Prevalence and management of severe asthma in the Nordic countries: findings from the NORDSTAR cohort

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Shareable abstract (@ERSpublications)
In nationwide cohorts of all asthma patients from three Nordic countries, the prevalence of severe asthma was comparable: 3.5–5.4% in adults and 0.3–1% in children. Many patients with severe asthma are not managed in specialist care. https://bit.ly/3vM1kMg

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Abstract

Background Real-life evidence on prevalence and management of severe asthma is limited. Nationwide population registries across the Nordic countries provide unique opportunities to describe prevalence and management patterns of severe asthma at population level. In nationwide register data from Sweden, Norway and Finland, we examined the prevalence of severe asthma and the proportion of severe asthma patients being managed in specialist care.

Methods This is a cross-sectional study based on the Nordic Dataset for Asthma Research (NORDSTAR) research collaboration platform. We identified patients with severe asthma in adults (aged ⩾18 years) and in children (aged 6–17 years) in 2018 according to the European Respiratory Society/American Thoracic Society definition. Patients managed in specialist care were those with an asthma-related specialist outpatient contact (only available in Sweden and Finland).

Results Overall, we identified 598 242 patients with current asthma in Sweden, Norway and Finland in 2018. Among those, the prevalence of severe asthma was 3.5%, 5.4% and 5.2% in adults and 0.4%, 1.0%, and 0.3% in children in Sweden, Norway and Finland, respectively. In Sweden and Finland, 37% and 40%

of adult patients with severe asthma and two or more exacerbations, respectively, were managed in specialist care; in children the numbers were 56% and 41%, respectively.
Conclusion In three Nordic countries, population-based nationwide data demonstrated similar prevalence of severe asthma. In children, severe asthma was a rare condition. Notably, a large proportion of patients with severe asthma were not managed by a respiratory specialist, suggesting the need for increased recognition of severe asthma in primary care.

Introduction

Globally, asthma is one of the most common chronic diseases. Although most asthma patients are well controlled on the available inhaled therapy, a minor group has severe disease that is associated with substantial burdens due to increased risk of exacerbations, high healthcare costs and risk of serious side-effects to oral corticosteroids (OCS) [1–5].

Insights into the prevalence of severe asthma and the management of severe asthma patients are important for many reasons. The health and economic benefits derived from successful management of severe uncontrolled asthma in specialist care are well documented [6, 7] and generally recommended by guidelines [8–10]. Nevertheless, evidence suggests that severe asthma remains under-recognised and often managed only in primary care, where the risk of not achieving asthma control is high [11–14]. With the emergence of monoclonal antibodies targeting specific inflammatory pathway in patients with severe asthma, there is an urgent need to better understand the current management strategies for these patients. Lastly, from a health economic and political perspective, prevalence estimates may support decision-makers in the allocation of scarce healthcare resources in the most appropriate and cost-effective way [15].

Available studies have estimated that the prevalence of severe asthma ranges from 2% to 10% of asthma patients [5, 11–20]. However, prior studies are generally limited by the use of different methodologies and the lack of unified definitions of severe asthma. Furthermore, most of the existing literature is based on smaller population studies [16] or registries containing only selected patient groups from single countries, limiting the comparability of results between different studies [15, 21–23]. In particular, large nationwide registry studies that investigate severe asthma in children and adolescents are lacking [24]. Updated data on severe asthma and its morbidity using unified definitions on severe asthma in large, unselected paediatric and adult asthma populations from several countries are highly warranted.

The Nordic Dataset for Asthma Research (NORDSTAR) research platform is unique in terms of having complete nationwide data from all asthma patients in the Nordic European countries [25]. The database contains detailed information on medical diagnosis, medication use, use of healthcare resources and costs, sociodemographics and mortality, thereby enabling us to investigate potential inter-country differences in the prevalence of severe asthma, its morbidity and management strategies of severe asthma without the risk of selection bias.

The aim of this study was to estimate the prevalence and management strategies of severe asthma in children and adults in Sweden, Norway and Finland.

Methods

Study design and data sources

This was a cross-sectional study based on data from NORDSTAR. For this study, NORDSTAR data from 2018 were extracted from nationwide registries available in Sweden, Norway and Finland. Data from Denmark were not available for 2018 and were consequently not included in the present study. Specifically, data were obtained from the national patient registries and the drug registries for Sweden and Finland, while for patients in Norway, only prescription data were available (supplementary table S1). These nationwide registers are based on routinely collected administrative data on all residents in each country. Within each country, information from the population registers was used to link individual-level information between the registries using the unique social security number that enables the linking of data collected throughout an individual's lifetime from birth (or immigration) to death (or emigration).

