Impact of Payor-Initiated Switching of Inhaled Corticosteroids on Lung Function

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Objectives To evaluate the impact of a payor-initiated formulary change in inhaled corticosteroid coverage on lung function in patients with asthma and on provider prescribing practices. This formulary change, undertaken in August 2016 by a Medicaid payor in Kentucky, eliminated coverage of beclomethasone dipropionate, a metered dose inhaler (MDI), in favor of mometasone furoate, available as MDI and dry powder inhaler (DPI).

Study design A retrospective chart review was conducted on children with asthma ages 6-18 years covered by the relevant payor from a university-based pediatric practice who were seen before the formulary change (February to July 2016) and after (February to July 2017). Spirometry data from each visit was compared using the paired Student *t* test.

Results Fifty-eight patients were identified who were initially on beclomethasone dipropionate and had spirometry available at both visits. Those who switched from an MDI to a DPI (n = 24) saw a decline in median predicted forced expiratory volume in 1 second from 98.5% to 91% (P = .013). A decline was also seen in forced expiratory flow at 25%-75%, from 89.5% predicted to 76% predicted (P = .041). No significant changes were observed in children remaining on an MDI. Seven patients discontinued inhaled corticosteroid therapy.

Conclusions This study suggests insurance formulary changes leading to use of a different inhaler device may have a detrimental impact on pediatric lung function, which may be a surrogate measure for overall asthma control. This could be due to a lack of adequate timely educational intervention as well as the inability of some children to use DPIs. *(J Pediatr 2021;234:128-33)*.

Inhaled corticosteroid (ICS) therapy is the cornerstone of chronic management for persistent asthma and has demonstrated superiority over nonsteroidal therapies in lung function improvements, symptom-free days, and inflammatory markers. Consistent, correct use of ICS has been linked to significant decreases in asthma morbidity and mortality, health care utilization, and costs.[1-3]

Multiple forms of ICS therapy are Food and Drug Administration (FDA)-approved for use in pediatric patients. Each has specific pharmacologic attributes and delivery devices that ideally allow practitioners to tailor selection of therapy.[4,5] The delivery mechanism is especially important in pediatric patients, as younger children may struggle to use devices that require an inspiratory effort to actuate the device or require long breath holds to optimize deposition.[6] With improper device use, oropharyngeal deposition may be increased, possibly resulting in oral candidiasis, dysphonia, pharyngitis, and higher rates of systemic absorption via the gastrointestinal system if swallowed.[7,8] Likewise, ICS particle size may be an important attribute to consider in pediatric patients, as ultra-fine formulations have superior peripheral airway distribution.[9,10]

Currently, ICS are delivered by 1 of 3 mechanisms: nebulization, a metered dose inhaler (MDI), or a dry powder inhaler (DPI).[11,12] Nebulized ICS therapy may be appropriate in very young children or those with special health care needs but overall is inefficient, time-consuming, and has limited therapy options. Standard MDIs use a propellent to deliver a dose of medication in either suspension or solution when the device is actuated by the patient or caregiver. To correct for timing and medication velocity, these devices should be used with a holding chamber and, in young children, a mask.[13] Although DPIs do not require holding chambers, they can be difficult for young children to use correctly, in part because they may have difficulty generating the needed inspiratory effort to trigger a dose or may have insufficiently long breath-hold.[6]

BDP	Beclomethasone dipropionate
DPI	Dry powder inhaler
FDA	Food and Drug Administration
FVC	Forced vital capacity
$FEF_{25\%-75\%}$	Forced expiratory flow at 25%-75%
FEV_1	Forced expiratory volume in 1 second
ICS	Inhaled corticosteroid
MDI	Metered dose inhaler
MF	Mometasone furoate

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The authors declare no conflicts of interest.

