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A Novel Questionnaire and Algorithm for Work-Related Asthma Screening and Surveillance: An EAACI Task Force Report

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ABSTRACT

Introduction: Work-related exposures contribute to one in six new-onset adult asthma cases and exacerbation of one in five existing cases, which together are termed 'work-related asthma' (WRA). A valid and standardized WRA questionnaire is needed for workplace surveillance and epidemiological studies. This project aimed to review evidence on WRA questionnaires and algorithms to propose a standardized instrument.

Methods: A scoping review was conducted using PubMed, Embase, and Cochrane databases up to March 2021. Search terms focused on asthma, occupational diseases, questionnaires, surveys, and algorithms.

High-quality studies were identified and data extracted on instrument construction, validation, and performance. Common questions were used to develop a questionnaire and algorithm for detecting suspected WRA.

Results: Six studies were included. The final WRA questionnaire consists of eight questions on general asthma symptoms, diagnosis, and medication; four on WRA symptoms; and two on work-related ocular-nasal symptoms. The algorithm calculates a WRA total score (WRATS) based on the general asthma and work-related symptoms. A score of ≥ 1 triggers a referral for further evaluation.

Conclusion: This is the first WRA questionnaire based on validated questionnaires. Evaluation of its performance and validation in diverse geographic and occupational settings are needed for further refinement and translation for broader applications.

1 | Introduction

Work-related exposures have a substantial adverse impact on asthma. Work-related asthma (WRA) includes occupational asthma (OA), which is either sensitizer or irritant-induced, that is caused by work, estimated as 16% of new adult-onset asthma [1]. It also includes work-exacerbated asthma, a phenotype of asthma that is caused for other reasons but is then exacerbated by work exposures, estimated as 21.5% of people with asthma [2]. Most OA reflects sensitization to a high or low-molecular weight agent in the workplace and has a better outcome with early diagnosis and removal from further exposure to the causative work sensitizer [3–5]. In addition, the diagnosis of irritant-induced OA and work-exacerbated asthma can also lead to improved asthma control by reducing work exposure to asthma triggers.

The diagnosis of OA is often delayed, mean 2–4 years after onset in some studies [6, 7]. Reported reasons for a delay in diagnosis include lack of knowledge among healthcare professionals or affected workers, or fear of reporting a suspected association with work by workers, due to concern about loss of income or job. Other reasons may include lack of specific questioning by the physician about a possible work association with asthma symptoms [7, 8].

Medical surveillance that includes a patient questionnaire on asthma has been associated with an earlier diagnosis of OA from diisocyanates, and milder asthma at the time of diagnosis, in studies from Ontario and Quebec in Canada [9, 10]. Similarly, for bakers [11, 12], workers exposed to complex platinum salts [13] and notably detergent workers [14], worker questionnaires have been used in addition to skin testing or serum-specific IgE in medical surveillance programs for the detection of OA.

Various asthma questionnaires have been used in occupational settings, each with their strengths and limitations. Previous standardized and validated instruments were too generic (the European Community Respiratory Health Survey—ECRHS population-based surveys) [15] and required adaptation with OA-specific job-exposure matrices (JEM) [16]. Earlier UK questionnaire initiatives aimed at being more specific for OA were inconclusive [17], while others identified items most useful in specialist centres [18]. Over the past decade, WRA questionnaires such as the WRASQ(L) were developed for surveillance [19], but required further validation for broader use [20].

In a workplace medical surveillance setting, one study reported that unstructured interviews successfully detected only one fifth of the OA cases that were subsequently identified [6]. In more recent years, diagnostic models using simple self-administered questionnaires [12] and scores based on clinical interviews, specific skin prick test (SPT) and non-specific bronchial hyperresponsiveness (NSBH) to predict OA from high molecular weight sensitisers [21] and validated in other European settings were proposed [22]. These approaches have been suggested to be useful when specific inhalation challenge tests to confirm OA are inaccessible, thereby reducing diagnostic delays that are associated with poorer prognosis.

To date, there has not been a simple, validated questionnaire for surveillance of WRA.

The aim of this Work-related asthma surveillance questionnaire and algorithm (WAQASS) Task Force was to review published studies that included a workplace questionnaire or algorithm and identify validated questions to develop a simple medical surveillance/epidemiological survey questionnaire and algorithm for use by occupational medicine practitioners or in epidemiological research settings, which could then be validated for further use.

2 | Methods

2.1 | Scoping Review

To identify published WRA questionnaires and algorithms, a literature search strategy was designed using a combination of Medical Subject Heading (MeSH) terms with keywords and Boolean operators that were mentioned in the title or abstract, and was restricted to human studies. The search terms addressed topics related to asthma, occupational diseases, questionnaires, surveys, and algorithms. Searches were performed in March 2021 on the three databases PubMed Central, Excerpta Medica Database (EMBASE), and Cochrane. The search strategies and the search items are presented in Appendix S1, specifically in Table S1a for databases PubMed and EMBASE and Table S1b for Cochrane. The references from the literature search were checked to eliminate duplicates and then reviewed in sequential Phases 1 and 2.

