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Environmental triggers of COPD symptoms: a cross sectional survey

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Abstract

Background: There is little published evidence on environmental triggers of COPD exacerbation, despite anecdotal reports from patients and clinicians. This study gathered data on reported triggers of COPD exacerbation among a well-characterized cohort of COPD patients. We hypothesized that patient reports of irritating chemical exposures would differ depending on disease characteristics including asthma co-morbidity and COPD severity.

Methods: We conducted a cross-sectional survey of 167 clinically-confirmed COPD patients who were participants in a COPD disease management program (DMG) in a large multi-specialty medical group practice. The survey included questions about specific daily activities and associated chemical exposures likely to be irritating to the respiratory system. Participants were asked whether exposure to these activities or products bothered their breathing, whether they avoided them or took additional medications to treat symptoms when exposed to them.

Results: More than half of the COPD patients surveyed reported that certain common dusty activities (sweeping, vacuuming, dusting), and exposures to cigarette smoke, wood smoke, vehicle exhaust, cleaning products, perfumes and other scented products (scented candles, insect spray, hair products) adversely affected their breathing. There was evidence that COPD patients with an asthma diagnosis respond more to volatile organic compounds and those with more severe disease were more likely to report being bothered by particulate exposures.

Conclusions: Common environmental exposures may adversely affect COPD patients by increasing their use of rescue medications and/or their risk of clinical exacerbation; these exposures may also lower quality of life when patients alter their activities to protect themselves from such exposures.

Keywords: COPD, Triggers, Symptoms, Asthma, Environmental exposures

Background

Chronic Obstructive Pulmonary Disease (COPD) affects over 10 million people in the United States, is the third leading cause of death and is responsible for over $15 billion in health care costs each year [1]. Tobacco smoking is the primary cause of COPD [2, 3], although air pollution and occupational exposures to a number of hazardous chemicals are also important preventable causes [4–11]. It has long been recognized that in the clinical management of COPD, the most important strategy is preventing the occurrence of acute episodes of COPD exacerbation [12, 13], followed by rapid medical response when exacerbations do occur [14]. It is thought that the most important trigger of COPD exacerbation is respiratory infection [15, 16], although there is also good evidence that urban air pollution can also increase risk of exacerbations [17]. Environmental tobacco smoke may also be a COPD trigger [18]. Beyond these three factors, little is known about other preventable triggering exposures.

At least two lines of evidence suggest that there may be environmental chemical exposures (other than urban air pollution and tobacco smoke) which increase the risk of COPD exacerbation. First, it is likely that the mechanism by which urban air pollution triggers exacerbations involves inflammatory processes which also underlie other health endpoints including asthma, bronchial hyperreactivity, acute loss of pulmonary function and cardiovascular disease.

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Under this assumption, it seems reasonable that other chemical exposures which act through respiratory inflammation and irritation pathways might also trigger COPD exacerbations. These might include volatile organic compounds and fine particulates in indoor air. There are a large number of such chemicals identified as triggers for asthma attacks [19], and we hypothesize that asthmagens – and particularly irritant asthmagens may also act as triggers of COPD exacerbations in susceptible patients. The second reason to investigate possible environmental chemical triggers of COPD exacerbation is that patients and their clinical care providers frequently recommend avoiding certain chemical exposures (household cleaning products, strong odors, gas fumes, dust) because they may trigger exacerbations, despite the fact that little or no formal evidence exists to support these recommendations [20, 21]. In focus groups of COPD patients (described further below), many expressed well-formed opinions about chemical exposures and activities which they seek to avoid in order to manage their disease and reduce risk of exacerbation which requires treatment with antibiotics and/or steroids. Patients and their providers often discuss strategies to avoid "flares" of symptoms – milder than full-blown exacerbations, but which often lead to increased use of rescue medications.

Asthma is a common co-morbidity with COPD [22] and we hypothesized that COPD patients who also had asthma might report different environmental irritants than COPD patients without asthma. We further hypothesized that as the course of COPD progresses, patients may change their sensitivities to environmental exposures either because these sensitivities may be modified by chronic airways inflammation and/or because their increasingly debilitating disease may limit their activities and therefore also their opportunities to be exposed to different chemicals. For example, once a patient can no longer do heavy housecleaning, their exposures to certain cleaning chemicals would be expected to decrease. To investigate potential effect modification by COPD severity, we used the standard GOLD classification [23].