Portions of this study were presented at the American College of Chest Physicians Annual International Meeting, October 19-23, 2019, New Orleans, LA.

https://doi.org/10.1016/j.jpeds.2021.03.008

Despite the multitude of ICS options and considerations, selection of a specific ICS is frequently dictated by insurance formulary coverage. Formularies are often changed abruptly and tailored toward adults, with limited pediatric specialist input.[14] There are scant data on the impact of insurance formulary changes on adherence and asthma control in pediatric asthma. In 2016, a major regional Medicaid provider in Kentucky discontinued coverage of beclomethasone dipropionate (BDP), an MDI, in favor of mometasone furoate (MF), available in both MDI and DPI forms. The reason for this change was not disclosed by the organization. Flunisolide (an MDI) and budesonide (DPI and nebulizer respules) were also available, though MF was preferred. In limited circumstances, BDP could be continued with a prior authorization. At the time of the change, MF was FDA approved in DPI form for ages 4 years and up and the MDI form was approved only for patients ages 12 years and up. Although the MDI form could be prescribed off-label to younger children, we hypothesized that the FDA indications would lead to increased DPI usage in younger children. The purpose of this analysis was to examine how these payor decisions changed ICS prescription patterns and to test whether children who were switched from MDI to DPI medications had differences in lung function compared with children who remained on an MDI.

Methods

We performed a retrospective chart review on children with asthma ages 6-18 years from a large, university-based group of general pediatric clinics with a predominately Medicaid population. Local institutional review board approval (University of Louisville institutional review board #18.0347) was obtained prior to collecting data. Using our electronic medical record system, patients with asthma ages 6-18 years were identified who were on the Medicaid plan of interest and were seen in the 6 months before the formulary change (February to July 2016, visit 1) and again during the same 6-month time span the following year (February to July 2017, visit 2). This allowed for an approximate 6-month transition period to any new medication and helped control for seasonal variations (**Figure 1**; available at www.jpeds.com). If a patient had multiple visits during these 2 periods for asthma, the last visit during February to July 2016 was used, and the first visit during February to July 2017 was used. This was to ensure the most recent data were obtained prior to the formulary change and that there was uniformity in capturing data from the second visits. Demographics, asthma medications, and spirometry measures were collected. For inclusion in the full analysis, patients had to have spirometry available at both visits.

Forced expiratory volume in 1 second (FEV_1) and forced expiratory flow at 25% - 75% ($FEF_{25\%-75\%}$) were selected as 2 spirometry measures commonly used in routine pediatric asthma care to serve as surrogates for overall asthma control. FEV_1 is specifically considered in the *National Heart, Lung, and Blood Institute* asthma guidelines for assessing severity and control for patients 5 years and above.[15] $FEF_{25\%-75\%}$ is a sensitive marker for predicting asthma morbidity in children as well as bronchodilator responsiveness.[16,17] Two-sided paired Student *t* tests were calculated to evaluate changes in these lung function measures between the 2 time periods. Statistical *t* test analysis was conducted using Excel 2016 (Microsoft Corporation).

Prescribing patterns were assessed for all patients on ICS in both time periods. GraphPad (GraphPad Software) was used to calculate a 2-tailed Fisher exact test to assess differences between prescribing MDI and non-MDI ICS between the 2 time periods.

Results

Our initial query generated a list of 111 patients with asthma, 58 of who were on BDP at visit 1, had complete spirometry data at both visits, and were included for full analysis (**Figure 2**). Demographics of these 58 patients are listed in **Table I**. Seventy of 111 patients were on either an ICS or combination ICS/long-acting beta-agonist at visit 1 with 67 (95.7%) receiving this therapy via an MDI, 1 patient using nebulized budesonide, and 2 patients using a DPI. At follow-up (visit 2), 67 of 111 patients were on ICS or ICS/long-acting beta-agonist and 39 of those were still on an MDI (58.2%) with 27 on a DPI and 1 patient on a nebulizer. The frequency of MDI and non-MDI prescriptions between the 2 time periods was statistically significant by a 2-tailed Fisher exact test (**Table II**; $P < .0001$).

Of those initially on BDP, 27 out of 58 (46.6%) patients remained on an MDI, 24 out of 58 (41.3%) had been switched to a DPI, and 7 patients were reported to no longer be on any ICS. **Figure 2** outlines what therapy was specifically being used at the second visit for each group. The average visit date for each group was calculated using Excel to assess for differences in seasonality which could bias results if different between the 2 groups. As reported in **Table I**, there was no major difference in visit timing between groups.