In Phase 1, the references were separated into those with and without abstracts. Only studies published in English were included. Each reference with an abstract was independently reviewed by two different members of the Task Force. They answered the following two questions based on the titles and abstracts of the references. The possible responses for each of the following questions were Yes, No, and Uncertain:

1. Does the study deal with a questionnaire for medical surveillance/epidemiological survey for WRA?
2. Does the study deal with an algorithm for medical surveillance/epidemiological survey for WRA?

A reference with an abstract was selected for full-text review if it fulfilled at least one of the following two criteria. Criterion 1 was based on answers to the two questions, which were fulfilled when both reviewers had recorded at least one Yes response to the two screening questions. Criterion 2 required at least one of the two Task Force members to have recorded a Yes or Uncertain response to at least one of the questions, and a word search of the title and abstract identified at least one of the three words, “algorithm” “valid” and “specificity.” References that fulfilled Criteria 1 and/or 2 were advanced to Phase 2.

The references that lacked abstracts underwent a similar review process but were based on the full text article. Two Task Force members each reviewed half of the full-text articles and responded to the two questions used with references that had

abstracts. A Yes answer to at least one of the questions was required to justify advancing to Phase 2.

Phase 2 involved conducting full-text reviews and applying selection criteria in two sequential steps. In Step 1, two different members of the Task Force independently reviewed each article and answered the following Yes/No questions:

1. Does the questionnaire referred to in the article include WRA questions?
2. Does the algorithm referred to in the article aim to identify WRA?

Articles that received Yes responses from both reviewers for a questionnaire or an algorithm or both were advanced to Step 2 of Phase 2. The primary purpose of Step 2 was to confirm that the questionnaires and algorithms were validated. Each article was reviewed by a single Task Force member, who recorded relevant details about study methods and findings on a data extraction form. Items on the forms completed by reviewers addressed quality aspects such as internal consistency, reproducibility, and validity [23]. Articles that included evidence for validation of the instruments intended to identify WRA cases were finally retained.

2.2 | International Survey on the Use of WRA Questionnaires

A voluntary survey was conducted using a snowball sampling method. Researchers, clinicians, and other experts who used questionnaires for work-related asthma surveys, screening, or surveillance were contacted to obtain and collate questionnaires in use and to form a reference group for ongoing research collaboration on the development of the questionnaire. An e-mail invitation was sent to potential reference group members who were identified by Task Force members as currently active in the field, and a survey link was sent to EAACI Environmental and Occupational Interest Group members as well. Furthermore, scientific societies including the American Thoracic Society, Spanish Allergy and Pneumology Societies, and Society of Occupational Medicine UK were contacted and requested to share the invitation with their members.

The survey inquired about the name and purpose of the questionnaire that the responder used; the languages and countries it was used in; whether it was modified from another questionnaire; and whether it was published (Appendix S2a). The responders were invited to share their questionnaire followed by a reminder if it was not received. Each questionnaire was evaluated by two reviewers. The questionnaires that included WRA-related questions (i.e., presence of respiratory, rhinitis, ocular or skin symptoms at work; time-relationship of symptoms and work shift; appearance and/or worsening and/or improvement of symptoms with work shift) were then selected for further analysis. In this analysis, an assessment was made as to whether the questionnaire included questions about general asthma; for different phenotypes of WRA; and symptoms related to work. The questionnaire was also evaluated to assess whether there was a specific focus on certain industry sectors or exposures; the presence of questions on the onset of symptoms related to exposure, improvement of asthma symptoms away from work or worsening with work, and whether a question of physician-diagnosed asthma was included.

Responders that were interested in participating in the reference group were contacted through a second survey to distinguish those collaborators that worked with WRA and to evaluate the context in which the questionnaire was used (Appendix S2b). The reference group was then formed based on information received about who had worked with WRA or had specific expertise in conducting surveys. Furthermore, at least one participant from each country was included in the group (Figure 1). Data obtained from the respondent questionnaires were analyzed using STATA 17 statistical software (StataCorp, College Station, Texas, USA).

2.3 | WRA Questionnaire and Algorithm Development

The actual questions from each original questionnaire of the selected articles were tabulated and sorted per component (general versus work-related asthma) and further stratified between upper or lower respiratory symptoms for each component. Questions that were selected for general asthma and upper airway symptoms were phrased according to the validated ECRHS III questionnaire (https://www.ecrhs.org/questionnaires-and-protocols).

The questions on work-related symptoms were then organized into two subcomponents: WRA symptoms and work-related ocular-nasal symptoms. All questions were organized in a logical sequence and numbered accordingly to produce the WAQASS questionnaire.

The WAQASS algorithm was developed using the framework of the algorithm proposed by the ERS taskforce statement [24] and further guided by the two algorithms [25, 26] and the scoring system developed by Suarthana et al. [27]. The scoring was based on the anticipated level of responses to the WAQASS questionnaire. All items in the questionnaire were previously validated in their respective study. They were listed, and each response was given equal weight based on the expert opinion of task force members. The cut-off chosen for referrals for further assessments to confirm WRA was also established based on the expert opinion of the members of the task force.

