Original Article

Asthma Is Associated With Increased Sickness Absence Among Young Adults

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What is already known about this topic? Asthma has been suggested to negatively affect sickness absence and other work-related outcomes, but there is limited evidence regarding the impact in young adults and factors that could modify this potential association.

What does this article add to our knowledge? Asthma, especially uncontrolled asthma and certain asthma phenotypes, was associated with higher sickness absence and productivity loss. The association may be stronger among those who are overweight than among those with a normal weight.

How does this study impact current management guidelines? The results highlight the importance of asthma prevention to reduce the negative health consequences and societal costs of asthma. Health care needs to support patients with asthma to achieve and maintain asthma control and weight management.

BACKGROUND: There is limited knowledge about how asthma affects sickness absence in young adulthood.
OBJECTIVE: To examine how asthma and different asthma phenotypes affect sickness absence among young adults and potential modifying factors. A secondary aim was to estimate productivity losses related to sickness absence for asthma.
METHODS: The study included 2391 participants from the Swedish population-based cohort BAMSE (Barn/Child, Allergy, Milieu, Stockholm, Epidemiology). Information on asthma, asthma phenotypes, and lifestyle factors was collected from questionnaires and clinical examinations at age approximately 24 years (2016-2019). Information on sickness absence for longer than 14 days was obtained from a national register for the years 2020 and 2021. Associations between asthma, asthma phenotypes, and sickness absence were analyzed with logistic regression models adjusted for sex, birth year, education, and overweight status.
RESULTS: At age 24 years, 272 (11.4%) fulfilled the definition of asthma. Sickness absence was more common among those with asthma than among those without (15.1% vs 8.7%; $P = .001$; adjusted odds ratio 1.73; 95% CI, 1.19-2.51). Analyses of asthma phenotypes showed that the association tended to be stronger for persistent asthma, uncontrolled asthma, and asthma in combination with rhinitis; no consistent differences were observed across phenotypes related to allergic sensitization or inflammation. The association tended to be stronger among those with overweight than among those with normal weight. Asthma, especially uncontrolled asthma, was associated with higher productivity losses from sickness absence.

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Abbreviations used
BAMSE- Barn/Child, Allergy, Milieu, Stockholm, Epidemiology
BMI- body mass index
COVID-19- coronavirus disease 2019
EUR- euro
FENO- fractional exhaled nitric oxide
LISA- Longitudinal Integrated Database for Health Insurance and Labour market studies
OR- odds ratio

CONCLUSIONS: Asthma may be associated with higher sickness absence and productivity losses. Achieving better asthma control and reducing allergic symptoms may reduce sickness absence among individuals with asthma. **© 2024 The Authors. Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).** **(J Allergy Clin Immunol Pract 2024;12:2364-71)**

Key words: *Asthma; Lifestyle factors; Productivity losses; Sickness absence*

INTRODUCTION

Asthma is one of the most common chronic diseases among adolescents and young adults, with an estimated prevalence of 12% to 14%.[1] Living with asthma implies a substantial disease burden for many patients. A large proportion of adolescents and young adults with asthma have an uncontrolled disease, characterized by restrictions in daily activities, disturbed night sleep, and impaired lung function.[2] Asthma, especially uncontrolled asthma, has in turn been associated with several negative consequences, such as impaired quality of life[3] and school performance.[4]

The disease burden of asthma in adolescence and young adulthood could potentially affect the introduction into working life. Previous studies have suggested that asthma relates to disability pension, unemployment, and sickness absence[5,6] and negatively affects job retention[7] and career path.[8] This was particularly evident among individuals with uncontrolled asthma[5] and adult-onset asthma, and among blue-collar workers.[6] Among patients with asthma, previous studies have suggested that disease severity,[9] and exposure to occupational vapors, gas, dust, or fumes,[10] may increase the risk of sickness absence. This is important because sick leave may have negative consequences beyond the underlying illness.[11,12] In addition, poorer asthma control has been associated with increased presenteeism (working when unwell), which was also related to poorer asthma-related quality of life and symptoms of depression and anxiety.[13]

However, there is limited knowledge about how asthma and different asthma phenotypes (with regard to, eg, age of onset, allergic sensitization, inflammation, and allergic comorbidity) affect sickness absence in young adulthood. There is also little knowledge of factors that may contribute to reduced sickness absence among young adults with asthma. Sickness absence has previously been reported to be influenced by lifestyle factors including obesity, smoking, and low physical activity.[14,15] Obesity has been shown to increase the risk of asthma, though asthma may also increase the risk of obesity.[16,17] Obesity in asthma has been associated with reduced quality of life, greater health care consumption, and poorer asthma control. However, there are few studies that have investigated how obesity and other potential modifying factors can affect sickness absence among individuals with asthma.

Knowledge about future work-related illness among young individuals with asthma, and factors that may influence this, is highly relevant for health care to provide appropriate support and improved care for this group. Investigating the role of different asthma phenotypes is important to identify particularly vulnerable groups that may need additional resources and high priority. The main aim of the study was therefore to examine how asthma affects sickness absence and potential modifying factors among young adults in a population-based cohort, with detailed information on asthma phenotypes, potential confounders, and linkage to objective register-based information on sickness absence. A secondary aim was to estimate the productivity losses related to sickness absence for asthma.

METHODS

Study population and study design

The study is based on the population-based birth cohort study BAMSE (Barn/Child, Allergy, Milieu, Stockholm, Epidemiology). The BAMSE cohort originally included 4089 children born and recruited between 1994 and 1996 in the central and northwestern parts of Stockholm, Sweden. The study participants have been followed with repeated questionnaires and clinical investigations throughout childhood, adolescence, and up to young adulthood.

