

Stable admission rate for acute asthma in Danish children since 1977

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Abstract Childhood asthma is consistently reported to have increased in recent decades in most westernized countries, but it is unknown if this increase is similar across severities. We aimed to study the time-trend of acute hospital admission and readmission for asthma of school-aged children in the recent 35 years in Denmark. We analyzed time-trends in the national incidence rate of hospitalization for acute severe asthma in children aged 5–15 in Denmark during the 35-year period 1977–2012 in the Danish national registry. Only in-patient admissions with a principal diagnosis of asthma (ICD-8: 493** or ICD-10: J45** or J46**) were included. Among children with asthma hospitalizations, we investigated the risk of readmission beyond 1 month of first admission. Admissions were summarized as rates per thousand person years at risk. The overall time-trend is stable with a rate of one admission per year per thousand children at risk and a per-year incidence rate ratio 0.999 [95 % CI 0.997–1.001]. The rate of any readmission decreased from approximately 20 per thousand children in the eighties to less than 10 in the early nineties before stabilizing at around 10 per thousand children from mid-nineties and onwards. During 35 years of nation-wide follow-up, we find a highly stable incidence rate of first hospital admission for acute severe asthma in

children. Moreover, rates of readmission halved during the seventies and stabilized in the last twenty years. In conclusion, our data suggest that the reported increase in childhood asthma is mainly due to less severe cases.

Keywords Asthma · Child · Denmark · Hospitalization · Incidence

Abbreviations

ICD International classification of diseases

Introduction

Acute hospitalization for asthma is traumatic to the child and her relatives, and it is a major part of the total direct cost of asthma management in the United States and Europe [1]. It is a main goal of asthma management to avoid asthma-related hospital admissions. Furthermore it is presumably “the tip of the iceberg” reflecting the general asthma control in the population.

The prevalence of childhood asthma has consistently been reported to have increased in recent decades in most westernized countries. In Denmark, one study found the prevalence has increased from 5.3 % in 1986 to 11.7 % in 2001 [2]. Likewise, the latest report from ISAAC on worldwide trends from 2007 [3] reported an increase.

Much of the research behind these claims relies on questionnaire data. Especially questions regarding “wheeze” could be biased, since much higher prevalence has been found in English speaking nations where such terms seem familiar. Therefore, it remains unclear whether these trends represent a consistent increase across severities of asthma.

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In this study, we used the unique National Danish hospital registry data; consistent for more than 35 years of complete national coverage of pediatric population in-patient hospital admissions and analyzed the time-trend of acute hospital admission and readmission for asthma of school-aged children in Denmark.

We analyzed time-trends in the national incidence of hospitalization for acute severe asthma in children aged 5–15 (both included) in Denmark during the 35-year period 1977–2012 in the Danish national registry.

Methods

Study population

The Danish National Patient Registry was established in 1977, and includes information on all in-patient hospitalization in Danish public hospitals comprising a personal identification number, dates of admission and discharge, and diagnoses at discharge classified according to the international classification of diseases versions 8 and 10 [4].

We identified all children born in Denmark 1972–2010 in the Danish Civil Registration System (CRS). From the CRS, information was retrieved regarding date of birth, and possible date of death or emigration, and children were followed in registries from age 5 to 15 for all asthma hospitalizations during 1977–2012.

Case definition

First admission

Children aged 5–15 years (both years included) with in-patient admissions with a principal diagnosis of asthma (1977–1993: ICD-8 493**; and 1994–2012: ICD-10 J45*, J46*) were considered as cases at their first in-patient admission.

Readmission

Inclusion criteria for analyses of readmission selected all children with any first admission in the age span 5–15 years. Children were considered as cases if they had any subsequent admission for asthma (same definition as above) more than 1 month after the first admission and before age 15.

