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SHORT REPORT

Suboptimal persistence with inhaled corticosteroid monotherapy among children with persistent asthma in the UK

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Abstract

Background: Long-term studies indicate that adherence to asthma controller therapy decreases over time, and persistence with therapy may be poor.

Methods: This primary care database study assessed persistence with therapy over one year after first prescription of inhaled corticosteroid (ICS) for children aged 2–14 years with a diagnosis of asthma. Children with intermittent asthma were excluded. Discontinuation was defined as no ICS prescription during the last three months of the follow-up year.

Results: 2220 of 7375 children receiving a first prescription for ICS had persistent asthma. Mean (±SD) age was 7.3 (±3.8) years; 59.5% were male. A total of 745 (33.6%) continued initial ICS, 133 (6.0%) received add-on therapy, 150 (6.8%) switched to another asthma therapy, and 1192 (53.7%) discontinued therapy. These percentages were similar for children aged 2–5 or 6–14 years.

Conclusion: Persistence with first-time ICS monotherapy is poor among children with persistent asthma.

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Introduction

Asthma management guidelines recommend regular use of an anti-inflammatory controller (preventer) medication when symptoms are not controlled by intermittent use of short-acting β_2-agonist (step 2 of the guidelines).[1-3] For children aged 5–12 years, current British Thoracic Society (BTS) asthma guidelines recommend an inhaled corticosteroid (ICS) as the first controller medication and, for children younger than 5 years, an ICS or leukotriene receptor antagonist.[1]

Regular long-term use of ICS has been shown to prevent hospitalisations for asthma,[4] while suboptimal adherence to ICS has been linked to poor asthma control.[5-8] Nonetheless, suboptimal adherence to prescribed controller therapy is common among both adults and children.[9-14] Long-term studies indicate that adherence to asthma controller therapy decreases over time,[15,16] and persistence with therapy may be poor.[17,18] 'Adherence' to asthma controller therapy can be defined as the proportion of doses taken as prescribed, while 'persistence' with therapy applies to duration of therapy, namely, the continued use of the prescribed medication over time.[18,19]

The objective of this observational study was to assess persistence with therapy after a first prescription for ICS monotherapy among children with persistent asthma, as recorded in a large primary care database.

Methods

Study design and patients

Data for this retrospective observational study were drawn from the UK MediPlus database, now known as the IMS Disease Analyzer UK[20] and described in detail elsewhere.[21] At the time of our study (November 2000 to October 2005), UK MediPlus contained information on approximately 2 million patient visits to a nationally representative sample of approximately 500 general practitioners (GPs) in the UK. Recorded information includes the reason for consultation, diagnosis, prescribed treatment, and secondary medical care, linked to encrypted patient identifiers.

We studied children aged 2–14 years with a diagnosis of asthma (international classification of diseases [ICD]-10

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Table 1. Categorisation of asthma severity according to number of inhaled short-acting β_2-agonist and oral corticosteroid prescriptions during the baseline year.[22]

Inhaled short-acting β_2-agonist	Oral corticosteroid	Asthma severity classification
≤1 prescription *and*	0 prescription	Mild intermittent*
	1 prescription	Mild intermittent*
	2 prescriptions	Moderate persistent
	≥3 prescriptions	Severe persistent
2–3 prescriptions *and*	0–1 prescriptions	Mild persistent
	2 prescriptions	Moderate persistent
	≥3 prescriptions	Severe persistent
4–6 prescriptions *and*	0 prescription	Mild persistent
	1–2 prescriptions	Moderate persistent
	≥3 prescriptions	Severe persistent
>6 prescriptions *and*	0–1 prescriptions	Moderate persistent
	≥2 prescriptions	Severe persistent

*Children with mild intermittent asthma were excluded from the study.

diagnostic codes J45 [asthma] and J46 [status asthmaticus]) who initiated ICS monotherapy (step 2 of the BTS guidelines) from November 2001 to October 2004. To be eligible for the study, children had to have data available for 12 months before and 12 months after the date of the ICS prescription (index date) and no prescription for controller therapy within six months before the index date. Asthma severity was estimated using the prescription history for short-acting β_2-agonist and oral corticosteroid during the baseline year, as described by Leidy *et al*.[22] (see Table 1). Children with intermittent asthma (step 1 of the BTS guidelines) were excluded from the study.

