

Characteristics and medical resource use of asthmatic subjects with and without work-related asthma

Catherine Lemiere, MD, MSc,^a Amélie Forget, MSc,^a Marie-Hélène Dufour,^b
Louis-Philippe Boulet, MD,^b and Lucie Blais, PhD^a Montreal, Quebec, Canada

Background: Asthma is work related when there is an association between symptoms and work. Occupational asthma (OA) is induced by the workplace, whereas work-exacerbated asthma (WEA) is triggered by the workplace but not induced by it.

Objective: We sought to compare the clinical characteristics and the use of medical resources between subjects with work-related asthma (WRA) and asthmatic control subjects without WRA, as well as between subjects with OA and subjects with WEA.

Methods: We performed a retrospective cohort study of the charts of subjects with WRA who were investigated between 2001 and 2004 in our centers. These subjects were matched according to sex, age, and FEV₁ to subjects with non-WRA investigated during the same period. All charts were linked to the information provided by the Régie de l'assurance maladie du Québec, including outpatient clinic visits and visits to the emergency department and hospitalizations during the year before and after the initial assessment in our centers.

Results: Three hundred fifty-one subjects had WRA (WEA, 145; OA, 206), whereas 384 subjects were asthmatic control subjects without WRA. Subjects with WRA had more asthma exacerbations than subjects with non-WRA. The risk factor of experiencing a severe asthma exacerbation was no greater for OA than for WEA (odds ratio, 1.15; 95% CI, 0.75-1.75).

Conclusion: WRA is associated with a larger use of medical resources than non-WRA.

Clinical implications: Improving the diagnosis and management of WRA is crucial for limiting the use of medical resources associated with this condition. (J Allergy Clin Immunol ■■■■;■■■:■■■-■■■.)

Key words: Occupational asthma, work-exacerbated asthma, work-related asthma, medical resource

Asthma is “work related” when there is an association between symptoms and work. Work-related asthma (WRA) includes 2 distinct categories: work-exacerbated asthma (WEA; ie, preexisting or coincidental new-onset adult asthma that is worsened by nonspecific factors in the workplace) and occupational asthma (OA; ie, adult asthma caused by workplace exposure and not by factors outside of the workplace).¹

It has been estimated that 18% to 34% of employed subjects with asthma report a worsening of their asthma in association with workplace exposures.²⁻⁵ WRA appears to be associated with a greater use of medical resources than non-work-related asthma (NWRA).⁶ Furthermore, there might be an association between work exposures and asthma severity.⁷ However, in the majority of studies, the diagnosis was not made on the basis of respiratory function test results, which might have led to misdiagnosis of asthma or WRA in some cases.

WRA is often considered a single entity without distinguishing OA from WEA. Indeed, differentiating OA from WEA is very difficult, even in clinical practice, where the clinicians have access to the functional characteristics of the subjects,⁸ and even more when the diagnosis is solely based on questionnaires. OA has been extensively studied during the last 20 years, but the data regarding WEA are scarce. It is unclear whether asthma severity differs between OA and WEA. Whether subjects with WEA use more or less medical resources than subjects with OA is unknown.

The aim of the present study was to compare the clinical characteristics and the use of medical resources between subjects with WRA and asthmatic control subjects without WRA, as well as between subjects with OA and subjects with WEA.

METHODS

Study design

A retrospective cross-sectional study of all the charts of subjects who were investigated for suspected WRA by means of specific inhalation challenge (SIC) tests between 2001 and 2004 was undertaken at Sacré-Coeur Hospital and Laval Hospital in the Canadian

From ^aHôpital du Sacré-Coeur de Montréal (Québec) and ^bUnité de Recherche en Pneumologie, Institut de Cardiologie et de Pneumologie de l'Université Laval, Hôpital Laval.

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Reprint requests: Catherine Lemiere, MD, MSc, Department of Chest Medicine, Sacré-Coeur Hospital, 5400 Gouin West, Montreal, Quebec, Canada, H4J 1C5. E-mail: catherine.lemiere@umontreal.ca.