3 | Results

3.1 | Scoping Review

The initial numerical yields from the systematic searching of the three databases are presented in the two tables in Appendix S1. The resulting 1651 references included 22 duplicates that were excluded to provide 1629 unique references. The fate of these 1629 references is described in the following text and summarized in Figure S1 in Appendix S1. They included 1550 with abstracts and 79 without abstracts. Phase 1 review of the 1550 references with abstracts produced 35 that fulfilled only Criteria 1, 51 that fulfilled only Criteria 2, and

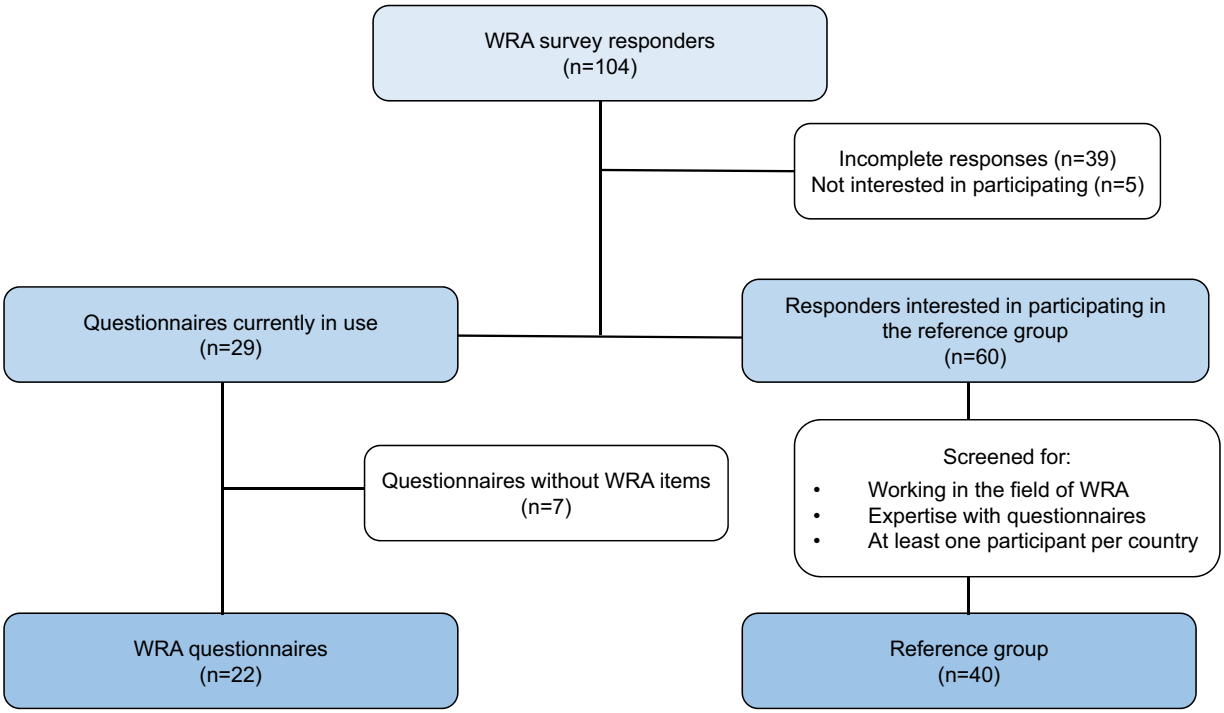

FIGURE 1 | Flowchart international survey of questionnaires and formation of reference group. WRA, work-related asthma.

22 that met both criteria, for a total of 108. From the review of articles for the 79 references without abstracts, 12 fulfilled the selection criteria of having at least one Yes answer to the two screening questions. The other 67 references included 45 with No to both questions, 1 was a duplicate that had been missed earlier in the review process, and 21 could not be evaluated. The final 21 articles included 17 that could not be located and 4 in a language other than English that had been missed in the initial selection of references for review. From the completion of Phase 1 reviews, a total of 120 references were advanced to Phase 2.

Phase 2 used full-text reviews of the 120 articles selected in Phase 1 to confirm that they dealt with a questionnaire and/or algorithm for medical surveillance/epidemiological survey for WRA. Phase 2 was accomplished in two sequential steps. The Step 1 review produced 39 references that addressed questionnaires and/or algorithms to identify WRA cases in primary level medical surveillance or research settings: 19 addressed questionnaires only, 5 addressed algorithms only, and 15 addressed both. In Step 2 of Phase 2, an additional critical review of study methods determined that six articles included evidence for validation of questionnaires and algorithms intended to identify WRA cases. These articles accounted for five questionnaires [12, 25, 27–29] (Appendix S3 contains the detailed summary information of questionnaire items) and two algorithms [25, 26] are described in Table 1. The symptom model by Suarthana et al. [27] after external validation, and the Pralong et al. [28] model, after bootstrapping, revealed similar values for area under the curve (AUC) = 0.69. The model by Jonaid et al. [12] produced an AUC of 0.87 after bootstrapping and contained work-related lower respiratory symptoms, work-related conjunctivitis, and medication use in the last year. Other questionnaires identified from reviewed articles are presented in Appendix S4, which demonstrated a diverse range of specific occupational contexts where they were used.

