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Beyond direct costs: individual and societal financial burden of asthma in young adults in a Danish nationwide study

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ABSTRACT

Introduction As a common chronic disease seen across all ages, asthma has the potential to incur high societal and individual costs from both direct healthcare costs and loss of productivity. Most previous studies use smaller, selected populations to assess the cost of asthma, possibly reducing generalisability. We, therefore, aimed to assess the total, nationwide economic burden of asthma by severity from both an individual and a societal perspective.

Methods The annual cost of asthma was assessed in a Danish nationwide cohort of patients aged 18–45 during 2014–2016 as excess healthcare costs, loss of income and welfare expenditure compared with controls (matched 1:4) using national registries. Asthma severity was defined as mild-to-moderate (steps 1–3 or step 4 without exacerbations) or severe (step 4 with exacerbations or step 5).

Results Across 63 130 patients (mean age 33, 55% female), the annual excess cost of asthma compared with controls was predicted to €4095 (95% CI €3856 to €4334) per patient. Beyond direct costs related to treatment and hospitalisations (€1555 (95% CI €1517 to €1593)), excess indirect costs related to loss of income (€1060 (95% CI €946 to €1171)) and welfare expenditure (eg, sick pay and disability pensions) (€1480 (95% CI €1392 to €1570)) were seen. Crude pooling of excess costs resulted in an annual societal cost of €263 million for all included patients.

Severe asthma (4.5%) incurred 4.4 times higher net costs (€15 749 (95% CI 13 928 to €17 638)) compared with mild-to-moderate disease (€3586 (95% CI €3349 to €3824)). Furthermore, patients with severe asthma experienced an annual loss of income of €3695 (95% CI €4106 to €3225) compared with controls.

Conclusion In young adults with asthma, a significant societal and individual financial burden of disease was seen across severities. Expenditure was mainly driven by loss of income and welfare utilisation, rather than direct healthcare costs.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Asthma is often considered to be a mild disease without larger impact by patients, and physicians are known to underestimate the impact of asthma on patients' lives, yet the full financial consequences of asthma are unknown and difficult to assess.

WHAT THIS STUDY ADDS

⇒ The present study estimates the financial burden of asthma in 63 130 Danish young adults in a nationwide fashion and finds annual excess costs of approximately €263 million. Furthermore, a considerable loss of income was seen for patients with severe disease.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The present study serves as an important reminder for patients, care providers and policy-makers that asthma is a chronic disease with significant financial implications for both individual patients and on a societal level.

INTRODUCTION

With an estimated €72 billion of annual costs attributed to asthma, it represents one of the costliest respiratory diseases in young adults in Europe.[1] As a chronic respiratory disease seen in individuals of all ages, asthma can affect the entire lifespan and thus incur costs on both personal and societal levels over several decades.[2]

Treatment with inhaled corticosteroids (ICS) is a cost-effective therapy capable of significantly lowering risk of acute exacerbations and mortality, while allowing many patients to live without major asthma-related limitations in their daily lives.[2 3] Despite the existence of an effective treatment, both poor asthma control and exacerbations remain common phenomena,[2 4] influenced by low adherence to ICS-based maintenance treatment, low referral rates of high-risk patients to specialists or even complacency towards the risks associated with uncontrolled asthma.[5–7] Asthma has been shown to be a substantial

burden to healthcare and welfare systems, as well as impairing quality of life for individual patients.[8–10]

Costs of disease analyses are one way of quantifying disease burden. Analyses typically include direct costs (eg, related to hospitalisation and treatment related), indirect costs (related to loss of productivity and personal income) and in some cases intangible costs (eg, loss of quality of life).[8] Previous studies on the cost of asthma, including those carried out in Denmark over two decades ago, have most often used self-reported data or population samples and extrapolated the costs found in selected individuals to the assumed prevalence of asthma.[11–15] As such, there is a scarcity of studies using nationwide cohorts for cost of asthma analyses without the need for extrapolation and with a reduction in the risk of selection bias, and thus allowing for precise estimation of the financial burden of asthma.

In the present study, we aimed to describe the cost of asthma in Denmark across disease severities, compared with the background population. Using a cohort comprising all ICS-treated young adults with asthma, we hypothesised that asthma carries a substantial financial burden for society at large and for young adults typically expected to be under education or be active participants of the workforce.

METHODS

Data sources and sharing

Data were linked on an individual basis by Central Person Registry (CPR) numbers and collected using the nationwide registries from Statistics Denmark, The Danish National Prescription Registry and The Danish Health Data Authority. Data are available on application to data sources, as required by Danish law.

Patients or the public were not involved in the design or conduct of the present research, yet patient organisations will be involved in dissemination of the present manuscript.

