Use of population data for assessing trends in work-related asthma mortality

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Purpose of review
Work-related asthma has been associated with poorer asthma control and frequent unscheduled healthcare visits, and can be fatal. Case reports of work-related asthma deaths are rare, but can initiate efforts to prevent additional cases. We reviewed relevant literature and data sources to evaluate whether analyzing mortality data at the population level can help identify potential sources of exposures that contribute to work-related asthma.

Recent findings
A limited number of population-based studies have addressed work-related asthma mortality. Data on asthma mortality are derived from death certificates using the International Classification of Diseases (ICD) as a standard for coding cause. However, no discrete code for work-related asthma is available. Analysis of asthma mortality relative to industries and occupations appears to identify high-risk jobs that were not identified by analyzing asthma morbidity data.

Summary
Beyond recognized work-related asthma deaths, it is possible that occupational exposures have contributed to other asthma deaths that have gone unnoticed and could potentially be identified by the analysis of mortality data at the population level. Such analyses in the United States appear to assist in recognizing high-risk occupations and industries. Additional analyses would be possible if a work-related asthma ICD code were available.

Keywords
morbidity, mortality, work-related asthma

INTRODUCTION

Work-related asthma is a subset of asthma that includes new-onset asthma that is caused by factors related to work or the workplace environment (i.e. occupational asthma) and preexisting or concurrent asthma that is worsened by factors related to work (i.e. work-exacerbated asthma) [1,2▪]. Work-related asthma has been associated with poorer asthma control and frequent unscheduled healthcare visits, and can be a fatal disease [3]. A limited number of population-based studies have addressed work-related asthma mortality and most published studies are case reports [4▪,5–7]. We reviewed literature and data sources on asthma deaths with an emphasis on their relationship to work in order to evaluate whether the analysis of population mortality data can help to identify jobs and exposures that contribute to work-related asthma.

ASTHMA EPIDEMIOLOGY

Asthma, a chronic and usually inflammatory disorder of the airways, is characterized by variable and recurring episodic wheezing, shortness of breath, chest tightness, cough, airflow obstruction, and bronchial hyperresponsiveness. It is one of the most prevalent lung diseases worldwide with an estimated 235 million people having asthma in 2015 [8]. In the United States, an estimated 25.7 million persons had asthma in 2010 [9]. Of these, 18.7 (72.8%) million were adults aged at least 18 years. Asthma prevalence among US adults has increased from 6.9% in 2001 to 8.2% in 2010 [9]. In 2009, adult asthma resulted in 7.2 million physician visits, 1.1 million emergency department visits, 600 000

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Curr Opin Allergy Clin Immunol 2019, 19:98–104
DOI:10.1097/ACI.0000000000000508

KEY POINTS

- Case reports of work-related asthma deaths remain a focus of preventive efforts because they serve as sentinel events.
- The analysis of asthma mortality data at the population level may help to identify sources of exposure that contribute to work-related asthma.
- It is not possible to estimate the full magnitude of asthma mortality in relation to work because no discrete code for work-related asthma is available in the current International Classification of Diseases.

hospital outpatient department visits, 299 000 hospitalizations, and 3262 deaths in the United States [10].

WORK-RELATED ASTHMA

Work-related asthma is a commonly occurring disease and an estimated 16.9% (range 8.6–44.0%) of adult-onset asthma is attributed to workplace exposures [11]. Among ever-employed adults with current asthma who participated in the Asthma Callback Survey in 29 states in the United States during 2012–2013, an estimated 15.2% had work-related asthma and an additional 40.8% had possible work-related asthma [12]. In this study, adults with work-related asthma were identified as those who reported having health professional-diagnosed work-related asthma, and adults with possible work-related asthma were identified as those who did not have a health professional-diagnosed work-related asthma but reported that their asthma was caused or made worse by chemicals, smoke, dust or mold in their current or previous job.