3.2 | International Survey of WRA Questionnaires

The international survey was answered by 104 members of the respective societies previously described. This component yielded 29 questionnaires, of which 7 questionnaires only contained general asthma questions (i.e., asthma control test), while the other 22 questionnaires included WRA-related questions that were evaluated for further details (Appendix S5). Among these questionnaires, five were based on the ECRHS and four on the Work-Related Asthma Survey Questionnaire (WRASQ). Three questionnaires were targeted for clinical purposes only, seven for epidemiological survey, six for medical screening and surveillance, and six for more than one of these purposes.

Most of the questionnaires included general asthma (18/22) and occupational allergic asthma (20/22) questions, whereas four had occupational irritant-induced asthma questions. A total of 14 questionnaires covered occupational conjunctivitis, 13 occupational rhinitis, and 5 occupational urticaria. Most questionnaires did not target specific industrial sectors (16/22) or exposure types (13/22). A total of 16 questionnaires included questions about the onset of symptoms related to work, 18 improvements of asthma away from work, and 20 worsening of asthma when working. Physician diagnosis of asthma was inquired in two questionnaires.

Another outcome of the international survey was the formation of a reference group, following the 104 responses to the international survey. Sixty respondents confirmed their willingness to be part of the WAQASS reference group. The

TABLE 1 | Summary of final papers accepted after literature search and review.

Author	Jonaid et al. [12]	Bolen et al. [29]	Pralong et al. [28]	Suarthana et al. [25]	Suarthana et al. [27]	Klees et al. [26]
Year	**2017**	**2007**	**2013**	**2008**	**2010**	**1990**
Country	The Netherlands	USA, Massachusetts	Canada, Quebec	Canada, Quebec	The Netherlands	USA
Questionnaire, Algorithm	Questionnaire	Questionnaire	Questionnaire	Questionnaire and Algorithm	Questionnaire	Algorithm
Work	Bakers	Various	Various	Animal health technology apprentices	Bakery workers	Various
Number of workers in study	438	95	169	314	Development: 867, Validation: 390	101
Means of administration	Self	(1) self for Q during serial testing, (2) interview for Q after serial testing	Self	Interview for Q, SPT and NSBH administered	Self	Interview for Q, clinical tests incl NSBH, serial PEF, FEV_1 increase pre to post BD, FEV_1 related to job
Means of comparison	Clinic objective testing	PEF for exacerbation	Specific inhalation challenge	Positive SPT to lab animal allergens, and respiratory symptoms at work	Sensitization to wheat allergens	Two: (1) clinician's diagnosis; (2) expert review of records
Main discriminating features	Work-related lower respiratory symptoms, work-related conjunctivitis and use of medication in the last year	During serial PEF testing: medication use increased on workdays, symptoms (cough attack, wheeze, chest tightness, or shortness of breath) increase on workdays	Asthma attack, Symptoms of wheezing, wheezing at work, dyspnea, cough	Asthma symptoms, Allergic symptoms	Naso-conjunctival symptoms, shortness of breath and wheeze, WR lower respiratory symptoms	Algorithm based on various symptoms and clinical tests but no separate results by these elements

(Continues)

TABLE 1 | (Continued)

Author	Jonaid et al. [12]	Bolen et al. [29]	Pralong et al. [28]	Suarthana et al. [25]	Suarthana et al. [27]	Klees et al. [26]
Year	**2017**	**2007**	**2013**	**2008**	**2010**	**1990**
Other information	Outcome evaluated in higher predicted workers with clinical assessments	Used to identify WEA among working asthmatics	Used Occupational Asthma Screening Questionnaire-11 (OASQ-11)	Used Q responses alone and combined with results from common allergen SPT and NSBH to methacholine	Predictive model from development set workers performed well in validation set of workers	Used to identify all types of WRA reported to state-based surveillance programs
Origin of Q or questionnaire items	ECRHS Q, supplemented with standard questionnaire items applied by occupational physicians in practice	Daily Q log with spirometry and a telephone Q	7 questionnaire items from IUATLD Q + four more questionnaire items on work-relatedness.	Used questionnaire items from validated IUATLD Q	Used questionnaire items from validated IUATLD and MRC-ECCS Qs	Questionnaire items vary by state, of uncertain origin, some questionnaire items likely from ATS-DLD-78-A
Asthma phenotype evaluated: IIA, WEA, AA, Mixed	Bakers' OA and OR	WEA	OA cases presumably all AA. Non-OA comparison group included WEA and IIA cases	Closest is AA, but two outcomes (lab animal SPT, resp. symptoms at work) included more than asthma	Closest is AA, but outcome of sensitization to wheat allergens included more than asthma	Mixed
Exposures of interest: HMW, LMW, IRR, Mixed	HMW	Mixed	Included HMW, LMW, and HMW + LMW	HMW	HMW	Mixed
Context used: work med surf, epi study, popn surv., clinical	Workers from workplace surveillance (Suarthana et al. 2010) with moderate or high risk from Q were validated by specialist medical investigations and assessment	Epi study, using serial PEF data as the diagnostic standard for WEA	Clinical, specialist referral level (workers referred for potential OA)	Work med surv.	Work med surv.	Popn surv.

