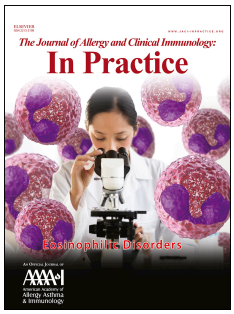
Journal Pre-proof



Work-related asthma and its impact on quality of life and work productivity

Eva Suarthana, MD, MSc, PhD, Nicole Le Moual, PhD, Catherine Lemière, MD, MSc, Jean Bousquet, MD, PhD, Stephie Pierre, BSc, Bernardo Sousa Pinto, MD, PhD, Alfi Afadiyanti Parfi, MD, MPH, Philippe Van Brussel, MD, Hormoz Nassiri Kigloo, MD, Olivier Vandenplas, MD, PhD, Paul K. Henneberger, MPH, ScD

PII: S2213-2198(23)01199-6

DOI: https://doi.org/10.1016/j.jaip.2023.10.044

Reference: JAIP 5131

To appear in: *The Journal of Allergy and Clinical Immunology: In Practice*

Received Date: 13 April 2023

Revised Date: 3 October 2023

Accepted Date: 23 October 2023

Please cite this article as: Suarthana E, Le Moual N, Lemière C, Bousquet J, Pierre S, Pinto BS, Parfi AA, Van Brussel P, Kigloo HN, Vandenplas O, Henneberger PK, Work-related asthma and its impact on quality of life and work productivity, *The Journal of Allergy and Clinical Immunology: In Practice* (2023), doi: https://doi.org/10.1016/j.jaip.2023.10.044.

Work-related asthma and its impact on quality of life and work productivity

Eva Suarthana, MD, MSc, PhD,[a,b] Nicole Le Moual, PhD,[c] Catherine Lemière, MD, MSc,[b,d] Jean Bousquet, MD, PhD,[e,f] Stephie Pierre, BSc,[b] Bernardo Sousa Pinto, MD, PhD,[g,h,i] Alfi Afadiyanti Parfi, MD, MPH,[b] Philippe Van Brussel, MD,[j] Hormoz Nassiri Kigloo, MD[a, k], Olivier Vandenplas*, MD, PhD,[l] Paul K. Henneberger*, MPH, ScD[m]

*Equally contributed

Authors' affiliation:

[a] Research Institute of the McGill University Health Center, Montréal, Canada;

[b] Research Centre, Centre Intégré Universitaire de santé et de services sociaux du Nord-de-l'île-de-Montréal, Montreal, Canada;

[c] Université Paris-Saclay, UVSQ, Univ; Paris-Sud, Inserm, Equipe d'Epidémiologie Respiratoire Intégrative, CESP, 94807, Villejuif, France;

[d] Faculty of Medicine, Université de Montreal, Montreal, Canada;

[e] Euforea, Brussels, Belgium;

[f] MACVIA-France, Fondation partenariale FMC VIA-LR, Montpellier, France;

[g] MEDCIDS - Department of Community Medicine, Information and Health Decision Sciences; Faculty of Medicine, University of Porto, Porto, Portugal;

[h] CINTESIS - Center for Health Technology and Services Research; University of Porto, Porto, Portugal;

[i] RISE - Health Research Network; University of Porto, Porto, Portugal;

[j] Service de Prévention et Protection au Travail - Centre de Service Interentreprises (CESI), Brussels, Belgium;

[k] Faculty of Medicine, University Laval, Quebec City, Quebec, Canada

[l] Department of Chest Medicine, Centre Hospitalier Universitaire UCL Namur, Université Catholique de Louvain, Yvoir, Belgium;

[m] National Institute for Occupational Safety and Health, Morgantown, West Virginia, United States;

Running head: Impact of work-related asthma

Correspondence: Eva Suarthana

McGill University Health Center, Royal Victoria Hospital – Glen Site

1001 Decarie Boulevard, Room D05.2543, Montreal, Quebec H4A 3J1

E-mail: eva.suarthana@mcgill.ca

Funding: This work was funded by a grant from the Fonds Scientifique CESI.

Role of the funding source: The funding source had no role in the analysis and interpretation of the data or in the preparation of the manuscript.

Conflicts of interest: There is no conflict to declare in relation to this article.

Authors' Contributions: OV, ES, and PV contributed to the conception and design of the study and acquisition of data. ES, OV, PKH, NLM, CL, JB, SP, BSP, and AAP contributed to data analysis and interpretation. ES, OV, PKH, NLM, CL, JB, BSP, and HNK contributed to the writing of the manuscript. All authors provided input into the drafting of the manuscript, critical feedback, and final approval. ES is the guarantor of the final content of the manuscript.

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.

Highlights Box

What is already known about this topic?

There is scarce and often discordant information on the impact of work-related asthma (WRA) on quality of life and work productivity compared to asthma unrelated to work.

What does this article add to our knowledge?

Asthmatics have a lower general health-related quality of life and overall work productivity compared to non-asthmatics, with greater impairment in subjects with WRA compared to non-WRA.

How does this study impact current management guidelines?

A more holistic approach to identifying and managing work-related airway disease in clinical practice is needed to reduce the global burden of asthma.

Keywords: Quality of life; Socioeconomic burden; Work productivity; Work-related asthma

Abstract

Background**:** The impact of Work-related asthma (WRA) on quality of life (QoL) and work productivity remains largely neglected/uncertain despite its high prevalence.

Objective: We aimed to investigate the association of WRA with QoL and work productivity as compared to subjects with asthma unrelated to work and those without asthma and rhinitis.

Methods**:** A cross-sectional survey was carried out among workers during their periodic occupational health visit in Belgium. The mini Asthma QoL Questionnaire (mAQLQ), Medical Outcome Study Short Form-8 (SF-8), and Work Productivity and Activity Impairment-General Health questionnaires were administered. Survey participants were divided into three groups: 1) WRA (current asthma with ≥2 respiratory symptoms at work, n=89); 2) non-WRA (current asthma without work-related respiratory symptoms, n=119); and 3) the reference group (no asthma and no lower respiratory, nasal, or eye symptoms; n=815). Associations of QoL and work productivity with WRA were evaluated by multivariable regression analyses.

Results: WRA and having poor asthma control were significantly associated with lower global mAQLQ scores compared to non-WRA. Asthmatic subjects had significantly lower physical and mental health components of the SF-8 instrument and overall work productivity compared to the reference group, with greater impairment in WRA than non-WRA. Moreover, workers with WRA had higher percentages of doctor visits and income reduction due to respiratory symptoms than non-WRA. Work-related rhinitis and depression were associated with reduced QoL, independent of the effect of WRA.

Conclusions: Comprehensive management of WRA should be done to reduce the worsening of QoL and work productivity of those affected.

Abstract word count: 250 of 250 maximum words

List of abbreviations:

ACT:	Asthma control test
CI:	Confidence interval
IQR:	Interquartile range
MCS:	Mental Component Summary
mAQLQ:	mini Asthma Quality of Life Questionnaire
OA:	Occupational asthma
OR:	Odds ratio
PCS:	Physical Component Summary
QoL:	Quality of Life
SF-8:	Medical Outcome Study Short Form-8 items
WEA:	Work-exacerbated asthma
WPAI-GH:	Work Productivity and Activity Impairment - General Health
WRA:	Work-related asthma
WRR:	Work-related rhinitis

INTRODUCTION

The Global Burden of Disease Study reported that asthma was deemed accountable for 21.6 million (95% uncertainty interval 17.1–27.0) disability-adjusted life-years (DALYs) in 2019, which was one-fifth of total DALYs from chronic respiratory disease[1].

Occupational exposure accounts for approximately 16% of all cases of adult-onset asthma[2]. The term "work-related asthma" (WRA) encompasses both occupational asthma (OA) and work-exacerbated asthma (WEA)[3, 4]. OA is defined as asthma caused by a specific exposure at work, while WEA is defined as "pre-existing or concurrent asthma that is worsened by workplace conditions[3]."