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Abbreviations used

ICS: Inhaled corticosteroid
 NWRA: Non-work-related asthma
 RADS: Reactive airways dysfunction syndrome
 OA: Occupational asthma
 SIC: Specific inhalation challenge
 WEA: Work-exacerbated asthma
 WRA: Work-related asthma

province of Quebec. The charts of asthmatic control subjects without WRA investigated during the same period were matched according to sex, age categories (younger or older than 45 years), and FEV₁ categories (lower than 50% of predicted value, 50% to 59% of predicted value, 60% to 79% or predicted value, and greater than 80% of predicted value) to the subjects with WRA. Each WRA chart was matched to a maximum of 3 non-work-related asthma (NWRA) cases.

Definitions

Asthma was defined according to the American Thoracic Society criteria.⁹ OA was defined as the worsening of asthma symptoms related to work with a positive SIC result, whereas WEA was defined as the worsening of asthma symptoms in the workplace with a negative SIC result.¹⁰ In this study OA refers only to OA with a latency period. Because the pathophysiology, investigation, management, and outcome of subjects with reactive airways dysfunction syndrome (RADS) differ substantially from those of subjects with OA with a latency period, cases of RADS were not included in the WRA group.

Procedures

The data collection was performed by a trained research assistant in each center. Demographic data were collected, as were data on work exposure, treatment, respiratory function tests, and results from sputum induction. During the investigation, spirometry,¹¹ methacholine challenge,¹² sputum induction,¹³ and SICs¹⁴ were performed as previously described. Atopy was defined by the presence of at least 1 positive skin prick test response to a battery of 22 common allergens with a wheal diameter equal to or greater than 3 mm.

All of the data were collected on the control day of the SIC, except for the data on PC₂₀, sputum induction, and final diagnoses, which were also collected on the last day of exposure, as well as on the last day of the SIC. For the subjects with NWRA, the data were collected on the day of the first assessment at Sacré-Coeur Hospital. The day of the first visit at Sacré-Coeur or Laval Hospital is referred to in the study as the index visit.

An authorization was obtained from the Commission d'accès à l'information du Québec for linking the medical charts to the information provided by the Régie de l'assurance maladie du Québec and MED-ECHO regarding the outpatient clinic visits, visits to the emergency department, and hospitalizations during the year before and after the initial visit at either Sacré-Coeur or Laval Hospitals.

The project was accepted by Sacré-Coeur and Laval Hospitals' ethics committees. The consultation of the medical charts was approved by the Professional Services Office in both Sacré-Coeur and Laval Hospitals.

Analysis

Descriptive statistics were used to summarize the clinical characteristics of the subjects. Normally distributed data were reported as the arithmetic mean and SD. Nonnormally distributed data were reported as the median and interquartile range. An ANOVA was

performed to compare the results between the different groups of subjects: subjects with OA, subjects with WEA, and control subjects with NWRA. The medical resource use (ie, visits to the clinic, visits to the emergency department, or hospitalizations) was assessed during the year before and after the index visit at either Sacré-Coeur Hospital or Laval Hospital.

The clinical and functional characteristics, as well as the use of medical resources, were also compared between the subjects who were already removed from exposure at the time of the index visit and those who were still working with an ANOVA.

A Poisson regression analysis was performed to compare the risk of a severe exacerbation during the year before and after the index visit between patients with OA and patients with WEA while adjusting for the following potential confounders: age, sex, atopy, smoking, PC₂₀, duration of exposure after onset of symptoms, molecular weight of agents, treatment with inhaled corticosteroids (ICSs), use of long-acting β_2 -agonists, removal from exposure, and visit to the clinic for any cause. A severe asthma exacerbation was defined by a visit to the emergency department or a hospitalization for asthma. Visits at the emergency department or hospitalization for asthma occurring within a 2-week period were considered the same exacerbation. Significance was accepted at the level of 95%. All analyses were performed with SAS, version 8.02 (SAS Institute, Inc, Cary NC).

RESULTS

A total of 897 charts were reviewed. Five hundred thirteen subjects were investigated for WRA during a 3-year period. Three hundred fifty-one subjects had WRA: 145 had WEA, and 206 had OA. Three subjects who were given diagnoses of RADS were not included in the WRA or control groups, as mentioned in the definition section. One hundred sixty-two subjects did not have asthma at the time of the investigation. The repartition of the various diagnoses is shown in Fig 1.

Three hundred eighty-four subjects were asthmatic control subjects without WRA.

The clinical characteristics of subjects with OA, WEA, and asthmatic control subjects are detailed in Table 1.

