

Eliminated patient fee and changes in dispensing patterns of asthma medication in children—An interrupted time series analysis

Elin Dahlén^{1,2} | Joris Komen^{2,3} | Eva W. Jonsson⁴ | Catarina Almqvist^{5,6} |
Inger Kull^{7,8} | Björn Wettermark^{1,2}

¹Centre for Pharmacoepidemiology, Department of Medicine, Karolinska Institutet, Stockholm, Sweden

²Public Healthcare Services Committee, Stockholm County Council, Stockholm, Sweden

³Department of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute of Pharmaceutical Science, Utrecht University, Utrecht, The Netherlands

⁴Clinical Epidemiology, Department of Medicine Solna, Karolinska Institutet, Clinical Pharmacology, Karolinska University Hospital, Stockholm, Sweden

⁵Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

⁶Pediatric Allergy and Pulmonology Unit at Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden

⁷Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, Stockholm, Sweden

⁸Sachs' Children and Youth Hospital, Södersjukhuset, Stockholm, Sweden

Correspondence

Elin Dahlén, Centre for Pharmacoepidemiology, Department of Medicine, Karolinska University Hospital Solna, T2 S-171 76 Stockholm, Sweden.
Email: elin.dahlen@ki.se

Funding information

Stockholm County Council

Abstract

In 2016, all prescription drugs included in the reimbursement system in Sweden were made available for children (age 0-17 years) without any patient fees. Our aim was to estimate the association between this intervention and the dispensing patterns of asthma medications among children. Dispensing data on asthma medications for all children living in Stockholm County during 2014-2017 were selected to include two years before (January 2014-December 2015) and after (January 2016-December 2017) the intervention. In an uncontrolled before and after study, the measures of utilization were as follows: the proportion of children with at least one dispensed asthma medication (prevalence); the number of children initiated on treatment after an 18-month drug-free period (incidence); the number of defined daily doses (DDDs) dispensed per child; and the number of children with at least two prescriptions with controller medication (inhaled corticosteroid or leukotriene receptor antagonist) dispensed during 18 months (persistence). In an interrupted time series (ITS) analysis, all measures were included except for persistence. Socio-economic status was defined using Mosaic data. The prevalence increased after the intervention (from 11.9% to 13.0%). However, the ITS analysis showed a positive trend already before the intervention, and consequently, the increase was not attributable to the intervention. For incidence, similar patterns were observed. There was an increase in dispensed volumes related to the intervention, 46.3 DDDs/child/month before and 51.1 after the intervention (P -value 0.01). The proportion of children with persistent asthma medication increased from 46.0% to 51.9% in children with low socio-economic status. In conclusion, the intervention was only modestly associated with changes in the dispensing patterns of asthma medication, with the volume dispensed per child increasing slightly, particularly in children with low socio-economic status.

KEYWORDS

asthma, co-payment, drug utilization, interrupted time series analysis, patient fee

1 | INTRODUCTION AND BACKGROUND

Pharmacological treatment is a cornerstone in asthma management, and although asthma medication is the second most commonly prescribed medication in children (prevalence 10%-25%),¹ many studies report low adherence to treatment with controller medication.²⁻⁴ One previously described reason for low adherence to asthma medication is limited financial resources.^{5,6}

In the Priority Medicines report, the World Health Organization (WHO) suggested medicine use in children to be a priority area in need of more attention, resources and research.⁷ Health professionals and policymakers apply a range of strategies to promote a more safe and effective use of medicines. The main strategies can be abbreviated with the “four Es”: Education, Engineering, Economics and Enforcement.⁸ Economical interventions include changes in insurance and reimbursement systems, patient co-payment, positive and negative financial incentives for physicians and rebate schemes for over-prescribing of agreed drugs. Changes in patient fees may be effective in influencing patient behaviour but it is difficult to set the appropriate levels of co-payment. Too high fees may limit those in need of medication to redeem their prescriptions, and too low fees may lead to overconsumption of medications and waste of resources. A Cochrane review showed that increased patient co-payment could lead to a decrease in prescription drug use and expenditure.⁹ However, effects on medication use of the opposite interventions, that is, reducing patient co-payment on medication use have, to the best of our knowledge, not been scientifically evaluated.

Equal health care has been one of the cornerstones in Swedish health policy over a number of decades.¹⁰ Social inequalities in health remain a major issue, and the government has recently commissioned an investigation into how inequalities in health can be reduced.¹¹ Equality also relates to medicine use, and a Swedish report has shown that 3% of the population claim that they do not redeem a prescription because of economic reasons.¹² In children with single parents, the proportion was twice as high. Therefore, the government introduced a change in the Swedish reimbursement system, and in January 2016, the legal decision of free medications to children (age 0-17 years) came into force.¹³ All prescription medications included in the reimbursement system became free of charge for children. The rationale behind the elimination of a patient fee was to increase access to medications regardless of social and financial conditions.