Study population

All Danish residents aged 18–45 redeeming at least two canisters of ICS-containing prescriptions during a 365-day period within the inclusion period of 2014–2016 were defined as having actively treated asthma and consequently included in the cohort. ICS redemption was defined as redeemed prescriptions belonging to the Anatomical Therapeutic Chemical codes R03BA, R03AK06–09, R03AK10–14, R03AL11–12, R03AL08–09.

A control group from the background population was supplied by Statistics Denmark based on 1:4 matching for age, sex, civil status (defined as married/cohabiting or living alone in the CPR), and residence at the case index date. Individuals without a valid CPR number (non-permanent residency, tourists, etc), with missing data in matching variables, or where no matching controls were found, were excluded (figure 1).

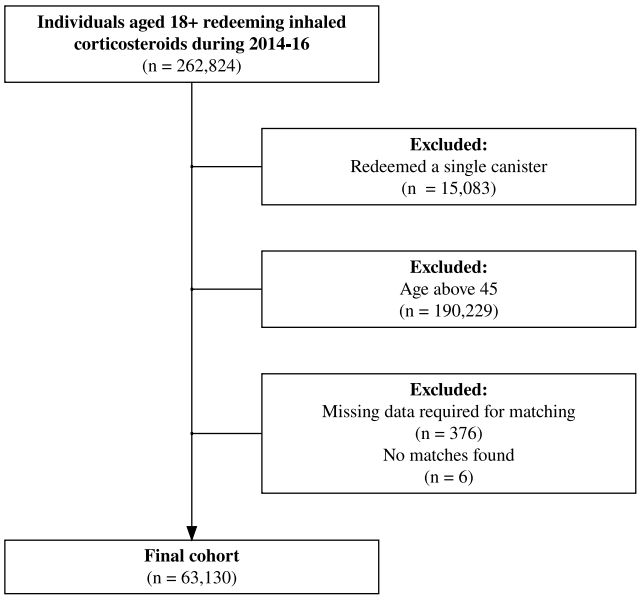

Figure 1 Flow chart describing patient inclusion and exclusion flow into the final cohort.

Observation period

Individual observation periods where created based on the index date (date of first ICS redemption) and patients were followed for up to 2 years postindex unless censored by date of emigration or death.

Asthma severity, control and definitions

Asthma severity is described by Global Initiative for Asthma (GINA) 2020 Treatment Steps,[2] based on annualised and standard-particle beclomethasone normalised doses, long-acting bronchodilators and leukotriene antagonist use as previously described.[6]

Possible severe asthma was defined according to GINA/International Severe Asthma Registry as GINA 2020 step 4 treatment with either ≥2 moderate or ≥1 severe/very severe exacerbation or GINA 2020 step 5 treatment.[2 16]

Moderate exacerbations were defined as redemption of at least 37.5 mg prednisolone for 5 days (totalling 187.5 mg). Severe exacerbations were defined as asthma-related hospitalisations (A-diagnosis of International Classification of Diseases (ICD)-10 DJ45 or A-diagnoses DJ96, DJ13–18 paired with a B-diagnosis of DJ45), with very severe exacerbations defined as admission to an intensive care unit and/or any severe exacerbations with a procedure code for intubation and/or mechanical ventilation. A wash-out period of ±14 days between exacerbations was used when calculating costs to distinguish new exacerbations from treatment failure/exacerbation progression.

Comorbidity

A modified, non-respiratory Charlson Comorbidity Index ('Charlson score') with updated weights was used to describe comorbidity burden in the cohort.[17]

Calculation of costs

Asthma-related costs

For hospitalisation, outpatient or emergency department contacts, costs were considered asthma-related if they were linked to events with an ICD-10 A-diagnosis of any DJ45-code, or costs linked to events with an ICD-10 A-diagnosis of DJ96, DJ13–18 in a patient with a concurrent ICD-10 B-diagnosis of DJ45. The latter always counts as asthma-related costs yet will only add to exacerbation burden if prednisolone has been redeemed according to the exacerbation criteria. All redemptions of medications with ATC code R03 were classified as asthma related. All remaining costs were classified as non-asthma expenditure.

Definitions of other costs

Direct costs: includes acquisition costs for drugs, healthcare visits in the primary sector, outpatient hospital visits including ER visits and hospital admissions.

Indirect costs: constitutes the difference in earnings between asthma patients and the control population, based on information on earned income.

Welfare-related costs: non-healthcare-related forms of welfare expenditure (eg, student grants, pension, early retirement, at-home assisted care, living at assisted homes and the state-paid portion of sick leave payments).

