

International exchange

Adherence to guidelines for drug treatment of asthma in children: potential for improvement in Swedish primary care

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ABSTRACT

Background Adherence to guidelines in general is poor. Because asthma is the most common chronic disease in Swedish children, identifying areas for improvement regarding drug treatment for asthma is crucial.

Aim To explore the utilisation patterns of anti-asthmatic drugs in children with asthma in relation to evidence-based guidelines.

Method All children visiting 14 primary healthcare centres in Stockholm, Sweden, who had their first prescription of anti-asthmatic agents dispensed between July 2006 and June 2007 were followed over 24 consecutive months. The children (1033 in total) were divided in two age groups: 0–6 years and 7–16 years. The outcome measurements were: the characteristics of the physicians initiating drug treat-

ment; the extent to which the children were initiated on the drugs recommended in the guidelines; and the amount and frequency of drugs dispensed over time and whether the dosage texts on the prescriptions contained adequate information.

Results In 54% of the older children and 35% of the younger children, only one prescription for anti-asthmatic drugs was dispensed during two years of follow-up following the first prescription. In school-aged children, 50% were initiated on inhaled short-acting bronchodilating beta2-agonists (SABA) in monotherapy. Among preschool children, 64% were initiated on SABA and inhaled corticosteroids in combination. In 41% of the prescriptions dispensed, the indication was stated and in 25% the mechanism of action was stated. Drug therapy was

initiated by a general practitioner in 42% of the younger children and 72% of the older children.

Conclusion There is a need for improvement in adherence to guidelines in important areas. Asthma, especially among children aged 7–16 years, is usually a chronic disease and should, in many cases, be treated with anti-asthmatics counteracting

inflammation. However, this was not the case in our study. In addition, the dosage texts written by the physicians did not follow recommendations and may negatively influence patient safety.

Keywords: anti-asthmatic agents, asthma, drug utilisation, general practitioner, primary care

How this fits in with quality in primary care

What do we know?

Asthma is a common disease in primary care. Many children with asthma have a chronic disease and should receive continuous anti-asthmatic drugs to counteract inflammation. Inhaled beta2-agonists could be used for monotherapy in very mild asthma, but are otherwise considered as rescue medication to be used as needed. There is room for improvement in adherence to guidelines in general. However, less is known about the adherence to guidelines for asthma treatment of children in primary care.

What does this paper add?

Asthma in children is usually not treated as a chronic disease. Only 47% of all children aged 7–16 years old in 14 Swedish primary healthcare centres who initiated asthma treatment redeemed a prescription of inhaled corticosteroids. This proportion should be 80%, according to guidelines. In 42% of the children, there was only one prescription dispensed in 24 months. This indicates that patient and physician adherence to guidelines and care is poor over time. In more than half of the investigated prescriptions, the dosage texts lacked information about indication and/or mechanism of action. Thus, the prescriptions did not follow the regulated requirements. Improvement of the dosage texts could be a potential way to improve care in the future.

Introduction

Asthma is the most common chronic disease among children in most industrialised countries.¹ The prevalence has been estimated at 8–10% of all Swedish children aged 0–16 years.²

Pharmacotherapy is the cornerstone of asthma treatment according to evidence-based international guidelines,³ as well as national and regional guidelines in Sweden.^{4,5} Similar to other countries, drugs to treat asthma in Sweden are not available over-the-counter and a prescription from a physician is required. In order to improve patient safety, the Swedish Medical Products Agency has stated that the dosage, mechanism of action, indication and duration of treatment should clearly be specified in the dosage text on all prescriptions.⁶

In the Swedish national and regional guidelines for management of asthma,^{4,5} it is stated that children aged 7–16 years with mild asthma should be treated in primary care. The term asthma should be used with care in younger children without atopic manifestations, especially below the age of 3 years, because up to 50% in this age group will have at least one episode of virus-induced wheezing without developing a recurrent wheeze.⁷ Children with recurrent obstructive

airway symptoms due to viral airway infections are diagnosed as virus-induced asthma even if the asthma often resolves by school age.¹ Preschool children (under 7 years old) should be treated by a paediatrician because treatment of asthma is more complicated in this age group. Most preschool children are referred to paediatricians by general practitioners (GPs). GPs subsequently initiate treatment with short-acting bronchodilating beta2-agonists (SABA). Previous research has highlighted that implementation of guidelines in primary care is a complex task.⁸ More needs to be done and understood, as there appears to be an appreciable gap between what is carried out by physicians and what should be done in clinical practice to achieve the targets and levels of care outlined in the guidelines.⁹ There is, however, limited knowledge on how guidelines for asthma are followed in primary care. This is partly due to the limited availability of data on prescribed and dispensed drugs. The development of the Swedish Prescribed Drug Register in 2005 has facilitated such studies.^{10,11} The aim of this study was to explore the dispensing patterns of anti-asthmatic drugs to children in relation to evidence-based guidelines. If areas for improvement can be identified, these can then be targets for strategies towards developing the care of children with asthma.