The aim of this study was to estimate the association between the eliminated patient fee and the dispensing patterns of asthma medications among children. Our hypothesis is that the elimination of a patient fee increased the dispensing of asthma medication—both the number of children treated

and the dispensed volumes per child. We also hypothesize that the effect is most profound among children with relatively low socio-economic status.

2 | MATERIAL AND METHODS

This was a population-based study of dispensing patterns of asthma medication in all children (age 0-17 years) in Stockholm County (n = 468 580 in January 2014 and 485 665 in January 2016). The study consisted of two sub-studies: an uncontrolled before and after comparison (a) and an interrupted time series analysis (b).

2.1 | Intervention

In January 2016, the legal decision of free medications to children came into force.¹³ All prescription medications included in the reimbursement system became free of charge for children regardless of whether the prescription was issued before or after 1 January 2016. Before 1 January 2016, all children and adults were included in a national reimbursement system for prescription medication, where a high-cost threshold system was applied. Before the intervention, each individual had to pay a maximum annual cost of 2200 SEK (approximately 214 EUR) for prescription medicines. All children in a family shared the same high-cost threshold; that is, a family with three children would pay a maximum of 2200 SEK per year for all their children's prescription medications. According to Swedish legislation, all prescriptions are valid up to 1 year after they have been issued and may be repeatedly dispensed until the total prescribed amount is purchased. A 3-month supply is the maximum amount patients can be dispensed at each refill to get their medication subsidized.

2.2 | Participants

Our study population was defined as children 0-17 years old who lived in Stockholm and had at least one dispensed prescription of asthma medication during 2014-2017. This time period allowed us to include 2 years (24 months of data) before (January 2014-December 2015) and after (January 2016-December 2017) the intervention. Asthma medications were defined by ATC codes as follows: Short-acting β_2 -agonists, SABA (ATC codes R03AC02, R03AC03); controller medication (Inhaled corticosteroids, ICS ATC codes R03BA or Leukotriene receptor antagonists, LTRAs R03DC or fixed combination of ICS and long-acting β_2 -agonists, LABA R03AK06-08 or R03AK11); and LABA (R03AC12, R03AC13); at least one of SABA, controller medication, or LABA was denoted as “any asthma medication.”

2.3 | Data sources

The population was selected from the administrative healthcare databases VAL held by the Stockholm County Council.¹⁴ The VAL databases include all healthcare contacts and recorded diagnoses from inpatient care, specialized ambulatory care and primary care along with data on all dispensed prescription medications from all pharmacies in the country to the citizens in the region. The prescription information is the same as in the national prescribed drug register, that is unique patient data on all prescription drugs dispensed anywhere in Sweden to inhabitants in the region since July 2010: amounts, expenditures and reimbursement, the age and sex of the patient, co-payments and prescriber category.¹⁵ The information has a high validity, with >99% of all prescriptions registered with unique identifiers. Information on all prescription medications dispensed to inhabitants in Stockholm County was included in the databases regardless of reimbursement status. The VAL databases also include demographic data on age, sex, death, migration and area of residence (Small Areas for Market Statistics, see below).

2.4 | Measurements

In the uncontrolled before and after study (a), five different outcome measures of utilization were calculated 2 years before and after the intervention, respectively:

- The proportion of children with dispensed asthma medications, that is period prevalence
- The number of children initiated on treatment, defined as children purchasing a first prescription after an 18-month asthma medication-free period, that is incidence
- The dispensed volume measured as the sum of defined daily doses (DDDs) per child
- The proportion of children with persistent medication measured as having at least two asthma controller medications (inhaled corticosteroid or leukotriene receptor antagonist) dispensed during an 18-month period (second dispensing date >first dispensing date), that is persistence. The 18-month time window was used based on our previous study in which we compared dispensing patterns of asthma medicines with patient-reported use.¹⁶
- The proportion of children with controller medication (inhaled corticosteroid or leukotriene receptor antagonist) of all children with dispensed asthma medications.

The outcome measurements selected were intended to reflect different types of changes in patient behaviour after the elimination of the patient fee.

In the interrupted time series (ITS) analysis (b), similar measures of prevalence, incidence and DDDs were used. We

did not analyse the number of children with persistent medication since the measurement was not feasible to calculate with monthly data.