As a part of a larger study of COPD exacerbation, we surveyed participants enrolled in the COPD disease management group (DMG) of a large medical group practice. The participants were administered a mailed questionnaire soliciting their input on exposures and activities which made their breathing worse. The objective of this paper is to summarize the findings of this investigation of self-reported environmental exposures reported by COPD patients to worsen their breathing symptoms. We also sought to identify patient characteristics (asthma comorbidity and COPD severity) which may affect sensitivity to different potentially triggering exposures.

Methods

All study materials and protocols were approved by the Reliant Medical Group Institutional Review Board.

Patient population

The study population was drawn from a large medical group practice in central Massachusetts. The area centers on Worcester County (population 785,000), comprising 62 towns and the city of Worcester, the third largest city in New England with a population of 175,454. As a part of its efforts to improve patient quality of life, compliance with care guidelines and control costs, the group medical practice maintains and staffs a COPD DMG. Patients are enrolled into the group by pulmonologists or primary care physicians after a diagnosis of COPD is made based on symptoms and spirometry. These patients are followed closely through periodic telephone contacts with a nurse, as well as clinic visits. Routine calls are made by a DMG nurse to all patients at least once every 4–6 months; more frequent calls are made if patients have unstable COPD or are experiencing frequent exacerbations. The purpose of the DMG is to educate patients and teach them to properly manage their disease with the overall goal of reducing the frequency and severity of their exacerbations, thus slowing their disease progression.

We invited participation from patients who were DMG members and who had consented to participate in an ongoing study of COPD exacerbation. All had received a physician's diagnosis of COPD, had received at least one antibiotic prescription in the 3 years prior to study enrollment; had experienced at least one exacerbation in the 15 month study period; and had no other lung diseases (e.g., interstitial lung disease, lung cancer, diffuse bronchiectasis) except asthma which is often misdiagnosed in COPD patients [22].

COPD severity was characterized using the GOLD (Global Initiative for Chronic Obstructive Lung Disease) stages [24]. The GOLD stages are: stage I (mild) FEV1/FVC < 0.70 and $FEV_1 \geq 80$ % of normal; Stage II (moderate) FEV1/FVC < 0.70 and FEV_1 50–79 % of normal; Stage III (severe) FEV1/FVC < 0.70 and FEV_1 30–49 % of normal; and Stage IV (very severe) FEV1/FVC < 0.70 and $FEV_1 < 30$ % normal, or <50 % normal with chronic respiratory failure present. The majority of these patients had COPD signs and symptoms meeting GOLD stages I through IV. However patients referred to the DMG with symptoms of COPD and normal FEV_1/FVC ratios were also included for study. Surveys were mailed to 167 eligible DMG members. The cover letter requested

that patients complete the survey and mail it back or call the study nurse for telephone administration of the survey. The research nurse called patients who did not return their surveys or call to have them administered by phone. Patients were compensated $20 for completing the survey.

Focus groups

We conducted 2 focus groups of patients recruited from the DMG. The first focus group was used to review our a priori list of products and activities that might be COPD triggers, and to add others if needed. The second focus group was used to pilot the exposure survey for readability and finalize the survey format. Comments and suggestions from patients were incorporated into our final survey.

Surveys

We developed a questionnaire organized into three main sections: 1) physical activities, 2) chemical exposures and 3) non-chemical triggers of COPD (such as upper respiratory tract infections, exertion and weather). The questionnaire was designed to collect data on relevant activities of daily living and exposures that might be associated with irritants and other potential triggers of COPD flares or exacerbations. A candidate list of activities and exposures was initially developed from Relationships of Indoor, Outdoor, and Personal Air (RIOPA) and National Human Exposure Assessment Survey (NHEXAS) questionnaires and workplace exposures were based largely on the American Thoracic Society (ATS) and European Respiratory Society questionnaires (including the vapors, dust, gas, fumes questions) [25–27].

