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Socioeconomic status is associated with healthcare seeking behaviour and disease burden in young adults with asthma – A nationwide cohort study

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Abstract

Introduction: Specialist management of asthma has been shown to associate with socioeconomic status (SES). However, little is known about the influence of SES on care burden in universal healthcare settings.

Methods: Patients aged 18–45 years using inhaled corticosteroids (ICS) were followed in national databases. Impact of asthma was investigated using negative binomial regression adjusted for age, sex, comorbidity, and GINA 2020 Step. Uncontrolled asthma was defined as >600 annual SABA puffs, ≥2 prednisolone courses and/or ≥1 hospitalization.

Results: A total of 60,534 (55% female, median age 33 (IQR 25–39)) patients were followed for 10.1 years (IQR 5.2–14.3)). Uncontrolled asthma resulted in 6.5 and 0.51 additional annual contacts to primary care and pulmonologists, respectively. Unscheduled and primary care burden was dependent on SES, increasing with rural residence, lower education, income and receiving welfare. Differences in planned respiratory care were slight, only seen among divorced, low income- or welfare recipients. Lower SES was consistently associated with an increased utilization of SABA and prednisolone. No dose–response relationship between ICS use and SES could be identified.

Conclusion: Lower SES in asthma is a risk factor for a predominance of unscheduled care and adverse outcomes, warranting further attention to patients' background when assessing asthma care.

Introduction

The high prevalence of asthma and associated variability in clinical manifestations pose a tremendous burden both for patients and healthcare systems on a worldwide scale.[1] Disease control, where patients experience few to none day-to-day symptoms, no restrictions in daily activities and are free from exacerbations, is the outmost goal of asthma management.[2] Treatment with inhaled corticosteroids (ICS) alone or in combination with a second controller makes disease control a realistic goal for the majority of patients.[2] However, despite the existence of an effective preventive treatment, uncontrolled asthma still poses a significant source of societal burden, morbidity and even mortality.[1,2]

Socioeconomic status (SES) is a well-established risk factor for developing chronic diseases based on associated physical and health literacy-related risk factors such as smoking, diet, workplace- and home exposures.[3,4] Lower SES has previously been associated with an increased risk of both incident and prevalent asthma,[5] and it is well established that

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indicators of SES, such as education and ethnicity, are present in various outcomes such as exacerbations.[6,7] In terms of ICS treatment for asthma in a Danish context, the odds of being treated with ICS is seemingly dependent income and education,[8] and even in the most severely affected patients, access to specialist care depend on their SES.[9]

A well-established link between health literacy and SES exists in asthma,[10] and a recent nationwide Welsh study highlights the increased burden of poor asthma outcomes depending on residential area deprivation.[11] Yet other factors seem important, as previous research has suggested that there exists a differential effect of SES on asthma outcomes depending on place of care, type of healthcare resource utilized, an effect seemingly independent of the larger organization of healthcare systems, such as insurance-based or universal access.[6] However, due to the common use of aggregate indexes for SES, little is known regarding what individual factors of SES are the main determinants of healthcare resource utilization (HRU) and, as much of the research on the topic is based on secondary care, the additional burden to primary care by asthma.

In the present study, utilizing a nationwide cohort of all individuals with actively treated asthma and universal linkage between Danish healthcare databases, we aimed to describe the HRU, healthcare-seeking behaviour and its interplay with SES in young adult asthma patients in comparison to the background population.

Methods

The REASSESS cohort

The REASSESS Danish Asthma cohort is built on the nationwide registers the Danish National Patient Register (NPR), the Danish Clinical Quality Program – Asthma (DrAstma), Statistics Denmark, and the Danish National Database of Reimbursed Prescriptions (DNDRP).

The cohort includes all Danish individuals aged 18–45 (at cohort entry, date of first redeemed canister of ICS) redeeming at least two ICS canisters in a calendar year during the case identification period of 2014–2018. Statistics Denmark provided a 1:1 age and sex-matched background population, based on a unique, random selection of individuals not fulfilling the cohort inclusion criteria.

Place of asthma management is based on registration in the DrAstma database, with registered individuals considered as managed in secondary care.

Ethics and data sharing

Study approvals were granted by the Greater Capital Region of Copenhagen's Data Safety Board (P-2019–142) and the Greater Capital Region of Copenhagen's Scientific Ethics Committee (H-19042597). Data is available upon reasonable request. Approval from data sources and data safety boards may be required as per Danish law.

