# The Burden of Work-related Asthma in Michigan, 1988–2018

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## Abstract

**Rationale:** Exposure to a variety of substances in the workplace can cause new-onset asthma or aggravate preexisting asthma, both of which are considered work-related asthma (WRA). Understanding trends in the nature and causes of WRA can assist in the diagnosis and management of adult patients with asthma.

**Objective:** To describe trends over 31 years of WRA surveillance in Michigan.

**Methods:** Michigan law requires reporting of all known or suspected cases of occupational disease. WRA was confirmed by review of a standardized telephone interview and patient medical records. Enforcement inspections at the workplaces of the WRA cases included air monitoring and evaluation for asthma and asthma symptoms among coworkers.

**Results:** The Michigan surveillance program identified 3,634 WRA cases from 1988 to 2018, including nine deaths. The cumulative incidence rate of WRA decreased from 3.5 to 2.0 cases per 100,000 workers. Cases most frequently worked in manufacturing (56%), health care (12%), and education (4%). The cumulative incidence rate of WRA decreased in each of those three industries, while increasing in retail trade and accommodations and food services. The most common exposures to known asthma inducers were to cleaning agents and isocyanates; the percentage exposed to cleaning agents increased from 5% to 20%, and the percentage exposed to isocyanates decreased from 20% to 7%. Fifty-one percent had not applied for workers' compensation benefits. Only 5% of the 571 workplaces where air sampling was performed were above the allowable exposure limit. Fifteen percent (1,622 of 10,493) of coworkers of the index cases reported onset of asthma since beginning to work at the facility or being bothered at work by daily or weekly chest tightness, shortness of breath, or wheezing.

**Conclusions:** The industries and exposures where Michigan adults develop WRA have changed during the past 31 years. The identification of WRA cases, including WRA deaths, underscores the need for continued vigilance to monitor changes in where and how workers are exposed to asthma-causing agents, physician consideration of workplace exposures in new-onset or worsening adult asthma, and adoption of workplace standards that reduce exposure and require workplace medical monitoring to prevent and reduce the morbidity and mortality of WRA.

**Keywords:** work-related asthma; asthma-causing agents; workplace; surveillance; epidemiology

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A man in his 50s died from an isocyanate-induced asthma attack, after working at an adhesive manufacturer for 5 years. He had no personal or family history of allergies or asthma. He smoked cigarettes since the age of 16 years. Spirometry performed by the company at hire was normal, with a forced expiratory volume in 1 second ($FEV_1$) 97% predicted. The day the decedent collapsed he was working in a mixing room where isocyanates were added to reactor vessels. He died in the hospital 6 days later without regaining consciousness. The patient had 18 medical encounters for his breathing difficulties before he died: four medical examinations provided by the company, five urgent care visits, seven visits to his primary care physician, and two visits to a pulmonologist. However, he was not removed from exposure to isocyanates. After his death, review of

medical records identified 5 of 18 coworkers with respiratory changes of concern. Appendix E1 in the online supplement has full details of this work-related asthma (WRA) death.

More than 300 workplace substances have been identified to cause new-onset asthma, and the list continues to grow (1, 2). Other substances can aggravate preexisting asthma, causing increased morbidity and medication requirements. WRA comprises both new-onset and work-aggravated asthma (3). An estimated 15% to 55% of all adult asthma is related to work (4–8). In some instances, WRA has been fatal (9, 10). WRA can occur in any industry or occupation. Variation in the industries, occupations, exposures, and costs related to WRA have been reported internationally (11–13). United States surveillance data have described WRA from exposure to cleaning agents (14), fragrances (15), isocyanates (16), metalworking fluids (17), and welding fume (18); at swimming facilities (19), schools (20), healthcare facilities (21), and wood-processing industries; and among hops production workers (22). The data have also described the industries and exposures by type of WRA (23, 24).

Since 1988, Michigan has received funding from the National Institute for Occupational Safety and Health for the development and continuation of a WRA surveillance and workplace intervention program. Other states have intermittently conducted WRA surveillance, but Michigan is the only state to track WRA for the entire 31 years. Furthermore, Michigan is the only state where the surveillance program is part of a regulatory program to conduct enforcement inspections at the workplaces of the WRA index cases.

The Occupational Safety and Health Administration (OSHA) sets workplace limits of exposure, termed the permissible exposure limit (PEL), which is an 8-hour time-weighted average exposure not to be exceeded during the workday. However, most asthma inducers do not have a PEL; of those with a PEL, most were not set to prevent WRA. Consequently, many WRA exposures are regulated under the general category of respirable nuisance dust, which has a PEL of 5 mg/m$^3$.

The WRA case classification criteria have previously been described (25). New-onset WRA is divided into asthma that typically develops after months to years of low-level exposure to a known asthma inducer (occupational asthma [OA]) and asthma that develops from a one-time high-level acute exposure to an irritant (reactive airways dysfunction syndrome [RADS]) (26). WRA from chronic exposure to low to moderate levels of irritants has also been described (27, 28). Work-aggravated asthma (WAA) occurs when an individual with preexisting asthma has an increase in respiratory symptoms and/or need for medications from workplace exposure(s).

This report summarizes the results of Michigan's WRA surveillance system from 1988 to 2018.

## Methods

### Case Identification

Case identification relied on healthcare provider reports, hospital discharge records, workers' compensation (WC) claims, and poison control center (PCC) reports. Additional sources included referrals of coworkers by the index case, death certificates, clinical laboratory reports for specific Immunoglobulin E allergy testing, self-referrals, and the Mine Safety and Health Administration. The authority to identify and collect information on these cases is based on Michigan Public Health Code (Article 368, Part 56, P.A. 1978, as amended) (29), requiring healthcare providers, hospitals, clinics, and employers to report known or suspected cases of occupational diseases to the state. All cases, regardless of reporting source, required confirmation of the diagnosis.

### Case Definition

A confirmed WRA case required: *1*) physician diagnosis of asthma, *2*) onset of respiratory symptoms associated with a job that resolved or improved away from work, and *3*) work with a known allergen, or an association between the work exposure and a decrease in peak flow or spirometry.

### Case Confirmation

We used a standardized telephone-administered questionnaire to obtain: sex; race; ethnicity (since 1994); age; cigarette use (current, ever, or never smoked [five or more packs of cigarettes or 12 ounces of tobacco in a lifetime was used to define ever smoked]); WC status; prior asthma and allergies; family allergies; history of: respiratory symptom development and persistence, asthma medication, and medical treatment for asthma; and lifetime work and exposure history (exposure to agents associated with asthma, exposure to spills or leaks). The questionnaire and medical records, including pulmonary function testing, were reviewed to confirm the diagnosis.

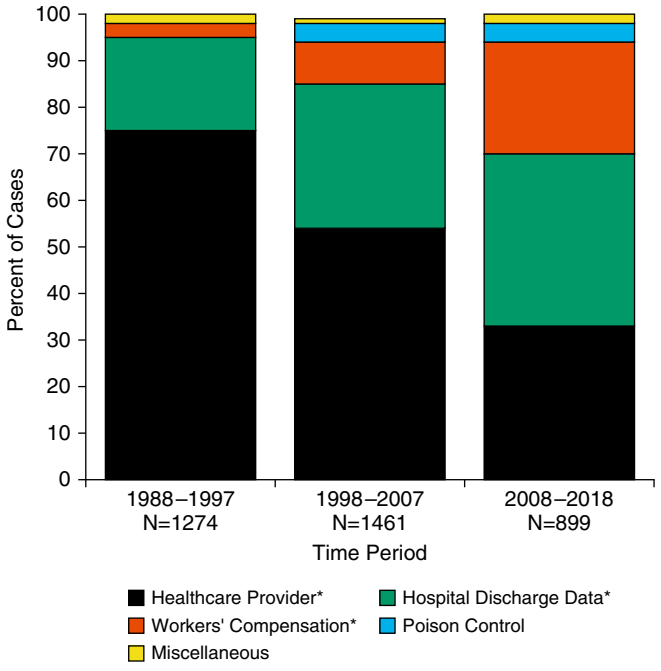


**Figure 1.** Percent of cases and ascertainment source for confirmed work-related asthma cases: Michigan, 1988–2018. *Time trend $P \leq 0.05$.

Michigan OSHA conducted enforcement inspections at the workplaces of the confirmed WRA cases. Workplaces were selected for inspection if the exposure was ongoing, if Michigan OSHA had jurisdiction and an enforceable standard relative to the exposure, and if the index case had new-onset WRA, not WAA. Each workplace location was generally inspected once, even if new cases were identified after an inspection. Inspection reports included air monitoring results for asthma-causing agents and a confidential standardized respiratory questionnaire administered to coworkers of the index cases.

To reduce the potential effect of year-to-year variability, we divided the 31-year surveillance data into three periods: 1988 to 1997, 1998 to 2007, and 2008 to 2018. Frequencies and cross-tabulations were calculated using Microsoft Access. For employment denominators to calculate cumulative incidence rates, we used the midpoint year data (1992, 2002, and 2012) for each time period and 2002 for all years combined from the Michigan Bureau of Labor Market Current Employment Estimates for 1992, the Bureau of Labor Statistics Quarterly Census of Employment and Wages for 2002 and 2012, and the Census of Agriculture State Data for all three periods. Additional time series analyses to test whether there were trends by year were conducted using the Cochran-Armitage test, SAS version 9.4. Industry was coded to the two-digit 2002 North American Industry Classification System.

The Michigan State University Human Research Protection Program (Biomedical and Health Institutional Review Board) approved this investigation with waiver of informed consent.

