ORIGINAL ARTICLE

Update of an occupational asthma-specific job exposure matrix to assess exposure to 30 specific agents

Nicole Le Moual,[1,2] Jan-Paul Zock,[3,4,5] Orianne Dumas,[1,2] Theodore Lytras,[3,4] Eva Andersson,[6] Linnéa Lillienberg,[6] Vivi Schlünssen,[7] Geza Benke,[8] Hans Kromhout[9]

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For numbered affiliations see end of article.

Correspondence to
Dr Nicole Le Moual, Inserm, U1168, VIMA: Aging and chronic diseases. Epidemiological and public health approaches, F-94807, Villejuif, France; nicole.lemoual@inserm.fr

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ABSTRACT

Objectives We aimed to update an asthmagen job exposure matrix (JEM) developed in the late 1990s. Main reasons were: the number of suspected and recognised asthmagens has since tripled; understanding of the aetiological role of irritants in asthma and methodological insights in application of JEMs have emerged in the period.

Methods For each agent of the new occupational asthma-specific JEM (OAsJEM), a working group of three experts out of eight evaluated exposure for each International Standard Classification of Occupations, 1988 (ISCO-88) job code into three categories: 'high' (high probability of exposure and moderate-to-high intensity), 'medium' (low-to-moderate probability or low intensity) and 'unexposed'. Within a working group, experts evaluated exposures independently from each other. If expert assessments were inconsistent the final decision was taken by consensus. Specificity was favoured over sensitivity, that is, jobs were classified with high exposure only if the probability of exposure was high and the intensity moderate-to-high. In the final review, all experts checked assigned exposures and proposed/improved recommendations for expert re-evaluation after default application of the JEM.

Results The OAsJEM covers exposures to 30 sensitisers/irritants, including 12 newly recognised, classified into seven broad groups. Initial agreement between the three experts was mostly fair to moderate (κ values 0.2–0.5). Out of 506 ISCO-88 codes, the majority was classified as unexposed (from 82.6% (organic solvents) to 99.8% (persulfates)) and a minority as 'high-exposed' (0.2% (persulfates) to 2.6% (organic solvents)).

Conclusions The OAsJEM developed to improve occupational exposure assessment may improve evaluations of associations with asthma in epidemiological studies and contribute to assessment of the burden of work-related asthma.

Key messages

What is already known about this subject?

- ► To evaluate the burden of work-related asthma in community-based epidemiological studies, assessment of occupational exposures is a crucial issue.
- ► An asthma-specific job exposure matrix (JEM) was constructed in the late 1990s and applied successfully in various studies on asthma or other immunological diseases.
- ► However, the number of identified asthmagens has tripled since the end of the 1990s and an update of this JEM is warranted.

What are the new findings?

- ► A new occupational asthma-specific JEM (OAsJEM) was created to evaluate exposure to 30 specific agents, based on consensus from international experts in the field.

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

- ► This new OAsJEM, developed to improve exposure assessment to occupational asthmagens, may be a valuable tool to improve evaluations of associations between occupational exposures and asthma phenotypes in epidemiological studies, and contribute to assessment of the burden of disease due to exposure to occupational asthmagens.

INTRODUCTION

Work-related asthma is the most common occupational lung disease in industrialised countries.[1] The proportion of asthma in adults attributable to occupational exposures is estimated to be around 15%.[2] The burden of work-related asthma is underestimated partly due to limited knowledge about occupational exposure to well-established asthmagens.[3] In addition, new asthmagens are constantly being reported.[4] Occupational asthma is classically described as induced by a sensitiser (immunological asthma) or by a unique high-level accidental exposure to an irritant agent (non-immunological asthma) at work.[1 3] However, recently chronic low-to-moderate level of exposure to irritants has also been recognised as a cause of work-related asthma.[5–9] Underlying biological mechanisms are complex and partly unknown especially for reactive chemicals and irritants.[3 10] It has been suggested that irritant-induced asthma may represent between 10% and 20% of occupational asthma, with an increase in recent years.[3 11]

The deleterious role of cleaning agents and disinfectants in asthma has been recognised in recent decades.[2 12 13] Other potential risk factors for asthma have received more attention recently especially occupational exposures to endotoxins, organic solvents, pesticides and chronic exposure to irritants in general.[1 5 14–17] Studying associations between such kinds of agents, which may be sensitisers (low molecular weight (LMW) chemicals) and/or lung irritants, and asthma is important for a better understanding of the disease.[3 10 12 17] Improvement of exposure assessment, especially for newly recognised agents, is a crucial but challenging issue[3 18] when studying work-related asthma in community-based cohorts.