Visit 1 median FEV_1 for all 58 subjects was 97% and median $FEF_{25\%-75\%}$ was 84%. When looking at the 24 patients initially on an MDI and then switched to a DPI, the median FEV_1 was 98.5% predicted prior to the change and 91% predicted afterward ($P = .013$). A decline was also seen in $FEF_{25\%-75\%}$ where the baseline median was 89.5% predicted prior to the change and 76% afterward ($P = .041$). Of those who remained on an MDI, there was no statistically significant change in FEV_1 or $FEF_{25\%-75\%}$. Data are presented in boxplot format in **Figure 3**.

Discussion

Our study demonstrates a significant decline in lung function in pediatric patients who switched inhaler types as a result of an ICS insurance formulary change which was not seen in patients whose inhaler type remained the same. After the payor mandated formulary changes, pediatricians' prescribing patterns changed from almost exclusively using MDIs in this age group to a near even mix between MDIs and DPIs.

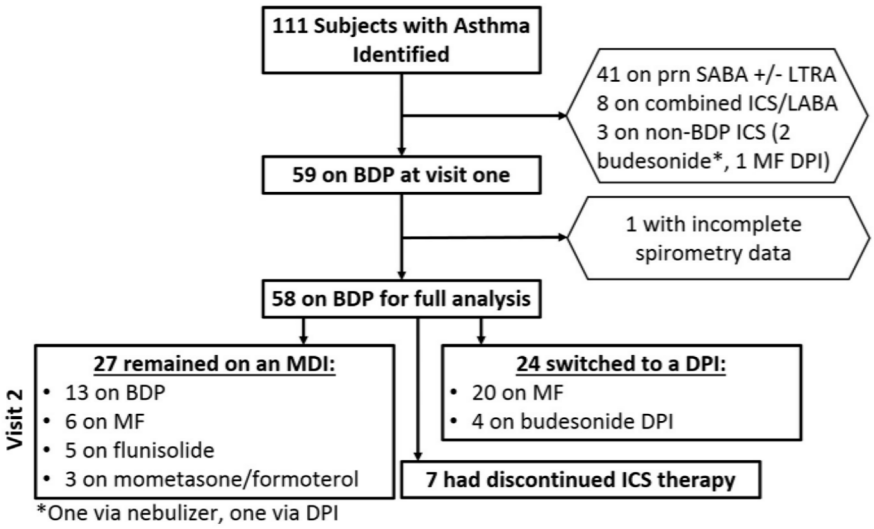

Figure 2. Subject selection and progression of therapies before and after the formulary change. SABA, short-acting beta-agonist; LTRA, leukotriene receptor antagonist; LABA, long-acting beta-agonist.

Pediatric asthma is different from adult asthma in that medication factors (pharmacodynamics) and medication delivery devices must be taken into careful consideration based on the age and maturity of the pediatric patient.[11] Generally, adolescents (13-18 years of age) are able to use the full range of MDIs and DPIs that are available for use in adults. Children ages 5-12 years can use an MDI with a valved holding chamber, if given appropriate instruction and coaching. Young children (<4-5 years of age) are often unable to generate the inspiratory flow rate necessary to effectively deliver the medication from a DPI and, therefore, require either a nebulizer or an MDI with a holding chamber and mask of appropriate size with a good fit.[13,18,19]

Prior research provides evidence that inhaler device changes without proper education can be detrimental to asthma control. A 2-year study was done in the United Kingdom in adolescents and adults with asthma where controller medications containing ICS devices were changed without a consultation with the physician. A total of 824 patients from 55 practices had a device switch. Over one-half (53%) of device switches were from DPIs to MDIs. A significantly higher number of patients experienced unsuccessful treatment (51% vs 38%) compared with those who had no switch on their medications. The authors concluded that switching ICS devices without a face-to-face consultation was associated with worsened asthma control and is, therefore, inadvisable.[20]

It should be noted from these studies that loss of asthma control can occur any time a switch without face-to-face consultation or hands-on teaching is done, whether the switch is from DPI to an MDI or vice versa. It is the recommendation of most authorities that patients with stable