## Results

From 1988 to 2018, 3,634 WRA cases were confirmed: 1,274 cases from 1988 to 1997, 1,461 from 1998 to 2007, and 899 from 2008 to 2018. Case reporting was from physicians (2,046, 56%), hospitals (1,040, 29%), WC (386, 11%), the Michigan PCC (100, 3%), index case referrals (45, 1%), death certificates (8, <1%), clinical laboratories (5, <1%), self-referrals (3, <1%), and Mine Safety and Health Administration (1, <1%) (Figure 1). Over time, healthcare provider reporting decreased ($P < 0.01$), hospital and WC reporting increased ($P < 0.01$), and PCC reporting did not change.

Overall, 2,905 (80%) cases were new-onset WRA (2,498 [69%] OA, 407 [11%] RADS), and 729 (20%) were WAA (Table 1). Of the 2,498 OA cases, 1,191 (48%) were exposed to a known allergen (1); for 1,307 (52%), a known allergen was not identified. OA cases decreased from 80% to 53% over time ($P < 0.01$). RADS cases did not significantly change. WAA cases increased from 11% to 37% ($P < 0.01$). The online supplement shows yearly changes for each characteristic listed in Table 1.

Females accounted for 54% of the WRA cases, which increased from 49% to 60% over time ($P < 0.01$) (Table 1). Overall, 2,720 (78%) were white, 683 (20%) African American, and 98 (3%) classified as other; 3% of all the cases reported Hispanic ethnicity. There were no significant changes over time among race or ethnicity.

Overall, 56% of the WRA cases ever smoked cigarettes, of whom 20% were current smokers. There was an increase over time among never smokers, from 37% to 51% ($P < 0.01$), and a decrease among ex-smokers, from 43% to 31% ($P < 0.01$). The percentage of current smokers remained unchanged. Forty-nine percent of subjects applied for WC, which did not change over time. Those who received WC benefits increased from 37% to 47% over time ($P < 0.01$).

WRA cases with a personal history of asthma or allergies increased from 47% to 63% over time ($P < 0.01$). Those with a family history of allergies increased from 41% to 46% over time ($P < 0.01$). Overall, 66% had at least one emergency department (ED) visit, and 35% were hospitalized at least once for their WRA. ED visits increased from 57% to 74% ($P < 0.01$), while hospitalizations remained the same over time. On average, WRA cases had five ED visits, and four hospitalizations (Table 1).

Nine (<1%) individuals died from an asthma attack from a workplace exposure

**Table 1.** Select characteristics of confirmed work-related asthma cases: Michigan, 1988–2018

| Characteristics | Time Period | | | |
|---|---|---|---|---|
| | All Years | 1988–1997 | 1998–2007 | 2008–2018 |
| Total No. of cases | 3,634 | 1,274 | 1,461 | 899 |
| Work-aggravated asthma | 729 (20) | 135 (11) | 258 (18) | 336 (37) |
| RADS | 407 (11) | 124 (10) | 196 (13) | 87 (10) |
| Occupational asthma | 2,498 (69) | 1,015 (80) | 1,007 (69) | 476 (53) |
| Female sex | 1,964 (54) | 626 (49) | 800 (55) | 538 (60) |
| Race | | | | |
| White | 2,720 (78) | 997 (79) | 1,093 (77) | 630 (76) |
| African American | 683 (20) | 239 (19) | 272 (19) | 172 (21) |
| Other | 98 (3) | 25 (2) | 47 (3) | 26 (3) |
| Hispanic ethnicity | 82 (3) | 24 (4) | 27 (2) | 31 (4) |
| Never smoked cigarettes | 1,529 (44) | 463 (37) | 632 (45) | 434 (51) |
| Current cigarette smokers | 685 (20) | 243 (20) | 295 (21) | 147 (17) |
| Ex-cigarette smokers | 1,285 (37) | 540 (43) | 479 (34) | 266 (31) |
| Applied for WC | 1,534 (49) | 568 (49) | 612 (49) | 354 (50) |
| If applied, awarded WC benefits | 578 (38) | 208 (37) | 204 (33) | 166 (47) |
| Personal history of asthma or allergies | 1,797 (51) | 588 (47) | 676 (48) | 533 (63) |
| Family history of allergies | 1,351 (44) | 462 (41) | 570 (47) | 319 (46) |
| Health care use | | | | |
| Emergency department visit | 2,242 (66) | 661 (57) | 956 (68) | 625 (74) |
| No. of visits, average ± SD | 5 ± 15 | 6 ± 17 | 5 ± 14 | 5 ± 12 |
| No. of visits, median | 2 | 2 | 2 | 2 |
| Total No. of visits, range | 1–300 | 1–300 | 1–200 | 1–150 |
| Hospitalization | 1,128 (35) | 426 (37) | 423 (33) | 279 (36) |
| No. of visits, average ± SD | 4 ± 10 | 4 ± 8 | 4 ± 13 | 3 ± 6 |
| No. of visits, median | 1 | 1 | 1 | 1 |
| Total No. of visits, range | 1–200 | 1–100 | 1–200 | 1–50 |

*Definition of abbreviations*: RADS = reactive airways dysfunction syndrome; SD = standard deviation; WC = workers' compensation.

Data are frequency (%), unless otherwise noted. Totals vary owing to missing information. Race was missing for 133, ethnicity was missing for 844, smoking was missing for 118, WC was missing for 511, personal history of asthma or allergies was missing for 128, family history was missing for 586, emergency department use was missing for 235, and hospitalization was missing for 412.

(*see* Table E1 in the online supplement). The decedents ranged from 19 to 77 years of age. Five were men. Five worked in manufacturing, and one each worked in construction, agriculture, food services, and automotive repair. Four were exposed to isocyanates, and one case each was exposed to secondhand cigarette smoke, milk tank cleaning agents, construction chemicals, mold machine release spray, and welding fume. Five of the decedents had new-onset WRA and four had WAA. The time from asthma diagnosis to death ranged from 1 to 37 years. Five individuals had spirometry; two were normal ($FEV_1 \geq 80\%$ predicted) and three decreased ($FEV_1 < 80\%$ predicted).

Of the 1,614 (44%) WRA cases tested for hyperreactivity, either methacholine challenge testing and/or spirometry with pre- and post-bronchodilation, 832 (52%) were positive (Table 2). WRA cases who had a test for hyperreactivity decreased from 53% to 34% over time ($P < 0.01$). Those with a positive result from either type of testing decreased from 60% to 45% ($P < 0.01$). Five percent of all WRA cases had a breathing test performed in relation to work. Sixty-eight percent of the 75 WRA cases who had peak flow, 73% of the 80 who had pre- and post-shift spirometry performed in relation to work, and 33% of the 12 WRA cases with specific bronchoprovocation had a positive result.

The cumulative incidence rate of WRA decreased from 3.5 during 1988 to 1997 to 2.0 cases per 100,000 Michigan workers during 2008 to 2018 ($P < 0.01$). The cumulative incidence rate of OA decreased from 2.8 to 1.1 ($P < 0.01$) and from 0.3 to 0.2 for RADS cases per 100,000 Michigan workers over time, and it increased for WAA from 0.4 to 0.8 ($P < 0.01$) (Figure 2).

Manufacturing was the primary industry, (2,052, 56% cases), followed by health care (452, 12%), education (163, 4%), retail trade (117, 3%), and accommodations and food services (112, 3%) (Table E2). Both the cumulative incidence rate and percentage of WRA cases in manufacturing decreased over time from 11.6 to 5.6 cases per 100,000 workers ($P < 0.01$) (Figure 3) and 71% to 37% ($P < 0.01$) (Figure 4). The cumulative incidence rate of WRA decreased in health care from 2.7 to 2.3 cases per 100,000 Michigan workers, but the percentage of cases in health care increased from 8% to 17% ($P < 0.01$). In education, the cumulative incidence rate decreased from 1.9 to 1.3 cases per 100,000 Michigan workers from 1998–2007 to 2008–2018 (1988–1997 denominator data unavailable), and the percentage of WRA cases increased from 3% to 6% ($P < 0.01$). In retail trade, the cumulative incidence rate and percentage of cases increased from 0.3 to 1.1 cases per 100,000 workers ($P < 0.01$) and 1% to 6% ($P < 0.01$). In accommodations and food services, the cumulative incidence rate increased from 0.7 to 1.5 during the first two periods, then decreased to 1.1 cases per 100,000 workers during 2008 to 2018, while the percentage of cases increased from 2% to 5% ($P < 0.01$). The inconsistent findings between percentages of cases and rates in health care, education, and accommodations and food services may in part be explained by the relatively small number of cases in a given time period (education and accommodations and food services) and/or the increasing workforce

**Table 2.** Breathing test results of confirmed work-related asthma cases: Michigan, 1988–2018

| Breathing Test Results | Time Period | | | |
|---|---|---|---|---|
| | 1988–1997 | 1998–2007 | 2008–2018 | All Years |
| Total No. of cases | 1,274 | 1,461 | 899 | 3,634 |
| Conducted any testing for hyperreactivity* | 672 (53) | 632 (43) | 310 (34) | 1,614 (44) |
| Positive result | 400 (60) | 292 (46) | 140 (45) | 832 (52) |
| Conducted any breathing test in relation to work | 67 (5) | 72 (5) | 40 (4) | 179 (5) |
| Any positive result | 41/67 (61) | 44/72 (61) | 23/39 (59) | 108/179 (61) |
| Peak flow meter, positive result | 20/28 (71) | 16/28 (57) | 15/19 (79) | 51/75 (68) |
| Pre- and post-shift spirometry, positive result | 17/20 (85) | 30/44 (68) | 11/16 (69) | 58/80 (73) |
| Specific bronchoprovocation, positive result | 4/9 (44) | 0/3 (–) | 0/0 (–) | 4/12 (33) |

Data are frequency (%). Totals vary owing to missing information. Testing for hyperreactivity was missing for 2,020, information for peak flow meter testing was missing for 814, information for before and after shift spirometry was missing for 805, and information for specific bronchoprovocation was missing for 1,080.
*Methacholine challenge test result or before and after bronchodilation result.

