Working while unwell: Workplace impairment in people with severe asthma

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Running title: Work impairment in severe asthma

Word count:

Abstract: 300

Main text: 3562, excluding tables and reference list.

Figure/table count: 7

Online supplement: Yes

Abstract

Background: Severe asthma affects quality of life; however, its impact on workplace productivity is poorly understood.

Objective: To compare workplace productivity – absenteeism and presenteeism – and impairment in daily activities in severe and non-severe asthma over time and identify characteristics associated with presenteeism in severe asthma.

Methods: The Severe Asthma Web-based Database (SAWD) is an ongoing observational registry from Australia, New Zealand and Singapore. At April 2017, 434 patients with severe asthma and 102 with non-severe asthma were enrolled (18 to 88 years; 59% female). Participants provided comprehensive clinical and questionnaire data at baseline and were followed-up every 6 months for 24 months. Absenteeism (percentage of time not at work), presenteeism (self-reported impairment at work) and impairment in daily activities outside work due to health problems in the last week were calculated.

Results: At baseline, 61.4% of participants with severe asthma and 66.2% with non-severe asthma under 65 years were employed. At younger ages (30-50 years), fewer severe asthma participants were employed (69% vs 100%). Presenteeism and impairment in daily activity were more frequently reported in severe asthma and in participants with poorer asthma control, poorer lung function and more past-year exacerbations ($p<0.01$). Over time, deteriorating asthma control was associated with increasing presenteeism. Although absenteeism was not different between severe and non-severe asthma, worse asthma control was associated with absenteeism ($p<0.001$). In participants with severe asthma, presenteeism was reported more frequently in those with poorer asthma control, poorer asthma-related quality of life and symptoms of depression or anxiety ($p<0.01$).

Conclusions and clinical relevance: Severe asthma was associated with impairment at work and outside the workplace. Improving asthma control and mental health may be important targets for optimising workplace productivity in severe asthma. Presenteeism and absenteeism may represent key metrics for assessing intervention efficacy in people with severe asthma of working age.

Keywords: Severe asthma; registry; workplace productivity; presenteeism; absenteeism; work disability.

Introduction

Severe asthma is a high impact disease that is often refractory to inhaled therapy. It affects up to 10% of patients with asthma yet accounts for most of the disease burden.[1] Recognised impacts of severe asthma include asthma exacerbations, poor health status and poor health-related quality of life,[2,3] which are likely to lead to impaired functioning at work and in other roles. Impairment at work – where illness impairs ability to work – may be associated with negative consequences over time, including extended sick leave, continued health impairment and greater healthcare utilisation, reduced work team cohesion, arrested work progression, reduced earnings, job insecurity and job loss.[4–7] To date there are scant data on the extent and determinants of workplace impairment in severe asthma. Quantifying workplace impairment can provide an understanding of the impact of severe asthma on the lives of patients and represents a crucial step for developing strategies to maximise workplace participation.

Most previous studies on workplace impairment in severe asthma report work absence yet fail to examine the potentially more widespread problem of presenteeism.[8,9] Presenteeism is defined as working at suboptimal capacity because of ill health. Compared to absenteeism, which is partial or complete absence from work due to illness, presenteeism is a relatively new indicator of workplace impairment.[10,11] Presenteeism is often underestimated yet is costly to the economy[12–14] and is associated with an increased risk of absenteeism in the future.[4]

The aim of this study was to quantify the impact of severe asthma on workplace productivity, by comparing absenteeism, presenteeism and impairment in daily activities over time in people with severe and non-severe asthma. The study also examined characteristics associated with presenteeism among people with severe asthma.

Methods

Study design

The Severe Asthma Web-based Database (SAWD) is an observational registry of patients enrolled through centres of the Australasian Severe Asthma Network (ASAN), which includes hospital-based severe asthma and respiratory clinics and private respiratory practices. SAWD comprises a cross-sectional observational study, a prospective cohort study and databank. Participating centres submit anonymised data to the web-based database where data is stored securely using REDCap electronic data capture tools[15] hosted at the Hunter Medical Research Institute, Australia. REDCap forms were modified from those initially developed by the Alfred Difficult Asthma Service, Melbourne.[16]

SAWD is conducted in accordance with the International Conference on Harmonisation Good Clinical Practice standards and the Declaration of Helsinki, and under the governance framework of the Thoracic Society of Australia and New Zealand. Ethical approval was obtained from relevant national, regional or local human research ethics committees or institutional review boards, according to country-specific requirements (Australia: HNEHREC 12/11/21/4.04, HREC/13/RAH/379, Alfred Hospital EC 391/13, HREC [Tasmania] Network H0014915 and SCGH HREC 2015-133; New Zealand: HDEC 12/CEN/69; and Singapore: SingHealth CIRB 2016/2550). All patients provided informed written consent prior to participating.

The detailed SAWD protocol is available on the Centre of Excellence in Severe Asthma website (http://www.severeasthma.org.au/tools-resources/toolkits/).

Participants

Adult patients with severe refractory asthma and a comparison group with non-severe controlled asthma were enrolled in the registry by staff at 26 centres in Australia, New Zealand and Singapore. Enrolment commenced in August 2013. The current study reports on patients enrolled until April 2017.

To be included in the registry, all patients required a confirmed asthma diagnosis with evidence of variable airflow limitation documented at baseline or during the previous 10 years. Patients were excluded if they were pregnant; had cognitive impairment that prevented completion of data collection forms; were highly dependent on medical care; had significant life limiting co-morbidity; had primary diagnosis of lung disease other than asthma; had current lung cancer or other blood, lymphatic or solid organ malignancy; were unable to attend study visits; and had current exacerbation at the baseline visit.

Patients were classified as having severe asthma if they met the European Respiratory Society (ERS)/American Thoracic Society (ATS) taskforce definition, where control is not achieved despite high level recommended treatment (refractory asthma and corticosteroid-resistant asthma) or where control can be maintained only with the highest level of recommended treatment.[2] Inclusion criteria for the severe asthma group were optimised management skills (inhaler technique, education, adherence, written asthma action plan); appropriate assessment and management of triggers and relevant comorbidity; use of maximal inhaled corticosteroid (ICS) therapy according to the Global Initiative for Asthma (GINA)[17] guidelines (> 1000µg beclomethasone equivalent) with a second controller (long acting beta agonist [LABA], long acting anti-muscarinic antagonist [LAMA], oral

corticosteroid (OCS) ≥ 50% of the previous year, montelukast or theophylline); and meeting at least one definition of uncontrolled asthma[2] (Online Supplement Table S1).

Inclusion criteria for the non-severe asthma group were use of maintenance inhaled controller therapy; asthma control defined as either Asthma Control Questionnaire 6-item (ACQ6)[18] ≤ 1.5 or Asthma Control Test (ACT)[19] ≥ 20; and stable disease with no respiratory infection, asthma exacerbation or change in maintenance therapy in the four weeks preceding screening.

Data collection and assessments

Clinical and patient-reported data were collected via face-to-face visits, telephone and mail at baseline and at 6-month intervals for 2 years. At the baseline assessment, patients were assessed for study eligibility and classified as having severe or non-severe asthma. Data collected in SAWD included demographic characteristics; asthma, allergy and general medical history; medication use and adherence; asthma control; severe exacerbations; spirometry; biomarkers; and patient-reported measures related to health status and asthma-related quality of life. Further details are contained in the journal Online Supplement and SAWD protocol (http://www.severeasthma.org.au/tools-resources/toolkits/).

Current employment and productivity were assessed via the Work Productivity and Activity Impairment Questionnaire: General Health V2.0 (WPAI:GH).[20] Absenteeism was calculated as a percentage of the number of hours of work missed due to health reasons divided by usual work hours. Presenteeism and impairment in daily activities were calculated using Likert scale responses regarding self-rated impairment due to health reasons at work and in

activities outside work, multiplied by 10 to scale between 0 and 100 (higher scores indicate greater impairment).

Statistical analysis

We computed descriptive characteristics of participants at baseline, comparing severe with non-severe asthma using Chi-square, Fisher's exact test, t-test and Wilcoxon rank-sum as appropriate. We examined whether asthma severity indicators were associated with being employed (in participants of working age; <65 years), absenteeism and presenteeism (in participants currently employed) and impairment in daily activity (in all participants) across repeated assessments. We used logistic or Gaussian generalised estimating equations (GEE), controlling for age, sex and assessment timepoint, modelling impairment as (1) a binary outcome (no reported problems versus some problems) and (2) a continuous outcome when values were greater than 0. We also examined whether severe exacerbations in the year before baseline were associated with baseline productivity indicators using logistic and linear regression. We tested whether the association between impairment and asthma severity differed over time by adding an interaction term between assessment timepoint and severity indicators. Finally, we examined the association between asthma-related characteristics and presenteeism at baseline in the severe asthma group via binary logistic or linear regression, controlling for age and gender. Analyses were completed in Stata IC/15 (StataCorp LLC, USA) and the "gee" package[21] in R statistical language (R Foundation, Austria).[22] Statistical significance was considered at $p < 0.05$.