Table I. Demographics of subjects initially on BDP

Demographics	Total (n = 58)*	MDI to MDI (n = 27)	MDI to DPI (n = 24)
Male sex	36/58 (62%)	16/27 (59%)	16/24 (67%)
Age (median with ranges)	11 y (6-18)	11 y (6-18)	11 y (7-16)
Race/ethnicity			
African American	48/58 (82.7%)	23/27 (85.2%)	18/24 (75%)
Caucasian	6/58 (10.3%)	2/27 (7.4%)	4/24 (16.7%)
Other race/ethnicity	4/58 (6.9%)	2/27 (7.4%)	2/24 (8.3%)
Asthma severity			
Mild intermittent asthma	5/58 (8.6%)	1/27 (3.7%)	2/24 (8.3%)
Mild persistent asthma	16/58 (27.6%)	6/27 (22.2%)	8/24 (33.3%)
Moderate persistent asthma	20/58 (34.4%)	10/27 (37%)	10/24 (41.7%)
Severe persistent asthma	1/58 (1.7%)	0/27 (0%)	1/24 (4.2%)
Unspecified asthma severity	16/58 (27.6%)	10/27 (37%)	3/24 (12.5%)
Average date of first PFT	5/8/2016	5/17/2016	5/1/2016
Average date of second PFT	4/18/2017	4/18/2017	4/21/2017

*Seven patients discontinued ICS use between the first and second visits.

Table II. Fisher exact test contingency table comparing MDI to non-MDI (DPI or nebulizer) prescriptions between the visits before and after the formulary change ($P < .0001$)

ICS Type	Visit 1	Visit 2	Total
MDI ICS	67	39	106
Non-MDI ICS	3	28	31
Total	70	67	137

