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Fragrances and work-related asthma–California surveillance data, 1993–2012

Justine Lew Weinberg, MSEHS, CIH[a], Jennifer Flattery, MPH[b], and Robert Harrison, MD, MPH[b]

[a]Public Health Institute, Contractors to the California Department of Public Health, Richmond, CA, USA; [b]California Department of Public Health, Richmond, CA, USA

ABSTRACT

Objective: Fragrance chemicals are used in a large array of products. Workers may be exposed to these chemicals in the workplace directly when used as air fresheners, or indirectly in personal care products used by coworkers or others. This study characterizes work-related asthma (WRA) cases associated with fragrance exposures in California workplaces from 1993 through 2012. *Methods*: We used the California Work-Related Asthma Prevention Program's surveillance database to identify individuals with physician-diagnosed WRA associated with the use of air fresheners and scented personal care products (perfumes, colognes, etc.). Cases were classified using previously published, standardized surveillance methods. *Results*: Perfume was the ninth most common exposure identified from 1993 through 2012. A total of 270 WRA cases associated with fragrance exposure were reported during this period, representing 3.8% of all confirmed cases. These 270 cases included 242 associated with perfume or cologne, 32 associated with air freshener, and 4 associated with both. Similar to non-fragrance cases, nearly a quarter of fragrance-associated cases were classified as new-onset asthma. Fragrance-associated cases were significantly more likely to be in office, health, and education jobs than non-fragrance-associated cases. When compared to non-fragrance cases, fragrance cases were significantly more likely to be female (94% vs 62%) and be classified as having work-aggravated asthma (38% vs 20%), yet had similar outcomes compared with cases associated with other exposures. *Conclusions*: Our surveillance data show that fragrance use in the workplace is associated with WRA. Prevention methods include employee education, enforced fragrance-free policies, well-designed ventilation systems, and good building maintenance.

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Introduction

One of the characteristics that makes fragrance chemicals useful—their volatility—also makes them a potential inhalation hazard. Fragrance chemicals are meant to be breathed in, and yet fragrance chemicals have been associated with asthma and other respiratory effects such as irritation and paradoxical vocal cord movement in a number of studies [1–18], including in the workplace setting. Up until the 1990s, the asthma signs and symptoms that patients experienced from fragrance exposure (i.e., declines in forced expiratory volume in one second [FEV_1], chest tightness, wheezing, rhinitis, cough, dyspnea) were thought to be due to the irritative effects of perfumes in patients with existing bronchial hyperreactivity [2]. However, specific inhalation challenge testing with perfumes and common fragrance ingredients has shown that fragrance ingredients can also have a causative role in new-onset asthma (NOA) [1–4, 8, 10, 12, 14]. The chemicals used in fragrances may not have a common mechanism and the pathogenic mechanisms are not fully understood [1, 2, 4, 11].

There has been reporting of sensitivity to perfume in the general population [5] and in individual occupational case studies [2, 7], but this is the first time state-based surveillance data about WRA associated with fragrance exposures have been examined. In the workplace, fragrances can be used directly in the form of air fresheners, which are intended either to cover up unwanted odors or to add a specific scent to a room. Fragrance chemicals can also be present because they are ingredients in personal care products used by workers, customers, clients, students, and patients.

It is well understood that each scented product can contain a large number of fragrance chemicals. A report produced by the Research Institute for Fragrance Materials states that a fragrance product may contain 50–300 different ingredients [19]. Of relevance in the context of indoor air and potential worker exposure is how many chemicals are emitted from these products. In one study, researchers tested emissions from 44 scented consumer products and detected almost 300 different fragrance chemicals. The number of fragrance chemicals emitted

CONTACT Justine Lew Weinberg justine.weinberg@cdph.ca.gov California Department of Public Health, Occupational Health Branch, 850 Marina Bay Parkway, Building P, 3rd Floor, Richmond, CA 94804, USA.

from each product ranged from 14 to 72 [20]. Another study investigated emissions from 25 different fragranced consumer products, including personal care products and air fresheners, and found 133 different volatile organic compounds (VOCs) with an average of 17 VOCs per product and a range from 6 to 20 VOCs [21].