Results

Baseline characteristics

SAWD comprised 536 participants, 434 (81%) with severe asthma and 102 (19%) with non-severe asthma. Follow-up data were available in SAWD for 334 participants at 6 months, 254 at 12 months, 161 at 18 months, and 109 at 24 months (70.8%, 66.5%, 55.5% and 47.8% of the sample due for assessment at April 2017, respectively). There were four known deaths and 12 study withdrawals. Participants who had follow-up data recorded, compared with those who did not, were more likely to have severe asthma and were slightly older at baseline, but did not significantly differ in other key characteristics including workplace characteristics and asthma control (Online Supplement Table S2).

At baseline, the mean age of participants was 55.0 years (SD = 15.3) and 59% were female. Participants with severe and non-severe asthma were similar in age, gender, race, and atopic and smoking status, although those with severe asthma had poorer health status according to several indicators (Table 1). As expected, participants with severe asthma had poorer lung function, poorer asthma control, more past-year exacerbations and were prescribed a higher dose of ICS than participants with non-severe asthma, although they reported a similar asthma duration (mean±SD duration for overall sample 31.0±19.1 years). Participants with severe asthma were highly symptomatic, with median ACQ6 score of 2.0 (IQR 1.2-2.8). There was little change in asthma control over time (Figure 1).

Participants with severe asthma were using a median of four maintenance respiratory medications (IQR 3-5), compared with two medications in the non-severe group (IQR 2-3, $p < 0.001$). All participants were using ICS at baseline. Use of ICS/LABA combination inhalers was common in the overall sample (91.8%) and more common in participants with

severe asthma (93.3% versus 85.3% in non-severe asthma, $p = 0.014$). In the severe asthma group, 24.4% were using maintenance oral corticosteroids and 19.1% were receiving omalizumab, whereas no participants with non-severe asthma used these medications.

Workplace productivity at baseline

Among participants of working age (<65 years; $N = 355$), 221 (62.3%) were employed at baseline, with little difference in the overall employment rate between severe and non-severe asthma (61.4% vs 66.2%, $p = 0.571$, Figure 2A). Discrepancies in employment rates between severe and non-severe asthma were apparent at younger ages (Figure 3). All participants with non-severe asthma between 30 and 50 years were employed ($N = 19$), whereas only 69% with severe asthma were employed (employed $N = 70$; not employed $N = 31$).

In the total sample, 243 participants (48.5%) were employed at baseline; 24.9% of workers reported some absenteeism and a majority of workers reported presenteeism in the past week (66.7%). At baseline, participants with severe asthma reported much higher presenteeism ($p < 0.001$) and activity impairment ($p = 0.002$) than those with non-severe asthma, but no significant difference in absenteeism (Figure 2A and 2B). In the severe asthma group, the rate of presenteeism was high, regardless of whether the participant had comorbid nasal polyps, rhinitis or allergic sensitisation (all $p > 0.05$, Figure 2C).

At baseline, presenteeism and activity impairment were strongly correlated ($\rho = 0.70$, $p < 0.001$), whereas absenteeism was less strongly correlated with presenteeism ($\rho = 0.39$, $p < 0.001$) and activity impairment ($\rho = 0.32$, $p < 0.001$). Absenteeism and presenteeism did not differ across sites (for sites with > 20 participants and after controlling for proportion of

severe participants). However, employment rates significantly differed across sites, ranging from 34.6% to 78.8% (X^2 (9) = 28.4, p = 0.001).

Asthma severity, workplace productivity and activity limitations

Across all assessments, participants with severe asthma were 3.2 times more likely to report presenteeism ($p < 0.001$) and 2.3 times more likely to report impairment in daily activity ($p < 0.001$) compared to participants with non-severe asthma, adjusting for age, gender and assessment timepoint (Figure 4A; Online Supplement Table S3). Compared with non-severe asthma, participants with severe asthma who reported productivity impairment did not have a greater degree of presenteeism, although they had a greater degree of activity impairment. Participants with severe asthma were not more likely to report absenteeism.

Poorer asthma control according to the ACQ6 was associated with greater likelihood of reporting absenteeism, presenteeism and impairment in daily activity, as well as a greater degree of impairment when the impairment was reported (Figure 4C; Table S3). Excluding participants with non-severe asthma from this analysis did not change the observed effects. Higher pre-bronchodilator FEV_1% was also associated with lower likelihood of presenteeism and activity impairment and higher likelihood of being employed (Figure 4B; Table S3).

More exacerbations (either OCS courses, hospitalisations, or emergency department visits) in the year before baseline were associated with lower likelihood of being employed and greater likelihood of presenteeism and impairment in daily activity, as well as a greater degree of activity impairment, at baseline (Figure 4D; Table S3). Use of maintenance oral corticosteroids was not associated with any of the workplace productivity indicators or activity impairment ($p > 0.05$).

Change in workplace productivity over time

The proportion of participants employed remained stable over time (not shown) as did the level of presenteeism reported, particularly among participants with severe asthma (Figure 2D). Overall, there was little evidence that the association between asthma severity and workplace productivity or activity impairment differed over the assessments (interaction $p > 0.05$). However, there was a significant interaction between assessment timepoint and ACQ6 in predicting presenteeism (interaction $p = 0.011$). Figure 5 shows that participants with the highest scores on ACQ6 reported increasing levels of presenteeism at later assessments, suggesting that patients with the worst asthma control and highest symptom burden were increasingly affected at work over time.

Predictors of presenteeism in people with severe asthma at baseline

In people with severe asthma at baseline, among a range of possible predictors, poorer asthma control scores, lower FEV_1%, more past-year exacerbations, poorer asthma quality of life, and symptoms of depression or anxiety were significantly associated with increased odds of reporting presenteeism, after controlling for age and gender (Figure 6; Table S4). The association between anxiety or depression symptoms and presenteeism remained statistically significant after adjusting for asthma control (anxiety symptoms OR = 1.11, 95% CI 1.01-0.22, $p = 0.024$; depression symptoms OR = 1.16, 95% CI 1.01-1.33, $p = 0.031$). Poorer asthma control and asthma quality of life, and, to a lesser extent, lower BMI were associated with a greater degree of presenteeism (Table S4). Medication use and immunological indicators (atopy, IgE, blood eosinophils) were not significantly associated with presenteeism (Figure 6; Table S4).

Discussion

Patients with severe asthma reported presenteeism and impairment in daily activity, but not absenteeism, more often than patients with non-severe asthma. Poorer asthma control was associated with a greater degree of absenteeism, presenteeism and impairment in daily activity, as well as worsening presenteeism over time. For each additional exacerbation per year, there was a 25% increase in reporting presenteeism. In people with severe asthma, presenteeism was associated with poorer asthma control, poorer asthma-related quality of life, and symptoms of depression or anxiety. These findings emphasise the importance of optimising asthma control, health status and mental health to promote participation of individuals with severe asthma in the workforce.

A key finding in this study was the high prevalence of presenteeism in asthma, which was significantly higher in severe asthma. The difference in presenteeism between severe and non-severe asthma was more prominent than impairment in non-work roles. Presenteeism, or "pushing through" at work to keep up with others, has been identified as a problem by severe asthma interviewees.[3] The severe asthma registry from China reported similar rates of employment and higher levels of presenteeism in patients with uncontrolled compared with controlled asthma (85.2% vs. 47.5% presenteeism, respectively).[23] Comparable findings have been observed in severe asthma clinics,[24] outpatient clinics[25] and from population-based representative random samples, although these studies typically include few participants on high-dose medication.[14,26–29] Studies assessing asthma-specific impairment, rather than general health impairment, also show that those with severe or uncontrolled asthma show greater impairment than controlled asthma.[30,31] However, using an asthma-specific version of the workplace productivity questionnaire may underestimate the true effect of severe asthma

on workplace productivity, given physical and mental health comorbidity is high in asthma and often contributes to symptoms.

Previous studies from severe asthma registries have generally only reported on unemployment indicators of workplace productivity, where 15-26% of patients with severe asthma are not working due to asthma.[8,9,32,33] Our study suggests that younger age groups may be most adversely affected. It also highlights exacerbations and lung function as predictors of current employment status. Unlike other registries, although absenteeism in the previous week was relatively frequently reported in SAWD (25% of overall sample), there was little difference between severe and non-severe asthma. In part, this may be because participants who were exacerbating at baseline were excluded from SAWD until they were stable and the recruitment of non-severe patients from hospital-based respiratory clinics who may have had more disease-related impairment. However, we did observe that a one-point increase in ACQ6 almost doubled the chance of reporting absenteeism. Previous studies comparing absenteeism in severe or uncontrolled asthma with controlled asthma over periods longer than a week report even higher prevalence of absenteeism (36-43%) in severe patients than our study.[34–38] Cost analyses show that differences in indirect costs to the economy due to lost workdays between uncontrolled and controlled asthma are striking (€466.86 versus €44.60/month, based on the ACT).[25] Taken together, substantial levels of absenteeism and work deficits show that there is an urgent need to achieve asthma control and reduce exacerbations in severe asthma to improve workplace participation.

Another important finding from this study is that productivity impairments changed little over time and differences between severe and non-severe asthma were maintained. There was also evidence that patients with the worst asthma control have greater presenteeism over time. Other longitudinal studies in severe asthma have similarly observed stable or worsening

workplace impairment over time in severe asthma.[39–41] These findings demonstrate the increased burden of severe asthma, and that effects of severe asthma on workplace productivity are enduring.

