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Burden of respiratory abnormalities in microwave popcorn and flavouring manufacturing workers

Ethan D. Fechter-Leggett[1], **Sandra K. White**[1,2], **Kathleen B. Fedan**[1], **Jean M. Cox-Ganser**[1], and **Kristin J. Cummings**[1]

[1]Respiratory Health Division, National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC), Morgantown, West Virginia, USA

[2](Current affiliation) Department of Pathology, University of Utah, Salt Lake City, Utah, USA

Abstract

Objectives—Diacetyl, a butter-flavour compound used in food and flavouring production, is a respiratory toxin. We characterized the burden of respiratory abnormalities in workers at popcorn and flavouring manufacturing facilities that used diacetyl as evaluated through U.S. National Institute for Occupational Safety and Health (NIOSH) health hazard evaluations.

Methods—We performed analyses describing the number and percentage of current and former workers from popcorn and flavouring manufacturing facilities where NIOSH administered a respiratory health questionnaire and spirometry testing who met case definitions of suspected flavourings-related lung disease. Case definitions were — Pathologist-reported: lung biopsy pathology report stating supportive of/consistent with constrictive bronchiolitis or bronchiolitis obliterans; Probable: obstructive/mixed spirometric pattern with forced expiratory volume in 1 second (FEV1) <60% predicted; Possible: obstructive/mixed spirometric pattern with FEV1 ≥60% or any spirometric restriction; Symptoms Only: normal spirometry plus exertional dyspnoea or usual cough.

Results—During 2000–2012, NIOSH collected questionnaire and spirometry data on 1407 workers (87.0% current, 13.0% former) at nine facilities in eight states. After applying case definitions, 4 (0.3%) were classified as Pathologist-reported, 48 (3.4%) as Probable, 234 (16.6%) as Possible, and 404 (28.7%) as Symptoms Only. The remaining 717 (51.0%) workers had normal spirometry without exertional dyspnoea or usual cough. Seven of 11 workers with biopsies did not meet the Pathologist-reported case definition, although four met Probable and three met Possible.

Address correspondence to Dr. Ethan D. Fechter-Leggett, Respiratory Health Division, National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC), 1095 Willowdale Road, Mailstop 2800, Morgantown, WV 26505, USA. Telephone: (304) 285-6030. iun8@cdc.gov.

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Conclusions—This approach demonstrates the substantial burden of respiratory abnormalities in these workers. A similar approach could quantify the burden of respiratory abnormalities in other industries that use diacetyl.

INTRODUCTION

Diacetyl is an alpha-diketone that confers a buttery smell and taste to food or flavouring agents.[1] Natural and synthetic forms of diacetyl have been used in the microwave popcorn and flavouring industries as a butter-flavouring compound because of this flavour profile, and diacetyl has been identified during volatile organic compound air sampling in these workplaces.[2, 3] In 2000, a cluster of advanced lung disease in former workers of a microwave popcorn facility (sentinel plant) was reported by the health department; the U.S. National Institute for Occupational Safety and Health (NIOSH) conducted air sampling and cross-sectional medical evaluations at the sentinel plant and concluded that occupational obliterative bronchiolitis among these workers was likely caused by respiratory exposure to diacetyl.[4, 5] Subsequent experimental studies revealed that respiratory exposure to diacetyl causes severe injury to the respiratory epithelium in animals, putting microwave popcorn and flavouring manufacturing workers who are exposed to diacetyl at risk for lung disease.[6–8]

Obliterative bronchiolitis, sometimes referred to as constrictive bronchiolitis obliterans[9] or bronchiolitis obliterans,[10] is a rare lung disease characterized by narrowing of the respiratory bronchioles, without affecting the alveolar walls or alveolar ducts, secondary to inflammation and fibrotic changes in response to tissue injury.[11] The clustering of cases of this rare lung disease at a facility that used diacetyl led to a series of NIOSH on-site medical investigations at other facilities that also used diacetyl, including additional microwave popcorn and flavouring manufacturing facilities, through the Health Hazard Evaluation (HHE) Program.[3, 5, 12–18] Historically, obliterative bronchiolitis was considered an obstructive lung disease, manifesting as fixed airway obstruction with decreased forced expiratory volume in 1 second (FEV1) and decreased FEV1 to forced vital capacity (FVC) ratio on spirometry testing.[11, 19] Hence, early investigations focused on identifying microwave popcorn and flavouring manufacturing workers with spirometric obstruction. At the sentinel plant, current workers overall had 3.3 times more airway obstruction than expected, and workers who had never smoked had 10.8 times more airway obstruction than expected, compared to national prevalences.[20] Following the sentinel plant investigation in 2000, subsequent NIOSH investigations over the next decade documented similar patterns of excess obstruction or workers with obliterative bronchiolitis in both microwave popcorn workers and flavouring manufacturing workers.[19, 21, 22] In one study that included 16 workplaces in California, flavouring manufacturing workers were 2.7 times more likely to have severe airways obstruction (defined as FEV1 <50% predicted) than the general population.[23]