Kennedy *et al*[19] proposed at the end of the last century an asthma-specific job exposure matrix (JEM) combined with an expert step, to evaluate occupational exposures to common asthmagens.[20] This method, by favouring specificity over sensitivity *via* an expert re-evaluation step, improved asthmagen assessment and reduced misclassification errors.[19] In some studies limited improvement of the additional expert re-evaluation step was observed, possibly due to imprecise available information regarding tasks.[21] This asthma-specific JEM is the most commonly used method in various populations both in and outside Europe[19] and has been adapted to country-specific workplace environments in Northern Europe and the UK.[15 22–24] Since the asthma-specific JEM was developed the number of suspected asthmagens has tripled.[3 4]

We aimed to develop a new occupational asthma-specific JEM (OAsJEM), combined with an expert re-evaluation step, to assess exposure to 30 specific sensitisers and/or irritants.

METHODS

The original asthma-specific JEM

Briefly, the original asthma-specific JEM,[19] is a two-dimensional table with a two-digit to four-digit International Standard Classification of Occupations, 1988 (ISCO-88) job code[25] axis crossed with a second axis of 18 asthmagens and four agents classified as low risk for asthma. Agents were classified into four broad groups: LMW asthmagens, high molecular weight (HMW) asthmagens, mixed environments and irritants peaks. In addition, job codes poorly defined and/or with heterogeneous exposures (88 out of all 506 two-digit to four-digit ISCO-88 job codes; 17%) were identified and classified as requiring 'an expert re-evaluation step' with linked comments and specific recommendations for reviewing each specific exposure (see online supplementary figure E1). When re-evaluation was needed in a study, the exposure attributed by the JEM was checked and modified if necessary by the expert directly, at the individual level, according to the participant's job, industry and tasks descriptions.

Two major strengths of this method were: (1) specificity favoured over sensitivity, that is, a job was classified as exposed to a specific asthmagen only if the probability to be exposed was high for an important number of subjects in that job (2) an expert re-evaluation step, performed after applying the JEM, for an a priori list of jobs (poorly defined or with heterogeneous exposures).[19] JEM combined with an expert re-evaluation step provided a more specific exposure assessment, by correcting for heterogeneity of exposures within occupations and thereby avoiding a classical drawback of most JEMs, and by so doing reducing the impact of misclassification error.

The asthma-specific JEM is commonly used (see online supplementary table E1 for more detail) and is freely available on a website (http://asthmajem.vjf.inserm.fr/), which was developed and launched in Vancouver in 2005 and hosted in France since 2011.

The new OAsJEM

A standardised procedure was used to develop the updated OAsJEM. First the list of agents was updated from the previous one (22 agents, categorised from a list of 150 substances from Chan-Yeung and Malo[20]) based on the recent literature.[1 3 5 7 26–28] The list was further improved during the process (online supplementary table E2) resulting in a final version consisting of seven large groups with 30 specific agents in total (table 1). The new agents were identified based on recent literature knowledge, mostly using information from two major literature reviews[1 5] for sensitiser and irritant-induced asthma, respectively.

A working group of three experts was assigned to each agent: each expert evaluated exposure to a number of specific agents varying from 3 to 19 agents, according to their agent of choice and expertise.

Classification of exposures was refined from yes/no to semi-quantitative metrics that is, high: high probability of exposure and moderate-to-high intensity; medium: low-to-moderate probability or low intensity of exposure, such as 'high probability and low intensity' or 'low probability and moderate to high intensity'; no: unlikely to be exposed (low probability and low intensity). Experts classified a job as 'high probability of exposure' when they considered that at least 50% of the workers were exposed. The expert re-evaluation recommendations were also improved with checking for (1) ISCO code for selected jobs (mostly the larger two-digit and three-digit ISCO-88 codes) and (2) exposure assessment for selected jobs (poorly defined and/or heterogeneous jobs). For the expert re-evaluation recommendations, period and country-specific work situations were taken into account, in addition to job, industry and tasks recorded by each participant.