Comparison between subjects with WRA and subjects with NWRA

Asthmatic subjects with and without WRA were matched on the basis of sex, age, and FEV₁. However, during the course of the study, we had to exclude subjects with NWRA identified initially because their medical charts were not retrieved. A greater number of charts reporting the data of female asthmatic subjects than of male asthmatic subjects were retrieved. Consequently, there were more women in the control group than in the WRA group, although the proportion of male and female subjects was not statistically different between groups. Nevertheless, the match was kept for age and FEV₁, which were similar between the groups. There were fewer non-smokers in the WRA groups than in the NWRA groups (32.5% vs 40.5%, $P = .005$, Table 1).

Subjects with WRA visited their physicians more frequently because of their asthma than asthmatic subjects without WRA before and after the index visit at Sacré-Coeur or Laval Hospital. Subjects with WRA were more

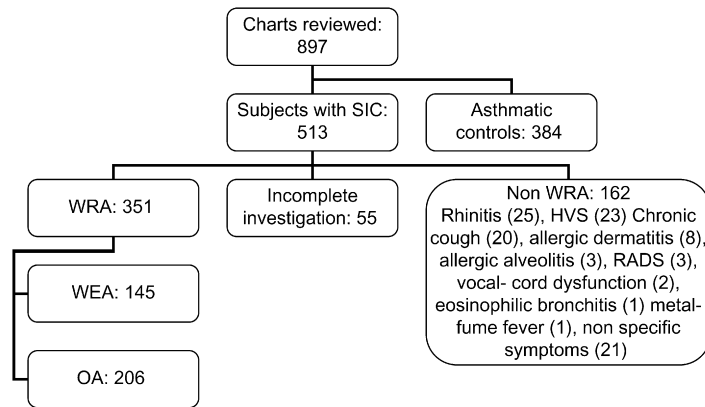


FIG 1. Repartition of the different diagnoses identified during the chart review. *HVS*, Hyperventilation syndrome.

TABLE I. Characteristics of subjects with OA, WEA, and NWRA

	WEA	OA	NWRA
N	145	206	384
Sex			
Male	101 (70%)	137 (67%)	200 (52%)
Female	44 (30%)	69 (33%)	194 (48%)
Age at first visit (y)	42.0 ± 12.0	40.1 ± 11.2	44.0 ± 15.4
Smoking habits (NS/CS/exS/MV)	47/44/53/1	67/53/8/0	142/65/147/30
Smokers (CS, exS; n [%])	97 (66.9)	61 (29.6)	212 (55.2)
Pack-years	18.2 ± 14.8	14.9 ± 11.8	21.8 ± 22.5
Atopy (n [%])	93 (68)	136 (70)	215 (56), n = 266
No. of subjects away from work at time of investigation	85 (59)	147 (71)	—
Duration between removal from work and first visit (mo)	2.6 ± 7.3	3.1 ± 6.5	—
Duration of symptoms before first visit (y)	4.8 ± 8.4	6.4 ± 8.2	8.5 ± 12.4
Duration of exposure before onset of respiratory symptoms (y)	8.6 ± 10.1	7.8 ± 8.6	—
Duration of exposure after onset of symptoms (y)	2.8 ± 4.3	4.0 ± 5.4	—
FEV ₁ (% predicted)	87.4 ± 16.1	87.6 ± 18.4	87.0 ± 17.0
FVC (% predicted)	96.3 ± 18.3	100.0 ± 32.1	97.6 ± 16.4
PC ₂₀ control day (mg/mL)	3.7 ± 4.8 (n = 129)	3.0 ± 6.4 (n = 169)	2.2 ± 4.0 (n = 359)
PC ₂₀ on last day of exposure (mg/mL)	3.8 ± 5.7 (n = 68)	1.7 ± 5.4* (n = 124)	—
Type of asthmatic reactions	None	Immediate: 58.0%; late: 21.0%; dual: 18.8%; atypical: 1.7%; early late: 0.6% (n = 181)	

NS, Nonsmoker; CS, current smoker; exS, exsmoker; MV, missing values; CS, current smoker, FVC, forced vital capacity.

**P* < .05.

often hospitalized for their asthma than subjects with WRA during the year preceding the initial assessment. In addition, subjects with WRA visited the emergency department more frequently because of their asthma than subjects with NWRA during the year after the index visit (Table II).