Statistics

The incidence rate is calculated as number of new cases divided by person years at-risk. All children contributed person-time from age 5 until age 16 or migration or death or final registry date (Dec 31st 2011), or first asthma

admission, if present. Trend is presented in the window 1988–2012 during which we follow a complete cohort of school-aged children without left-truncation of data. In Fig. 2, the time trend is visualized with a non-parametric LOWESS smoother using a bandwidth of 0.5 years. The linear trend across 1988–2012 is calculated as the effect of calendar year on the number of admissions in a Poisson regression with log link and log to person-years of observation as offset.

Readmissions are investigated among children with any first admission. In Cox regression analysis children are followed from first admission till readmission. They are censored at age 16, migration or death whichever comes first. Rates are compared by year at first admission (5 year intervals 1977–2012) and are stratified by age (1 year intervals) at first admission in a Cox regression to adjust for non-complete cohort until 1988. Pairwise comparisons of the rate of readmission between categories of calendar time are summarized by a letter-based representation [5] and are adjusted for multiple testing using the single step procedure [6].

Admissions and person years are summarized using the SAS macro developed by Rostgaard [7].

Analyses were performed in SAS 9.3 (SAS Institute Inc., Cary, NC, USA) and R version 3.1.2.

Ethics

The study was based on data from national registries and was approved by the Danish Data Protection Agency (J.no. 2012-41-0388). Subjects were not contacted as a part of the study; hence the ethics committee did not require written informed consent.

Results

2.3 million children (51 % male) born in Denmark 1972–2006 are followed during 20.6 million person-years in the ages 5–15 through 1977–2012. Due to changing birth rates over the study period, the number of person years varies slightly over time. Figure 1 depicts the number of person years in the entire period. From 1988 onwards a complete cohort of Danish born children aged 5–15 are investigated for 1.6 million person years.

Excluding 3339 same person admission within a month (31 days), we find 33,219 unique in-patient childhood asthma hospitalizations in 22,023 children (14,143 boys, and 7880 girls) during 1977–2012.

Incidence

Figure 2 shows the national yearly incidence of first asthma admissions of school-aged children. The incidence

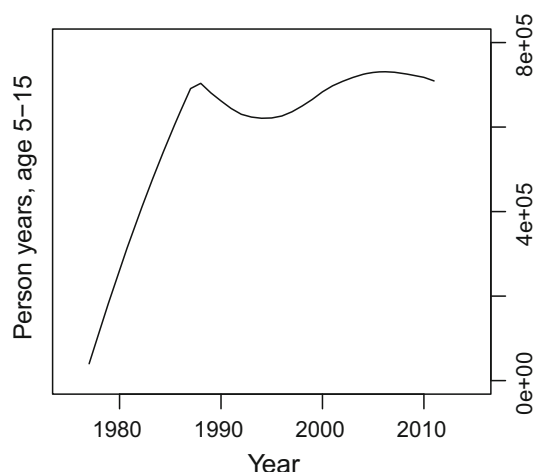


Fig. 1 Person years of observation in children aged 5–15 in Denmark

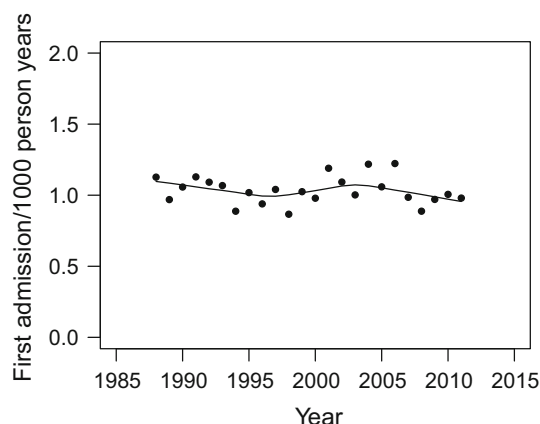


Fig. 2 Asthma admissions in Denmark per 1000 school-aged children at risk 1988–2012

of childhood asthma in Denmark during 1988–2012 is stable with an overall rate of 1.04 [1.02–1.05] first admission in 1000 children per year. More boys than girls have asthma—overall the rate for boys is 1.258 [1.234–1.282] in 1000 boys per year, whereas the rate for girls is 0.743 [0.724–0.762] in 1000 girls per year.