In a follow-up at age approximately 24 years (2016-2019), participants answered a questionnaire "24-year Questionnaire" (n = 3064 [75%]) focusing on symptoms of allergic disease and asthma, including detailed questions on asthma control and medications. Most participants (n = 2270 [56%]) also attended a clinical examination including blood sampling and measurements of fractional exhaled nitric oxide (FENO) and anthropometrics.[18] Blood samples were analyzed for IgE antibodies (n = 2235) using Phadiatop (cat, dog, horse, timothy [grass], birch, mugwort, *Dermatophagoides pteronyssinus* [house dust mite], and *Cladosporium* [mold]) and Fx5 (milk, egg, soy, peanut, cod, fish, wheat) with ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden) and eosinophil cell count (n = 2185) (Department of Clinical Chemistry, Karolinska University Hospital, Stockholm, Sweden). FENO (n = 1922) was measured using NIOX VERO (Circassia, Oxford, UK) at a velocity of 50 mL/s in accordance with the American Thoracic Society and European Respiratory Society guidelines.[19] The main study population included participants who had been working and for whom there were data on sickness benefits received in 2020 or 2021 and data on asthma status at 24 years (n = 2391). In a subanalysis, the study population was broadened to include data from 2019 (n = 2494), to rule out that the association between asthma and sickness absence could be attributed solely to the coronavirus disease 2019 (COVID-19) pandemic.

A flowchart of the included study population can be found in Figure E1 in this article's Online Repository at www.jaci-inpractice.org. The study was approved by the Swedish Ethical Review Authority (2022-06298-02). Informed consent was obtained from all participants.

Exposure assessment

Asthma was defined as doctor-diagnosed asthma (ever) in combination with breathing difficulties in the last 12 months and/or any asthma medication use in the last 12 months, based on responses to the 24-year Questionnaire.

Among individuals with asthma, subgroups were identified. Uncontrolled/partly controlled asthma was defined in accordance with the modified Global Initiative for Asthma definition,[20] based on frequency of symptom, activity limitations, night-time awakening, and frequency of reliver medication (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). Asthma was also analyzed in relation to onset and remission, as adult-onset (asthma at age 24 years, but not at 16 years) or persistent asthma (asthma at both age 16 and 24 years), and in combination with allergic sensitization (based on measured IgE levels against Phadiatop or Fx5), type 2 inflammation (based on blood eosinophils and/or FENO values), and with questionnaire-reported symptoms of rhinitis. Full descriptions and definitions of these asthma phenotypes are provided in Table E1.

Definition of outcomes

Information on days with sickness absence benefits was obtained from the Longitudinal Integrated Database for Health Insurance and Labour market studies (LISA). LISA includes information on sickness absence benefits paid by the Social Insurance Agency to individuals in Sweden 16 years and older; benefits are paid for spells longer than 14 days among those employed. Sickness absence was defined according to the Social Insurance Agency as a period of connected payments for sickness absence, preventive sickness absence rehabilitation, or occupational injury benefits.[21] We analyzed any registered net days with sickness absence longer than 14 days, categorized as yes/no, in the period 2020 to 2021, among participants who had been working in at least 1 of these years. The time period was chosen to fall after the 24-year Questionnaire completion, which occurred in 2019. Information on occupational status was obtained from the LISA register and referred to 1 month (November) each year. Diagnoses (*International Classification of Diseases, Tenth Revision* codes) linked to the first case of sickness absence were obtained from the Micro-Data for Analysis of the Social Insurance System (MiDAS database) held by the Swedish Social Insurance Agency.

Productivity losses related to sickness absence in 2020 and 2021. These were estimated from a societal perspective,[22] which involves the costs to society of the hypothetical lost production from when the individual was sickness absent from work. Society's loss of production was estimated using the human capital approach at the average cost of employment.[22,23] This was calculated by multiplying the number of net days with sickness absence (converted into months) by the sum of the average monthly salary in 2021 for the age group 25 to 34 years (3271 euro [EUR])[24] and the social security contribution from employers (31.42%).[25] The costs were presented in 2021 values in EUR using the 2021 exchange rate (1 EUR = 10.1485 SEK).

Definition of lifestyle factors and covariables

Body mass index (BMI) was calculated from height and weight measured at the clinical examination at age 24 years and categorized as underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), or obesity (≥30 kg/m^2). Among 577 individuals with missing information on measurements, self-reported information on BMI was obtained from 564 through the questionnaire.

Physical activity at age 24 years was based on the questionnaire-reported amount of vigorous (eg, lifting heavy weights, aerobics, or high-speed bicycling) and moderate (eg, bicycling at normal speed and carrying light objects) physical activity in the last 12 months. The means for the summer and winter seasons were calculated. Levels of physical activity were defined in accordance with the international physical activity questionnaire guidelines[26]: *High levels of physical activity*, greater than or equal to 7 h/wk of moderate to vigorous activity or greater than or equal to 3.5 h/wk of vigorous activity, and *low/moderate levels*, less than 7 h/wk of moderate to vigorous activity and less than 3.5 h/wk of vigorous activity.

Smoking, education level, and doctor-diagnosed depression (ever) were self-reported at the 24-year follow-up. Smoking was categorized as yes (daily smoking and occasional smoking) or no (past or no smoking).