Asthmagen exposure in the workplace has been associated with poor asthma control[5, 6].WRA may considerably impact the socioeconomic conditions of the affected subjects since it most often implies job changes to avoid or reduce exposure[4, 7]. In addition, WRA may be associated with increased use of healthcare resources and/or an impaired health-related quality of life (QoL)[8-13]. Unfortunately, studies assessing the impact of WRA on QoL or work productivity either had a small sample size[12], lacked a non-asthmatic control group[11], and/or showed conflicting results[8]. In fact, despite being potentially preventable and associated with improved QoL if addressed properly, WRA has been relatively neglected from a clinical and scientific point of view[1].

Our study aimed to simultaneously compare WRA to both non-WRA asthma cases and a non-asthmatic reference group from a general workforce survey, which not only evaluated the association between WRA with health-related QoL but also with work productivity.

MATERIALS AND METHODS

Study Design and Population

A cross-sectional questionnaire-based survey was conducted on a sample of workers employed in various industrial sectors in the French-speaking part of Belgium. The design of this survey has been previously described[14]. The participants were recruited at the time of their periodic visit to medical examination centres of an occupational health service (*Service de Prévention et Protection au Travail - Centre de Service Interentreprises*, CESI) from 2008 to 2011. Periodic examination of salaried workers by internal or external occupational health services is mandatory in Belgium. All workers who attended a medical examination on a selected day were asked to participate. The study days were randomly allocated after weighting for the annual activity of each examination center. For all assessments when pre-existent questionnaires were applied, we used their validated versions in French. The study protocol was approved by the Ethics Committee of the *Centre Hospitalier Universitaire UCL Namur* (approval no. B0392006772) and written informed consent was obtained from each participant.

Procedures

Screening Questionnaire

A two-step integrated questionnaire was administered under the supervision of clinical research assistants. In the first step, the participants were asked to complete a "screening questionnaire", aimed at identifying those with asthma as well as those with rhinitis[14]. The screening questionnaire gathered information on: (1) demographic, medical, and occupational characteristics; (2) asthma and rhinitis symptoms as well as their relationship with work exposure and medications; (3) general health-related QoL using the Medical Outcome Study Survey Short Form-8 (SF-8) (four-week recall French version 1.0 for Belgium provided by QualityMetric Incorporated, Lincoln, Rhode Island); and (4) impairment in work productivity due to general health assessed through the Work Productivity and Activity Impairment-General Health (WPAI-GH) generic instrument (*www.reillyassociates.net)*. Participants with a self-reported or physician-based diagnosis of asthma who had wheezing or whistling sounds in the chest (apart from colds) in the last 12 months or were currently taking any medication for asthma were considered as having current asthma.

In the second step, all subjects who screened positive for current asthma were invited to complete an "asthma-specific questionnaire" during the same visit.

Asthma-Specific Questionnaire

Participants screened for asthma were administered an "asthma-specific questionnaire" that aimed to collect information pertaining to the level of asthma control (Asthma Control Test, ACT)[15, 16] and asthma-related quality of life (Mini Asthma Quality of Life Questionnaire, mAQLQ)[17]. Participants with current asthma who merely have one respiratory symptom at work were excluded from the study.

Rhinitis-Related Questionnaire

Rhinitis-related questionnaires, including rhinitis-specific QoL, work-disability, and healthcare utilization due to rhinitis, were administered to participants with a symptom-based diagnosis of rhinitis or with a self-reported or physician-based diagnosis of allergic rhinitis[18].

Identification of Diseases

The screening questionnaire included items on respiratory symptoms extracted from the European Community Respiratory Health Survey (ECRHS) questionnaire[19]. The list of definitions of symptoms/diseases and outcomes is presented in **Table E 1**.

'Ever asthma' was defined by an affirmative answer to one of the following two questions: (1) "Did you ever suffer from asthma or 'asthmatic bronchitis'?" (i.e. self-reported asthma) or (2) "Has a doctor ever told you that you have asthma or 'asthmatic bronchitis?" (i.e. physician-based asthma). Those participants with self-reported or physician-based asthma (ever asthma) were categorized as having current asthma if they also provided a positive answer to any of the following questions: (1) "Have you had wheezing or whistling sounds in your chest apart from colds in the last 12 months?" or (2) "Are you currently taking any medicine for asthma?". Poor asthma control was defined as having an ACT score ≤ 19[16].

WRA was considered when participants reported current asthma[19] and experienced at least two asthma symptoms related to work exposure identified using the following question "*when you are at work or during the hours following your work shift do you notice the onset of any of the following symptoms: wheezing, chest tightness, shortness of breath, or cough?"* [20]. Asthma unrelated to work (non-WRA) was considered present when the worker reported current asthma without asthma symptoms related to work exposure.

A diagnosis of current rhinitis was assigned to participants reporting that they regularly experienced at least two nasal symptoms (i.e. runny nose, stuffy nose, or sneezing), apart from a cold or flu, during the last 12 months[14, 21]. Subjects were regarded as having allergic rhinitis in the presence of either self-reported or physician-based allergic rhinitis[22]. Work-related

rhinitis was defined by the presence of current rhinitis and at least two nasal symptoms at work[14]. Work-related conjunctivitis was identified by reporting itchy and red eyes at work.

Comorbidity

Information on co-morbidities was collected through a questionnaire. Participants were asked if they had ever been diagnosed with Diabetes, cancer, headaches, cardiovascular diseases, arterial hypertension, gastrointestinal diseases, musculoskeletal disorders, arthritis and chronic dermatitis. Information on respiratory-based comorbidities including chronic bronchitis and emphysema were also asked among workers who reported asthma. The term "chronic phlegm" is used most frequently in Belgium to designate COPD.

Outcome Measures

Quality of Life

Health-related QoL was assessed using two validated instruments: (1) the generic SF-8 questionnaire administered to all participants and (2) the mAQLQ[17] which was completed by participants who reported current asthma.

The SF-8 questionnaire is a shortened generic instrument assessing eight health concepts (general health, physical functioning, physical role, bodily pain, vitality, mental health, role emotional, and social functioning) that are summarized into two aggregate scores: The Physical Component Summary (PCS) and the Mental Component Summary (MCS) measures. The SF-8 raw scales are transformed into 0-100 scales, with higher scores indicating better health status. The summary measures are standardized using scoring algorithms to have a mean value of 50 and a standard deviation of 10.

The mAQLQ is a 15-item self-administered questionnaire designed to evaluate asthma-specific QoL by addressing four domains: symptoms (5 items); limitations in daily activities (4 items); emotional function (3 items); and exposure to environmental stimuli (3 items). The degree of impairment during the preceding two weeks is scored on a 7-point scale ranging from 1 (severe impairment) to 7 (no impairment) for each item. The answers are summarized into four domain scores and a mean global score.

Work Productivity

The impact of general health on work productivity was assessed in all participants using the French version of the WPAI-GH self-administered instrument (*www.reillyassociates.net)*[23]. This questionnaire is designed to produce four outcome measures evaluated over the last seven days: (1) the work time missed due to general health (i.e. absenteeism); (2) the productivity

impairment while working due to health (i.e. impaired presenteeism); (3) the overall work impairment as the sum of absenteeism and impaired presenteeism, and (4) the impairment in usual off-work activities. These metrics are expressed as percentages from 0% to 100%, with higher percentages indicating greater impairment. The generic "general-health" version of the WPAI was used because this instrument is generalizable across diseases and allowed for comparing impairment in work productivity between participants with and without asthma. The existence of "any overall work impairment" was defined as having a WPAI-GH score >0.