Socio-economic status was defined using Mosaic data.¹⁷⁻¹⁹ Mosaic is an area-based classification system based on Small Areas for Market Statistics (SAMS). In Stockholm County, 1345 SAMS were defined. One SAMS area included on average 1700 inhabitants, so all individuals living in a SAMS area were assigned to the same mosaic category. In total, over 100 variables are included in the mosaic classification originated from demographic data (education and family composition), economic data (income and wealth), urbanity (population density) and dwelling data. These data are categorized into 14 segments. The mosaic segments were summarized to three different categories: low, middle and high socio-economic status.

2.5 | Statistical analyses

In sub-study (a), we used an uncontrolled before and after design. We calculated the proportion of children with asthma medications as the number of individuals with dispensed asthma medications divided by the total number of children 2 years before and 2 years after the intervention, respectively. We also calculated the absolute and relative differences in prevalence before and after the intervention.

In sub-study (b), we used an ITS analysis to analyse the association between the intervention and a change in utilization patterns of asthma medication.²⁰⁻²² The outcome was repeatedly measured each month to create a trend over time, starting from January 2014 and ending in December 2017. With this, we created a pre- and post-intervention timeframe of 2 years, giving an equal distribution of seasons and seasonal trends before and after the intervention. We used a segmented regression model to determine two associations: the direct effect (change in level) and the trend (change in slope) before and after the intervention. We checked for autocorrelation using the Durbin-Watson statistic and by visual inspection of the autocorrelation functions and corrected for this if needed with an autoregressive term in the time series model. For illustrative purposes, we presented linear segmented regression lines in Figure 2A-C.

Pre-specified stratifications by socio-economic status and type of asthma medications were performed.

We performed a sensitivity analysis using data for diabetic medications to act as a control group. All children with at least one dispensed prescription of diabetic medication (ATC-code A10) during 2014-2017 were included in the analysis. Insulins (accounting for 96% of all diabetic medications for children) were not part of the intervention since these medications were free of charge for patients already before January 2016. Furthermore, the dispensing patterns for

diabetic medications do not show the same seasonal variation as asthma medications.

SAS Enterprise Guide 7.1 (SAS Institute Inc) was used for the data extraction and processing of data. The statistical package IBM SPSS Statistics for Windows, version 23 (IBM corp.), was used for all statistical analyses in sub-study (b).

3 | RESULTS

The overall study population is shown in Table 1. The total number of children living in the region increased with 3.6% from January 2014 to January 2016, but the distribution in terms of sex, the proportion of children in each age category and the distribution within different socio-economic categories remained the same (Table 1).

3.1 | Sub-study (a)—uncontrolled before and after comparison

The total number of dispensed prescriptions of asthma medication was larger after the intervention with a relative difference of 19.3% (Table 2; Figure 1). The prevalence of dispensed asthma medication increased from 11.9% to 13.0% after the intervention. A slightly higher incidence was seen after the intervention (8.0% before and 8.5% after). Larger volumes of asthma medications were dispensed to each child after the intervention (124 DDDs/child before and 137 DDDs/child after). Also, the proportion of children with persistent use of asthma controller medication increased from 48.3% to 52.2% after the intervention. Across all measures, boys redeemed a larger number of prescriptions and a larger proportion of boys than of girls were dispensed asthma medications (Table S1).

The prevalence of dispensed asthma medication was lowest in children with low socio-economic status (10.9% before and 12.5% after the intervention). The relative change in prevalence was highest in this group of children (13.5% CI

13.3-13.7 low vs 8.6% CI 8.5-8.7 high socio-economic status). The proportion of children with persistent asthma medication increased from 46.0% to 51.9% in children with low socio-economic status (relative difference 12.9%; Table 2).

3.2 | Sub-study (b)—interrupted time series analysis

The ITS analysis indicated that the prevalence of dispensed asthma medication increased directly after the intervention (6572 children in December 2015 and 6896 children in January 2016); however, the difference was not statistically significant (Table 3). The number of incident children (children initiated on therapy each month after an 18-month drug-free period) increased with 372 children directly after the intervention (P -value 0.393). Larger volumes of asthma medication were dispensed to children after the intervention, 51.1 DDDs/child/month after the intervention compared to 46.3 before (P -value 0.01). A negative trend, that is a declining rate of increase, was seen in all measures after the intervention, but there were no statistically significant differences (Figure 2A–C).

The number of children with dispensed asthma medicines showed a numerical increase across all socio-economic groups, although not statistically significant (Table 4). The same patterns were seen for incidence. However, there was a significant difference in volumes with the number of DDDs/child increasing most in the lowest socio-economic group (3.9; P -value 0.010).

The number of children with SABA appeared to increase directly after the intervention, even though the rate of increase declined over time. Among children with dispensed controller medication, the number of prevalent children and the DDDs/child appeared to increase after the intervention. However, no results were statistically significant (Table 4).

There was no association between the eliminated patient fee and changes in the dispensing patterns for diabetic medication ($P > 0.1$ for prevalence, incidence and number of DDDs/child; data not shown).