In addition, we addressed important methodological points during the process: (1) all experts evaluated exposure independently from each other. In case of disagreement, the final decision was taken by consensus within the experts' team and (2) specificity was favoured over sensitivity for high level of exposure only (not for 'medium' exposure).

At the beginning, all ISCO job codes were classified as 0: 'non exposed', if these jobs were classified unlikely to be exposed according to three existing JEMs (asthma-specific,[19] ALOHA[29 30] and Northern[15 26]) or 1: 'exposure assessment warranted', if classified by one of these three JEMs as potentially exposed to asthmagens, irritants or dusts, gases and fumes. In a first step, for all jobs classified as 'exposure assessment warranted', for a given agent a first evaluation of exposure (high, medium, no) was attributed by each of the three experts independently. The experts' decisions were based on assessments from existing JEMs and especially the asthma-specific, Northern europe Job-Exposure Matrix (N-JEM) and ALOHA JEMs[15 19 29 30] and on recent literature. In a second step, all exposure assessments were reviewed and compared. If the assessment was unanimous and consistent with previous evaluations (for 'old' agents from the asthma-specific JEM) the job was classified as such; if not (jobs with at least one expert disagreeing or inconsistent with the previous evaluation), we used a standardised procedure and sent it to the three experts: an Excel file including information on the three initial evaluations, an exposure rating proposed by NLM with comments/justifications, and opportunities for further comments/justifications from each expert, who were asked to send back the file completed with comments on the proposal. If all experts agreed, a final rating was made; in case of disagreement, the final decision was taken by consensus after a discussion (using

Table 1 List of individual agents classified in seven large groups—new occupational asthma-specific JEM

Agents, n=30	HMW sensitiser	Mites	Microbial exposure	LMW sensitiser	Irritants	Highly reactive chemicals	Biocides
Animals	1						
Fish/shellfish	1						
Flour	1						
Foods	1						
Plants-related dusts	1						
House dust mites	1	1					
Storage mites	1	1					
Plant mites	1	1					
Enzymes	1						
Latex	1						
Textiles	1		1		1		
Moulds			1		1		
Endotoxin			1		1		
Drugs	1			1			
High-level chemical disinfectants				1	1	1	1
Aliphatic amines				1	1	1	
Isocyanates				1	1	1	
Acrylates				1	1	1	
Epoxy resins				1	1	1	
Persulfates/henna				1	1	1	
Wood	1			1	1		
Metal				1	1		
Metal working fluids			1	1	1		
Herbicides					1		1
Insecticides					1		1
Fungicides					1		1
Indoor cleaning					1		
Bleach					1	1	1
Organic solvents					1	1	
Exhaust fumes					1		

The 12 new agents (out of 30), identified in bold, were chosen based on the knowledge from recent literature.[1 5]
Animals: exposure to animals in agriculture industry, research labs—land mammals and birds;
Foods: work with milk, eggs, peanuts, tree nuts, soy, … mostly powders (process used to obtain powder may affect allergenic properties)—fish/shellfish and flour are not included in foods;
Other plant-related dusts: flour is not included;
Enzyme: those used as improver in bread dough, or in washing detergents manufacturing …;
Textile: work with cotton or synthetic fibres, which explain its classification in three groups (HMW, microbes, irritants);
Drugs: mostly HMW agents[19] (Kennedy, personal communication) but potentially also LMW[1];
Wood: mostly LMW agents[19] but potentially also HMW[1 27 28];
High-level chemical disinfectants: high-level disinfectant or chemical sterilising agents (eg, glutaraldehyde, chlorhexidine, ethylene oxide, hydrogen peroxide);
Indoor cleaning: cleaning products/detergents or low/intermediate-level disinfectants.
Seven large groups:
HMW *sensitisers* (n=13), of which mites is a subcategory (three sensitisers);
Microbial exposure (n=4);
LMW sensitisers (LMW, n=10);
Chronic exposure to irritants (n=19 agents including nine agents also classified as LMW sensitisers because for these nine agents both mechanisms are possible[1 3 5 19]), of which ***highly reactive chemicals*** (eight agents) and biocides (five agents) are two subcategories.
HMW, high molecular weight; JEM, job exposure matrix; LMW, low molecular weight.

information from the file) with the three experts during a conference call or a face-to-face meeting. Decisions regarding evaluations and recommendations are illustrated for latex in the online supplementary tables E3, E4. The final step consisted of a complete review and feedback by all experts on the assigned exposures, their consistency and expert-step recommendations on exposure and code checking.

