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Asthma control in severe asthma and occupational exposures to inhalable asthmagens

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ABSTRACT

Introduction Work-related asthma accounts for ≥25% of asthma in working-age populations, though the relationship between work exposures and symptoms is frequently missed, leading to poor health and employment outcomes. We hypothesised that inhalable exposures at work are associated with poor asthma control in severe asthma (SA).

Methods We searched the Birmingham (UK) Regional NHS SA Service clinical database (n=1453 records; 1 March 2004 to 1 March 2021) and undertook a cross-sectional study using baseline data collected at diagnosis. We included all employed patients aged 16–64 with documented current occupation (n=504), and collected socio-demographic, general health and asthma-specific data, including Asthma Control Questionnaire 7 (ACQ7) score. The Occupational Asthma Specific Job-Exposure Matrix (OAsJEM) was employed to determine the likelihood of exposure to respiratory sensitisers, irritants, cleaning agents and detergents; associations between exposures and ACQ7 were investigated using binary and multinomial regression.

Results Frequently reported occupations were care assistants (7%) and nurses (6%); 197/504 (39%) patients were exposed to an asthmagen, including respiratory sensitisers (30%), airway irritants (38%) and cleaning products/disinfectants (29%). ACQ7 score was available for 372/504 (74%) patients, of whom 14% had adequate control (ACQ7=0–1.5). After adjustment for major confounders there were no significant associations between inhaled asthmagens and ACQ7 score (either as binary or multinomial outcomes).

Conclusion JEM-determined workplace exposures to inhaled asthmagens are not associated with asthma control in SA; 29–39% of patients may have current exposure to workplace asthmagens. Routine collection of lifetime occupational data including current job role and level of exposure, in the national asthma registry, would give further insights into this relationship.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ A significant proportion of asthma in adult life is caused or exacerbated by workplace exposures, though the link between exposure and disease control is frequently missed. There are no such data from populations of patients with severe asthma (SA).

WHAT THIS STUDY ADDS

⇒ There was no significant association between asthma control at diagnosis of SA and workplace exposures to asthmagens, though 29-39% of working patients were likely to be exposed to respiratory sensitisers or irritants, determined by a job-exposure matrix.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Prospective and routine collection of data relating to lifetime and current job role in the UK national SA registry would allow further evaluation of the relationship between exposure and asthma control.

INTRODUCTION

Severe asthma (SA) describes asthma that is uncontrolled despite adherence to high-dose inhaled corticosteroids and long-acting beta agonists, and exclusion of other contributory factors.[1] SA can be considered separately from mild or moderate asthma, due to its accurate phenotyping, associated high-cost treatments and multidisciplinary, holistic and personalised approaches to patient care.[2] Living with SA impacts workability, and once socio-demographic factors are accounted for, uncontrolled symptoms, low asthma-related quality of life and poor physical and mental health status, have all been associated with unemployment and work disability; indeed lower-than-expected employment rates are seen in SA populations.[3 4] However, the role of workplace inhalable exposures in causing or exacerbating asthma, referred to as work-related asthma (WRA), has not been evaluated from the perspective of an SA population.

The burden and the health and social costs of WRA are high: occupational asthma (OA) alone is estimated to cost the UK economy £1 billion each decade.[5] OA accounts for one

in six incident cases of asthma in working life, and work-exacerbated asthma (WEA) is a prevailing issue affecting approximately one in four patients with pre-existing asthma.[6 7] There is also a clear social gradient, with WRA disproportionately affecting those undertaking skilled and unskilled manual work in the UK.[8] WRA diagnosis is missed ≤50% of the time,[9 10] enquiry about the relationship between work and symptoms is largely absent in both primary and secondary care[9 11] and the median time to see a specialist with symptoms is 4 years.[12] As a result, affected workers suffer poor health and employment outcomes in terms of accelerated lung function decline, and job and financial loss[7]; yet these costs are largely avoidable with early diagnosis and removal from causative exposures. We have hypothesised that inhalable exposures at work are likely to play a significant causative and/or exacerbating role in SA populations, and independently and negatively impact on disease control.