TABLE 1 Population characteristics for children in Stockholm County at the start of the study period (January 2014) and at elimination of the patient fee, that is the intervention (January 2016)

Population characteristics	Children in January 2014 (N = 468 580)	Children in January 2016 (N = 485 665)
Girls	227 839 (48.6%)	235 589 (48.5%)
Age categories		
Age 0-1	58 561 (12.5%)	58 837 (12.1%)
Age 2-5	116 731 (24.9%)	117 368 (24.2%)
Age 6-11	158 945 (33.9%)	167 073 (34.4%)
Age 12-17	134 343 (28.7%)	142 387 (29.3%)
Socio-economic status		
Low	165 056 (35.2%)	170 226 (35.1%)
Middle	73 475 (15.7%)	78 680 (16.2%)
High	225 573 (48.1%)	235 422 (48.5%)
Missing	4476 (0.96%)	1337 (0.28%)

TABLE 2 Dispensing patterns of asthma medications among children 0-17 years of age before (January 2014-December 2015) and after (January 2016-December 2017) the eliminated patient fee, that is intervention

Dispensed asthma medications in total and by socio-economic status (SES)	January 2014-December 2015 (N = 468 580)	January 2016-December 2017 (N = 485 665)	Absolute differences (After-Before)	Relative differences ([After-Before]/Before) (%)
No. of prescriptions				
Total	235 147	280 527	45 380	19.3
High SES	118 911	134 190	17 279	12.8
Middle SES	37 882	48 257	10 375	27.4
Low SES	75 009	97 475	22 466	30.0
Prevalence of asthma medication				
Total	11.9%	13.0%	1.1%	8.9
High SES	12.5%	13.0%	0.6%	8.6
Middle SES	12.3%	13.8%	1.5%	9.3
Low SES	10.9%	12.5%	1.7%	13.5
Prevalence of controller medication				
Total	8.6%	9.4%	0.7%	8.3
High SES	9.0%	9.4%	0.4%	4.1
Middle SES	8.8%	9.9%	1.1%	13.0
Low SES	7.8%	9.0%	1.2%	15.0
Incidence of asthma medication^a				
Total	8.0%	8.5%	0.6%	7.1
High SES	8.2%	8.4%	0.2%	2.8
Middle SES	8.3%	9.2%	0.9%	10.7
Low SES	7.4%	8.4%	1.0%	13.4
DDDs/child				
Total	124	137	13	10.5
High SES	129	140	11	8.6
Middle SES	121	133	11	9.3
Low SES	119	136	16	13.5
Proportion of children with persistent medication^b				
Total	48.3%	52.2%	3.9%	8.1
High SES	49.7%	52.6%	2.9%	5.8
Middle SES	48.5%	51.6%	3.1%	6.5
Low SES	46.0%	51.9%	5.9%	12.9
Proportion of children with controller medication/all asthma medications				
Total	72.3%	72.0%	-0.3%	-0.4
High SES	72.5%	72.1%	-0.5%	-0.6
Middle SES	71.8%	72.1%	0.3%	0.4
Low SES	72.1%	71.8%	-0.3%	-0.4

^aAfter an 18-month asthma drug-free period.

^bAt least two asthma controller medications dispensed during 18 months.

4 | DISCUSSION

In this population-based study of all children aged 0-17 years in Stockholm, Sweden, we found an increase in the proportion of children with dispensed asthma medications after the

eliminated patient fee. However, the ITS analysis showed that there was a positive trend already before the intervention, and consequently, the increase in number of children was not attributable to the intervention. For incidence, similar patterns were observed although there was an increase in

the dispensed volumes of asthma medication (DDDs/child) related to the intervention. This was most profound in children with low socio-economic status. The persistence of drug use, that is the proportion remaining on treatment, was higher after the intervention. Since this was not possible to assess in the ITS, it is unclear whether there was a positive trend already before the intervention or if it was an effect of the intervention.

In the uncontrolled before and after study, there was an increase in the prevalence, the incidence, the number of DDDs/child and the proportion of children with persistent medication after the intervention. There are no published studies on