Basic characteristics of the asthma-specific JEM and the new OAsJEM are compared in table 2.

Data analysis

The initial evaluations of exposure to a specific agent obtained by each of the three experts were independently compared. Comparisons of chance-corrected agreement between three pairs of experts per agent were undertaken by estimating Cohen's κ. The agreement was interpreted as follows: poor (<0), slight (0–0.2), fair (0.2–0.4), moderate (0.4–0.6), substantial (0.6–0.8) and almost perfect (0.8–1.0) agreement.[31] Prevalence of jobs classified exposed and with an

Table 2 Comparison of basic characteristics of the asthma-specific JEM and the new OAsJEM

	Asthma-specific JEM[19]	New OAsJEM
Number of agents or groups of agents	22	30
HMW sensitiser	9	13
LMW sensitiser	5	10
Mixed exposure	3	(13)
Microbial exposures	–	4
Irritants, high peaks	1	–
Irritants, chronic exposure	3	19
Classification	No/yes	No/medium/high
Exposure at low risk for asthma identified	Yes	No
Standardised expert re-evaluation step (revising job codes, agents)	Yes	Yes
Number of experts to assess each agent	One and consultation of coauthors, and three European occupational epidemiologists for the final version of the method	Three per agent (eight in total)

HMW, high molecular weight; JEM, job exposure matrix; LMW, low molecular weight; OAsJEM, occupational asthma-specific JEM.

expert re-evaluation step, for each agent, was assessed after the final assessment of exposure at the ISCO-88 code level.

RESULTS

The revised OAsJEM (table 1) included exposure evaluations to 30 specific asthmagens (HMW (n=13) and LMW (n=10) agents) and exposure to irritants (n=19). The 12 new agents evaluated through the OAsJEM are marked in bold (such as acrylates, epoxy resins). Exposures were classified into seven broad groups (table 1): HMW sensitisers, mites (subcategory of HMW), microbial exposures, LMW sensitisers, chronic exposure to irritants, highly reactive chemicals, biocides (last two subcategories of irritants). Two agents were classified as both potentially HMW and LMW sensitisers (drugs, wood) as their classification was inconsistent in the literature.[1 19 27 28] Most LMW sensitisers were also classified as irritants. Compared with the previous asthma-specific JEM,[19] 'mixed environments' and 'low risk exposure' as well as 'high irritant peaks', 'environmental tobacco smoke' (ETS) were no longer included in the OAsJEM (online supplementary table E2).

Values of initial agreements between two experts varied strongly by agent (table 3; for example, the three κ values varied from 0.08 to 0.54 for fish/shellfish and from 0.21 to 0.29 for plants) and were mostly fair to moderate (0.2–0.5). The κ values varied overall from −0.01 to 1.00. Agreement could not be estimated for agents added after the first step (three categories of mites and pesticides, online supplementary table E2). For mites, experts decided by consensus after comparison of their first evaluations to split them into three subcategories. We also decided a posteriori to assess exposures to three subcategories of pesticides (herbicides, insecticides, fungicides).

Table 4 illustrates the percentage of jobs classified as exposed or with an expert re-evaluation step for the 30 agents. Out of 506 two-digit to four-digit ISCO-88 job codes, agents classified as exposed ranged from 0.2% (persulfates/henna) to 17.4% (organic solvents) and as highly exposed from 0% (acrylates, enzymes, storage mites) to 2.6% (organic solvents, exhaust fumes). For 14 agents, such as epoxy resins (1.8%) and flour (0.6%), less than 3% of the jobs were classified as exposed to high level or medium level. Overall, more jobs were classified exposed with the OAsJEM, compared with the original JEM (table 4), mostly explained because specificity was not favoured to evaluate medium level. However, for high level exposure the percentages were mostly lower with the OAsJEM (0.2% to 2.6%) than with the old JEM (0.2% to 5.5%). Examples of jobs classified at a high exposure level are given in the