There is increasing evidence that the spirometric abnormalities of individuals with obliterative bronchiolitis are not limited to purely obstructive patterns. Some patients with biopsy-confirmed obliterative bronchiolitis have had normal spirometry,[24–26] spirometric restriction,[25, 26] or mixed restriction and obstruction.[4, 25, 26] Because of this range of spirometric findings that includes normal, spirometry testing alone might not be sensitive

enough to detect all cases of obliterative bronchiolitis. Respiratory symptoms are also part of the overall respiratory disease burden and might be more sensitive to detecting flavourings-related lung disease than spirometry. Textbook descriptions of obliterative bronchiolitis describe respiratory symptoms of exertional dyspnoea and usual cough,[10] which have been documented in microwave popcorn workers to be as high as 2.6 times national prevalences.[20] At one flavouring manufacturing plant, workers who used flavouring ingredients had 4.7 times the odds of reporting work-related usual cough than workers who did not use flavouring ingredients.[27]

Considering the range of spirometry results found in individuals with obliterative bronchiolitis and the excess exertional dyspnoea and chronic cough found in microwave popcorn and flavouring manufacturing workers, a narrow focus on the classic finding of spirometric obstruction in obliterative bronchiolitis might underestimate the true burden of respiratory morbidity in diacetyl-exposed workers. Therefore, we sought to characterize the overall burden of respiratory abnormalities documented by the NIOSH HHE Program investigations during 2000–2012 at microwave popcorn and flavouring manufacturing facilities that used diacetyl in production processes, including all spirometric findings and the traditionally described symptoms of exertional dyspnoea and usual cough.

METHODS

Facility Selection

NIOSH conducts workplace health hazard evaluations after receiving a request from company management, three current workers, or a labour union representative, as authorized by U.S. federal regulations (42 CFR 85),[28] or from a federal, state, or local government agency. We included the nine facilities that used diacetyl in production processes that were evaluated by NIOSH during 2000–2012 as part of the HHE program where NIOSH administered a respiratory health questionnaire and spirometry testing. Two of these evaluations were requested by management, four by employees, and three by state health departments.

Study Population

All current workers were invited to participate in the medical evaluation at all facilities, except one facility where current worker invitations to participate were limited to those who worked in the production rooms, quality control laboratory, warehouse, and maintenance areas. Former workers were recruited to participate in the medical evaluations primarily by informal referral by co-workers. However, at one facility, former workers were also actively recruited through newspaper advertisements and telephone calls using rosters provided by facility management or temporary agencies that supplied the plant with employees. For the current analysis, workers who met the following were included in the study population: (1) current or former worker from a microwave popcorn or flavouring manufacturing facility evaluated through a NIOSH HHE investigation during 2000–2012, (2) completed a NIOSH-administered respiratory health questionnaire, and (3) completed NIOSH-administered spirometry testing.

Case Definitions

We developed case definitions to classify each worker's possibility of flavourings-related lung disease. To put the burden of respiratory abnormalities among these workers into the context of how obliterative bronchiolitis has historically been conceptualized, we used classic textbook descriptions of obliterative bronchiolitis of obstructive deficits, shortness of breath, and chronic cough[10] as a framework. Because of the documented range of spirometric abnormalities in patients with biopsy-confirmed obliterative bronchiolitis, we also incorporated restriction, mixed restriction and obstruction, and normal spirometry into case definitions. Case definitions were as follows: Pathologist-reported — lung biopsy pathology report stating supportive of or consistent with constrictive bronchiolitis or bronchiolitis obliterans; Probable — spirometric obstruction or mixed restriction/obstruction with FEV1 <60% predicted; Possible — spirometric obstruction or mixed restriction/obstruction with FEV1 ≥60% predicted or any spirometric restriction; Symptoms Only — normal spirometry plus exertional dyspnoea or usual cough; Normal Spirometry, No Symptoms — normal spirometry plus neither exertional dyspnoea nor usual cough.

Data Sources

We used worker-reported exertional dyspnoea and usual cough information obtained from the NIOSH-administered, cross-sectional questionnaire at each facility. Symptom information was assessed using the same questions among all facilities that were adapted from the American Thoracic Society (ATS) standardized respiratory symptom questionnaire.[29] We obtained lung biopsy information from published HHE reports and case reports in the scientific literature.[4, 12, 15, 20, 21, 30] We calculated tenure as the total amount of time employed by the company, including work in office and other non-production jobs and excluding time spent away from the facility during extended medical leave.