This list was then narrowed by identifying the subset that were likely to be found in home and community settings where patients were likely to go (stores, restaurants, gas stations, etc.). The candidate list included activities and exposures associated with agents in the following categories: known asthmagens, respiratory irritants, "non-specific dusts" as referred to by the American Thoracic Society vapor dust gas fume questions, volatile organic compounds, combustion aerosols, bioaerosols and tobacco smoke [10, 11, 19, 28–31].

For each of the activities (Appendix), exposures and products we asked the following questions: would exposure to any of these activities (exposures, products) bother your breathing or make it harder to breathe? Do you avoid exposure to this activity? Have you ever needed to start antibiotics or steroids after exposure to this product? If you do get exposed to this activity, how do you handle it? (Possible responses: I remove myself from the activity; I increase my daily rescue medications; Other (Please Specify)). We chose a range of possible responses from the mildest – that the exposure "bothered" their breathing to the clinically relevant reporting of having to use additional medications to regain the ability to breathe comfortably. Data presented below include patients who answered yes to any of these questions indicating that these activities or products trigger symptoms that worsen their breathing. We refer to anything that engendered an affirmative on the spectrum of adverse responses (from bothered to taking additional medications) as a "symptom trigger".

Patient susceptibility

We hypothesized that COPD patients might report different types and severities of adverse responses to irritant exposures depending on characteristics of their underlying disease. Specifically, we hypothesized that: 1) those patients with more severe disease as defined by the GOLD criteria might have different types of responses to triggering exposures than those with less severe disease; and 2) COPD patients who also had received a diagnosis of asthma might show a different pattern of responses to irritant and sensitizing exposures than those without an asthma diagnosis. We grouped GOLD stages I and II – mild and moderate COPD versus III and IV – severe and very severe. Post-bronchodilator spirometry was missing for 12 patients, and for these we used their baseline spirometry to assign their GOLD stage. The standard ATS survey questions on doctor-diagnosed asthma were used to identify COPD patients who also had asthma: "Have you ever had asthma? If yes, was it confirmed by a doctor?" [32].

Data analysis

Data were entered into an ACCESS database, edited and cleaned. The final dataset was analyzed in SAS (SAS Institute Inc., Version 9.3, Cary, NC,). Cleaned survey data were exported into SAS. The potential modifying effects of COPD severity or asthma diagnosis were investigated by calculating prevalence ratios comparing the frequency of reporting a particular exposure as bothersome in one group (severe/very severe COPD or those with asthma) versus a comparison population (mild/moderate COPD, no asthma).

Results

Surveys were mailed to 167 COPD patients, and we received responses from 145 (87 %). The mean age of the respondents was 72 years, 56 % were female and almost all were white (Table 1). Approximately two thirds of patients had severe or very severe COPD (GOLD Stages 3 or 4). Ninety seven percent of patients had a smoking history with an average of 52 pack years. More than half were on

Table 1 Characteristics of COPD patients surveyed

	Overall	Asthma diagnosis	
	(*n* = 145)	No (*n* = 87)	Yes (*n* = 58)
Age (years)	71.6 (8.8)[a]	71.9 (9.0)	71.2 (8.7)
Female	56 % (82)[b]	59 % (51)	53 % (31)
Race: White	97 % (140)	99 % (86)	93 % (54)
Black	2.1 % (3)	1.2 % (1)	3.5 % (2)
Other	1.4 % (2)	0 %	3.5 % (2)
GOLD stage			
1 Mild	2 % (3)	3.5 % (3)	0 %
2 Moderate	23 % (33)	24 % (21)	21 % (12)
3 Severe	51 % (73)	51 % (44)	50 % (29)
4 Very severe	16 % (23)	18 % (16)	12 % (7)
Normal FEV_1/FVC with COPD Symptoms	7 % (10)	2.3 % (2)	14 % (8)
Inadequate spirometry[c]	2 % (3)	1.2 % (1)	3.5 % (2)
Smoking status			
Current	16 % (22)	21 % (18)	7.7 % (4)
Ex	81 % (118)	80 % (70)	83 % (48)
Never	4.1 % (6)	0 %	10 % (6)
Pack years	52 (32.3)[a]	54.9 (26.9)	47.6 (39.2)
Regular home oxygen	54 % (76)	60 % (50)	45 % (26)
Regular nebulizer use	79 % (109)	76 % (63)	84 % (46)
FEV_1 improvement post-bronchodilator ≥15 %	18 % (25)	18 % (15)	19 % (10)