Table 3 Cohen's κ values—new occupational asthma-specific JEM (OAsJEM)

Agents, n=24*	Cohen's κ values between pairs of experts (1 and 2/1 and 3/2 and 3; ordered by ascending κ values)
Animals†	0.39/0.47/0.56
Fish/shellfish	0.08/0.52/0.54
Flour	0.50/0.67/0.83
Foods†	0.18/0.24/0.78
Plants-related dusts†	0.21/0.26/0.29
Enzymes	0.00/0.22/0.33
Latex	0.48/0.53/0.59
Textile†	0.36/0.45/0.69
Moulds	0.18/0.18/0.44
Endotoxin	0.15/0.18/0.31
Drugs†	0.22/0.42/0.44
High-level chemical disinfectants†	0.09/0.15/0.37
Aliphatic amines	−0.01/0.14/0.18
Isocyanates	0.08/0.21/0.35
Acrylates	0.31/0.34/0.80
Epoxy resins	0.35/0.43/0.85
Persulfates and henna	1.00/1.00/1.00
Wood†	0.35/0.37/0.41
Metal	0.25/0.31/0.52
Metal working fluids	0.35/0.39/0.49
Indoor cleaning†	0.28/0.40/0.50
Bleach	0.16/0.28/0.32
Organic solvents	0.24/0.26/0.41
Exhaust fumes	0.29/0.40/0.53

Unweighted Cohen's κ values of three pairs of experts (expert 1 and expert 2/expert 1 and expert 3/expert 2 and expert 3) per agent. For each agent, Cohen's κ values were calculated between a pair of experts, using exposure evaluations for 506 job codes, and reported in ascending values.

*No evaluation of κ was available (see online supplementary table E2) for specific mites (house dust, storage, plant) and specific pesticides (herbicide, insecticide, fungicide). For evaluation of mites in general the three values varied from 0.15 to 0.29

†***Animals***: exposure to animals in agriculture industry, research labs—land mammals and birds;

Foods: work with milk, eggs, peanuts, tree nuts, soy, … mostly powders (process used to obtain powder may affect allergenic properties), fish/shellfish and flour are not included in foods;

Other plants-related dusts: flour is not included;

Enzymes: those used as improver in bread dough, or in washing detergents manufacturing …;

Textiles: work with cotton or synthetic fibres, which explains its classification in three groups (HMW, microbes, irritants);

Drugs: mostly HMW agents[19] (Kennedy, personal communication) but potentially also LMW[1];

Wood: mostly LMW agents[19] but potentially also HMW[1 27 28];

High-level chemical disinfectants: high-level disinfectant or chemical sterilising agents (eg, glutaraldehyde, chlorhexidine, ethylene oxide, hydrogen peroxide);

Indoor cleaning: cleaning products/detergents or low/intermediate-level disinfectants.

HMW, high molecular weight; JEM, job exposure matrix; LMW, low molecular weight.

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Table 4 Percentage of jobs classified as exposed or with an expert re-evaluation

	Asthma-specific JEM	New OAsJEM		
		Exposure level, %*		Expert re-evaluation, %*
Agents	Exposed, %	Medium or high	High only	
Animals	*2.2*	3.4	1.2	4.2
Fish/shellfish	*0.2*	2.2	0.8	1.8
Flour	*0.6*	0.6	0.4	0.8
Foods	–	1.0	0.2	1.8
Plants-related dusts	*0.8*	3.4	0.6	4.9
House dust mites	– †	0.8	0.2	1.2
Storage mites	– †	3.4	0.0	0.8
Plant mites	– †	2.8	0.4	4.3
Enzymes	*0.2*	1.0	0.0	1.4
Latex	*2.2*	4.2	1.2	4.5
Textile	*3.2*	3.2	0.6	3.4
Moulds	*1.2*	6.3	0.6	3.0
Endotoxin	–	5.5	1.6	3.8
Drugs	*1.2*	1.2	0.4	2.0
High-level chemical disinfectants	*0.8*	7.1	0.6	4.7
Aliphatic amines	–	2.0	0.6	3.6
Isocyanates	*1.0*	1.4	0.2	2.2
Acrylates	–	2.0	0.0	3.2
Epoxy resins	–	1.8	0.8	1.8
Persulfates/henna	–	0.2	0.2	0.0
Wood	*0.0*	3.6	1.0	2.0
Metal	*5.5*	9.3	1.4	8.1
Metal working fluids	*0.8*	2.0	1.0	1.6
Herbicides	–	3.2	1.4	2.0
Insecticides	–	4.2	1.8	2.4
Fungicides	–	4.0	1.8	1.0
Indoor cleaning	–	4.2	0.6	1.8
Bleach	–	2.2	0.4	1.6
Organic solvents	–	17.4	2.6	5.5
Exhaust fumes	*4.0*	11.9	2.6	7.1