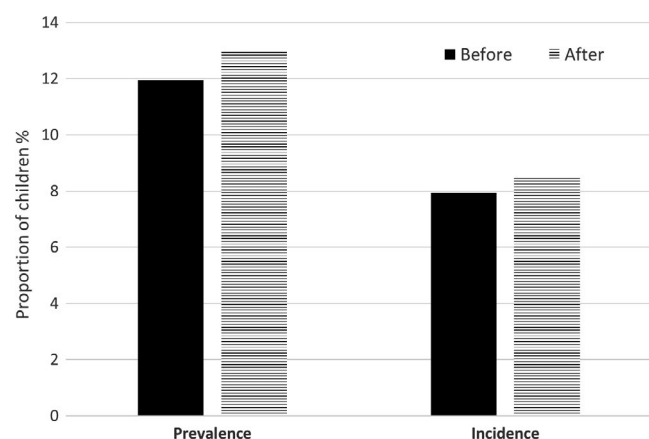


FIGURE 1 Proportion of children with ≥ 1 asthma medication (prevalence) and initiating therapy after an 18-month drug-free period (incidence) before (January 2014-December 2015) and after (January 2016-December 2017) the eliminated patient fee, that is the intervention

similar interventions. However, our findings are supported by previous studies on increased co-payment showing opposite effects.^{5,6} In US children 5 years and older, an increase in cost-sharing for asthma medication resulted in a reduction in medication use (percentage of days covered by a prescription asthma medication; total expenditure on asthma medications) and higher rates of asthma hospitalizations.⁵ Among US citizens aged 12-64 years, even a small increase in patient co-payments (\$5) resulted in lower medication use and higher unintended use of healthcare services.⁶

In sub-study (b), the ITS analysis showed that the intervention did not affect the prevalence nor the incidence of asthma medication. In contrast, the number of DDDs/child increased as an effect of the intervention. The highest increase in volumes of dispensed asthma medication was observed among children in areas with low socio-economic status. The impact of income on the dispensing patterns of asthma medication in children has previously been shown by Gong et al²³ They found that children to parents with the lowest income had a lower incidence of asthma (measured as at least two dispensed asthma medications, hazard ratio 0.8) compared with children to parents with the highest income. Among children with asthma in Ontario, Canada, an increase in the proportion of family income spent out-of-pocket on asthma medication was associated with exacerbations requiring urgent care.²⁴ It has also been found that children with asthma are significantly less likely to receive inhaled corticosteroid prescriptions if they come from low-income families than from high-income families, independent of type of drug insurance.²⁵ That is in line with our findings that controller medication was dispensed more often after the intervention,

TABLE 3 The association between the eliminated patient fee, that is the intervention on 1 January 2016 on the dispensing patterns of asthma medication in children in Stockholm County by socio-economic status (SES)

Model	Level effect	P-value	Trend (change in slope)	P-value
Total model				
No. of prevalent children	893.552	0.395	-9.020	0.922
No. of incident children	371.867	0.393	-0.704	0.984
Mean DDDs/child	3.381	0.010	-0.046	0.699
Low SES				
No. of prevalent children	432.483	0.221	-4.270	0.893
No. of incident children	145.185	0.318	-2.346	0.847
Mean DDDs/child	3.870	0.010	-0.027	0.815
Middle SES				
No. of prevalent children	147.956	0.424	-1.120	0.945
No. of incident children	69.031	0.371	-0.641	0.917
Mean DDDs/child	2.553	0.047	0.070	0.460
High SES				
No. of prevalent children	306.000	0.554	-7.301	0.871
No. of incident children	159.376	0.449	0.838	0.960
Mean DDDs/child	2.324	0.068	-0.086	0.455