The International Fragrance Association (IFRA) publishes an online list of fragrance ingredients that member companies have used in products. The current list, based on the IFRA 2011 use survey, contains nearly 3000 materials [22]. According to IFRA's description, the member companies that contributed to the list "represent approximately 90% of the world's production volume of fragrances." How well this self-reported list represents the entire universe of fragrance chemicals is unclear, however estimates of about 2,700–4,000 chemicals have been reported elsewhere [7, 19].

Among the lists of fragrance ingredients are aldehydes, phenols, ketones, terpenes, and other VOCs [19, 22] that are respiratory tract irritants and which may exacerbate asthma and laryngeal disorders. In addition, among the chemicals found in fragrances are substances that can cause asthma in people who have not had asthma before. Substances that can cause asthma *de novo*—either as a sensitizer or irritant—are known as asthmagens [23]. Several chemicals that meet established criteria for asthmagens [23] are found among the chemicals on the IFRA Transparency list [22]. For example, one of these, eugenol, documented to cause NOA [3, 4], was found in the emissions of more than 20% of tested products [20]. Two others, styrene and acetic acid, were also found in a number of products. In another study, researchers measured the volatile emissions from 14 room fragrance products and found 108 chemicals. Among the chemicals detected were the asthmagens eugenol, carene, acetic acid, and methyl methacrylate [24]. Steinemann et al. [21] also found carene and formaldehyde in fragranced products. Other asthmagens among the IFRA list include triethanolamine, zinc oxide, benzalkonium chlorides, didecyldimethylammonium chloride, fenugreek, and turpentine oil [22].

In addition, dozens of chemicals containing carbon-carbon double bonds (C=C) are found both on the IFRA list and in studies of emissions from the fragranced products. Principal among these are terpenes, aldehydes, and alcohols. Essential oils are mostly comprised of terpenes. Importantly, chemicals with C=C bonds react with ambient ozone to form secondary pollutants such as formaldehyde (an asthmagen), ultrafine particles, and chemical irritants [25–30].

In order to characterize work-related asthma (WRA) associated with fragrance exposures, we analyzed data from the California WRA surveillance database for the years 1993 through 2012. The goal of this analysis is to promote recognition and identification of WRA due to fragrance chemical exposures in the workplace and help guide prevention efforts.

Methods

Previous publications have described the criteria used to confirm and classify surveillance cases of WRA [31–33]. From 1993 to 2005, California relied primarily on a single statewide reporting mechanism that requires physicians to notify the state and insurance carriers of suspected work injury or illness, Doctor's First Reports of Occupational Injury and Illness (DFRs). The DFR system is a legislatively mandated California reporting mechanism for all occupational injuries or illnesses, including WRA. In addition to DFRs, since 2006, potential WRA cases have also been routinely identified by reviewing workers' compensation data from the Workers' Compensation Information System (WCIS), as well as all hospital discharge and emergency department records, referred to as patient discharge data (PDD) and emergency department data (ED). All PDD and ED records were reviewed with a primary diagnosis of a Ninth International Classification of Diseases (ICD-9) codes of asthma (493.0–493.9) where either workers' compensation was expected payer, or there was an external cause of injury code indicating the asthma occurred at the workplace (E493.1–E493.3). Potential cases were identified in the WCIS using an algorithm that included either an indication of asthma in the accident description text field, or an ICD-9 of 493.0–493.9 accompanied by other codes (part of body, cause of injury, nature of injury) denoting the incident was respiratory or related to chemical exposure. Codes and descriptions for other respiratory disorders such as vocal cord dysfunction were excluded. DFRs account for 42% of potential cases across all reporting years, but only 20% of potential cases in 2012, as half (50%) of all potential cases are now identified through WCIS data.