Medication dose, asthma severity and control definitions

GINA 2020 guidelines were used to define treatment steps,[2] and ICS dose were calculated as average daily ICS dose exposure during the study period based in redeemed prescriptions. Doses reported as standard-particle beclomethasone dipropionate equivalents as follows: Below low (<200 mcg/day), Low (200-599 mcg/day), Moderate (600-1200 mcg/day) and High (>1200 mcg/day) doses .[2]

Possible severe asthma was defined according to the International Severe Asthma Registry and GINA 2020 guidelines as GINA 2020 Step 4 (with either at least two systemic corticosteroid prescriptions or ≥1 respiratory (ICD-10 code DJ) hospitalization) or GINA Step 5 (regardless of exacerbations).[12] A moderate exacerbation was defined as a prescription of at least 37.5 mg an oral corticosteroid (OCS) (prednisolone) for 5 days or more. A severe exacerbation was defined as a respiratory hospitalization with ICD-10 code DJ. Excessive SABA use was defined as redemption of at least 600 annual doses of Short-acting beta$_2$ agonists (SABA) during the inclusion period.[13]

Comorbidities

A modified, non-respiratory Charlson Comorbidity Index ("Charlson score") was used to describe the burden of comorbidity. Updated weights by Quan et al.[14,15] were used for calculation.

Statistics and healthcare resource utilization

Descriptive data is presented as median (interquartile range, IQR) or n (%). For groupwise comparisons Wilcoxon rank-sum test or Chi-squared test of independence were used depending on continuous or categorical data.

Healthcare burden was assessed during a retrospective period (a graphical overview is available in Figure 1) defined as:

- Retrospective resource utilization period start: Date of first ICS container redemption from 1/1/2004-31/12/2018 unless below the age 18 as of 1/1/2004, where cohort entry was defined as first redemption after the day of the 18th birthday.
- Retrospective resource utilization period end: 31/12/2018 unless censored by 1) death or 2) emigration. For controls/background population, observation

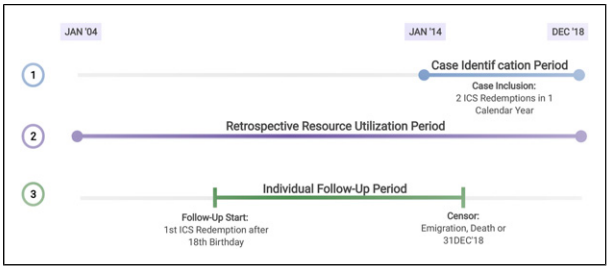

Figure 1. Graphical overview of 1) Identification and inclusion of patients to the REASSESS cohort, 2) Span of the retrospective resource utilization period and 3) Creation of patient-level individual follow-up periods.

periods are set to the matching asthma patient's observational period.

Annual HRU is presented as incidence rates (IR) as annualised number of contacts with 95% confidence intervals (CI) based on bivariable negative binomial regression. Relative increases in HRU between different markers of SES was performed using multivariable negative binomial regression with observational time used as the offset variable and adjustment for covariates age, sex, GINA 2020 Treatment Step and comorbidity. Zero-inflated and Hurdle models were fitted to ensure uniform performance with no significant variation in estimates or CIs. Results are presented as incidence rate ratios (IRR) with accompanying 95% CIs.

Markers of SES used for analyses were civil status, area of residence, level of education, annual income, workforce attachment and worker designation. For detailed definitions, please see.[16]

Burden of asthma in primary care

Healthcare resource utilisation in primary care was defined as: General practice – any contact to general practice during retrospective period – or Other – any contact to the primary care sector, such as physiotherapists, psychologists etc. Of note, Danish nationwide registries do not allow for differentiation between scheduled/unscheduled or respiratory/non-respiratory contacts in primary care.

Burden of asthma in secondary care

Healthcare resource utilisation in secondary care was defined as Outpatient visits, Emergency Department (ED) contacts or Hospital admissions – either Respiratory (ICD-10 group DJ or R04-07 for ED contacts, ICD-10 DJ for hospital admissions) or Non-respiratory as coded in the NPR. Due to issues with access to secondary care NPR data after 2017, analyses in secondary care are limited to data between 2004–2017 and observational periods have been adjusted accordingly.