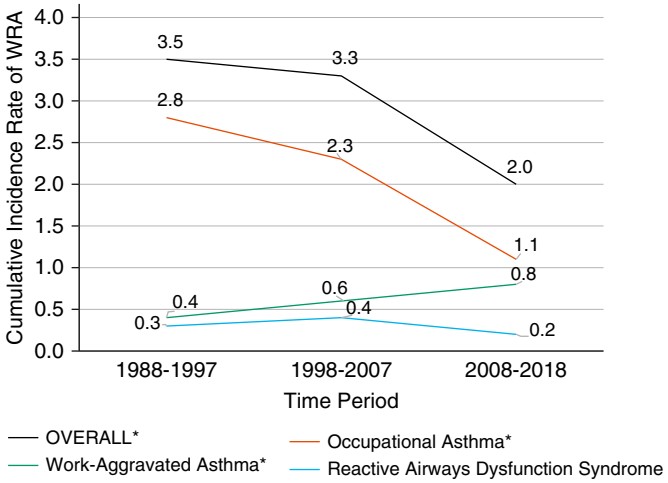


**Figure 2.** Cumulative incidence rate of work-related asthma (WRA) per 100,000 workers, overall and by type of asthma: Michigan, 1988–2018. We used the midpoint year of each time period (1992, 2002, and 2012) for the counts of Michigan employment for the denominators for the cumulative incidence rates by time period (1988–1997, 1998–2007, and 2008–2018) from the State of Michigan Bureau of Labor Market Current Employment Estimates for 1992, the Bureau of Labor Statistics Quarterly Census of Employment and Wages for 2002 and 2012, and the Census of Agriculture State Data for all three periods. *Time trend $P \leq 0.05$.

(health care and accommodations and food services).

Figure 5 and Table E3 show the changes over time for the top workplace exposures: cleaning agents, isocyanates, metalworking fluids, manufacturing and office, and all other low- (i.e., chemicals, metals) and high- (i.e., organic material) molecular-weight exposures. WRA cases exposed to cleaning agents increased from 5% to 20% over time ($P < 0.01$), while those exposed to isocyanates decreased from 20% to 7% ($P < 0.01$). Metalworking fluid exposures decreased from 12% to 4% ($P < 0.01$). All other high-molecular-weight compounds increased from 7% to 13% ($P < 0.01$). There was no significant change over time for WRA cases associated with other manufacturing exposures, office exposures, and all other low-molecular-weight compounds.

The confirmed cases worked in 2,601 facilities. Michigan OSHA inspected 806 of those facilities and conducted air sampling during 571 (71%) of the inspections. Thirty (5%) inspections identified an exposure to a known asthma inducer above the enforceable PEL. Companies inspected with exposures above the PEL decreased from 5% to 4% and then increased to 10% over time. During the inspections, 10,493 coworkers of the index cases completed the confidential respiratory questionnaire; 1,622 (15%) reported being bothered at work by daily or weekly chest tightness, shortness of breath, or wheezing, or having new-onset asthma since beginning to work at the facility. Symptomatic coworkers decreased over time from 18% to 12% (Table 3).

## Discussion

Since 1988, the Michigan surveillance system confirmed 3,634 WRA cases, primarily through physicians and hospital discharge data (Figure 1). Nine individuals died from an asthma attack due to a workplace exposure (Table E1 and Appendix E1 in the online supplement). The reports submitted to the state have decreased by 29% from 1988 through 1997 to 2008 through 2018 (Table 1). We attribute the decrease to physician reporting fatigue, even though reporting is required by Michigan law, and workplace improvements in some industry sectors. Evidence of reporting fatigue is illustrated by the increase in hospital reporting and decrease in reporting by individual healthcare providers over time (Figure 1). This may also explain the increase in the percentage of WAA cases (Table 1), which are more commonly reported by hospitals. Surveillance systems internationally have also reported a downward trend in WRA, although England noted a small increase in reports during 2015 to 2017 (30); we have not seen a similar increase in Michigan.

When an adult seeks care for new-onset or preexisting asthma, healthcare professionals may focus on treating symptoms rather than also taking a workplace exposure history (31, 32). Workers themselves may not recognize the association of work with their symptoms or may have financial concerns including job loss (33, 34). This underrecognition has been noted internationally (28, 35, 36). Even when recognized, delays of 2 to 5 years between onset of symptoms and the diagnosis of WRA have been reported (37). The Michigan worker who died from isocyanates, with 18 medical encounters from the onset of symptoms to his death, illustrates how these factors can result in tragic and avoidable consequences (Appendix E1). We are not aware of any data to suggest that underrecognition of WRA has changed over time.

Improved workplace engineering and controls, such as enclosure of work processes, product substitution, and use of personal protective gear, especially for certain exposures in manufacturing such as metalworking fluids and isocyanates, could also account for the decrease in WRA cases. For example, despite a slight increase in the number of facilities using isocyanates in Michigan, from 107 in 2014 to 111 in 2016, the number of cases of isocyanate-induced asthma continues to decrease (38, 39). The overall decrease of WRA cases reported in manufacturing may explain the increase of WRA cases among women over time, as manufacturing is typically overrepresented by men.

However, WRA associated with some exposures has increased, especially cleaning products. Cleaning product exposures are found across all industries, generally with less-standardized work practices than those applied in a manufacturing setting.

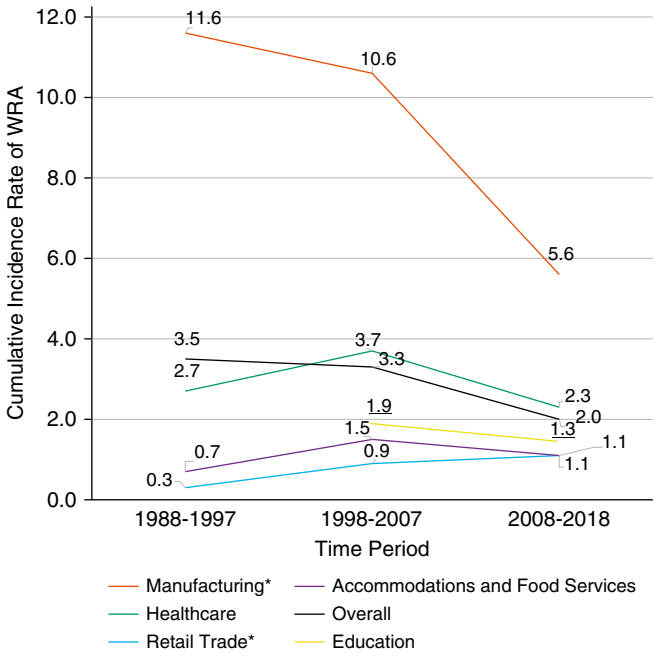


**Figure 3.** Cumulative incidence rate of work-related asthma (WRA) per 100,000 workers, overall and by industry, reported as source of exposure for confirmed WRA cases: Michigan, 1988–2018. We used the midpoint year of each time period (1992, 2002, and 2012) for the counts of Michigan employment overall and by industry for the denominators for the cumulative incidence rates by time period (1988–1997, 1998–2007, and 2008–2018) from the State of Michigan Bureau of Labor Market Current Employment Estimates for 1992, the Bureau of Labor Statistics Quarterly Census of Employment and Wages for 2002 and 2012, and the Census of Agriculture State Data for all three periods. *Time trend $P \leq 0.05$.

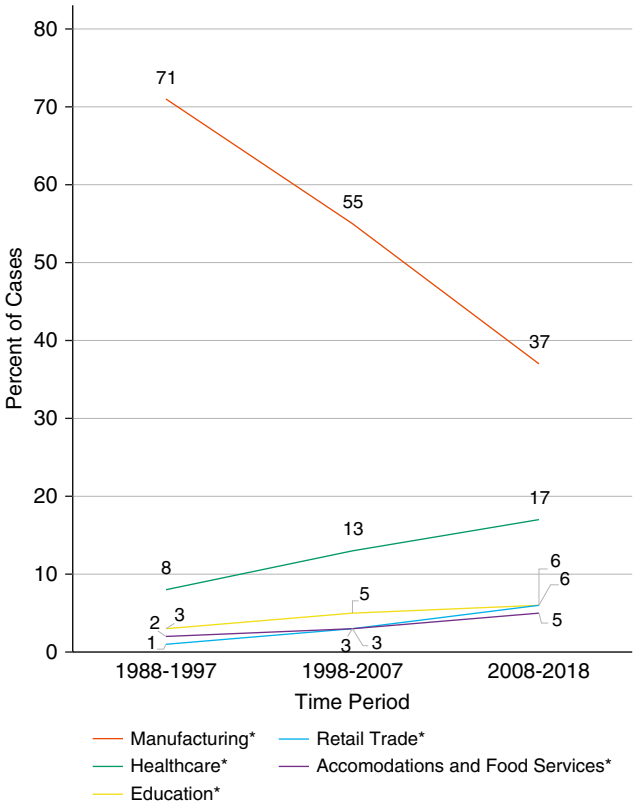


**Figure 4.** Top five industries reported as source of exposure for confirmed work-related asthma cases: Michigan, 1988–2018. *Time trend $P \leq 0.05$.

Accordingly, cleaning product exposures are more difficult to control (40). Increased use, inappropriate use, and ingredient changes in disinfectants may also help explain the increase in WRA cases associated with cleaning products. Despite lack of evidence that their use is effective in preventing infectious disease in schools, daycare, and food establishments (41, 42), and even for some situations in healthcare facilities (43), disinfectants are regularly used across all industries.