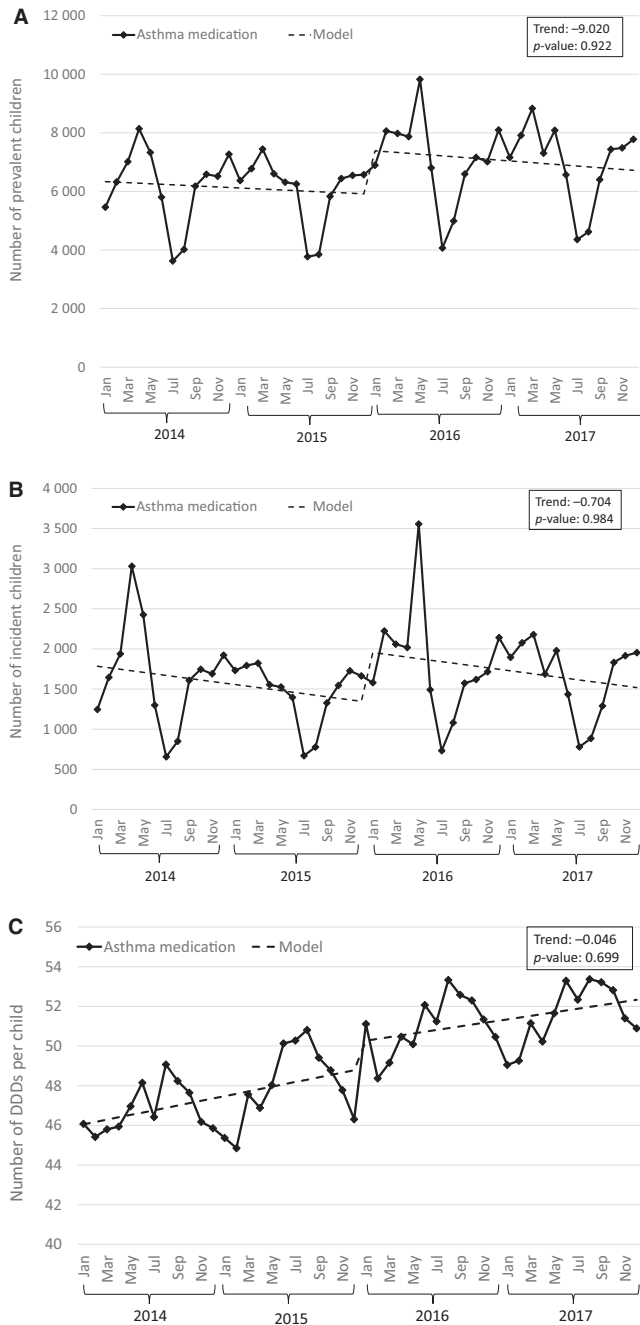


FIGURE 2 Segmented linear regression, interrupted by the elimination of patient fee, that is the intervention, measured as number of prevalent children (A), number of incident children after an 18-month drug-free period (B) and number of dispensed DDDs/child (C)

especially among children with low socio-economic status. A meta-analysis of seven studies including various types of medications showed 11% increased odds of non-adherence to medications in populations with co-payment systems compared with non-co-payment groups.²⁶ Furthermore, among patients in primary care in Catalonia (Spain; age >14 years), even a small increase in patient co-payment (€1) did affect the initial medication non-adherence (not filling a prescription

for a newly prescribed medication, analgesics 50%, treatments for chronic disease 12% and penicillin 12%).²⁷

In general, the intervention had relatively small effects on the dispensing patterns of asthma medication in children. This might be explained by the fact that there already was a positive trend for all measures before the intervention was carried out. It could be that there had been increased focus on pharmacological asthma treatment in children due to recently updated national guidelines²⁸ before the intervention, and therefore, only small effects of the intervention were seen. However, the proportion of children with persistent controller medication as well as the number of DDDs/child increased after the intervention. That may imply that children were not dispensed sufficient amounts of asthma medication before it became free of charge. Nor were there any major differences in groups with different socio-economic status. It could be explained by the fact that the previous reimbursement system for prescription medications among children in Sweden did not disfavour children in low-income families, and therefore, only small measurable socio-economic discrepancies did exist before the intervention. Another interpretation could be that the intervention was not known by families with children with asthma and therefore did not affect their pattern of redeeming prescriptions. In that case, the absence of effect may be a signal of other needs for action to improve the drug utilization among children with asthma.

Nevertheless, an increase of 3.4 more DDDs/child/month is a modest change and extrapolated to a clinical situation; this may not affect the asthmatic child's health outcome.

4.1 | Strengths and weaknesses

Our study has several strengths. Firstly, we included all children in a whole region, regardless of reimbursement status and family socio-economics. Secondly, we used the ITS design, which is the strongest quasi-experimental design in interventional research.²² We included monthly measurements 2 years before and after the intervention, thus including a large number of measurement points. We also performed a sensitivity analysis including data on diabetic medications. Thirdly, we made an uncontrolled before and after comparison as a complement to the ITS design. The combined results from the separate sub-studies can provide a more robust discussion of whether the intervention had an effect or not. In sub-study (a), we had the opportunity to measure persistence of asthma medication for 2-year periods before and after the intervention. Furthermore, the prevalence and incidence measures were more feasible to calculate for a longer period (ie 2 years when studying asthma medications in children).

The aggregated socio-economic measure is a limitation. The Mosaic measure includes over 100 variables, but maybe only a few of them may influence the dispensing patterns

TABLE 4 The association between the eliminated patient fee, that is the intervention on 1 January 2016 on the dispensing patterns of asthma medication in children in Stockholm County by medication group and socio-economic status (SES)