Regardless of the reporting source, standardized telephone interviews were attempted with each potential case-patient for confirmation and classification, as well as to characterize exposures, employment and medical history, outcomes, and other occupational and non-occupational risk factors. In addition, medical record review was conducted for all cases reported from ED and PDD, as well as for DFR and WCIS cases with inadequate information for case confirmation. For each case, up to three exposures were recorded as being associated with asthma symptoms, either by the patient or as chronicled in medical records.

Cases were confirmed using previously published National Institute for Occupational Safety and Health surveillance criteria [31–33] if they had a health care provider diagnosis consistent with asthma documented in medical records and an association between symptoms

and work. All cases were confirmed using this standardized surveillance case definition. The term "confirmed" is used for surveillance and not clinical purposes, as objective testing for asthma was not required under this definition [31–33]. Objective testing in addition to a health care provider diagnosis of asthma was not performed. Information collected through interviews and medical record review was used to further classify WRA cases as either NOA or work-aggravated asthma (WAA), based on their first WRA incident. If cases had a history of asthma within 2 years of beginning the job where their first work-related incident began and a work exposure worsened their asthma symptoms, they were classified as WAA. New-onset cases were further delineated into 1) reactive airways dysfunction syndrome (RADS), or asthma without latency that develops after a worker experiences an acute exposure to an irritating agent and symptoms appear immediately, lasting at least 3 months; or 2) occupational asthma, or asthma with latency that develops over time after repeated exposures to an irritant or sensitizer with symptoms that worsen when in the workplace. Some cases have adequate information to confirm that the case is work-related, but inadequate temporal information to distinguish whether asthma first started before any workplace exposure began. These cases could not be reached for interview and are considered "confirmed, but not classified." Industry and occupation were coded using the 2000 Bureau of Census Occupation Codes and the 2002 North American Industry Classification System Codes, and all exposures were coded using the Association of Occupational and Environmental Clinics (AOEC) coding system [23]. Additional questions were asked in the interview regarding occupational history and non-occupational medical history, including: "Have you ever had allergies to dust, grasses, or molds?" and "Have any parents, brothers, sisters or children ever had asthma?"

Cases were identified as associated with fragrances if exposures to perfume or air freshener were coded (AOEC codes 320.23 and 320.42, respectively). Air freshener exposures included products intended to mask odors in the air by emitting fragrance, including sprays, plug-ins, and oils. Perfume exposures included scented body care products, including perfume, cologne, or scented lotions. We used SAS version 9.3 (SAS Institute Inc., Cary, NC) for analyses. To compare select characteristics between fragrance and non-fragrance cases, Fisher's Exact test, *t*-test, and chi-square statistics were used and considered statistically significant at p-values <0.05.

Results

A total of 7,163 confirmed cases of WRA were identified in California from 1993 through 2012, the most recent year for which all interview and medical record review data are complete. The majority of cases (4370, or 61%) were confirmed using medical record information, and an additional 2,793 cases were confirmed using telephone interviews (39%). Of all confirmed cases, 270 (3.8%) were associated with exposure to fragrances as defined above. Fragrance-associated cases (hereafter referred to as "fragrance cases") included 242 associated with perfume or scented body products, 32 associated with air freshener, and 4 cases associated with both. Two-thirds of fragrance cases reported only fragrance exposures. Perfume was the ninth most common exposure among all cases in this time period. All confirmed WRA cases were ascertained through DFRs (58%), WCIS (34%), ED (7%) and PDD (1%), and there was no significant difference between fragrance and non-fragrance-associated cases (hereafter termed "non-fragrance cases") by reporting source. Fragrance cases were significantly more likely to be interviewed (58% vs 38%, $p < 0.0001$).