Determinants of presenteeism and other indicators of workplace impairment, beyond asthma control, have seldom been examined, indicating this as an area for further investigation. We identified poorer asthma control, poorer asthma-related quality of life, and more depression and anxiety symptoms as characteristics associated with presenteeism in severe asthma. The findings for depression and anxiety are novel, yet are not unexpected, given studies in non-asthma populations.[42,43] Effects of depression and anxiety on productivity may be even more profound than asthma control,[44] highlighting the importance of improving mental health in severe asthma. We identified few other predictors of presenteeism among a range of demographic, asthma and health status characteristics. Concordant with the current study, previous studies indicate that atopy and eosinophil levels are not associated with absenteeism.[6,45] While patients on multiple asthma medications have greater work and activity impairment,[27,46] effective new treatments, including biological agents, have been shown to reduce workplace impairment.[38,41,47]

We identified several limitations of this study. As SAWD is an observational registry, data are subject to selection bias, other unknown bias and confounding, and effects over time are not controlled. However, the strength of registry data is the generalisability of the findings due to the heterogeneity of the population. Registry data is an important complement to randomised controlled trial data, providing practice-based evidence. This study also used a convenience rather than random sample, so the representativeness of this sample of severe and non-severe asthma in general is not clear. Nevertheless, the sample characteristics are consistent with other registry samples although prevalence of atopy is higher in SAWD.[8,9,48]

There were limitations in the measurement of workplace productivity. This study examined self-reported impairment over seven days, which, although positive in terms of the reliability of the estimate, may underestimate longer-term effects. Extended follow-up, including real-time sampling of workplace productivity, and verification with objective indicators of workplace performance would be a novel improvement to assessing workplace productivity in severe asthma. Data regarding the effects of asthma on probability of early retirement or employment choices would also be informative. SAWD did not collect information on type of employment, socioeconomic status, education, retirement age or whether participants access disability pensions, which further data collection could address. Finally, some data were incomplete, patients were lost to follow-up and follow-up assessments were yet to be completed at the time data were extracted from SAWD. However, baseline differences between participants who did and did not contribute follow-up data were minimal.

Workplace productivity loss is common in people with severe asthma, which may have significant consequences for their physical, financial, social and emotional wellbeing. Work impairment in severe asthma is associated with greater healthcare utilisation and more exacerbations over time.[6,30] Beyond presenteeism and absenteeism, people with severe asthma work less, switch jobs, are prevented from entering some professions, take disability leave and retire early, all of which may pose significant risks to their financial stability.[3,7–9,30,33,49] They report lower earnings compared with controlled asthma.[28,29,35,37] People with severe asthma worry about their work and non-work activity limitations and their finances, reporting fear that health costs will be unmanageable due to restrictions on their ability to work.[3] They report workplace discrimination and stigma due to asthma[7] and experience negative emotions of giving up work.[50] An adverse cycle may ensue whereby workplace

impairment due to asthma symptoms and exacerbation generates stress that leads to further impairment, even when asthma symptoms resolve.

People with severe compared with non-severe asthma have a high symptom and disease burden, which significantly contributes to impairment at work and during other activities. We show that people with severe asthma, particularly those with poorer asthma control, are more likely to experience impairment at work. Patients in this registry, and others, are comprehensively monitored and optimally treated, however symptom control remained suboptimal. There is an urgent need for improvement in asthma control to safeguard against losses to financial and psychological wellbeing from work impairment. Although expensive, novel asthma therapies that improve asthma control and quality of life may have benefits to an individual's productivity and the broader economy. Concentrating only on absenteeism as a measure of workplace impairment may miss the important issue of presenteeism: working while unwell at suboptimal capacity. Absenteeism and presenteeism may be key metrics for assessing intervention efficacy among people with severe asthma of working age.

Conflict of interest statement

Sarah Hiles' salary is supported by a grant from GlaxoSmithKline. **Vanessa M McDonald** has received speaker fees for unrelated work, grants for organising education unrelated work, and research funds for unrelated work from AstraZeneca, Menarini and GlaxoSmithKline. **Jeffrey Bowden** reports personal fees from AstraZeneca and GlaxoSmithKline during the conduct of the study. **Mark Hew** has undertaken contracted research for AstraZeneca, Sanofi, Novartis and GlaxoSmithKline; delivered education talks for GlaxoSmithKline, AstraZeneca and Novartis; participated on advisory boards/consultancies for AstraZeneca, GlaxoSmithKline and Seqirus; for all of which his employer (Alfred Health) has been reimbursed. **Christine Jenkins** has received payments for speaking at symposia, chairing sessions and attending advisory board meetings of several major pharmaceutical companies that manufacture medications for asthma. **Naghmeh Radhakrishna** has received speaker fees from Mundipharma, Boehringer Ingelheim and AstraZeneca. **Helen Reddel** reports grants, personal fees and non-financial support from AstraZeneca; grants, personal fees and non-financial support from GlaxoSmithKline; personal fees from Merck; personal fees from Novartis; personal fees from Teva; personal fees from Mundipharma; personal fees from Boehringer Ingelheim outside the submitted work. **Michael Sutherland** reports personal fees from AstraZeneca outside the submitted work. **Peter G Gibson** has received research grants and speaker fees from AstraZeneca, GlaxoSmithKline and Novartis. All other co-authors declare no conflict of interest.

Acknowledgments

This study was funded through grants from AstraZeneca, GlaxoSmithKline, Novartis, Boehringer Ingelheim and Roche. We thank the Thoracic Society of Australia and New Zealand for providing governance and the Woolcock Institute of Medical Research and the Hunter Medical Research Institute. We thank the study participants and members of the Australasian Severe Asthma Network, including SAWD site investigators, clinical research staff, staff involved in data entry staff and personnel involved in statistical and information technology support throughout the project.

Figure captions

Figure 1. Asthma Control Questionnaire (ACQ6; higher scores indicate less control) and Asthma Control Test (ACT; lower scores indicate less control) across assessments for participants with severe and non-severe asthma.

Figure 2. Workplace productivity in participants with severe and non-severe asthma. (A) Proportion of participants who reported being employed, absenteeism, presenteeism and impairment in daily activity at baseline; (B) Median levels of absenteeism, presenteeism and impairment in daily activity at baseline; (C) Proportion of participants with severe asthma reporting presenteeism according to comorbidity of nasal polyps, rhinitis or allergic sensitisation at baseline; (D) Median levels of presenteeism across study assessments. ** $p < 0.01$; *** $p < 0.001$.

Figure 3. Percentage of participants employed across age groups.

Figure 4. Associations between asthma severity indicators and being employed or reporting impairments in productivity (versus no reported impairment). Analyses were generalised estimating equations with exchangeable correlation structure, controlling for sex, age and assessment timepoint and clustered by assessment timepoint. Data from all five assessments were used except for the exacerbations analyses where only baseline data were used. Confidence intervals were calculated from robust standard errors. Abbreviations: ACQ6: Asthma Control Questionnaire 6-item; CI: confidence interval; FEV_1%: forced expiratory volume in 1 second % predicted (10 unit change); OCS: oral corticosteroid; OR: odds ratio.

Figure 5. Interaction between Asthma Control Questionnaire (ACQ6) and assessment visit predicting workplace presenteeism, predicted from generalised linear model analysis. Participants with the highest values of ACQ6 (poorest asthma control) reported increasing levels of presenteeism across the five assessments (ACQ6*assessment interaction $p = 0.011$).

Figure 6. Associations between asthma severity characteristics, health status characteristics and immunological indicators at baseline. Abbreviations: CI: confidence interval; FEV_1%: forced expiratory volume in 1 second percent predicted (10 unit change); HADS: Hospital Anxiety and Depression Scale: N: number; OR: odds ratio.

Table 1. Baseline demographic, clinical and quality of life characteristics according to severity group.

	Severe asthma N = 434		Non-severe asthma N = 102		*p*
Demographic characteristics					
Age (years), mean (SD)	54.8	(14.9)	56.0	(16.9)	.506
Gender, N (%)					
Female	260	(59.9)	56	(54.9)	
Male	174	(40.1)	46	(45.1)	.372
Race, N (%)					
White	290	(85.3)	76	(79.2)	
Asian	32	(9.4)	18	(18.8)	
Pacific islander	6	(1.8)	1	(1.0)	
Other	12	(3.5)	1	(1.0)	.061
Smoking status, N (%)					
Never smoked	267	(62.2)	66	(66.0)	
Ex-smoker	149	(34.7)	34	(34.0)	
Current smoker	13	(3.0)	0	(0)	.223
Pack years, median (IQR)	10.5	(2.4, 26.8)	5.9	(1.0, 13.8)	.018
Number of comorbid conditions, median (IQR)	3.0	(2.0, 4.0)	2.0	(1.0, 3.0)	<.001
Asthma characteristics					
Asthma duration (years), mean (SD)	30.7	(19.0)	32.4	(19.4)	.419
ACQ6, median (IQR)	2.0	(1.2, 2.8)	0.7	(0.3, 1.0)	<.001