(Continues)

TABLE 1 | (Continued)

Author	Jonaid et al. [12]	Bolen et al. [29]	Pralong et al. [28]	Suarthana et al. [25]	Suarthana et al. [27]	Klees et al. [26]
Year	**2017**	**2007**	**2013**	**2008**	**2010**	**1990**
Frequency of administration	Unclear whether more than one workplace Q administration	Daily self-recording and a single telephone interview	Once	Baseline and annually for 3years, but appeared to use only baseline and 3-year data	Once	Once
Questionnaires/algorithms validated	Reg model with 12 candidate predictors from the Q assessed.	Comparisons made of Q data with serial PEF readings	Reg model with 8 items from Q, age, exposure duration	Reg model with data from 2 symptom clusters: asthma symptoms, allergic symptoms	Reg model with 5 symptom clusters and bakery type; 6-point Score based on model	Algorithm in Table 1
Performance of Questionnaires/Algorithms	Multivariate logistic regression model: ROC area (95% CI) after bootstrapping: 0.87, Calibration: HL test value 0.94 Bootstrapping was used to internally validate the model Not externally validated	From Q during serial PEF testing: medication use (sens = 62%, spec = 65%, Youden's Index = 0.27), symptoms (sens = 62%, spec = 54%, Youden's Index = 0.16)	Discriminative ability of 8-symptoms in Model-1: AUC = 0.69. When added age and work duration to create Model-2: AUC = 0.80. Calibration of both models was good ($p = 0.32$ model 1; $p = 0.74$ model 2). Bootstrapping was used to internally validate the model Not externally validated	Q model with and without SPT and/or NSBH had good calibration. Ability of Q model to discriminate sensitized from non-sensitized apprentices comparable to SPT or NSBH testing alone (AUC = 0.73). Bootstrapping was used to internally validate the model Not externally validated	Application of model in external validation set had reasonable discrimination (AUC = 0.69) and good calibration after small adjustment of intercept. Score 2–3 (intermediate probability) had sens = 88%, spec = 43%; Score 5–6 (high probability) sens = 46%, spec = 89%	2 standards. MD Dx WRA: sens = 54%, spec = 100%. Expert review: sens = 68%, spec = 100%
Fit regression models	Yes	Not performed	Yes	Yes	Yes	No

Abbreviations: A, algorithm; AA, allergic asthma; ATS-DLD-78-A, The 1978 adult respiratory questionnaire developed by the American Thoracic Society (ATS) and the Division of Lung Diseases (DLD) of the US National Heart, Lung, and Blood Institute (NHLBI); AUC, area under the curve, as indicator of validity; BD, bronchodilator; ECRHS, European Community Respiratory Health Survey; epi study, epidemiologic study; FEV_1, forced expiratory volume in 1 s; HL test, Hosmer-Lemeshow test; HMW, high-molecular weight; IIA, irritant-induced asthma; IRR, irritants; IUATLD, International Union Against Tuberculosis and Lung Disease; LMW, low-molecular weight; MD Dx WRA, Physician diagnosed work-related asthma; MRC-ECCS, Medical Research Council (MRC) Questionnaire on respiratory symptoms (from the United Kingdom) and the European Community for Coal and Steel (ECCS) Questionnaire for studying chronic bronchitis and emphysema; NSBH, non-specific bronchial hyperresponsiveness; OA, occupational asthma; PEF, peak expiratory flow; popn surv., population based surveillance; Q, questionnaire; Reg model, regression model; ROC, receiver operator characteristic; sens, sensitivity; spec, specificity; SPT, skin prick test for allergy; WEA, work-exacerbated asthma; work med surv., workplace medical surveillance.

reference group finally comprised 40 participants that responded to the second survey, which provided further insights into their practices and experience in diverse settings (Figure 1). Respondents were from 26 different countries, with 15 participants from Europe, 13 from Africa, 7 from Asia, 4 from North America, and 1 from South America. Twenty-six reference group members reported the context in which they are involved with WRA aspects. In 13 cases, this was in clinical practice, 3 in epidemiologic population surveys, and 4 in workplace surveys, with the remaining 6 involved in at least two of these contexts.

3.3 | WAQASS Questionnaire and Algorithm

Questions from the six accepted articles were pooled and sorted. The selection of specific questions for incorporation was based on a process in the following order:

- Level of evidence as per summary evidence of the six validated studies—only those questions that were significant in the final models in these studies were chosen (Table 1).
- All questions were incorporated into their respective components, irrespective of how many times they were present across the studies.
- Where a similar question of a particular sub-component was present in more than one study, the question from the more recently cited study was chosen, unless the clarity of the question from an earlier cited study was formulated in a better way or if it was more explicit by mentioning a time period for the particular symptom.
- None of the questions from "secondary level" evidence of validation were included, although most of these questions consistently appeared in other studies that had primary level evidence of validation. Furthermore, the variables of "age" and "duration of work" were also not included.

The proposed WAQASS questionnaire for WRA screening and surveillance is presented in Figure 2. It contains eight questions on general asthma symptoms, diagnosis, and medication; four on work-related asthma symptoms; and two on work-related ocular-nasal symptoms.