During each NIOSH HHE, spirometry was conducted by NIOSH-trained technicians using a dry rolling-seal volume spirometer following ATS guidelines in effect at the time of the respective medical evaluation.[31, 32] In the current analysis, all spirometry tests were interpreted based on the 2005 ATS interpretive guidelines.[33] For participants with multiple spirometry tests because of their participation in longitudinal follow-up evaluations, we used the first interpretable quality test. We defined an interpretable quality test as one with at least two trials that met the ATS acceptability criteria[31, 32] with the highest two values of FVC and FEV1 each repeatable within 250 ml.

Statistical Analyses

The data analysis was part of a research study reviewed and approved by the NIOSH Institutional Review Board. We used SAS version 9.4 software (SAS Institute, Cary, North Carolina, USA) to perform analyses describing the number and percentage of workers meeting each case definition; to summarize demographic characteristics, spirometric parameters, and reported symptoms; and to perform statistical comparisons. We assessed for differences in sex, age, Body Mass Index (BMI), smoking status, and tenure among all possible pairs of case definitions. Because age, BMI, and tenure were not normally distributed, we used the nonparametric Kruskal-Wallis and Mann-Whitney tests. For sex and smoking status, we used Pearson's chi-square or Fisher's exact tests. For overall tests, we

considered p≤0.05 statistically significant. For all pairwise comparisons (10 total pairs), we applied a Bonferroni correction and considered p≤0.005 statistically significant.

RESULTS

During 2000–2012, NIOSH collected respiratory symptom data and performed spirometry on 1407 microwave popcorn or flavouring manufacturing workers (87.0% current, 13.0% former) at nine facilities in eight states (table 1). Overall, most workers were male (57.4%), white (81.1%), and their median age was 36 (range: 18–72) years. Among all workers, 44.1% were never smokers (44.9% of current workers and 38.8% of former workers) and 55.9% were ever (current or former) smokers. Median BMI fell within the adult "overweight" category of 25.0–29.9[34] at 27.8. The median number of years worked (tenure) overall was 2.8, with former workers having a lower median tenure (1.0 years) than current workers (3.6 years). Eleven lung biopsies came from current (n=8) and former workers (n=3).

After applying case definitions for flavourings-related lung disease, four (0.3%) were classified as Pathologist-reported, 48 (3.4%) as Probable, 234 (16.6%) as Possible, and 404 (28.7%) as Symptoms Only (figure 1). The remaining 717 (51.0%) workers had normal spirometry without exertional dyspnoea or usual cough. Additional findings (not mutually exclusive) on the four biopsies from workers who met the Pathologist-reported case definition included granulomas (2 workers), respiratory bronchiolitis (2 workers), and emphysema (1 worker). Of the seven workers with biopsies that did not meet the Pathologist-reported case definition, four met the Probable and three met the Possible case definitions. Pathologies (not mutually exclusive) noted in these biopsies that did not meet the Pathologist-reported case definition included granulomas (3 workers), respiratory bronchiolitis (3 workers), chronic fibrous pleuritis (2 workers), interstitial fibrosis (2 workers), peribronchial inflammation (1 worker), and emphysema (1 worker).

Demographics of all workers by case definition are presented in Table 2. Pathologist-reported cases of obliterative bronchiolitis were identified in both current and former workers. One worker meeting the Pathologist-reported case definition had a tenure of less than six months. The Probable group was significantly older than the Possible, Symptoms Only, and Normal Spirometry, No Symptoms groups; the Probable group also had significantly longer tenure than the Possible and Symptoms Only groups. Additionally, the Possible group was significantly older than the Symptoms Only and Normal Spirometry, No Symptoms groups. Sex and smoking status did not significantly differ between pairwise comparisons of Pathologist-reported, Probable, Possible, and Symptoms Only groups. BMI significantly differed only between the Pathologist-reported and Possible groups.

Overall, 20.3% of all workers had abnormal spirometry results, and 41.2% reported exertional dyspnoea and/or usual cough. Spirometry results and symptoms reported among all workers by case definition are presented in Table 3. Most (79.2%) of the workers classified as Probable had a mixed pattern on spirometry. Almost half (49.6%) of the workers classified as Possible had an obstructive pattern on spirometry while 43.6% of these workers had a restrictive pattern. All (100%) of workers classified as Pathologist-reported

and nearly all (95.8%) classified as Probable reported exertional dyspnoea and/or usual cough. Of the workers classified as Possible, 43.5% reported exertional dyspnoea, 31.6% reported usual cough, and 22.0% reported both. Of those classified as Symptoms Only, 77.3% reported exertional dyspnoea, 52.5% reported usual cough, and 29.4% reported both. Among all workers reporting exertional dyspnoea or usual cough with available symptom onset information, 68.8% reported post-hire onset of at least one of these respiratory symptoms.

Figure 2 displays case classifications by worker type (current or former worker). Approximately half (55.6%) of current workers and 19.7% of former workers had normal spirometry and reported neither exertional dyspnoea nor usual cough, while the remaining (44.4% of current workers and 80.3% of former workers) were classified as Symptoms Only or worse. Approximately 18.0% of current workers and 35.5% of former workers were classified as Possible, Probable, or Pathologist-reported.

