these earlier reports. However, our study did not have information on pesticide dose, so we were unable to determine if exposure dose differed for cases exposed to Type I versus Type II pyrethroids.

## Limitations

This study has several limitations. First, acute illness/injury associated with pesticide exposure are likely under-reported. Case identification by states relies on a passive surveillance system, so persons who do not seek medical treatment or advice from poison control centers are not captured as cases. Other factors contributing to under-reporting include misdiagnosis, and health care provider’s failure to report pesticide-related illness/injury to public health authorities. Second, some individuals may have been incorrectly labeled as having acute pesticide-related illness/injury. This is because symptoms for acute illnesses associated with pesticides are non-specific and not pathognomonic, and diagnostic tests are not available or rarely performed. Furthermore, most of the cases included in our analyses were classified as possible meaning they were based on subjective data, without objective verification of health effects and exposure. Third, this data is subject to incomplete information on cases. Missing information for some of these cases could have led to misclassification or exclusion from statistical analyses. Furthermore, pesticide products contain both active and other ingredients (e.g., propellants, carriers, and solvents). Information on the other ingredients was not available to NIOSH. Even if detailed product information was available, it would be very difficult to identify the specific ingredient responsible for each illness/injury. Fourth, the cases captured by SENSOR-Pesticides/PISP may not be representative of all cases of acute pyrethrin/pyrethroid illness/injury. For example, some Western states have more robust pesticide illness and injury surveillance programs, and

**TABLE VIII.** Contributing Factors for Pesticide Exposure among Individuals With Acute Illness/Injury Cases Due To Pyrethrin and Pyrethroid Exposures, 2000–2008

Contributing factors	Exposed to pyrethrins and pyrethroids all cases <sup>a</sup>			Only exposed to pyrethrins and/or pyrethroids <sup>b</sup>		
	Total, no. (%) <sup>c,d</sup>	Workers, no. (%) <sup>c,d</sup>	No. (%) <sup>c,d</sup>	Total, no. (%) <sup>c,d</sup>	Workers, no. (%) <sup>c,d</sup>	Non-workers, no. (%) <sup>c,d</sup>
One or more contributing factors identified	3,301	1,111	2,190	2,160	610	1,550
Drift from application site	412 (12)	221 (20)	191 (9)	72 (3)	32 (5)	40 (3)
Spill/splash of liquid or dust	417 (13)	148 (13)	269 (12)	316 (15)	105 (17)	211 (14)
Failure to evacuate during pesticide application	362 (11)	124 (11)	238 (11)	256 (12)	79 (13)	177 (11)
Inadequate ventilation	330 (10)	178 (16)	152 (7)	253 (12)	142 (23)	111 (7)
Improper storage	281 (9)	22 (2)	259 (12)	211 (10)	19 (3)	192 (12)
Early re-entry into treated area	234 (7)	122 (11)	112 (5)	136 (6)	49 (8)	87 (6)
Excessive application of pesticide	140 (4)	21 (2)	119 (5)	104 (5)	11 (2)	93 (6)
Failure to leave treated area post-application	129 (4)	7 (1)	122 (6)	104 (5)	5 (1)	99 (6)
Application equipment failure	96 (3)	53 (5)	43 (2)	61 (3)	32 (5)	29 (2)
Decontamination not adequate/timely	88 (3)	19 (2)	69 (3)	68 (3)	10 (2)	58 (4)
PPE inadequate/not worn	70 (2)	53 (5)	17 (1)	46 (2)	32 (5)	14 (1)
Notification of pesticide application lacking/ineffective	70 (2)	48 (4)	22 (1)	51 (2)	32 (5)	19 (1)
Preexisting asthma, allergy, or chemical sensitivity	33 (1)	11 (1)	22 (1)	20 (1)	5 (1)	15 (1)
Applicator not properly trained/supervised	32 (1)	25 (2)	7 (<1)	17 (1)	12 (2)	5 (<1)
Illegal pesticide used/illegal dumping	19 (1)	11 (1)	8 (<1)	16 (1)	10 (2)	6 (<1)
Other <sup>e</sup>	32 (1)	9 (1)	23 (1)	22 (1)	3 (<1)	19 (1)
Label violation not otherwise specified	432 (13)	82 (7)	350 (16)	324 (15)	53 (9)	271 (17)
No label violation identified/person still poisoned	378 (11)	86 (8)	292 (13)	261 (12)	63 (10)	198 (13)
Unknown	1,673	581	1,092	1,047	308	739
Total	4,974	1,692	3,282	3,207	918	2,289

<sup>a</sup>There were 4,974 cases exposed to mixtures that included pyrethrins and/or pyrethroids and another pesticide that was not a pyrethrin or pyrethroid.