METHODS

Setting

The Birmingham Regional NHS Severe Asthma Service (BRSAS) hosted by University Hospitals NHS Foundation Trust, is commissioned by National Health Service (NHS) England to provide holistic inpatient and outpatient care for patients with SA from central England, UK. Patients are referred from both primary and secondary care with severe or difficult-to-treat asthma and receive multidisciplinary evaluation and management that also includes phenotype-appropriate biological therapy and bronchial thermoplasty.

Clinical database

For every attending patient, socio-demographic-related, disease-related and treatment-related characteristics are recorded routinely in an electronic database (Dendrite Clinical Systems, Reading, UK), which is also used for periodic reporting to the UK national SA registry. 93% of patients are referred from secondary care, 7% from primary care and 84% receive a final diagnosis of SA. We have previously published a summary of all patients in the clinical database (2004–2021) with respect to their employment status (employed or not),[4] and this constituted the sample population for this study.

Study design

We undertook a retrospective, cross-sectional study using data variables obtained from the Dendrite clinical database, in order to examine any association between asthma control and workplace exposures to inhalable asthmagens.

Eligibility

We included any patient aged 16–64 inclusive, who was employed and not in full-time education, for whom current occupation had been given (see study flow chart in figure 1).

Data gathering

For each included patient, we extracted the following 'baseline' data variables (ie, at the time of data entry, which was usually at first attendance): socio-demographics (age, gender, index of multiple deprivation decile (1=most deprived, 10=least deprived),[13] smoking status, current occupation), general health (body mass index (BMI), comorbidities, presence of atopy) and asthma-related factors (spirometric indices, Asthma Control Questionnaire 7 (ACQ7) score,[14] Asthma Quality of Life Questionnaire score,[15] maintenance oral corticosteroids, peripheral eosinophil count, hospital admissions and rescue treatments). Atopy was defined as sensitisation to ≥1 aeroallergen by specific IgE or skin prick testing. Asthma-related comorbidities were those deemed by the authors to be respiratory complications of asthma (eg, allergic bronchopulmonary aspergillosis, inducible laryngeal obstruction); major non-asthma-related comorbidities were musculoskeletal (eg, spondylosis, osteoarthritis), cardiovascular (eg, ischaemic heart disease, hypertension), metabolic (eg, diabetes mellitus, Addison disease), psychological (eg, anxiety, depression, psychosis), gastrointestinal (eg, gastro-oesophageal reflux disease, irritable bowel syndrome), cancer or chronic respiratory (eg, interstitial lung disease, chronic obstructive pulmonary disease, cystic fibrosis). Frequencies of any missing data are shown in the appropriate places in the results and tables.

Coding of occupation and evaluation of exposures

Source data on current occupation is recorded using open text and remains uncoded within the Dendrite database. Two WRA experts (GIW and CR) independently attributed patients' occupations to a specific job code from the International Standard Classification of Occupations, 1988 (ISCO-88).[16] For individual cases where there was disagreement, review by a third subject expert (CCH) allowed a majority decision to be made. Occupational exposures were evaluated using the recently updated Occupational Asthma-specific Job Exposure Matrix (OAsJEM), whose design and structure are described in detail elsewhere.[17] OAsJEM assigns ISCO-88-coded occupations to three expert-derived categories: 'high' (high probability of exposure and moderate-to-high intensity), 'medium' (low-to-moderate probability or low intensity) and 'unexposed', for 30 respiratory sensitiser and airway irritant exposures, including cleaning products and/or disinfectants. A second step using individuals' specific occupational context is also incorporated into the OAsJEM, which requires the researcher (here GIW and CR independently) to decide whether to adjust scores for probability or intensity exposure on a case-only basis. In the present study, occupations were determined to be either 'exposed' (assigned high or medium category) or