We examined the distribution of ICS monotherapy with respect to choice of drug and the mean number of ICS prescriptions written per patient over the follow-up year (prescriptions could have been for more than one inhaler). Treatment patterns were classified into four categories:

- continuation of initially prescribed ICS without change
- add-on (added long-acting β_2-agonist [LABA] or montelukast to ICS)
- switch (changed to another ICS, LABA, ICS-LABA combination, or montelukast)
- discontinuation (no ICS prescription during the last 3 months of the follow-up period).

Descriptive statistics were used to summarise study results. Ethics committee approval was not required for this study as the MediPlus data are anonymised.

Results

From a total of 7375 children receiving an initial prescription for ICS, we identified 2220 children with persistent asthma. The mean (±SD) age overall was 7.3 (±3.8) years, and 1321/2220 (59.5%) patients were male (Table 2). The majority of children (1909/2220, 86.0%) had mild persistent asthma; 262 (11.8%) had moderate and 49 (2.2%) severe persistent asthma.

Table 2. Demographic characteristics, asthma severity, and persistence with therapy of 2220 children who received inhaled corticosteroid monotherapy, by age category.

	Age 2–5 years (n=899)	Age 6–14 years (n=1321)
Age, mean (SD)	3.5 (1.1)	10.0 (2.5)
Male sex, n (%)	546 (60.7)	775 (58.7)
Asthma severity, n (%)		
Mild	752 (83.7)	1157 (87.6)
Moderate	115 (12.8)	147 (11.1)
Severe	32 (3.6)	17 (1.3)
Persistence with ICS, n (%)		
Continuation	331 (36.8)	414 (31.3)
Add-on therapy	41 (4.6)	92 (7.0)
Switched asthma therapy	48 (5.3)	102 (7.7)
Discontinuation	479 (53.3)	713 (54.0)

Three-quarters (1740 or 78.4%) of the initial ICS prescriptions were for beclometasone, 261 (11.8%) were for fluticasone, and 219 (9.9%) for budesonide. The mean number of ICS prescriptions recorded during the follow-up year was 3.1 (SD 2.2; range, 1–17). Half of children had one (25%) or two (24%) total ICS prescriptions; 18% received three; 14%, four; 7%, five; and 12%, six or more prescriptions. While the record of number of treatment days supplied by each prescription was incomplete in the database, the average supply for each prescription, when recorded, was most commonly 30 days.

Overall, 745 (33.6%) children continued their initial ICS therapy, 133 (6.0%) received add-on therapy, 150 (6.8%) switched to another asthma therapy, and 1192 (53.7%) discontinued therapy. These percentages were similar in the two age-group categories of 2–5 years and 6–14 years (Table 2). Figure 1 depicts persistence with therapy according to asthma severity and Figure 2 the persistence with therapy according to ICS drug type.

Discussion

Persistence with ICS was poor, as captured in this retrospective database study, among children with persistent asthma initiating ICS monotherapy from November 2001 to October 2004. Over half (54%) of children in the study discontinued asthma controller therapy according to our *a priori* definition. Moreover, during the year, two-thirds (67%) of children received three or fewer ICS prescriptions, representing a 3- to 6-month supply at most, depending on prescription type.

Figure 1. Persistence with inhaled corticosteroid monotherapy after a first prescription, by level of asthma severity, for 2220 children with persistent asthma. "Continuation" was defined as initially prescribed ICS without change; "add-on," as added long-acting β_2-agonist (LABA) or montelukast to ICS; "switch," as change to another ICS, LABA, ICS-LABA combination, or montelukast; and "discontinuation," as no ICS prescription during the last 3 months of the follow-up year.