Socioeconomic and healthcare utilization related to respiratory symptoms

The participants also completed a questionnaire that inquired whether they ever had to change or leave their job or reduce working time because of their respiratory symptoms. This questionnaire also collected information about workdays missed, visits to physicians (general practitioners and specialists) and hospitalizations due to respiratory symptoms over the last 12 months. Respiratory sickness absence was defined as one or more days of work loss due to respiratory symptoms in the previous year [24].

Data Analysis

Survey participants were divided into three groups: WRA, non-WRA, and the reference population (defined as participants who did not report either asthma or any lower respiratory, nasal, or eye symptoms). Continuous variables were presented as medians and interquartile ranges (IQR) and categorical variables as percentages. The chi-squared or Fisher's exact test was used for comparing categorical variables, and the Mann-Whitney or Kruskal-Wallis test for continuous variables. Multivariable linear regression analysis was used to evaluate factors associated with the mAQLQ overall score and SF-8 PCS/MCS scores. Multivariable logistic regression analysis was used to evaluate the determinants of any work productivity impairment. For each outcome modelled, we fit a base model composed of the main determinant (the presence of WRA or non-WRA) and the potential confounders (age, sex, smoking habits, BMI, education level, and current job duration). Other clinical factors (comorbidities) for the modelled outcome with a univariable p-value <0.10 were added to the base model. Multivariable regression analysis with backward stepwise selection, using an exclusion criterion of p-value >0.10, was carried out to obtain the final models. Statistical analysis was performed using the IBM SPSS Statistics version 25 (IBM Corp, USA). Statistical significance was defined by $p \leq 0.05$. We did not impute missing values. Post hoc power calculation using G*Power version 3.1.9.6 revealed that with 56 WRA and 74 non-WRA we could detect 0.9 mean difference of the mini AQLQ global score with 5% alpha and 99% power.

RESULTS

Participants

Of 2,954 eligible workers invited to participate in the survey, 2,686 (90.9%) agreed to complete the questionnaires (**Figure 1**). Valid information on respiratory symptoms was obtained from 2,611 (88.4%) workers. Among the 252 (9.6%) subjects with current asthma, 89 (35.3%) were categorized as having WRA, and 119 (47.2%) as non-WRA. Forty-four (17.5%) participants with current asthma who experienced only one respiratory symptom at work were excluded from both the WRA and non-WRA groups and not included in the data analyses. Non-asthmatic workers who reported neither lower respiratory, nasal, nor eye symptoms were regarded as the reference group (n=815).

Workers' characteristics

Workers with WRA and non-WRA were younger and had a higher prevalence of physician-based diagnosis of depression compared with workers in the reference group (**Table I**). Two-thirds of the WRA group were females, whereas the proportion of females in the non-WRA and the reference groups were close to 50%. Workers with WRA showed lower ACT scores (i.e. poorer asthma control) and had a higher prevalence of work-related rhinitis, work-related conjunctivitis, chronic phlegm, and physician-based diagnosis of depression when compared with workers with non-WRA (p-values range: <0.001 to 0.006). The use of asthma treatments, including short-acting and long-acting β_2-agonists, and inhaled corticosteroids, was similar between workers with WRA and non-WRA.

Quality of Life Impairment

Asthma-Specific Quality of Life

Subjects with WRA showed significantly lower mAQLQ in overall and subdomain scores than those with non-WRA, indicating a higher level of QoL impairment (**Table II**). Univariable and multivariable associations with overall mAQLQ score are detailed in **Table III**. The multivariable linear regression analysis conducted among subjects with current asthma revealed that a greater impairment in asthma-specific QoL was independently associated with poor asthma control (i.e. ACT score ≤19), WRA, and work-related rhinitis.

General Health-Related Quality of Life

Analysis of the SF-8 questionnaire (**Table IV**) revealed that the median PCS score was worse in participants with WRA (46.4) and non-WRA (51.8) as compared to the reference group (54.4, p<0.01). Subjects with WRA and non-WRA also showed lower MCS scores (45.7 and

297 50.7, respectively) than the reference group (52.4, p<0.01). The PCS and MCS scores were
298 significantly lower in subjects with WRA than those with non-WRA or the reference group
299 (**Table IV**). Univariable and multivariable analyses of the factors that determined physical
300 health impairments are summarized in **Table Va.** In the final multivariable model, being
301 female, having non-WRA, having WRA, and having depression and other comorbidities were
302 significantly and independently associated with lower PCS scores. Compared to the reference
303 group, the PCS scores were lower by averages of 6.9 points (95% CI -8.8; -5.3; *P*<0.001) for
304 the WRA group and 2.2 points (95% CI -3.7; -0.9; *P*=0.002) for the non-WRA group.
305
306 Univariable and multivariable regression models with mental health impairment as the
307 dependent variable are summarized in **Table Vb.** Similarly, being a female, having non-WRA,
308 having WRA, and having depression, and other comorbidities were significantly and
309 independently associated with lower MCS scores. Having WRA lowered the MCS scores by
310 4.6 points (95% CI -6.5, -2.7; *P*<0.001), while having non-WRA lowered the MCS scores by
311 2.1 points (95% CI -3.7, -0.5; *P*=0.011).
312
313 **Work Productivity Impairment**
314 *Asthma-Related Work Disability and Healthcare Utilization*
315 Respiratory-related work disability was reported by 10.4% of workers with WRA and none
316 (0%) in the non-WRA group (*P*=0.003) (**Table II**). Thirteen percent of the WRA group and
317 12% of the non-WRA group reported missed workdays or respiratory absences in the past 12
318 months (*P*=0.320). However, workers with WRA had higher percentages of at least one visit
319 to their general practitioner (67.2%) as well as income reduction due to respiratory symptoms
320 (13.8%) than those with non-WRA (46.3%, *P*=0.011 and 3.6%, *P*=0.024, respectively).
321 *General Health-Related Work Productivity*
322 **Table IV** shows that the WRA group had the highest proportion (17.9%) of workers with any
323 work time missed due to general health (absenteeism) in the last seven days compared with
324 both non-WRA (4.5%) and the reference group (2.6%) (*P*=0.001). Workers with WRA also
325 had the highest proportions of any impairment at work (presenteeism), any overall work
326 impairment and any activity impairment compared with the non-WRA and reference groups
327 (all *P*<0.001). **Table VI** displays the univariable and multivariable associations between
328 sociodemographic and clinical characteristics and any overall work impairment based on
329 WPAI-GH. In the final multivariable regression model (**Table VI**), having WRA increased the
330 risk of having any overall work impairment more than four-fold (OR=4.5; 95% CI 2.5; 8.1;

P<0.001), while having non-WRA increased the risk by more than two-fold (OR=2.0; 95% CI 1.2; 3.5; *P*=0.008). An additional analysis among asthmatics shows that asthma control was not associated with work productivity (**Table E 2**).

DISCUSSION

This study shows that workers with WRA had significantly lower asthma QoL in all domains compared to those with non-WRA. Workers with WRA and non-WRA had significantly lower physical and mental health status and overall work productivity compared to the reference group, with greater impairment in WRA than non-WRA. Consistent with published literature [4, 7, 10] workers with WRA had a higher percentage of doctor visits and income reduction due to respiratory symptoms than non-WRA.

These main findings were consistent with our evaluation of the impact of rhinitis that workers with work-related rhinitis (WRR) and non-WRR had significantly lower physical and mental health status and overall work productivity compared to workers without nasal symptoms, with greater impairment in WRR than non-WRR[14]. Our current study suggests that work-related rhinitis was associated with a reduced asthma-related QoL, independently from having WRA.