Methods

Study population and design

This was a retrospective observational study of dispensed anti-asthmatic drugs during a 2-year period. The drugs were prescribed to a cohort of children visiting 14 primary healthcare centres (PHCs) in northern Stockholm, Sweden. The PHCs were recruited to a study evaluating the effect of an educational intervention to improve the management and treatment of asthma. This study describes the utilisation of anti-asthmatic drugs at baseline.

Inclusion criteria were children aged 0–16 years who were dispensed at least one prescription for the treatment of asthma between July 2006 and June 2007, following a 1-year period without any prescribed anti-asthmatic drugs. All children dispensed with an anti-asthmatic drug were then followed for 24 consecutive months after the first dispensing date. All patients had at least one of the prescriptions issued from the participating PHCs. However, the study also included all prescriptions dispensed to patients issued by physicians other than the GPs at these PHCs.

Data collection

All data were collected from the Swedish Prescribed Drug Register, containing data on all dispensed ambulatory prescriptions for the entire Swedish population (99.7% coverage) from July 2005.¹⁰ According to Swedish legislation, all prescriptions are valid for up to 1 year after they are issued and may be repeatedly dispensed until the prescribed amount is reached. Three months is the maximum prescription time that patients are allowed to qualify for subsidised drugs.¹²

Data analysis

The children were studied in two age groups: 0–6 years (preschool) and 7–16 years (school age). This is because, according to the national guidelines at the time of the study, the management and treatment of asthma differs for these two age groups.⁴

The analyses were undertaken to determine the extent to which:

- treatment was initiated by GPs versus by paediatricians
- the children were initiated on the drugs or drug combinations.

The guidelines recommended:

- the amount of drugs dispensed over time. Defined daily doses (DDD) were used to estimate the

volumes dispensed.¹³ Absolute DDD values, defined for adults only, were 0.8 mg for salbutamol, 2 mg for terbutaline and 0.8 mg for budesonide (the most commonly prescribed anti-asthmatic drugs)

- that the dosage texts on the prescriptions contain adequate information clearly stating the mechanism of action. They should be written in Swedish without abbreviations that could be misinterpreted by the patient.

Based on the recommended drugs for the treatment of asthma^{3–5} the following combinations of drugs were included in the analysis: inhaled SABA, inhaled long-acting beta2-agonists (LABA), inhaled corticosteroids (ICS), fixed combination therapy, and montelukast, the only leukotriene receptor-antagonist currently registered in Sweden.

Analyses of the dosage texts were limited to three products. Two of these were SABA products: terbutaline, administered by dry powder inhaler (DPI), accounting for 12% of prescriptions; and salbutamol, administered by pressurised metered dose inhaler (pMDI) accounting for 27% of prescriptions. The third product was the ICS budesonide administered by pMDI (21% of prescriptions). The reason for choosing these three drugs was that they were the most frequently prescribed anti-asthmatics to children at the 14 PHCs at the time for the study. In addition, we wanted to study whether the mechanism of action and indication for the drugs were clearly stated for the two different substances, SABA and ICS.

The dosage texts were studied from a patient perspective. Variations in the dosage texts were analysed qualitatively and then graded as pass or fail. Texts with the same content were graded as equal with no consideration given to minor variations in phrasing, e.g. 'for asthma' vs 'against asthma'.

An indication stated on the prescription was graded as 'pass' if it fulfilled the indication for the drug stated in the Summary of Product Statistics (SPC). The specific effect or action of the drug on the lung should be stated for acceptance of mechanism of action.

Statistical analysis

Standard descriptive statistics (number and proportions) were used to describe the study cohort and the utilisation patterns. The obtained data were processed in Microsoft Excel v. 2003, SYSTAT II v. 2004 (SYSTAT Software, Richmond, CA, USA) and SAS v. 9, 1.3 SP 3, 2004 (SAS Institute, Cary, NC, USA).