DISCUSSION

Many of the early investigations and case reports of microwave popcorn and flavouring manufacturing workers focused on lung biopsy results and obstruction/mixed spirometry patterns for defining flavourings-related lung disease. Across all facilities included in this study, only 11 workers had information on lung biopsies published in HHE reports or the scientific literature, and only four of these 11 had published information that noted the biopsies were supportive of or consistent with constrictive bronchiolitis or bronchiolitis obliterans. While the NIOSH investigations detected biopsy-confirmed obliterative bronchiolitis cases in current and former workers from both microwave popcorn and flavouring manufacturing facilities,[5, 12, 15] we demonstrate in this paper that the actual burden of respiratory morbidity in these workers encompasses a larger picture than these few biopsies illustrate. Our results also highlight that biopsy-confirmed flavourings-related lung disease was diagnosed in a worker with less than six months tenure.

Using our case definition approach, we found that almost half of all workers (about 45% of current workers and 80% of former workers) were categorized as Symptoms Only or worse. Although FEV1 percent predicted values for the Probable and Possible case definitions are artificially bound to <60% predicted or ≥60% predicted, respectively, corresponding to the 2005 ATS interpretive guidelines cut-off for moderate severity,[33] the median FEV1 percent predicted values provide a context of lung function impairment severity within each case definition. For example, the Probable case definition required FEV1 to be less than 60% predicted, and the workers who met this case definition had a median FEV1 of about 46% predicted. The FEV1 parameters also demonstrate the spectrum of abnormalities and clinical findings that workers with biopsy-confirmed flavourings-related lung disease exhibit, considering one of the workers classified as Pathologist-reported had an FEV1 of 83% predicted while another had an FEV1 of 21% predicted.

In the current study, about half of the workers classified as Possible had spirometric restriction, and while our case definition scheme required any worker with spirometric restriction to be placed in this category, these workers (approximately 7% of all workers)

could have previously been overlooked as a group possibly having flavourings-related lung disease, despite documented restriction in some individuals with biopsy-confirmed obliterative bronchiolitis.[25, 26] Although spirometric restriction has been associated with higher BMI, BMI of the Probable, Possible, Symptoms Only, and Normal Spirometry, No Symptoms groups did not significantly differ in pairwise comparisons, indicating that being overweight or obese wasn't the sole driver of spirometric abnormalities. A previous study summarizing spirometry results of workers at a flavouring manufacturing facility found 3.7 times more spirometric restriction than expected as well as higher odds of excessive FEV1 declines over time in workers with high potential for flavourings exposure compared with workers with lower potential for flavourings exposure.[35] Another study of persons exposed to dust from the World Trade Center revealed evidence of spirometric restriction that the authors attributed to an obstructive process and air trapping within the small airways.[36] Spirometric restriction in a population of workers from microwave popcorn and flavouring manufacturing facilities might be indicative of a broader functional spectrum of flavourings-related lung disease affecting the small airways.[37] Hence, these workers with spirometric restriction, especially in combination with exertional dyspnoea and/or usual cough, could be showing early signs of flavourings-related lung disease.

The proportion of never smokers in this group of workers (about 44%) is lower than the general population during the study period, which ranged from 55 to 61%;[38] however, smoking alone probably does not account for the burden of respiratory morbidity seen in these workers, as documented in previous studies.[20, 26, 27] Our results demonstrate that respiratory abnormalities were not limited to current or former smokers, and smoking status did not significantly differ between pairwise comparisons of groups of workers with respiratory abnormalities. For the never smokers in these groups, their respiratory abnormalities must be ascribed to factors other than current or former smoking. Among diacetyl-exposed workers at the sentinel plant, both never smokers and current/former smokers had excess risk of having obstruction, shortness of breath, and chronic cough; in fact, never smokers had almost seven times *more* excess risk than current/former smokers of having obstruction and almost two times *more* excess risk of shortness of breath.[20] Besides smoking history, known occupational exposure to flavouring agents such as diacetyl is important information physicians should consider when evaluating the respiratory health of these workers.[37]

The combination of classic symptoms of exertional dyspnoea and usual cough, excess spirometric abnormalities including obstruction, and occupational exposure to a known respiratory toxin, creates a burden of evidence suggestive of possible subclinical or undiagnosed flavourings-related respiratory disease in these microwave popcorn and flavouring manufacturing workers. A comprehensive review and risk assessment published by NIOSH addressing occupational exposure to diacetyl acknowledges that although diacetyl causes obliterative bronchiolitis, exposure to diacetyl might also be responsible for a spectrum of respiratory disease.[37] Almost 70% of workers reported their exertional dyspnoea or usual cough began post-hire; still, the presence of pre-hire symptoms does not preclude development of respiratory abnormalities due to occupational exposures. The continuum of symptoms and respiratory impairment as summarized in the current study is consistent with the notion that flavourings-related lung disease might actually be a spectrum