Socioeconomic status and asthma healthcare seeking behaviour

Investigated as the relative number of redeemed doses of ICS, SABA and OCS during individual follow-up periods in adjusted regression models as described above.

R 4.1 (The R Foundation, AU) and the MASS-package[17] was used for statistical analyses. p-values ≤ 0.05 were considered to be statistically significant. Figures created using BioRender or ggplot2.[18]

Results

The present study comprises 60,534 Danish asthma patients aged 18–45 currently on ICS treatment during 2014–2018 followed retrospectively for up to 15 years in national registries. The median age at the end of the study period was 33 (IQR 25, 39) and 55% of patients were female. Median follow-up time was 10.1 years (IQR 5.2, 14.3) for a total of 1.148.669 person-years (Table 1).

Of asthma patients included, 19% fulfilled the criteria for being uncontrolled and 5.7% were classified as having possible severe asthma. An overview of asthma treatment and GINA 2020 steps is provided in Table 1.

Burden of asthma in primary care

A total of 12,375,858 primary care visits were registered during the observation period, of which 8,960,924 (72,4%) were contacts to general practitioners (GP). Close to all (97–100%) asthma patients and controls had at least one contact to primary care during the study period, yet the number of annual contacts to GPs were significantly higher in mild-to-moderate (IR 8.91 (8.86–8.97) and possible severe asthma (IR 12.80 (12.46–13.14)), versus 5.52 (5.48–5.55) annual contacts for the background population (Figure 2(a)). Similar increases were seen when stratifying according to controlled and uncontrolled asthma versus the background population (Figure 2(b)). An overview of contact prevalence and unadjusted annual contacts can be found in Table 2.

In adjusted models, mild-to-moderate and possible severe asthma saw relative increases in GP contacts of IRR 1.64 (1.62–1.65) and 2.27 (2.22–2.33), respectively. Similar numbers were seen for non-GP primary care contacts (Table 3).

Burden of asthma in secondary care

Non-respiratory contacts were seen in 26–48% of individuals in the background population, whereas 4–5% of the background population had a respiratory secondary care

Table 1. Demographics of 60,534 patients with actively treated asthma and an age- and sex matched control group followed for up to 15 years.

Demographics	Controls, *N* = 60,534[a]	Asthma cohort, *N* = 60,534[a,b]	*p*-value
Age	33 (25, 38)	33 (25, 38)	>0.9
Female	33,056 (55%)	33,056 (55%)	>0.9
Education level			<0.001
Primary and basic education	16,979 (28%)	17,929 (30%)	
Vocational training	17,909 (30%)	16,950 (28%)	
Higher education	24,788 (42%)	25,250 (42%)	
Missing	858	405	
Charlson score ≥2	284 (0.5%)	486 (0.8%)	<0.001
Secondary care asthma management		10,694 (18%)	*N*/A
Uncontrolled asthma		11,531 (19%)	*N*/A
Possible severe asthma		3,475 (5.7%)	*N*/A
GINA 2020 step			*N*/A
Step 1		25,497 (42%)	
Step 2		13,092 (22%)	
Step 3		13,411 (22%)	
Step 4		6,005 (9.9%)	
Step 5		2,529 (4.2%)	
Daily exposed inhaled corticosteroid dose			*N*/A
Below low		25,497 (42%)	
Low		21,911 (36%)	
Moderate		9,380 (15%)	
High		3,746 (6.2%)	

[a]Statistics presented: n (%); median (IQR).
[b]Statistical tests performed: Wilcoxon rank-sum test; chi-square.