Results

A total of 1033 children aged 0–16 years were initiated on anti-asthmatic drugs during July 2006 to June 2007. This corresponds to 6% of all children in this age group visiting the 14 PHCs during the study period. Slightly more than half of all children (51%) were aged 0–6 years and 45% were girls.

Asthma treatment was initiated in a paediatric outpatient clinic for 52% of the preschool children and by GPs in primary care for 42%. Among the school-aged children, almost three-quarters (72%) received their asthma treatment from GPs in primary care, 16% had their treatment initiated at a paediatric outpatient clinic. Other healthcare providers such as hospital-based specialists or school-health initiated treatment in 6% of the preschool children and 12% of the school-aged children.

Choice of drug for initiation

Most children (89%) were initiated on SABA as monotherapy or SABA in combination with ICS (Table 1).

Among the preschool children (0–6 years), the majority (64%) were initially dispensed a combination of ICS and SABA. SABA as monotherapy was most common among the school-aged children (7–16 years), where it was initially dispensed in 50% of the children. Anti-asthmatic drugs other than SABA and ICS were dispensed in fewer than 8% of the children (Table 1).

Persistence and dispensed volumes per patient

A total of 42% of the children were only dispensed one prescription during the 24 months' follow-up, whereas 13% had more than four prescriptions dispensed.

The school-aged children, in general, had fewer prescriptions dispensed than the preschool children (Figure 1).

Table 1 Number of patients with their first anti-asthmatic drugs dispensed July 2006–June 2007 after a 1-year drug-free wash-out period (children were from 14 primary healthcare centres in Stockholm)

| Drugs | 0–6 years | | | 7–16 years | | | All children (0–16 years) <i>n</i> (%) |
|--|-----------------------|----------------------|-----------------------|-----------------------|----------------------|-----------------------|--|
| | Girls <i>n</i> (%) | Boys <i>n</i> (%) | Total <i>n</i> (%) | Girls <i>n</i> (%) | Boys <i>n</i> (%) | Total <i>n</i> (%) | |
| SABA and ICS | 149 (65) | 189 (63) | 338 (64) | 70 (30) | 95 (35) | 165 (33) | 503 (49) |
| SABA monotherapy | 68 (30) | 91 (30) | 159 (30) | 127 (55) | 123 (46) | 250 (50) | 409 (40) |
| ICS monotherapy | 6 (3) | 18 (6) | 24 (5) | 11 (5) | 13 (5) | 24 (5) | 48 (5) |
| Fixed combination ^a and SABA | 1 (<1) | 0 (0) | 1 (<1) | 17 (7) | 20 (7) | 37 (7) | 38 (4) |
| LABA monotherapy | 0 (0) | 0 (0) | 0 (0) | 5 (2) | 10 (4) | 15 (3) | 15 (1) |
| LABA, ICS and SABA | 0 (0) | 0 (0) | 0 (0) | 2 (1) | 5 (2) | 7 (1) | 15 (1) |
| Montelukast monotherapy | 1 (<1) | 1 (<1) | 2 (<1) | 0 (0) | 2 (1) | 2 (<1) | 4 (<1) |
| Other combinations ^b | 4 (2) | 2 (1) | 6 (1) | 1 (<1) | 2 (1) | 3 (1) | 9 (1) |
| All patients initiated on therapy | 229 (100) | 301 (100) | 530 (100) | 233 (100) | 270 (100) | 503 (100) | 1033 (100) |

^a Fixed combination of ICS and LABA. ^b Other combinations of the above-mentioned drugs. SABA, short-acting beta2-agonists; ICS, inhaled corticosteroids; LABA, long-acting beta2-agonists.

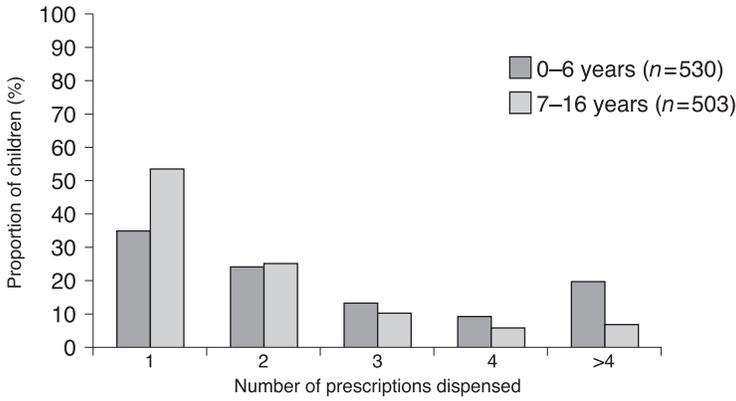


Figure 1 Number of anti-asthmatic drug prescriptions dispensed to each patient over a 24-month period