Other pervious studies also suggest that workers with WRA, either OA or WEA, tend to have impaired QoL and/or work productivity. A cross-sectional study in Tunisia showed that most OA patients had a poor quality of life, but there was no control group[11]. In another study of 43 German bakers with allergic OA, a third of the participants reported “Moderate” problems in the ‘anxiety/depression’ dimension. Although the overall quality of life was high, asthma symptoms triggered by exposure to dust showed the greatest impairment[12]. A large survey of workers with asthma related to workplace dampness and mold exposure was conducted in Finland. It used the SF-12 questionnaire and found that patients with WRA had significantly lower QoL in physical but not mental components compared to patients with asthma-like symptoms and those with upper respiratory symptoms[9]. On the contrary, Moullec et al.[8]. compared workers with WRA and non-asthmatics and did not find significant differences in SF-36 scores except for the emotional dimension. Nevertheless, they found that OA workers were more likely to change jobs than WEA and non-asthmatic workers. They also found that the QoL of workers with WRA remained impaired long after the diagnosis, which indicated the sustained impairment even after being removed from the workplace exposure. Workers with WRA also had more clinical visits compared to non-asthmatic workers. Knoeller and colleagues used the Behavioral Risk Factor Surveillance System health-related QoL indicators to evaluate the ever-employed adults with current asthma in the United States. WRA was

defined as adults with current asthma who reported that[1] they were ever told by a doctor or other health professional that their asthma was related to any job they ever had,[18] or their asthma was caused or made worse by exposure in the workplace. They showed that workers with WRA were significantly more prone to have poor self-rated health, impaired physical and mental health, as well as activity limitations than those with non-WRA[13].

We would like to highlight our findings that female sex and depression were associated with both worse physical and mental domains of QoL and impaired work productivity, independent of the effect of WRA. These findings were consistent with our previous study of work-related rhinitis, in which female sex and depression were associated with impaired QoL and overall work productivity, independent of the effect of work-related rhinitis[14]. A previous study among Canadian workers also found a high prevalence of mental health problems among those with WRA[8]. Screening for mental health problems such as anxiety and depression should be considered in guidelines for occupational physicians treating WRA patients to avoid poorer results of QoL in all domains.

Strength and limitations

To the best of our knowledge, our study is one of the largest to evaluate the impact of WRA on health related QoL and work productivity compared to non-WRA and non-asthmatic subjects in the general workforce population using validated instruments for assessing QoL and work-productivity. The survey instruments used in the study, such as the mAQLQ-M, had been validated[25]. SF-8 demonstrated a good reflection of physical, mental, and overall health[26] and has been validated in numerous populations[27]. Nevertheless, given the cross-sectional design of our study, one should interpret our findings with caution. Ideally, a longitudinal study (e.g. a cohort of workers exposed to occupational sensitizers) could be more suitable to demonstrate the impact of the development of WRA on the decline in QoL. WPAI-GH is a commonly used tool to evaluate work and activity impairment, but it only evaluates impairment in the past seven days[23].

There were 186 (17.6%) subjects with at least one missing sociodemographic and/or clinical characteristic, with most missing information being on body mass index and/or job duration. Therefore, the multivariable analyses were conducted with 80-90% of those who completed the QoL or work productivity questionnaires. Despite the high number of missing values, the proportions of missing characteristics were not significantly different across the WRA, non-WRA, and reference groups. Moreover, the distributions of the mAQLQ overall score, SF-8

PCS/MCS scores, and any work productivity impairment were comparable (i.e. no statistically significant difference) between the group with and without missing values.

Due to the questionnaire design, we could not distinguish between the two major types of WRA cases (OA versus WEA) or the types of agents responsible for these cases. Therefore, this study was unable to investigate differences stratified by these characteristics. Information on whether asthma onset was pre-existing to the current job, was only available in 83% of subjects with current asthma. Sixteen of 73 (21.9%) subjects in the WRA group with asthma onset information had asthma that existed prior to the current job. This number was too low to compare OA and WEA cases. In addition, periodic examination of workers by an occupational health service is obligatory in Belgium, but only for salaried workers. Therefore, some categories of self-employed workers with a high risk of WRA (i.e. bakers, farmers, wood workers, and hairdressers) might have been underrepresented in our study population. Nevertheless, the prevalence of asthma in our population (9.6%) was similar to that reported in a previous survey of the Belgian population (7.2%)[28] and in the European Union (8.2% in adults)[29].

Conclusions

To conclude, both WRA and non-WRA were associated with lower general health-related QoL as well as overall work productivity compared to the non-asthmatics, with an incrementally greater impairment in WRA compared to non-WRA. Work-related rhinitis and depression appeared to be associated with reduced QoL, independent of the effect of WRA. These findings suggest that comprehensive management of work-related airway disease should be done to reduce the worsening of QoL and the work productivity of those affected, thus contributing to reducing the global burden of asthma. Moreover, we suggest thorough mental health screenings for patients with WRA.

REFERENCES

1. Diseases GBD, Injuries C. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1204-22.
2. Blanc PD, Annesi-Maesano I, Balmes JR, Cummings KJ, Fishwick D, Miedinger D, et al. The Occupational Burden of Nonmalignant Respiratory Diseases. An Official American Thoracic Society and European Respiratory Society Statement. American journal of respiratory and critical care medicine. 2019;199(11):1312-34.
3. Tarlo SM, Lemiere C. Occupational asthma. The New England journal of medicine. 2014;370(7):640-9.
4. Henneberger PK, Redlich CA, Callahan DB, Harber P, Lemiere C, Martin J, et al. An official american thoracic society statement: work-exacerbated asthma. American journal of respiratory and critical care medicine. 2011;184(3):368-78.
5. Dumas O, Varraso R, Boggs KM, Descatha A, Henneberger PK, Quinot C, et al. Association of hand and arm disinfection with asthma control in US nurses. Occupational and environmental medicine. 2018;75(5):378-81.
6. Le Moual N, Carsin AE, Siroux V, Radon K, Norback D, Toren K, et al. Occupational exposures and uncontrolled adult-onset asthma in the European Community Respiratory Health Survey II. The European respiratory journal. 2014;43(2):374-86.
7. Vandenplas O. Socioeconomic impact of work-related asthma. Expert Rev Pharmacoecon Outcomes Res. 2008;8(4):395-400.
8. Moullec G, Lavoie KL, Malo JL, Gautrin D, L'Archeveque J, Labrecque M. Long-term socioprofessional and psychological status in workers investigated for occupational asthma in quebec. Journal of occupational and environmental medicine. 2013;55(9):1052-64.
9. Karvala K, Uitti J, Luukkonen R, Nordman H. Quality of life of patients with asthma related to damp and moldy work environments. Scand J Work Environ Health. 2013;39(1):96-105.
10. Lemiere C, Forget A, Dufour MH, Boulet LP, Blais L. Characteristics and medical resource use of asthmatic subjects with and without work-related asthma. The Journal of allergy and clinical immunology. 2007;120(6):1354-9.
11. Henchi MA, Omrane A, Amri C, Bouzgarrou L, Rassas I, Mahfoudhi A, et al. The Quality of Life and Professional Future among Tunisian Workers Suffering from Occupational Asthma. Recent Pat Inflamm Allergy Drug Discov. 2017;11(1):64-70.
12. Bittner C, Garrido MV, Harth V, Preisser AM. IgE Reactivity, Work Related Allergic Symptoms, Asthma Severity, and Quality of Life in Bakers with Occupational Asthma. Adv Exp Med Biol. 2016;921:51-60.
13. Knoeller GE, Mazurek JM, Moorman JE. Health-related quality of life among adults with work-related asthma in the United States. Qual Life Res. 2013;22(4):771-80.
14. Vandenplas O, Suarthana E, Rifflart C, Lemiere C, Le Moual N, Bousquet J. The Impact of Work-Related Rhinitis on Quality of Life and Work Productivity: A General Workforce-Based Survey. J Allergy Clin Immunol Pract. 2020;8(5):1583-91 e5.
15. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, et al. Development of the asthma control test: a survey for assessing asthma control. J Allergy Clin Immunol. 2004;113(1):59-65.
16. Schatz M, Sorkness CA, Li JT, Marcus P, Murray JJ, Nathan RA, et al. Asthma Control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. The Journal of allergy and clinical immunology. 2006;117(3):549-56.