[a]Mean (std. deviation)
[b]Percent (n)
[c]Excluded from analyses comparing mild/moderate versus severe/very severe COPD

some form of oxygen therapy to reduce or prevent the complications of hypoxemia. Forty percent of this population of COPD patients reported ever having a doctor diagnosis of asthma. Asthmatics and non-asthmatic participants were fairly similar in most respects. However, fourteen percent of the asthmatics had normal FEV_1/FVC ratios compared to 2 % of the non-asthmatics ($p = 0.007$). In addition asthmatics were less likely to be smokers. For example, about 8 % the percent of asthmatics reported current smoking compared to 21 % of non-asthmatics ($p = 0.04$).

A wide range of activities and products were reported by patients as making their breathing worse (Fig. 1 shows those reported by at least 50 % of the population – see Appendix for the complete set). These were generally either activities which generated particulates such as sweeping or vacuuming, or dusting, or else they involved exposure to volatile organic compounds such as paint thinner, perfumes, and scented candles. The smoking of tobacco products (active or passive) and sweeping or vacuuming were the most frequently reported (74, 70 % respectively) symptom triggers, followed by paint thinner (62 %), cleaning supplies (60 %) and wood smoke (60 %).

The frequency of reporting different symptom triggers varied depending on both disease severity and on whether or not the patient reported a diagnosis of asthma along with their COPD (Figs. 2 and 3). Those COPD patients with disease categorized as severe or very severe were at least 50 % more likely (prevalence ratio > 1.5) to report being adversely affected by several activities involving