Comparison between subjects with WEA and subjects with OA

The demographic and functional characteristics of the subjects with OA were very similar to those of the subjects

with WEA (Table I). The following comparisons made between OA and WEA were crude and not adjusted for any confounding variables. The exposure to the occupational agents during SICs induced a change in airway responsiveness only in subjects with OA (Table I). There was an increase in sputum eosinophil counts after exposure to the offending agent during SIC (6.8% [22.9%]) compared with the baseline value (2.5% [5.1%], *P* < .01) only in subjects with OA. There was a statistically significant increase in sputum neutrophil counts after SIC (54.0% [38.3%]) to occupational agents compared with

TABLE II. Use of medical resources in subjects with WRA and NWRA

	Before index visit		After index visit	
	WRA (n = 351)	NWRA (n = 381)	WRA (n = 351)	NWRA (n = 381)
Visits to clinic for any cause [mean $\pm$ SD; n (%)]	9.8 $\pm$ 7.4*; 337 (96.0)	8.6 $\pm$ 7.2*; 370 (97)	16.0 $\pm$ 8.3*; 350 (99.7)	10.6 $\pm$ 8.5*; 379 (99.5)
Visits to clinic for asthma [mean $\pm$ SD; n (%)]	4.1 $\pm$ 4.3*; 263 (74.9%)*	1.2 $\pm$ 1.7*; 214 (56.2)*	10.0 $\pm$ 6.0*; 341 (97.1)	3.1 $\pm$ 2.2*; 365 (95.8)
Visits to emergency department for asthma [mean $\pm$ SD; n (%)]	0.3 $\pm$ 0.8; 59 (16.8)	0.2 $\pm$ 0.7; 48 (12.6)	0.2 $\pm$ 0.6*; 43 (12.2)*	0.04 $\pm$ 0.2*; 11 (2.9)*
Hospitalizations for asthma [mean $\pm$ SD; n (%)]	0.04 $\pm$ 0.2*; 13 (3.7)*	0.008 $\pm$ 0.7*; 3 (0.8)*	0.0 $\pm$ 0.2; 6 (1.7)	0.0 $\pm$ 0.1; 3 (0.8)

The number of subjects who had at least 1 visit to the clinic or emergency department or 1 hospitalization is shown.

*Comparisons between WRA and NWRA during the year before the first visit or during the year after the first visit with a *P* value of .05 or less.

TABLE III. Use of medical resources in the year before and after the index visit in subjects with OA and WEA

	WEA		OA	
	Off work at time of visit 1 (n = 59)	At work at time of visit 1 (n = 86)	Off work at time of visit 1 (n = 32)	At work at time of visit 1 (n = 174)
Use of medical resources during year before index visit				
Visit to clinic for any cause [mean $\pm$ SD; n (%)]	9.9 $\pm$ 8.9; 56 (94.9)	12.4 $\pm$ 7.7; 85 (98.8)	6.5 $\pm$ 5.2; 31 (96.9)	9.2 $\pm$ 6.8*; 165 (94.8)
Visit to clinic for asthma [mean $\pm$ SD; n (%)]	2.9 $\pm$ 5.1; 34 (57.6)	5.6 $\pm$ 4.3*; 73 (84.9)*	2.1 $\pm$ 2.8; 17 (53.1)	4.2 $\pm$ 4.0*; 139 (79.9)*
Visit to emergency department for asthma [mean $\pm$ SD; n (%)]	0.2 $\pm$ 0.6; 9 (15.3)	0.3 $\pm$ 0.9; 14 (16.3)	0.3 $\pm$ 0.9; 6 (18.8)	0.3 $\pm$ 0.8; 30 (17.2)
Hospitalization for asthma [mean $\pm$ SD; n (%)]	0.1 $\pm$ 0.2; 3 (5.1)	0 $\pm$ 0*; 0 (0)	0.03 $\pm$ 0.2; 1 (3.1)	0.1 $\pm$ 0.2; 9 (5.2)
Use of medical resources in year after index visit				
Visit to clinic for any cause [mean $\pm$ SD; n (%)]	21.2 $\pm$ 9.0; 59 (100)	15.7 $\pm$ 8.0*; 85 (98.8)	19.2 $\pm$ 10.4; 32 (100)	13.9 $\pm$ 6.7*; 174 (100)
Visit to clinic for asthma [mean $\pm$ SD; n (%)]	12.8 $\pm$ 6.0; 58 (98.3)	8.8 $\pm$ 5.3*; 84 (97.7)	13.0 $\pm$ 9.0; 29 (90.6)	9.0 $\pm$ 5.1*; 170 (97.7)*
Visit to emergency department for asthma [mean $\pm$ SD; n (%)]	0.4 $\pm$ 1.2; 10 (16.9)	0.1 $\pm$ 0.3*; 7 (8.1)	0.3 $\pm$ 0.7; 4 (12.5)	0.2 $\pm$ 0.5; 22 (12.6)
Hospitalization for asthma [mean $\pm$ SD; n (%)]	0.3 $\pm$ 0.2; 2 (3.4)	0 $\pm$ 0; 0 (0)	0.09 $\pm$ 0.4; 2 (6.3)	0.0 $\pm$ 0.2; 2 (1.1)