17. Juniper EF, Guyatt GH, Cox FM, Ferrie PJ, King DR. Development and validation of the Mini Asthma Quality of Life Questionnaire. Eur Respir J. 1999;14(1):32-8.
18. Hoy R, Burdon J, Chen L, Miles S, Perret JL, Prasad S, et al. Work-related asthma: A position paper from the Thoracic Society of Australia and New Zealand and the National Asthma Council Australia. Respirology. 2020;25(11):1183-92.
19. Burney PG, Laitinen LA, Perdrizet S, Huckauf H, Tattersfield AE, Chinn S, et al. Validity and repeatability of the IUATLD (1984) Bronchial Symptoms Questionnaire: an international comparison. Eur Respir J. 1989;2(10):940-5.
20. Vandenplas O, Delwiche JP, Evrard G, Aimont P, van der Brempt X, Jamart J, et al. Prevalence of occupational asthma due to latex among hospital personnel. Am J Respir Crit Care Med. 1995;151(1):54-60.
21. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. Eur Respir J. 1995;8(3):483-91.
22. Shaaban R, Zureik M, Soussan D, Neukirch C, Heinrich J, Sunyer J, et al. Rhinitis and onset of asthma: a longitudinal population-based study. Lancet. 2008;372(9643):1049-57.
23. Reilly MC, Tanner A, Meltzer EO. Work, classroom and activity impairment instruments. Validation studies in allergic rhinitis. Clin Drug Invest. 1996;11(5):278-88.
24. Kim JL, Blanc PD, Villani S, Olivieri M, Urrutia I, van Sprundel M, et al. Predictors of respiratory sickness absence: an international population-based study. Am J Ind Med. 2013;56(5):541-9.
25. Adams RJ, Ruffin RE, Smith BJ. Validity of a modified version of the Marks Asthma Quality of Life Questionnaire. J Asthma. 2000;37(2):131-43.
26. Wirtz MA, Schulz A, Brahler E. Confirmatory and bi-factor analysis of the Short Form Health Survey 8 (SF-8) scale structure in a German general population sample. Health Qual Life Outcomes. 2021;19(1):73.
27. Lang L, Zhang L, Zhang P, Li Q, Bian J, Guo Y. Evaluating the reliability and validity of SF-8 with a large representative sample of urban Chinese. Health Qual Life Outcomes. 2018;16(1):55.
28. Wijnant SRA, Lahousse L, De Buyzere ML, Brusselle GG, Rietzschel ER. Prevalence of Asthma and COPD and Blood Eosinophil Count in a Middle-Aged Belgian Population. *Journal of Clinical Medicine*. 2019; 8(8):1122. https://doi.org/10.3390/jcm8081122
29. Selroos O, Kupczyk M, Kuna P, Lacwik P, Bousquet J, Brennan D, et al. National and regional asthma programmes in Europe. Eur Respir Rev. 2015;24(137):474-83.

512 **Figure legends:**

513 **Figure 1.** Flowchart of the study recruitment.

514

Table I. Demographic and clinical characteristics of participants with work-related asthma, asthma unrelated to work, and the reference population.

Characteristics	Missing values[d]	Work-related asthma (WRA) (n=89)	Non-work-related asthma (non-WRA) (n=119)	Reference group (n=815)	*P*-value[e]
Sex, female	0/0/3	59 (66.3)	54 (45.4)	383 (47.2)	0.002
Age, year	2/1/19	38.1 (30.5 - 47.4)	37.5 (30.4 - 45.9)	40.7 (32.5 – 48.5)	0.023
Smoking status:	0/0/12				0.050
Current smoker		37 (41.6)	39 (32.8)	216 (26.9)	
Ex-smoker		13 (14.6)	21 (17.6)	147 (18.3)	
Never smoker		39 (43.8)	59 (49.6)	441 (54.9)	
Body mass index:	4/6/61	25.3 (23.01 -27.9)	24.1 (21.9 – 27.1)	24.8 (22.5 - 27.8)	0.174
Normoweight		39 (45.9)	66 (58.4)	369 (48.9)	0.193
Overweight (≥25 kg/m^2)		46 (54.1)	47 (41.6)	385 (51.1)	
Education level					0.127
>12 years	1/0/26	28 (31.8)	54 (45.4)	300 (38)	
≤12 years		60 (68.2)	65 (54.6)	490 (62)	
Current job duration	8/7/70	6.3 (2.02 -11.1)	5.5 (1.8 -11.6)	7.0 (2.1-16.0)	0.164
Asthma pre-existing to current job	16/17/-	57 (78.1)	84 (82.4)	n/a	0.240
Use of asthma treatment	0/0/-	67 (75.3)	85 (71.4)	n/a	0.535
SABA	33/47/-	35 (62.5)	39 (54.2)	n/a	0.344
LABA	33/47/-	17 (30.4)	18 (25.0)	n/a	0.500
ICS	33/47/-	18 (32.1)	21 (29.2)	n/a	0.717
Oral corticosteroid	33/47	3 (5.4)	1 (1.4)	n/a	0.318
Asthma control:					
ACT score		21.0 (17.0; 23.0)	23.0 (21.0; 24.0)	n/a	<0.001
ACT score ≤19	30/46/	27 (45.8)	13 (17.8)	n/a	0.001
Associated conditions:					
Allergic rhinitis[a]	1/0/-	67 (76.1)	89 (74.8)	n/a	0.824
Work-related rhinitis[b]	1/0/-	31 (34.8)	7 (5.9)	n/a	<0.001
Work-related conjunctivitis[c]	0/0/-	22 (24.7)	6 (5.0)	n/a	<0.001
Chronic phlegm	1/3/-	25 (28.4)	15 (12.9)	n/a	0.006
Depression, physician-based	0/0/1	24 (27.0)	17 (14.3)	69 (8.5)	<0.001
Non-respiratory non-depression comorbidity	0/0/0	30 (33.7)	42 (35.3)	324 (39.8)	0.387

Legend: Data are presented as numbers (% of available data) of subjects or medians (interquartile ranges). Values in boldface are statistically significant.

ACT: Asthma Control Test; ICS: Inhaled corticosteroid; Na: not applicable; LABA; long-acting β_2-agonist; SABA; short-acting β_2-agonist.

[a] Allergic rhinitis is defined as either self-reported or physician-based allergic rhinitis;

[b] Work-related is rhinitis defined by current rhinitis (the presence of at least two nasal symptoms on a regular basis during the last 12 months) associated with at least two nasal symptoms at work;

[c] Work-related conjunctivitis as itchy and red eyes at work

[d] Missing data for WRA, non-WRA and reference groups, respectively.

[e] Between WRA, non-WRA and the reference group

Table II. Asthma-specific quality of life (mAQLQ) and socioeconomic outcomes in work-related asthma and asthma unrelated to work.