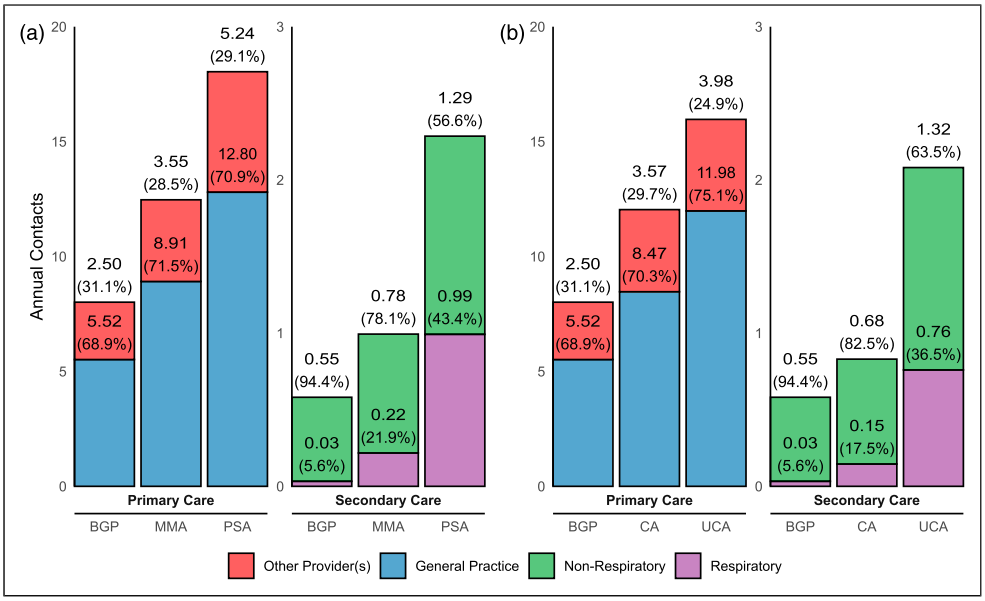

Figure 2. Annualized healthcare resource utilization for 60,534 actively treated asthma patients stratified by A) mild-to-moderate asthma (MMA) and possible severe asthma (PSA) or B) controlled (CA) and uncontrolled asthma (UCA), as well as an age- and sex-matched background population (BGP).

Table 2. Healthcare resource utilization during 15 years of 60,534 young adults with actively treated asthma and an age- and sex-matched control group, estimated using negative binomial regression.

Healthcare resource utilization	Controls, *N* = 60,534[a]	Mild-to-moderate asthma, *N* = 57,059[a]	Possible severe asthma, *N* = 3,475[a]
Primary care HRU			
General practitioner	58,424 (97%)	56,189 (98%)	3,467 (100%)
Annual contacts	5.52 (5.48–5.55)	8.91 (8.86–8.97)	12.80 (12.46–13.14)
Other	54,554 (90%)	53,762 (94%)	3,405 (98%)
Annual contacts	2.50 (2.47–2.52)	3.55 (3.52–3.59)	5.24 (5.05–5.44)
Of which dental care	22.9%	17.6%	13.0%
Of which physiotherapist or chiropractor	44.4%	45.1%	52.9%
Of which primary care specialist	23.6%	26.9%	24.5%
Of which psychologist or psychiatrist	8.8%	10.0%	9.1%
Of which other care providers	0.3%	0.3%	0.5%
Secondary care HRU			
Respiratory outpatient care	2,816 (4.7%)	12,040 (21%)	1,803 (52%)
Annual visits	0.01 (0.01–0.01)	0.13 (0.13–0.14)	0.47 (0.42–0.54)
Non-respiratory outpatient care	29,092 (48%)	32,116 (56%)	2,616 (75%)
Annual visits	0.29 (0.29–0.30)	0.40 (0.40–0.41)	0.62 (0.58–0.66)
Respiratory emergency care	2,690 (4.4%)	6,443 (11%)	850 (24%)
Annual visits	0.01 (0.01–0.01)	0.02 (0.02–0.02)	0.05 (0.05–0.06)
Non-respiratory emergency care	28,139 (46%)	30,454 (53%)	2,356 (68%)
Annual visits	0.11 (0.11–0.12)	0.16 (0.16–0.16)	0.21 (0.20–0.22)
Respiratory hospitalization	2,469 (4.1%)	7,245 (13%)	1,523 (44%)
Annual hospitalizations	0.01 (0.01–0.01)	0.03 (0.03–0.03)	0.17 (0.15–0.19)
Non-respiratory hospitalization	15,896 (26%)	18,293 (32%)	1,729 (50%)
Annual hospitalizations	0.06 (0.06–0.06)	0.10 (0.10–0.10)	0.19 (0.18–0.20)

[a]Statistics presented: any contact during study period – n (%); annual contacts (95% CI).

Table 3. Relative healthcare resource utilization among 60,534 young adults with actively treated asthma and background population controls adjusted for age, sex, education level and comorbidity estimated using negative binomial regression and stratified by asthma severity.