Exacerbation costs: costs for exacerbations are calculated based on healthcare resource utilisation (not including individual or societal costs) during 28 days from the start of the exacerbation event. Exacerbations with less than 28 days of follow-up due to censoring were not included.

Statistical analyses

A generalised linear model regression model with a gamma distribution and a log-link was used to predict costs and test differences in costs between cases and controls as described in.[18] The gamma-distributed log-link model is used due to a continuous outcome variable (cost) where zeroes are present and a need to weight individuals' exposure time as described in.[19]

Costs were estimated for a 2-year period postindex and subsequently annualised. Weighting for exposure time was used should individuals censor before the end of the 2-year period. Models are adjusted for Charlson score and education, besides the matching already performed. Costs were estimated for an individual with primary education and no comorbidity. For regression models comparing subgroups of patients without the use of controls, age, sex, marital/cohabiting status and residence was adjusted for. Due to non-convergence, GINA step-stratified and disease severity-stratified analyses are only reported as pooled costs. Costs presented are unadjusted for inflation and are converted to Euro at an exchange rate of €1=DKK7.45.

All statistical analyses were performed using SAS V.9.4 (SAS Institute). Graphics were generated using ggplot2.

RESULTS

The current cohort comprises 63 130 patients with actively treated asthma (mean age was 33% and 55% of patients were female). One-third of patients resided in the Capital Region, and most patients were either employed (61%) or were currently under education (20%). Minor differences in education level and socioeconomic status were found between patients and their controls. Patients were assigned to GINA 2020 Treatment steps, with step 1 (33%) and step 3 (31%) being the most common (table 1).

The overall economic burden of asthma

Across the entire cohort, the net cost per patient was estimated to €4095 (95% CI €3856 to €4334), representing the difference in direct healthcare costs, indirect costs due to loss of income, and welfare transfer payments between patients and their controls.

Direct healthcare costs for asthma patients totalled €3025 (95% CI €2977 to €3073) annually, approximately twice of the expenditure for controls without asthma, corresponding to an increase in direct expenditure of €1555 (95% CI €1517 to €1593) annually (figure 2A). Medication acquisition costs were the largest driver of direct costs (€918 (95% CI €903 to €932) annually), yet only 50.6% (€465 (95% CI €458 to €433)) were classified as asthma related. Asthma-related outpatient care and hospitalisation incurred annual costs corresponding to €188 (95% CI €185 to €191) and €99 (95% CI €97 to €100) per patient, respectively (figure 2B). Out of the direct healthcare costs for patients with asthma, 24.1%–37.7% were directly attributable to asthma, depending on inclusion of primary care expenditure (figure 2C).

Indirect costs were calculated as foregone income as compared with controls and corresponded to €1060 (95% CI €946 to €1171) annually. Societal welfare expenditure was significantly increased compared with controls and amounted to €1485 (95% CI €1392 to €1570) per patient per year (figure 2A). In terms of welfare expenditure, disability pensions (€1639 (95% CI €1595 to €1683)) and social security (€751 (95% CI €714 to €789)) were the largest drivers of cost (table 2).

Economic burden of asthma by disease severity

A U-shaped relationship between cost of disease and GINA steps was observed, with step 2 being associated with the lowest annual cost (1902 (95% CI €1404 to €2397)), as compared with both step 1 (€3181 (95% CI €2800 to €3560)) and steps 3–5 (€3981 (95% CI €3548 to €4413) to €14 496 (95% CI €12 350 to €16 726), respectively). Substantial increases across all types of expenditure were seen, and a full specification of direct costs are available in online supplemental table 1. Indirect costs and welfare expenditure remained the major financial burden across all GINA Steps (figure 3A).

When stratified asthma severity, substantial differences in costs between patients with mild-to-moderate and possible severe asthma were seen. In mild-to-moderate asthma,

Table 1 Demographics of 63 130 patients aged 18–45 with actively treated asthma, and a 1:4 age, sex, marital/cohabiting status and residence-matched control group