*Comparison between subjects still at work and those removed from exposure with a *P* value of .05 or less.

the baseline value (42.6% [33.0%], *P* = .05) only in subjects with WEA.

Subjects with OA who were away from work at the time of the investigation had a higher FEV₁ (95.7% $\pm$ 19.7%) than those who were still exposed at their workplace (86.2% $\pm$ 17.9%, *P* = .01), whereas there was no difference in the FEV₁ values of the subjects with WEA who were removed from exposure (86.7% $\pm$ 17.9%) at the time of the investigation compared with the subjects with WEA who were still working (88.0% $\pm$ 14.9%, *P* = .6). Subjects with OA were exposed more frequently to high-molecular-weight agents (47.6%) than subjects with WEA (21.2%, *P* < .01). The SICs were performed at the workplace in 6 subjects with OA and in 26 subjects with WEA. In these instances the subjects were exposed to a mix of agents, and a specific agent could not be

identified. The types of occupational agents to which the subjects were exposed were the following: chemicals (OA, 10.1%; WEA, 24.8%); isocyanates (OA, 17.0%; WEA, 21.2%); proteins (OA, 28.6%; WEA, 13.0%); cereals (OA, 18.0%; WEA, 7.5%); metals (OA, 7.3%; WEA, 7.5%); wood dust (OA, 13.6%; WEA, 6.8%); and latex (OA, 2.4%; WEA, 1.4%).

Subjects with OA and WEA who were still exposed at their workplace at the time of the investigation had to visit their physician more frequently during the year preceding the index visit compared with the subjects who had already been removed from exposure before the index visit (Table III).

Having OA was not a greater risk factor for severe asthma exacerbation than having WEA before or after the index visit. The occurrence of severe asthma

TABLE IV. Risk for the occurrence of severe asthma exacerbations in the year before or after the first assessment at Sacré-Coeur or Laval Hospitals comparing patients with OA and patients with WEA

Independent variables	Adjusted risk ratio (95% CI) of occurrence of severe asthma exacerbation in year before index visit	Adjusted risk ratio (95% CI) of occurrence of severe asthma exacerbation in year after index visit
Diagnosis of OA (vs WEA)	1.15 (0.75-1.75)	1.0 (0.61-1.64)
FEV ₁ (<80% of predicted value)	2.14 (1.42-3.23)	1.75 (1.08-2.85)
Duration of exposure before onset of symptoms	—	NR
<4 y	0.61 (0.4-0.93)	—
Missing values	0.68 (0.17-2.8)	—
Addition of a LABA	NR	1.79 (1.10-2.92)
Away from work at diagnosis	NR	1.71 (1.03-2.84)

NR, Not retained; LABA, long-acting β_2 -agonist.

exacerbations during the year preceding the index visit was associated with a longer duration of exposure before the onset of symptoms and with an FEV₁ of less than 80% of predicted value after controlling for age, sex, atopy, smoking, PC₂₀, duration of exposure after onset of symptoms, molecular weight of agents, treatment with ICSs, use of long-acting β_2 -agonists, removal from exposure, and visit to the clinic for any other cause (Table IV). The occurrence of severe asthma exacerbations during the year after the index visit was associated with markers of asthma severity, such as FEV₁, treatment with a long-acting β_2 -agonists, and removal from exposure at the time of the investigation after controlling for age, sex, atopy, smoking, PC₂₀, duration of exposure before and after onset of symptoms, molecular weight of agents, treatment with ICSs, and visit to the clinic for any other cause (Table IV).