Relative healthcare resource utilization	Controls, N = 60,534[a]	Mild-to-moderate asthma, N = 57,059[a]	Possible severe asthma, N = 3,475[a]
Primary care contacts			
General practice	Ref	1.64 (1.62–1.65)	2.27 (2.22–2.33)
Other providers	Ref	1.43 (1.41–1.45)	2.01 (1.93–2.08)
Secondary care contacts			
Outpatient care			
Respiratory	Ref	5.65 (5.42–5.88)	16.47 (15.26–17.79)
Non-respiratory	Ref	1.38 (1.36–1.40)	1.94 (1.85–2.02)
Emergency care			
Respiratory	Ref	3.27 (3.11–3.43)	8.93 (8.07–9.89)
Non-respiratory	Ref	1.35 (1.33–1.37)	1.80 (1.73–1.88)
Hospitalizations			
Respiratory	Ref	4.46 (4.24–4.69)	23.69 (21.49–26.17)
Non-respiratory	Ref	1.47 (1.43–1.51)	2.61 (2.45–2.79)

[a]Statistics presented: Adjusted Incidence Rate Ratios (95% Confidence Intervals).

contact. In asthma, respiratory contacts were relatively common and increased with severity.

In adjusted analyses, mild-to-moderate and possible severe asthma saw increases across all types of secondary care contacts, especially respiratory. Notably, even non-respiratory contacts were increased according to asthma severity, with IRRs ranging from 1.35 (1.33–1.37) to 2.61 (2.45–2.79), depending on contact type (Table 3).

Influence of socioeconomic status on respiratory care healthcare seeking behaviour

To investigate the differential behaviours across SES on healthcare seeking behaviours towards respiratory care, adjusted relative incidence were calculated for six different measures of SES (Figure 3).

In terms of primary care, the increases in GP consultation rates were seen with most markers of low/poor SES such as rural residence, vocational or basic education, lower income or being outside the labour force. Notable exceptions were being married (IRR 1.08 (1.06–1.11)) or separated (IRR 0.89 (0.88–0.90)) (Figure 3).

For scheduled respiratory outpatient care, fewer variations and smaller effects depending on SES parameters were seen. Factors associated with increased scheduled care were being separated, low income and being outside the labour force (Figure 3).

Significant increases in unscheduled respiratory care were seen with lower SES parameters such as rural residence, vocational or basic education, decreasing level of income and being outside the labour force. Being separated was associated with lower rates of unscheduled respiratory care at IRR 0.91 (0.86–0.96) (Figure 3).

Interplay of socioeconomic status and asthma control

When assessing ICS use, no dose–response relationship was found across all six measures of SES. However, those with vocational or primary/basic education only had significantly lower rates of ICS use than patients with higher education (IRR 0.89 (0.88–0.90) and IRR 0.92 (0.91–0.94), respectively. Being married, living in non-metropolitan areas, moderate to low income and manual labour were all associated with slightly lower use of ICS (Figure 4).

In contrast to ICS, both OCS and SABA use were clearly associated with markers of lower SES such as with transfer income and primary/basic education demonstrating the strongest associations (Figure 4).

Discussion

In the present study, we've demonstrated that asthma – even well controlled asthma – represents an additional burden on both primary care, non-respiratory and respiratory secondary care, and that the burden often is negatively associated with many measures of SES. Furthermore, we've shown distinct healthcare seeking behaviours across SES, with patients with lower SES showing increased reliance on unscheduled healthcare and rescue treatments such as SABAs or OCS bursts.

Burden of asthma in across care sectors

In a previous Finnish study, primary care management of asthma was shown to entail one asthma-related assessment every three years on average, despite guidelines recommending