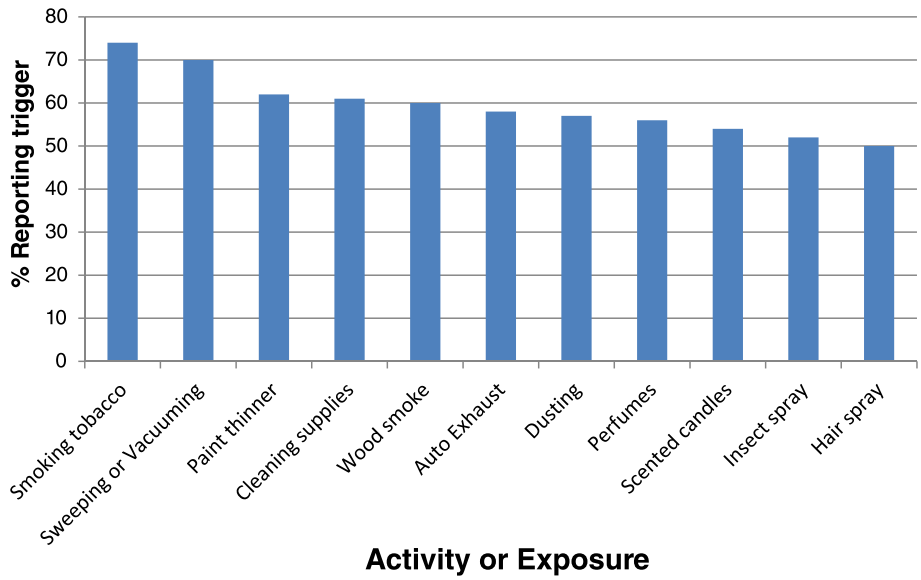

Fig. 1 Self-reported symptom triggers affecting at least 50 % of COPD patients

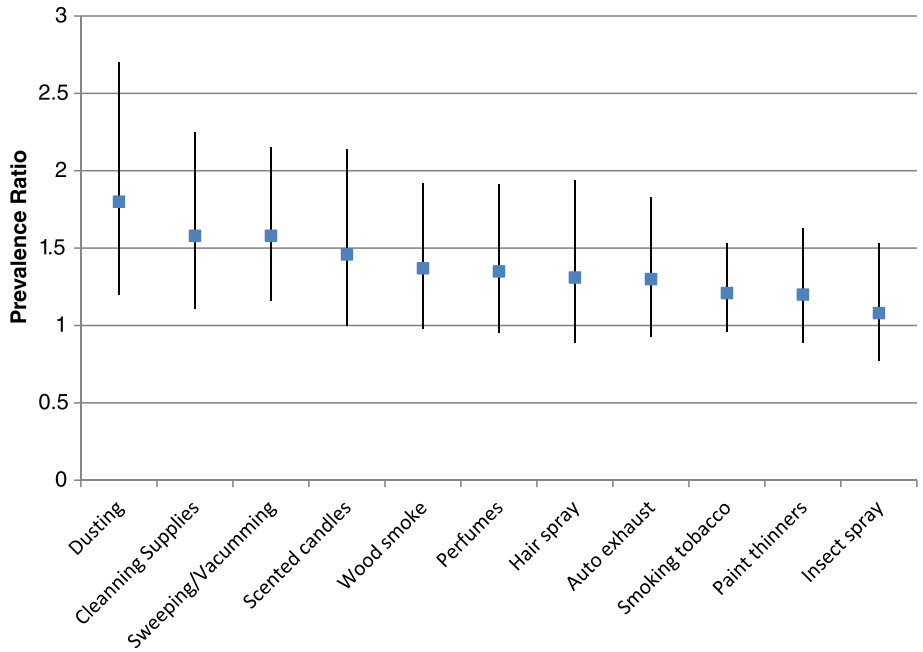

Fig. 2 Self-reported symptom triggers. Prevalence ratios for severe/very severe versus mild/moderate COPD* .*Mild/Moderate: COPD diagnosis normal FEV/FVC Ratios and Gold Stages 1, 2; Severe/Very Severe COPD includes Gold Stages 3 and 4. Error bars represent 95 % confidence intervals

exposure to particulates – dusting, cleaning with cleaning supplies, sweeping and vacuuming, than those with mild or moderate disease. Several other exposures including scented candles and wood smoke seemed to be more frequently reported by those with more severe COPD.

COPD patients who reported that they had been told by a doctor that they had asthma reported a somewhat different pattern of symptom triggers. They were more likely to report that exposures to several volatile organic compounds triggered their symptoms than those

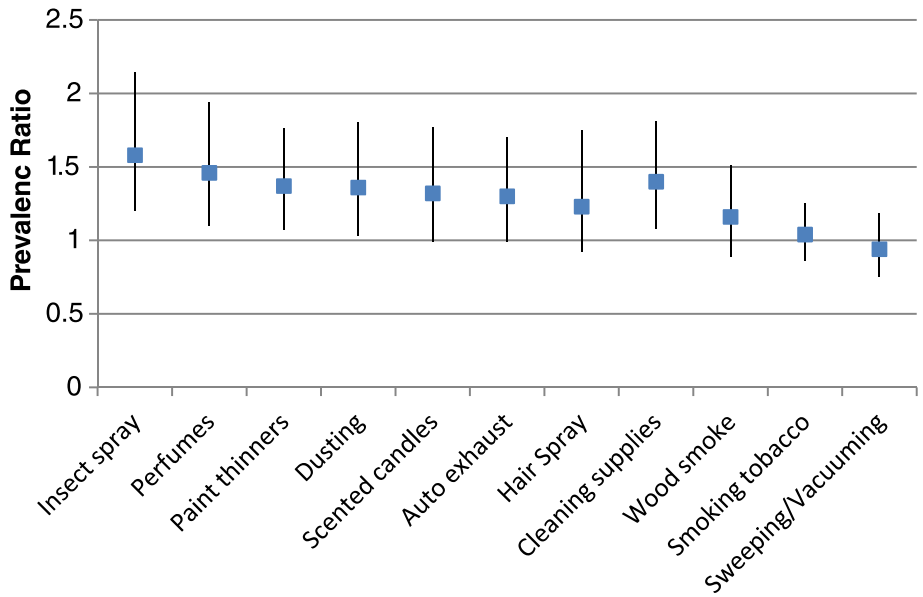

Fig. 3 Self-reported symptom triggers comparing those with and without doctor diagnosed asthma*. *Patient responded yes to both questions: Have you ever had asthma? Was it confirmed by a doctor? Error bars represent 95 % confidence intervals

without asthma diagnoses. These exposures included insect sprays, perfumes, cleaning supplies and paint thinner (Fig. 3).