	Asthma population (N=63 130)*	Controls (N=252 473)*	P value†
Age	33	33	NS
Female	34 657 (55)	138 250 (55)	NS
Marital status			NS
Married/cohabiting	34 623 (55)	138 457 (55)	
Never married/divorced	28 507 (45)	114 016 (45)	
Region			NS
Capital Region	21 262 (34)	85 029 (34)	
Outside of the Capital Region	41 868 (66)	157 444 (66)	
Education			<0.0001
Primary and secondary	25 087 (40)	97 362 (39)	
Vocational	16 069 (25)	67 984 (27)	
Higher education	21 376 (34)	84 187 (33)	
Unknown	598 (1)	2967 (1)	
Socioeconomic status			<0.0001
Employed	38 536 (61)	163 582 (65)	
Unemployed	6497 (10)	22 078 (9)	
Disability pension	3448 (5)	7368 (3)	
Currently under education	12 632 (20)	47 588 (19)	
Other/unknown	2013 (3)	11 848 (5)	
Charlson Index			<0.0001
0	62 642 (99)	250 905 (99)	
1	161 (0.3)	518 (0.2)	
≥2	326 (0.5)	1050 (0.4)	
GINA 2020 treatment step			
Step 1	20 817 (33)	N/A	
Step 2	11 205 (18)	N/A	
Step 3	19 559 (31)	N/A	
Step 4	9567 (15)	N/A	
Step 5	1982 (3.1)	N/A	
Possible severe asthma‡	2859 (4.6%)	N/A	

Significant; p>0.05.
*Statistics presented: n (%); mean.
†Tests used: χ^2, Wilcoxon.
‡Defined as either step 4 with at least two moderate or one severe exacerbation or step 5 irrespective of exacerbation burden.
GINA, Global Initiative for Asthma; NS, not statistically.

annual costs were estimated to €3586 (95% CI €3349 to €3824) with an even spread between healthcare, welfare costs and forgone income at 37.5%, 36.2 and 26.4%, respectively. For possible severe asthma, annual costs were €15 749 (95% CI €13 928 to €17 638), of which 39.3%, 37.2% and 23.5% were attributable to healthcare, welfare costs and forgone income, respectively (figure 3B).

Patients' and societal financial burden of asthma

Cost of disease on a patient level can be further described as forgone income and eventual social security and welfare transfer compensation. For asthma patients overall, an annual earned income loss of €1060 (95% CI €946 to €1171) was seen when compared with controls. The loss of earned income was offset by increases in public welfare transfers to an estimated total annual loss of net income of €310 (95% CI €88 to €502). In contrast to the modest loss of total income for those with mild-to-moderate disease, patients with possible severe asthma experienced an estimate of loss of earned income corresponding to €3695 (95% CI €3225 to €4106), a loss not fully compensated by social security and welfare transfers