ACQ6 ≥ 2 (N, %)	229	(54.0)	0	(0)	<.001
ACT total score, median (IQR)	15.0	(11.0, 19.0)	21.0	(19.0, 23.0)	<.001
Pre-bronchodilator					
FEV_1 % predicted, mean (SD)	66.9	(21.2)	79.7	(19.4)	<.001
FVC % predicted, mean (SD)	81.4	(20.3)	88.7	(15.0)	<.001
FEV1/FVC % predicted, mean (SD)	0.8	(0.2)	0.9	(0.1)	<.001
Post-bronchodilator					
FEV_1 % predicted, mean (SD)	73.1	(21.9)	83.5	(19.3)	<.001
FVC % predicted, mean (SD)	85.6	(18.3)	90.4	(15.6)	.015
FEV_1/FVC % predicted, mean (SD)	0.8	(0.2)	0.9	(0.1)	<.001
ICS daily dose, µg beclomethasone equivalent units, median (IQR)	2000.0	(1600.0, 2000.0)	720.0	(400.0, 800.0)	<.001
Number of respiratory medications, median (IQR)	4.0	(3.0, 5.0)	2.0	(2.0, 3.0)	<.001
Severe exacerbations in the past year					
Number of OCS initiations, median (IQR)	2.0	(0.0, 4.0)	0.0	(0.0, 1.0)	<.001
Ever hospitalised, N (%)	96	(22.1)	2	(2.0)	<.001
Ever visited emergency department, N (%)	104	(24.0)	4	(3.9)	<.001
Atopy, N (%)	214	(79.6)	67	(81.7)	.753
IgE ≥ 30 kU/L, N (%)	278	(89.4)	19	(76.0)	.055
Blood eosinophils (10^9/L), median (IQR)	0.2	(0.1, 0.4)	0.3	(0.2, 0.4)	.576
Quality of life and mental health					

characteristics					
AQLQ, median (IQR)					
Activity	5.1	(3.9, 5.9)	6.5	(5.9, 6.7)	<.001
Symptoms	4.8	(3.6, 5.8)	6.1	(5.7, 6.6)	<.001
Emotions	5.0	(3.4, 6.2)	6.4	(5.8, 6.8)	<.001
Environment	5.2	(3.8, 6.2)	6.2	(5.5, 6.5)	<.001
Total	5.0	(3.8, 5.8)	6.2	(5.7, 6.6)	<.001
HADS anxiety score, median (IQR)	6.0	(3.0, 10.0)	5.0	(2.0, 8.0)	.033
HADS depression score, median (IQR)	4.0	(2.0, 7.0)	2.0	(1.0, 4.0)	<.001

1 ACQ6: Asthma Control Questionnaire 6-item; ACT: Asthma Control Test; AQLQ: Asthma
2 Quality of Life Questionnaire; BMI: body mass index; FVC: forced vital capacity; FEV_1:
3 forced expiratory volume in 1 second; GINA: Global Initiative for Asthma; HADS: Hospital
4 Anxiety and Depression Scale; ICS: inhaled corticosteroids; OCS: oral corticosteroids.
5

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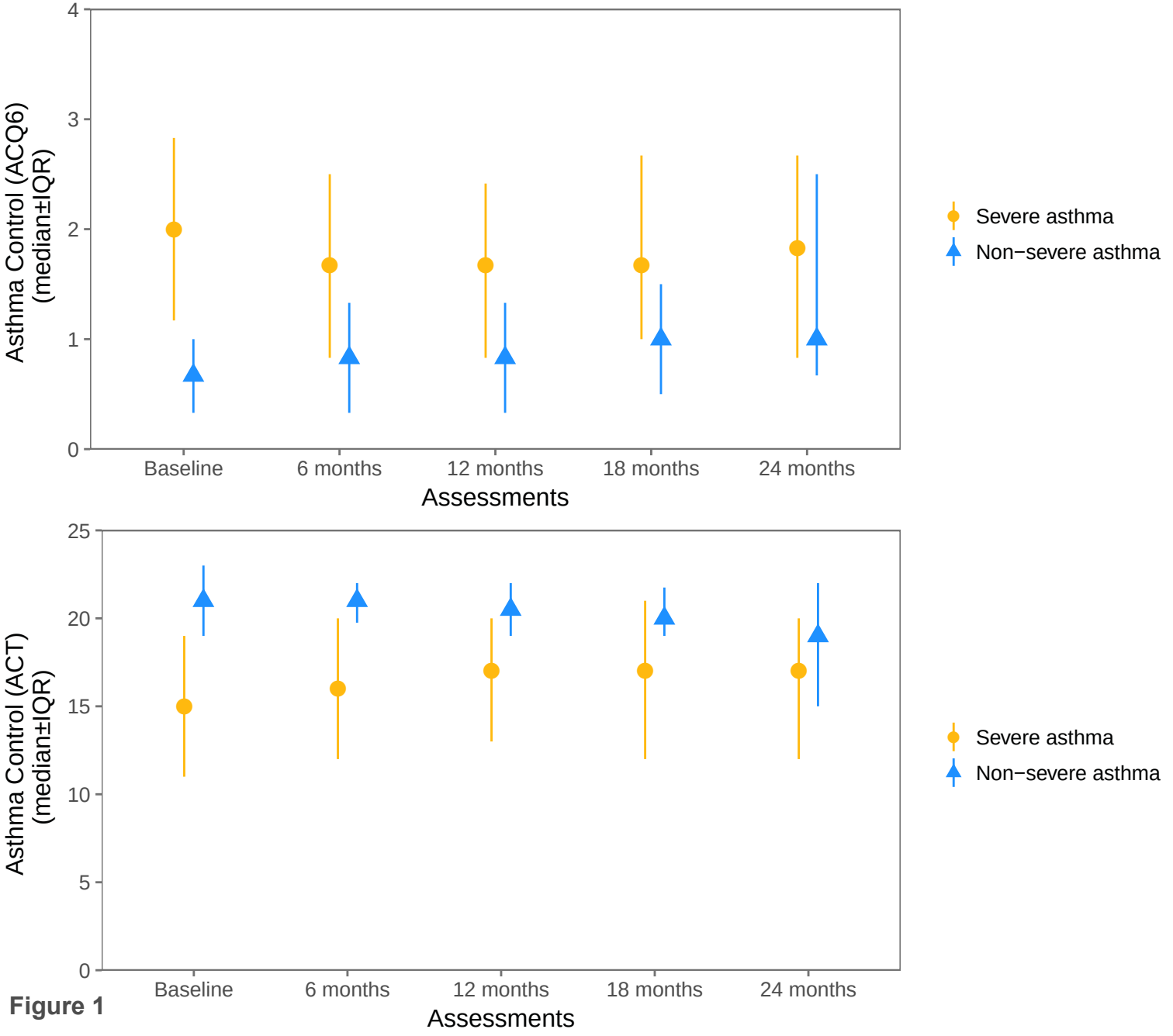
Asthma Control (ACQ6)
(median±IQR)
4
3
2
1
0
Baseline
6 months
12 months
18 months
24 months
Assessments
Severe asthma
Non−severe asthma
Asthma Control (ACT)
(median±IQR)
25
20
15
10
5
0
Baseline
6 months
12 months
18 months
24 months
Assessments
Severe asthma
Non−severe asthma