In the second column, in italics: percentage of jobs classified exposed by the original asthma-specific JEM.[19]

*percentage of jobs classified exposed at high or medium level and at high level, respectively out of 506. For 14 agents, the percentages of jobs classified exposed were less than 3%.

†0.4 for mites and insect antigens in general according to the original asthma-specific JEM.[19]

JEM, job exposure matrix; OAsJEM, occupational asthma-specific JEM.

online supplementary table E5. Overall, the percentage of jobs classified with an expert re-evaluation by the new OAsJEM (table 4) varied from 0% (persulfates/henna) to 8.1% (metal). Considering only the 390 four-digit ISCO-88 job codes (online supplementary table E6), after exclusion of the 116 less precise codes (two-digit and three-digit), the percentages of jobs classified as highly exposed were similar. In addition, around 20% of the jobs (113 out of 506 codes, mostly two-digit and three-digit codes) were identified as 'code checking required'.

DISCUSSION

We developed an OAsJEM to update and to improve occupational exposure assessment for 30 specific asthmagens and irritants, classified into seven large groups, for 506 two-digit to four-digit ISCO-88 job codes. The initial agreement observed between three experts per agent was fair to moderate in most cases and final decisions regarding exposure assessment were taken by consensus. These results stress the importance of evaluating occupational exposures among a working group of at least two experts. The expert re-evaluation step was improved and country-specific and time-specific issues (eg, replacement of latex powered gloves) were taken into account.

A priori or a posteriori choice of specific exposure evaluation

Agents included in the category 'at low risk for asthma' in the original JEM[19] may be considered instead of 'chronic low-to-moderate level of exposure to irritants' which may also induce asthma.[3 6 7 26] Improvement of occupational exposure assessment during the entire working life is crucial[18] for a better understanding of the underlying mechanisms of irritant-induced asthma.

Therefore, for the new OAsJEM we excluded the 'Low risk' category and added specific irritants potentially at risk for asthma such as indoor cleaning agents, pesticides, endotoxins, aliphatic amines, acrylates, epoxy resins, persulfates/henna and organic solvents.[1 3] In the original JEM,[19] the literature at the time suggested that only industrial cleaning products, which contain highly reactive chemicals, mostly used in hospitals, were associated with asthma compared with cleaning products used at home or in offices. However, this has been refuted in recent literature.[2 3 12 13] Cleaning products and disinfectants are ubiquitous agents used in many places (such as hospital, office, home) and are now considered among the most common lung irritants.[3 10] Bleach is considered one of the main airway irritants among cleaning products and has been shown to induce acute irritative asthma earlier known as reactive airways dysfunction syndrome (RADS).[17] Therefore, we have added *bleach* as a subcategory of indoor cleaning products.