A comparison of fragrance cases with non-fragrance cases by a variety of characteristics is presented in Table 1. When compared to non-fragrance cases, fragrance cases were significantly more likely to be female (94% vs 62%), older (median age 48 vs 42), and be classified as having WAA (38% vs 20%), but did not differ significantly by race, ethnicity, or smoking history. Cases associated with fragrance were significantly more likely to have a history of allergy (74% vs 66%) and a family history of asthma (58% vs 47%).

Fragrance cases also differed from non-fragrance cases in the occupations that employed them when their WRA began. Table 2 shows the distribution of cases by occupation categories. Fragrance cases were significantly less likely to be in protective services, production, transportation and moving, agriculture and forestry, building and grounds maintenance, installation, repair and maintenance, and construction and mining jobs. Two-thirds of the fragrance cases were in occupations where 70% or more of the workforce is composed of women: education, health care, and office and administrative support [34].

As presented in Table 3, fragrance cases were significantly more likely to still be exposed in the workplace (50% vs 26%). They were also more frequently associated with being in the same job where their work-related breathing problems first began (67% vs 60%) and to have had breathing problems in the prior 2 weeks (62% vs 55%), but these differences were not statistically significant. Fragrance cases were significantly more likely to have had their workers' compensation claim denied (30% vs 21%).

Illustrative Case report: Registered Nurse—WRA from perfume exposure

A 47-year-old nurse was working in the emergency department and developed an immediate onset of cough

Table 1. Selected characteristics of work-related asthma cases by fragrance exposure, California Surveillance Data, 1993–2012.

	Fragrance-associated		Non-fragrance-associated		Total		
Characteristics	#	%	#	%	#	%	*p*-value
Total	270	(100)	6,892	(100)	7,163	(100)	**<0.01**
Sex[*]							
Male	17	(6)	2639	(38)	2656	(37)	
Female	253	(94)	4253	(62)	4506	(63)	
Age							
<20	0	(0)	124	(2)	124	(2)	**0.03**
20–29	23	(9)	1211	(18)	1234	(17)	**<0.01**
30–39	40	(15)	1560	(23)	1600	(22)	**0.03**
40–49	94	(35)	1899	(28)	1993	(28)	**0.01**
50–59	91	(34)	1576	(23)	1667	(23)	**<0.01**
60–64	14	(5)	354	(5)	368	(5)	0.97
≥65	8	(3)	122	(2)	130	(2)	0.15
Unknown	0	(0)	47	(1)	47	(1)	0.17
Race[a]							
White	113	(67)	1859	(63)	1972	(63)	0.29
Black	15	(9)	395	(13)	410	(13)	0.09
Asian	6	(4)	187	(6)	193	(6)	0.15
Native American	7	(4)	87	(3)	94	(3)	0.38
Other	27	(16)	411	(14)	438	(14)	0.45
Ethnicity[a]							
Hispanic	35	(21)	699	(24)	734	(24)	0.51
Not hispanic	130	(79)	2227	(76)	2357	(76)	
WRA classification							
Work-aggravated	103	(38)	1366	(20)	1469	(21)	**<0.01**
New onset	63	(23)	1642	(24)	1705	(24)	0.85
RADS	8	(3)	263	(4)	271	(4)	0.47
Occupational asthma	55	(20)	1379	(20)	1434	(20)	0.88
Confirmed, not classified	104	(39)	3885	(56)	3989	(56)	**<0.01**
History of allergy[b]	105	(74)	1611	(66)	1716	(66)	**0.04**
Family history of asthma[b]	86	(58)	1185	(47)	1271	(47)	**0.01**
Smoking history[b]	53	(35)	927	(36)	980	(36)	0.81

[*]Sex is missing for one non-fragrance case.
[a]Race and ethnicity were collected from telephone interviews or medical records, which were available for just under half of total cases identified.
[b]Variable collected from telephone interview, therefore missing for over half of total cases identified. Percentages refer to proportion of respondents who answered the question.