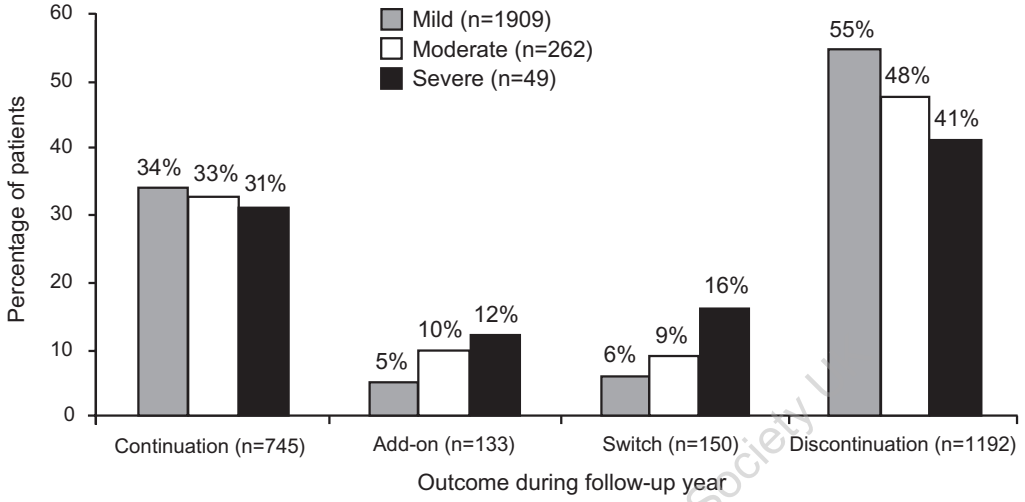
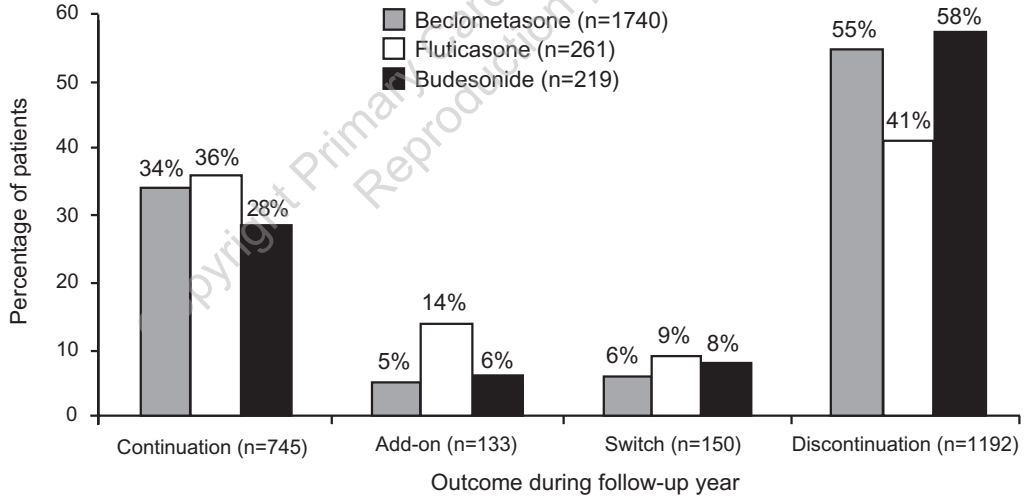


Figure 2. Persistence with each of the three drugs prescribed as first inhaled corticosteroid monotherapy for 2220 children with persistent asthma. "Continuation" was defined as initially prescribed ICS without change; "add-on," as added long-acting β_2-agonist (LABA) or montelukast to ICS; "switch," as change to another ICS, LABA, ICS-LABA combination, or montelukast; and "discontinuation," as no ICS prescription during the last 3 months of the follow-up year.



Other authors report suboptimal persistence with asthma controller therapy for first-time users of ICS. In the Netherlands, a large database study found 49% persistence at 100 days and <10% persistence at one year after start of ICS monotherapy among patients aged 35 years and younger; the results were similar when stratified by age.[17] Jones and co-workers[19] reported 25% and 22% persistence with ICS monotherapy at six and nine months, respectively, in their study of pharmacy claims data in the US. In another study in the Netherlands, children were more likely to continue with their asthma medications if they received their first prescription for asthma medication at age 2 or 3 years (versus ≤1 year) or if they received prescriptions for β_2-agonist and ICS (versus just β_2-agonist).[23]