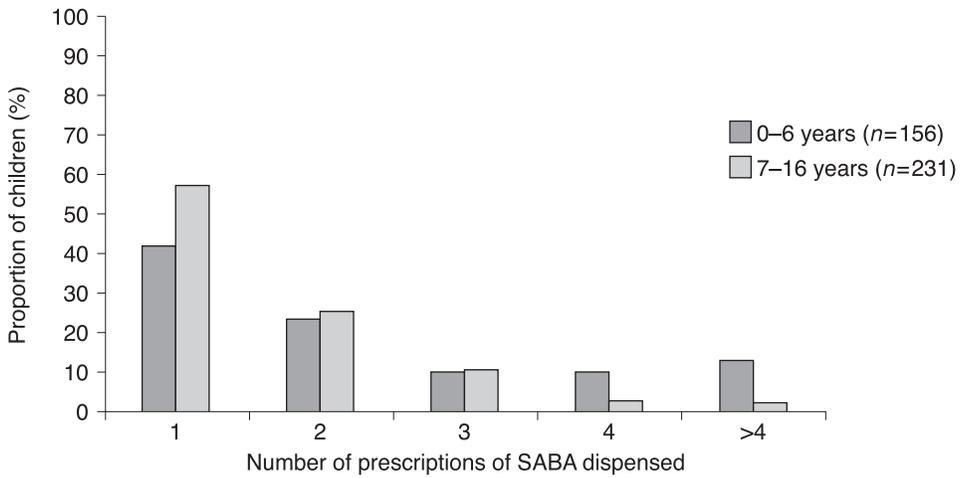


Figure 2a Number of dispensed prescriptions of SABA in mono-therapy over the 24-month follow-up period

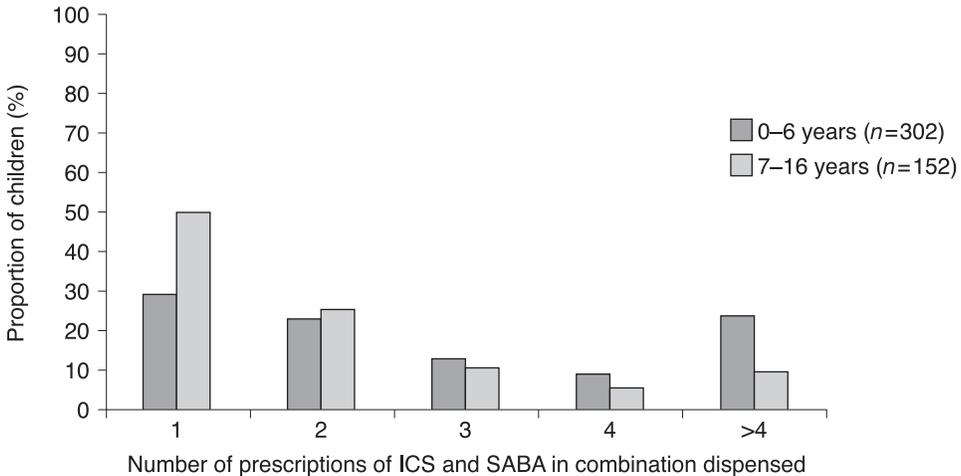


Figure 2b Number of dispensed prescriptions of SABA and ICS in combination over the 24-month follow-up period

Children treated with SABA in monotherapy were most likely to have fewer prescriptions dispensed during the study period (Figure 2a). Few patients were dispensed large volumes of SABA, measured as DDD, during the period studied, and the majority

were dispensed small volumes (Figure 3). Of the total amount of SABA dispensed per month, measured as DDD, 8% of preschool and 6% of school-aged children were dispensed 30% of the SABA DDDs per month.