Study population

The study population was identified in a stepwise manner as illustrated in figure 1. The source population included all citizens in Sweden, Norway and Finland who were aged ⩾6 years in 2018. From the source population, asthma patients were identified as those with either at least one asthma International Classification of Diseases, 10th revision (ICD-10) diagnosis (J45–J46) registered in specialist care during 2018 and/or dispensation with an Anatomical Therapeutic Chemical Classification (ATC) code R03

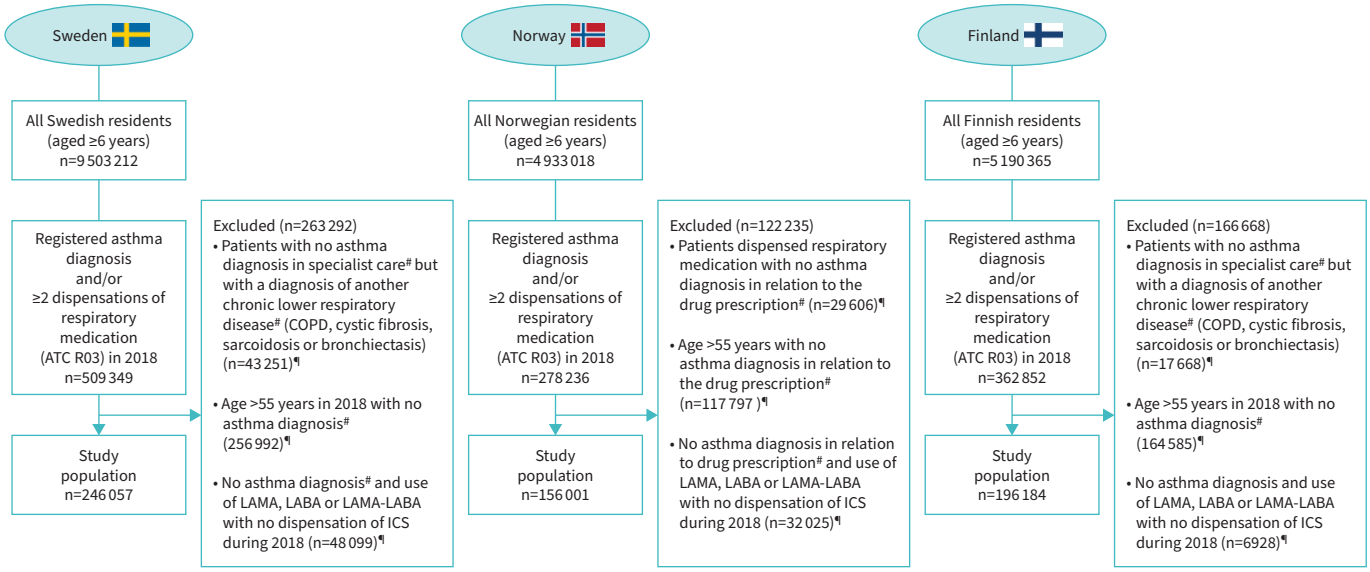

FIGURE 1 Flowchart illustrating selection of the study population with inclusion and exclusion criteria. ATC: Anatomical Therapeutic Chemical Classification; LAMA: long-acting muscarinic antagonist; LABA: long-acting β_2-agonist; ICS: inhaled corticosteroid. #: during 2018 or the preceding 5 years; ¶: not mutually exclusive.

(except for omalizumab) on at least two occasions in 2018. In Norway, information about diagnoses was available from the prescription registry, where indications for treatment are registered. The applied exclusion criteria attempted to eliminate likely nonasthmatic patients from the analyses (figure 1), but only pertained to patients with no ICD-10 asthma diagnosis, *e.g.* if a patient had an asthma ICD-10 diagnosis, they were included regardless of comorbidities or age >55 years.

Definition of severe asthma

Severe asthma was defined according to the European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines [9]. For patients aged ⩾12 years, it included high-dose inhaled corticosteroids (ICS) (corresponding to dispensing ICS with an average daily dose of ⩾1600 µg budesonide or equivalent) and at least one dispensed prescription with a second controller including long-acting β_2-agonists (LABA), long-acting muscarinic antagonists (LAMA), xanthines or leukotriene receptor antagonists (LTRA) and/or a dispensed biological therapy (anti-IgE, anti-interleukin (IL)-5/IL-5r) and/or high OCS exposure in 2018. To reflect a significant steroid exposure comparable to daily use of OCS, high OCS exposure was defined as filled OCS prescriptions corresponding to an average of ⩾5 mg per day during 2018 corresponding to ⩾1825 mg total dispensed OCS [26]. For patients aged <12 years, those with severe asthma were defined as those requiring high-dose ICS (corresponding to dispensing ICS prescriptions of an average daily dose of ⩾800 µg budesonide or equivalent) and at least one dispensed prescription of a second controller and/or dispensed biological therapy (anti-IgE, anti-IL5) in 2018. Patients aged 6–12 years were not included in the severe group based on high OCS exposure.

Additional study definitions

Several different definitions were used to characterise patients and study outcomes (supplementary table S2). Exacerbations were defined as either a dispensation with burst OCS (ATC code H02AB) or an asthma-related emergency department (ED) visit in 2018 or as an asthma-related hospital admission in 2018. High short-acting β-agonist (SABA) use was defined as dispensations of ⩾600 doses (puffs) of SABA in 2018 [11, 12, 27]. Uncontrolled asthma was a composite measure defined as either 1) two or more OCS dispensations and/or asthma-related ED visits and/or 2) one or more asthma-related admission and/or 3) high SABA use (of ⩾600 doses (puffs)) in 2018.