In addition, we excluded unspecific exposure categories: one a priori, agriculture, and five a posteriori, bacteria, high peaks exposure to irritants, ETS, highly reactive chemicals and dusts, gases, fumes in general. *Agriculture* workers are exposed to many agents associated with asthma.[3] These agents are often heterogeneous in terms of mechanisms, as they may include both allergens, such as animal proteins, and irritants, such as pesticides and cleaning products. Large groups make it difficult to disentangle immunological or non-immunological mechanisms involved in occupational asthma. Following discussion within the expert group, it was decided a posteriori to exclude *bacteria* assessment because it was closely linked to endotoxins. In addition, we assumed that associations observed between bacteria and asthma may be explained by the presence of endotoxins. For *high peak exposure to irritants* many workers such as freight handlers (gassed containers), police officers, farmers, animal caretakers and animal transporters, may be exposed. However, only one study in which the asthma-specific JEM was applied (a case control study in Taiwan,[32] table E1), found an association between irritant peaks and non-atopic asthma (OR 4.2 (1.5 to 11.8)). Given that these peaks are induced during incidents, we considered that the JEM methodology is not the best approach to evaluate such exposure. In the same way, we decided to exclude the category ETS from this new OAsJEM, because ETS assessment at job level might be of poor quality. Indeed, nowadays workers are unexposed to ETS in most workplaces, due to new smoking regulations, which may depend strongly on country and period. In addition, the large group *highly reactive chemicals* was evaluated through exposure assessment of eight specific agents (see table 1). We have not evaluated exposure to dusts, gases and fumes as a group as it may not be relevant for asthma,[33] and it is especially important to define groups that allow disentangling sensitisers from irritating agents when studying the underlying mechanism.

The study experts decided by consensus a posteriori (at step 2) to split 'mites' into three subcategories and to add an evaluation of exposures to three subcategories of pesticides (herbicides, insecticides, fungicides) based on the existing ALOHA JEM.[29 30]

Evaluations of specific exposures

Initial agreement between exposure evaluations of two experts (out of three) varied according to agents and was mostly fair to moderate, which is consistent with previous observations.[34 35] However, it is difficult to compare agreement for each specific agent with earlier findings as few comparable studies are available. The lack of initial congruence between experts underlines the importance of evaluating occupational exposures within a review team of at least two experts. For all the agents, a small percentage of jobs, out of 506, were classified exposed at high level. For half of the agents, less than 3% of the jobs were classified exposed at high or medium level. Compared with the original JEM, more jobs were classified exposed in general but less at high level with the OAsJEM. In the original JEM less than 3% of the jobs were classified exposed, except for three agents (textile, metals, exhaust fumes). As expected, the exposure assessment evaluated through the new OAsJEM was more specific for high level of exposure but more sensitive for medium level.

Occupational asthma-specific JEM

Due to the lack of a gold standard, a formal validation of the OAsJEM estimates is not possible, which is a classical limitation of JEMs.[35 36] It has been suggested that updating a JEM may increase the validity.[37] In addition, the development of the OAsJEM was based on recent literature and knowledge from multidisciplinary international experts, using a standardised procedure to take a final decision by consensus. The OAsJEM has been updated from the original asthma-specific JEM, which has been used in at least 51 publications to date, and has been regarded as a valuable and robust standardised tool for evaluating exposure to asthmagens.[6 38] Published papers using this method allowed evaluating (1) efficiency and accuracy of the method and (2) healthy worker effect, asthma-related and allergy-related phenotypes, occupational exposures in other diseases such as lymphoma and autism, maternal occupational exposure and child health (table E1, online supplement). The original asthma-specific JEM[19] was the sole JEM set-up to evaluate exposure to asthmagens in epidemiological surveys, and was previously adapted twice to take into account country-occupation specificities.[15 23]

This updated OAsJEM may improve the evaluation of associations between occupational exposures and asthma phenotypes in epidemiological studies and contribute to assessment of the burden of disease due to occupational asthmagens. In order to use the OAsJEM in optimal conditions, we recommend the following steps previously advised in the original JEM:[19] first coding jobs by an experienced occupational coder and then applying the JEM with an expert re-evaluation step, blinded to disease status. In order to limit misclassification errors and to perform both job coding and the expert re-evaluation step in an optimal way, recording well-described tasks for each job is crucial in epidemiological surveys. During the expert re-evaluation step it is important to keep in mind that the OAsJEM was built to promote specificity for high level of exposure to asthmagen. Other important points include (1) taking into account, for some identified exposures, time of exposure occurrence and in which country, (2) following the recommendations of the re-evaluation step written for each job, for both ISCO code and exposure assessment checking and (3) performing the expert re-evaluation step with at least two experts, independently. In the update, we have tried to limit the number of expert re-evaluations to improve feasibility of this additional step. Some analyses[7 33] performed in large cohorts suggest that it is possible to use the JEM without an expert re-evaluation step, especially after exclusion of poorly defined or heterogeneous jobs (such as those classified as needing an expert re-evaluation step). In addition, information regarding task descriptions, specific workplace conditions (ventilation, personal respiratory protection use …) or target tasks, as recorded in occupational epidemiology studies,[39] may improve evaluations of exposure assessment from the OAsJEM agents by decreasing misclassification errors at the re-evaluation step.