Outcomes	**Missing values**	**Work-related asthma (WRA)** (n=89)	**Non-work-related asthma (non-WRA)** (n=119)	***P*-value**
mAQLQ domains:				
Global	45/33	5.3 (4.2 - 6.3)	6.3 (5.7 - 6.7)	<0.001
Symptoms	44/30	5.0 (3.4 - 5.8)	6.2 (5.2 - 6.6)	<0.001
Activities	43/33	6.0 (4.6 - 6.5)	6.8 (6.0 - 7.0)	<0.001
Emotions	42/30	5.7 (4.3 - 7.0)	6.7 (6.0 - 7.0)	0.001
Environment	42/31	5.0 (4.0 - 6.1)	6.0 (5.3 - 7.0)	<0.001
Respiratory-related work disability[a]	36/22	7 (10.4)	0 (0)	0.003
Respiratory sickness absence, last 12 mo[b]	37/27	13 (21.0)	12 (14.6)	0.320
Any income reduction due to respiratory symptoms[c]	36/24	9 (13.8)	3 (3.6)	0.024
Hospitalization due to respiratory symptom	22/36	4 (6.0)	3 (3.5)	0.701
Visit general practitioner due respiratory symptom	22/37	45 (67.2)	38 (46.3)	0.011
Visit a specialist due to respiratory symptom	22/36	19 (28.4)	20 (24.1)	0.554

Legend: Data are presented as numbers (percentages) of subjects or medians (interquartile ranges), and p-values are for comparing WRA to non-WRA. AQLQ: Asthma Quality of Life Questionnaire. Values in boldface are statistically significant.

[a] Defined as ever having had to change or leave the job or reduce working time due to respiratory symptoms;

[b] Defined as at least one work day lost due to respiratory symptoms;

[c] Slight or substantial income reduction (self-reported)

Table III. Univariable analysis and multivariable model for the mini Asthma Quality of Life Questionnaire global score – among asthmatics.

Characteristics	Univariable associations		Final Multivariable model	
	Median (IQR)	*P*-value	Unstandardized β coefficient (95% CI)	*P*-value
Sex*		0.007		
Female	5.7 (4.9 - 6.4)			
Male	6.2 (5.4 - 6.7)			
Age; yr*		0.590		
<35 years	5.7 (4.9 - 6.5)			
35-45 years	6.2 (5.1 – 6.5)			
≥ 45 years	6.2 (5.1 – 6.5)			
Smoking habit*		0.702		
Never smoker	6.0 (5.2 - 6.4)			
Ex-smoker	5.7 (4.8 - 6.7)			
Current smoker	6.1 (5.1 - 6.5)			
Body mass index*		0.03		
<25 kg/m^2	6.3 (5.4 - 6.6)			
≥25 kg/m^2	5.7 (4.9 – 6.4)			
Education level*		0.729		
>12 years	6.1 (5.3 - 6.5)			
≤12 years	6.1 (4.9 – 6.5)			
Current job duration*		0.064		
<5.0 years	5.7 (4.3 - 6.4)			
≥ 5.0 years	6.03 (5.4 - 6.5)			
Asthma pre-existing to current job				
Yes	5.7 (4.9 - 6.4)	0.006		
No	6.4 (5.7-6.7)			
Asthma control*		<0.001		
ACT score >19	6.3 (5.7 – 6.7)		Reference	
ACT score ≤19	4.8 (3.7 - 5.4)		-1.4 (-1.8; -1.1)	<0.001
Asthma*				
Non-WRA	6.3 (5.7 - 6.7)	<0.001	Reference	
WRA[a]	5.3 (4.2 – 6.3)		-0.4 (-0.7; -0.01)	0.044
Asthma medication		0.001		
No	6.2 (5.5 – 6.7)			
Yes	5.4 (4.1 – 6.3)			
Allergic rhinitis[b]		0.282		
Absent	6.2 (5.4 - 6.6)			
Present	6.0 (5.0 - 6.5)			
Work-related rhinitis[c]		0.017		
Absent	6.3 (6.1 - 7.0)		Reference	
Present	5.6 (5.0 - 6.4)		-0.4 (-0.8; -0.02)	0.061
Work-related conjunctivitis[d]		0.637		
Absent	6.0 (5.1 - 6.5)			
Present	6.1 (5.1 - 6.4)			
Chronic phlegm*		0.004		
Absent	6.1 (5.4 - 6.5)			
Present	5.0 (3.9 - 6.3)			
Depression, physician-based		0.677		
Absent	6.0 (5.1 - 6.5)			
Present	5.9 (4.8 - 6.5)			

Non-respiratory non-depression comorbidity		0.393		
Absent	6.0 (5.0 - 6.5)			
Present	6.1 (5.2 - 6.6)			

Legend: ACT: Asthma Control Test; AQLQ: Asthma Quality of Life Questionnaire; IQR: Interquartile range; n/a: not available; SF-8: Medical Outcome Study Short Form-8; WPAI-GH: Work Productivity and Activity Impairment-General Health.
Analysis was done in the WRA and non-WRA groups because AQLQ is an asthma-specific questionnaire. Multivariable analysis was done on 106 subjects and incorporated well-known confounders such as age, sex, smoking habits, body mass index, allergic rhinitis and other covariates with a *P*-value <0.1 in univariable analyses (marked with asterisk (*)).

[a] Work-related asthma is defined as current asthma associated with ≥2 work-related asthma symptoms.
[b] Allergic rhinitis is defined as either self-reported or physician-based allergic rhinitis.
[c] Work-related rhinitis is defined as current rhinitis with ≥2 work-related rhinitis symptoms.
[d] Work-related conjunctivitis is defined by red and itchy eyes at work.

Table IV. General health-related quality of life (SF-8) and Work productivity impairments in participants with work-related asthma and non-work-related asthma compared with the reference population [a,b]

Outcomes	**Missing values**	**Work-related asthma (WRA)** (n=89)	**Non-work-related asthma (non-WRA)** (n=119)	**Reference Group** (n=815)	**P value Non-WRA vs. Reference Groups**
SF8-Physical Component Summary	1/5/42	46.4 (38.6-51.5)	51.8 (46.4-56.2)	54.4 (50.0-56.9)	0.001
SF8-Mental Component Summary	1/5/42	45.7 (36.6-52.4)	50.7 (43.9-56.3)	52.4 (48.2-57.5)	0.016
Any work time missed (absenteeism)	11/8/90	14 (17.9)	5 (4.5)	19 (2.6)	0.469
Any impairment at work (presenteeism)	19/11/132	33 (47.1)	25 (23.1)	58 (8.5)	<0.01
Any overall work impairment	21/11/139	31 (45.6)	27 (25.0)	58 (8.6)	<0.01
Any activity impairment	7/6/56	45 (54.9)	32 (28.3)	77 (10.1)	<0.01

Legend:
Data are presented as numbers (% of available data) of subjects or medians (interquartile ranges). SF-8: Medical Outcome Study Short Form-8; WPAI-GH: Work Productivity and Activity Impairment-General Health. Values in boldface are statistically significant.

[a] Comparison between the three groups were all significant (p values <0.001)

[b] Comparison between the WRA vs. non-WRA groups, as well as WRA vs. Reference groups were all significant (p values <0.01)

Table Va. Univariable analysis and multivariable model for physical components of general health quality of life (SF-8 PC) in all subjects

.