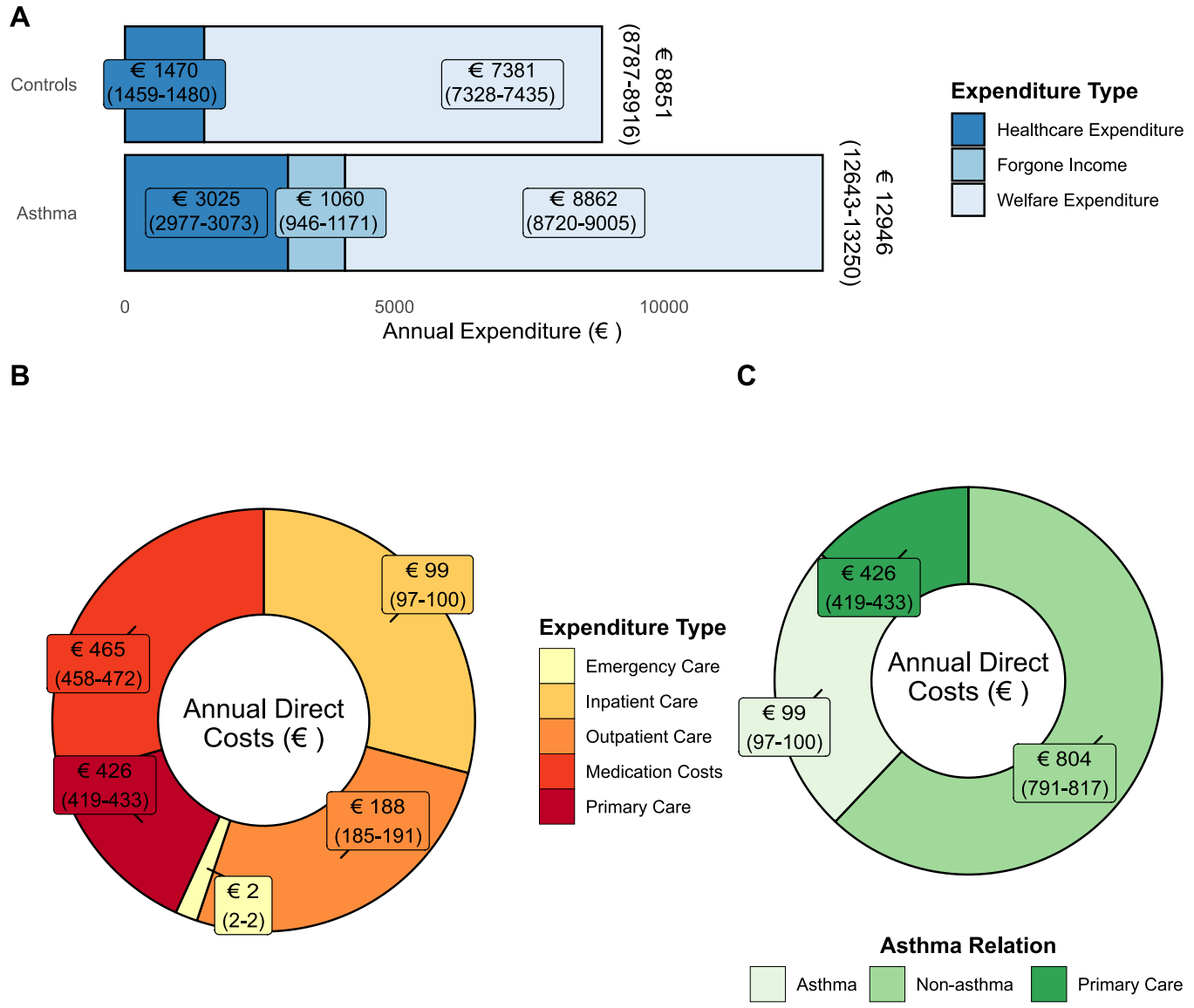

Figure 2 (A) Total annual expenditure in 63 130 patients with actively treated asthma aged 18–45 years as compared with a 1:4 age, sex, marital/cohabiting status and residence-matched control group. (B) Healthcare-related direct costs of asthma in cases only, stratified by type of expenditure. (C) Healthcare-related direct costs of asthma in cases only, stratified by their relation to asthma. Note that costs related to primary care are unable to be classified as asthma or non-asthma.

and thus resulting in a total loss of net income estimated to €1387 (95% CI €137 to €2500) annually (table 3).

Pooling of crude, unadjusted differences in mean excess total costs from indirect costs, healthcare and welfare expenditure between patients and controls was used for estimation of the nationwide cost of asthma (table 4). The total annual cost of asthma in patients aged 18–45 in Denmark was estimated to €263 million.

DISCUSSION

Based on a nationwide cohort of 63 130 young adults with asthma, we estimated the annual cost of asthma per patient to be €4095, of which 37.9% represented direct costs, 25.9% indirect costs and 36.1% increases in welfare-related societal costs. Costs of disease were highly dependent on severity of disease, with possible severe asthma demonstrating a 4.4-fold increase in costs compared with mild-to-moderate disease. Finally, we show that in patients with possible severe asthma, a significant drop in annual net income is seen and is only partly compensated by societal welfare measures.

In previous Scandinavian studies, the annual cost of asthma has been estimated to range between €1768[15] and €1270 (after adjustment for inflation, €1=DKK7.45),[12] both significantly lower than the average annual cost of €4095 seen in the present study. However, we use a nationwide cohort with complete, individual-level records of all publicly funded healthcare and welfare costs, as well as taxation records for estimating loss of income and adjust for incremental expenditure using a control group, in

Table 2 Detailed specification of estimated annual welfare expenditure in 63 130 patients aged 18–45 with actively treated asthma compared with controls

	Asthma versus controls		Across severity			
	Asthma population (N=63 130)*	Controls (N=252 473)*	Mild to moderate asthma (N=60 271)*	Controls (N=241 037)*	Possible severe asthma (N=2859)	Controls (N=11 436)*
Welfare costs						
Sick pay	359 (353–365)	323 (321–326)	346 (341–352)	318 (316–320)	649 (601–702)	447 (432–464)
Student grants	1392 (1370–1415)	1378 (1368–1388)	1414 (1392–1438)	1393 (1383–1404)	897 (831–702)	1010 (975–1047)
Social security	3677 (3619–3737)	2926 (2905–2948)	3582 (3524–3641)	2894 (2873–2915)	5876 (5437–6350)	3684 (3554–3818)
Unemployment benefits	456 (449–463)[NS]	454 (451–458)	452 (445–460)[NS]	449 (446–452)	532 (493–575)	592 (572–614)
Disability pension	3735 (3676–3795)	2096 (2081–2112)	3405 (3350–3462)	2051 (2036–2067)	12 321 (11 402–13 315)	3131 (3021–3244)
Housing and child benefits	1086 (1069–1104)	1136 (1678–1145)	1059 (1042–1077)	1110 (1102–1118)	1681 (1554–1818)	1788 (1724–1855)

All costs in Euro (€) and presented with 95% CIs.
Significant, p>0.05.
*A 1:4 age, sex, marital/cohabiting status and residence-matched control group.
NS, not statistically.

comparison to previous studies on asthma cost primarily relying on self-report and extrapolation of costs. We, therefore, arguably provide a more robust estimate of the actual costs of asthma. Despite differences in methods, the distribution between direct, indirect and societal costs of asthma were comparable both to previous Scandinavian[12 15] and international[11 20] studies with direct costs representing approximately 30%–40% of the total costs.