Model	Level effect	P-value	Trend (change in slope)	P-value
SABA ^a total model				
No. of prevalent children	886.950	0.276	-2.843	0.968
No. of incident children	348.158	0.368	-4.472	0.886
Mean DDDs/child	0.320	0.486	-0.031	0.388
SABA Low SES				
No. of prevalent children	420.385	0.139	-1.610	0.949
No. of incident children	135.830	0.300	-2.978	0.785
Mean DDDs/child	0.264	0.550	-0.027	0.413
SABA Middle SES				
No. of prevalent children	164.777	0.253	0.335	0.978
No. of incident children	63.570	0.353	-1.449	0.790
Mean DDDs/child	0.470	0.374	0.008	0.829
SABA High SES				
No. of prevalent children	301.500	0.438	-4.015	0.902
No. of incident children	149.869	0.419	-1.166	0.937
Mean DDDs/child	0.228	0.656	-0.046	0.232
Controller ^b total model				
No. of prevalent children	690.073	0.358	-6.641	0.922
No. of incident children	25.115	0.611	3.807	0.372
Mean DDDs/child	2.334	0.094	-0.071	0.685
Controller Low SES				
No. of prevalent children	361.146	0.152	-2.239	0.923
No. of incident children	9.726	0.517	0.613	0.630
Mean DDDs/child	3.014	0.060	-0.063	0.712
Controller middle SES				
No. of prevalent children	108.075	0.414	-0.860	0.943
No. of incident children	5.916	0.523	0.790	0.264
Mean DDDs/child	1.455	0.349	0.063	0.599
Controller high SES				
No. of prevalent children	217.236	0.560	-6.616	0.841
No. of incident children	12.556	0.630	2.059	0.361
Mean DDDs/child	1.794	0.229	-0.094	0.595

^aShort-acting β_2 -agonist (SABA) defined by ATC codes R03AC02 + R03AC03.

^bController medication defined as inhaled corticosteroids (R03AB or R03AK) or leukotriene receptor antagonists (R03DC).

of asthma medication in children. Also, the socio-economic groups are created from area of residence, which assumes that all inhabitants in the same area have the same socio-economic status. The effect of the intervention across different socio-economic categories may be diluted in our study due to the aggregated Mosaic data.

Also, only the capital region of Sweden was included in the study. Including the entire country would increase the number of participants in the study which in turn might lead to significant results in some measures that are now non-significant. The volume measure DDD is widely used, but is not

adapted for children.²⁹ However, since the age distribution of children and the proportion of children dispensed a controller medication were similar before and after the intervention, the errors with DDD in children would most likely be distributed evenly across the two periods.

Furthermore, the seasonality in the dispensing patterns for asthma medications in children may not be fully controlled for in the ITS analyses. However, we did include 24 months of data before and after the intervention, yielding an even distribution of seasons around the intervention. Finally, there may have been factors other than the

studied intervention that influenced the dispensing patterns of asthma medication in children during the study period. The updated national recommendations for asthma and chronic obstructive pulmonary disease were published in November 2015,²⁸ but the potential effect of them on the dispensing patterns of asthma medication would not be seen immediately afterwards.³⁰ On the other hand, a preliminary version of the national guidance was made public in 2014, which may have influenced the utilization patterns before they were finalized.

In conclusion, the prevalence and incidence of asthma medication in children was higher after the eliminated patient fee; however, utilization increased already before the intervention and the specific effect attributable to the intervention seems to be limited. Nevertheless, the volume of dispensed asthma medication per child increased, particularly in children with low socio-economic status.

ACKNOWLEDGEMENTS

We would like to acknowledge professor Marion Bennie for professional language edits. This study was supported by the Stockholm County Council.

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose pertaining to this work.