Statistical analyses

Differences in background factors in relation to asthma were analyzed with χ^2 tests. Associations between asthma, asthma phenotypes, and any sickness absence in 2020 and 2021 were analyzed with logistic regression models. We included 1 crude model and 1 adjusted model. Confounders in the adjusted model were selected on the basis of directed acyclic graphs (see Figure E2 in this article's Online Repository at www.jaci-inpractice.org) and by evaluating their influence on the estimates through including them one by one in the logistic regression model. The final adjusted model included sex, birth year, education, and BMI status. Smoking, physical activity, dietary factors (soft drink and fast-food consumption), stress, and sleep did not significantly influence the association between asthma and sickness absence and were therefore not included in the final model. The analysis between asthma and sickness absence was further stratified by sex, BMI status (overweight/obesity vs normal weight/underweight), and physical activity level (high vs low/moderate). Interactions between asthma and sex, BMI status, and physical activity, respectively, were evaluated by including interaction terms in the regression model.

Several sensitivity analyses were performed. First, we included data on sickness absence from the year 2019, as described above. Next, the results were presented for the years 2019, 2020, and 2021 separately for those who were working the respective year (n = 1953, 2038, and 2218, respectively). The main analysis was further adjusted for distance work, for which data were available from a subpopulation at a later follow-up at age approximately 26 years. The analyses were further adjusted for self-reported doctor-diagnosed depression (ever).

The average costs in relation to asthma and asthma control were presented together with SDs and bias-corrected bootstrap-estimated 95% CIs with 2000 iterations.[27] Because of the nonnormally distributed data, differences between the groups were assessed using Wilcoxon rank-sum test, which is a nonparametric test suitable for data with a nonnormal distribution. The excess net days with sickness absence and excess productivity losses related to asthma were estimated through zero-inflated Poisson regression[28] adjusted for sex.

RESULTS

Description of the study population

The study population (n = 2391) consisted of 54.3% females. The mean age when answering the 24-year follow-up in the period 2016 to 2019 was 22.5 years (range, 21.5-25.2 years). At

age 24 years, 272 (11.4%) fulfilled the definition of asthma (see Table E2 in this article's Online Repository at www.jaci-inpractice.org). Among those with asthma, most (60%) had persistent asthma (asthma at both 16 and 24 years) and 32.3% had uncontrolled asthma. Moreover, 74.4% had an allergic asthma, whereas 39.9% had type 2 asthma (asthma with high eosinophils and/or high FENO). Most participants with asthma (63.7%) also had rhinitis (Table I).

Participants with asthma were more likely to be overweight than participants without asthma (36.2% vs 23.0%; $P = .001$) and had higher levels of physical activity. There were no differences in the proportions with male sex, post−secondary education, smoking, or self-reported depression (Table I).

Association between asthma and sickness absence

In total, 226 (9.5%) participants had at least 1 episode of sickness absence longer than 14 days in the year 2020 or 2021. Sickness absence was more common among participants with asthma than among those without asthma (15.1% vs 8.7%; $P = .001$). This result corresponded to a crude odds ratio (OR) of 1.86 (95% CI, 1.29-2.67) for the association between asthma and sickness absence, which remained in the adjusted models (OR_{adj}, 1.73; 95% CI, 1.19-2.51; see Table E3 in this article's Online Repository at www.jaci-inpractice.org). The association between asthma and sickness absence was similar among females (OR_{adj}, 1.74; 95% CI, 1.10-2.75) and males (OR_{adj}, 1.62; 95% CI, 0.83-3.18), with no significant interaction between sex and asthma ($P = .68$).

Figure 1 shows the associations between different asthma phenotypes and sickness absence (crude and adjusted estimates are presented in Table E3). Compared with participants with no asthma, those with persistent asthma had an increased risk of sickness absence (OR_{adj}, 1.95; 95 % CI, 1.20-3.15), which was not observed among those with adult-onset asthma. When investigating sickness absence in relation to asthma control, uncontrolled asthma was significantly associated with sickness absence (OR_{adj}, 1.93; 95% CI, 1.06-3.49), compared with no asthma. For controlled asthma, the estimate was lower and not statistically significant (OR_{adj}, 1.51; 95% CI, 0.94-2.43). For asthma phenotypes related to allergic sensitization and type-2 inflammation, the estimates were relatively similar across phenotypes. In investigations of asthma in combination with rhinitis, the association was significant only among those with both asthma and rhinitis (OR_{adj}, 2.00; 95% CI, 1.27-3.15), not among those with asthma but no rhinitis.

Role of lifestyle factors

When the prevalence of sickness absence was investigated in relation to asthma and overweight, sickness absence was found to be most prevalent in the group with both overweight and asthma (20.4%, n = 20), compared with 12.1% (n = 21) among those with asthma without overweight, 11.8% (n = 57) among those with overweight and no asthma, and 7.8% (n = 127) among those with neither overweight nor asthma. In contrast, similar proportions of sickness absence were observed among those with asthma and low versus high levels of physical activity (Table II). In the adjusted regression analyses, there was no significant interaction between asthma and overweight or physical activity. The association was significant only among those with overweight (OR_{adj}, 2.09, 95% CI, 1.17-3.71, compared with OR_{adj}, 1.55, 95% CI, 0.94-2.55, among those without overweight; Table II).

Sensitivity analyses

When the study period was extended (by including data from 2019), the association between asthma and sickness absence remained significant (OR_{adj} 1.68; 95% CI, 1.19-2.36). Relatively similar results were observed when analyzing the years 2019, 2020, and 2021 separately; however, the difference in sickness absence related to asthma was significant only in the year 2021 (see Table E4 in this article's Online Repository at www.jaci-inpractice.org). Adjusting for distance work had no major impact on the association between asthma and sickness absence in the subpopulation with information on this variable (OR_{adj}, 1.82, 95% CI, 1.14-2.92, compared with crude OR, 2.00, 95% CI, 1.27-3.15). When self-reported doctor-diagnosed depression was adjusted for, the association was slightly attenuated but remained statistically significant (OR_{adj}, 1.64; 95% CI, 1.12-2.42).