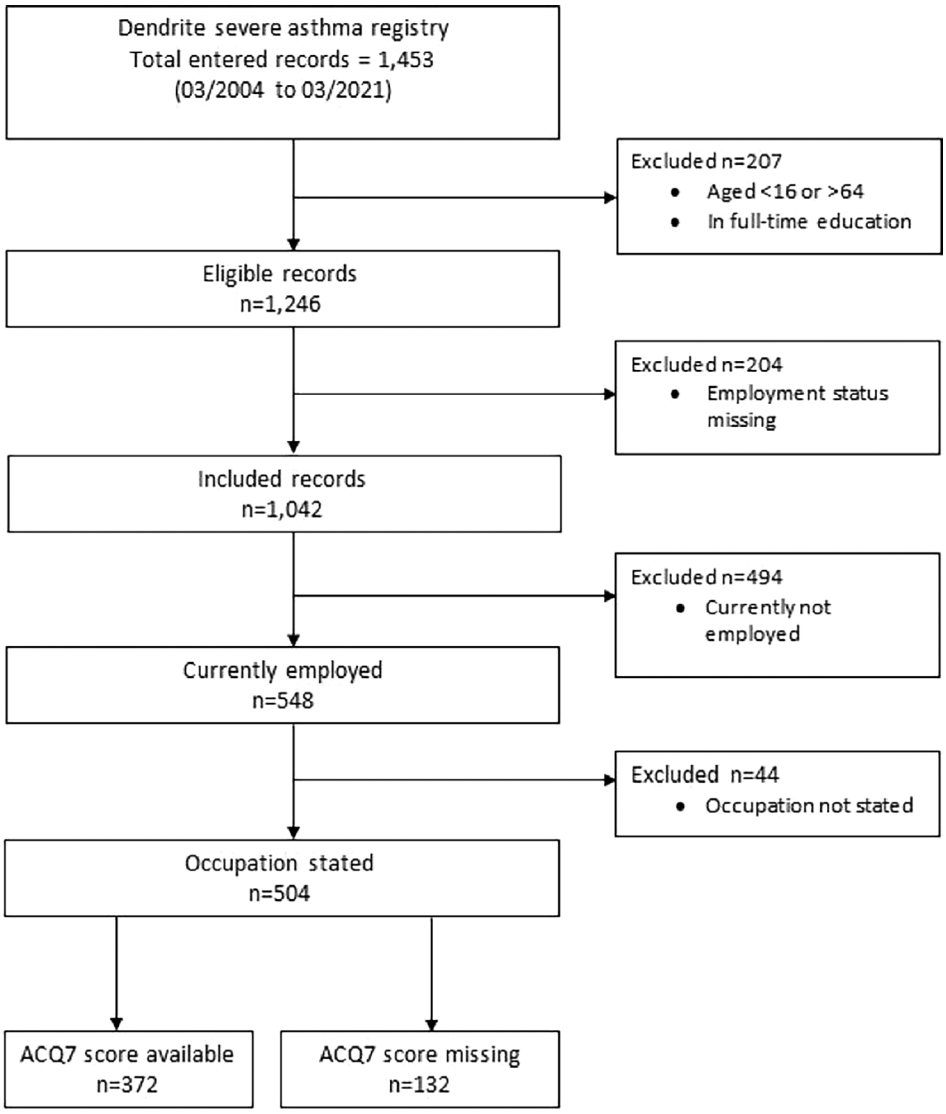

Figure 1 Study flow chart showing selection of included patients. ACQ7, Asthma Control Questionnaire 7.

'unexposed', to (1) any workplace asthmagen (ie, sensitiser and/or irritant; n=30 agents), (2) any respiratory high molecular weight (HMW) or low molecular weight (LMW) sensitiser (±irritant; n=21 agents), (3) any airway irritant (±sensitiser; n=19 agents) or (4) any LMW sensitiser or irritant cleaning product and/or disinfectant (n=3 agents).