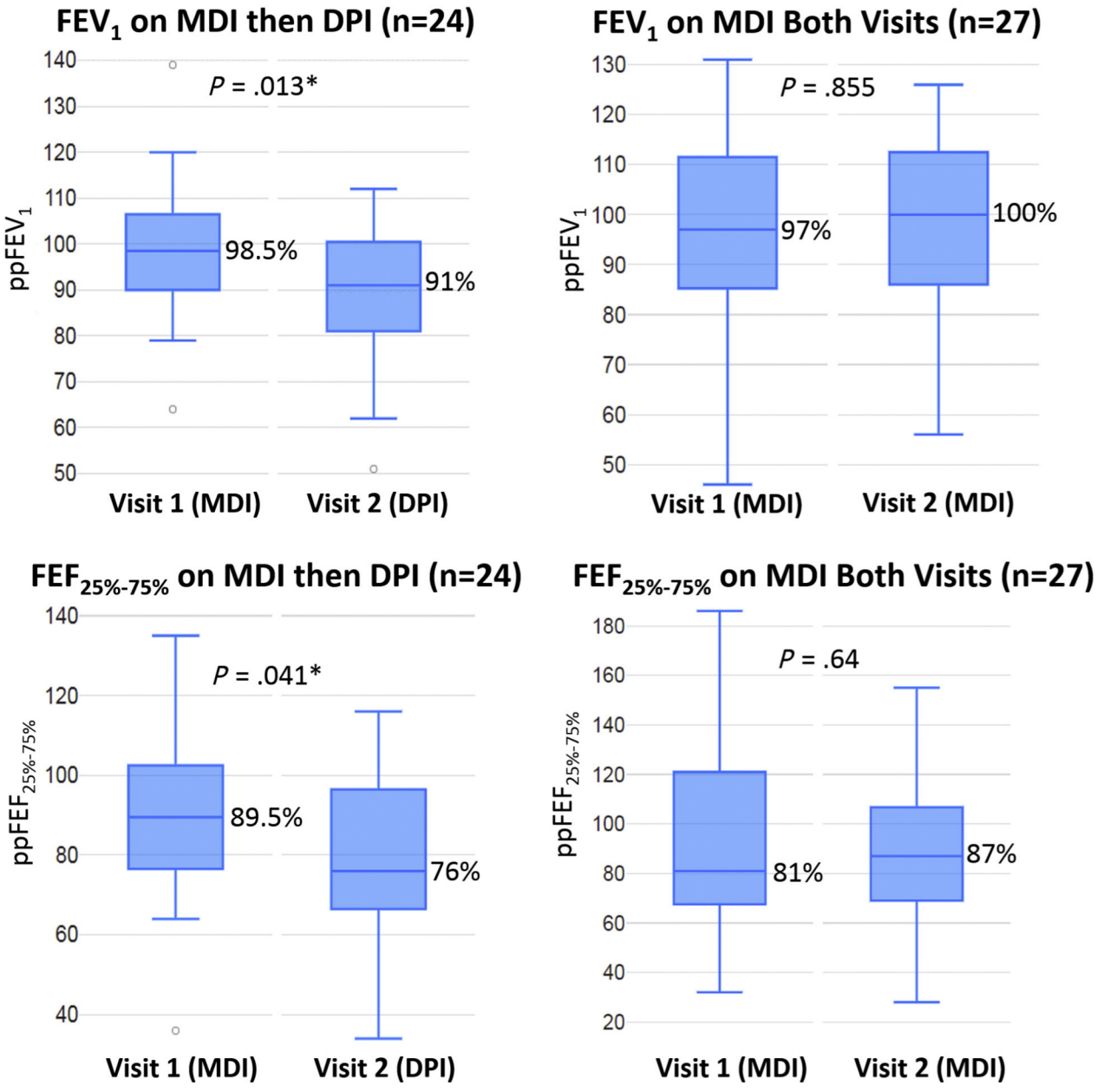

Figure 3. Boxplots illustrating minimum, first quartile, median, third quartile, and maximum values demonstrating changes in FEV_1 and $FEF_{25\%-75\%}$ for patients switched to an DPI vs maintained on an MDI.

disease remain on their current device. If a switch is considered, it should be first discussed with patient and their family, and the physician should consider the patient's preference, their age, and their cognitive ability to correctly use the device, and the availability of the preferred drug in the preferred device.[21]

The situation described herein specifically illustrates a case of nonmedical switching and its potential consequences. Nonmedical switching refers to a change in medication to a clinically similar but distinct option that is not based on clinical effectiveness, tolerability, or adherence. Insurance plans have long utilized these changes in an attempt to limit costs. These changes may include the preferential use of generics or incentive formularies. An American Medical Association policy strongly discourages non-medical switching in ambulatory patients with chronic diseases.[22]

Numerous studies have shown a negative impact of nonmedical switching on patient outcomes. A recent systemic review summarizing these studies showed that nonmedical switching had a negative impact on clinical, economic, health care utilization, and medication-taking behavior domains.[14] Physicians surveyed felt that nonmedical switching created ethical concerns (decreased clinical judgement and autonomy), diverted their clinical time, had

adverse effects on practice burden (increased pharmacy calls and nonoffice patient contact) while potentially worsening clinical care (possibly increased side effects and medication errors) and physician well-being.[23]

Nonmedical switching impacts the quadruple aim of healthcare, which emphasizes the clinical decision-making collaboration between a provider and their patient.[24] This relationship is particularly crucial in asthma management because therapeutic choices are predicated on individual patient, medication bioavailability, and device-related factors. Without ensuring appropriate ability to use correct device technique and lack of physician-patient partnership, the impact on adherence, asthma control, and health care utilization could be significant.

Nonmedical switching has received significant attention lately because of its negative impact on health care in the US and in Europe. Any added confusion to patients and their families about medications and devices along with lack of timely communication between patients and their providers can ultimately lead to patient's inability to use the medication correctly. Indeed, our study suggests that an abrupt formulary change of asthma controller medications from MDI to DPI had a detrimental impact on pediatric asthma control with decline in lung function when the formulary change involved a transition to a different inhaler type. After the abrupt switch, lung function declined only in those who were switched to a different type of inhaler but remained the same if a similar type of inhaler was used.

A large body of evidence on nonmedical switching from 2000 to 2015, involving multiple chronic disease states including asthma has shown no clinical, economic, or health services utilization improvements 90% of the time when patients were doing well on their current medications. For 100% of these patients, nonmedical switching led to poorer medication adherence.[25] In a systematic review of 79 articles, correlates of adherence to ICS use in pediatric asthma were studied; the most commonly reported were family level correlates (socioeconomic status, race/ethnicity, health behaviors, and asthma knowledge).[26] The authors stress the importance of the dynamic interaction between the individual, family, and health care provider, which influences the degree of adherence to ICS use. Frequent inhaler changes by insurance companies result in artificial barriers within the medical system leading to poor adherence and loss of asthma control.