Estimated cost of sickness absence in relation to asthma

Table E5 in this article's Online Repository at www.jaci-inpractice.org summarizes the cost estimates of the productivity losses related to net days of sickness absence in the period 2020 to 2021 in relation to asthma and asthma control at 24 years. The mean net days among those with asthma was 9.1 days, compared with 6.6 days among those without asthma. Accordingly, the estimated productivity losses were significantly higher among those with asthma (1280 EUR compared with 933 EUR among those with no asthma; $P < .001$) and even higher among those with uncontrolled asthma (1973 EUR) ($P = .003$). Table III presents estimated excess costs related to asthma estimated through zero-inflated Poisson regression. The estimated average excess productivity losses in the period 2020 to 2021 were 369 EUR ($P < .001$) per person among individuals with asthma and 1117 EUR for individuals with uncontrolled asthma, compared with those without asthma. Investigating the years 2020 and 2021 separately, the estimated average annual excess productivity losses related to asthma were 508 EUR in 2020 while they were 140 EUR lower compared with those without asthma in 2021.

Causes of sickness absence

Diagnoses linked to the first case of sickness absence after the year 2020 in relation to asthma are presented in Table E6 in this article's Online Repository at www.jaci-inpractice.org. Among the 33 participants with asthma who had available information on diagnoses, 6 of 33 (18.2%) were registered as "diseases of the respiratory system," compared with 10 of 170 (5.9%) among those without asthma. In contrast, "mental and behavioral disorders" seemed to be more common among participants without asthma (60 of 170 [35%]) compared with among participants with asthma (7 of 33 [21.2%]).

DISCUSSION

In the present study based on 2391 young adults from a population-based cohort study, asthma was associated with higher sickness absence and related productivity losses. The association with sickness absence tended to be stronger for uncontrolled asthma, persistent asthma, and asthma combined with rhinitis, whereas no consistent differences were observed across phenotypes related to allergic sensitization or inflammation.

TABLE I. Description of the study population stratified by asthma at 24 y

Variable	No asthma 24 y	Asthma 24 y	*P* value*
Male sex (n = 2391)	980 (46.3)	112 (41.2)	.11
Post−secondary education*† (n = 2380)	764 (36.2)	108 (40.0)	.22
Smoking† (n = 2385)	448 (21.2)	51 (18.8)	.37
Overweight‡ (n = 2378)	484 (23.0)	98 (36.2)	<.001
High level of physical activity† (n = 1905)	990 (58.6)	141 (65.6)	.049
Depression, doctor-diagnosed† (n = 2310)	241 (11.8)	36 (13.7)	.36
Allergic sensitization (n = 1784)§	629 (40.1)	160 (74.4)	<.001
Type 2 inflammation (n = 1515)‖	289 (21.9)	77 (39.9)	<.001
Rhinitis (n = 2366)†	560 (26.7)	172 (63.7)	<.001

ppb, Parts per billion.
Values are n (%).
**P* values comparing asthma vs no asthma obtained through χ^2 tests.
†Self-reported at the 24-y follow-up.
‡Measured or self-reported at the 24-y follow-up.
§Measured at the 24-y follow-up.
‖Defined as high blood eosinophils ($\geq 0.3 \times 10^9$ cells/L) or high FENO (≥25 ppb) measured at the 24-y follow-up.

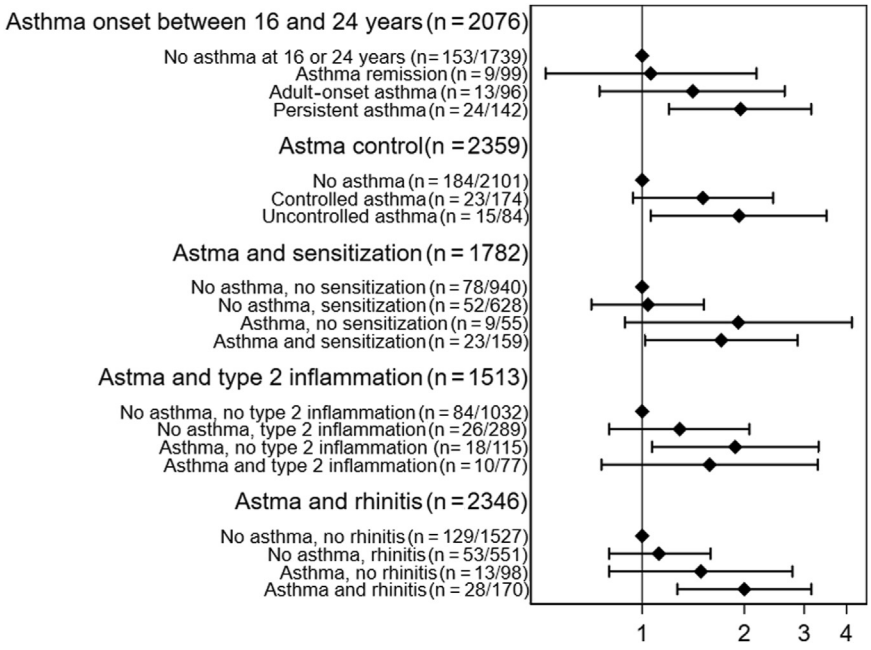

FIGURE 1. Adjusted associations between asthma phenotypes and sickness absence in the period 2020 to 2021, displayed as ORs with 95% CIs, analyzed with logistic regression models adjusted for sex, birth year, education, and BMI status. The numbers represent the number of cases with sickness absence out of the total numbers in each category.