Statistical analysis

We examined data for normality using Normal Q–Q plots and Shapiro-Wilk tests, and summarised data for the whole sample using frequency counts, mean and SD (continuous data, normal distribution), median and IQR (continuous data, non-normal distribution) and percentages (categorical data). Data were grouped as follows: (1) availability of ACQ7 data, that is, present or absent, (2) binary: adequate disease control (ACQ7 score ≤1.5) or poor disease control (ACQ7 score >1.5)[18] or (3) multinomial: into tertiles for ACQ7 score. We examined the relationship between independent variables and ACQ7 score by hypothesis testing using Student's t-tests (continuous data, normal), Mann-Whitney U tests (continuous data, non-normal) and Kendall tau-B (ordinal data), and by univariate binary or multinomial logistic regression; for continuous data, linear assumptions were tested using the Box-Tidwell transformation. Multivariate binary and multinomial logistic regression analyses were undertaken to adjust for the following potential confounders (age, gender, presence of atopy, smoking status (ex-or current vs never), BMI (<25 vs ≥25), presence of ≥1 major non-asthma-related comorbidity) using a main effects model. Goodness of fit was examined using the Hosmer-Lemeshow test, and co-linearity between variables was examined visually using linear regression plots. All tests were performed using Statistical Package for the Social Sciences (SPSS; IBM, Armonk, USA) at the 95% significance level. The UK SA registry has database ethical approval from the Office of Research Ethics Northern Ireland (15/NI/0196) and all patients provide written informed consent for research and audit before data is

entered locally at BRSAS. In addition, this project was registered with University Hospitals Birmingham NHS Foundation Trust as a service improvement project (CARMS number 19297).

RESULTS

Baseline characteristics

There were 1453 records in the Dendrite SA registry entered between 01 March 2004 and 01 March 2021, of which 1042 were included, and of whom 548 were employed (figure 1). Occupation was either not stated or incomprehensible in 44 cases, so 504 were suitable for further analyses. Median age was 44 (IQR=33–52), 340/504 (68%) were women, 141/504 (28%) were current or ex-smokers, 338/504 (75%) were atopic and 184/504 (38%) had major non-asthma-related comorbidities. Median forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC)%=65% (IQR=52–77), and median pre-bronchodilator FEV_1%=73 (IQR=59–79). Demographic and disease-related characteristics of employed patients are summarised in table 1.

Occupation and inhalable exposures

There was agreement between experts in coding of jobs in 439/504 (87%) cases; a majority verdict using a third expert was found for the other 65 cases. The most frequently reported occupations (table 2) were: care assistants (7%), adult nurses (6%), office workers (5%) and teachers (5%). Using the OAsJEM 197/504 (39%) were deemed exposed to any inhalable asthmagen, 149/504 (30%) to HMW or LMW respiratory sensitiser, 192/504 (38%) to an airway irritant and 144/504 (29%) to an LMW sensitising- or irritant cleaning product or disinfectant.

ACQ7 score/asthma control

ACQ7 score was available for 372/504 participants (74%; mean=2.9, SD=1.2) and there was significantly more major non-asthma-related comorbidity (41% vs 30%; p=0.03) and greater frequency of exposure to respiratory sensitisers (32% vs 22%; p=0.03), compared with those where no ACQ7 given (table 1). The frequency distribution for ACQ7 score, where given, is shown in figure 2. Among patients with available ACQ7, 51/372 (14%) had adequate asthma control (determined by ACQ7 score 0–1.5) and thus 321/327 (86%) poor asthma control (ACQ7 score >1.5). Hypothesis testing revealed that BMI (kg/m^2) was higher in the poor control group (median=31 vs 27; p=0.01) with a larger proportion having BMI≥25 (79% vs 63%; p=0.01). Both median pre-bronchodilator FEV_1/FVC% and %predicted pre-bronchodilator FEV_1 were lower in the poor control group (69% vs 74%, p=0.005; 77% vs 96%, p<0.001, respectively). Data for all variables grouped by ACQ7 score are shown in table 3. There were no significant differences between ACQ7 score and exposure to any inhalable asthmagens, or when grouped by nature of exposure (sensitiser, irritant, disinfectant/cleaning product), on hypothesis testing.

Binary and multinomial regression analyses

With ACQ7 score as the dependent variable, either as a binary outcome (≤1.5 vs >1.5) or multinomial (tertiles) outcome, there were no significant associations with any inhaled asthmagen, before or after adjustment for major confounders. Univariate and multivariate regression analyses are shown in table 4.