Figure 1

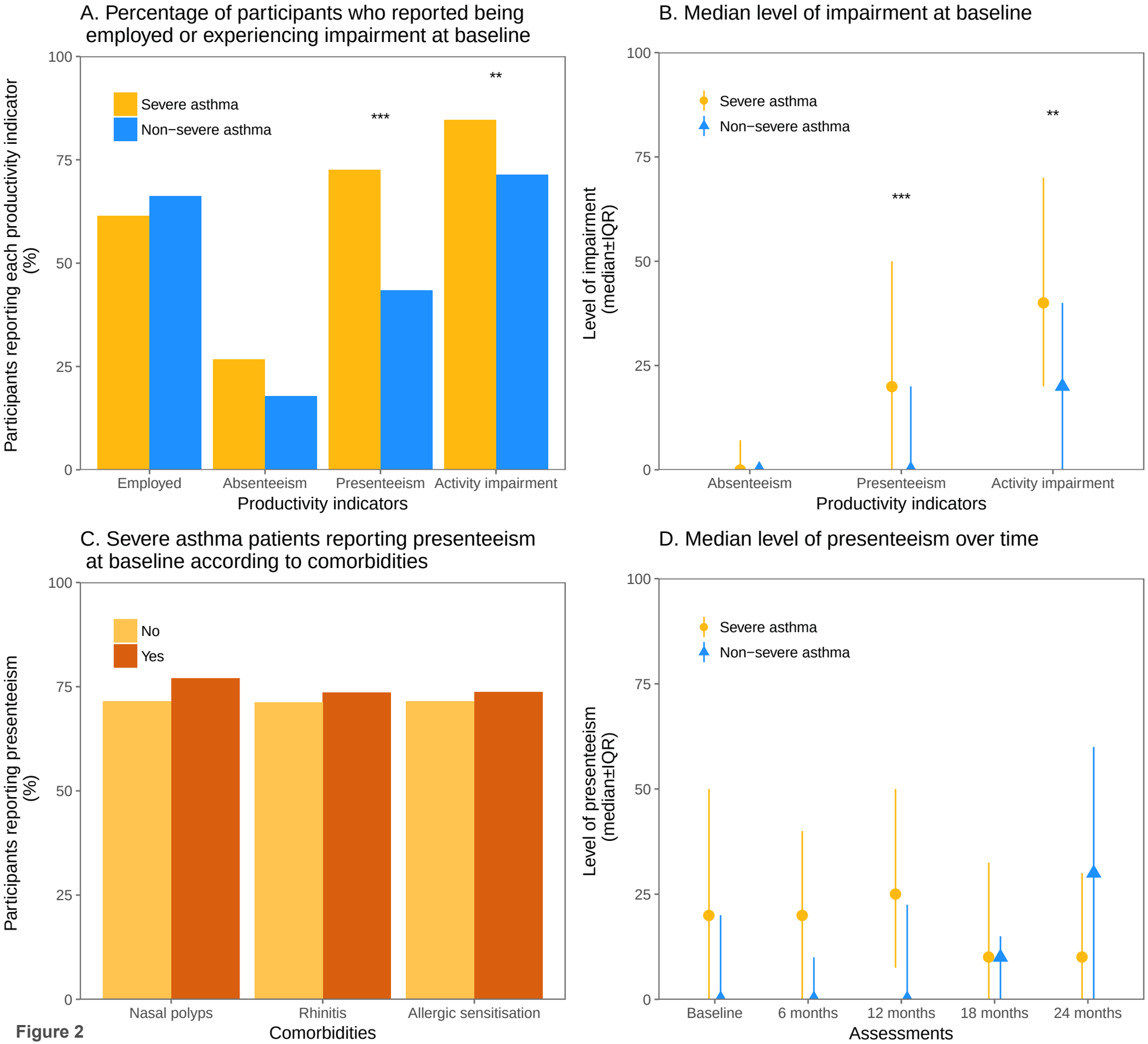
A. Percentage of participants who reported being employed or experiencing impairment at baseline
Participants reporting each productivity indicator (%)
Severe asthma
Non−severe asthma
***
**
Employed
Absenteeism
Presenteeism
Activity impairment
Productivity indicators
B. Median level of impairment at baseline
Level of impairment (median±IQR)
Severe asthma
Non−severe asthma
***
**
Absenteeism
Presenteeism
Activity impairment
Productivity indicators
C. Severe asthma patients reporting presenteeism at baseline according to comorbidities
Participants reporting presenteeism (%)
No
Yes
Nasal polyps
Rhinitis
Allergic sensitisation
Comorbidities
D. Median level of presenteeism over time
Level of presenteeism (median±IQR)
Severe asthma
Non−severe asthma
Baseline
6 months
12 months
18 months
24 months
Assessments

Figure 2

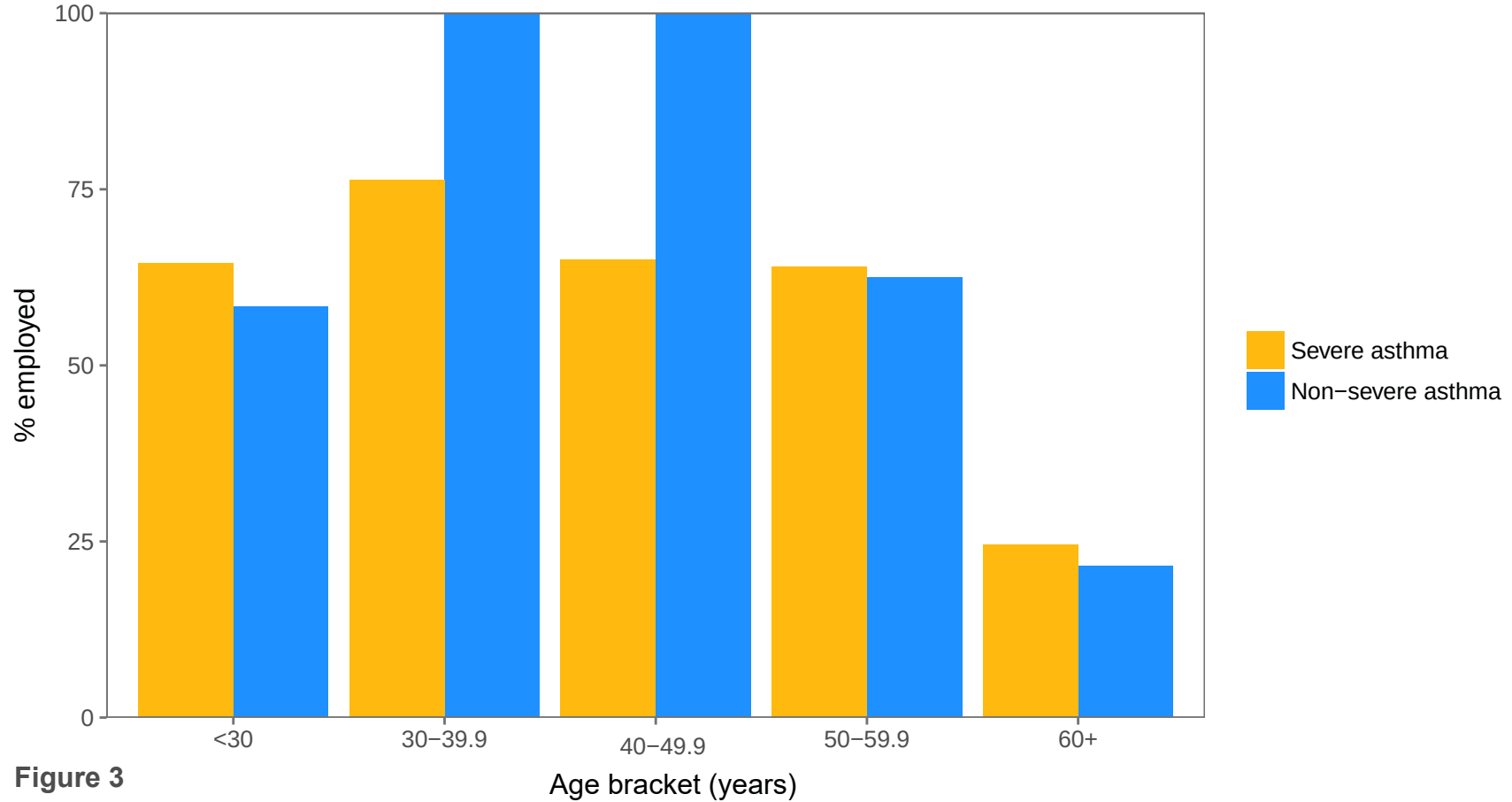
100
75
50
25
0
% employed
<30
30−39.9
40−49.9
50−59.9
60+
Age bracket (years)
Severe asthma
Non−severe asthma

Figure 3

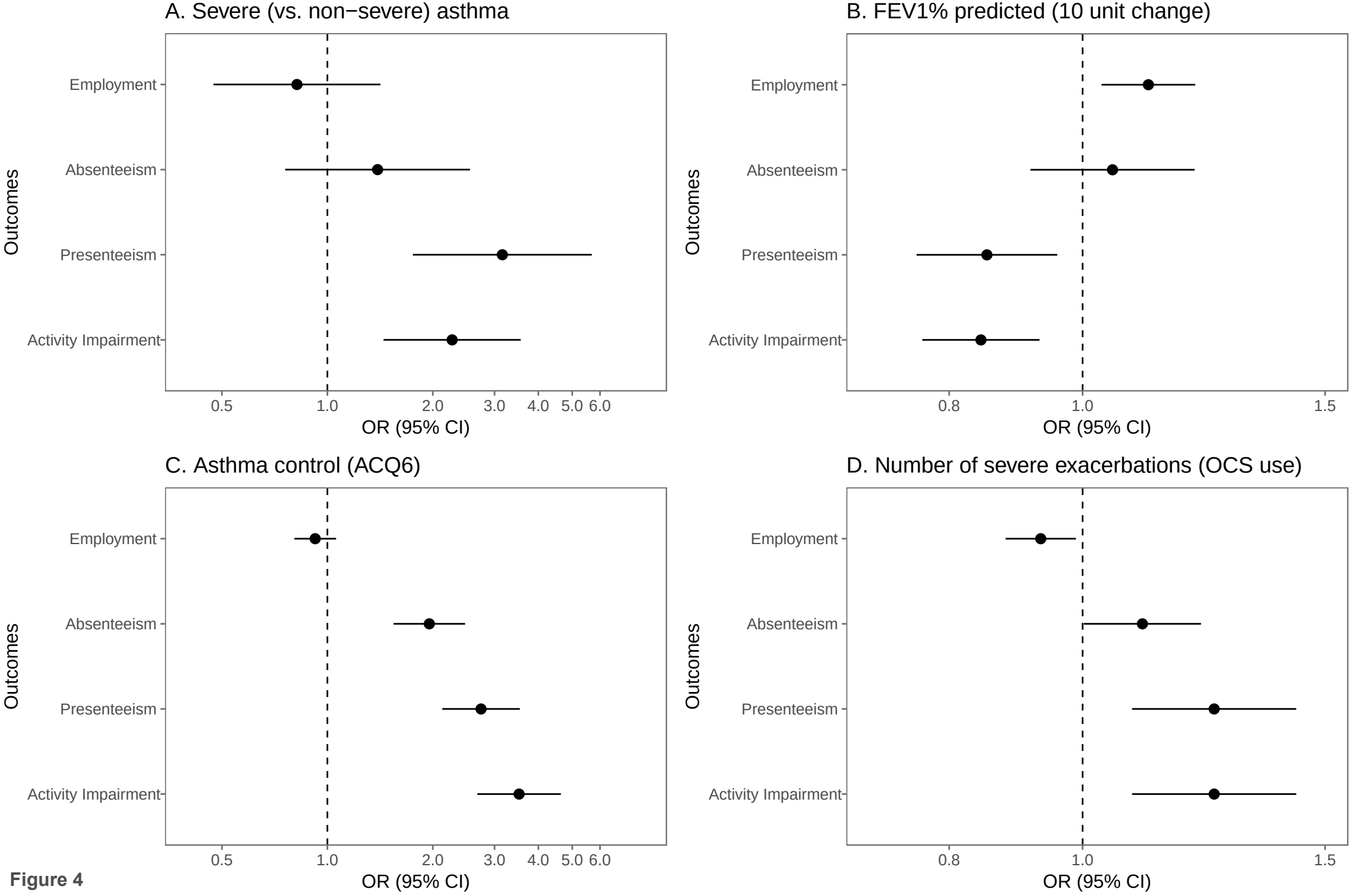
A. Severe (vs. non−severe) asthma
B. FEV1% predicted (10 unit change)
C. Asthma control (ACQ6)
D. Number of severe exacerbations (OCS use)
Outcomes
Employment
Absenteeism
Presenteeism
Activity Impairment
0.5
1.0
2.0
3.0
4.0
5.0
6.0
0.8
1.0
1.5
OR (95% CI)