Regardless of the reason for overall decreased reporting of WRA, evidence suggests that surveillance systems, including Michigan's, identify less than half of all WRA cases. The American Thoracic Society (ATS) 2003 consensus statement estimated that 15% of adult asthma is caused by work (4). In the 2005 Behavioral Risk Factor Surveillance System random sample of Michigan, Minnesota, and Oregon residents, more than half reported their asthma was caused or made worse by any job they ever had (6). Washington found similar results examining their Behavioral Risk Factor Surveillance System data from 2006 to 2009, wherein 55% of respondents reported their asthma was caused or made worse by their work (7). In 2011, a second ATS consensus statement estimated that 21.5% of adults with asthma have WAA (5). The combined estimates from these consensus statements and studies suggest that up to 55% of all adult asthma is work related, which is consistent with the estimate in a 2018 ATS educational document (8). To understand the magnitude of underreporting, we can apply these estimates to the Michigan adult asthma population, which would suggest a prevalence of 97,500 Michigan adults with WRA (4). Using capture-recapture analysis, we would expect a WRA incidence of 228 to 801 Michigan adults (44).

There is a significant cost associated with WRA. The estimated annual WRA cost for medical care and lost time in the United Kingdom was $100 million, with 49% of the cost borne by the patient, 48% by the state, and 3% by the employer (11). Using primarily data from WC, Washington estimated costs of >$3 million dollars for 1,285 cases identified from 2001 to 2008 (22). Michigan does not have cost estimates. However, Michigan workers likely bear a high percentage of the costs associated with WRA, given that only 49% applied for WC benefits, and less than half of those applying received benefits, even though there was a significant increase over time in the percentage of individuals awarded WC if they applied, from 37% to 47% (Table 1). WC is a useful benefit for a chronic disease like WRA, covering partial wage replacement and having no deductible for medical care, including costly asthma medication.

We examined the time trends of multiple factors/outcomes over the 31 years, and although the changes over time make sense, with multiple comparisons it is possible that some of the statistically significant changes were due to chance alone.

Poor documentation of asthma likely contributes to the small percentage of individuals who received WC in Michigan; only 50% of patients had pulmonary function tests and only 5% had pulmonary function tests performed in relationship to work (Table 2). This reflects the standard of medical care in the United States, where the diagnosis of asthma and WRA is frequently made from the patient's history and response to a trial of asthma medication, despite National Heart, Lung, and Blood Institute guidelines recommending a measure of hyperreactivity (45). More frequent use of objective pulmonary function testing performed in relation to work would give healthcare providers more confidence to determine when to advise their patients to leave their workplace exposure. Numerous expert guidelines outlining diagnostic tools for healthcare practitioners in their assessment of a worker with suspected WRA are available (28, 36).

There are no screening tests and/or history that sufficiently predict whom to exclude from workplace exposure to asthma-causing agents. Personal habits like cigarette smoking and individual susceptibility measured through personal or family history of allergies do not predict who will develop WRA (3, 46). About half of the patients with WRA identified through the Michigan surveillance system had no personal or family history of allergies, and 80% were not smoking cigarettes at the time their asthma symptoms developed (Table 1). The increase seen in the percentage of

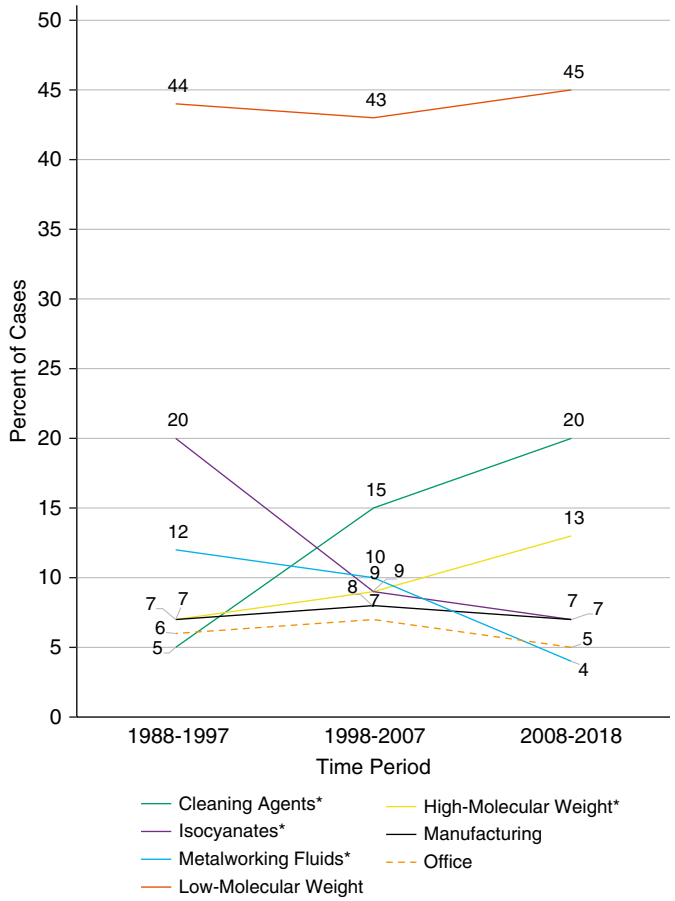


**Figure 5.** Most commonly reported exposures at work for confirmed work-related asthma cases: Michigan, 1988–2018. *Time trend $P \leq 0.05$.

non–cigarette smokers presumably reflects the decreased prevalence of cigarette smoking in the general population and possibly the tendency for physicians to be more likely to diagnose WRA if the patient does not smoke.

Most facilities where the patient developed WRA were in compliance with OSHA exposure standards, yet high percentages of symptomatic coworkers were identified in those facilities (Table 3). Accordingly, healthcare providers should use caution when factoring exposure-monitoring results into their diagnostic and management decisions. Workers can develop new-onset WRA and experience WAA from exposures well below established OSHA PELs or after nonroutine exposures, such as leaks or spills.

Inspections decreased over time for several reasons: inspections were conducted for new-onset WRA, not WAA; inspections were conducted where there were potential OSHA-enforceable standards for the suspected exposure; there was a decrease over time in WRA cases from manufacturing, where there were more likely to be OSHA-enforceable standards; and, generally, each location was inspected once because there was less likelihood of identifying additional standard violations once a company was inspected by Michigan OSHA for a WRA case, even if new cases were reported from that company after the inspection was completed.

Fifty-two percent of the new-onset non-RADS cases reported in the Michigan surveillance system were to substances not known to cause WRA (1); these either represent cases caused by chronic irritant exposures (27, 28), substances not yet identified to cause an immunologically mediated WRA, or the inability to properly identify that the cases were exposed to a known cause of OA.

Given that one cannot predict who will develop WRA in the workplace, and that exposures to asthma-causing agents are often well below permissible limits, workplace medical monitoring is an important secondary prevention opportunity to reduce the burden of WRA (47). The longer a person with asthma remains exposed to an asthma-causing agent in the workplace, the more likely their asthma will become a chronic problem (46, 48). A review of companies using isocyanates in Michigan showed that only 30% provided periodic medical surveillance (47, 49). Periodic medical monitoring of workers exposed to known asthma-causing agents can help identify workers with asthma-like symptoms early, so that they can be removed from exposure, decrease

**Table 3.** Michigan OSHA inspections at facilities with work-related asthma cases: Michigan, 1988–2018

| | Time Period | | | |
|---|---|---|---|---|
| | 1988–1997 | 1998–2007 | 2008–2018 | All Years |
| Total No. of inspections | 437 | 266 | 103 | 806 |
| Inspections where air sampling performed for known asthma inducer, *n* | 296 | 203 | 72 | 571 |
| Known asthma inducer above Michigan OSHA PEL | 15 (5) | 8 (4) | 7 (10) | 30 (5) |
| Coworkers interviewed about respiratory health, *n* | 6,293 | 3,200 | 1,000 | 10,493 |
| Coworkers bothered at work by daily or weekly chest tightness, shortness of breath, or wheezing or onset of asthma since beginning work at this facility | 1,125 (18) | 380 (12) | 117 (12) | 1,622 (15) |

*Definition of abbreviations*: OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit.
Data are frequency (%) unless otherwise noted.

morbidity, and increase the likelihood of clinical remission (50). These elements and challenges of effective medical monitoring have been well described (28, 35, 51). Medical monitoring alone without appropriate exposure restrictions, such as that which occurred in the Michigan WRA death from isocyanates, illustrates the danger of an incomplete medical surveillance program (Appendix E1).

## Conclusions

The industries and exposures where adults develop WRA changed over the past 31 years. The identification of WRA cases, including WRA deaths, underscores the need for continued vigilance to monitor changes in where and how workers are exposed to asthma-causing agents.

Healthcare providers should consider the workplace in new-onset and worsening adult asthma. The potential that >50% of adults with asthma have exposures at work that cause or aggravate their asthma emphasizes why healthcare providers and asthma education programs must address work exposures in diagnosing and managing adult asthma (4–8, 46). Breathing tests for patients with suspected WRA would assist practitioners in advising their patients whether to leave the exposure and when to file for WC benefits.