The potential loss of asthma control secondary to payor-initiated nonmedical switching is likely to have adverse impacts on healthcare utilization and, therefore, increase the already staggering economic burden of asthma in the US. A recent study estimated the economic burden of asthma in the US to be close to $81.9 billion in 2013; $3 billion in losses because of missed work and school days, $29 billion because of asthma-related mortality, and $50.3 billion in medical costs[27] with $5.92 billion dollars in direct costs for pediatric asthma specifically.[28] Based on a probabilistic computer model that linked state-specific estimates of population growth, aging, asthma prevalence, and asthma control levels, the burden of uncontrolled asthma excess health care cost for the next 20 years are estimated to be $300.6 billion ($963.5 billion when indirect costs are added).[29] Although this study is unable to quantify the economic impact of this particular formulary change, future studies should be designed to do so and address whether short- term economic benefits to payors are outweighed by higher long-term costs related to increased health care utilization.

This study has several limitations. It is retrospective in nature, and we were unable to assess what specific inhaler education was provided to families. Assessment of asthma control was limited to analysis of lung function. Information on measures of increased health care utilization such as exacerbations, emergency department use, and provision of rescue medications was unavailable. We were also unable to systematically assess specific reasons for the higher rates of DPIs prescribed. This could have been due to the ages stipulated in FDA approval, unfamiliarity with the different available products, ordering methods in the electronic medical record system, true preference for DPIs, or other reasons. Finally, specific dosing regimens in each group were not able to be examined and could contribute to the study's findings if patients in the DPI group were systematically receiving lower effective ICS doses. If this is the case, the loss of lung function observed would still be secondary to payor initiated nonmedical switching.

Our data suggests abrupt insurance formulary changes (payor-initiated nonmedical switching) leading to the use of a different inhaler device likely had a detrimental impact on pediatric lung function. This is likely secondary to patient and family confusion on proper device use due to a lack of adequate timely educational intervention as well as the inability for some younger children to use DPIs. We suggest insurance formulary changes should be minimized but, when required, they should take into account the unique needs of the pediatric population and should be clearly communicated in advance to providers, pharmacists, and families. Future research should be done to examine whether the loss of lung function demonstrated in this study translates clinically into increases in systemic steroid exposure, emergency department visits, and hospital admissions, as well as into increases in total asthma health care costs. ■

Submitted for publication Dec 13, 2020; last revision received Mar 3, 2021; accepted Mar 5, 2021.

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Data Statement

Data sharing statement available at www.jpeds.com.

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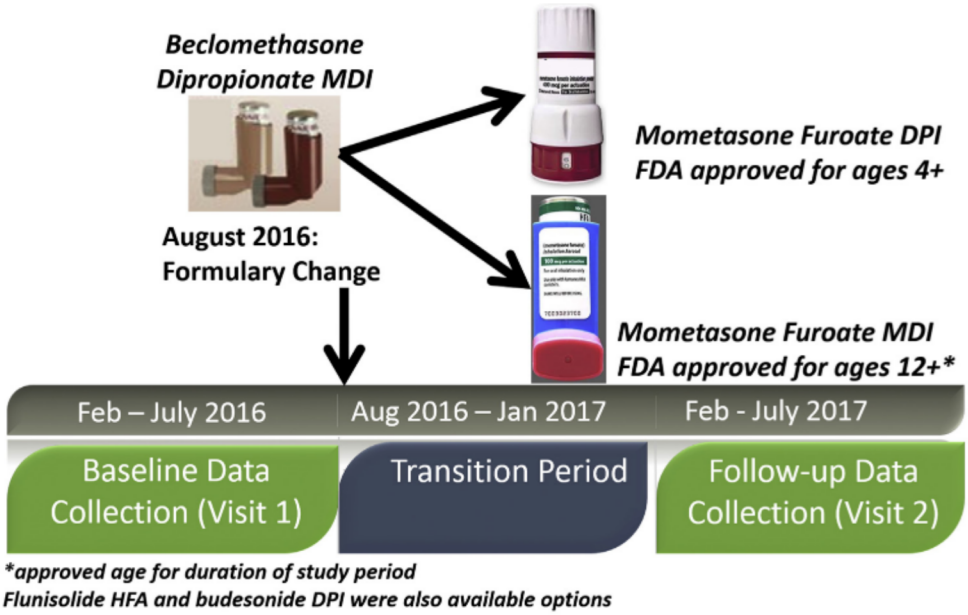

Figure 1. Study timeline.