The indirect costs of asthma

In the present study, indirect costs were represented by foregone income and societal costs by welfare expenditure. Indirect costs are highly reliant on the societal context on which they are analysed, as well as the choice of design. Pertinent examples of context-dependent differences are the American cost of asthma studies,[14 21] where absenteeism-related indirect costs represented 3.7%–6.7% of total annual costs, presumably attributable to significant differences in welfare and healthcare organisation in the USA compared with the Danish universal healthcare and 'flexicurity' welfare models.

While the present study estimates loss of productivity as forgone income, it fails to address intangible productivity losses attributed to asthma, such as presenteeism, which is often defined as attending school or work with a consequent lower rate of productivity due to disease.[22] Sadatsafavi *et al*[23] reported that the prevalence of presenteeism is approximately threefold to that of absenteeism, corroborated by a Singapore-based study by Finkelstein *et al*[24] who found presenteeism to account for 67%–87% of the total cost of asthma depending on level of disease control. Furthermore, due to limitations in the databases used, sick leave payments for periods below 30 days are not included in the present cost analyses, calling for prospective studies to estimate the impact of asthma on shorter-term absenteeism. As such, while the indirect costs found in the present study seem high compared with earlier studies, they are arguably still to some extent underestimating the societal impact of asthma, both in terms of absenteeism and presenteeism-related costs.

In line with most previous studies, disease severity was highly associated with increased cost of disease.[15 25–27] Interestingly, we found GINA 2020 step 2 to be associated with approximately 40% lower annual excess costs than step 1, a difference arguably driven by patients with poor adherence and thus low ICS exposure leading to increased asthma burden. Overall, cost of asthma was disproportionally driven by increases in welfare expenditure and forgone income for patients with possible severe asthma. However, we found that while the Danish welfare model reduces the financial impact of asthma in patients with mild-to-moderate disease, patients with possible severe asthma experienced significant financial losses (ca. €3700 in earned income lost annually compared with controls, only in-part compensated for by the Danish welfare system). While the exact annualised numbers pale in comparison to previous findings on forgone