Figure 4

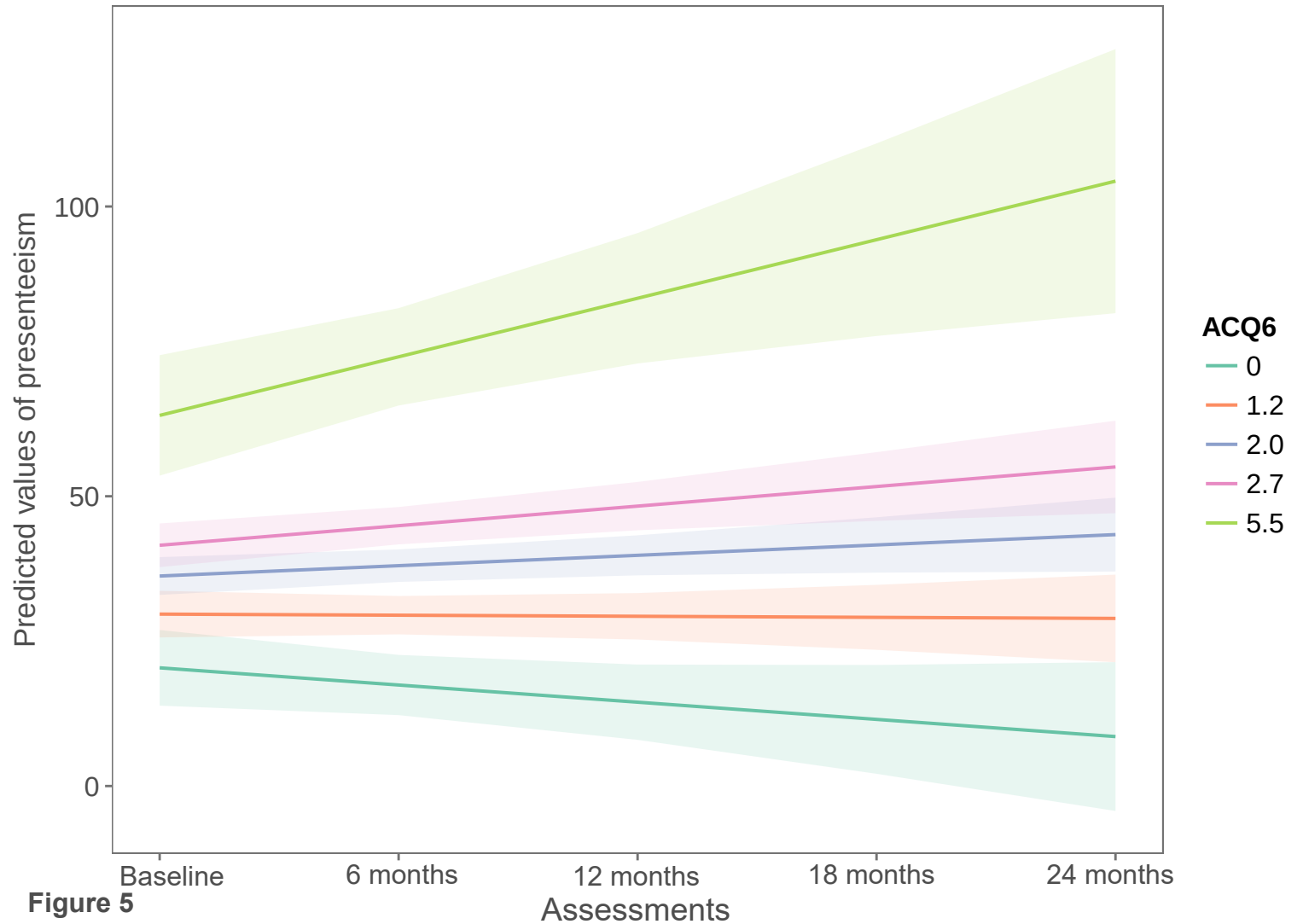
Predicted values of presenteeism
100
50
0
Baseline
6 months
12 months
18 months
24 months
Assessments
ACQ6
0
1.2
2.0
2.7
5.5

Figure 5

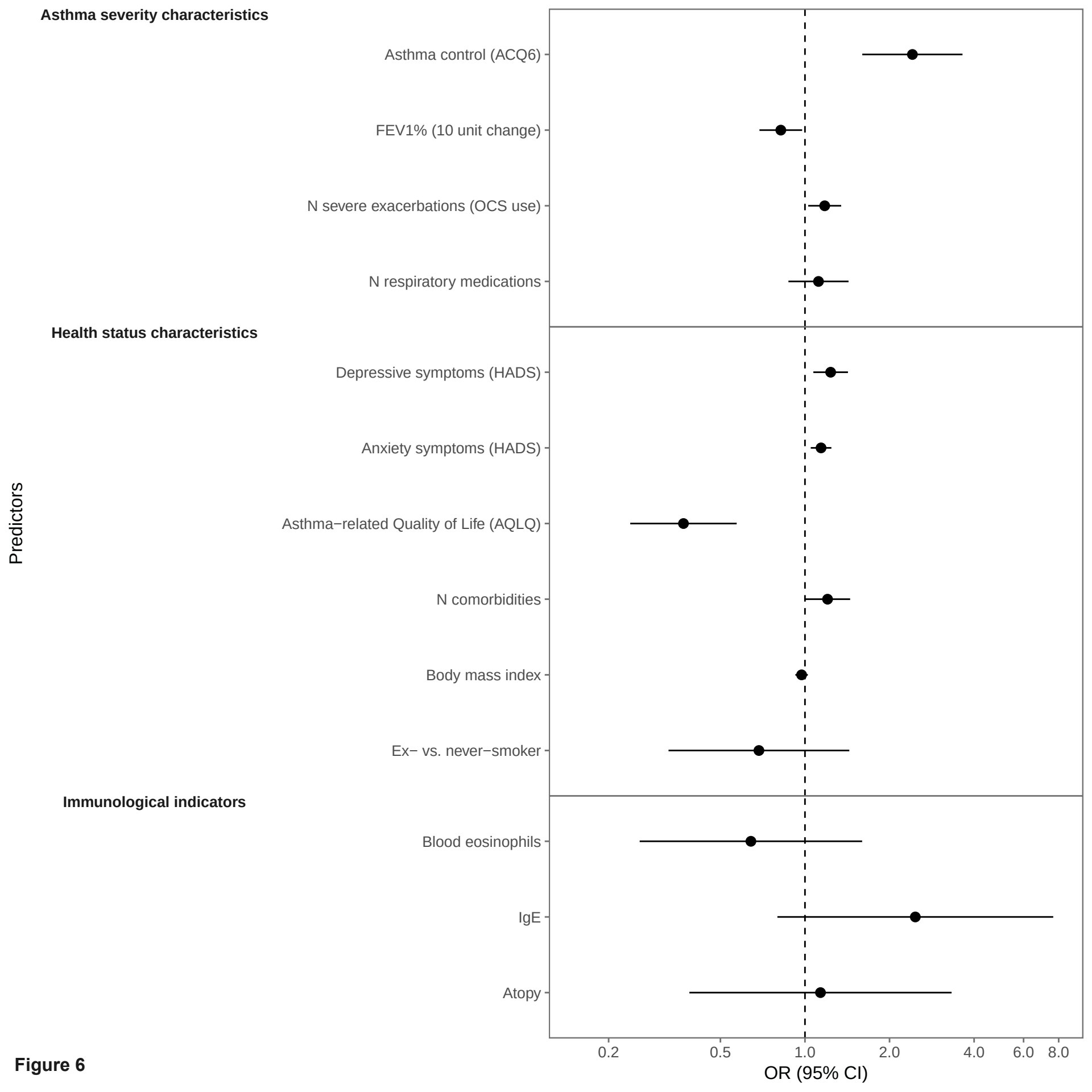
Asthma severity characteristics
Asthma control (ACQ6)
FEV1% (10 unit change)
N severe exacerbations (OCS use)
N respiratory medications
Health status characteristics
Depressive symptoms (HADS)
Anxiety symptoms (HADS)
Asthma−related Quality of Life (AQLQ)
N comorbidities
Body mass index
Ex− vs. never−smoker
Immunological indicators
Blood eosinophils
IgE
Atopy
Predictors
0.2
0.5
1.0
2.0
4.0
6.0
8.0
OR (95% CI)

Figure 6

Online supplement

Severe Asthma Web-based Database (SAWD) Additional methods and results for *Working while unwell: Workplace impairment in people with severe asthma (Hiles et al.)*

Contents

Methods

Protocol

The detailed SAWD protocol is available on the Centre of Excellence in Severe Asthma website (http://www.severeasthma.org.au/tools-resources/toolkits/).