The WAQASS algorithm is intended to be used in medical surveillance to guide actions based on responses to the questions and the computation of the total score (Figure 3).

Asthma evaluation occurs in two steps:

- Ask general asthma questions to compute the *general asthma total score (GATS)*
- If affirmative, then proceed to work-related asthma symptoms to obtain the *work-related asthma symptom score (WRASS)*

The specificity of the questions for WRA increases if:

- Asthma-related symptoms occur *at work* or *immediately on returning home* from work
- Asthma-related symptoms start *within 24 h after an incident at work* involving exposure to high levels of vapors, gases, dust, or fumes
- Asthma-related symptoms *improve* on *extended periods away from work*
- Work-related *nasal or ocular* symptoms present, which are assigned their own work-related ocular-nasal symptom score (WRONSS)

The work-related asthma total score (WRATS) is computed by summing the WRASS and the WRONSS.

If the GATS > 0, this prompts further questioning to assess for the presence and scoring of work-related asthma symptoms (WRASS) and work-related ocular-nasal symptoms (WRONSS). If the WRATS is ≥ 1, this prompts specialist referral for occupational history, clinical assessment, and tests to confirm WRA diagnosis, so that the worker can be managed accordingly. If the GATS is > 0 but the WRATS is < 1, then the worker is managed by the physician according to general asthma/rhinitis guidelines, and the worker is enrolled for ongoing regular surveillance.

4 | Discussion

4.1 | When/How to Use the WAQASS Questionnaire and Algorithm

Worldwide, especially in developing countries, WRA remains under-recognized and poorly diagnosed [30]. Diagnosing WRA is challenging due to delayed referral by general practitioners [31]. The European Respiratory Society Task Force on the Management of Work-related Asthma recommended the administration of a brief respiratory questionnaire to workers as the first step in a worker surveillance program for WRA [24]. Furthermore, the use of a standardized questionnaire for epidemiological surveys would enhance the comparability of findings across studies, thereby providing further insights on WRA disease burden and its risk factors.

The WAQASS questionnaire constitutes a further refinement of questionnaires and approaches used previously. Depending on the context, the questionnaire can be either self-administered or interviewer/nurse assisted either in medical surveillance or research settings. The former method is used where literacy levels are generally high and the latter where levels are low. The first component of the proposed questionnaire contains questions on general asthma as contained in the ECRHS III questionnaire, which has been previously validated and used in various countries and contexts [32]. Given the united airway concept [33] and to establish an association with the workplace, the second component of the proposed questionnaire comprises work-related asthma and ocular-nasal symptoms. It is important to supplement these questions with context-specific exposure information where this is appropriate and taking into consideration the ability of workers to provide such information in a reliable manner. This is based on the premise that exposures vary in different work settings, are multiple and quite diverse, with specific exposure information often difficult to obtain from individual workers.

WAQASS QUESTIONNAIRE	
	Score
Asthma-related symptoms	
1.1 Have you had wheezing or whistling in your chest at any time in the last 12 months?	
____Yes (1) ____No (0)	
1.2 Have you woken up with a feeling of tightness in your chest at any time in the last 12 months?	
____Yes (1) ____No (0)	
Note: For questions 1.3-1.6, "attack" is regarded as an episode of a flare-up or sudden worsening of symptom/s	
1.3 Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last 12 months?	
____Yes (1) ____No (0)	
1.4 Have you had an attack of shortness of breath that came on following strenuous activity or exercise at any time in the last 12 months?	
____Yes (1) ____No (0)	
1.5 Have you been woken by an attack of shortness of breath at any time in the last 12 months?	
____Yes (1) ____No (0)	
1.6 Have you been woken by an attack of coughing at any time in the last 12 months?	
____Yes (1) ____No (0)	
Asthma diagnosis	
2. Have you ever had asthma?	
____Yes (1) ____No (0)	
2.1 IF 'YES': Was this confirmed by a doctor?	
____Yes (1) ____No (0)	
Asthma medication	
3.1 Have you used any inhaled medicines to help your breathing at any time in the last 12 months?	
____Yes (1) ____No (0)	

FIGURE 2 | WAQASS questionnaire.

Optional question for countries in which inhaled medicines are generally not accessible	
3.2 Have you used any pills, capsules, tablets or medicines, other than inhaled medicines or antibiotics, to help your breathing at any time in the last 12 months?	
____Yes (1) ____No (0)	
GENERAL ASTHMA TOTAL SCORE (GATS)	
Work-related asthma symptoms	
4.1 Does being at your current workplace ever cause:	
4.1.1 Wheezing	
____Yes (1) ____No (0)	
4.1.2 Shortness of breath	
____Yes (1) ____No (0)	
4.1.3 Cough	
____Yes (1) ____No (0)	
4.1.4 A feeling of chest tightness	
____Yes (1) ____No (0)	
4.1.5 Asthma attack/s (episode of a flare-up or sudden worsening of symptoms)	
____Yes (1) ____No (0)	
4.2. Do you have any of the following breathing problems once you have returned home after work:	
4.2.1 Wheezing	
____Yes (1) ____No (0)	
4.2.2 Shortness of breath	
____Yes (1) ____No (0)	
4.2.3 Cough	
____Yes (1) ____No (0)	
4.2.4 A feeling of chest tightness	
____Yes (1) ____No (0)	
4.2.5 Asthma attack/s (episode of a flare-up or sudden worsening of symptoms)	
____Yes (1) ____No (0)	