The most clinically significant response to an exposure or activity was having to take additional medications to control symptoms. Several exposures were found to frequently require this level of response by the patients (Table 2). For example, nearly one quarter of those who said they were bothered by wood smoke said that they sometimes had to use medications to control their symptoms after this exposure. About a third of the COPD patients reported that air fresheners bothered their breathing (Appendix), and of those, about one in five said they needed to use additional medications following this exposure. Perfumes and car and truck exhaust had very similar levels of symptoms and medication usage.

Discussion and conclusions

Chronic disease management has been shown to improve symptoms, quality of life and other outcomes (emergency room visits and inpatient admissions) in COPD patients [12, 13, 33]. It is important that patients know and control triggers and symptoms of COPD exacerbations. To date, viral respiratory infections have been understood to be the primary trigger for exacerbations, and so prevention strategies have emphasized annual flu and pneumonia vaccines. While there is good evidence for this recommendation, there is a lack of additional evidence-based prevention strategies provided to COPD patients. Disease management programs often recommend that patients identify and avoid factors that can make COPD symptoms worse. One such program, "Living Well with COPD" has a list of possible triggers [20] that contains many of the exposures that we report, but there does not appear to be any formal quantitative evidence to support these recommendations.

Table 2 Symptom triggers most frequently reported to require additional rescue medications

Exposure/Activity	% (n) of those bothered[a]	95 % CI[b]
Wood smoke	24.6 (65)	(14.8, 36.9)
Air fresheners	21.7 (46)	(10.9, 36.4)
Perfume	21.5 (65)	(12.3, 33.5)
Vehicle exhaust	19.4 (67)	(10.8, 30.9)
Cleaning	18.5 (65)	(9.9, 30.0)
Barbeque	17.7 (34)	(6.8, 34.5)
Gas	17.6 (17)	(3.8, 43.4)
Household cleaners	17.4 (69)	(9.3, 28.4)
Markers	16.7 (18)	(3.6, 41.4)
Dusting	16.7 (60)	(8.3, 28.5)
Glue	16.2 (37)	(6.2, 32.0)
Vacuuming OR sweeping	18.8 (80)	(10.9, 29.0)

[a]Percent of patients reporting that the activity (exposure, product) bothered their breathing who said they needed to take additional breathing medications following the activity
[b]Exact 95 % confidence interval for proportion

There are a large number of known environmental triggers of asthma attacks [19]. Many COPD patients have both a reversible and fixed component to their disease. Good clinical management of COPD seeks to limit exposures that could cause an inflammatory response, worsening the reversible obstruction. There is much less known about which substances might initiate this inflammatory response in COPD patients, but the overlap between the two diseases suggests that it is reasonable to investigate asthmagens as potential irritants for COPD patients.

Our primary inclusion criterion was membership in the DMG which was based on a clinician's judgement. However, since there were some Gold 0 subjects (normal FEV_1/FVC but with COPD symptoms), we investigated the impact of excluding Gold 0 subjects, as well as three patients who were missing spirometry data and found little difference. For example in Table 2, the three most commonly reported irritants requiring additional rescue medications were wood smoke, air fresheners and perfume, which changed from 24.6 to 23.0 %, 21.7 to 20.9 % and 21.5 to 20.6 % respectively.

We stratified the analysis to investigate variations in patterns of triggers within the COPD patient population. These results suggested that not all patients respond the same way to these symptom triggers. Although the mechanism for such a response is unclear, the results suggest that perhaps COPD patients with an asthma diagnosis respond more to volatile organic compounds while those with more severe disease were more likely to report being affected by common particulate exposures.

A limitation of this investigation is that we were not studying clinical exacerbation but rather self-reported irritation of breathing and the need for rescue medication. While these self-reports are subjective and did not necessarily lead to a full-blown exacerbation, we believe that the findings are nonetheless relevant. If patients are using rescue medication, and avoiding certain environments or activities in order to protect themselves, we believe this indicates a material impact on health and quality of life that clinicians and patients will want to take seriously. The observation that asthma co-morbidity and COPD severity appeared to modify the pattern of reported triggers may suggest potential lines of research for further studies which may improve our ability to prevent environmentally-triggered exacerbations.