Procedure

Data collected included demographic characteristics; smoking status; medical and allergy history; asthma history and triggers; medication use and adherence; asthma control; exacerbations; spirometry, atopic status (skin prick test/serum specific IgE test) and patient-reported measures related to health status and asthma-related quality of life. Questionnaires were used with permission. Longitudinal patient-reported data were collected via telephone/mail out/face-to-face visits and submitted to the database with relevant clinical data.

Inclusion criteria for severe and non-severe asthma groups are described in **Table S1**. Comparison of participants with and without data for follow-up assessments is described in **Table S2**.

Measures

Medical information

Comorbidities, allergy history, asthma and concomitant medications were recorded. Height and weight without shoes were also recorded.

Table S1. Inclusion criteria for entry to SAWD.

For all participants	
Able to provide informed written consent	
AND	
Adults (≥ 18 years)	
AND	
Confirmed asthma diagnosis with confirmed variable airflow limitation at visit 1 or documented within the past 10 years: Bronchodilator response > 200mL and/or > 12% (post-bronchodilator FEV_1 following administration of 400µg salbutamol, pMDI with spacer; after 10 minutes) **AND/OR** Airway hyperresponsiveness in response to any standard challenge agent (e.g., methacholine, histamine, hypertonic saline, mannitol, adenosine monophosphate, exercise) **AND/OR** Peak flow variability >12% over at least 1 week **AND/OR** FEV_1 variability >12% within 2 months	
AND	
No: • Pregnancy • Cognitive impairment preventing completion of data forms • High dependence on medical care • Significant life limiting co-morbidity • Primary diagnosis of lung disease other than asthma • Current lung cancer or other blood, lymphatic or solid organ malignancy • Inability to attend study visits • Current exacerbation at baseline visit (repeat screening when stable)	
AND	AND
For severe asthma	**For non-severe asthma**
TREATMENT REQUIREMENT: >1000µg BDP equivalent (high daily ICS dose)[1] **AND** 2nd controller (LABA, LAMA, oral corticosteroids ≥ 50% of the past year, montelukast or theophylline)	Using maintenance inhaled controller therapy
AND	AND

UNCONTROLLED ASTHMA**:**	CONTROLLED ASTHMA:
Poor symptom control: ACQ6 consistently > 1.5, ACT < 20 or 'not well controlled' by NAEPP/GINA guidelines **AND/OR** Frequent severe exacerbations: 2 or more bursts of systemic corticosteroids (> 3 days each) in the previous year **AND/OR** Serious exacerbations: at least one hospitalisation, ICU stay or mechanical ventilation in the previous year **AND/OR** Persistent airflow limitation: FEV_1< 80% predicted (in the face of a reduced FEV_1/FVC) pre-bronchodilator.	ACQ6 ≤ 1.5 or ACT ≥ 20 **AND** Stable disease with no respiratory infection, asthma exacerbation, or change in maintenance therapy in the 4 weeks preceding screening
AND	
Optimised management skills (inhaler technique, education, adherence, written asthma action plan)	
AND	
Triggers and relevant co-morbidities have been assessed and managed	

ACQ6: Asthma Control Questionnaire-6; ACT: Asthma Control Test; BDP: Beclomethasone equivalent dose; FEV_1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; GINA: Global Initiative for Asthma; ICS: Inhaled corticosteroid; ICU: Intensive care unit; LABA: Long acting beta agonist agent; LAMA: Long acting anti-muscarinic antagonist; NAEPP: National Asthma Education and Prevention Program.

Table S2. Comparison of baseline demographic, clinical and quality of life characteristics according to whether or not participants completed at least one follow-up assessment.

	No follow-up data available N = 178		**Follow-up data available N = 358**	
Severe asthma	134	(75.3)	300	(83.8)
Demographic characteristics				
Age (years), mean (SD)	52.7	(16.7)	56.1	(14.4)
Male, N (%)	69	(38.8)	151	(42.2)
Race, N (%)				
White	112	(73.7)	254	(89.4)
Asian	33	(21.7)	17	(6.0)
Pacific islander	4	(2.6)	3	(1.1)
Other	3	(2.0)	10	(3.5)
Smoking status, N (%)				
Never smoked	131	(73.6)	202	(57.5)
Ex-smoker	41	(23.0)	142	(40.5)
Current smoker	6	(3.4)	7	(2.0)
Pack years, median (IQR)	10	(2.5, 26.5)	9	(2.0, 25.5)
BMI, median (IQR)	28.7	(25.3, 33.3)	29.3	(25.7, 34.4)
Number of comorbid conditions, median (IQR)	2	(2, 4)	3	(2, 5)
Asthma characteristics				
Asthma duration (years), mean (SD)	31.2	(19.3)	30.9	(19.0)
ACQ6, median (IQR)	1.5	(0.7, 2.7)	1.7	(0.8, 2.6)
ACQ6 ≥ 2 (N, %)	75	(42.9)	154	(43.9)
ACT total score, median (IQR)	17	(12.0, 21.0)	16	(12.0, 20.0)
ACT < 20 (N, %)	56	(31.8)	100	(30.0)
GINA control				
Controlled (N, %)	16	(9.5)	12	(3.7)
Partially controlled (N, %)	49	(29.0)	84	(25.9)
Uncontrolled (N, %)	104	(61.5)	228	(70.4)
Pre-bronchodilator				
FEV_1 % predicted, mean (SD)	70.7	(22.6)	68.9	(20.8)
FVC % predicted, mean (SD)	83.8	(22.0)	82.4	(18.2)
FEV_1/FVC % predicted, mean (SD)	0.8	(0.2)	0.8	(0.2)
Post-bronchodilator				
FEV1 % predicted, mean (SD)	76.5	(24.4)	74.7	(20.2)
FVC % predicted, mean (SD)	87.4	(19.2)	86.3	(17.2)
FEV_1/FVC % predicted, mean (SD)	0.7	(0.1)	0.7	(0.1)
ICS daily dose, µg beclomethasone equivalent units, median (IQR)	1600	(800.0, 2000.0)	2000	(1280.0, 2000.0)

Number of respiratory medications, median (IQR)	3	(2.0, 4.0)	4	(3.0, 4.0)
Atopy, N (%)	75	(76.5)	206	(81.4)
IgE ≥ 30 kU/L, N (%)	91	(86.7)	206	(89.2)
Blood eosinophils (10^9/L), median (IQR)	0.3	(0.2, 0.4)	0.2	(0.1, 0.4)
Quality of life and mental health characteristics				
AQLQ, median (IQR)				
Activity	5.5	(4.1, 6.3)	5.4	(4.3, 6.3)
Symptoms	5.2	(3.9, 6.1)	5.1	(4.0, 6.1)
Emotions	5.4	(3.6, 6.4)	5.4	(4.0, 6.4)
Environment	5.2	(4.0, 6.2)	5.5	(4.2, 6.2)
Total	5.2	(4.0, 6.2)	5.2	(4.2, 6.2)
HADS anxiety score, median (IQR)	6	(3.0, 10.0)	5	(3.0, 9.0)
HADS depression score, median (IQR)	3	(1.0, 7.0)	4	(2.0, 7.0)
Workplace characteristics				
Employed, N (%)	94	(53.7)	149	(45.7)
Reported absenteeism, N (%)	24	(27.6)	32	(23.2)
Degree of absenteeism, median (IQR)	0	(0.0, 5.1)	0	(0.0, 0.0)
Reported presenteeism, N (%)	62	(70.5)	88	(64.2)
Degree of presenteeism, median (IQR)	20	(0.0, 30.0)	20	(0.0, 40.0)
Reported activity impairment, N (%)	140	(80.5)	266	(82.9)
Degree of activity impairment, median (IQR)	30	(10.0, 70.0)	40	(10.0, 70.0)

ACQ6: Asthma Control Questionnaire 6-item; ACT: Asthma Control Test; AQLQ: Asthma Quality of Life Questionnaire; BMI: body mass index; FVC: forced vital capacity; FEV_1: forced expiratory volume in 1 second; GINA: Global Initiative for Asthma; HADS: Hospital Anxiety and Depression Scale; ICS: inhaled corticosteroids.