FIGURE 2 | (Continued)

The WAQASS algorithm aims to serve as a framework to formalize decision-making and improve the efficiency of ongoing medical surveillance programs. It begins with a set of general asthma questionnaire items to identify workers with asthma, either by having asthma symptoms, an asthma diagnosis, or receiving treatment for asthma. This step excludes workers without evidence of asthma from ongoing steps in the algorithm. For those who fulfill these asthma criteria, the subsequent group of

4.3 If 'YES' to either 4.1 or 4.2: Do these breathing problems diminish or stop during the weekend or during holidays?	
____Yes (1) ____No (0)	
4.4 Have you ever been involved in an incident at work that exposed you to high levels of vapours, gases, dusts or fumes?	
____Yes (0) ____No (0)	
4.4.1 If 'YES' to 4.4: Did you experience respiratory symptoms within 24 hours following the incident?	
____Yes (1) ____No (0)	
WORK-RELATED ASTHMA SYMPTOM SCORE (WRASS)	
Work-related ocular-nasal symptoms	
5.1 Do you have sneezing, runny or a blocked nose, which start at or are aggravated by your work?	
____Yes (1) ____No (0)	
5.2 Do you have itchy, watery or red eyes, which start at or are aggravated by your work?	
____Yes (1) ____No (0)	
WORK-RELATED OCULAR-NASAL SYMPTOM SCORE (WRONSS)	
WORK-RELATED ASTHMA TOTAL SCORE (WRATS) = WRASS + WRONSS	

FIGURE 2 | (Continued)

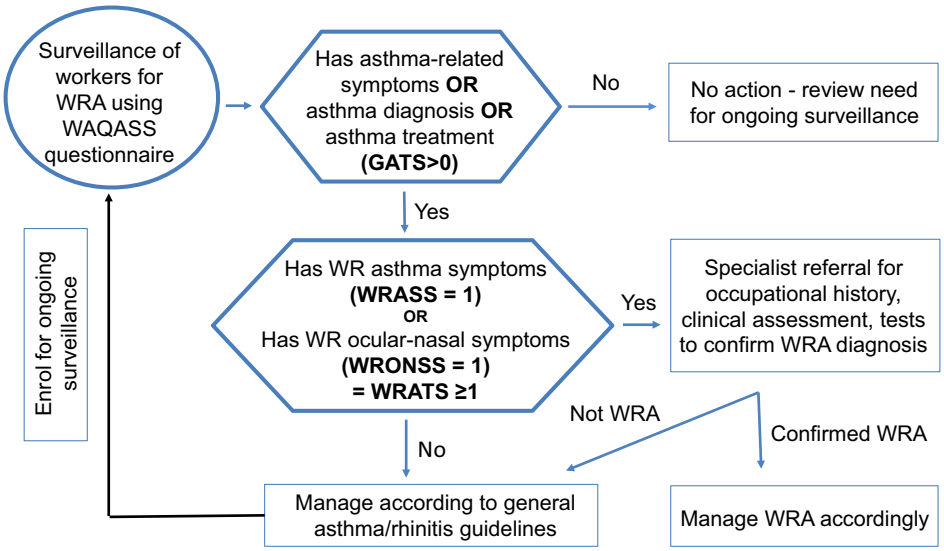

FIGURE 3 | WAQASS algorithm for primary care setting workplace surveillance. GATS, general asthma total score (Q1.1–3.2); WRASS, work-related asthma symptom score (Q4.1–4.4), WRONSS, work-related ocular-nasal symptom score (Q5.1–5.2), WRATS, work-related asthma total score (WRASS + WRONSS).

questions aims to assess the association between the lower respiratory and ocular or nasal symptoms with workplace exposure. Further diagnostic workup by a specialist is recommended for workers who have work-related symptoms.

This algorithm has chosen the threshold cut-off score of WRATS ≥ 1 for referral, is based on expert opinion of the panel based on clinical as well as historical performance of the identified questionnaires and algorithms. In the study reported by Suarthana [27], work-related upper and lower respiratory symptoms were found to have equal *clinical significance*, as reflected by the equal weighting in the predictive model. The expert panel opted to assign an equal weighting to both components, such that workers presenting with symptoms from either component were deemed eligible for referral for further diagnostic evaluation. Furthermore, the expert opinion for the proposed threshold is also based on the *performance of the questionnaires or algorithms*, the specific aspects of which are summarized in Table 1. It is evident that the sensitivity and specificity varied widely for the three studies that reported these values [26, 27, 29]. The sensitivity ranged between 46% and 88%, while the specificity was between 43% and 100%. With these results as a guide for the likely performance of the new algorithm, it is not possible to predict how it will perform since the questionnaire was compiled from individual questions from one or more of these questionnaires. While the assessment of the model's diagnostic performance remains an important consideration, this was beyond the scope of the current study. The panel recommended therefore that a validation study of the entire questionnaire would be an important next step in order to assess the impact of differential symptom weighting on the diagnostic accuracy and referral outcomes.