Asthma management in specialist care was defined as a specialist visit (not an ED visit), where asthma ICD-10 codes J45–J46 were the primary or secondary diagnosis. The patients, who did not fulfil the criteria for specialist asthma management, were considered to have been treated in primary care. Asthma

management in specialist care was only reported for patient data derived from Finland and Sweden, as no data on primary *versus* specialist care were available for Norway.

Other measures included comorbidities, use of antibiotics and hospital admissions for pneumonia (refer to supplementary tables S3–S5 for definitions).

Analyses

The prevalence of asthma in 2018 was estimated in the populations aged ⩾6 years in Sweden, Norway and Finland, as the proportion of severe asthma in the current asthma populations in each country. The prevalence measures were calculated separately in the paediatric populations (aged 6–17 years) and in the adult populations (aged ⩾18 years). The study was descriptive in nature with calculation of frequencies and proportions (n, %), mean±SD and median (interquartile ranges). All study outcomes were evaluated separately in subsamples of patients with mild-to-moderate asthma and severe asthma.

No hypothesis tests analysing differences between the countries were conducted, as the data from each country were derived from separate nationwide registries, and despite the application of uniformed study definitions, the differences in the data registration could vary between the countries. Statistical analyses were performed using R (version 4.1.0; R Foundation for Statistical Computing, Vienna, Austria).

All data in this study were pseudo-anonymised and contained no direct identifiable patient information. Patient consent is not required in the Nordic countries for registry-based studies.

Results

The prevalence of severe asthma in Sweden, Norway and Finland

In total, the study populations consisted of 598 242 children and adults with asthma (Sweden n=246 057, Norway n=156 001, Finland n=196 184) (figure 1). When stratified by age, the prevalence of asthma in patients aged ⩾18 years was 2.3% in Sweden, 3.1% in Norway and 3.7% in Finland. Of the prevalent asthma cases, 3.5%, 5.4% and 5.2%, respectively, had severe asthma, according to the ERS/ATS definition (figure 2, table 1). For children aged 6–17 years, the prevalence of asthma was 4.1% in Sweden, 3.5% in Norway and 4.4% in Finland, of whom 0.4%, 1.0% and 0.3%, respectively, had severe asthma (figure 2, table 2). In adults (age ⩾18 years), the prevalence of both overall asthma and severe asthma was higher among females than males, whereas in children aged 6–17 years, asthma and severe asthma were more prevalent in males (tables 1 and 2). The mean±SD age of mild-to-moderate adult asthma patients ranged from 44±15 to 48±17 years, whereas the mean±SD age of severe asthma patients ranged from 56±16 to 60 ±16 years between countries.

Asthma medication use

In adult patients fulfilling the definition of severe asthma, the mean±SD daily budesonide equivalent was 1375±960 µg in Sweden, 1314±875 µg in Finland and 1030±902 µg in Norway (table 1). In all countries, most adult patients with severe asthma were prescribed LABA as the second controller (82–86%). Larger proportions of severe asthma patients with dispensations of LAMA were found in Norway (38%) and Sweden (25%) compared to Finland (6%). Furthermore, 53% of patients with severe asthma in Sweden, 66% in Norway and 63% in Finland had high OCS exposure. Lastly, in Norway, 11% and 8% of severe asthma patients were on anti-IgE or anti-IL-5 therapies, respectively. Since information about hospital-administered medication was not available in the registries in Sweden and Finland, dispensations of biologicals are not presented in these countries.

In children with severe asthma, the controllers most frequently dispensed, apart from ICS, were LABA and LTRA (table 2). In Norway, 34% of children with severe asthma filled at least one OCS prescription; in Sweden and Finland, the numbers were 52% and 51%, respectively. Moreover, in Norway, 26% of children with severe asthma were treated with anti-IgE and 25% used anti-IL-5 therapies.

Asthma control outcomes according to asthma severity

In adult patients with severe asthma, the proportions of those patients who had two or more exacerbations were 67%, 61% and 63% in Sweden, Norway and Finland, respectively (table 3). Furthermore, 7–10% of these patients had one or more one ED visits, and 8–11% had at least one asthma-related hospital admission. The proportion of children with severe asthma who had two or more exacerbations varied from 14% in Norway to 37% in Sweden and Finland (table 4). Furthermore, in children with severe asthma, 2–10% and 4–5% had asthma-related ED visits and admissions, respectively (table 4).