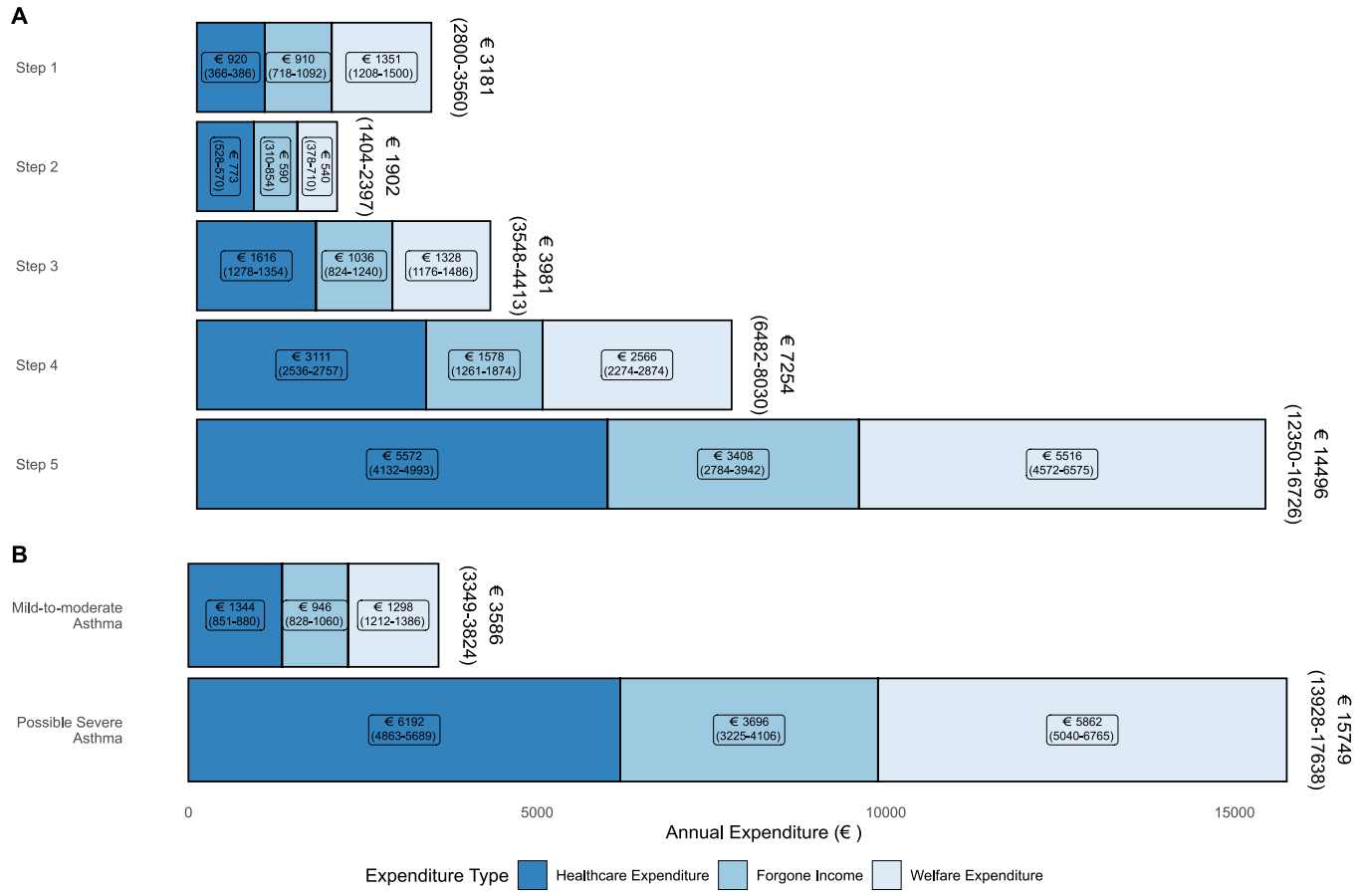

Figure 3 Total annual excess expenditure in 63 130 patients with actively treated asthma aged 18–45 years as stratified by (A) GINA 2020 Treatment Steps and (B) mild-to-moderate and possible severe asthma. Costs are calculated as increases in expenditure as compared with a matched control group. GINA, Global Initiative for Asthma.

income in Chronic obstructive pulmonary disease,[18] the life course financial consequences for these young adults are far from minor, considering that most patients have just started contributing to the labour market or were still under education, and thus are expected to work for an additional four to six decades.

Reducing the cost of asthma

With an increasing prevalence and rising medical costs, the cost of asthma is expected to—and has historically—increased.[27] Direct, patient-facing medical expenditure increased with 15.1% (after adjusting for inflation) in the present study when compared with a previous Danish analysis by Mossing and Nielsen,[12] contrasting the relatively unchanged levels in Finland.[28] However, when seen from a societal level, a quadrupling of medication costs was seen in the USA, and a threefold increase was observed in Finland.[8 28] The increasing costs combined with a higher number of patients call for initiatives to improve asthma care to reduce the financial burden on society.

On a smaller scale, many of the treatments used for asthma, including ICS in combination with long-acting beta$_2$ agonists, are cost-effective,[3] yet despite this the financial burden of asthma remains significant. Larger scale asthma programmes, such as the Finnish Asthma Programme holds promise in reducing the financial burden of asthma. Despite seeing a threefold increase in asthma patients and overall medication expenditure, Finland experienced a 14% reduction in overall costs of asthma between 1987 and 2013, often attributed to a 10-year asthma programme that significantly decreased hospitalisation rates and productivity losses.[28] The Finnish Asthma Programme serves as proof that early diagnosis, increased attention to ICS-based maintenance treatment and close collaboration between primary and secondary care, as well as promotion of asthma knowledge, can significantly impact the overall costs of asthma.

While larger national initiatives such as the Finnish Asthma Programme are few and far in-between, recent developments in asthma treatment such as ICS/formoterol for maintenance and reliever use[2] and the advent of more widespread use of biologic treatments could lead to future reductions in the disease burden of asthma, calling for further studies to assess cost-effectiveness and perhaps even cost-saving properties of these novel treatment strategies once broader scale implementation is seen. It should be noted, however, that the cost-effectiveness of biologics has been challenged, primarily due to the current high prices and the highly selective criteria used

Table 3 Overview of indirect costs (forgone income) and welfare expenditure in 63 130 patients aged 18–45 with actively treated asthma