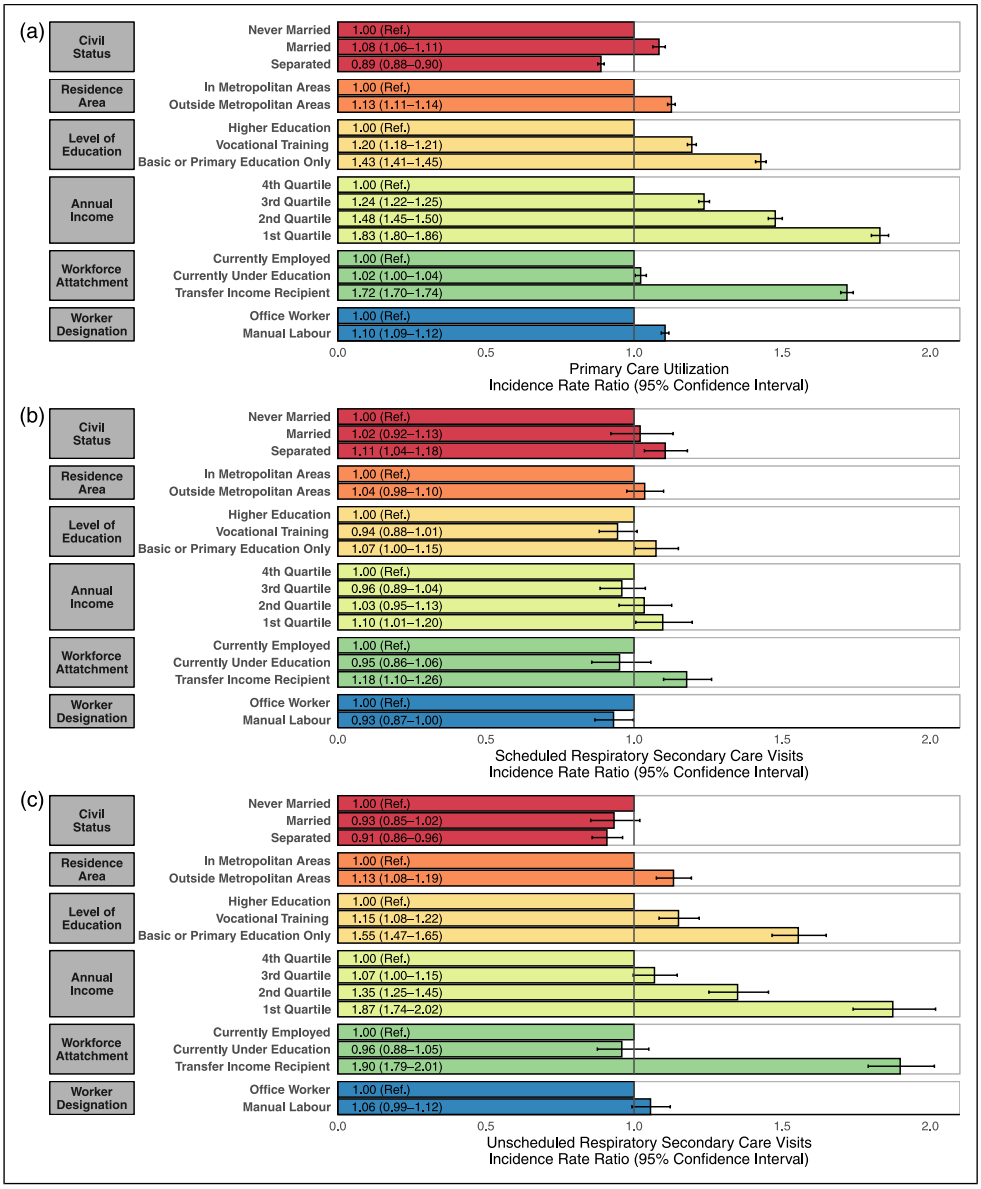

Figure 3. Relative use of a) primary care, b) scheduled (outpatient care) respiratory secondary care and c) unscheduled (emergency department and hospitalization) respiratory secondary care in 60,534 patients with actively treated asthma stratified by markers of socioeconomic status and adjusted for age, sex, Charlson score and GINA 2020 treatment step.

regular assessments.[2,19] The present study found that patients with asthma had approximately three to seven additional annual contacts to GPs in comparison to the background population. Previous studies have demonstrated that asthma accounts for 11–40% of primary care contacts,[20–22] suggesting that asthma in itself is a minor driver of primary care contacts and that annual assessments in the present study can be assumed to be in line with the findings of Takala et al.[19] The "spill over" burden of asthma found in primary and non-respiratory care in the present study has previously been shown in childhood asthma.[21] The "spill over" burden of non-respiratory care, however, was dependent on disease severity and control – suggesting that increasing asthma control could bring potential positive effects to other specialties and sectors.