DISCUSSION

This cross-sectional study found that after adjustment for major known confounders, JEM-determined workplace exposures to airborne asthmagens were not associated with poor asthma control in patients referred to a regional NHS severe and difficult-to-treat asthma service. Application of the OAsJEM indicated that patients were likely to be exposed at high-intensity or medium-intensity to airborne airway irritants or sensitisers in the workplace, in 29–39% of cases. The main strength of this study is the availability of a whole baseline data set for a large regional NHS SA service, although with missing data. Besides any unidentified errors in transcribing data that may have occurred, the potential for information bias from clinical variables remains low since data had been entered at the point of clinical assessment using objective measurements (eg, blood count, BMI), via medical records (eg, comorbid diagnoses) or using standardised tools (eg, ACQ7 score). We have tried to understand the effect of confounding by demographic factors (eg, deprivation, gender, age) through models built using multivariate logistic regression.

It is then necessary to consider the limitations of the study. The UK SA registry does not currently report data on patients' work and workplace exposures, nor on rates of diagnosed work-related disease.[19] The Birmingham clinical database, which feeds into the UK SA registry, does retain some data on employment (yes/no) and current occupation (open comment), though this is insufficient to determine whether patients are genuinely exposed at the time of clinical review and database entry (eg, long-term sickness absence), and it is assumed for this study that all are present at work and neither working from home nor absent. Moreover, there are no data on the presence of workplace exposure control measures that may be in place to mitigate any risk that is assumed by the JEM, so prevalence estimates do not take these into account. JEMs are used to overcome the recall bias associated with self-reporting of exposures for population-based studies, and in general, do not allow for individual variations in the work process and workers' tasks. Determining exposures using OAsJEM involves matching a patient's job with the most appropriate code in the occupational classification (here, ISCO-88), and then, a second step of expert attribution according to the specific context of an individual worker. However,

Table 1 Baseline characteristics of all employed patients, and comparison of variables between those with and without data for Asthma Control Questionnaire 7 (ACQ7) score

		All employed (n=504)	With data for ACQ7 (n=372; 74%)	Data missing for ACQ7 (n=132; 26%)	Hypothesis testing
Age	Median (IQR)	44 (33–52)	45 (32–53)	43 (34–51)	p=0.43
Female gender	Number (%)	340 (68)	251 (68)	89 (67)	p=0.99
IMD decile (ordinal; 1=most deprived, 10=least deprived)	Median (IQR)	5 (2–8)	6 (3–8)	5 (2–7)	p=0.11
BMI (missing=34)	Median (IQR)	30 (25–35)	30 (25–35)	29 (25–34)	p=0.53
Current or ex-smokers (missing=4)	Number (%)	141 (28)	106 (29)	35 (27)	p=0.75
Presence of atopy (missing=56)	Number (%)	338 (75)	280 (77)	58 (69)	p=0.14
Presence of non-asthma-related major comorbidities (missing=22)	Number (%)	184 (38)	146 (41)	38 (30)	**p=0.03**
Exacerbations requiring rescue oral corticosteroids in the preceding 12 months	Median (IQR)	5 (2–8)	5 (2–8)	4 (3–7)	p=0.87
Hospital admissions in the preceding 12 months	Median (IQR)	0 (0–2)	0 (0–2)	0 (0–2)	p=0.89
Maintenance oral corticosteroids (missing=22)	Number (%)	161 (33)	119 (32)	42 (37)	p=0.38
Pre-BD FEV_1	Median (IQR)	2.2 (1.6–2.9)	2.1 (1.6–2.7)	1.9 (1.4–2.6)	p=0.99
Pre-BD %predicted FEV_1	Median (IQR)	73 (52–92)	77 (56–92)	66 (49–83)	p=0.25
Pre-BD %predicted FVC	Median (IQR)	3.3 (2.7–4.1)	3.3 (2.7–4.0)	3.4 (2.6–4.1)	p=0.47
Pre-BD %predicted FVC	Median (IQR)	92 (78–104)	92 (78–102)	87 (73–103)	p=0.90
Pre-BD FEV_1/FVC%	Median (IQR)	65 (52–77)	70 (59–79)	67 (53–80)	p=0.33
AQLQ total score (ordinal 0=worse, 7=better)	Mean (SD)	4.0 (1.2)	4.0 (1.2)	3.9 (1.1)	p=0.49
Eosinophilia (>0.3×10^9/L) (missing=244)	Number (%)	153 (59)	122 (57)	31 (67)	p=0.19
Exposed to any inhalable asthmagen	Number (%)	197 (39)	153 (41)	44 (33)	p=0.12
Exposed to an HMW or LMW respiratory sensitiser	Number (%)	149 (30)	120 (32)	29 (22)	**p=0.03**
Exposed to an airway irritant	Number (%)	192 (38)	149 (40)	43 (33)	p=0.13
Any LMW sensitising- or irritant-cleaning product or disinfectant	Number (%)	144 (29)	111 (30)	33 (25)	p=0.29