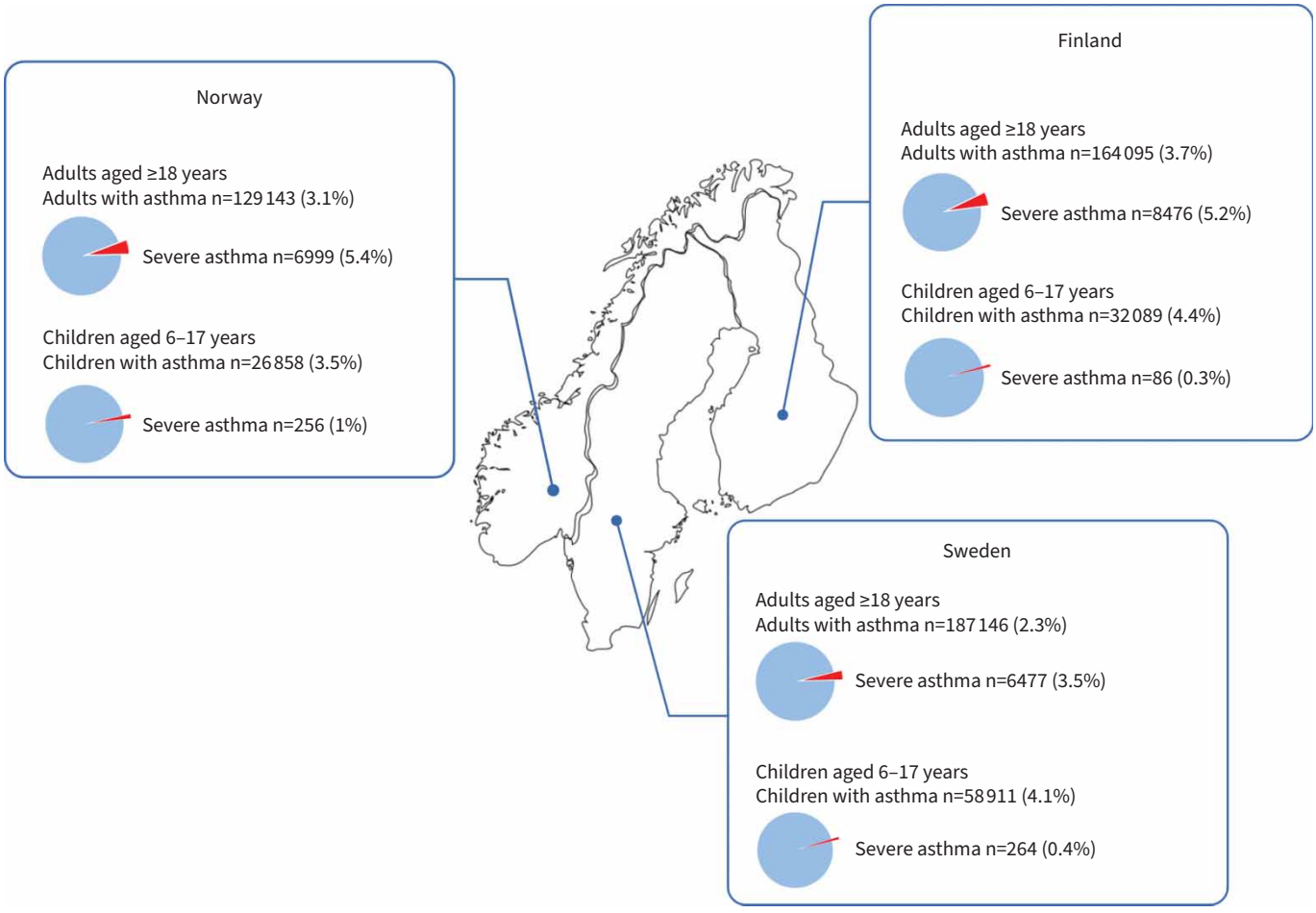

FIGURE 2 Prevalence of asthma and severe asthma in children and adults in Sweden, Norway and Finland.

Overall, uncontrolled asthma (defined as at least two OCS dispensations/asthma-related ED visits and/or having an asthma-related admission and/or high SABA use) was observed for the majority of adult patients with severe asthma, *i.e.* 80% in Sweden, 78% in Finland and 77% in Norway (table 3). The corresponding proportions for children with severe asthma were smaller in all countries, *i.e.* 70% in Sweden, 53% in Finland and 55% in Norway (table 4). In patients with mild-to-moderate asthma, uncontrolled asthma was in the range 19–24% in adults, and 12–24% in children.

Patients with severe asthma were more likely to have been prescribed antibiotics against respiratory infections in all three countries in both children and adults when compared to mild-to-moderate asthma (tables 3 and 4). Admissions with pneumonia were similarly more prevalent in severe asthma patients compared to patients with mild-to-moderate asthma in both adults and in children (tables 3 and 4).

Management of severe asthma in specialist care

In adults with severe asthma and two or more exacerbations, 37% and 40% were seen by a specialist in secondary care in Sweden and Finland, respectively (figure 3). Furthermore, among those with high OCS exposure, 36% and 39% were managed in specialist care. In children with severe asthma and two or more exacerbations, the proportions of patients with a specialist care contact were 56% and 41% in Sweden and Finland, respectively.