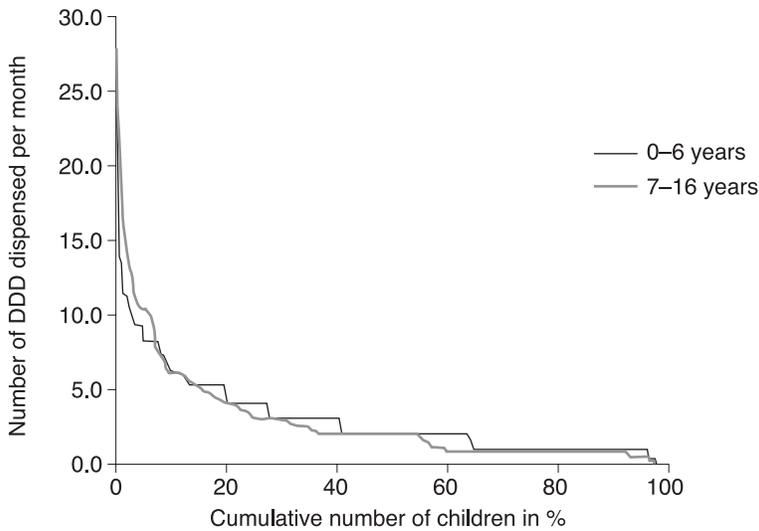


Figure 3 Proportion of patients dispensed different volumes of SABA

Table 2 Number and proportions of prescriptions dispensed where either indication or mechanism of action was stated and examples of how the most common dosage texts were stated

| Drug | Indication stated <i>n</i> (%) | Mechanism of action stated <i>n</i> (%) | Example of the most common dosage texts |
|-------------|-----------------------------------|---|---|
| Salbutamol | 557 (39) | 471 (33) | 1–2 doses 3–4 times daily when coughing. Muscle-relaxing To be inhaled 1–4 times daily as needed 1 inhalation every third hour as needed Airway-widening |
| Terbutaline | 294 (46) | 173 (27) | 1–2 inhalations as needed 1–2 inhalations as needed against asthma 1–2 inhalations as needed. Airway-widening |
| Budesonide | 434 (40) | 142 (13) | 2 inhalations 2–3 times daily for one week until the cough has disappeared After that half the dose should be given for one more week. Against inflammation in the airways 1 inhalation twice daily According to prescription |

Children who first collected combinations of ICS and SABA had more prescriptions dispensed than children who started with SABA in monotherapy (Figure 2b).

Dosage texts

The total numbers of prescriptions dispensed during the observation period were: salbutamol, 1428; terbutaline, 639; and budesonide, 1092. A total of 566 (salbutamol), 328 (terbutaline) and 420 (budesonide) different ways of expressing the dosage were identified

on the prescriptions. Table 2 shows the number of prescriptions dispensed where the indication or the mechanism of action was stated and examples of the most common dosage texts.

Discussion

The main finding of our study was that asthma in children aged 7–16 years was not correctly treated

pharmacologically as a chronic disease. Nevertheless, asthma, at least in most children aged 7 years and older, is a chronic disease. This means that continuous or intermittent treatment with anti-asthmatic drugs is indicated.¹ For children with exercise-induced asthma, intermittent treatment with SABA might be sufficient and as a symptom reliever SABA should also always be prescribed to all children with asthma. From earlier studies^{14,15} it is known that 80% of children with asthma in this age group are sensitised to perennial allergens, mainly furred pets. Preventing exposure to allergens in sensitised children is therefore important. However, the presence of animal dander is common in school dust¹⁶ and exposure triggers asthma and airway inflammation in the sensitised child.¹⁷ Children sensitised and exposed to perennial allergens should, according to the guidelines, be treated continuously with drugs targeting the asthmatic inflammation such as ICS.^{3–5,14} In our study, only 47% of children in this age group were initiated on any kind of anti-inflammatory drug for asthma. Under half (45%) only had one prescription of ICS and only 10% had more than four prescriptions of ICS dispensed.

One explanation as to why only a limited number of children seemed to be initiated on, and even fewer had prescriptions dispensed for, anti-inflammatory maintenance treatment might be that, because we studied dispensed drugs, we missed children that received a prescription for ICS but never redeemed it. However, similar data were obtained in a Dutch study assessing asthma prescription patterns for children.¹⁸ In the Dutch study, fewer than 40% of children with physician-diagnosed asthma received a prescription for an anti-inflammatory drug during the 1-year observation period, and fewer than 20% had three or more prescriptions. Preschool children treated with ICS in combination with SABA were the group that had most prescriptions dispensed during the observation period.

More obvious symptoms of the disease of asthma and/or greater parental influence in younger children compared with older ones might explain the better adherence to guidelines in the dispensing patterns to preschool children. It is known that a decrease in symptoms often leads to a discontinuation of therapy with ICS.¹⁹ Many adolescents are also reluctant to accept drug treatment.²⁰

SABA in monotherapy had the least number of prescriptions dispensed in both age groups. A Dutch study including oral SABA, which in preschool children in Sweden is often used as a diagnostic tool, has shown that more than 30% of children treated with asthma medication did not have doctor-diagnosed asthma.²¹ Because oral SABA was excluded in our study, and inhaled anti-asthmatics, especially in preschool children, are complicated to administer, it is reasonable to believe that most of the preschool

children in our study had asthma. However, some of the school-aged children initiated on SABA in monotherapy, who had the drug dispensed only once, may not have an asthma diagnosis. In some of these cases, SABA might have been prescribed merely as a diagnostic tool.