Moreover, the association tended to be stronger among those with overweight, although the interaction between overweight and asthma did not reach significance. Although far from all sickness absence were related to asthma, analyses of diagnoses linked to each sickness absence case showed that diseases of the respiratory system tended to be more common among those with asthma, whereas mental and behavioral disorders tended to be less common. The higher levels of sickness absence associated with asthma were then quantified in terms of the productivity losses to society that they entail.

The results are in line with previous studies observing higher rates of sickness absence, disability pension, unemployment, or health-related periods of work interruption among patients with asthma.[5-8] Like our study, previous studies have shown that poor asthma control and disease severity are associated with higher sickness absence compared with well-controlled and less severe asthma.[5,9] For example, a large Danish register-based study including 60,534 patients with asthma aged 18 to 45 years found that uncontrolled asthma, defined on the basis of short-acting β-agonist use and exacerbations, was associated

TABLE II. Associations between asthma and sickness absence in the period 2020 to 2021, analyzed with logistic regression models stratified by physical activity and overweight at 24 y

	Any sickness absence 2020 and 2021						
	Low/moderate physical activity			High physical activity			
Asthma status	n (%)	OR*	95% CI	n (%)	OR*	95% CI	*P* value interaction
No asthma (n = 1690)	47 (6.7)	Reference	—	89 (9.0)			
Asthma (n = 215)	9 (12.2)	1.90	0.88-4.09	17 (12.1)	1.35	0.77-2.38	.47
	No overweight			Overweight			
	n (%)	OR	95% CI	n (%)	OR†	95% CI	*P* value interaction
No asthma (n = 2107)	127 (7.8)	Reference	—	57 (11.8)	Reference	—	
Asthma (n = 271)	21 (12.1)	1.55	0.94-2.55	20 (20.4)	**2.09**	**1.17-3.71**	.50

Bold represent statistically significant associations.
*Adjusted for sex, birth year, education, and BMI status.
†Adjusted for sex, birth year, and education.

TABLE III. Excess net days with SA in 2020 and 2021 and estimated excess costs related to asthma in EUR estimated through zero-inflated Poisson regression adjusted for sex

	Excess net days with SA in 2020 and 2021		Excess cost of SA in 2020 and 2021 (EUR)	
Comparison group	β	95% CI	β	95% CI
Asthma vs no asthma	2.6	−1.9 to 9.0	369.4	−265.3 to 1266.2
Uncontrolled asthma vs no asthma	7.9	−0.85 to 22.7	1117.4	−455.4 to 2690.2
Uncontrolled asthma vs controlled asthma	8.0	−1.16 to 18.1	1125.4	−218.4 to 2469.2

SA, Sickness absence.

with higher sick leave compared with controlled asthma.[5] In our study, uncontrolled asthma was found to yield higher net days of sickness absence and consequently higher productivity losses compared with no asthma. Previous studies have also shown that sick leave may have negative consequences for the individual,[11,12] highlighting the importance of asthma prevention and control, for both the individual and the society.

In the present study, the association between asthma and sickness absence was stronger in persistent than in adult-onset asthma. This is in contrast to other studies, which have observed a stronger association with work disability in adult-onset asthma than in childhood-onset asthma among Danish and Finnish adults aged 20 to 44 years and 20 to 65 years, respectively.[7,29] In these studies, the authors argued that the stronger association with adult-onset asthma could be explained by a more severe disease, less adaptation, reduced compliance to treatment, differing career choices, and a higher proportion of work-related asthma triggered by harmful occupational exposures.[7,29] In contrast, persistent asthma is generally more strongly associated with allergy and rhinitis,[30] which was found to contribute to higher sickness absence. Moreover, persistent asthma has been associated with poorer lung function and more severe disease among young adults,[31] which may explain the stronger association observed in our sample.

To our knowledge, no previous studies have investigated the role of other asthma phenotypes such as allergic asthma and type 2 asthma. We hypothesized that the association should have been stronger among asthma with sensitization and type 2 asthma because these are more linked with concurrent allergic symptoms. However, non−type 2 asthma may be a more difficult-to-treat phenotype and has also been linked to obesity, which have been associated with increased sickness absence.[15]

Few studies have investigated factors that may influence sickness absence among patients with asthma. In the present study, sickness absence was highest among participants with both asthma and overweight (20.4% compared with 12.1% among those with asthma and no overweight). Moreover, the association between asthma and sickness absence was observed only among those with overweight in the stratified analyses. Although no significant interaction was observed between asthma and overweight—potentially due to low power—the results suggest that the association may be stronger in case of overweight. Physical activity, however, was not related to sickness absence among participants with asthma. These results are somewhat different from those of a Norwegian cross-sectional study, which found increased odds of sick leave related to asthma but not to increased BMI, and no interaction between asthma and BMI status in relation to sick leave longer than 14 days.[32]

The COVID-19 pandemic may have affected those with asthma differently than those without asthma. This was also suggested by the cost analyses, with excess productivity losses related to sickness absence in 2020 among those with asthma, whereas the opposite was seen in 2021. This may be explained by fear of infection among those with asthma in the beginning of the pandemic and less acceptance of asthma symptoms such as coughing in the public. Therefore, we extended the time period to include sickness absence data also in 2019, as a sensitivity analysis. We also analyzed the years 2019, 2020, and 2021 separately, with relatively similar results. Moreover, we

performed a sensitivity analysis adjusting for distance work, because the possibility to work from home may enable working during milder sickness periods, especially during the pandemic when people with mild symptoms also were asked to stay home. Lastly, we adjusted for depression, because this may be related to both asthma and sickness absence. However, the results remained significant in all these sensitivity analyses, suggesting that neither the COVID-19 pandemic, distance work, nor depression fully explains the observed association.