Discussion

In this study, utilising nationwide registry data in NORDSTAR, the prevalence of severe asthma in adult asthma patients ranged between 3.5% and 5.4% in Sweden, Norway and Finland. Severe asthma in children was a rare condition, with the prevalence in asthma patients ranging from 0.3% to 1.0%. Moreover, severe asthma patients frequently had indicators of poor asthma control, use of antibiotics

TABLE 1 Characteristics of asthma patients aged ⩾18 years in Sweden, Norway and Finland in 2018

	Sweden		Norway		Finland	
	Mild-to-moderate	Severe	Mild-to-moderate	Severe	Mild-to-moderate	Severe
Current asthma population	187 146 (2.3)[§§]		129 143 (3.1)[§§]		164 095 (3.7)[§§]	
	180 669 (96.5)[ff]	6477 (3.5)[ff]	122 144 (94.6)[ff]	6999 (5.4)[ff]	155 619 (94.8)[ff]	8476 (5.2)[ff]
Demographics						
Age, years	43.7±14.6	56.3±16.1	47.9±16.7	59.7±15.8	45.3±16.0	59.1±16.4
Age group						
18–44 years	91 676 (49)	1464 (23)	50 715 (42)	1205 (17)	77 730 (50)	1681 (20)
⩾45 years	88 993 (51)	5013 (77)	71 429 (58)	5794 (83)	77 889 (50)	6795 (80)
Female	106 234 (59)	3991 (62)	69 523 (57)	4108 (59)	94 458 (61)	5433 (64)
Comorbidities[#]						
Allergy[¶,+]	56 600 (31)	3095 (48)			33 814 (22)	2819 (33)
Rhinitis[§]	37 362 (21)	2484 (38)			28 269 (18)	2653 (31)
Nasal polyposis[f]	3552 (2)	478 (7)			2281 (1)	321 (4)
Asthma medications						
SABAi	125 255 (69)	4670 (72)	79 510 (65)	5296 (76)	110 258 (71)	6472 (76)
ICS + ⩾1 controllers	98 345 (54)	5621 (87)	80 820 (66)	5925 (84)	83 419 (54)	11 065 (88)
ICS + ⩾2 controllers	25 569 (14)	3125 (38)	21 248 (17)	3521 (50)	20 126 (13)	3743 (45)
ICS + ⩾3 controllers	2614 (1)	839 (13)	2458 (2)	863 (12)	1194 (1)	644 (8)
Daily budesonide equivalent dose, µg	382±341	1365±960	361±349	1030±902	411±378	1314±875
LABA	94 564 (52)	5499 (85)	80 727 (66)	6000 (86)	77 037 (50)	6988 (82)
LAMA	9217 (5)	1635 (25)	12 848 (11)	2665 (38)	2121 (1)	479 (6)
XANT	298 (0.2)	184 (3)	541 (0)	304 (4)	1482 (1)	749 (9)
LTRA	26 927 (15)	2516 (39)	17 258 (14)	1990 (28)	28 329 (18)	3762 (44)
Any OCS[##]	39 316 (22)	5085 (79)	21 236 (17)	5513 (79)	29 867 (19)	6703 (79)
High OCS exposure[¶¶]	0 (0)	3431 (53)	0 (0)	4604 (66)	0 (0)	5360 (63)
Anti-IgE[++]			0 (0)	800 (11)		
Anti-IL-5[++]			0 (0)	551 (8)		

Data are presented as n (%) or mean±SD. SABAi: inhaled short-acting β-agonist; ICS: inhaled corticosteroid; LABA: long-acting β_2-agonist, LAMA: long-acting muscarinic antagonist; XANT: xanthines; LTRA: leukotriene receptor antagonist; OCS: oral corticosteroid; IL: interleukin. [#]: data not available in Norway; [¶]: Anatomical Therapeutic Chemical Classification (ATC) code S01G cannot be captured in Finnish data, which may underestimate the prevalence of allergy; [+]: defined as at least two prescriptions with R06 and/or S01G or an International Classification of Diseases, 10th revision (ICD-10) diagnosis J45.0 or J3; [§]: defined as at least two prescriptions with R01AD or an ICD-10 diagnosis with J30-J32; [f]: defined as an ICD-10 diagnosis with J33; [##]: at least one prescription with OCS (ATC code H02AB); [¶¶]: filled OCS prescriptions corresponding to an average of ⩾5 mg per day (~⩾1825 mg total dispensed OCS); [++]: data not available in Sweden and Finland; [§§]: in relation to the overall nationwide population; [ff]: in relation to the overall asthma population.

against respiratory infections and pneumonia-related admissions. Notably, 12–24% of patients with mild-to-moderate asthma in both age groups had indicators of recurrent exacerbations, indicating potential undertreatment in this group. Lastly, in both children and adults, a large proportion of patients with severe asthma who experienced recurrent exacerbations were not currently managed by a respiratory specialist.

A strength of the present study was the consistent application of study definitions and methodology to assess the prevalence of severe asthma across three countries, ensuring comparability of the results. Another strength is the sample size of our study, which included nearly 600 000 patients with asthma in 2018. This is one of the largest asthma populations studied so far. Furthermore, by using nationwide population data, we minimised potential responder and selection biases, which limit epidemiologic studies based on self-reported questionnaires or registries that only cover selected patient groups. Conversely, the use of registry data can also be perceived as a limitation due to the lack of clinical information, such as measures of daily symptoms, smoking history and lung function. Therefore, the outcomes of our study represent proxies for uncontrolled asthma.