<sup>b</sup>There were 547 (11%) cases exposed to pyrethrins, 1,682 (34%) cases exposed to only 1 pyrethroid, 686 (14%) cases exposed to 2 more pyrethroids only, and 273 (5%) cases exposed to a combination of pyrethrins and/or pyrethroids. These cases might also be exposed to the synergists piperonylbutoxide (PBO) or MGK-264.

<sup>c</sup>The denominators to calculate percentages were the total number of cases for which one or more contributing factors were identified.

<sup>d</sup>Cases may have had more than one contributing factor, therefore the sum of the percentages exceeds 100.

<sup>e</sup>The "other" category includes contributing factors that do not fit in the specified categories and includes instances of pesticide fires, exposure due to slips and falls, and accidental ingestion not due to improper storage (i.e., ate a spider that had been sprayed with insecticide).

have better mechanisms to capture work-related cases. This may explain the higher rates of work-related illness/injury observed in the West. In addition, some non-work-related cases might have been missed because NIOSH advises states to prioritize work-related cases when staffing limitations preclude follow-up of all cases. Finally, contributing factors for most SENSOR-pesticides cases were coded retrospectively, so misclassification was possible. In addition, because contributing factors were identified for only 66% of cases, full knowledge about contributing factors in all cases could alter the conclusions and interpretations in this report.

## CONCLUSIONS

The magnitude and severity of acute pyrethrin/pyrethroid-related illness/injury is relatively low. However, our findings suggest that acute illness/injury associated with

exposure to pyrethrins and/or pyrethroids are increasing in the non-occupational setting as the usage of these pesticides increases. An increased risk for dyspnea and wheeze was associated with exposure to pyrethrins and several pyrethroids: permethrin, phenothrin, tetramethrin, cypermethrin, Type I pyrethroids, Type II pyrethroids, mixtures containing two or more pyrethroids only, and mixtures containing pyrethrins and pyrethroids only. Paresthesias were most strongly associated with exposure to Type I pyrethroids.

Among the 3,301 cases with information on contributing factors, 704 (21%) were cases attributed to total release fogger exposures. As a result of a 2008 CDC report on illnesses/injuries related to total release foggers [CDC, 2008], EPA changed label requirements to address the factors that commonly contributed to exposure, including directions to promptly leave the treated structure, directions on the length of time to stay out of the structure, instructions on how long

the treated structure should be aired out upon return, and a recommendation to place a notice on doors leading to treated areas announcing when re-entry was permitted. The deadline for implementing EPA's label changes was September 2012. One additional preventive measure not included in the revised label is that applicators should be alert and careful not to use total release foggers when other persons are in the treated area.

Since many acute illnesses associated with pyrethrins and/or pyrethroid exposures were caused by inadequate ventilation, applicators should also make sure that there is adequate ventilation before persons return to the treated area. In homes, this involves direct ventilation of treated areas (i.e., using fans, and opening windows and doors) [U.S. Department of Housing and Urban Development, 2006] and in other buildings, it involves proper operation and maintenance of heating, ventilation and air conditioning systems [CDC, 2011]. Improper storage (8%) and spills/splashes of pesticides (13%) contributed to a large proportion of illnesses and injuries associated with pyrethrins and/or pyrethroids. Increased efforts to educate the public on pesticide safety, handling, and storage, including putting pesticides in proper containers, might reduce these illnesses. Of the 639 pyrethrin/pyrethroid-related cases below the age of 15 years, 218 (34%) occurred because the pesticide was in reach of a child. Including child safety devices on pesticide containers might reduce such illnesses. Thirteen percent of illnesses were due to exposure from off-target drift. To prevent illnesses associated with drift, pesticide applicators should use available drift management measures and equipment, including new validated drift reduction technologies as they become available [US EPA, 2012b]. Improved compliance with the EPA Worker Protection Standard (WPS) could reduce illnesses/injuries related to agricultural exposures. The WPS requires that handlers using agricultural pesticides avoid application that could contact other persons directly or through pesticide drift [US EPA, 1995]. Finally, minimizing the use of pesticides, including pyrethrins and pyrethroids, by adopting integrated pest management (IPM) strategies can reduce the incidence of acute pesticide-related illness/injury [Cornell University Cooperative Extension, 2009].

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