of respiratory disease, the most severe of which is obliterative bronchiolitis, with earlier stages manifesting as only respiratory symptoms and a range of spirometric patterns. This concept is perhaps best illustrated by our finding that the Symptoms Only group was significantly younger with shorter tenure, despite not significantly differing in BMI or smoking status, compared to groups of more severely affected workers. Our finding that seven of 11 biopsies did not meet the Pathologist-reported case definition but did exhibit other evidence of lung damage could be explained by the patchy nature of the pathologic changes in the lungs associated with obliterative bronchiolitis; a range of lung tissue pathologies representing obliterative bronchiolitis itself; or other respiratory diseases such as hypersensitivity pneumonitis, interstitial fibrosis, smoking-related respiratory bronchiolitis-interstitial lung disease, and emphysema in these workers.[4, 26, 37, 39, 40]

This study has a few limitations. First, this group of current and former workers is not representative of all workers in the microwave popcorn and flavouring manufacturing industries, because we identified facilities based on participation in NIOSH's HHE program; however, worker participation at each facility was generally high among current workers.[3, 5, 12–18, 22, 37] Second, former workers were recruited for participation in the medical evaluations differently than current workers, precluding formal comparison between the two groups of workers; this limitation is inherent in most HHE evaluations so therefore could not have been reasonably avoided. The high percentage of former workers classified as Symptoms Only or worse could reflect ill former workers being more motivated than healthy former workers to participate in the medical evaluation or the healthy worker effect whereby symptomatic workers exited the workforce. It is also possible that former workers might have been employed before exposure controls, if any were in use at the facility, were implemented and thus occupational exposure to diacetyl might have been higher for these former workers than for current workers at the time of the NIOSH medical evaluation. Third, only HHEs where NIOSH administered a respiratory health questionnaire and spirometry testing were included in analyses in order to take advantage of the standardized respiratory symptoms questions and maximize our confidence in the spirometry results' quality. Several other HHE investigations have been performed in other facilities where diacetyl was found where NIOSH did not administer a questionnaire and perform spirometry testing. The details of these additional investigations have been discussed elsewhere,[37] and overall findings are consistent with the current study. Finally, we did not have information about workers' past or subsequent diagnoses that might account for their respiratory abnormalities (e.g., asthma, interstitial lung disease), workplace smoking policies, or cotinine levels to examine secondhand smoke exposures; without this knowledge, we are unable to definitively attribute workers' respiratory abnormalities specifically to flavourings-related lung disease. We also did not consider job-level exposure information that might have provided further insights into the relationship between workers' respiratory abnormalities and occupational exposure to flavourings; however, the Probable group was older and had a longer tenure than groups of less severely affected workers, further supporting occupational exposures as a potential contributing factor in their respiratory abnormalities. Job- or task-level data would be useful to incorporate in future analyses to identify similarities or differences between microwave popcorn and flavouring manufacturing workers.

CONCLUSIONS

Our case definition approach demonstrates the substantial burden of respiratory abnormalities in current and former workers at microwave popcorn and flavouring manufacturing facilities visited by NIOSH as part of the HHE program during 2000–2012. Although diacetyl exposure causes obliterative bronchiolitis, the overall burden of respiratory morbidity in microwave popcorn and flavouring manufacturing facility workers is substantially larger than the few biopsies reported in the literature illustrate. Flavourings-related lung disease likely exhibits a spectrum of respiratory function abnormalities, including spirometric obstruction, restriction, and mixed obstruction/restriction, and further research is needed addressing the role of spirometric restriction in under-recognised flavourings-related lung disease. Considering naturally-occurring diacetyl and other alpha-diketones are produced or used during various food production processes, a similar approach could be used to quantify the burden of respiratory abnormalities in other industries where flavouring chemicals are found.

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SUMMARY BOX

What is already known about this subject?

Occupational exposure to flavouring chemicals including diacetyl, a butter-flavouring alpha-diketone, causes the rare and severe lung disease obliterative bronchiolitis.

What are the new findings?

Using a case definition approach, we found current and former workers at nine microwave popcorn or flavouring manufacturing facilities across eight states exhibited a substantial burden of reported exertional dyspnoea and usual cough as well as a range of spirometric abnormalities.

How might it impact on policy or clinical practice in the foreseeable future?

Workers with relevant occupational exposures to diacetyl and other flavouring chemicals who have abnormal or an excessive decline in lung function should be further evaluated for flavourings-related lung disease, even if spirometry results do not exhibit an obstructive pattern.