Our prevalence estimates of severe asthma ranging from 3.5% to 5.4% align well with previous population-based studies that have reported prevalence estimates of severe asthma in adults of 2% to 10% [5, 11–20]. Despite this agreement, we cannot exclude that we have overestimated the prevalence of severe asthma, since our study was register-based and therefore was limited by no possibility to distinguish between difficult-to-treat and true severe asthma. However, a common cause of difficult-to-treat asthma is poor adherence [28, 29]. In the Nordic countries, asthma inhalation medication is only partly reimbursed, and we therefore assume that patients who fill their prescriptions also adhere to their treatment. In contrast

TABLE 2 Characteristics of asthma patients aged 6–17 years in Sweden, Norway and Finland in 2018

	Sweden		Norway		Finland	
	Mild-to-moderate	Severe	Mild-to-moderate	Severe	Mild-to-moderate	Severe
Current asthma population	58 911 (4.1)[§§]		26 858 (3.5)[§§]		32 089 (4.4)[§§]	
	58 647 (99.6)[ff]	264 (0.4)[ff]	26 602 (99.1)[ff]	256 (1.0)[ff]	32 003 (99.7)[ff]	86 (0.3)[ff]
Demographics						
Age, years	11.1±3.4	11.6±3.3	11.5±3.4	11.4±3.3	11.3±3.4	13.2±2.7
Female	24 445 (42)	105 (40)	11 324 (43)	100 (39)	13 143 (41)	38 (44)
Comorbidities[#]						
Allergy[¶,+]	23 015 (39)	157 (59)			9413 (29)	31 (36)
Rhinitis[§]	10 209 (17)	83 (31)			5681 (18)	23 (27)
Nasal polyposis[f]	61 (0.1)	<5			16 (0.05)	<5
Asthma medications						
SABAi	48 006 (82)	231 (88)	21 847 (82)	220 (86)	24 919 (78)	65 (76)
ICS + ⩾1 controllers	18 822 (32)	214 (81)	9906 (37)	211 (83)	11 426 (35)	70 (81)
ICS + ⩾2 controllers	4668 (8)	108 (41)	1659 (6)	94 (37)	3045 (9)	25 (29)
ICS + ⩾3 controllers	81 (0.1)	8 (3)	16 (0.1)	5 (2)	5 (0.02)	<5
Daily budesonide equivalent dose, µg	184±182	758±565	174±198	830±656	169±172	1128±1075
LABA	13 353 (23)	180 (68)	8567 (32)	184 (72)	8651 (27)	67 (78)
LAMA	212 (0.4)	12 (5)	42 (0.2)	16 (6)	8 (0.02)	<5
XANT	9 (0.02)	<5	<5	<5	8 (0.02)	<5
LTRA	11 800 (20)	149 (56)	3667 (14)	119 (46)	7099 (22)	29 (34)
Any OCS[##]	6104 (10)	137 (52)	993 (4)	88 (34)	1533 (5)	44 (51)
High OCS exposure[¶¶]	27 (0.05)	71 (27)	16 (0)	56 (22)	12 (0.04)	39 (45)
Anti-IgE[++]			<5	66 (26)		
Anti-IL-5[++]			<5	65 (25)		

Data are presented as n (%) or mean±SD. SABAi: inhaled short-acting β-agonist; ICS: inhaled corticosteroid; LABA: long-acting β_2-agonist, LAMA: long-acting muscarinic antagonist; XANT: xanthines; LTRA: leukotriene receptor antagonist; OCS: oral corticosteroid; IL: interleukin. [#]: data not available in Norway; [¶]: Anatomical Therapeutic Chemical Classification (ATC) code S01G cannot be captured in Finnish data, which may underestimate the prevalence of allergy; [+]: defined as at least two prescriptions with R06 and/or S01G or an International Classification of Diseases, 10th revision (ICD-10) diagnosis J45.0 or J3; [§]: defined as at least two prescriptions with R01AD or an ICD-10 diagnosis with J30-J32; [f]: defined as an ICD-10 diagnosis with J33; [##]: at least one prescription with OCS (ATC code H02AB); [¶¶]: filled OCS prescriptions corresponding to an average of ⩾5 mg per day (~⩾1825 mg total dispensed OCS); [++]: data not available in Sweden and Finland; [§§]: in relation to the overall nationwide population; [ff]: in relation to the overall asthma population.

to the prevalence of severe asthma estimates, our findings regarding the prevalence of asthma in adults (2–4%) are lower than estimates from other population studies that have indicated a prevalence of approximately 6–10% [30–33]. This may be explained by our exclusion of patients aged >55 years without a diagnosis in secondary care. At the same time, the total adult population did not have an upper limit, which naturally has skewed the overall prevalence proportion towards a lower number in adults. In

TABLE 3 Asthma control outcomes in asthma patients aged ⩾18 years in Sweden, Norway and Finland in 2018