The main strength of the study is the unique combination of detailed information on asthma phenotypes, including longitudinal data and objective markers of disease, with objective register-based information on sickness absence, which allowed investigations of aspects that are not possible in nationwide registers. Another strength is the estimation of productivity losses from a societal perspective, which provides evidence on the economic impact for society of not addressing asthma health needs. One limitation is the relatively small sample size compared with fully register-based studies, which limited the power to detect smaller differences, especially in the stratified analyses. Another limitation is that the register only included sickness absence longer than 14 days, and we therefore could not investigate short-term sickness absence and related productivity losses, which may be more strongly connected to asthma.[33] Moreover, we were unable to adjust for type of occupation due to few individuals in each occupation. Lastly, the productivity loss estimations were not adjusted for potential confounders due to the small numbers of individuals in the subgroups. The differences in productivity losses between those with and without asthma should therefore be interpreted with caution and investigated further.

CONCLUSIONS

Asthma—especially persistent asthma, uncontrolled asthma, and asthma in combination with rhinitis—may be associated with more sickness absence. Asthma may also be associated with higher productivity losses related to sickness absence. Achieving better asthma control and moving toward normal weight may reduce sickness absence among individuals with asthma and overweight, though more studies on lifestyle factors in relation to sickness absence and asthma are needed. The results show the importance of asthma prevention and management to reduce the negative health consequences and costs of asthma. Moreover, health care providers need to offer the appropriate care, support, and treatment for patients with asthma to maintain asthma control and reduce concurrent allergic symptoms.

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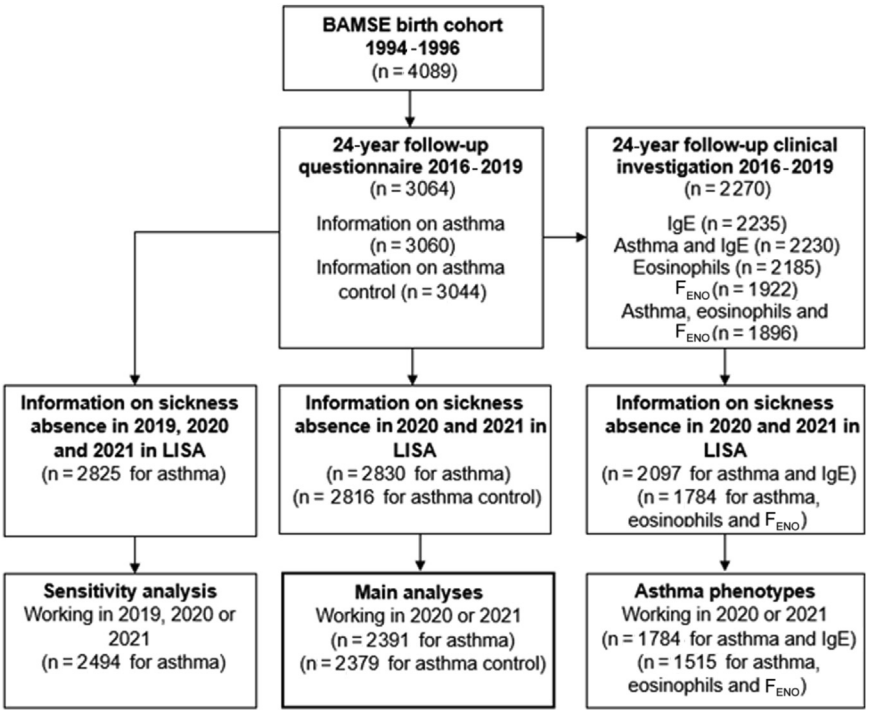

FIGURE E1. Flowchart of the included study populations.

TABLE E1. Description and definitions of the included asthma phenotypes

Asthma phenotype	Description and definition	Categories
Asthma onset and remission	Asthma onset and remission between 16 and 24 y categorized into 4 groups	• No asthma (no asthma at age 16 or 24 y) • Adult-onset asthma (asthma at age 24 y, but not at 16 y) • Persistent asthma (asthma at both age 16 and 24 y) • Asthma remission (asthma at age 16 y but not 24 y)
Asthma control	Asthma control at 24 y. Uncontrolled/partly controlled asthma was defined as fulfilling the definition of asthma in combination with at least 1 of the following symptoms as described in the modified Global Initiative for Asthma definition[E1]: breathing difficulties at least 2 times per week in the last 4 wk, any night-time awakening due to breathing difficulties in the last 4 wk, activity limitation due to breathing difficulties in the last 4 wk, and use of a symptom reliever at least 2 times/wk	• No asthma • Controlled asthma • Uncontrolled asthma
Asthma in combination with sensitization	Asthma in combination with allergic sensitization at 24 y. Allergic sensitization was defined as a positive ($\geq$0.35 kU_A/L) Phadiatop (cat, dog, horse, timothy, birch, mugwort, *Dermatophagoides pteronyssinus* [house dust mite] and *Cladosporium* [mold]) or Fx5 (milk, egg, soy, peanut, cod, fish, wheat) test result	• No asthma, no sensitization • No asthma, sensitization • Asthma, no sensitization • Asthma and sensitization
Asthma in combination with type 2 inflammation	Asthma in combination with high blood eosinophils and/or FENO at 24 y (using the cutoffs $\geq 0.3 \times 10^9$ cells/L and $\geq$25 ppb, respectively, to define high levels[E2])	• No asthma with low FENO and low eosinophils • No asthma with high FENO and/or high eosinophils • Asthma with low FENO and low eosinophils • Asthma with high FENO and/or high eosinophils
Asthma in combination with rhinitis	Asthma in combination with rhinitis at 24 y. Rhinitis was defined as symptoms from the eyes or nose due to furred animals or pollen (without having a cold/flu) in the last 12 mo, based on the 24-y questionnaire	• No asthma, no rhinitis • No asthma, rhinitis • Asthma, no rhinitis • Asthma and rhinitis