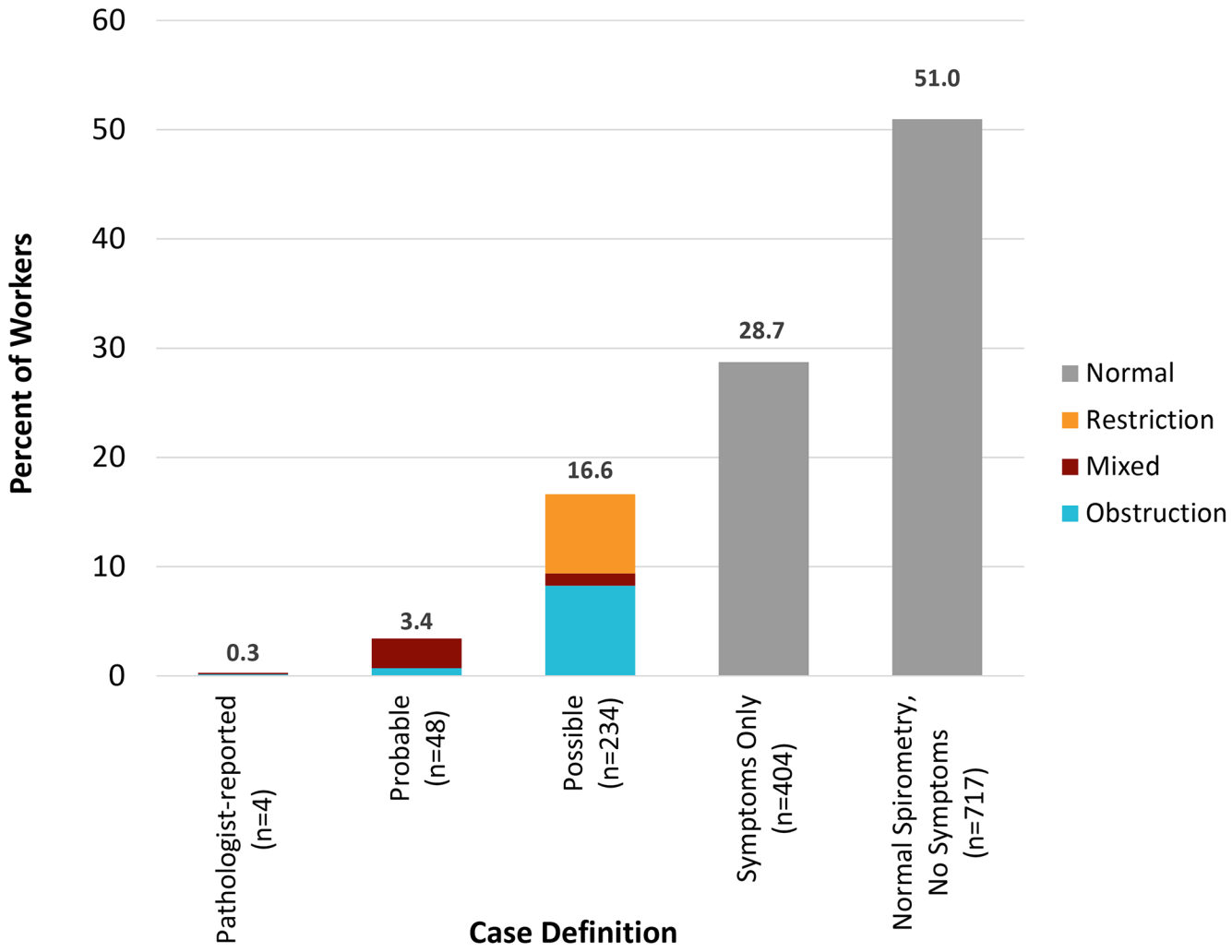

Figure 1.

Case definition classification and spirometry results of all workers (N=1407). Numbers above bars represent percent of all workers meeting that case definition.