Our findings of poor persistence with ICS were consistent for the two age groupings of 2–5 years and 6–14 years, as well as among asthma severity and ICS drug type categories. A limitation of this observational study is that the diagnosis of asthma was based on coding in the database; moreover, the

asthma severity determinations were based on prescribing information for the baseline year, as severity was not specifically coded. We cannot rule out the possibility that some children who were classified as having persistent asthma had intermittent asthma instead. The fact that all children had a database diagnostic code for asthma suggests that a therapeutic trial although possible was unlikely. If the ICS had been prescribed before the diagnosis then a therapeutic trial would be likely, but after diagnosis it implies commencement of regular preventive therapy. Also supporting the persistent asthma classification is the fact that the children included in this study represented just 30% (2220/7375) of the children receiving a first prescription for ICS during the study period. Moreover, the data were consistent for older children with less diagnostic doubt. Finally, the patients in the moderate and severe asthma categories, who are the least likely to have been misclassified as having persistent asthma, had discontinuation rates of 48% and 41%, respectively, not much lower than the percentage of those with mild persistent asthma who discontinued (55%).

The severity classifications were based on the algorithm of Leidy *et al*.,[22] which was assessed statistically in a healthcare claims database by examining the relationship between severity level and clinical variables, including deaths, hospitalisations, emergency room visits, and care from an allergist or pulmonologist. To our knowledge the algorithm has not been validated clinically or published as a full paper. Birnbaum and co-workers[24] report that the Leidy algorithm, in conjunction with an asthma guideline-based classification using ICS daily dose information and derived from an administrative claims database, generally categorised patients as having more severe asthma than an approach using pulmonary function testing. Therefore, it is possible that use of the Leidy algorithm led to an overestimation of asthma severity in this study. Patients prescribed fluticasone were numerically more likely to receive add-on therapy and less likely to discontinue ICS therapy during the year, which could indicate that fluticasone was prescribed for patients considered to have more troublesome symptoms.

Our findings are dependent on the accuracy of recorded data. By studying prescriptions over a full 12 months after the index date we hoped to minimise the effect of seasonal variations in asthma symptoms and prescribing. We defined discontinuation of therapy as no prescription during the last three months of the outcome year. Because it is possible that patients were using ICS intermittently and their supply of prescribed ICS lasted longer than we estimated, it would have been ideal to follow patients for a longer period to assess persistence. Moreover, it would have been of interest to examine asthma-related outcomes in conjunction with prescribing patterns. It is also possible that patients discontinued therapy because of lack of adequate benefit for reasons that could include poor inhaler technique.

We cannot ascertain whether children did not persist with therapy because it was found that they did not actually have asthma or that they had intermittent asthma and did not need ICS. Thus, because of this diagnostic uncertainty, we cannot rule out the possibility that, rather than lacking persistence with therapy, children were initially over-treated.

In conclusion, our findings suggest that persistence with first-time ICS monotherapy is poor among children with persistent asthma. Lack of persistence with ICS could lead to suboptimal asthma control. These data suggest that persistence with controller therapy should be routinely evaluated for children with asthma, and further study is needed to identify means of improving persistence with therapy for those children who require regular controller therapy.

Conflict of interest declaration

Qiaoyi Zhang, Stephanie D Taylor, and Vasilisa Sazonov-Kocevar are employees of Merck & Co., Inc.

Neither Mike Thomas nor any member of his close family has any shares in pharmaceutical companies. In the last three years he has received fees for acting as a consultant for MSD, Schering, and GSK and has received speaker's honoraria for speaking at sponsored meetings from the following companies marketing respiratory and allergy products: AstraZeneca, Boehringer Inglehiem, GSK, MSD, Schering-Plough, Teva. He has received honoraria for attending advisory panels with Altana, AstraZeneca, BI, GSK, MSD, Merck Respiratory, Schering-Plough, Teva. He has received sponsorship to attend international scientific meetings from GSK, MSD, AstraZeneca. He has received funding for research projects from GSK, MSD, AstraZeneca. He holds a research fellowship from Asthma UK. He is an Associate Editor of the *PCRJ*, but was not involved in the editorial review of, nor the decision to publish, this article.

David Price has consultant arrangements with Aerocrine, BI, Dey Pharmaceuticals, GSK, MSD, Novartis, Schering-Plough, and Teva. He or his team have received grants and research support for research in respiratory disease from the following organisations: UK National Health Service, Aerocrine, AstraZeneca, BI, GSK, MSD, Novartis, Pfizer, Schering Plough, and Teva. He has spoken for: BI, GSK, MSD, Pfizer, and Teva.

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