The use of SABA in monotherapy may also indicate milder asthma, whereas ICS in combination with SABA may indicate moderate to severe asthma.³ In a study by Zuidgeest *et al*, it was found that persistence of asthma medication prescribed in the first year of life was positively associated with doctor-diagnosed asthma and use of inhaled corticosteroids.²²

Children initiated on drugs other than SABA in monotherapy or SABA and ICS in combination were few, which is in line with the guidelines.^{3–5}

According to the guidelines,^{4,5} GPs can initiate treatment with SABA in preschool children, but a paediatrician should initiate treatment with ICS. However, in this age group, asthma is often related to upper airway infections,¹ which are primarily treated by GPs. The fact that the majority in this age group were initiated on ICS and SABA in combination meant that many of the preschool children had their ICS treatment initiated by a GP, which is not in accordance with the current guidelines. However, especially in some areas, this is a large group of patients. To avoid delays, GPs experienced in managing childhood asthma have sometimes initiated ICS treatment in cooperation with a local paediatrician, often after a phone consultation.

Most children (72%) in the 7–16 years age group had their treatment initiated in primary health care, which is in line with the guidelines.

Overall, the dosage texts gave insufficient information and may be a potential patient safety problem. For budesonide, the only ICS studied, only 13% of the dispensed drugs had a mechanism of action stated on the prescription. Because budesonide was studied only with a pMDI device, one argument could be that this was only prescribed to preschool children who often have individualised treatment or special prewritten 'ICS schedules'.⁵ However, this should be stated in the dosage text as 'according to prescription'. The fact that insufficient dosage texts are common is supported in a study by Abramson *et al*²³ where prescribing errors occurred at high rates among community based primary care providers. Even if only a small number of these resulted in adverse drug events – 9% in a study by Bates *et al*²⁴ – these adverse events are preventable.

Insufficient information in the dosage text could also make it more difficult for the pharmacist dispensing the drug to give adequate information to the patient. To ensure patient safety, this often results in time-consuming phone calls with the providers for prescription clarification.²⁵

A strength of our study is that since the Swedish Prescribed Drug Register has an almost 100% coverage of all prescriptions dispensed,⁹ we can give a complete overview of all drugs for asthma dispensed during any period studied.

A weakness of our study is that the drug-free period to define initiations was only 1 year. Patients with just one drug dispensed during the observation period may have been dispensed drugs for asthma more than 12 months previously. However, this does not change our conclusion. If this was the case, it is reasonable to believe that these patients had mild asthma and may have had the same drugs prescribed for a long time.

Finally, it is important to acknowledge that dispensed drugs may not be the same as prescribed drugs. Because we do not have data on prescriptions that were never redeemed, the study may underestimate prescribers' decision making and their adherence to guidelines. However, the patients can actually take only what is dispensed. High-quality treatment should be reflected in the dispensed drugs, unless there is widespread use of anti-asthmatics prescribed to someone else, for instance, a relative, or medications purchased abroad. This may be the case for a few individuals, but is not likely to affect the overall findings. We are also aware that dispensed drugs are not necessarily the same as actual use of the drug. Nevertheless, despite these limitations, we believe that the longitudinal data on dispensed drugs for asthma for a large group of children revealed important information on the utilisation of these drugs in a real-life primary healthcare setting, identifying many areas for improvement.

Conclusion

There is a need for improvement in adherence to guidelines in important areas, especially among children aged 7–16 years. Fewer than expected were treated with ICS and very few had regular treatment with ICS. Because asthma is a chronic disease that can cause deterioration of lung function and increasing bronchial hyper-responsiveness due to progressive airway inflammation, it is important that the patients receive information on how the anti-asthmatic drugs work. Clearly stating the mechanism of action and indication in the dosage text could be one way of achieving this.

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ETHICAL APPROVAL

The Ethics Committee of the Karolinska Institutet, Sweden approved the study. The study conforms to the Declaration of Helsinki 59th WMA, General Assembly, Seoul, Korea, October 2008.

PEER REVIEW

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CONFLICTS OF INTEREST

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