The overall time trend is stable with a per-year incidence rate ratio (IRR) of 0.999 [0.997–1.001]. The overall trend is the same adjusted for gender. The minor fluctuations in trend are mainly due to fluctuations in incidence amongst boys, however this follows the same pattern as the person years of observations, reflecting the changing age distribution over time.

Readmissions

5282 children (64 % boys) have at least one readmission more than 1 month after the first asthma for asthma at age 5–15. The majority (72 %) of readmissions occur within 2 years after the first admission.

Table 1 Risk of readmission by calendar year at first admission (Cox regression stratified by age at first admission)

Year	Cox regression	
	HR [95 % CI]	Letter-based-comparison of rates ^a
1977–1981	Ref	A
1982–1986	0.96 [0.86–1.07]	A
1987–1991	0.65 [0.58–0.73]	B
1992–1996	0.43 [0.38–0.48]	C
1997–2001	0.54 [0.48–0.60]	D
2002–2006	0.57 [0.51–0.63]	BD
2007–2011	0.52 [0.46–0.59]	D

^a Calendar year groups with the same letter are not significantly different

Risk of readmission differs by age at first admission and calendar year at first admission. Table 1 shows the Hazard Ratios for readmission by year (5-year intervals) at first admission from an age-stratified Cox regression. The risk of readmissions has decreased since 1977–81, to a low-point during 1992–1996, but stabilized from mid 1990s onwards where the trend in readmission rates is similar, but inflated, to the minor fluctuations in overall trend and observation years.

Discussion

Primary findings

The stable incidence of 1 child per thousand per person year through our 35 years of observation extends our report 2 decades ago on a stable incidence of acute asthma hospitalizations of school children during 1978–1993 [8]. Likewise the decreasing readmission rates were reported during 1978–1993, and now we show that these have since stabilized.

Strengths and limitations

The Danish National Patient Registry is considered unique and of very high quality [4]. The registrations are compulsory and necessary for government reimbursement, which results in complete coverage—and for the pediatric population there are no alternatives to public hospitals. This gives us the exclusive opportunity for a complete nation-wide population cohort of standardized observation followed over 35 years.

To avoid left-truncation of the data, we only investigated the incidence trends from 1988 onwards where a complete cohort can be followed. We consider this data

restriction compulsory to obtain un-biased estimates of the actual incidence. When investigating the readmissions the stratified Cox regression analysis can account for the truncation, and therefore we were able to investigate readmission for the full 35 years span.

We excluded same-month admissions in same child, since these could be the result of moving a child from one department to another, or simply reflect the same asthmatic period where the child was discharged too soon. This ensures that changing discharge procedures do not bias our analyses of readmissions.

Various political reforms of the Danish health care system have taken place during recent decades. We only investigate the in-patient admission category which has existed in the entire span of registry, and leave out out-patient admissions which were introduced in Denmark in 1994. Most importantly for the hospital admission was the shift from ICD-8 to ICD-10 in 1994. The fact that we do not observe any shift during this change reassures us that asthma diagnosis is stable and in-patient acute hospital admissions for asthma is robust against such changes.

Still, we cannot rule out changes in admission practice over time, and in fact others have dismissed 5 year stable hospitalization rates by indications of changing admission criteria [9]. However, we find that hospitalization rates may be a less biased marker of disease incidence and disease control in the society than other assessments, such as symptom history and prescribed treatment, which are prone to changes in disease perception, management strategy and definition over time.

Interpretation

Time trends

Asthma is a complex and heterogeneous disease. Hospitalized asthmatics represent the most severe cases that have been filtered through primary care and hospital admission criteria. Uncontrolled milder asthmatics may also contribute, but we interpret the incidence of first hospitalization for acute severe asthma as a surrogate marker of the incidence of moderate to severe asthma disease [10], and thereby as the “tip of the iceberg” of the general asthma incidence.