Over 300 factors and agents have been associated with work-related asthma [13]. Lists of agents causing work-related asthma are continuously revised as new factors and asthmagens are reported [13,14▪,15,16]. An updated list of agents that cause occupational asthma with key references is available online [17▪▪]. A 2018 review by Dao and Bernstein [18] summarized major causes of occupational asthma and provided a list of occupations that place workers at risk. In addition, the authors outlined steps in evaluating patients with suspected occupational asthma [18].

Compared with adults with nonwork-related asthma, adults with work-related asthma have poorer asthma control [3] and more frequent asthma-related healthcare visits, emergency department visits and hospitalizations for a similar level of airflow obstruction and airway responsiveness [19].

A recent report indicated that during 2011–2016, an estimated 11 million (6.8%) adults in the United States employed at any time in the previous year had current asthma [20]. Among those, 44.7% (4.9 million) experienced at least one asthma attack, and 9.9% (1.1. million) had at least one asthma-related emergency department visit in the previous year. The prevalence of current asthma, asthma attacks, and asthma-related emergency department visits was elevated in certain industries and occupations suggesting increased risks for these health outcomes associated with workplace exposures [20]. For example, among those with current asthma, workers in the education, training, and library occupations had the highest (51.5%) prevalence of asthma attacks, and workers in personal care and service occupations had the highest (17.4%) prevalence of emergency department visits in the past 12 months.

RISK OF ASTHMA ATTACKS AND DEATH

The American Thoracic Society has defined asthma exacerbations as 'events characterized by a change from the patient's previous status' [21]. Severe exacerbations may be unresponsive to treatment with bronchodilators and corticosteroids and require urgent action to prevent hospitalization or death. Workers with asthma may develop asthma exacerbations after exposure to allergic or nonallergic (irritant) factors in the workplace [22]. An estimated 21.5% of adults with asthma experience asthma exacerbations in relation to work [23]. Prevention of severe asthma exacerbations is important because exacerbations have been associated with an accelerated decline of respiratory function [23,24].

Characteristics of patients with asthma who are at high risk for asthma-related death have been summarized by the National Asthma Education and Prevention Program (NAEPP) Expert Panel [24]. Risk factors were grouped in three areas related to: asthma history: previous severe exacerbation (e.g. requiring intubation or admission to an ICU for asthma), two or more hospitalizations for asthma in the past year, three or more emergency department visits for asthma in the past year, hospitalization or emergency department visit for asthma in the past month, using more than two canisters of short-acting beta agonists per month, difficulty perceiving asthma symptoms or severity of exacerbations, lack of a written asthma action plan, sensitivity to *Alternaria* spp.; social history: low socioeconomic status or inner-city residence, illicit drug use, major psychosocial problems; and presence of comorbidities: cardiovascular disease, other chronic lung disease, chronic psychiatric disease. In a 2016 review, D'Amato *et al.* [25] reported similar

risk factors and discussed in detail patient characteristics associated with asthma exacerbations and asthma-related deaths.

WORK-RELATED ASTHMA DEATH CASE REPORTS

Information on work-related asthma deaths is available from case reports. For example, a death from work-related asthma was attributed to exposure to shark cartilage in a mill worker, a tragic event that was investigated by the National Institute for Occupational Safety and Health (NIOSH) in the United States [6]. In addition, the authors discussed previous reports of fatal occupational asthma associated with various agents in printing, pharmaceutical industries, food processing, agriculture, foundries, and autobody industries. State-based surveillance in the United States has also revealed individual work-related asthma deaths. The four states that conducted work-related asthma surveillance during the 1990s into the 21st century identified cases using multiple data sources (e.g. reports form healthcare providers, hospital discharge data, workers' compensation data, death certificates) [26–28]. Identification of such patients triggers a follow-up investigation, which includes evaluating worksite factors potentially responsible for asthma and screening other workers for asthma at the implicated worksite. Despite multiple limitations, these systems offer a unique opportunity to identify work-related asthma cases and related exposures [27,29]. Surveillance in the state of Michigan during 1988–2015 yielded 3417 work-related asthma cases. Among these, seven deaths occurred during 1988–2008 [5,7], and one death occurred in 2015 [28]. The relevant exposures included an isocyanate-containing polyurethane bed liner material that a worker sprayed inside a van [5], and workplace secondhand tobacco smoke exposure experienced by a waitress [7]. Folletti *et al.* [30] in their review of published articles on cleaning agents and asthma identified reports of inhalation accidents in cleaners associated with acute irritant-induced asthma and work-exacerbated asthma [31], but no studies reported on work-related asthma deaths attributed to cleaning agents.