	Sweden		Norway		Finland	
	Mild-to-moderate	Severe	Mild-to-moderate	Severe	Mild-to-moderate	Severe
Patients	180 669	6477	122 144	6999	155 619	8476
Recurrent exacerbations[#] (⩾2 exacerbations)	14 185 (8)	4335 (67)	6557 (5)	4285 (61)	8167 (5)	5370 (63)
Asthma-related ED visit	5616 (3)	480 (7)			3767 (2)	825 (10)
Asthma-related hospital admission	2404 (1)	517 (8)			2642 (2)	925 (11)
High SABA use	33 103 (18)	2457 (38)	24 877 (20)	3292 (47)	23 227 (15)	3458 (41)
Uncontrolled asthma[¶]	43 985 (24)	5167 (80)	29 120 (24)	5395 (77)	30 070 (19)	6587 (78)
Antibiotics	28 029 (16)	2220 (34)	26 145 (21)	3348 (48)	57 642 (37)	4882 (58)
Hospital attendance with pneumonia	2197 (1)	455 (7)			3337 (2)	1002 (12)

Data are presented as n or n (%). ED: emergency department; SABA: short-acting β-agonist. [#]: defined as either a dispensation with burst oral corticosteroid (OCS) (Anatomical Therapeutic Chemical Classification code H02AB), or an asthma-related ED visit in 2018, or as an asthma-related hospital admission; [¶]: defined as at least two OCS dispensations and/or asthma-related ED visits and/or at least one asthma-related admission and/or high SABA use (of ⩾600 doses (puffs)).

TABLE 4 Asthma control outcomes in asthma patients aged 6–17 years in Sweden, Norway and Finland in 2018

	Sweden		Norway		Finland	
	Mild-to-moderate	Severe	Mild-to-moderate	Severe	Mild-to-moderate	Severe
Patients	58 647	264	26 602	256	32 003	86
Recurrent exacerbations[#](≥2 exacerbations)	1969 (3)	98 (37)	111 (0)	36 (14)	244 (8)	32 (37)
Asthma-related ED visit	2762 (5)	26 (10)			706 (2)	<5
Asthma-related hospital admission	308 (0.5)	11 (4)			234 (1)	<5
High SABA use	12 634 (22)	125 (47)	5915 (22)	121 (47)	3600 (11)	18 (21)
Uncontrolled asthma[¶]	14 091 (24)	186 (70)	5998 (23)	142 (55)	3902 (12)	46 (53)
Antibiotics	8205 (14)	70 (27)	3337 (13)	81 (32)	10 643 (33)	40 (47)
Hospital attendance with pneumonia	375 (0.6)	12 (5)			275 (1)	<5

Data are presented as n or n (%). ED: emergency department; SABA: short-acting β-agonist. [#]: defined as either a dispensation with burst oral corticosteroid (OCS) (Anatomical Therapeutic Chemical Classification code H02AB), or an asthma-related ED visit in 2018, or as an asthma-related hospital admission; [¶]: defined as at least two OCS dispensations and/or asthma-related ED visits and/or at least one asthma-related admission and/or high SABA use (of ⩾600 doses (puffs)).

children, we found that severe asthma was a rare condition. Only a few studies have previously assessed the prevalence of severe asthma in children with estimates of 2.1% [19] and 4.5% [34] in two birth cohort studies, and estimates from 2% to 18% in a study using different European healthcare databases [5] However, compared to the present study, less strict definitions for severe asthma were used in these studies, which could explain the discrepancies.

Although the prevalence of severe asthma was similar across the countries, some noteworthy differences were also observed with respect to treatment patterns in adults that appeared to vary in Norway compared to Sweden and Finland. These differences may be real, but they may also be explained by a difference in the Norwegian data compared to the Finnish and Swedish data. Notably, we observed a lower mean ICS