DISCUSSION

This study showed that WRA is associated with a greater use of medical resources than NWRA. Indeed, subjects with WRA visited their physicians more frequently because of their asthma, went more frequently to the emergency department, and were more frequently hospitalized than asthmatic subjects without WRA for a similar level of airflow obstruction and airway responsiveness.

Our study is consistent with the findings from Breton et al,⁶ who reported that subjects with WRA were more likely to report having an exacerbation of asthma, visit the emergency department, and visit a physician for worsening asthma compared with individuals with NWRA. However, with regard to that study, the diagnosis of asthma was solely based on questionnaires and included no objective testing for asthma.

Le Moual et al⁷ showed significant associations between severe adult-onset asthma and exposure to any occupational asthmogens. However, with regard to that study, asthma severity and control were difficult to detangle because the definition of asthma severity was based on a score calculated according to the frequency of attacks,

persistent symptoms, and hospitalization, which are also criteria of asthma control. In the present study we also found that subjects with WRA had more visits to the clinic, visits to the emergency department, or hospitalizations for asthma than subjects with NWRA. However, subjects with WRA had an FEV₁ within the normal range, as well as mild airway hyperresponsiveness, which are not characteristics of severe asthma. Although our study did not allow us to assess whether the asthma severity was greater among subjects with WRA than among subjects with NWRA because the groups were matched on FEV₁, it is likely that subjects with WRA had poorer control than subjects with NWRA.

As in other studies,^{8,15} we found that subjects with OA and WEA were very similar clinically. However, exposure to occupational agents during SICs induced changes in airway responsiveness and eosinophilic inflammation only in subjects with OA, suggesting different underlying pathophysiologic mechanisms in these 2 conditions.

To the best of our knowledge, this is the first study to show that OA and WEA have a very similar use of medical resources. Furthermore, the diagnoses of OA and WEA were not risk factors for the occurrence of severe asthma exacerbations. The only factors that were found to be associated with the occurrence of asthma exacerbations were markers of asthma severity. OA and WEA were distinguished according to the results of the SIC. Although SICs are the current reference tests for diagnosis of OA, these test results are sometimes false negative. It might be possible that some subjects with WEA actually had OA and were misclassified. However, the investigation performed for WRA in Quebec is extensive and leaves little room for missing a diagnosis of OA. Therefore if there was some misclassification, this was likely to be minimal and unlikely to have affected the results.

In both groups subjects who were removed from exposure had a lower level of medical resource use than subjects who were still working. However, and in contrast with subjects with OA, subjects with WEA who were removed from exposure had a similar FEV₁ as those who remained exposed. These results are consistent with a previous study in which the functional improvement of the

subjects with WEA seemed less than that in the subjects with OA, although this study was underpowered to be fully confident with this finding.¹⁶ The functional improvement of subjects with OA after removal from exposure is consistent with previous studies.^{17,18}

The subjects with OA and WEA who were still at work at the time of the first assessment had a more significant decrease in medical resource use in the year after the first visit than those who were removed from exposure at the time of the first investigation. A large majority of the subjects who were working at the time of the first assessment might have left their workplace during the following year, resulting in an improvement of their asthma control, whereas the subjects who were already removed from work might not have had further improvement in their asthma control. In Quebec almost all subjects who are given diagnoses of OA are removed from exposure. Although WEA is not recognized as an occupational disease and compensated as such by the Quebec Workers Compensation Board, the majority of subjects with WEA leave their workplace because of their respiratory symptoms.¹⁶ In the present study 59% of subjects with WEA had already left their workplace at the time of the investigation. Whether improving the respiratory environment, wearing a mask, or improving asthma treatment can allow workers with WEA to stay at their workplaces remains to be determined.

Subjects with WRA experienced asthma symptoms several years before being assessed in a tertiary care center to investigate the relationship between their asthma and their workplace. This delay in the diagnosis of WRA is likely to be responsible for a poor prognosis, especially for subjects with OA. Increased efforts should be made to improve the primary and secondary prevention of WRA.

In conclusion, this study emphasizes the importance of an early recognition of WRA to improve the control of asthma in those workers and limit their use of medical resources. Although the pathophysiology between WEA and OA differs, there is no significant difference between these 2 conditions in terms of clinical characteristics and use of medical resources. There is a need for prospective studies to assess whether an optimal management of WEA can allow the maintenance of these workers at their workplace or if they should be removed from exposure, like subjects with OA.

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