Despite scarcity of regular asthma assessments, follow-up and timely referrals to specialist care are vital for optimal asthma management,[2,23] patients are reluctant to attend.[24] A notion of asthma as a less than serious disease seems prevalent,[25] despite broad impacts on quality of life and mental health for patients across asthma severities.[26,27] Additionally, the present study shows implications not just isolated to pulmonologists, but across primary and secondary care specialities, warranting further awareness to

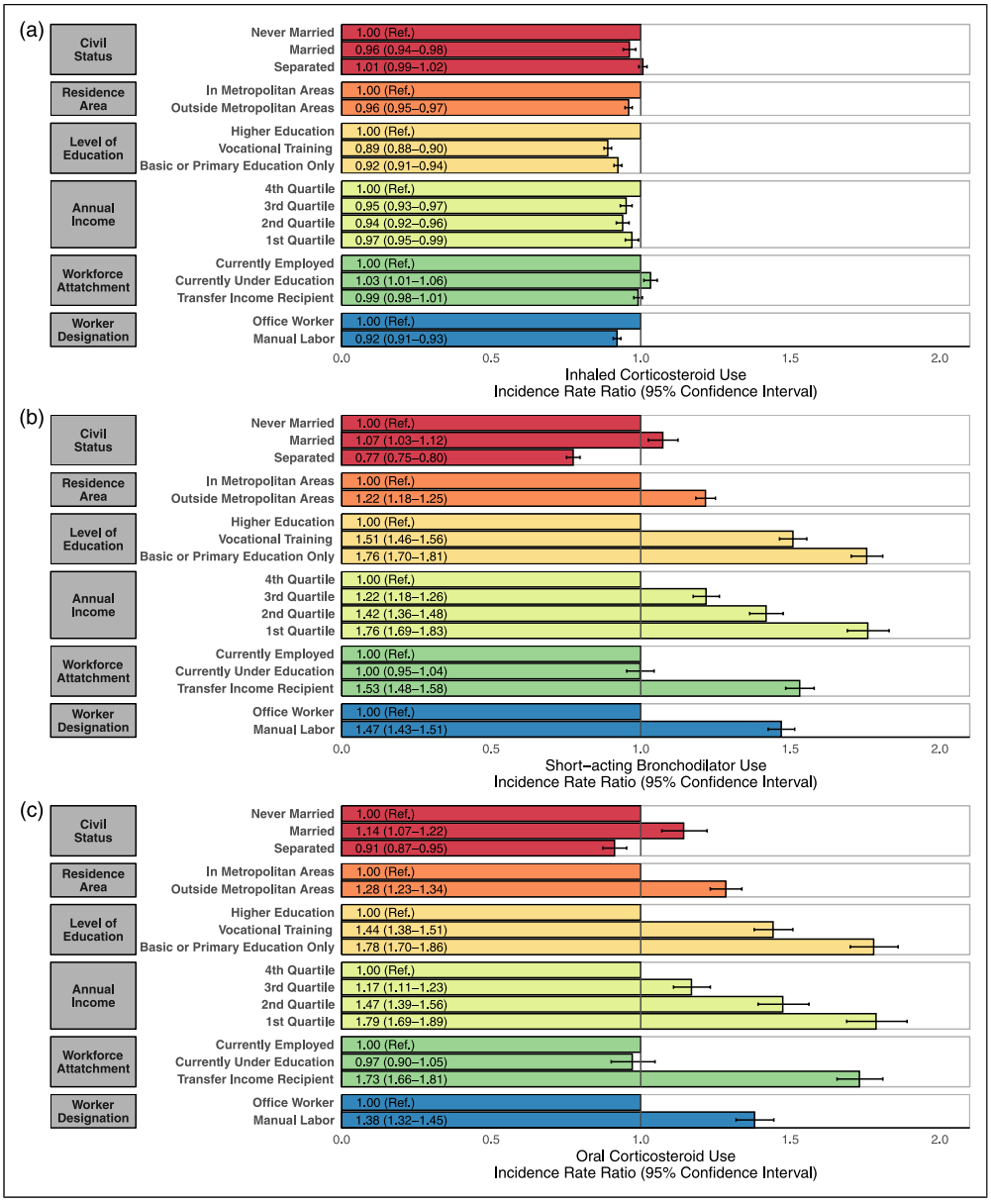

Figure 4. Relative number of redeemed doses of a) inhaled corticosteroids, b) short-acting bronchodilators and c) oral corticosteroid (OCS) bursts, in 60,534 patients with actively treated asthma stratified by markers of socioeconomic status and adjusted for age, sex, Charlson score and GINA 2020 treatment step.

the implications of asthma across care sectors and specialities.