Bold values indicate <0.05 is significant at 95% confidence level.
AQLQ, Asthma Quality of Life Questionnaire; BD, bronchodilator; BMI, body mass index; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; HMW, high molecular weight; IMD, index of multiple deprivation; LMW, low molecular weight.

as data had not been collected specifically for this study, given open comments were often brief (eg, teacher, nursery nurse, secretary) meaning no further interpretation was possible, or at least had to be assumed and thus may have led to an information bias. There were only a small number of included patients with normal asthma control (mean ACQ7 score=2.9, SD=1.2; proportion with ACQ7>1.5=86%), reducing the likelihood of observing small effect sizes. Moreover, although rates of missing data were on the whole low, the proportion of missing data for ACQ7 was relatively higher (26%) and can be attributed to failure on the part of healthcare professionals to carry out the assessment at the baseline visit, for some individuals.

It was not possible to adjust for the type or degree of treatment prescribed at baseline, due to the extent of missing treatment data (eg, presence and dose of inhaled corticosteroids missing in 35% of cases within the whole

Table 2 Most frequently reported occupations among 504 patients with severe asthma included in further analyses. Any occupation with frequency count ≥5 is displayed

Occupation	Frequency (%)	Examples, where specified
Care assistant	34 (7)	Residential home, nursing home, domiciliary, paediatric, primary care, hospital ward, critical care.
Adult nurse	26 (6)	Emergency department, medical ward, surgical ward, critical care, hospice.
Office worker	22 (5)	Charity, public relations company, local council, warehouse, community healthcare, telesales, retail companies.
Teacher	21 (5)	Primary, secondary.
Teaching assistant	19 (4)	Primary, secondary, special needs.
Retail assistant	19 (4)	Pharmacy, convenience shop, golf course shop, supermarket fish counter, clothes shop, department store.
Clerical administrator	14 (3)	Business, finance, sales, information technology, customer service, transport, healthcare.
Cleaner	10 (2)	Domestic, healthcare, school, office.
Barbers and hairdressers	9 (2)	
Paediatric nurse	7 (2)	Children's ward, neonatal.
Nursery nurse	7 (2)	
Bank clerk	7 (2)	
Receptionist	6 (1)	Medical, hospital, commercial, manufacturing.
Catering assistant	5 (1)	School meals, restaurant.
Social worker	5 (1)	Child protection, council housing, community mental health.

database). Most patients had been referred as difficult-to-treat cases from secondary care asthma services (86%), so it seems unlikely that patients would have been without inhaled corticosteroids at all. The direction of any relationship between variables with significant associations is unclear, due to the retrospective and cross-sectional