Exposure standards and practices to reduce exposures, along with a requirement for medical monitoring, should be adopted in the workplace. Appropriate exposure restrictions should be implemented when symptomatic individuals are identified through medical monitoring. Increased awareness by healthcare providers of the role work plays in adults with asthma would reduce the morbidity and mortality of WRA. ■

**Author disclosures** are available with the text of this article at www.atsjournals.org.

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**Online Data Supplement**

**The Burden of Work-Related Asthma in Michigan, 1988-2018**

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Supplemental Table 1 Summary of Nine Work-Related Asthma Deaths, Michigan, 1988-2018

| Year | Age at Death | Sex | Exposure | Industry/Occupation | Asthma Type | Years With Asthma | FEV1 on Last Baseline Spirometry Done Before Death |
|---|---|---|---|---|---|---|---|
| 1998 | 67 | F | Mold Machine Release Spray | Rubber & Plastic Parts Manufacturing/ Machine operator | OA | 16 | 59% of Predicted |
| 2003 | 45 | M | Isocyanates | Auto Detailing/ Truck bed liner sprayer | OA | 1 | None |
| 2004 | 19 | F | Second Hand Cigarette Smoke | Restaurant/Waitress | Aggravated | 16 | None |
| 2004 | 75 | F | Chlorine, HCL & Phosphoric Acid | Agriculture/Farmer Cleaning Milk Tanks | Aggravated | Unknown | 84% of Predicted |
| 2005[1] | 50 | M | Isocyanates | Adhesive Manufacturing/ Production worker | OA | 4 | 97% of Predicted |
| 2006 | 77 | F | Toluene Diisocyanate | Auto Seat Manufacturing/ Machine operator | OA | 26 | 33% of Predicted |
| 2007 | 54 | M | Welding Fumes, Chemicals | Plastic Car Parts Manufacturing/ Welder | Aggravated | 37 | 36% of Predicted |
| 2013 | 21 | M | Construction | Construction/Laborer | Aggravated | Child | None |
| 2015 | 43 | M | Isocyanates | Rubber & Plastic Parts Manufacturing/ Casting room machine operator | OA | 1 | None |

[1] Full case history in Appendix 1.

Supplemental Table 2 Industry of Work-Related Asthma Cases, Michigan, 1988-2018

| | Time Period | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 1988-1997 | | | 1998-2007 | | | 2008-2018 | | |
| Industry[1] | Rate | # (%) | Employees[2] | Rate | # (%) | Employees | Rate | # (%) | Employees |
| Agriculture, Forestry, Fishing, & Hunting | 0.9 | 4(<1) | 46,562 | 1.5 | 12 (1) | 79,883 | 0.9 | 8 (1) | 80,304 |
| Mining | | 5 (<1) | | 8.8 | 6 (<1) | 6,799 | 2.9 | 2 (<1) | 6,303 |
| Utilities | | 3 (<1) | | 2.4 | 5 (<1) | 20,502 | 5.3 | 12 (1) | 20,458 |
| Construction | | 32 (3) | | 1.8 | 37 (3) | 204,876 | 2.2 | 32 (4) | 132,219 |
| Manufacturing | 11.6 | 910 (71) | 787,800 | 10.6 | 809 (55) | 762,165 | 5.6 | 333 (37) | 535,815 |
| Wholesale Trade | 1.5 | 22 (2) | 151,600 | 0.8 | 14 (1) | 174,805 | 0.2 | 3 (<1) | 158,882 |
| Retail Trade | 0.3 | 17 (1) | 486,000 | 0.9 | 48 (3) | 530,118 | 1.1 | 52 (6) | 448,234 |
| Transportation & Warehousing | 1.2 | 14 (1) | 116,300 | 2.6 | 35 (2) | 136,910 | 1.6 | 22 (2) | 123,849 |
| Information | | 6 (<1) | | 1.4 | 11 (1) | 77,265 | 1.1 | 7 (1) | 57,777 |
| Finance & Insurance | 0.1 | 2 (<1) | 141,700 | 1.1 | 17 (1) | 153,864 | 1.1 | 16 (2) | 135,796 |
| Real Estate & Rental & Leasing | 0.4 | 2 (<1) | 46,600 | 2.0 | 11 (1) | 55,552 | 1.1 | 6 (1) | 48,252 |
| Professional, Scientific & Technical Services | 0.4 | 9 (1) | 216,000 | 0.6 | 16 (1) | 258,722 | 0.3 | 7 (1) | 248,860 |
| Management of Companies & Enterprises | -- | 0 | 59,700 | 0.1 | 1 (<1) | 68,416 | 0.2 | 1 (<1) | 54,601 |
| Administrative & Support & Waste Management | 0.6 | 10 (1) | 156,900 | 1.0 | 27 (2) | 265,300 | 1.4 | 43 (5) | 277,033 |
| Educational Services | | 40 (3) | | 1.9 | 73 (5) | 384,438 | 1.3 | 50 (6) | 343,525 |
| Healthcare & Social Assistance | 2.7 | 105 (8) | 392,800 | 3.7 | 194 (13) | 518,224 | 2.3 | 153 (17) | 606,008 |
| Arts, Entertainment & Recreation | 1.3 | 5 (<1) | 38,900 | 1.6 | 11 (1) | 68,144 | 2.8 | 16 (2) | 51,268 |
| Accommodation & Food Services | 0.7 | 20 (2) | 292,100 | 1.5 | 49 (3) | 336,905 | 1.1 | 43 (5) | 350,187 |
| Other Services (except Public Administration) | | 22 (2) | | 2.3 | 31 (2) | 136,616 | 2.1 | 30 (3) | 127,241 |
| Public Administration | | 44 (3) | | 3.0 | 46 (3) | 151,348 | 2.8 | 52 (6) | 171,797 |
| Unknown | | 2 (<1) | | | 8 (1) | | | 11 (1) | |
| Total | 3.5 | 1,274 | 3,610,462 | 3.3 | 1,461 | 4,470,093 | 2.0 | 899 | 4,015,999 |

Data are rate per 100,000, frequency and percentage, and total number of employees.

[1]Industry was coded to the 2-digit 2002 North American Industry Classification System (NAICS).

[2]We used the midpoint year of each time period (1992, 2002 and 2012) for the counts of Michigan employment overall and by industry for the denominators for the cumulative incidence rates by time period (1988-1997, 1998-2007 and 2008-2018) from State of Michigan Bureau of Labor Market Current Employment Estimates (CES) for 1992, the Bureau of Labor Statistics (BLS) Quarterly Census of Employment and Wages (QCEW) for 2002 and 2012, and for Agriculture from the Census of Agriculture State Data for all three periods. We used the 2002 midpoint BLS QCEW and Census of Agriculture data for the denominator for the cumulative incidence rate for all years combined. Some rates are not calculated because denominator data was not available for that industry group during that time period.

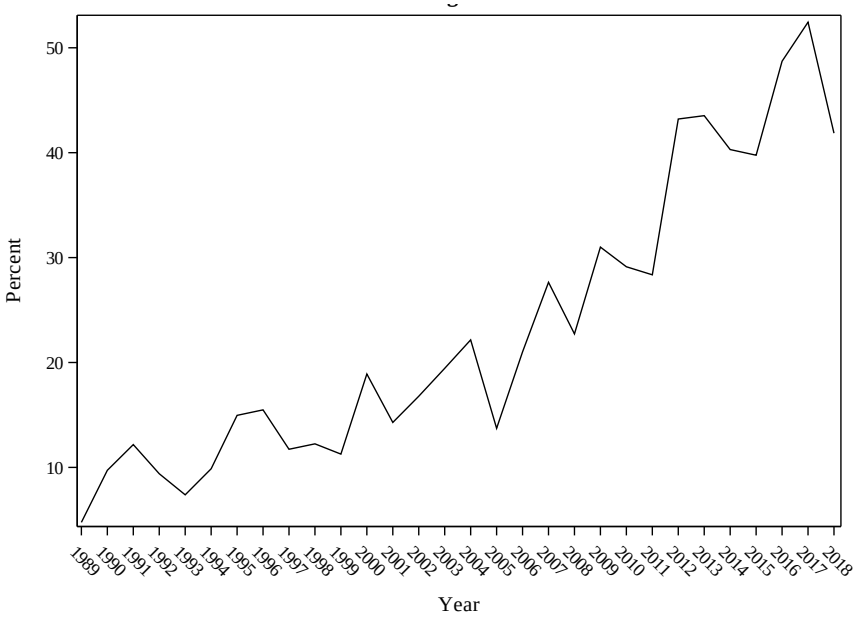
Supplemental Table 3 Work-Related Asthma Cases by the Five Most Common Types of Exposures and All of the Other High- and Low-Molecular-Weight Compounds, Michigan, 1988-2018

| | Time Period | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 1988-1997 | | 1998-2007 | | 2008-2018 | | All Years | | Percent Change |
| Total number of WRA Cases | 1,270 | | 1,455 | | 887 | | 3,612 | | |
| Agent[1] | # | % | # | % | # | % | # | % | |
| Cleaning agents | 58 | (5) | 211 | (15) | 177 | (20) | 446 | (12) | +300% |
| Isocyanates | 253 | (20) | 136 | (9) | 64 | (7) | 453 | (13) | -65% |
| Metalworking fluids | 153 | (12) | 141 | (10) | 35 | (4) | 329 | (9) | -67% |
| Manufacturing chemicals | 89 | (7) | 119 | (8) | 59 | (7) | 267 | (7) | No change |
| Office exposures | 72 | (6) | 98 | (7) | 40 | (5) | 210 | (6) | -17% |
| All other high-molecular weight compounds | 90 | (7) | 128 | (9) | 113 | (13) | 331 | (9) | +86% |
| All other low-molecular weight compounds | 555 | (44) | 622 | (43) | 399 | (45) | 1,576 | (44) | +2% |

Definition of abbreviation: WRA = work-related asthma.
Data are frequency and percentage, and percent change from first to most recent time period.
[1]Agent was missing for 4 cases 1988-1997, 6 cases 1998-2007 and 12 cases 2008-2018.