and chest tightness after exposure to perfume worn by a coworker. Her respiratory symptoms temporarily improved with an albuterol nebulizer. However, she experienced recurrent cough, chest tightness, and wheezing after exposure to another coworker's perfume. Over the next few years, she required emergency treatment with epinephrine injection, albuterol, and intravenous Solu-Medrol®, and was admitted to the hospital on multiple occasions for acute chest tightness after exposure to perfume and other scented products worn by coworkers. There was no associated dysphonia or other laryngeal symptoms. Her medical history was negative for seasonal allergies or asthma. She smoked 2–3 cigarettes per day for 25 years. Physical examination showed poor air movement without audible wheezing or other adventitious sounds. Pulmonary function studies showed an FEV_1 of 1.35 L (52% predicted), forced vital capacity (FVC) of 1.76 L (49%) and FEV_1/FVC ratio of 87% (108% predicted). There was a significant increase in FEV_1 following bronchodilator administration. There was a significant increase in specific airway resistance after the inhalation of a 0.2% solution of methacholine (after phosphate buffered saline = 3.7, maximum = 8.4; % change 227%). High-resolution chest computerized tomography (CT) scan showed mild bilateral interstitial prominence of both lungs. Bronchoscopic biopsy of the left upper and left lower lobes showed a small amount of chronic inflammation, alveolar lining hyperplasia, and scattered histiocytes. Viral, fungal, and bacterial cultures were negative. She was treated by her pulmonologist with inhaled corticosteroids, albuterol nebulizer, and zafirlukast. She was provided with medical restrictions (no exposure to scented products and other chemicals, dusts or fumes), but was unable to work due to severe respiratory symptoms.

Discussion

An association with fragrances was reported in nearly 4% of all WRA cases confirmed in California surveillance data over a 20-year period. When compared to non-fragrance cases, fragrance cases were significantly more likely to be women and nearly twice the proportion of classified cases were considered WAA. It is

Table 2. Distribution of fragrance-associated and non-fragrance-associated work-related asthma cases by occupation categories, California Surveillance Data, 1993–2012.

	Fragrance-associated		Non-fragrance-associated		*p*-value	
Occupation categories*	#	%	#	%	#	%
Management	8	3.2	251	4.1		0.50
Business and finance	8	3.2	159	2.6		0.54
Computer and math	6	2.4	29	0.5		**<0.01**
Architecture and engineering	1	0.4	66	1.1		0.31
Life, physical, and social sciences	1	0.4	131	2.1		0.06
Community and social services	6	2.4	112	1.8		0.49
Legal services	3	1.2	28	0.5		0.09
Education and library	24	9.7	265	4.3		**<0.01**
Arts, entertainment, and media	1	0.4	47	0.8		0.52
Health practitioners	49	19.8	559	9.1		**<0.01**
Health services support	17	6.9	239	3.9		**0.02**
Protective services	3	1.2	580	9.4		**<0.01**
Food services	4	1.6	186	3.0		0.20
Building and grounds maintenance	3	1.2	360	5.9		**0.01**
Personal care services	4	1.6	121	2.0		0.69
Sales	8	3.2	275	4.5		0.35
Office	89	35.9	1,171	19.0		**<0.01**
Agriculture and forestry	0	0	104	1.7		**0.04**
Construction and mining	0	0	318	5.2		**0.01**
Installation, repair, and maintenance	0	0	146	2.4		**0.01**
Production	4	1.6	536	8.7		**<0.01**
Transportation and moving	9	3.6	465	7.6		**0.02**
Total	248	100	6148	100		

*Census Occupation Codes, 2000.
Occupation was not reported for 22(8.1%) of fragrance-associated cases and 745 (10.8%) of non-fragrance-associated cases.
Categories in bold have more than the overall average 3.9% fragrance-associated cases.

well established that adult women have a higher prevalence of asthma in the general population than men [35–38]. Previous studies using WRA surveillance data from multiple states also document that a higher proportion of people with WRA are females and that females have a higher proportion of WAA [33]. In addition, market survey research shows that more women wear fragrance than men (85% vs 63%), making work settings with a high proportion of female workers more likely to be affected by perfume exposures [34, 39, 40]. However, it is noteworthy that a similar proportion of fragrance and non-fragrance cases were classified as NOA using the surveillance definition, indicating that fragrance is not just a source for exacerbation, as it was also associated with new physician-diagnosed asthma.