As illustrated by the surveillance data from Michigan, work-related asthma deaths are rare: only 8 of 3417 (0.23%) work-related asthma cases resulted in death. However, the extreme nature of these events often stimulates a series of alerts, fact sheets, and publications that have the goal of preventing workers from experiencing similar exposures and outcomes. For example, the February 2003 asthma death of a worker in Michigan after spraying an isocyanate-containing bed liner inside a cargo van was followed by a series of notices and articles. The Michigan Fatality Assessment and Control Evaluation (MIFACE) program conducted an investigation and generated a case report [32] and the state work-related asthma surveillance program published a summary in an autumn 2003 newsletter [33]. The Washington State Department of Labor and Industries published a related Hazard Alert in March 2003, [34] a Hazard Alert Update in February 2004 [35], and a guide for safe application of spray on truck bed liners in June 2004 [36]. A report of the Michigan case appeared in the peer-reviewed medical literature in 2005 [5]. Also, a column on OSHA Compliance Issues addressed this issue in a professional journal in March 2006 [37]. In September 2006, NIOSH published an alert [38] and a related fact sheet [39] about preventing asthma and death among workers who spray the truck bed liners. During the same era, the Washington State Department of Labor and Industries published peer-reviewed articles about measured levels of methylene-diphenyl isocyanate (MDI) exposure experienced by workers in the spray-on truck bed lining industry [40] and a description of work-related asthma cases attributed to MDI exposure in this industry that received workers' compensation [41].

It is possible that case reports and cases identified via surveillance are unable to fully reveal the occupational contribution to asthma mortality as the association of an asthma death with occupational exposures can go unnoticed [42–46]. For example, previous studies reported that some physicians take inadequate occupational histories from their asthma patients and do not refer suspected cases to occupational medicine or pulmonary physicians for additional evaluation [42,43]. In a 2013 study, 4.7% of incident asthma cases reported their healthcare professional told them they had work-related asthma, but when self-identified cases of work-related asthma were considered as well the proportion was 18.2% [45]. With this in mind, the analysis of mortality data at the population level has the potential to fill in gaps left by other data sources, and therefore contribute to prevention.

ASTHMA MORTALITY DATA SOURCE

The primary source of information on asthma mortality at the population level are death certificates and the International Classification of Diseases (ICD) is the international standard for reporting causes of death [47,48]. Depending on the adopted revision, researchers use relevant codes for identifying asthma deaths and assessing trends [25,49–59]. In general, each successive revision expands disease categories to provide more detailed information. For example, ICD 9th revision (ICD-9) provides a single

code for asthma (493) whereas ICD 10th revision (ICD-10) provides two codes (J45, asthma; and J46, status asthmaticus). In the United States, multiple-cause mortality data are available on an annual basis beginning with data year 1968, and they are classified according to the ICD-10 starting with data year 1999.

The ICD-10 was recently reviewed for modifications and the 11th revision is currently available on the WHO web site [47]. In the ICD-11, the CA23 code for asthma includes expanded categories for allergic and nonallergic asthma (with subcategories for asthma exacerbation and status asthmaticus), other forms of asthma or bronchospasm (including aspirin-induced asthma and exercise-induced bronchospasm), and unspecified asthma. No discrete code for work-related asthma is available.