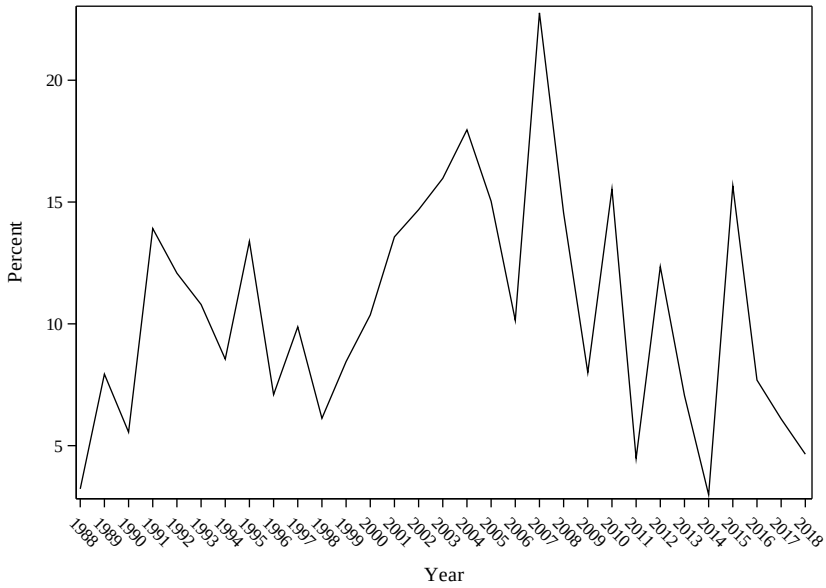
Supplemental Graphs. Trend Analysis by Year Using the Cochran-Armitage Test for Select Characteristics of Confirmed Work-Related Asthma Cases, Michigan, 1988-2018

