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Title:

Working while unwell: Workplace impairment in people with severe asthma

Date:

2018-06-01

Citation:

Hiles, S. A., Harvey, E. S., McDonald, V. M., Peters, M., Bardin, P., Reynolds, P. N., Upham, J. W., Baraket, M., Bhikoo, Z., Bowden, J., Brockway, B., Chung, L. P., Cochrane, B., Foxley, G., Garrett, J., Hew, M., Jayaram, L., Jenkins, C., Katelaris, C., ... Gibson, P. G. (2018). Working while unwell: Workplace impairment in people with severe asthma. *Clinical and Experimental Allergy*, 48 (6), pp.650-662. <https://doi.org/10.1111/cea.13153>.

Persistent Link:

<https://hdl.handle.net/11343/283882>

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Article type : Original Article-Asthma and Rhinitis

Working while unwell: Workplace impairment in people with severe asthma

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/cea.13153](https://doi.org/10.1111/cea.13153)

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19 **Running title:** Work impairment in severe asthma

20 **Word count:**

21 Abstract: 300

22 Main text: 3618, excluding tables and reference list.

23 Figure/table count: 7

24 Online supplement: Yes

25 Abstract

26 **Background:** Severe asthma affects quality of life; however, its impact on workplace
27 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 ($p<0.01$).

Conclusion 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 ($> 1000\mu\text{g}$ beclomethasone equivalent) with a second controller (long acting beta agonist [LABA], long acting anti-muscarinic antagonist [LAMA], oral corticosteroid (OCS) $\geq 50\%$ 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; referred to as "reported impairment") and (2) a continuous outcome when values were greater than 0 (referred to as "level or degree of impairment"). 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 FEV₁% 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 FEV₁%, 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). Symptoms of depression or anxiety and asthma control were independently associated with reporting presenteeism when simultaneously entered into regression analyses (OR [95%CI]: depressive symptoms 1.16 [1.01-1.33], $p = 0.031$ and ACQ6 2.14 [1.39-3.31], $p = 0.001$; anxiety symptoms 1.11 [1.01-1.22], $p = 0.025$ and ACQ6 2.28 [1.48-3.49], $p < 0.001$, controlling for age and gender). 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.

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

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

1 Another important finding from this study is that productivity impairments changed little over
2 time and differences between severe and non-severe asthma were maintained. There was also
3 evidence that patients with the worst asthma control have greater presenteeism over time.
4 Other longitudinal studies in severe asthma have similarly observed stable or worsening
5 workplace impairment over time in severe asthma.[39–41] These findings demonstrate the
6 increased burden of severe asthma, and that effects of severe asthma on workplace
7 productivity are enduring.

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

21 We identified several limitations of this study. As SAWD is an observational registry, data
22 are subject to selection bias, other unknown bias and confounding, and effects over time are
23 not controlled. However, the strength of registry data is the generalisability of the findings
24 due to the heterogeneity of the population. Registry data is an important complement to
25 randomised controlled trial data, providing practice-based evidence. This study also used a
26 convenience rather than random sample, so the representativeness of this sample of severe
27 and non-severe asthma in general is not clear. Nevertheless, the sample characteristics are
28 consistent with other registry samples although prevalence of atopy is higher in
29 SAWD.[8,9,48] There were limitations in the measurement of workplace productivity. This
30 study examined self-reported impairment over seven days, which, although positive in terms
31 of the reliability of the estimate, may underestimate longer-term effects. Extended follow-up,
32 including real-time sampling of workplace productivity, and verification with objective

1 indicators of workplace performance would be a novel improvement to assessing workplace
2 productivity in severe asthma. It would be particularly useful for verifying the impact of
3 mental health problems on presenteeism in severe asthma, independent of possible biased
4 self-reporting due to negative self-evaluation. Data regarding the effects of asthma on
5 probability of early retirement or employment choices would also be informative. SAWD did
6 not collect information on type of employment, socioeconomic status, education, retirement
7 age or whether participants access disability pensions, which further data collection could
8 address. Finally, some data were incomplete, patients were lost to follow-up and follow-up
9 assessments were yet to be completed at the time data were extracted from SAWD. However,
10 baseline differences between participants who did and did not contribute follow-up data were
11 minimal.