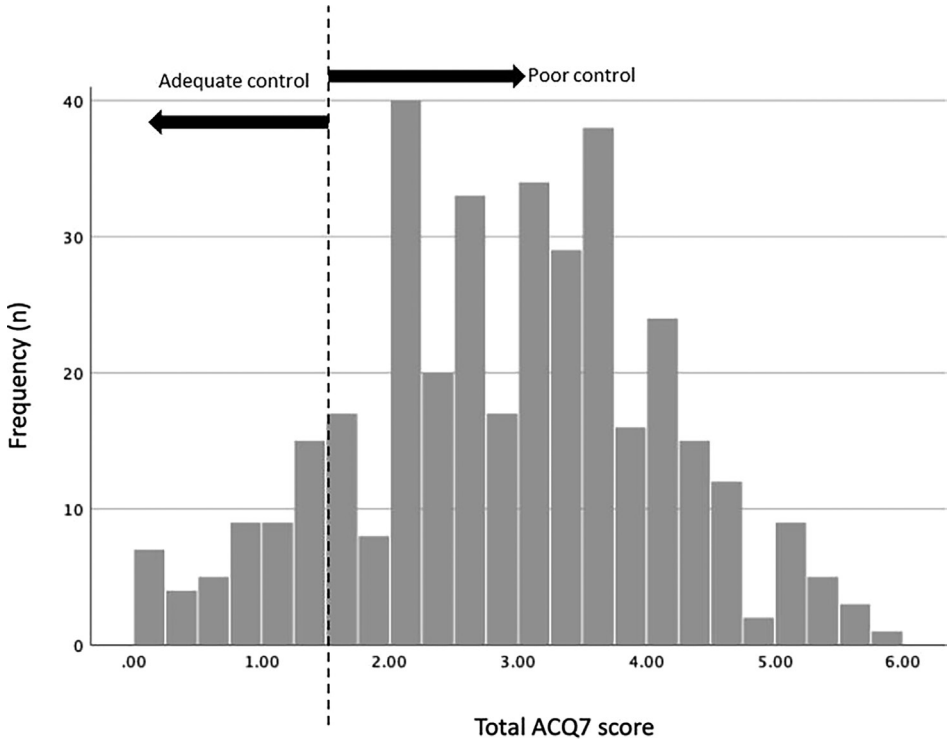

Figure 2 Histogram showing frequency distribution of total Asthma Control Questionnaire 7 (ACQ7) scores among all included patients. Adequate control=ACQ7 score ≤1.5; poor control=ACQ7 score >1.5.

Table 3 A comparison of baseline characteristics between patients with adequate asthma control (ACQ7≤1.5) and poor asthma control (ACQ7>1.5)

		Adequate control ACQ7≤1.5 (n=51; 14%)	Poor control ACQ7>1.5 (n=321; 86%)	Hypothesis testing
Age	Median (IQR)	45 (33–52)	45 (34–53)	p=0.90
Female gender	Number (%)	31 (62)	220 (69)	p=0.33
IMD decile (1=most deprived, 10=least deprived)	Median (IQR)	6 (5–8)	5 (3–8)	p=0.16
BMI (missing=34)	Median (IQR)	27 (24–32)	31 (26–35)	**p=0.01**
BMI<25 (missing=34)	Number (%)	19 (37)	67 (21)	**p=0.01**
Current and ex-smokers (missing=4)	Number (%)	15 (29)	91 (28)	p=0.87
Presence of atopy (missing=56)	Number (%)	37 (73)	243 (78)	p=0.43
Presence of non-asthma-related major comorbidities (missing=22)	Number (%)	18 (36)	128 (42)	p=0.44
Maintenance oral corticosteroids (missing=22)	Number (%)	16 (31)	103 (33)	p=0.87
Any inhalable asthmagen	Number (%)	21 (41)	132 (41)	p=0.99
Any sensitising agent	Number (%)	18 (35)	102 (32)	p=0.62
Any airway irritant	Number (%)	20 (39)	129 (40)	p=0.90
Any LMW sensitising- or irritant- cleaning product or disinfectant	Number (%)	15 (29)	96 (30)	p=0.94

Some missing data for ACQ7 score (n=132), so valid percentages given, where data are categorical. Lung function parameters are not included since ACQ7 score includes forced expiratory volume in 1 s and are therefore co-linear.
Bold values indicate <0.05 is significant at 95% confidence level.
ACQ7, Asthma Control Questionnaire 7; BMI, body mass index; IMD, index of multiple deprivation; LMW, low molecular weight.

design and cannot be assumed to be causative-based solely on this study. The given occupational data do not take into account the consequences of previous employment, which may have been difficult to navigate for a worker and necessitated job change. Finally, there may be a healthy worker effect[20] whereby more severely affected patients with work-related disease have left their employment by the time of assessment, reducing the overall work effect on asthma control within the study; this is an inevitable limitation of cross-sectional study design in working populations.