Trend of Work-Aggravated Asthma, 1988-2018



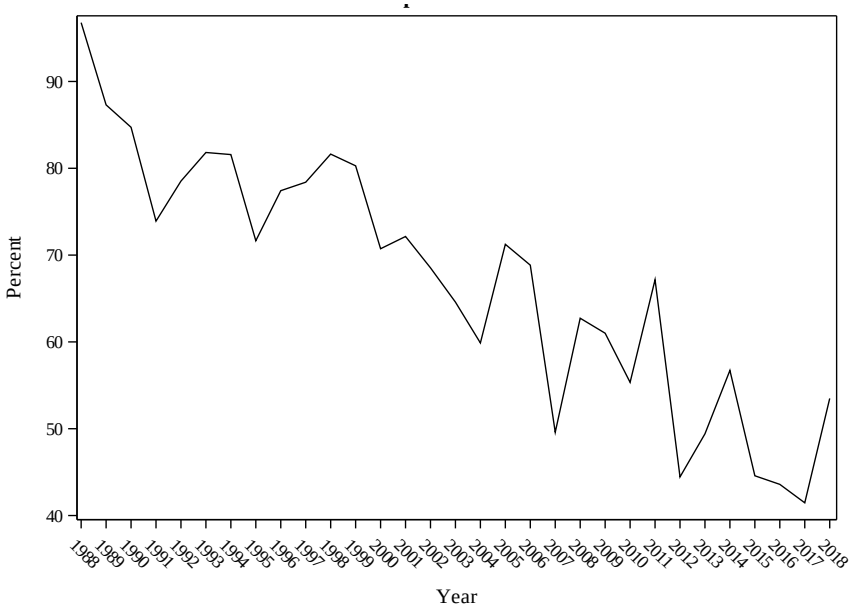

*Cochran-Armitage Trend Test: Two-sided P-value<0.001.*

Trend of RADS, 1988-2018




*Cochran-Armitage Trend Test: Two-sided P-value=0.7315.*

Trend of Occupational Asthma, 1988-2018

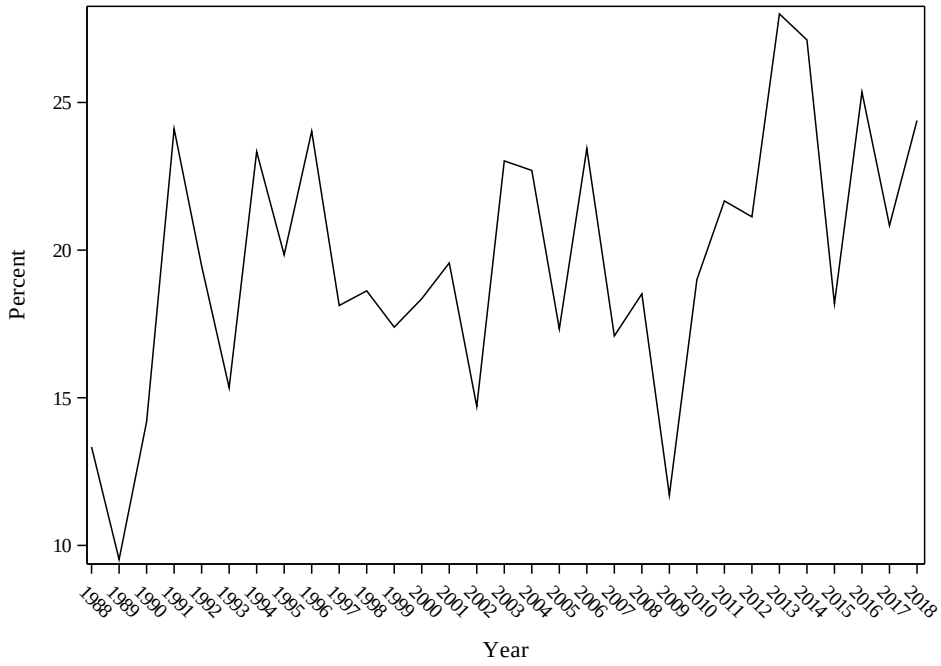



*Cochran-Armitage Trend Test: Two-sided P-value<0.0001.*

Trend of White Population among Work-Related Asthma, 1988-2018

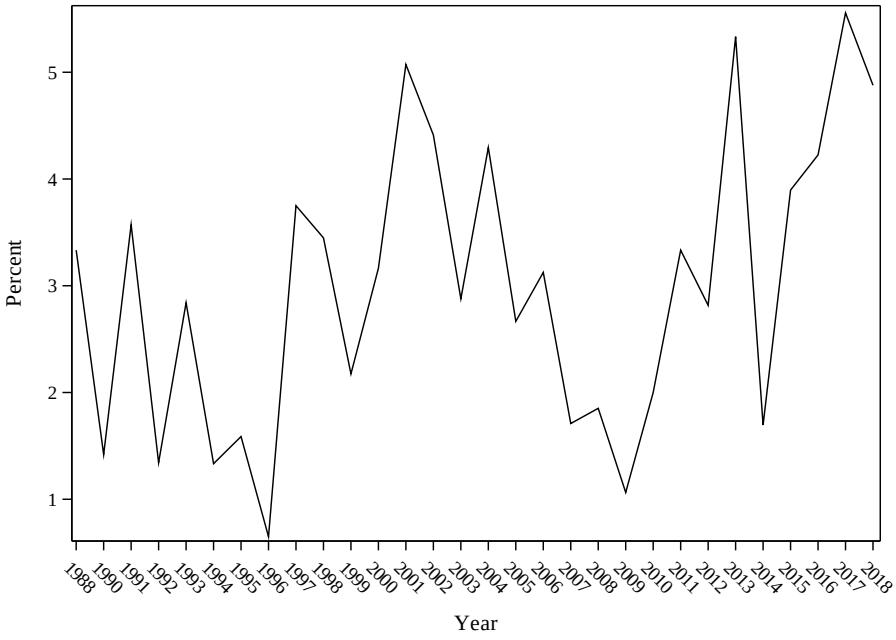

*Cochran-Armitage Trend Test: Two-sided P-value=0.1033.*

Trend of African American Population among Work-Related Asthma, 1988-2018



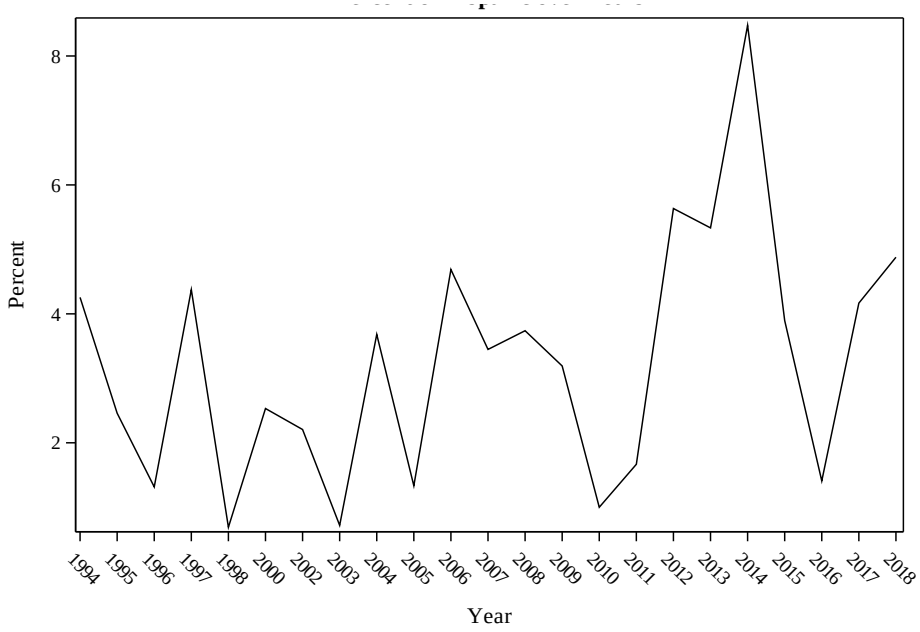

*Cochran-Armitage Trend Test: Two-sided P-value=0.3284.*

Trend of Other Races among Work-Related Asthma, 1988-2018



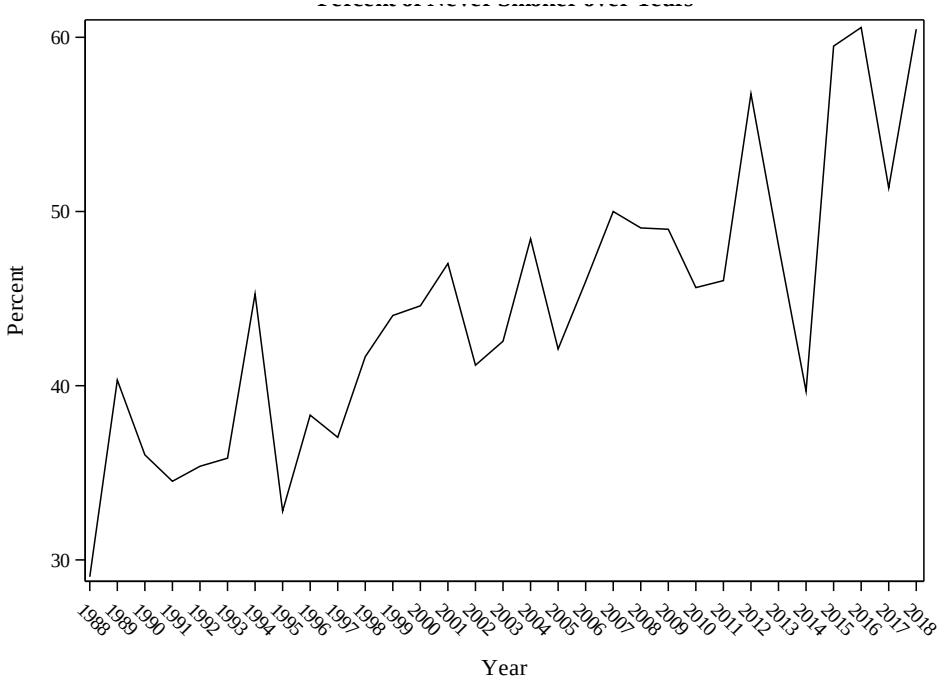

*Cochran-Armitage Trend Test: Two-sided P-value=0.0779.*

Trend of Hispanic Population among Work-Related Asthma, 1994-2018



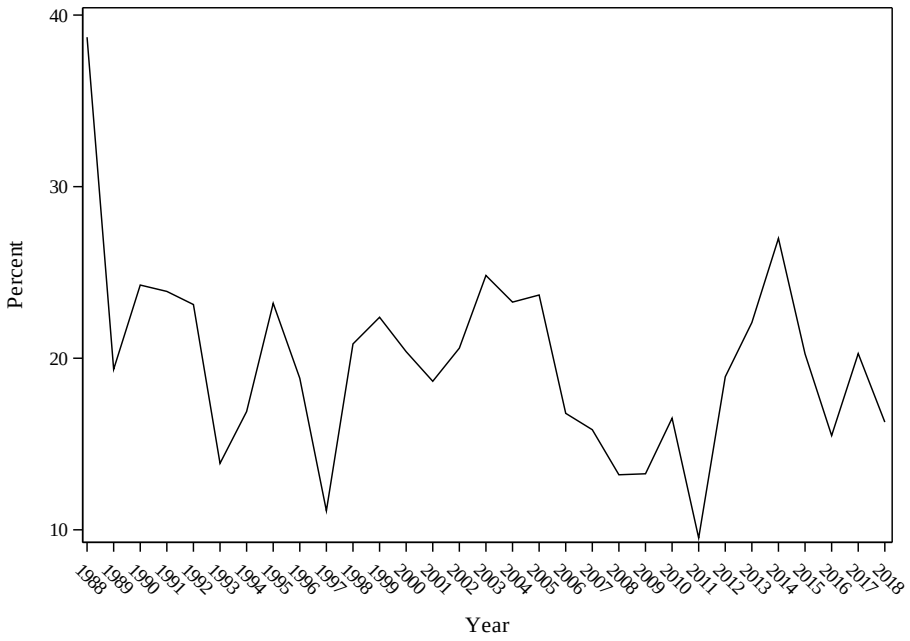

*Cochran-Armitage Trend Test: Two-sided P-value=0.2332.*

Trend of Never Smokers among Work-Related Asthma, 1988-2018




*Cochran-Armitage Trend Test: Two-sided P-value<0.0001.*

Trend of Current Smokers among Work-Related Asthma, 1988-2018

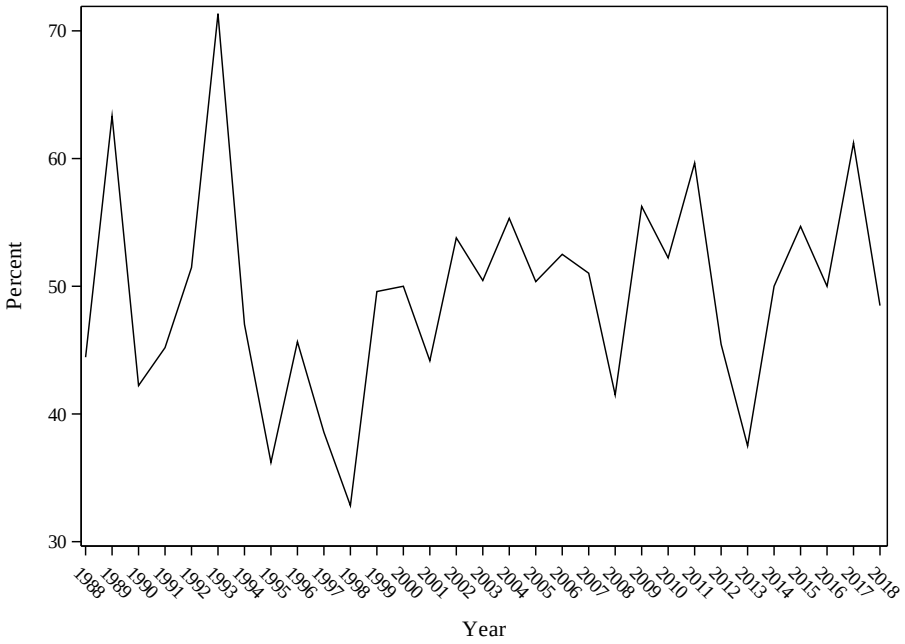



*Cochran-Armitage Trend Test: Two-sided P-value=0.3144.*

Trend of Ex-Smokers among Work-Related Asthma, 1988-2018

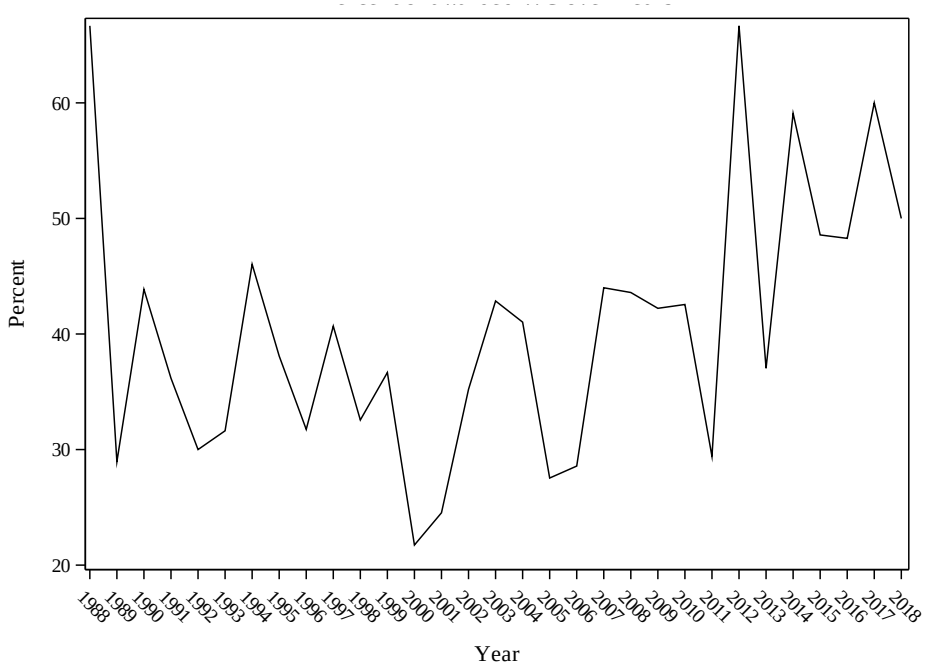

*Cochran-Armitage Trend Test: Two-sided P-value<0.0001.*

Trend of Workers Applied for WC among Work-Related Asthma, 1988-2018




*Cochran-Armitage Trend Test: Two-sided P-value=0.5738.*

Trend of Workers Awarded WC among Work-Related Asthma, 1988-2018

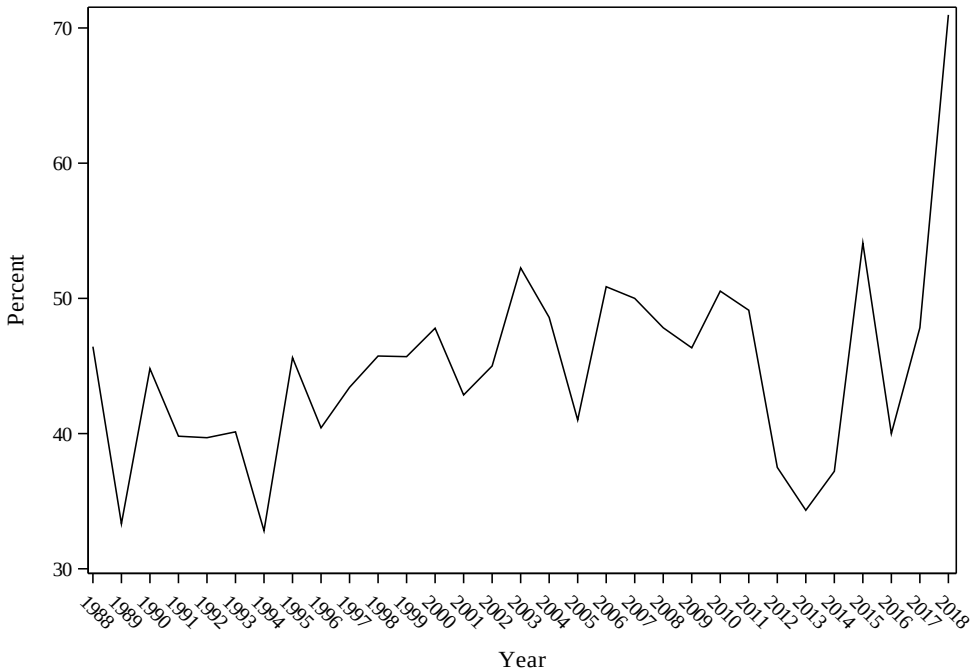



*Cochran-Armitage Trend Test: Two-sided P-value<0.001.*

Trend of Personal History of Asthma or Allergies among Work-Related Asthma, 1988-2018