12 Workplace productivity loss is common in people with severe asthma, which may have
13 significant consequences for their physical, financial, social and emotional wellbeing. Work
14 impairment in severe asthma is associated with greater healthcare utilisation and more
15 exacerbations over time.[6,30] Beyond presenteeism and absenteeism, people with severe
16 asthma work less, switch jobs, are prevented from entering some professions, take disability
17 leave and retire early, all of which may pose significant risks to their financial stability.[3,7–
18 9,30,33,49] They report lower earnings compared with controlled asthma.[28,29,35,37]
19 People with severe asthma worry about their work and non-work activity limitations and their
20 finances, reporting fear that health costs will be unmanageable due to restrictions on their
21 ability to work.[3] They report workplace discrimination and stigma due to asthma[7] and
22 experience negative emotions of giving up work.[50] An adverse cycle may ensue whereby
23 workplace impairment due to asthma symptoms and exacerbation generates stress that leads
24 to further impairment, even when asthma symptoms resolve.

25 People with severe compared with non-severe asthma have a high symptom and disease
26 burden, which significantly contributes to impairment at work and during other activities. We
27 show that people with severe asthma, particularly those with poorer asthma control, are more
28 likely to experience impairment at work. Patients in this registry, and others, are
29 comprehensively monitored and optimally treated, however symptom control remained
30 suboptimal. There is an urgent need for improvement in asthma control to safeguard against
31 losses to financial and psychological wellbeing from work impairment. Although expensive,
32 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

SA Hiles' salary was funded by a grant from GlaxoSmithKline during the conduct of the study. **VM 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. **M Peters** reports personal fees from GlaxoSmithKline for CME lectures and advisory board participation, personal fees from AstraZeneca, for CME lectures and personal fees from Novartis for advisory board participation outside the submitted work. **PN Reynolds** reports grants from TSANZ during the conduct of the study. **JW Upham** reports personal fees from Novartis, GlaxoSmithKline, AstraZeneca and TEVA outside the submitted work. **J Bowden** reports personal fees from AstraZeneca and GlaxoSmithKline during the conduct of the study. **LP Chung** reports fees for presentation and attendance at board meetings from AstraZeneca, GlaxoSmithKline, Menarini and Boehringer Ingelheim for work unrelated to the current manuscript. **M 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. **C Jenkins** reports personal fees from Novartis, AstraZeneca and Boehringer Ingelheim, and grants and personal fees from GlaxoSmithKline, outside the submitted work. **V Kritikos** reports other support from AstraZeneca outside the submitted work. **N Radhakrishna** has received speaker fees from Mundipharma, Boehringer Ingelheim and AstraZeneca. **H 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. **J Rimmer** reports unrelated honoraria from GlaxoSmithKline, Stallergenes, Seqirus and AstraZeneca. **M Sutherland** reports personal fees from AstraZeneca outside the submitted work. **PG 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.

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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; FEV₁ %: 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; FEV₁ %: 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	<i>p</i>
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)	.060
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)	.208
Pack years, median (IQR)	10.5 (2.4, 26.8)	5.9 (1.0, 13.8)	.018
BMI, median (IQR)	30.0 (25.9, 34.8)	27.4 (24.8, 30.3)	<.001
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 $\geq$ 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)	81.5 (20.3)	88.7 (15.0)	<.001
FEV1/FVC % predicted, mean (SD)	0.82 (0.17)	0.91 (0.14)	<.001
Post-bronchodilator			
FEV ₁ % predicted, mean (SD)	73.1 (21.9)	83.5 (19.3)	<.001
FVC % predicted, mean (SD)	85.7 (18.3)	90.4 (15.6)	.016
FEV ₁ /FVC % predicted, mean (SD)	0.66 (0.14)	0.72 (0.12)	<.001
ICS daily dose, μ g beclomethasone equivalent units, median (IQR)	(1600.0, 2000.0)	(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,	104 (24.0)	4 (3.9)	<.001