In the WAQASS algorithm, workers with evidence of asthma, as well as workers with work-related ocular or nasal symptoms (WRONS) but who do not have WRA symptoms, should be referred for further evaluation by a specialist. After taking relevant clinical and occupational histories, a more detailed assessment will be made to determine whether further diagnostic tests for WRA are needed. In some WRA cases, the patients initially report only work-related rhinitis symptoms, which should be taken into account given that they may represent a precursor to the development of WRA [6].

4.2 | Strength, Limitations, and Future Research

One possible limitation of the approach in the review of the literature is that a scoping review rather than a systematic review was conducted. Although the literature search was systematic, it is possible that other relevant references could have been identified if a different set of search terms and additional databases had been used. However, Munn et al. have suggested that scoping reviews are preferred over systematic reviews when the objective of a project is to identify knowledge gaps or scope a body of literature [34]. The Task Force members therefore considered that a scoping review was appropriate for this project, and it was the collective expert opinion of members that few, if any, relevant published articles were missed given the process that was followed. Furthermore, the six selected questionnaires/algorithms were validated internally or externally, further strengthening the approach that was used and confidence in the instruments that were included.

The WAQASS algorithm was derived from published validated questionnaires and models including the prognostic models to predict animal health apprentices who would develop laboratory animal sensitization and respiratory symptoms at work [25]. The models evaluated a questionnaire, with and without common diagnostic tests (i.e., SPT and NSBH to methacholine). These models could serve as a framework to identify individuals with a high probability of developing OA in the future and could be used to support career counseling and health surveillance programs. However, in these models, the predictive value of adding SPT and/or NSBH testing for OA seemed to be limited in a relatively healthy population. The ability of the questionnaire alone to discriminate sensitized from non-sensitized apprentices was comparable to that of SPT or BR testing on its own. Furthermore, their use in pre-employment or pre-placement screenings is uncertain since the predictive value of the model was relatively low. The WAQASS algorithm itself is, therefore, not aimed at pre-employment or pre-placement screening.

It is important to note that existing evidence may be biased toward questionnaires for identifying allergic occupational asthma caused by high molecular weight (HMW) agents, since this phenotype is relatively easier to study due to well-understood mechanisms and available diagnostic tools. Furthermore, the Task Force focused on detecting WRA and did not specifically search for questionnaires to detect WRONS. Therefore, the algorithm is unlikely to identify all workers with WRONS unless they also have asthma symptoms. However, there are some situations where it would be helpful to identify non-asthmatic workers with WRONS due to their increased risk of developing WRA. For example, detergent enzyme industry workers who are sensitized and have WRONS may be moved to different areas away from exposure [14].

Taking a thorough occupational and medical history is essential in confirming the diagnosis of WRA. The choice of diagnostic tests to further investigate workers referred from the primary level is beyond the scope of this Task Force. However, Vandenplas et al. recommended confirming occupational asthma with NSBH using a methacholine or histamine challenge test accompanied by immunological sensitization to workplace agents using either specific SPT or specific IgE as the first line of diagnostic tests [35]. The second line of tests may include either serial peak expiratory flow recordings, or NSBH test off-work versus at work, or specific inhalation challenges (SIC), depending on their availability in clinical practice. In line with this recommendation, Canadian researchers demonstrated that adding NSBH test and specific SPT with workplace agents to a clinical interview model resulted in an excellent discriminative ability in identifying workers at a high risk of having positive SIC in workers exposed to HMW agents [21]. The models were successfully validated using European data as previously highlighted [22].

5 | Conclusion

As with any model, evaluation of the validity and clinical usefulness of the WAQASS questionnaires in decision-making is essential. Hence, the next step is to initiate a multinational collaborative study to validate the WAQASS questionnaires and

algorithm, including transcultural validation in different languages, and testing whether results are consistent across different ways of administering the questionnaires (e.g., full-length or abbreviated form, self- vs. interviewer-administered, online digital- vs. paper-based). Furthermore, an evaluation of its performance and validation in workplace-based medical surveillance and epidemiological research settings is required to enable further refinement.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

Author Contributions

All authors contributed to the conceptualization of the work. Mohamed F. Jeebhay and Hille Suojalehto were the chair and secretary of the Task Force, respectively. Mohamed F. Jeebhay, Hille Suojalehto, Paul Henneberger, Susan M. Tarlo, and Eva Suarthana were members of the coordinating and drafting group. All other members, Paul Cullinan, Irmeli Lindström, Paola Mason, Xavier Munoz, Monika Raulf, Marcela Valverde, and Jolanta Walusiak-Skorupa, contributed to the development of the questionnaire and algorithm as well as the manuscript. All authors have read and agreed on the published version of the manuscript.

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Conflicts of Interest

Susan Tarlo has performed clinical consultations of patients at the request of the Ontario Workplace Safety and Insurance Board (WSIB) and the WSIB appeals tribunal. She has also received research funding from WSIB. The remaining authors declare no conflicts of interest in relation to this work.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.