Our findings of a long-term stable incidence of childhood asthma hospitalizations seems to contrast the consistent reports of increased asthma prevalence in industrialized countries through the recent half century [11]. In the same time period there has been a general increase in the awareness and a labeling shift towards asthma. We cannot know if improved treatments outbalance underlying increasing disease incidence, such that our overall observation of a stable admission incidence reflects

better control in an increased number of asthmatic children. However, we find it unlikely that a major asthma epidemic has occurred without leaving an imprint in the admission rates for asthma, suggesting that the increased asthma prevalence reported may be driven by increase in the milder segment of childhood asthma and pre-school aged children who are not included in our analysis.

In fact, others who have emphasized consistent data sources have also concluded relative stable rates of childhood asthma [12–14]. This makes it even more intriguing what reports of increasing incidence in fact are reporting? Self-reported asthma symptoms and allergies have definitely been rising [15]. This would fit the labelling shift in childhood asthma and not the actual disease incidence.

We have purposely downplayed the smaller disease incidence fluctuations that are visible from Fig. 2 as these may be chance findings. Alternatively, they may reflect real changes from environmental exposures. For instance smoking bans have been introduced in many countries with variations in stringency during the past decade. Several studies have reported drops in childhood asthma admissions in the period after the legislations. Specifically, a 2010 Scottish study reported a drop in childhood asthma hospitalizations after a peak in 2006, and this was interpreted as a result of the ban of tobacco in restaurants [16]. A more recent and larger study from England, where similar legislation was introduced in 2007, also reported a significant albeit smaller effect of the smoke ban on pediatric asthma admission rates [17].

The Danish population is comparable to the Scottish and English in many respects, including culture and access to public free healthcare. Legislation against smoking was initiated in 1995 in Denmark. In August 2007 the law was extended, now including public restaurants much alike the Scottish. Interestingly we see a drop in the Danish asthma hospitalizations around 2006 i.e. more than a year before the introduction of the smoking ban. Also evident from Fig. 2 is that the local peak around 2004 was preceded by a rise starting around the mid-nineties, actually when the first restrictions were introduced. Both the English and the Scottish study covers a much shorter period of time (1997–2010 and 2001–2009) compared with our 35 years of observation. Indeed, this will affect the baseline trend of hospitalizations and thereby the prediction of a counterfactual post legislation trend.

Smoking and secondhand smoke exposure are well-known risk factors for asthma and asthma exacerbations. But environmental short-term changes should be interpreted with great caution, and inferring causal relations from isolated time trends could be biased by random longer-term fluctuations. In conclusion, our long-term analysis argues no specific effect from tobacco ban on acute asthma hospitalization.

Readmissions

We have reported a drop in readmissions for asthma 2 decades ago [8] where we interpreted this as an indication of improved disease control inasmuch as first-admissions where frequent before regular treatment was initiated while readmission was a better reflection of control after the diagnosis was made. The fact that the low-point in readmission during 1992–1996 was followed by stabilization from mid 1990s onwards where the trend in readmission rates is similar, but inflated, to the minor fluctuations in overall trend could therefore be interpreted as no further improvements in asthma management in the recent two decades.

Conclusion

In summary, this nationwide analysis of asthma hospitalization of children in the recent 35 years shows a stable incidence of first-admissions, suggesting a stable incidence of this particular asthma phenotype among school-aged children.

Milder cases may therefore be contributing to alleged increase in asthma incidence.

The stable rate of readmissions for childhood asthma suggests that there has been no or little improvement in asthma management in the recent 2 decades.

Authors contributions The guarantor of the study is HB, from conception and design to conduct of the study and acquisition of data, data analysis, and interpretation of data. AS was responsible for data acquisition and analysis, interpretation and writing the manuscript. CBP contributed substantially to the analyses and interpretation of the data, and provided important intellectual input. All authors have agreed that the accuracy and integrity of any part of the work has been appropriately investigated and resolved and all have approved the final version of the manuscript. The corresponding author had full access to the data and had final responsibility for the decision to submit for publication. No honorarium, grant, or other form of payment was given to anyone to produce the manuscript.

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Compliance with ethical standards

Conflict of interest None.

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