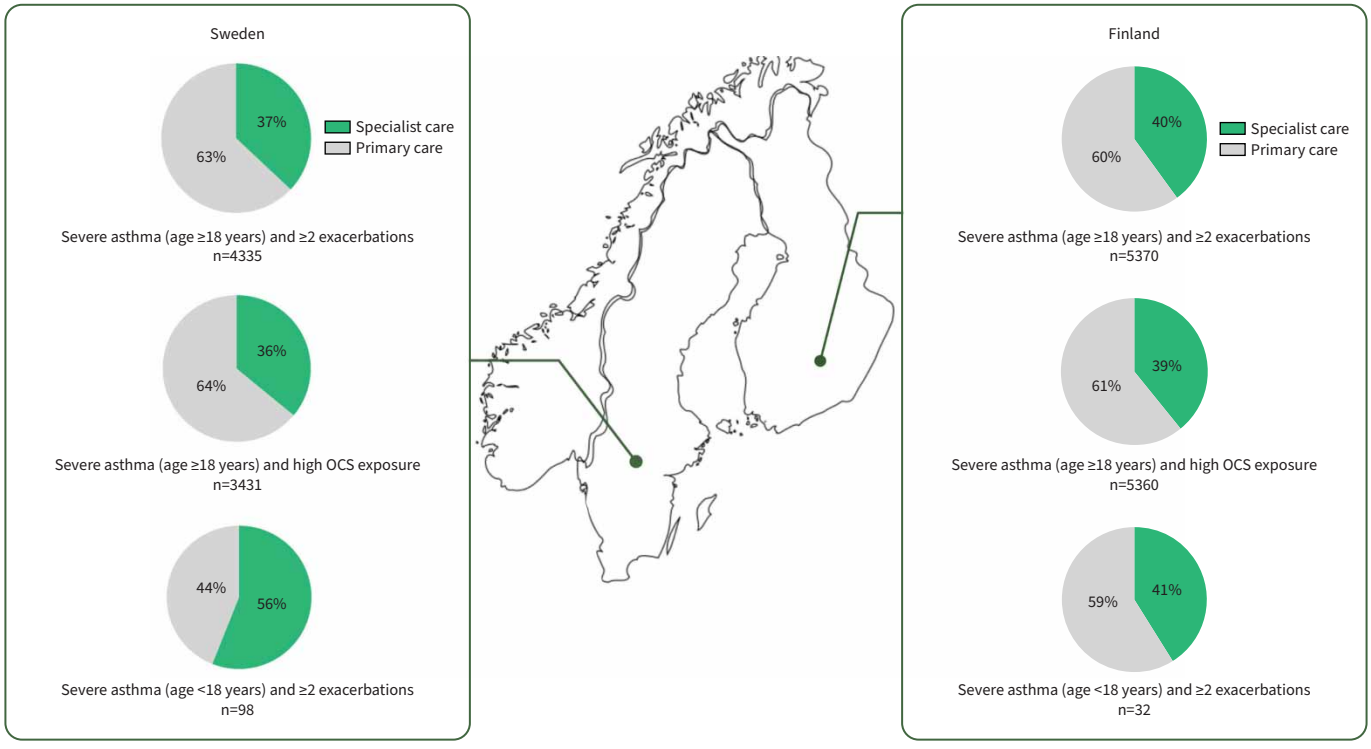

FIGURE 3 Management of severe asthma and recurrent exacerbations or high oral corticosteroid (OCS) exposure in children and adults in Sweden and Finland.

dose dispensed in adult severe asthma patients in Norway. Several reasons could explain this. Firstly, information about hospital-administered biological treatment was available in Norway, whereas no such data were available for Sweden and Finland. In Norway, nearly 20% of patients with severe asthma were treated with either anti-IgE or anti-IL-5 therapies, thereby being included as severe asthma with no requirement of high-dose ICS. Conversely, in Norway, information about diagnoses was only available as indications for treatment and not as separate ICD-10 codes from patient registries. Consequently, we speculate that in Norway, some patients with, for example, COPD and high OCS exposure might be misclassified as having severe asthma. This speculation is further supported by the observation of higher LAMA use in Norway (38%), compared to the other countries (25% in Sweden and 6% in Finland), which could indicate some degree of misclassification of COPD patients as severe asthma patients. In turn, such a possibility could also explain why a lower median ICS dose was observed in Norway.

The use of daily OCS is an important criterion in most of the definitions of severe asthma [8, 9]. Unfortunately, identifying daily OCS use is generally challenging, when using registry-based prescription data. Consequently, to estimate a cumulated steroid burden reflecting a daily use of OCS, adult patients with high-dose OCS exposure (with dispensed OCS prescriptions corresponding to an average daily dose of $\geqslant$5 mg per day) were classified as having severe asthma. In all three countries, a high proportion of high-dose OCS exposure was seen in adults with severe asthma, which may partly be explained by our inclusion of high-dose OCS users in our severe asthma definition. Likewise, as exacerbations were mostly driven by OCS prescriptions, the high proportion of exacerbations in patients with severe asthma could be, to some extent, caused by high-exposure OCS as a key inclusion criterion in adults with severe asthma. Furthermore, we cannot exclude that OCS were prescribed for other indications than asthma, such as inflammatory diseases, which could have led to some misclassification. However, although not all patients with severe asthma used ICS $\geqslant$1600 µg budesonide equivalent daily, few patients with high-dose OCS exposure had not been dispensed any ICS at all.

Finally, we found that patients with severe asthma and frequent exacerbations or high OCS exposure were often not treated in specialist care. This is a challenge also identified by other studies from the United Kingdom [13, 35], Denmark [11, 12] and Sweden [14] and is a great cause for concern. Since the benefits of management of severe asthma in specialist care are well documented [6], it should be a key priority to secure timely and appropriate referral of symptomatic asthma patients to specialist care in any healthcare system. Furthermore, with the emergence of new biological treatments and their availability in hospital settings, patients managed in primary care or by a private respiratory specialist will only have limited access to these treatments. However, it should be noted that the register data used, and the definitions applied in this study may have led to some degree of misclassification of level of management. For instance, registry data do not capture patients treated by respiratory specialists outside the hospitals, which could explain part of the gap, especially in the paediatric population.

In conclusion, to our knowledge, this is one of the largest studies to date having examined the prevalence of severe asthma in unselected population samples of nearly 600 000 asthma patients using complete nationwide registry data from multiple countries. The prevalence of severe asthma in asthma patients was comparable between three Nordic countries with variations from 3.5% to 5.4% in adults and 0.3% to 1.0% in children. Indicators of uncontrolled asthma were prevalent in patients with severe asthma in both children and adults, and many patients with severe asthma and recurrent exacerbations were currently only managed in primary care. Since the benefits from systematic assessment by respiratory specialist of severe asthma are well documented and effective biological therapies for severe asthma are only available in hospital settings, our findings highlight the need for increased focus on identifying patients with severe asthma in primary care.

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