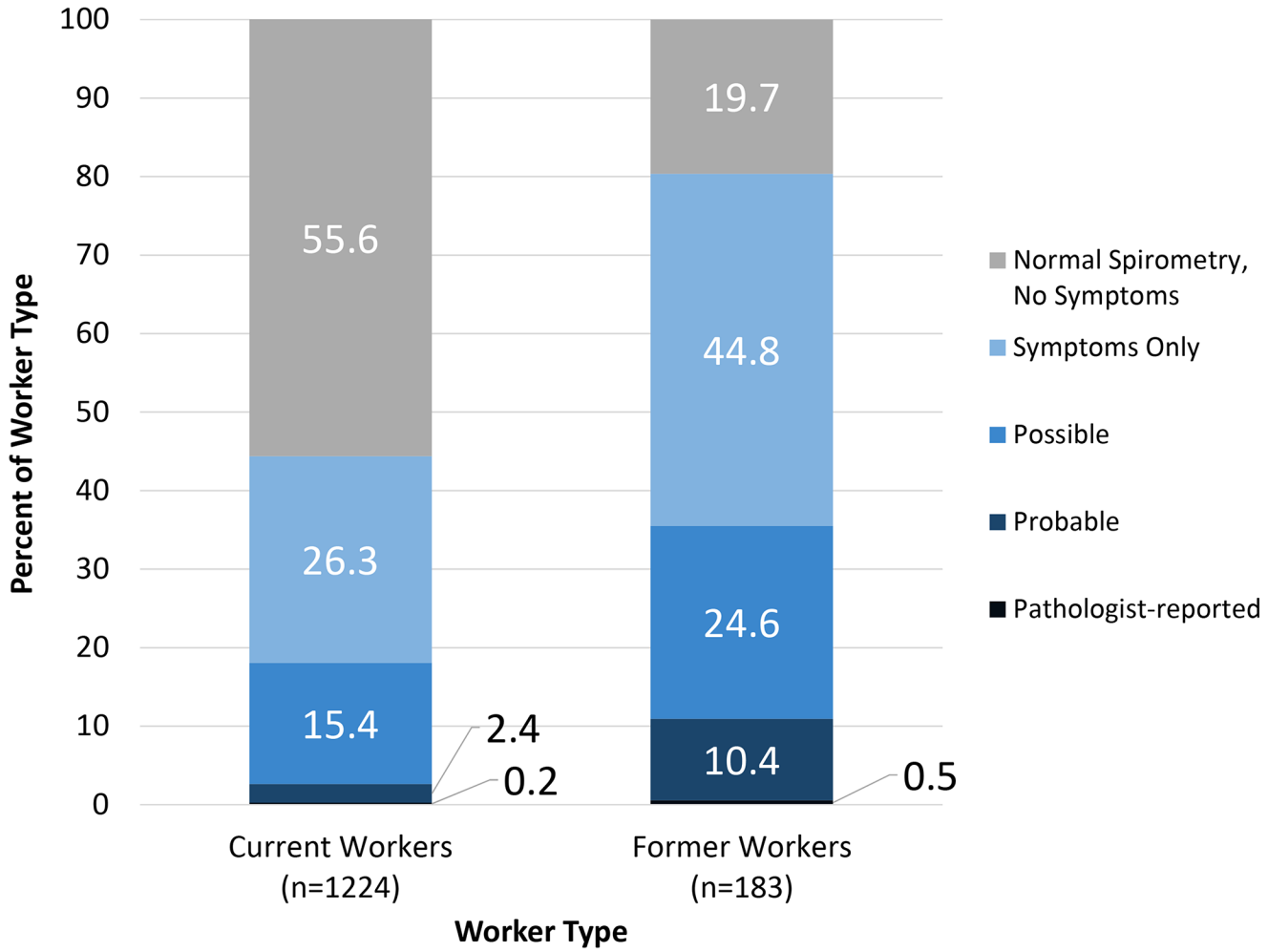

Figure 2.
Case definition classification of all workers by worker type (N=1407). Numbers within bars represent percent of worker type meeting that case definition.

Table 1.

Demographics of microwave popcorn and flavouring manufacturing workers (N=1407)

Worker type, n (%)	
Current	1224 (87.0)
Former	183 (13.0)
Sex, n (%)	
Male	808 (57.4)
Female	599 (42.6)
Race/ethnicity, n (%)	
White	1141 (81.1)
Hispanic	181 (12.9)
Black	42 (3.0)
Other	34 (2.4)
Asian	9 (0.6)
Smoking status, n (%) [*]	
Never smoker	620 (44.1)
Current smoker	544 (38.7)
Former smoker	242 (17.2)
Age, median (range), years	36 (18–72)
Body Mass Index, median (range)	27.8 (15.7–61.0)
Tenure, median (range), years [†]	2.8 (<0.5–37.5)

[*] Missing=1.

[†] Missing=4.

Table 2.

Demographics of all workers, by case definition (N=1407)

	Pathologist-reported (n=4)	Probable (n=48)	Possible (n=234)	Symptoms Only (n=404)	Normal Spirometry, No Symptoms (n=717)
Worker type, n (column %)					
Current	3 (75.0)	29 (60.4)	189 (80.8)	322 (79.7)	681 (95.0)
Former	1 (25.0)	19 (39.6)	45 (19.2)	82 (20.3)	36 (5.0)
Sex, n (column %) *					
Male	3 (75.0)[a,b]	24 (50.0)[a,b]	134 (57.3)[a,b]	194 (48.0)[a]	453 (63.2)[b]
Female	1 (25.0)[a,b]	24 (50.0)[a,b]	100 (42.7)[a,b]	210 (52.0)[a]	264 (36.8)[b]
Age (years) *					
Median	47[a,b,c,d]	48[a]	41[b]	35[c,d]	35[d]
Mean	46	47	40	37	37
Range	38–51	24–68	19–71	18–66	18–72
Body Mass Index *					
Median	22.2[a]	28.0[a,b]	28.2[b]	28.0[a,b]	27.4[a,b]
Mean	21.9	28.4	29.5	29.2	28.2
Range	19.9–23.2	15.7–52.3	16.8–50.9	16.9–61.0	16.5–47.6
Smoking status, n (column %) *†					
Never smoker	3 (75.0)[a,b]	17 (35.4)[a,b]	87 (37.3)[a]	134 (33.2)[a]	379 (52.9)[b]
Current smoker	1 (25.0)[a,b]	22 (45.8)[a,b]	116 (49.8)[a]	205 (50.7)[a]	200 (27.9)[b]
Former smoker	0 (0.0)[a,b]	9 (18.8)[a,b]	30 (12.9)[a]	65 (16.1)[a]	138 (19.2)[b]
Tenure (years) *‡					
Median	3.3[a,b,c]	6.3[a]	2.5[b,c]	2.4[c]	3.0[a,c]
Mean	5.8	7.3	4.7	4.8	5.1
Range	<0.5–16.1	<0.5–30.4	<0.5–27.8	<0.5–33.1	<0.5–37.5