The new OAsJEM is available for free on the website (http://oasjem.vjf.inserm.fr). In order to keep it up to date, we would appreciate receiving a notification through the website or by email to the corresponding author, when the application of the OAsJEM in an epidemiological study will result in a publication.

Strengths and limitations

The major strength of this OAsJEM is that initial exposure assessments were undertaken by experts independently from each other and final evaluations were taken by consensus, through a standardised procedure. Furthermore, we incorporated improvements based on other JEMs, such as ALOHA and Northern-JEM developed by experts from our team, to evaluate exposure assessment to pesticides and acrylates or epoxy resins, respectively. We finally checked that for all jobs with an expert re-evaluation step the default exposure assessment for a specific agent was the most likely one. In addition, the standardisation of an expert re-evaluation step with precisely written recommendations may be helpful for non-experts. Furthermore, this method has previously shown its efficiency and usefulness to evaluate associations between occupational exposures and diseases (online supplementary table E1).

The present method also has limitations. As with any JEM, non-differential misclassification remains but is somewhat reduced by incorporating up-to-date knowledge from eight experts for the evaluated agents. We acknowledge that the additional expert assessment step may be time-consuming and money-consuming which may induce difficulties in applying the method in large epidemiological studies. However, the expert step is mostly intended to improve precision of exposure estimates in studies of moderate size and limited power. Our list of 30 asthmagens was not exhaustive but was in accordance with most agents identified in recent papers.[1 5 40] This method does not intend to identify new occupational risks, but may improve estimates for the most common agents known or suspected to have an adverse effect on work-related asthma till now.[3 4] We developed the OAsJEM for the two-digit to four-digit ISCO-88 job codes, the most commonly used classification in Europe.[34] However, the ISCO-88 classification was originally defined for economic statistical purposes, which may not be optimal for evaluation of occupational exposures. For example, the five-digit nternational Standard classifcation odf Occupations, 1968 (ISCO-68) is a much more detailed classification and might be more accurate to evaluate occupational exposures, in spite of its lack of representation of more contemporaneous jobs. In future developments, it would be useful to adapt the OAsJEM for ISCO-68 and potentially International Standard classifcation odf Occupations, 2008 (ISCO-08) job codes. For certain agents, OAsJEM exposure assessment may be improved by applying agent-specific JEMs with quantitative exposure assessment, for example for endotoxins,[41] wood dusts,[42] solvents and exhaust fumes (FINJEM). Applying the new OAsJEM in ongoing prospective epidemiological respiratory health studies, such as Epidemiological study on the Genetics and Environment of Asthma (EGEA)[43] and European Community Respiratory Health Survey (ECRHS)[38] studies, in which the original JEM has been applied, will allow for comparisons of the original and updated asthma JEMs.

CONCLUSIONS

In conclusion, we have developed an updated OAsJEM that allows evaluation of retrospective occupational exposure assessment to 30 specific asthmagens and irritants for all ISCO-88 job codes. This OAsJEM, developed to improve occupational asthmagen exposure assessment, may improve the evaluation of the association between occupational exposures and asthma phenotypes in epidemiological studies and contribute to assessment of the burden of work-related asthma.

Author affiliations
[1]Univ Versailles St-Quentin-en-Yvelines, UMR-S 1168, F-78180, Montigny le Bretonneux, France
[2]Inserm, U1168, VIMA: Aging and chronic diseases. Epidemiological and public health approaches, Inserm, F-94807, Villejuif, France
[3]Barcelona Institute of Global Health (ISGlobal), Barcelona, Spain
[4]University Pompeu Fabra (UPF), Barcelona, Spain
[5]CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain
[6]Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden
[7]Department of Public Health, Danish Ramazzini Centre, Aarhus University and National Research Center for the Working Environment, Copenhagen, Denmark
[8]Monash Centre for Occupation and Environmental Health, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia
[9]Department of Environmental Epidemiology, Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands

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