	Asthma versus controls		Across severity			
	Asthma population (N=63 130)*	Controls (N=252 473)*	Mild to moderate asthma (N=60 271)*	Controls (N=241 037)*	Possible severe asthma (N=2859)	Controls (N=11 436)*
Earnings						
Earned income†	13 637 (13 420 to 13 857)	14 697 (14 591 to 14 803)	13 636 (13 415 to 13 861)	14 581 (14 475 to 14 639)	13 753 (12 730 to 14 858)	17 448 (16 836 to 18 083)
Difference	**−1060 (−1.171 to −946)**		**−945 (−1.060 to −778)**		**−3695 (−4106 to −3225)**	
Welfare transfers						
Transfer income‡	8862 (8720 to 9005)	7382 (7328 to 7435)	8577 (7937 to 8719)	7279 (7225 to 7333)	15 490 (14 323 to 16 751)	9628 (9283 to 9986)
Difference	**1480 (1392 to 1570)**		**1298 (712 to 1386)**		**5.862 (5040 to 6765)**	
Housing and child benefits§	1086 (1069 to 1104)	1137 (1128 to 1145)	1059 (1042 to 1077)	1110 (1102 to 1118)	1681 (1554 to 1818)	1788 (1724 to 1855)
Difference	**−51 (−59 to −41)**		**−51 (−60 to −41)**		**−107 (−170 to −37)**	
Total net income	**23 735 (23 370 to 24 132)**	**24 045 (23 872 to 24 220)**	**23 493 (23 111 to 23 882)**	**23 766 (23 591 to 23 942)**	**29 445 (27 228 to 31 841)**	**30 832 (29 728 to 31 978)**
Annual loss of net income§	−310 (−502 to −88)		−273 (−480 to −60)		−1387 (−2500 to −137)	

Bold values represent calcucated values, non-bold values are values from regression model(s).
*A 1:4 age, sex, marital/cohabiting status and residence-matched control group.
†The indirect cost of asthma is defined as the difference in earned annual income between patients and controls.
‡Includes public transfer income from sick pay, student grants, social security, unemployment benefits and disability pension.
§Sources of income that are traditionally not considered to be welfare related for individual patients, but for their families.

Table 4 Overview of mean, unadjusted direct, indirect and welfare expenditure in 63 130 patients aged 18–45 with actively treated asthma compared with controls

	Asthma versus controls	
	Asthma population (N=63 130)*	Controls (N=252 473)*
Direct costs	2801	1364
Indirect costs†	1613	
Welfare costs‡	5784	4664
Net costs per patient§	4170	
Total pooled annual costs for all cases¶	263 252 100	

All costs in €.
*A 1:4 age, sex, marital/cohabiting status and residence-matched control group.
†The indirect cost of asthma is defined as the difference in earned annual income between patients and controls.
‡Includes public transfer income from sick pay, student grants, social security, unemployment benefits and disability pension.
§Calculated as the difference in expenditure between cases and controls.
¶Calculated as the per-patient net cost times the number of included patients.

for eligible patients.[29 30] While the present study fails to account for the impact of biologics and ICS/formoterol for maintenance and reliever use, we can conclude that asthma—regardless of severity—is far from without financial consequences for both patients and society at large.

Limitations

The present study is strengthened by its nationwide design, a high degree of data completeness in the validated registries used, and the use of objective data free from selection and recall bias. However, several limitations are worth noting. First, the present study uses a previously published[6] method for assessing ICS treatment as exposed dose, which is closer to real-world exposed dose than the prescribed dose typically used in GINA Step-assessment—yet direct comparison to prescribed GINA 2020 steps should be done with caution. Second, the use of actively treated asthma as the case definition makes asthma-related costs incurred by the control population possible, as individuals with ICS-naïve (or severely non-adherent) asthma can be included as controls. However, the diminutive asthma-related costs recorded in controls (€7 annually) strengthens the case definition used. Costs related to asthma comorbidity (eg, polyposis and allergies) are not included, which could underestimate the true direct costs of asthma in select subpopulations. Third, the definition of asthma used in the present cohort is based on pharmacy redemption data and uses a widely used definition in Danish pharmacoepidemiology,[31 32] yet data on formal diagnoses such as objective

asthma testing is unavailable. Fourth, while nationwide cohort, artificial selections in terms of age and treatment criteria have been used, possibly reducing generalisability to other age groups. The two ICS canister criterium also exclude patients with the mildest forms of asthma, such as the SABA-only treated population, which further limits generalisability to all asthma patients. Finally, asthma-related primary care costs cannot be reliably characterised due to data limitations.

CONCLUSION

In this nationwide study using public records and healthcare data without self-report and/or data extrapolation, we found that the annual cost of asthma (€4095 per patient) in young adults is approximately twice of what previous Scandinavian studies have reported. Furthermore, possible severe asthma was a driver of overall costs, but patients also suffered a substantial personal loss of net income despite the existence of a robust welfare system. Interventions aimed at reducing asthma-related absenteeism could potentially attenuate both individual and societal financial losses attributable to asthma.

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