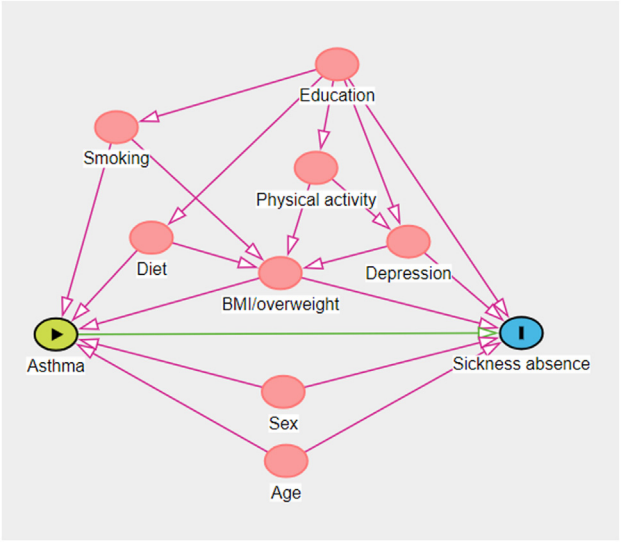

FIGURE E2. Directed acyclic graph showing possible associations between the main exposure, outcome, and potential confounders. Created with DAGitty (https://www.dagitty.net/).

TABLE E2. Prevalence of asthma, rhinitis, and asthma phenotypes at age 24 y in the study population

Variable	Females	Males	Total	*P* value*
Asthma at 24 y				.11
No	1139/1299 (87.7)	980/1092 (89.7)	2119/2391 (88.6)	
Yes	160/1299 (12.2)	112/1092 (10.3)	272/2391 (11.4)	
Rhinitis at 24 y				.50
No	882/1288 (68.5)	752/1078 (69.8)	1634/2366 (69.1)	
Yes	406/1288 (31.5)	326/1078 (30.2)	732/2366 (30.9)	
Asthma onset between 16 and 24 y				.09
No asthma at 16 or 24 y	958/1145 (83.7)	796/948 (84.0)	1754/2093 (83.8)	
Asthma remission	44/1145 (3.8)	55/948 (5.8)	99/2093 (4.7)	
Adult-onset	58/1145 (5.1)	38/948 (4.0)	96/2093 (4.6)	
Persistent asthma	85/1145 (7.4)	59/948 (6.2)	144/2093 (6.9)	
Asthma control at 24 y				.23
No asthma	1139/1293 (88.1)	980/1086 (90.2)	2119/2379 (89.1)	
Controlled asthma	103/1293 (8.0)	73/1086 (6.7)	176/2379 (7.4)	
Uncontrolled asthma	51/1293 (3.9)	33/1086 (3.0)	84/2379 (3.5)	
Asthma and sensitization at 24 y				<.001
No asthma, no sensitization	592/1023 (57.9)	348/761 (45.7)	940/1784 (52.7)	
No asthma, sensitization	296/1023 (28.9)	333/761 (43.8)	629/1784 (35.3)	
Asthma, no sensitization	43/1023 (4.2)	12/761 (1.6)	55/1784 (3.1)	
Asthma and sensitization	92/1023 (9.0)	68/761 (8.9)	160/1784 (9.0)	
Asthma and type 2 inflammation				<.001
No asthma, no type 2 inflammation	632/874 (72.3)	401/641 (62.6)	1033/1515 (68.2)	
No asthma, type 2 inflammation	123/874 (14.1)	166/641 (25.9)	289/1515 (19.1)	
Asthma, no type 2 inflammation	78/874 (8.9)	38/641 (5.9)	116/1515 (7.7)	
Asthma and type 2 inflammation	41/874 (4.7)	36/641 (5.6)	77/1515 (5.1)	
Asthma and rhinitis				.20
No asthma, no rhinitis	830/1288 (64.4)	706/1078 (65.5)	1536/2366 (64.9)	
No asthma, rhinitis	299/1288 (23.2)	261/1078 (24.2)	560/2366 (23.7)	
Asthma, no rhinitis	52/1288 (4.0)	46/1078 (4.3)	98/2366 (4.1)	
Asthma and rhinitis	107/1288 (8.3)	65/1078 (6.0)	172/2366 (7.3)	

Values are n/N (%).
*P values obtained by χ^2 tests.