Exacerbations

Severe exacerbations were identified as documented use of oral corticosteroids prescribed or supervised by a physician, need for parenteral corticosteroids, admission to hospital, stay in an intensive care unit or mechanical ventilation, emergency department visit or an unscheduled doctor visit. For each exacerbation type, number of exacerbations was recorded at baseline (exacerbations in the last 12 months) and at each follow-up assessment (exacerbations in the last 6 months).

Spirometry and biomarkers

Pre and post-bronchodilator spirometry was performed according to ATS/ERS standards.[2] Sputum was induced using nebulised 4.5% or 0.09% saline (depending on lung function) and processed. Biomarker levels (serum immunoglobulin E [IgE], blood eosinophils, full blood count), skin prick test results, fractional exhaled nitric oxide (FeNO) and induced sputum inflammatory cell counts were submitted to SAWD when available. Optionally entered were data from other investigations, including polysomnography, 24 hour pH monitoring, high resolution computed tomography (HRCT) chest and sinus CT.

Asthma control, quality of life and health status

Asthma control was assessed with three measures:

(1) Asthma Control Questionnaire-6 (ACQ6),[3] a six-item questionnaire that measures control from 0 (“good control”) to 5 (“extremely poor control”);
(2) Asthma Control Test (ACT),[4] a five-item questionnaire where low scores indicate poor control and high scores indicate good control (score range 5-25); and
(3) Control according to the Global Initiative for Asthma (GINA) control criteria,[1] which provides a category for asthma control based on the presence of five symptoms, either

"controlled" (score of 0, no symptoms present), "partially controlled" (score of 1 or 2) or "uncontrolled" (3, 4 or 5).

Asthma-related quality of life was assessed using the Juniper Asthma Quality of Life Questionnaire – standardised (AQLQ),[5] a 32-item questionnaire measuring quality of life across four domains (symptoms, activity limitation, emotional function and environmental stimuli).

Anxiety and depression symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS), where higher scores indicate greater symptoms of anxiety or depression (anxiety subscale 0-21; depression subscale 0-21).[6]

Productivity

Workplace productivity was assessed via the Work Productivity and Activity Impairment Questionnaire: General Health V2.0 (WPAI:GH).[7] The questionnaire asks whether the respondent is employed and the number of hours worked or missed from work for health or other reasons in the last seven days. It also asks for a self-rating of the extent to which their health problems affected their functioning at work and their functioning in daily non-work activity on 11-point Likert scales, where 0 is no problems and 10 is that their health problems completely prevented them from working or completing daily activities.

Absenteeism is calculated as a percentage of the number of hours of work missed due to health reasons by the possible work hours (i.e., the sum of actual hours worked and hours missed due to health reasons). Presenteeism is calculated using the Likert scale responses regarding their self-rated impairment at work due to health reasons, multiplied by 10 to scale between 0 and 100. Activity impairment is calculated similarly, using the Likert scale responses regarding their self-related impairment in completing non-work daily activities, multiplied by 10 to scale between 0 and 100.

Results

Table S3 shows the relationship between measures of asthma severity and (1) whether participants reported being employed or impaired in their work or daily activity, and (2) for those who reported impairment, the degree of impairment.

Table S4 shows associations between characteristics of people with severe asthma and (1) whether participants reported presenteeism, and (2) for those who reported presenteeism, the degree of impairment.

Table S3. Associations between asthma severity measures and workplace productivity, described as both the presence of impairment (versus no reported impairment) and the continuous level of impairment among people who reported some degree of impairment.

	Reported the impairment (binary)			Level of impairment (continuous)		
	OR	**(95% CI)**	***p***	**B**	**(95% CI)**	***p***
Severe vs. non-severe asthma (reference: non-severe asthma) associated with:						
Employment	0.82	(0.48, 1.41)	.477			
Absenteeism	1.38	(0.75, 2.53)	.293	10.13	(-5.39, 25.65)	.201
Presenteeism	3.15	(1.75, 5.67)	<.001	6.78	(-1.53, 15.09)	.109
Impairment of daily activity	2.26	(1.44, 3.55)	<.001	16.02	(11.18, 20.86)	<.001
Level of asthma control (ACQ6) associated with:						
Employment	0.92	(0.81, 1.05)	.236			
Absenteeism	1.95	(1.54, 2.47)	<.001	5.23	(0.35, 10.11)	.036
Presenteeism	2.75	(2.13, 3.55)	<.001	10.06	(7.90, 12.22)	<.001
Impairment of daily activity	3.52	(2.68, 4.63)	<.001	10.94	(9.63, 12.25)	<.001

Lung function (pre-bronchodilator FEV_1% 10 point increase) associated with:						
Employment	1.12	(1.04, 1.21)	.005			
Absenteeism	1.05	(0.92, 1.21)	.460	-3.49	(-7.45, 0.47)	.084
Presenteeism	0.85	(0.76, 0.96)	.011	0.08	(-1.61, 1.77)	.928
Impairment of daily activity	0.84	(0.76, 0.93)	.001	-2.17	(-3.29, -1.05)	<.001
Number of past-year severe exacerbations (OCS use) associated with:						
Employment at baseline	0.93	(0.87, 0.99)	.030			
Absenteeism at baseline	1.11	(1.00, 1.23)	.054	1.59	(-0.93, 4.11)	.217
Presenteeism at baseline	1.25	(1.08, 1.44)	.003	1.02	(-0.16, 2.20)	.090
Impairment of daily activity at baseline	1.24	(1.08, 1.42)	.002	1.46	(0.84, 2.08)	<.001
At least one past-year hospitalisation associated with:						
Employment at baseline	0.59	(0.35, 1.02)	.057			
Absenteeism at baseline	1.94	(0.89, 4.22)	.093	-7.00	(-26.05, 12.05)	.471
Presenteeism at baseline	1.55	(0.65, 3.70)	.327	4.20	(-5.05, 13.45)	.373
Impairment of daily activity at baseline	1.45	(0.75, 2.82)	.266	7.78	(1.34, 14.22)	.018

At least one past-year emergency department visit associated with:						
Employment at baseline	0.57	(0.34, 0.97)	.039			
Absenteeism at baseline	2.09	(0.94, 4.63)	.069	0.61	(-20.52, 21.74)	.955
Presenteeism at baseline	2.67	(1.05, 6.81)	.040	8.40	(-0.66, 17.46)	.069
Impairment of daily activity at baseline	2.44	(1.18, 5.07)	.017	7.58	(1.28, 13.88)	.018

Notes: Analyses were generalised estimating equations (GEE) with exchangeable correlation structure, using assessment timepoint as the clustering variable and controlling each analysis for sex, age and assessment timepoint. Data from all five assessments were used except for the analyses with exacerbations, where only baseline data were used. Confidence intervals were calculated from robust standard errors. Employment was analysed among participants of working age <65 years (N = 355), presenteeism and absenteeism analysed among people currently employed (N = 243) and impairment of daily activity analysed among all participants (N = 536).

ACQ6: Asthma Control Questionnaire 6-item; CI: confidence interval; FEV_1%: forced expiratory volume in 1 second percent predicted; OCS: oral corticosteroids.

Table S4. Associations between characteristics and workplace presenteeism among people with severe asthma at baseline.

	Reported presenteeism (binary)			Level of presenteeism (continuous)		
	OR	**(95% CI)**	***p***	**B**	**(95% CI)**	***p***
Asthma characteristics						
ACQ6	2.41	(1.60, 3.64)	<.001	8.06	(4.20, 11.92)	<.001
FEV_1% predicted (10 unit change)	0.82	(0.69, 0.98)	.026	-0.36	(-2.52, 1.80)	.747
Number of past-year exacerbations (OCS use)	1.18	(1.03, 1.35)	.019	0.62	(-0.61, 1.85)	.323
Number of respiratory medications	1.12	(0.87, 1.45)	.388	2.56	(-0.50, 5.62)	.104
Demographic and health status characteristics						
Ex-smoker (reference: never smoker)	0.69	(0.33, 1.45)	.317	6.10	(-4.09, 16.29)	.243
Body mass index	0.97	(0.91, 1.03)	.302	0.72	(0.05, 1.39)	.036
Number of comorbid diseases	1.19	(0.96, 1.48)	.109	2.18	(-0.29, 4.65)	.085
AQLQ total score	0.37	(0.25, 0.56)	<.001	-7.69	(-11.14, -4.24)	<.001
HADS anxiety score	1.14	(1.05, 1.23)	.002	0.60	(-0.30, 1.50)	.193
HADS depression score	1.23	(1.09, 1.38)	.001	0.98	(-0.20, 2.16)	.103
Immunological indicators						
Atopy (reference: no atopy)	1.14	(0.38, 3.42)	.819	6.51	(-7.94, 20.96)	.380
IgE > 30 kU/L (reference: IgE ≤ 30 kU/L)	2.47	(0.78, 7.85)	.126	15.26	(-3.18, 33.70)	.108
Blood eosinophils (10^9/L)	0.64	(0.28, 1.49)	.300	0.83	(-13.22, 14.88)	.908

Notes: All analyses controlled for age and gender.

ACQ6: Asthma Control Questionnaire 6-item; AQLQ: Asthma Quality of Life Questionnaire; CI: Confidence interval; FEV_1%: forced expiratory volume in 1 second; HADS: Hospital Anxiety and Depression Scale.

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