Asthma healthcare seeking behaviour and control across socioeconomic strata

Despite being conducted in a country with low, albeit increasing,[28] levels of disparity which may limit external validity, we demonstrate distinct patterns of HRU and healthcare seeking behaviour across socioeconomic strata. Shifting healthcare seeking behaviours have previously been demonstrated in a recent systematic review, where lower SES was associated with increased unscheduled (ED visits and hospitalizations) secondary care utilization, in contrast to primary care.[6] In the present study, as well a recent Welsh study, no clear relationship between scheduled respiratory outpatient visits and SES was found.[11] We have previously demonstrated a strong association between higher SES and specialist referral for possible severe asthma patients,[9] which in the light of present findings suggest that secondary care attendance is less dependent on SES than the

referral itself and that referrals of eligible patients indeed are lacking.[23] In contrast to previous studies demonstrating a neutral or slightly negative relationship between lower SES and primary care utilization,[6,11] the present cohort demonstrated a clear relationship between primary care utilization and lower SES, perhaps attributable to differences in registration and classification of asthma-related contacts in primary care between the studies.

The increased reliance on unscheduled care and rescue medication in asthma with lower SES can be interpreted as a multidimensional phenomenon, reliant on factors such as health literacy, self-management skills and treatment adherence.[6,29] While the effects in the present study was smaller than earlier research, ICS use in Denmark has previously been shown to associate with income.[8] Low use of ICS relative to SABA[11] is a challenge for achieving population-wide increases in disease control, though increased reimbursement of ICS costs seemingly only increases ICS use in children of families with low SES,[30] thus indicating that health literacy and personal beliefs regarding asthma treatment deserves attention on par with increasing access to ICS. Additionally, parental SES at childhood affects their children's asthma outcomes regardless of current SES,[31] highlighting that while single factors such as income are powerful associations and predictors of (future) use, public health interventions are often more complex and require engaging multiple factors of disparity including individual, household and population levels.

The issue of socioeconomic disparity in asthma control is complex and often creates a catch 22, as increases in welfare use such as temporary sick leave as well as more frequent and longer periods of unemployment[32,33] are seen in asthma, creating a theoretical cycle between deteriorating asthma control and possible increased deprivation from prolonged detachment from the labour force. The present study demonstrated an increased incidence of SABA and OCS use, as well as unscheduled respiratory care with decreasing SES. Combined with previous findings of patients with lower SES suffering from an increased severity of hospitalizations,[6] it could be argued that SES is an important factor in assessing asthma risk and patients' future engagement with healthcare providers and calls for targeted interventions based on relative deprivation.

Limitations

The present study is an observational study based on registry data and is as such limited by inherent weaknesses hereof. First, markers of SES are proxies for additional health status-related factors such as smoking and occupational exposures which we are unable to investigate due to data limitations. Second, the use of prescription data for classifying disease severity assumes administration of redeemed medication doses and the diagnosis of asthma based on ICS use fails to incorporate traditional diagnostic methods such as reversibility testing, leading to some uncertainty regarding accuracy of the asthma diagnosis, yet the method is routinely used in Danish epidemiology.[34,35] Third, classification of healthcare contacts assumes correct registration in Statistics Denmark, but as databases used are administrative in nature and proper registration as necessary for reimbursement, correct registration is assumed to be prioritized both in primary and secondary care. Fourth, the inclusion criteria in the present study excludes severely non-adherent and/or SABA-only treated asthma who could be included in the background population controls, yet only 5.6% of secondary care contacts in controls were respiratory, ergo can classification bias argued to be minor. Finally, and in continuation of the previous limitation, exploration of socioeconomic parameters is limited by systematic exclusion of the most disadvantaged that do not have the means or resources for fulfilling the ICS inclusion criteria, and thus introducing selection bias.

Several strengths are in favour of the present study, such as being based on the nationwide and centrally registered nature of Danish registries allowing for low rates of missing data, low selection bias and non-biased data extraction.

Conclusion

In this nationwide cohort of young adults with asthma, socioeconomic status was heavily intertwined in access to and utilization of both respiratory and non-respiratory care in both primary and secondary care. Patients belonging to lower socioeconomic strata skewed towards the use of rescue courses of both short-acting bronchodilators and prednisolone, as well as unscheduled respiratory care and hospitalizations. However, attendance – in contrast to referral – to specialist care was largely unaffected by socioeconomic status, signalling that increased attention is warranted towards at-risk asthma patients with lower socioeconomic status.

Declaration of conflicting interests

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