Characteristics	Univariable associations		Final Multivariable model	
	Median (IQR)	*P*-value	Unstandardized β coefficient (95% CI)	*P*-value
Sex*		<0.001		
Female	52.9 (46.4 - 56.4)		-1.6 (-2.6; -0.6)	0.001
Male	54.5 (49.4 – 57.1)		Reference	
Age*		<0.001	-0.1 (-0.1; -0.05)	<0.001
<35 years	55.4 (50.8 – 57.7)			
35-45 years	54.2 (48.8 - 56.7)			
≥ 45 years	52.9 (50.8 – 57.8)			
Smoking habit*		0.064		
Never smoker	54.2 (48.5 - 56.7)			
Ex-smoker	52.7 (46.4 -56.5)			
Current smoker	54.3 (48.7 – 56.9)			
Body mass index*		<0.001		
<25 kg/m^2	54.8 (49.9 – 57.3)		Reference	
≥25 kg/m^2	52.9 (46.3 – 56.3)		-1.7 (-2.7; -0.7)	0.001
Education level*		0.573		
>12 years	54.2 (48.4 - 56.7)			
≤12 years	54.1 (48.1 – 56.7)			
Current job duration*		<0.001		
<5.0 years	54.9 (50.1 - 57.5)			
≥ 5.0 years	53.6 (46.8 - 56.4)			
Asthma pre-existing to current job				
Yes	49.8 (43.5– 55.6)	0.978		
No	51.7 (44.4-54.2)			
Asthma control		<0.001		
ACT score >19	51.7 (45.8 - 56.2)			
ACT score ≤19	41.2 (37.0 - 48.4)			
Asthma*		<0.001		
Absent	54.4 (49.9 – 56.7)		Reference	
Non-WRA	51.8 (46.4 - 56.2)		-2.3 (-3.7; -0.9)	0.002
WRA[a]	46.4 (38.6 - 51.5)		-6.9 (-8.7; -5.3)	<0.001
Depression, physician-based*		0.001		
Absent	54.3 (48.7 – 56.7)			
Present	51.3 (44.1 – 55.7)			
Non-respiratory non-depression comorbidity*		<0.001		
Absent	54.7 (49.9 – 57.2)		Reference	
Present	52.8 (44.6 – 56.2)		-2.3 (-3.4; -1.3)	<0.001

Legend: ACT: Asthma Control Test; IQR: Interquartile range; n/a: not available; WRA: work-related asthma. Multivariable analysis was done on 822 subjects and incorporated well-known confounders such as age, sex, smoking habits, body mass index, allergic rhinitis and other covariates with a *P*-value <0.1 in univariable analyses (marked with asterisk (*)). Asthma control was not included because the information was only available among asthmatics.

[a] Work-related asthma is defined as current asthma associated with ≥2 work-related asthma symptoms.
[b] Allergic rhinitis is defined as either self-reported or physician-based allergic rhinitis.
[c] Work-related rhinitis is defined as current rhinitis with ≥2 work-related rhinitis symptoms.
[d] Work-related conjunctivitis is defined by red and itchy eyes at work.

Table Vb. Univariable analysis and multivariable model for mental components of general health quality of life (SF-8 MC) in all subjects

.

Characteristics	Univariable associations		Final Multivariable model	
	Median (IQR)	*P*-value	Unstandardized β coefficient (95% CI)	*P*-value
Sex*		<0.001		
Female	50.0 (43.5 – 56.0)		-2.4 (-3.5; -1.3)	<0.001
Male	53.9 (49.3 – 57.4)		Reference	
Age*		0.447		
<35 years	52.1 (46.8 – 57.3)			
35-45 years	52.1 (47.1 - 57.5)			
≥ 45 years	51.0 (43.0 – 57.5)			
Smoking habit*		0.248		
Never smoker	52.1 (47.0 - 57.5)			
Ex-smoker	52.4 (46.1 - 57.5)			
Current smoker	51.3 (44.8 - 57.3)			
Body mass index*		0.279		
<25 kg/m^2	52.3 (46.9 - 57.5)			
≥25 kg/m^2	51.3 (45.0 – 57.4)			
Education level*		0.458		
>12 years	51.5 (46.7 – 57.3)			
≤12 years	52.0 (46.3 – 57.5)			
Current job duration*		0.047		
<5.0 years	52.3 (48.1 - 57.5)			
≥ 5.0 years	51.4 (45.2 - 57.4)			
Asthma pre-existing to current job				
Yes	49.4 (42.1 - 54.8)	0.505		
No	49.6 (39.0-54.6)			
Asthma control		0.016		
ACT score >19	49.9 (42.9 – 55.0)			
ACT score ≤19	46.1 (40.3 - 51.6)			
Asthma*		<0.001		
Absent	52.4 (48.2-57.5)		Reference	
Non-WRA	50.7 (43.9 -56.3)		-2.1 (-3.7; -0.5)	0.009
WRA[a]	45.7 (36.6 - 52.4)		-4.6 (-6.5; -2.7)	<0.001
Depression, physician-based*		<0.001		
Absent	52.3 (48.1 – 57.5)		Reference	
Present	43.7 (37.1 – 52.3)		-7.6 (-9.3; -5.8)	<0.001
Non-respiratory non-depression comorbidity*		0.006		
Absent	52.5 (46.8– 57.5)		Reference	
Present	50.8 (45.6 – 56.6)		-2.1 (-3.3; -0.9)	<0.001

Legend: ACT: Asthma Control Test; IQR: Interquartile range; n/a: not available; WRA: work-related asthma. Multivariable analysis was done on 822 subjects and incorporated well-known confounders such as age, sex, smoking habits, body mass index, allergic rhinitis and other covariates with a *P*-value <0.1 in univariable analyses (marked with asterisk (*)). Asthma control was not included because the information was only available among asthmatics.

[a] Work-related asthma is defined as current asthma associated with ≥2 work-related asthma symptoms.
[b] Allergic rhinitis is defined as either self-reported or physician-based allergic rhinitis.
[c] Work-related rhinitis is defined as current rhinitis with ≥2 work-related rhinitis symptoms.
[d] Work-related conjunctivitis is defined by red and itchy eyes at work.

Table VI. Univariable analysis and multivariable model for work productivity (WPAI-GH) in all subjects

Characteristics	Univariable associations		Final Multivariable model	
	Median (IQR)	*P*-value	Unstandardized β coefficient (95% CI)	*P*-value
Sex*		0.034		
Female	86 (55.8)		1.4 (0.9; 2.1)	0.093
Male	68 (44.2)		Reference	
Age*		0.747		
<35 years	46 (31.1)			
35-45 years	46 (31.1)			
≥ 45 years	56 (37.8)			
Smoking habit*		0.035		
Never smoker	82 (53.6)			
Ex-smoker	38 (24.8)			
Current smoker	33 (21.6)			
Body mass index*		0.035		
<25 kg/m^2	65 (45.5)		Reference	
≥25 kg/m^2	78 (54.5)		1.5 (0.9; 2.2)	0.055
Education level*		0.051		
>12 years	72 (47.4)		Reference	
≤12 years	80 (52.6)		0.7 (0.5; 1.0)	0.070
Current job duration*		0.986		
<5.0 years	61 (43.0)			
≥ 5.0 years	81 (57.0)			
Asthma pre-existing to current job				
Yes	42 (87.5)	0.229		
No	6 (12.5)			
Asthma control		0.004		
ACT score >19	17 (53.1)			
ACT score ≤19	15 (46.9)			
Asthma*		<0.001		
Absent	96 (62.3)		Reference	
Non-WRA	27 (17.5)		2.0 (1.2; 3.5)	0.008
WRA[a]	31 (20.1)		4.5 (2.5; 8.1)	<0.001
Depression, physician-based*		0.037		
Absent	131 (85.1)		Reference	
Present	23 (14.9)		1.8 (0.9; 3.3)	0.085
Non-respiratory non-depression comorbidity*		0.003		
Absent	77 (50.0)		Reference	
Present	77 (50.0)		1.9 (1.2; 2.9)	0.004

Legend: ACT: Asthma Control Test; IQR: Interquartile range; n/a: not available; OR: Odds ratio; 95% CI: 95% confidence interval; WPAI-GH: Work Productivity and Activity Impairment-General Health; WRA: work-related asthma.
Multivariable analysis was done on 713 subjects and incorporated well-known confounders such as age, sex, smoking habits, body mass index, allergic rhinitis and other covariates with a *P*-value <0.1 in univariable analyses (marked with asterisk (*)). Asthma control was not included because the information was only available among asthmatics.

[a] Work-related asthma is defined as current asthma associated with ≥2 work-related asthma symptoms.
[b] Allergic rhinitis is defined as either self-reported or physician-based allergic rhinitis.
[c] Work-related rhinitis is defined as current rhinitis with ≥2 work-related rhinitis symptoms.
[d] Work-related conjunctivitis is defined by red and itchy eyes at work.