* Overall significant difference at p≤0.05 among five case definition groups. All pair combinations along a row without a superscript in common are statistically significantly different at p≤0.005 (Bonferroni correction).

† Missing=1 (Possible, 1).

‡ Missing=4 (Probable, 1; Symptoms Only, 1; Normal Spirometry, No Symptoms, 2).

Table 3.

Spirometry results and symptoms of all workers, by case definition (N=1407)

	Pathologist-reported (n=4)	Probable (n=48)	Possible (n=234)	Symptoms Only (n=404)	Normal Spirometry, No Symptoms (n=717)
Spirometry results, n (column %)					
Obstruction	2 (50.0)	10 (20.8)	116 (49.6)	—	—
Mixed	2 (50.0)	38 (79.2)	16 (6.8)	—	—
Restriction	0 (0)	—	102 (43.6)	—	—
Normal	0 (0)	—	—	404 (100.0)	717 (100.0)
FVC percent predicted (%)					
Median	73.0	72.7	82.1	98.6	101.1
Mean	76.0	69.0	87.9	99.8	102.1
Range	60.3–97.5	36.2–100.6	59.0–123.1	76.5–138.0	80.9–137.6
FEV1 percent predicted (%)					
Median	32.7	46.4	79.5	97.8	100.9
Mean	42.4	44.1	78.9	99.0	101.7
Range	20.9–83.3	14.3–59.8	55.8–99.8	74.6–134.8	77.2–142.6
Symptoms reported, n (%) [*]					
Exertional dyspnoea [†]	3 (75.0)	43 (91.5)	101 (43.5)	310 (77.3)	0 (0)
Post-hire onset [‡,§]	3 (100.0)	32 (80.0)	55 (67.1)	177 (64.8)	—
Usual cough [¶]	4 (100.0)	31 (64.6)	74 (31.6)	212 (52.5)	0 (0)
Post-hire onset [‡,**]	4 (100.0)	24 (80.0)	43 (63.2)	127 (65.8)	—
Both [††]	3 (75.0)	28 (59.6)	51 (22.0)	118 (29.4)	0 (0)
Post-hire onset (both) [‡,‡‡]	3 (100.0)	22 (81.5)	28 (65.1)	62 (62.6)	—
Either or both [§§]	4 (100.0)	46 (95.8)	124 (53.2)	404 (100.0)	0 (0)
Post-hire onset (at least one) [‡,¶¶]	4 (100.0)	34 (79.1)	70 (68.0)	242 (67.4)	—

[*] Exertional dyspnoea assessed using question adapted from American Thoracic Society – Division of Lung Diseases (ATS-DLD) standardized questionnaire[29] question 13A as “Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?” Usual cough assessed using ATS-DLD question 7A “Do you usually have a cough?”

[†] Missing=9 (Probable, 1; Possible, 2; Symptoms Only, 3; Normal Spirometry, No Symptoms, 3).

[‡] Post-hire onset defined as worker-reported symptom onset occurring after worker-reported earliest hire date at the facility.

[§] Of those reporting exertional dyspnoea. Post-hire information missing for n=59 (Probable, 3; Possible, 19; Symptoms Only, 37).

[¶] Missing=1 (Normal Spirometry, No Symptoms, 1).

[**] Of those reporting usual cough. Post-hire information missing for n=26 (Probable, 1; Possible, 6; Symptoms Only, 19).

[††] Missing=10 (Probable, 1; Possible, 2; Symptoms Only, 3; Normal Spirometry, No Symptoms, 4).

‡‡Of those reporting both exertional dyspnoea and usual cough. Post-hire information missing for n=28 (Probable, 1; Possible, 8; Symptoms Only, 19).

§§Missing=5 (Possible, 1; Normal Spirometry, No Symptoms, 4).

¶¶Of those reporting at least one of exertional dyspnoea or usual cough. Post-hire information missing for n=69 (Probable, 3; Possible, 21; Symptoms Only, 45).

FVC, forced vital capacity; FEV1, forced expiratory volume in one second.