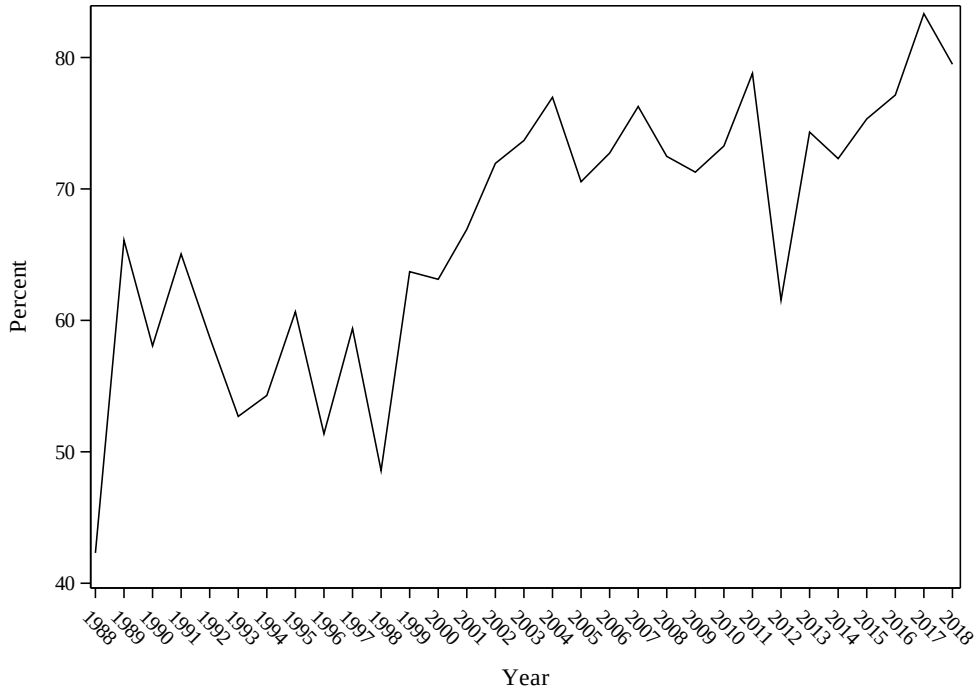

*Cochran-Armitage Trend Test: Two-sided P-value=0.0077.*

Trend of Family History of Allergies among Work-Related Asthma, 1988-2018



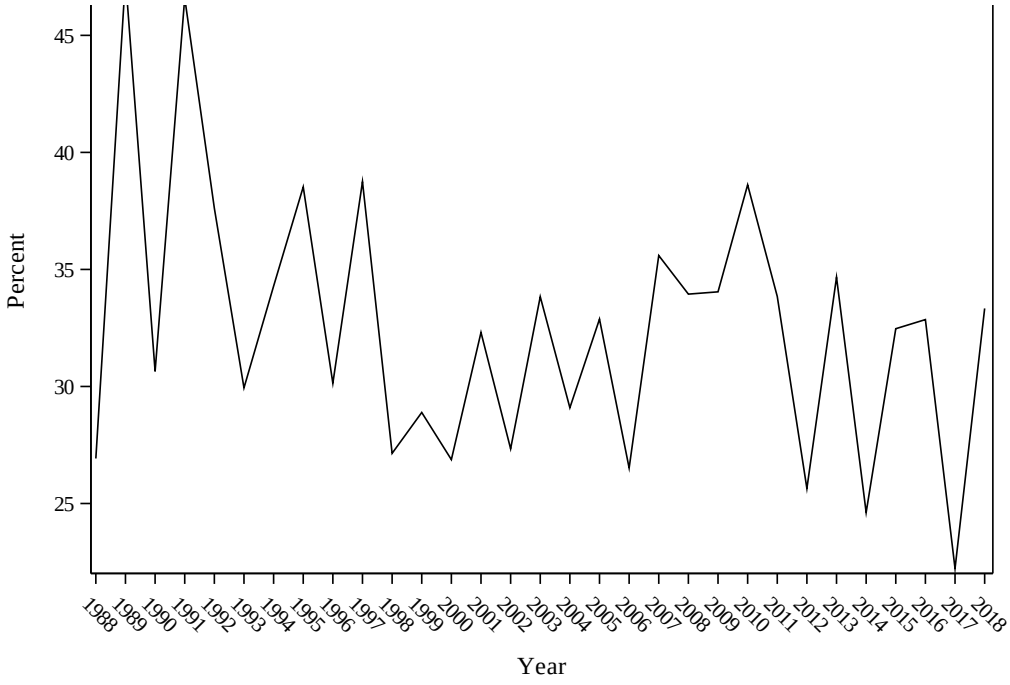

*Cochran-Armitage Trend Test: Two-sided P-value=0.0077.*

Trend of Emergency Department Visits among Work-Related Asthma, 1988-2018




*Cochran-Armitage Trend Test: Two-sided P-value<0.0001.*

Trend of Hospitalization among Work-Related Asthma, 1988-2018




*Cochran-Armitage Trend Test: Two-sided P-value=0.3202.*

APPENDIX 1

## Case History- Work-Related Asthma death from exposure to isocyanates in an adhesive manufacturing factory

A man in his 50's died from an isocyanate-induced asthma attack in a factory that made adhesives. He had worked at this company for five years. He had no personal or family history of allergies or asthma per his family and medical records. He had smoked cigarettes since the age of 16. Spirometry performed by the company at the time of hire was normal at FEV1 97% of Predicted.

The decedent first sought medical care for breathing difficulties at an urgent care facility six months after beginning to work at the factory. After two more visits to the urgent care facility over the next six months, the provider in the urgent care facility recommended the patient find a primary care provider. The primary care provider diagnosed him with asthma. On subsequent visits to the primary care doctor, the doctor noted the relationship between his asthma symptoms and exposure to isocyanates at work and increased his asthma medication. Over the next three years, the patient continued to experience symptoms in relationship to work and went to urgent care twice in addition to his regular primary care provider. In addition, the company provided an annual evaluation and spirometry, which was performed by a local family practitioner. His spirometry on the fourth annual testing required by the company showed a 1.18 liter decrease in his FEV1. The medical record of that encounter stated the patient should stop smoking with no recommendation regarding work restrictions. A year later, the patient asked his primary care physician for medical restrictions to be sent to the company. Although the primary care physician recognized that the patient's symptoms were related to work and that the frequent need to use oral steroids was not the "best route", he did not feel comfortable writing the restriction and referred the patient to a pulmonologist. The patient had two visits with a pulmonologist. The pulmonologist documented the patient had hyperreactivity with a 12% improvement in his FEV1 with a bronchodilator. He had no evidence of COPD, with a normal diffusing capacity and the absence of air trapping on lung volumes. His peak flow testing showed a clear worsening with work. The pulmonologist indicated the patient could continue to work but should return in two months for clinical reevaluation and spirometry. The patient collapsed at work prior to the return visit.

In total, the patient had 18 medical encounters for his breathing difficulties before he died. His medical encounters included four medical exams provided by the company, five urgent care visits, seven visits to his primary care physician, and two visits to a pulmonary specialist.

Each physician from whom he sought medical care noted something about his exposure to isocyanates or chemicals and his breathing symptoms or asthma in relation to work. His primary care physician made no recommendations regarding work restrictions, and did not refer him to a pulmonologist until the patient himself inquired whether there was a medical reason he could leave this job.

On the day of his fatal asthma attack, the decedent had been working third shift in a mixing room where isocyanates were added to reactors and the finished product was unloaded from these reactors. Towards the end of his shift, the decedent was observed staggering from a warehouse area, signaling to co-workers that he could not breathe. He may have used his asthma inhaler, as a co-worker noticed he had it in his hand. A co-worker helped the decedent to a break room, where he collapsed in the doorway. His co-workers provided oxygen. Police

arrived five minutes later and began cardiopulmonary resuscitation. The decedent suffered cardiac arrest. An automatic external defibrillator indicated against shocking the patient. EMS personnel arrived next and transported him to a nearby hospital. A spontaneous pulse was regained after approximately 25 minutes of resuscitation efforts, but the decedent never regained consciousness and died in the hospital six days later. An autopsy ruled out an acute myocardial infarction, pulmonary emboli, stroke or acute rupture of an organ. His pulmonary microscopic exam showed chronic changes of asthma.

The company was inspected twice by MIOSHA after this death, and cited for: a serious violation of the Medical Services and First Aid Standard for failing to send the decedent for medical evaluation when, on multiple occasions, he complained of respiratory difficulties at work; an other-than-serious violation for failing to record the death on the MIOSHA Injury and Illness 300 log; and a serious violation in a second inspection for an inadequate respiratory protection program. At the time of inspection, review of medical records of five of 18 co-workers of the decedent were identified with respiratory changes of concern for which no follow up testing had been performed.

A visual abstract was included with the 9 26 2019 submission of the manuscript. There were no changes to the visual abstract associated with this 10 21 2019 revision.