Death certificates include information on the causal chain of morbid conditions that led to death [60]. When two or more causes are recorded on the certificate, the underlying cause of death defined as 'the disease or injury which initiated the train of morbid events leading directly to death, or the circumstances of the accident or violence which produced the fatal injury' is selected. Any cause of death that is neither the direct, intervening, originating antecedent nor underlying is considered a contributing cause of death [47,60].

MORTALITY DATA LIMITATIONS

Previous studies examined the quality of information from death certificates [61] and researchers recognize data limitations in studying asthma mortality [48]. Frequently mentioned is a lack of cause of death validation against medical records and the possibility of misclassification. For example, asthma deaths might be mistakenly classified as COPD [52,55,57]. Moreover, asthma may be under-ascertained as a cause of death, in particular in an older population [55,56]. Other important issues are limited comparability and accuracy of cause-of-death statistics for assessing trends over time when new ICD versions or revisions are introduced [48,58,61,62]. Anderson *et al.* conducted a comparability study for 113 selected causes of death between ICD-9 and ICD-10 for the United States [62]. For asthma, the authors found a comparability ratio of 0.8855 [63] indicating that asthma was less likely to be selected as the underlying cause of death in ICD-10 than in ICD-9.

As underlying cause-of-death data may underestimate the burden of asthma-related mortality, some researchers have examined deaths for which asthma was listed on the death certificate as either the underlying or a contributing cause of death (i.e. identifying any mention of the disease) [49,56]. For example, McCoy *et al.* [56] found that 45% of all asthma-related deaths in the United States reported for 1990–2001 had asthma listed as the underlying cause of death. A similar proportion (42%) was reported by Fuhrman *et al.* [49] using French mortality data for 2004–2005. The authors of both studies indicated that using multiple-cause of death allows for a better understanding of asthma mortality burden and interpretation of mortality trends when the rules for assigning the underlying cause change [49,56].

None of the ICD revisions includes a distinct code for work-related asthma. Thus, trends in work-related asthma deaths cannot be assessed directly. Steenland *et al.* [64], estimated that 11–21% of asthma deaths might be attributable to occupational exposures. Using this estimate and the US National Vital Statistics System's multiple cause-of-death data for 1999–2016, Patel *et al.* reported that among persons aged 15–64 years, 3664–6994 asthma deaths might be attributable to occupational exposures during 1999–2016 (1573–3002 among men and 2091–3992 among women) [4▪]. Despite the authors' findings that the annual age-adjusted asthma death rate per 1 million persons declined from 1999 to 2016, they could not assess the trend in work-related asthma deaths because of the absence of a separate ICD code for work-related asthma.

The lack of information on asthma deaths in relation to work was evident in other studies [49,56,65]. For example, Gullach *et al.* [65] reviewed Danish 2000–2006 sudden death cases that occurred in persons aged 1–35 years with uncontrolled asthma, using death certificates, medical records, and autopsy reports to identify cases. Among 625 sudden deaths, 49 (8%) decedents had uncontrolled asthma. An acute asthma attack was identified as a cause of death in 13 (27%) of the 49. Remaining deaths were attributed to sudden cardiac death. Although the location of death for 17 decedents was a public place, no additional information on work-relatedness of these deaths was reported.