TABLE E3. Associations between asthma phenotypes and sickness absence in 2020-2021, analyzed with logistic regression models

	Any sickness absence 2020-2021			
	Crude		Adjusted	
Asthma phenotype	**OR**	**95% CI**	**OR***	**95% CI**
Asthma 24 y (n = 1875 and 1865)				
No asthma	Reference	—	Reference	—
Asthma	**1.86**	**1.29-2.67**	**1.73**	**1.19-2.51**
Asthma onset between 16 and 24 y (n = 1642 and 1634)				
No asthma at 16 or 24 y	Reference	—	Reference	—
Asthma remission (16 y, not 24 y)	1.04	0.51-2.10	1.06	0.52-2.17
Adult-onset (24 y, not 16 y)	1.63	0.89-2.99	1.41	0.75-2.63
Persistent asthma (16 and 24 y)	**2.07**	**1.30-3.31**	**1.95**	**1.20-3.15**
Asthma control 24 y (n = 1866 and 1856)				
No asthma	Reference	—	Reference	—
Controlled asthma	1.57	0.99-2.50	1.51	0.94-2.43
Uncontrolled asthma	**2.27**	**1.27-4.05**	**1.93**	**1.06-3.49**
Asthma and sensitization 24 y (n = 1409 and 1408)				
No sensitization, no asthma	Reference	—	Reference	—
No asthma, sensitization	1.00	0.69-1.44	1.04	0.71-1.52
Asthma, no sensitization	**2.16**	**1.02-4.58**	1.92	0.89-4.15
Asthma and sensitization	**1.86**	**1.13-3.06**	**1.71**	**1.02-2.87**
Asthma and T_H2 inflammation (n = 1205 and 1204)				
No asthma, no type 2 inflammation	Reference	—	Reference	—
No asthma, type 2 inflammation	1.12	0.70-1.77	1.29	0.80-2.07
Asthma, no type 2 inflammation	**2.08**	**1.20-3.60**	**1.88**	**1.07-3.31**
Asthma and type 2 inflammation	1.69	0.84-3.40	1.58	0.76-3.29
Asthma and rhinitis (n = 1855 and 1845)				
No asthma, no rhinitis	Reference	—	Reference	—
No asthma, rhinitis	1.16	0.83-1.62	1.13	0.80-1.59
Asthma, no rhinitis	1.67	0.91-3.07	1.49	0.80-2.77
Asthma and rhinitis	**2.12**	**1.36-3.30**	**2.00**	**1.27-3.15**

Bold represent statistically significant estimates.
*Adjusted for sex, birth year, education, and BMI status.

TABLE E4. Prevalence of sickness absence in 2019, 2020, and 2021 in relation to asthma at 24 y among participants who were working at the respective year

	Any sickness absence (yes/no), n (%)		
Year	**No asthma 24 y**	**Asthma 24 y**	***P* value***
2019 (n = 1953)	82 (4.8)	18 (7.5)	.071
2020 (n = 2038)	113 (6.3)	22 (9.6)	.054
2021 (n = 2218)	96 (4.9)	26 (10.3)	<.001

**P*-value obtained by X^2 tests.

TABLE E5. Net days with SA in 2020 and 2021 and estimated costs in EUR

	Net days with SA in 2020 and 2021		Cost of SA in 2020 and 2021 (EUR)		Excess costs in 2020 and 2021 (EUR)		
Variable	**Mean**	**95% CI†**	**Mean**	**95% CI†**	**Mean**	**95% CI†**	***P* value***
Asthma at 24 y							
No (n = 2119)	6.6	5.0 to 8.9	932.5	704.2 to 1207.4	Reference	—	
Yes (n = 272)	9.1	5.5 to 14.1	1280.4	770.8 to 1990.6	347.9	−205.2 to 1132.4	<.001
Asthma control at 24 y							
No asthma (n = 2119)	6.6	5.0 to 8.6	932.5	704.2 to 1207.4	Reference	—	
Controlled asthma (n = 176)	6.3	3.3 to 11.2	889.5	464.5 to 1578.4	−43.0	−598.0 to 644.6	.06
Uncontrolled asthma (n = 84)	14.0	5.3 to 25.3	1972.7	752.8 to 3567.6	1040.2	−78.4 to 2949.4	.003

**P* value for difference in costs obtained through Wilcoxon rank-sum tests.
†Bootstrap-estimated bias-corrected CIs, 2000 iterations.

TABLE E6. Diagnoses linked to the first case of sickness benefit in 2020-2021 among participants in the study population with and without asthma at 24 y

Diagnose code	**No asthma 24 y (n = 170), n (%)**	**Asthma 24 y (n = 33), n (%)**
Missing	25 (14.7)	5 (15.2)
A/B—Certain infectious and parasitic diseases	3 (1.8)	1 (3.0)
C—Neoplasms	1 (0.6)	0 (0.0)
E—Endocrine, nutritional, and metabolic diseases	1 (0.6)	0 (0.0)
F—Mental and behavioral disorders	60 (35.0)	7 (21.2)
G—Diseases of the nervous system	3 (1.8)	0 (0.0)
I—Diseases of the circulatory system	4 (2.4)	1 (3.0)
J—Diseases of the respiratory system	10 (5.9)	6 (18.2)
K—Diseases of the digestive system	3 (1.78)	0 (0.0)
L—Diseases of the skin and subcutaneous tissue	1 (0.6)	0 (0.0)
M—Diseases of the musculoskeletal system and connective tissue	14 (8.02)	3 (9.1)
O—Pregnancy, childbirth, and the puerperium	13 (7.6)	3 (9.1)
R—Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified	8 (4.7)	1 (3.0)
S/T—Injury, poisoning, and certain other consequences of external causes	13 (7.6)	4 (12.1)
U07—Codes for special purposes	10 (5.9)	2 (6.1)
Z—Contacts with health care for special measures and care	1 (0.6)	0 (0.0)

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