Figure 1.

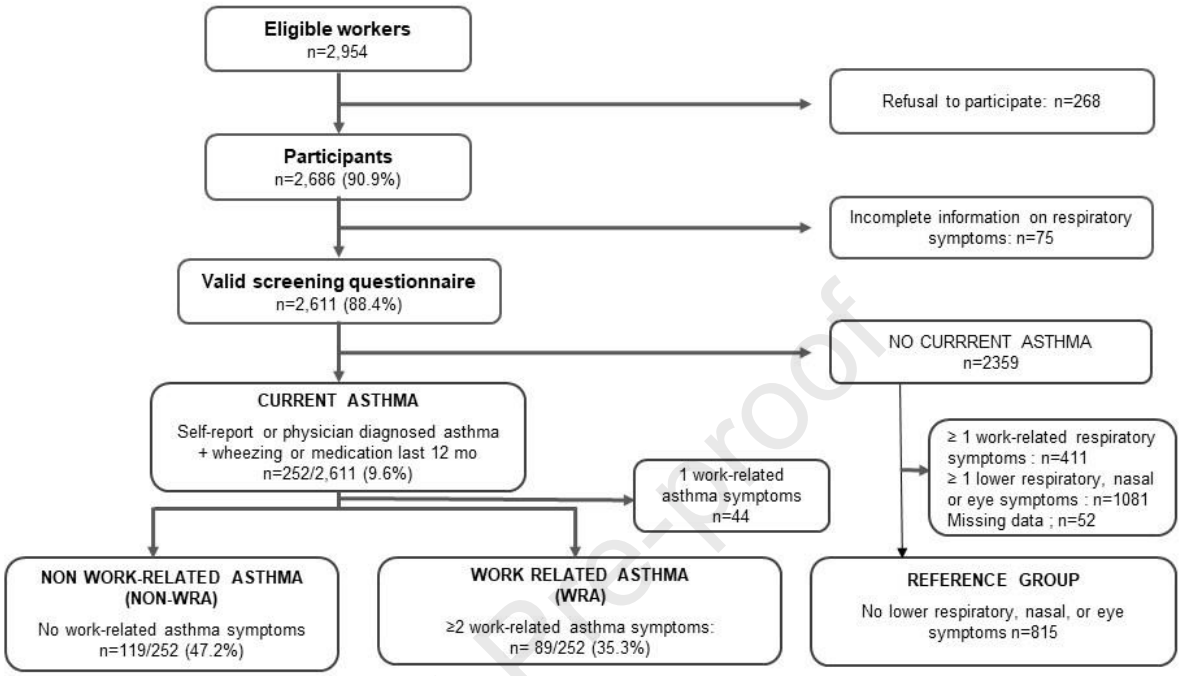


Table E 1. Definition of symptoms/diseases and outcomes.

Symptom/disease	Questions/criteria
Asthma (1)	• Self-reported asthma: "*Did you ever suffer from asthma or 'asthmatic bronchitis'?*" OR • Physician-based asthma "*Has a doctor ever told you that you have asthma or 'asthmatic bronchitis'?*"
Current asthma (1)	• Self-reported or physician-based asthma AND • *"Have you had wheezing or whistling sounds in your chest apart from colds in the last 12 months?"* OR • *"Are you currently taking any medication for asthma?"*
Work-related asthma (WRA)	• Current asthma AND • A least two asthma symptom at work: *"When you are at work or during the following hours; do you experience: Wheezing; chest tightness; shortness of breath; or cough?"*
Occupational asthma (OA)	• Current asthma AND • Onset of asthma during exposure to the current job AND • A least two asthma symptoms at work: *"When you are at work or during the following hours; do you experience: Wheezing; chest tightness; shortness of breath; or cough?"*
Work-exacerbated asthma (WEA)	• Current asthma AND • Onset of asthma prior to the current job AND • A least two asthma symptoms at work: *"When you are at work or during the following hours; do you experience: Wheezing; chest tightness; shortness of breath; or cough?"*
Current rhinitis (2)	• At least two nasal symptoms: *"In the last 12 months (when you did not have a cold or the flu); have you regularly had any of the following symptoms: Stuffy nose; runny nose; or episodes of sneezing?"*
Allergic rhinitis	• Self-reported or physician-based allergic rhinitis
Work-related rhinitis (3, 4)	• Current rhinitis AND • A least two nasal symptoms at work: "*When you are at work or during the following hours; do you notice the onset or worsening of: Stuffy nose; runny nose; or episodes of sneezing?*"
Work-related conjunctivitis	Itchy and red eyes at work
Quality of Life (QoL)	• Asthma-specific: Asthma Quality of Life Questionnaire (AQLQ) (5) • Generic: Medical Outcome Study Short Form-8 (SF-8) (*www.qualitymetric.com*) (6)
General health-related work productivity impairment	• Work Productivity and Activity Impairment-General Health (WPAI-GH) (*www.reillyassociates.net*) (6)
Respiratory-related work disability	• Respiratory-related work disability: *"Have you ever had to change your job or task or reduce your working time due to respiratory symptoms?"* (7) • Number of work days missed due to respiratory symptoms during the last 12 months

- Respiratory-related sickness absence: At least one self-reported work day missed due to respiratory symptoms in the last 12 months (8)

References

1. Burney PG, Laitinen LA, Perdrizet S, Huckauf H, Tattersfield AE, Chinn S, et al. Validity and repeatability of the IUATLD (1984) Bronchial Symptoms Questionnaire: an international comparison. Eur Respir J. 1989;2(10):940-5.
2. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. Eur Respir J. 1995;8(3):483-91.
3. Vandenplas O, Delwiche JP, Evrard G, Aimont P, van der Brempt X, Jamart J, et al. Prevalence of occupational asthma due to latex among hospital personnel. Am J Respir Crit Care Med. 1995;151(1):54-60.
4. Storaas T, Steinsvag SK, Florvaag E, Irgens A, Aasen TB. Occupational rhinitis: diagnostic criteria, relation to lower airway symptoms and IgE sensitization in bakery workers. Acta oto-laryngologica. 2005;125(11):1211-7.
5. Juniper EF, Guyatt GH, Epstein RS, Ferrie PJ, Jaeschke R, Hiller TK. Evaluation of impairment of health related quality of life in asthma: development of a questionnaire for use in clinical trials. Thorax. 1992;47(2):76-83.
6. Vandenplas O, Suarthana E, Rifflart C, Lemiere C, Le Moual N, Bousquet J. The impact of work-related rhinitis on quality of life and work productivity: A general workforce-based survey. The journal of allergy and clinical immunology In practice. 2020;8:1583-91.e5.
7. Blanc PD, Ellbjar S, Janson C, Norback D, Norrman E, Plaschke P, et al. Asthma-related work disability in Sweden. The impact of workplace exposures. Am J Respir Crit Care Med. 1999;160(6):2028-33.
8. Kim JL, Blanc PD, Villani S, Olivieri M, Urrutia I, van Sprundel M, et al. Predictors of respiratory sickness absence: an international population-based study. Am J Ind Med. 2013;56(5):541-9.

Table E 2. Multivariable analysis for work productivity (WPAI-GH) in asthmatics

	P-value	OR	95% CI	
			Lower	Upper
Age (years)	.731	1.009	.957	1.064
Sex, female	.058	2.813	.965	8.196
BMI ≥25 kg/m^2	.568	.735	.256	2.114
Smoker	.095	2.410	.859	6.759
Education level ≤12 years	.893	1.077	.367	3.155
Current job duration ≥ 5.0 years	.766	.836	.257	2.718
ACT score ≤19	.190	2.068	.698	6.125
WRA	.180	.499	.180	1.380
Depression, physician-based	.935	.941	.218	4.062
Non-respiratory non-depression comorbidity	.698	1.249	.405	3.848