COMPARING ASTHMA MORBIDITY AND MORTALITY

In evaluating working adults with asthma, it is important to determine whether occupational exposures have contributed to the onset or exacerbation of symptoms [22]. Death certificates are not designed to collect this information. Alternatively, information from records for emergency department visits and hospital stays might be a valuable source for determining work-relatedness of asthma deaths [66]. A recent study in the United States

Table 1. Industries and occupations with elevated asthma prevalence and corresponding proportionate mortality ratios

	Current asthma prevalence [20] (95% confidence interval)	PMR for asthma [4▪] (95% confidence interval)
Total	6.8% (6.7–7.0)	1.0, null value
Industry		
Social assistance[a]	10.3% (8.8–11.8)	Female, 1.35 (1.00–1.79)
Healthcare	8.2% to 8.8%	Female, 1.12 (1.00–1.27) Male, 1.04 (0.74–1.42)
Misc. manufacturing	4.8% (3.3–6.3)	Male, 1.45 (1.13–1.86) Female, 0.75 (0.50–1.07)
Occupation		
Community and social services occupations	7.6% (6.5–8.8)	Female, 1.46 (1.02–2.01)
Healthcare support occupations	8.8% (7.6–10.0)	Female, 1.15 (0.95–1.39)
Office and administrative support occupations	8.0% (7.5–8.6)	Male, 1.25 (0.97–1.61) Female, 0.90 (0.77–1.04)
Sales and related occupations	7.1% (6.5–7.7)	Male, 1.17 (0.95–1.61) Female, 1.09 (0.92–1.30)

[a]Includes child care workers; child, family, and school social workers; personal and home care aides; social and community service managers; and social and human service assistants (https://www.bls.gov/iag/tgs/iag624.htm).

reported an increased prevalence of asthma, asthma attacks, and emergency room visits for asthma among workers in certain industries and occupations [20]. These findings might be because of occupational exposures or self-selection of people with asthma into jobs they might consider free from exposure to asthmagens [67]. Moreover, in US studies, a disproportionate number of workers with asthma, especially in certain industries and occupations, may have inadequate or possibly no health insurance coverage [68]. These workers may have poorly managed and controlled asthma and may be more likely to have unscheduled healthcare visits.

Examining data from two recently published US studies revealed similarities and differences between asthma morbidity [20] and mortality [4▪] relative to industries and occupations. An important caveat is that the two studies presented data for somewhat different categories of industries and occupations, which prevented a more complete comparison of the two types of data. Nevertheless, elevated proportionate mortality ratios (PMRs) for asthma were matched by elevated prevalence estimates for the social assistance (workers in this industry provide a wide variety of social assistance services directly to their clients) and healthcare industries (Table 1). By occupation, the elevated PMRs were matched by elevated prevalence estimates for healthcare support occupations, and office and administrative support occupations. However, in miscellaneous manufacturing industries, elevated PMRs were not matched by elevated asthma prevalence estimates. Similarly, elevated PMRs by occupation were not matched by elevated prevalence estimates for community and social services occupations, and sales and related occupations. The finding of elevated asthma mortality concurrent with morbidity that is not elevated suggests that the excess deaths are not the result of adults with asthma purposely selecting a job to avoid troublesome workplace exposures. This would be especially true for the industry category of miscellaneous manufacturing, which has an elevated PMR matched with an asthma prevalence of 4.8% that is less than the overall estimate of 6.8%. In summary, these comparisons of morbidity and mortality data suggest that when examining data by industry and occupation, asthma-specific mortality might indicate potential problems with workplace exposures and access to appropriate asthma care that are not revealed by asthma-specific morbidity.

CONCLUSION

Early identification of work-related asthma cases and workplace follow-up could prevent asthma-related cases and deaths [1,2▪,24,26]. The analysis of mortality data at the population level appears to add insight regarding potential sources of exposure that contribute to work-related asthma, complementing existing reports of asthma morbidity and mortality. However, the magnitude of asthma mortality in relation to work cannot be sufficiently recognized as no discrete code for work-related asthma is available in the ICD.

Acknowledgements

We would like to thank Mr. Arialdi M. Miniño, National Center for Health Statistics, and Dr Brie Hawley,

National Institute for Occupational Safety and Health for their helpful comments.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

Financial support and sponsorship

Centers for Disease Control and Prevention (CDC), National Institute for Occupational Safety and Health.

Conflicts of interest

There are no conflicts of interest.

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