Fragrance cases were significantly more likely to have their workers' compensation claims denied than non-fragrance cases (30% vs 21%) and significantly more likely to still be exposed on the job (50% vs 26%). However, outcomes for fragrance cases did not differ from non-fragrance cases by severity, as indicated by the need for hospital-based intervention: they report similar proportions of ER visits and hospitalizations. These data illustrate how these cases are often not taken seriously or considered work-related. Our data document many cases of preexisting asthma that are worsened by

Table 3. Interviewed fragrance-associated and non-fragrance-associated work-related asthma cases, by selected outcomes, California Surveillance Data, 1993–2012.

	Fragrance-associated		Non-fragrance-associated		Total		
Outcomes/impacts	#	%	#	%	#	%	*p*-value
Problems in last 2 weeks	94	(62)	1393	(55)	1487	(55)	0.09
Still works at job	102	(67)	1550	(60)	1652	(60)	0.06
Still exposed at job	76	(50)	650	(26)	726	(27)	**<0.01**
ER visit	97	(63)	1550	(61)	1647	(61)	0.65
Hospitalized	19	(13)	387	(15)	406	(15)	0.36
Know others with breathing problems	94	(68)	1396	(65)	1490	(65)	0.47
Filed workers' compensation claim	91	(68)	1358	(61)	1449	(61)	0.11
Awarded claim	50	(59)	812	(67)	862	(69)	0.11
Denied claim	26	(30)	257	(21)	283	(22)	**<0.05**
Pending claim	7	(8)	115	(10)	122	(10)	0.70
Claim status unknown	2	(2)	24	(2)	26	(2)	0.82

fragrance exposures, yet many cases report that these are considered non-occupational by clinicians and employers even when the source of exposure originates in the workplace. Examples include the use of air fresheners provided by the employer or job-required interactions with fragrance-wearing patients or customers. When exposure to fragrance chemicals is considered objectively as a workplace exposure to a mixture of chemicals, often containing both irritants and asthmagens, it becomes clear that these exposures are important and need to be prevented. Further evidence that asthma due to fragrances is real and not psychological in origin is found in studies of anosmic patients and other subjects who could not smell the test fragrance having asthmatic reactions [8, 12]. Nor is a large dose of fragrance needed to cause a respiratory reaction—researchers have noted that barely noticeable dilutions have caused immediate and alarming symptoms [9].

Our surveillance data suggest that all types of WRA—WAA and NOA including RADS and chronic irritant-induced asthma—are associated with fragrance exposures. The documented experience of our case-patients, including repeated asthma exacerbations and emergency room visits brought about by subsequent fragrance (and other chemical) exposures, both on- and off-the-job, is mirrored by that found in published reports of workers exposed to fragrance compounds [2–4]. It is possible that, in our dataset, a subset of those diagnosed with WRA may have laryngeal disorders [15, 16, 18, 41–43]; we are unable to determine the extent of misclassification. Recent studies bringing attention to the need for the appropriate differential diagnosis of laryngeal disorders and the development of better diagnostic methods will likely improve our surveillance as well as improve treatment for patients [15, 17, 41, 42]. Workplace interventions would help prevent all respiratory disorders associated with fragrance.

It should not be controversial that fragrances can exacerbate and cause asthma and other respiratory system effects. They are largely comprised of VOCs, some of which are irritants and sensitizers and which also react with ambient ozone to create other irritants and sensitizers. It is noteworthy that fragrances are associated with a substantial proportion of NOA. Perfumes, individual fragrance chemicals, and their byproducts are recognized as irritants [6, 25, 30, 44–46], and the dominant theory proposed by several researchers suggests a spectrum of irritant-induced asthma with RADS at one end and NOA caused by chronic low-level exposures at the other [44, 47–52]. There is not a known threshold for sensitization or triggering of asthma nor is it known what the effects are of exposure to a combination of dozens of fragrance chemicals and their reaction by-products. Combined effects in environments with one or more sensitizing agents as well as one or more irritants have been proposed as a possibility for potentiation or enhancement of immunologic sensitization [46, 47].