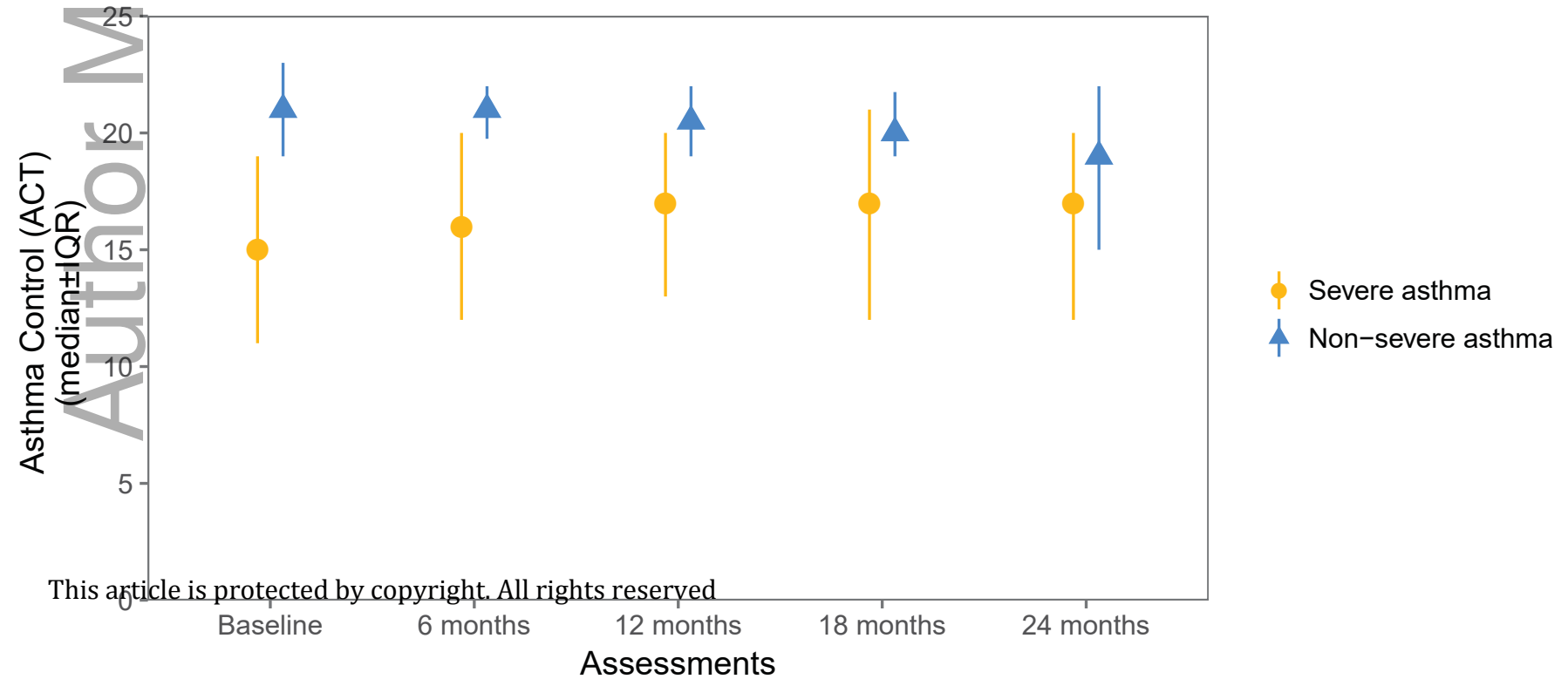
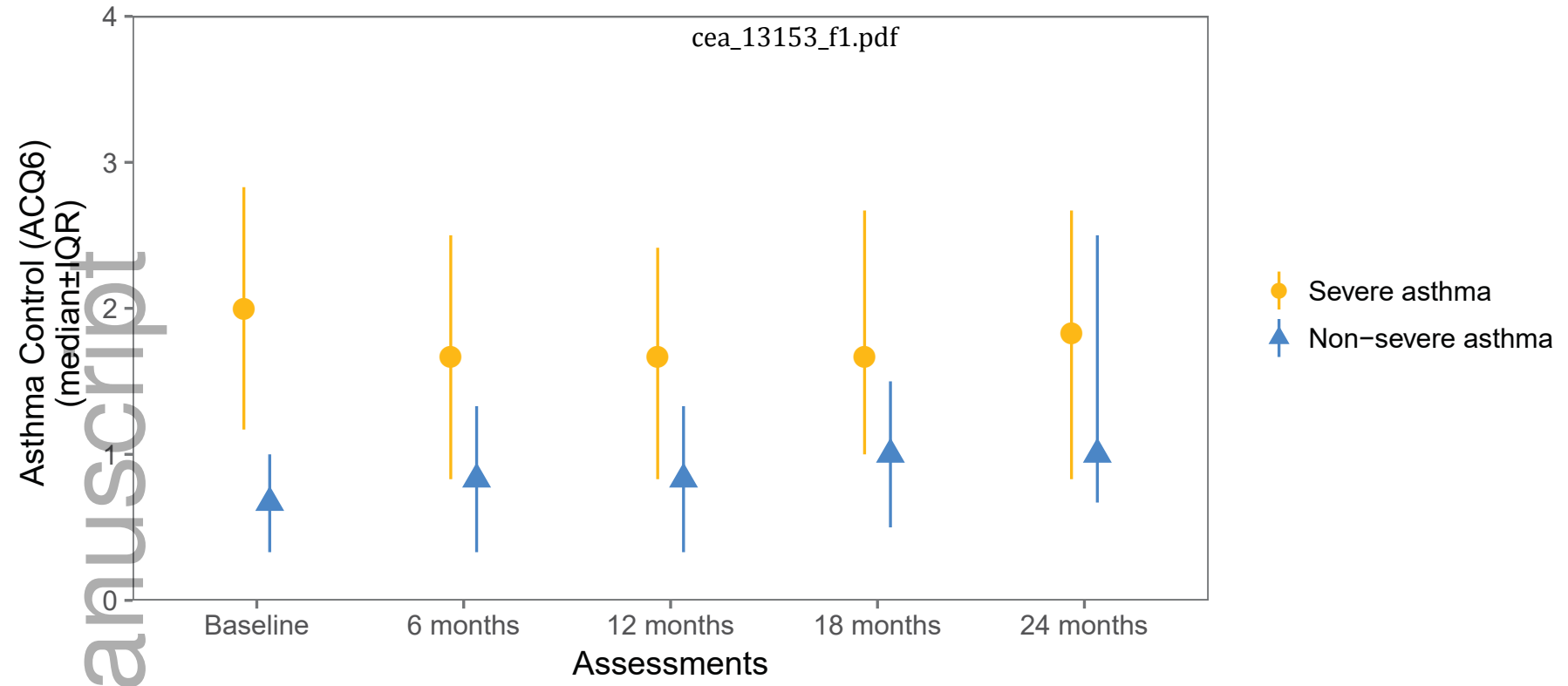
N (%)			
Atopy, N (%)	214 (79.6)	67 (81.7)	.753
IgE $\geq$ 30 kU/L, N (%)	278 (89.4)	19 (76.0)	.055
Blood eosinophils ($10^9/L$), median (IQR)	0.2 (0.1, 0.4)	0.3 (0.2, 0.4)	.576