REFERENCES

- Clavenna A, Bonati M. Drug prescriptions to outpatient children: a review of the literature. *Eur J Clin Pharmacol*. 2009;65(8):749-755.
- Breekveldt-Postma NS, Koerselman J, Erkens JA, van der Molen T, Lammers JW, Herings RM. Treatment with inhaled corticosteroids in asthma is too often discontinued. *Pharmacoepidemiol Drug Saf*. 2008;17(4):411-422.
- Cochrane MG, Bala MV, Downs KE, Mauskopf J, Ben-Joseph RH. Inhaled corticosteroids for asthma therapy: patient compliance, devices, and inhalation technique. *Chest*. 2000;117(2):542-550.
- Ingemansson M, Wettermark B, Jonsson EW, et al. Adherence to guidelines for drug treatment of asthma in children: potential for improvement in Swedish primary care. *Qual Prim Care*. 2012;20(2):131-139.
- Karaca-Mandic P, Jena AB, Joyce GF, Goldman DP. Out-of-pocket medication costs and use of medications and health care services among children with asthma. *JAMA*. 2012;307(12):1284-1291.
- Campbell JD, Allen-Ramey F, Sajjan SG, Maiese EM, Sullivan SD. Increasing pharmaceutical copayments: impact on asthma medication utilization and outcomes. *Am J Manag Care*. 2011;17(10):703-710.
- Ivanovska V, Mantel-Teeuwisse Aukje K., Van Dijk L. Background Paper 7.1 Priority Medicines for Children, Priority Medicines for Europe and the World. "A Public Health Approach to Innovation". 2013.
- Wettermark B, Godman B, Jacobsson B, Haaijer-Ruskamp FM. Soft regulations in pharmaceutical policy making: an overview of current approaches and their consequences. *Appl Health Econ Health Policy*. 2009;7(3):137-147.
- Luiza VL, Chaves LA, Silva RM, et al. Pharmaceutical policies: effects of cap and co-payment on rational use of medicines. *Cochrane Database Syst Rev*. 2015;5:CD007017.
- Anell A, Merkur S. Sweden health system review. 2012. Contract No.: 5.
- Lundberg O. Swedish Commission for Equity in Health– A Summary of the interim report. 2006.
- Annika A. *Att avstå från receptförskrivna läkemedel- en kartläggning av vem och varför*. Sweden: University of Gothenburg; 2007.
- Additional Act SFS 2015: 968 to the Pharmaceutical Benefits Act (2002:160 5§).
- Carlsson AC, Wandell P, Osby U, Zarrinkoub R, Wettermark B, Ljunggren G. High prevalence of diagnosis of diabetes, depression, anxiety, hypertension, asthma and COPD in the total population of Stockholm, Sweden - a challenge for public health. *BMC Public Health*. 2013;13:670.
- Wallerstedt SM, Wettermark B, Hoffmann M. The first decade with the Swedish prescribed drug register - a systematic review of the output in the scientific literature. *Basic Clin Pharmacol Toxicol*. 2016;119(5):464-469.
- Dahlen E, Almqvist C, Bergstrom A, Wettermark B, Kull I. Factors associated with concordance between parental-reported use and dispensed asthma drugs in adolescents: findings from the BAMSE birth cohort. *Pharmacoepidemiol Drug Saf*. 2014;23(9):942-949.
- InsightOne Experia MIS. Mosaic™ Sweden 2015.
- Douglas L, Szatkowski L. Socioeconomic variations in access to smoking cessation interventions in UK primary care: insights using the Mosaic classification in a large dataset of primary care records. *BMC Public Health*. 2013;13:546.
- Sharma A, Lewis S, Szatkowski L. Insights into social disparities in smoking prevalence using Mosaic, a novel measure of socioeconomic status: an analysis using a large primary care dataset. *BMC Public Health*. 2010;10:755.
- Jandoc R, Burden AM, Mamdani M, Levesque LE, Cadarette SM. Interrupted time series analysis in drug utilization research is increasing: systematic review and recommendations. *J Clin Epidemiol*. 2015;68(8):950-956.
- Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. *Int J Epidemiol*. 2017;46(1):348-355.
- Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. *J Clin Pharm Ther*. 2002;27(4):299-309.
- Gong T, Lundholm C, Rejno G, Mood C, Langstrom N, Almqvist C. Parental socioeconomic status, childhood asthma and medication use—a population-based study. *PLoS ONE*. 2014;9(9):e106579.
- Ungar WJ, Paterson JM, Gomes T, et al. Relationship of asthma management, socioeconomic status, and medication insurance characteristics to exacerbation frequency in children with asthma. *Ann Allergy Asthma Immunol*. 2011;106(1):17-23.
- Kozyrskyj AL, Mustard CA, Simons FE. Socioeconomic status, drug insurance benefits, and new prescriptions for inhaled corticosteroids in schoolchildren with asthma. *Arch Pediatr Adolesc Med*. 2001;155(11):1219-1224.

26. Sinnott SJ, Buckley C, O'Riordan D, Bradley C, Whelton H. The effect of copayments for prescriptions on adherence to prescription medicines in publicly insured populations; a systematic review and meta-analysis. *PLoS ONE*. 2013;8(5):e64914.
27. Aznar-Lou I, Pottegård A, Fernández A, et al. Effect of copayment policies on initial medication non-adherence according to income: a population-based study. *BMJ Qual Saf*. 2018;27(11):878-891.
28. The National Board of Health and Welfare. *Nationella riktlinjer för vård vid astma och kronisk obstruktiv lungsjukdom (KOL)*. Stockholm: Socialstyrelsen; 2015.
29. WHO Collaborating Center for Drug Statistics Methodology, Oslo. Guidelines for ATC classification and DDD assignment, 2018.
30. Grimshaw JM, Thomas RE, MacLennan G, et al. Effectiveness and efficiency of guideline dissemination and implementation strategies. *Health Technol Assess*. 2004;8(6):iii-iv, 1-72.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Dahlén E, Komen J, Jonsson EW, Almqvist C, Kull I, Wettermark B. Eliminated patient fee and changes in dispensing patterns of asthma medication in children—An interrupted time series analysis. *Basic Clin Pharmacol Toxicol*. 2019;125:360–369. <https://doi.org/10.1111/bcpt.13268>