Our surveillance data also illustrate that primary prevention is needed. Of highest importance in the industrial hygiene hierarchy of controls is the elimination of hazards. One possible approach would be to avoid specific chemicals, but this is currently impossible due to lack of disclosure by manufacturers. Product hazard evaluation is hampered by the lack of regulations requiring full disclosure of product ingredients. For example, eugenol has been documented as causing NOA [3, 4]. However, manufacturers are not required to disclose fragrance ingredients, so an employer or worker may not know whether eugenol is a fragrance component in a given product. One study found that, out of 133 different fragrance VOCs discovered by product analysis, only one was listed on any of the product labels and only two were found on product safety data sheets (SDSs) [21]. Occupational Safety and Health Administration Hazard Communication Standard regulations allow a manufacturer, importer, or employer to withhold the chemical identity of a substance in a mixture from the SDS in the case of "trade secrets" [53]. Other product labeling laws also allow the use of the term "fragrance" instead of the chemicals that comprise the fragrance [21, 54].

A more protective approach to prevent both WRA and other respiratory disorders would be implementing workplace purchasing policies that prohibit the use of air fresheners and fragranced cleaning products [55] and fragrance-free policies that restrict the use of perfumes, colognes, and scented personal care products by employees and others in the workplace. Employee education about the types of chemicals used in fragrances and their possible health effects may help overcome the resistance such a policy might meet. Anecdotal information obtained from our interviews shows that employers lack fragrance-free policies or that coworkers do not follow the existing policies. To assist workplaces we developed educational materials and a model fragrance-free policy, which were released in 2015 [56]. There is not currently a specific requirement in California for workplace fragrance-free policies; however we encourage workplaces to adopt them voluntarily.

Some health care providers have extended fragrance-free policies to their patients by requesting or requiring that patients not wear scented products [57, 58]. Other workplaces where workers deal with the public, particularly without an appointment, may find it difficult to implement such a requirement. In such workplaces possible controls might include the use of supplemental fans to

direct airflow past a worker and toward the customer or client.

In this study, jobs in indoor settings, such as those found in office buildings and in health care environments, had a significantly higher proportion of fragrance cases when compared to jobs in outdoor settings. A well-designed and maintained building ventilation system, effective humidity control, and good building maintenance will help to eliminate odors that cause many to turn to air fresheners in the first place. Effective ventilation will also dilute and clear out the chemicals found in cleaning products and personal care products. Ozone-emitting equipment sold as "air cleaners" or "air purifiers" should be banned from workplaces because they produce ozone, which is a lung irritant, and because ozone can react with other chemicals to produce secondary pollutants, as was previously discussed.

Full disclosure of all ingredients, as is currently done by some product manufacturers [59, 60], would assist health and safety professionals in evaluating products used in workplaces. Requiring this from all product manufacturers might also provide incentive to reformulate with safer ingredients. In addition, full disclosure could help health care providers and researchers pinpoint chemicals for diagnostic (e.g., challenge and sensitivity testing) purposes.

Also needed is more research to better determine the true number of asthmagens among the list of fragrance chemicals. For example, respiratory sensitization is not currently included in the battery of safety assessments used for fragrance chemicals [19]. Publishing case reports that include clinical tests meeting the criteria to determine whether a substance is an asthmagen [23] would add knowledge to help regulators, health professionals, product manufacturers, and employers protect workers and prevent WRA.