Appendix

Table 3 Summary of all symptom triggers

Activity or exposure	Percent (n) of all respondents ($n = 145$) who answered yes to:	
	"Breathing was bothered" or "it was harder to breathe"	Took action[a] in response to exposure/ activity
Having a respiratory infection or cold	75 (108)	81 (118)
Spending time in the hot weather or humidity	81 (117)	87 (126)
Dusty activities like sweeping, wood working, raking, or using fertilizers	64 % (93)	82 (119)
Shoveling or clearing snow off your car	61 % (88)	76 (110)
Increase in physical activity	72 (105)	77 (111)
Spending time in the cold air or in cold weather	67 (97)	75 (108)
Mowing or trimming the lawn or using snow blower	58 % (84)	73 (106)
Suffering from allergies	48 (70)	57 (82)
Exercising	63 (91)	67 (97)
Smoking of tobacco products (cigarettes, pipes, cigars or other)	57 % (82)	74 (107)
Other yard work or gardening	48 % (71)	66 (96)
Paint thinners and solvents	43 % (62)	62 (90)
Suffering from increased stress or intense emotions	50 (72)	56 (81)
Bug/Insect spray	39 % (56)	52 (76)
Use of a wood smoke fire (pellet stove, woodstove, campfire, etc.)	45 % (65)	60 (87)
Car or truck exhaust	46 % (67)	58 (84)
Having a non-respiratory virus (i.e., stomach bug, flu)	25 (36)	36 (52)
Perfumes, colognes or body sprays	45 % (65)	56 (81)
Sweeping (inside or outside)	48 % (70)	61 (89)
Vacuuming	47 % (68)	61 (88)_
Household cleaning products (cleaners, waxes, polishes)	48 % (69)	60 (87)
Scented candles or incense	40 % (58)s	54 (79)
Hair spray or hair gel or hair mousse	38 % (55)	50 (72)
Cleaning with cleaning supplies (cleaners, waxes, and polishes)	45 % (65)	61 (88)
Having a sinus infection	39 (57)	48 (69)
Dusting	41 % (60)	57 (82)
Glues or epoxy (for example during hobbies or art class)	26 % (37)	41 (59)
Animals or pets	19 % (28)	34 (49)
Barbequing, frying or sautéing food	23 % (34)	37 (54)
Nail polish or nail polish remover	28 % (42)	39 (57)
Swimming or around an indoor or outdoor pool	28 % (41)	42 (61)
Paint (for example hobbies or art class) or white out	32 % (47)	47 (68)
Air fresheners (Plug in Wall dispensers, sprays, etc.)	32 % (46)	44 (64)
Furniture spray or polish	32 % (47)	45 (65)
Filling the car with gas or diesel fuel	23 % (34)	34 (50)
Scented laundry products (detergents, laundry softeners or drier sheets)	20 % (29)	30 (44)
Cooking with a gas stove	12 % (17)	25 (36)
Spray deodorant	23 % (33)	35 (51)
Picking up or wearing dry cleaning	6 % (9)	19 (27)
Writing or drawing with felt tipped markers or highlighters	12 % (18)	21 (31)
Hand sanitizers (liquid, gel, wipes)	10 % (15)	19 (27)
Cosmetics	10 % (14)	17 (25)
Copier machine or printer	8 % (11)	17 (24)

[a]Reported yes to at least one of the following questions: 1) Do you avoid exposure to this activity? 2) Have you ever needed to start Antibiotics or Steroids after exposure to this product? 3) If you do get exposed to this activity, how do you handle it? a) I remove myself from the activity. b) I increase my daily rescue medications. c) Other (Please specify)

Abbreviations

ATS: American Thoracic Society; COPD: Chronic obstructive pulmonary disease; DMG: Disease Management Group.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

SRS had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. SRS and DK contributed to the study conception and design, analysis and interpretation of data, drafting the manuscript for important intellectual content, as well as reading and approving the final manuscript. RG and RD contributed to study analysis and interpretation of the data and review of the manuscript. RR contributed to the study conception and design and interpretation of data analysis and review of final manuscript for important intellectual content. All authors read and approved the final manuscript.

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