Published work suggests, at least indirectly, that a proportion of patients with SA may also have WRA. For instance, Vandenplas *et al*[21] established a multinational European cohort of consecutive patients with OA (n=997), all with sensitiser-induced OA confirmed using specific inhalation challenge testing. 16% of included patients met their definition of SA, which comprised the need for high-level treatment (ie, Global Initiative for Asthma (GINA) treatment step 4–5), plus ≥1 of (1) 'poor symptom control' defined by the use of short-acting beta agonists ≥1 per day, (2) ≥2 severe exacerbations in the previous year or (3) airflow obstruction. WEA is common and has a prevalence similar in magnitude to OA, occurring in a median of 22% of adults with asthma.[6] Data on health outcome are limited to a small number of cross-sectional studies but these show that WEA is associated with lower health-related quality of life (comprising mood, breathlessness, social disruption and health concern) than non-WRA, and greater self-rated disease severity, treatment use and work-related stress.[22 23]

This study indicates a significant proportion of patients with SA may be exposed to airway sensitisers and irritants, health, social care and education account for much (22%) of this work. Population studies and data from reporting schemes indicate that those in public-facing roles particularly, are exposed to a range of agents with both chlorine-based and quaternary ammonium-based cleaning agents and disinfectants featuring prominently; in addition, we have seen similar exposures in office workers with OA, traditionally considered to be low risk for WRA.[24 25] A recent study from the French NutriNet-Santé cohort, observed significant associations between occupational exposures to sensitisers, irritants, cleaning products and disinfectants and uncontrolled adult-onset asthma, when compared with both normal participants and those with controlled asthma.[26] It is perhaps then a surprise that a similar result was not observed in the current study, and differences may be explained at least in part, by the limitations of using a specialist clinical data set as outlined above. It would be unwise to dismiss outright the role of workplace exposures in SA, given their estimated prevalence and we advocate using both the SA disease registry and prospective longitudinal study of asthma outcome, that would variously take into account work-relatedness of symptoms, the latency of inhaled exposure, mitigating factors (eg, engineering controls, respiratory protective equipment) and job changes. Broadening the national

Table 4 Summary of univariate and multivariate binary and multinomial logistic regression analyses, with ACQ7 score as the independent variable, either adequate versus poor control (binary) or ACQ7 tertiles (multinomial) as the sample distribution

		Binary logistic regression		Multinomial logistic regression			
				Unadjusted OR		Adjusted OR	
		Unadjusted OR (95% CI); p value	Adjusted OR (95% CI); p value	Highest tertile vs ref	Middle tertile vs ref	Highest tertile vs ref	Middle tertile vs ref
Any inhalable asthmagen	Number (%)	1.00 (0.55 to 1.82); p=0.99	0.98 (0.52 to 1.82); p=0.94	0.99 (0.60 to 1.63); p=0.96	0.92 (0.55 to 1.52); p=0.74	1.03 (0.60 to 1.74): p=0.93	0.87 (0.51 to 1.48); p=0.60
Any sensitising agent	Number (%)	0.85 (0.46 to 1.59); p=0.62	0.79 (0.42 to 1.51); p=0.48	0.95 (0.56 to 1.61); p=0.86	0.75 (0.44 to 1.28); p=0.29	0.95 (0.55 to 1.65); p=0.86	0.70 (0.39 to 1.23); p=0.21
Any airway irritant	Number (%)	1.04 (0.57 to 1.91); p=0.90	0.99 (0.53 to 1.85); p=0.97	1.02 (0.62 to 1.69); p=0.94	0.95 (0.57 to 1.58); p=0.84	1.06 (0.62 to 1.80); p=0.83	0.89 (0.52 to 1.53); p=0.68
Cleaning agent/ disinfectant	Number (%)	1.02 (0.54 to 1.96); p=0.94	0.88 (0.44 to 1.78); p=0.73	0.99 (0.58 to 1.69); p=0.97	0.80 (0.46 to 1.39); p=0.47	0.92 (0.51 to 1.65): p=0.78	0.74 (0.40 to 1.36); p=0.33

Missing data for ACQ7 score in n=132. Adequate control (ACQ7≤1.5) was the reference group for the binary logistic regression analyses. ACQ7 tertiles were as follows: lowest=0–2.41; middle=2.42–3.50; highest=3.51–5.85; the lowest ACQ7 tertiles was the reference group in the multinomial regression analyses.
ACQ7, Asthma Control Questionnaire 7 .

registry data requirement at baseline and follow-up to include current job role and level of exposure, would give important insights into the contribution and impact of workplace exposures on SA.

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