There are limitations in our data. Previous studies have described the many stages within illness surveillance where a case may be missed and result in underreporting [61]. A worker must recognize they have asthma symptoms associated with work, be willing to report their work-related illness to a supervisor or clinician, and have access to health care; the clinician must be able and willing to assess the relationship of the symptoms with work and report it; the report must make its way into the surveillance system; and the surveillance program must be able to identify, select, and confirm that the case is WRA [59]. Evaluations of underreporting of WRA in California suggest that at least 2/3 of WRA cases are not captured by the surveillance system, and it is unknown if there is bias in case capture [35, 62, 63]. Therefore, it is possible the data are not representative of all cases of WRA in California. Because the surveillance case definition relies on an asthma diagnosis identified in medical records, and we did not perform a separate clinical evaluation, it is possible that some cases could be misclassified as asthma when they are actually upper airway disorders [15, 41, 43]. Similarly, it is likely that some WRA cases are misclassified as other upper airway disorders and therefore not captured by surveillance. Chemical exposures were most likely to be identified during the telephone interview attempted for each case reported, since patients described the WRA asthma incident in detail. Medical records infrequently included specific exposure information, more often focusing only on clinical presentation and treatment of the patient. However, interviews were only completed for 39% of cases and previous studies have demonstrated that women are more likely to complete the interview than men [31], which could introduce bias. Interviews also provide the key temporal information used to differentiate if a worker had preexisting asthma before their first work-related incident or if their asthma is new-onset due to work-related exposures. Cases that lack this temporal information are classified as "confirmed, but not classified," since they meet the case definition for WRA, but further classification is not possible. Over half of the cases identified fall into this category, largely because they could not be reached for interview and the necessary temporal information is rarely in medical records. It is unknown if this large proportion of unclassified cases biases the results when comparing fragrance with non-fragrance cases. This also suggests that the number of fragrance cases may be underestimated since some uninterviewed cases that were classified as "non-fragrance" may have had fragrance exposures; interviews often provide detailed exposure information. Based on statements made to us by the interviewed patients, we speculate that workers may hesitate to complain about or seek medical care for WRA brought on by fragrances due to fear of not being believed at work or feeling that it is not their place to complain about the personal care product choices of coworkers. It is possible that some patients may not mention fragrance to their providers because they do not recognize it as an exposure or providers may dismiss this information. While cases could report up to three exposures, two-thirds of the fragrance cases reported only fragrance exposures. When other agents were reported, they were often exposures where fragrance could still have been the putative agent, such as in cleaning products. Also, in this dataset some populations might be over- or underrepresented. Women, for example, seek medical care at higher rates than men [36–38], and workers who fear retribution in the workplace may not want to risk reporting a work-related health issue. Also, some professions that have better health benefits, nurses and teachers, for example, might

be more likely to see a doctor than other workers would. Additionally, patients who experience other reactions to chemicals, like rash, headache, or rhinitis, may be more likely to report asthma exacerbations to a physician than other patients. Because fragrance chemicals are not disclosed on labels or SDSs, we are unable to determine if a case-patient was exposed to a known asthmagen. Finally, these cases do not include exposures reported by the patient as due to cleaning agents or other commercial products, but where the fragrance in the product may have been the true causative agent.

Conclusions

Fragrance use in the workplace is associated with WRA cases identified through surveillance, and the outcomes of fragrance cases are similar to WRA cases associated with other work exposures. Just as an employer would limit or control the introduction of other airborne chemicals and contaminants into a workplace (cigarette smoke, solvents, etc.), an employer wishing to prevent worker illness should also prevent exposures to fragrance chemicals. Prevention methods include employee education, enforced fragrance-free policies, well-designed ventilation systems, and good building maintenance. Smoking in the workplace, once viewed as a personal choice issue, has been restricted in workplaces, largely due to concerns about secondhand smoke [64, 65]. Fragrance use by employees and others in the workplace, because of the health implications, should be viewed in a similar light. Further research is needed to better characterize the health and economic burden that the use of fragrances brings to workers and employers.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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