Quality of life and mental health

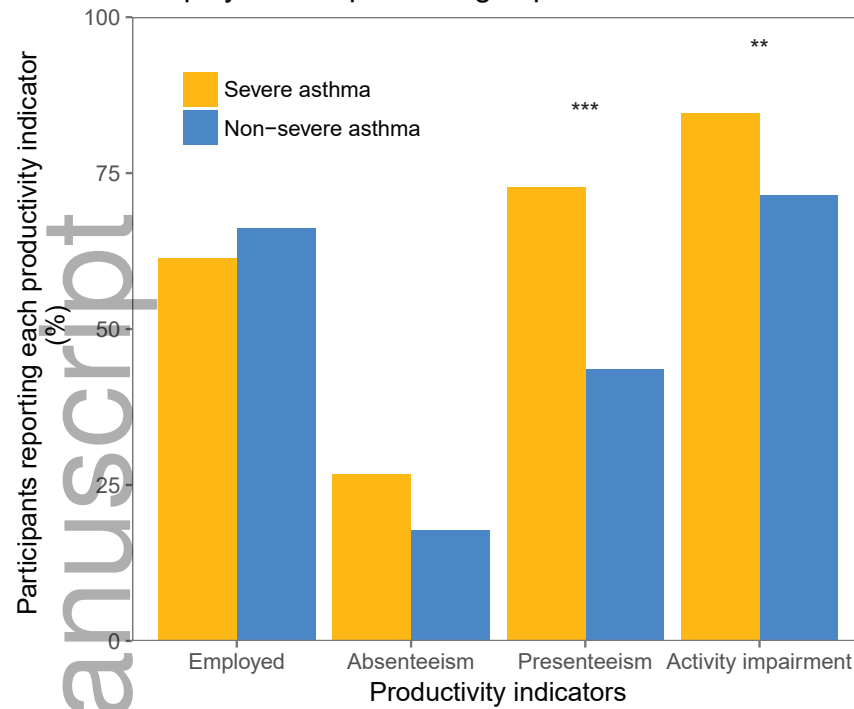
characteristics

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

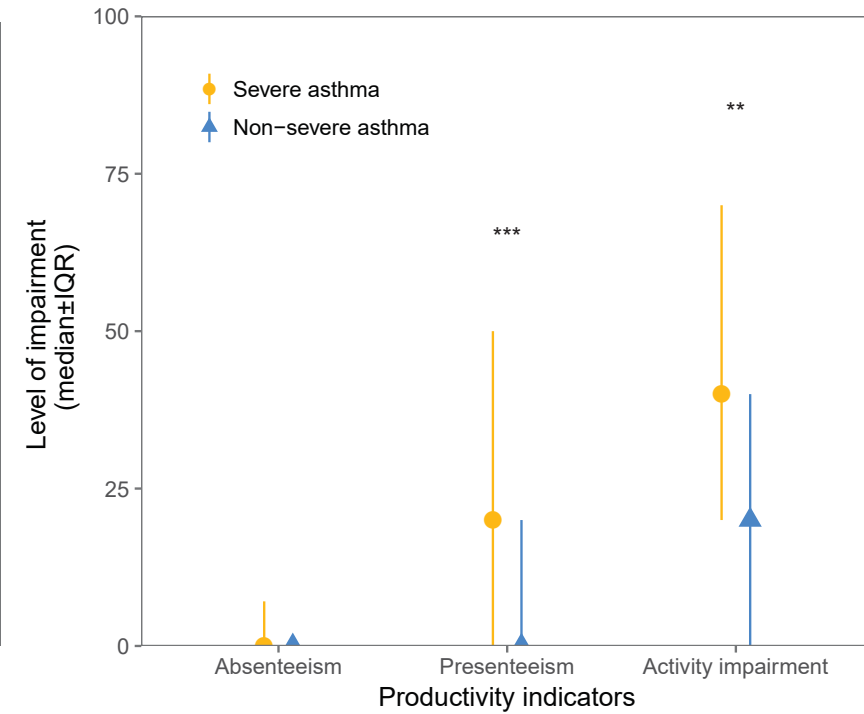
- 1 ACQ6: Asthma Control Questionnaire 6-item; ACT: Asthma Control Test; AQLQ: Asthma
- 2 Quality of Life Questionnaire; BMI: body mass index; FVC: forced vital capacity; FEV₁:
- 3 forced expiratory volume in 1 second; GINA: Global Initiative for Asthma; HADS: Hospital
- 4 Anxiety and Depression Scale; ICS: inhaled corticosteroids; OCS: oral corticosteroids.



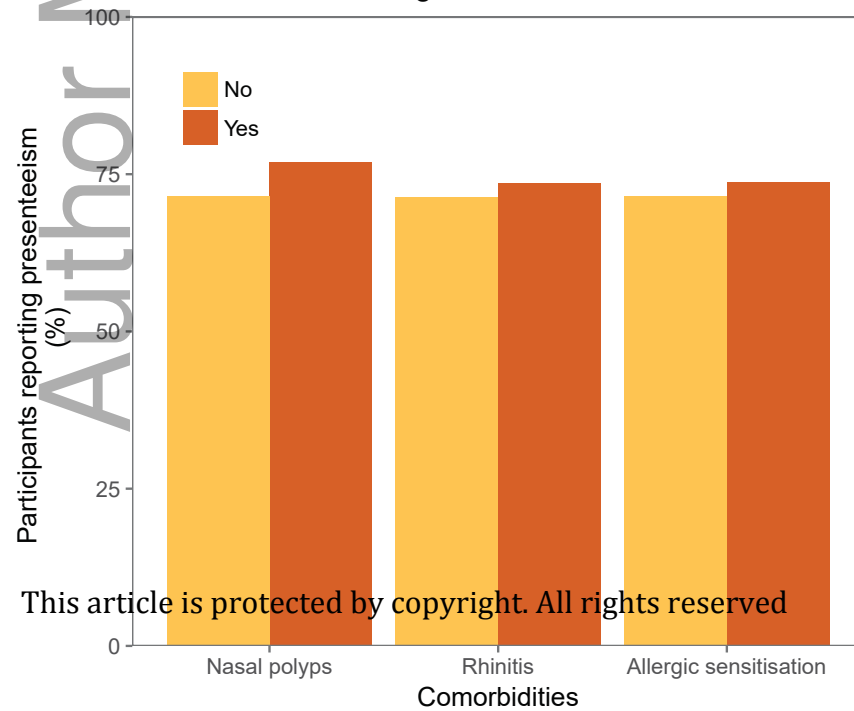
A. Percentage of participants who reported being employed or experiencing impairment at baseline



B. Median level of impairment at baseline



C. Severe asthma patients reporting presenteeism at baseline according to comorbidities



D. Median level of presenteeism over time

