including those who were naive to inhaled corticosteroids (ICSs) and leukotriene receptor antagonist (LTRA) medications and those who had been treated with low-dose ICSs or LTRAs at any point in the 6 months before enrollment but still experiencing symptoms warranting daily controller medication.

METHODS. This study was a multicenter, randomized, double-blind, double-dummy clinical trial. A run-in period of 2 to 8 weeks, depending on history of previous exacerbation requiring systemic corticosteroids and on current usage of step 2 therapy, was used to assess asthma severity and control. Treatment occurred over 48 weeks as three 16-week treatment arms via randomized, placebo-controlled crossover including: daily ICSs (fluticasone 44 mcg, 2 inhalations twice daily), daily LTRAs (4 mg at bedtime), and as-needed ICSs (fluticasone 44 mcg, 2 inhalations) co-administered with open-label, short-acting bronchodilator (90 mcg, 2 inhalations). No washout period was performed; however, the first 2 weeks of data were not analyzed in calculation of asthma control days (ACDs). Caregivers recorded symptoms, health care use, and medication use in electronic diaries at bedtime. Biomarkers included aeroallergen sensitization and blood eosinophil counts. Primary analysis was based on determination of differential response and 3 pre-specified factors (aeroallergen sensitization, previous exacerbation, and sex).

RESULTS. Of those enrolled, 230 had analyzable data; 74% (170/230) of subjects were differential responders to treatment (defined as time to asthma exacerbation at least 4 weeks longer or number of annualized ACDs at least 31 days more compared with another treatment), with the highest probability of best response being daily ICSs ($P <$ .0001) associated with greater ACDs and less exacerbations. Aeroallergen sensitization ($P = .0036$), blood eosinophil counts of 300 μL or greater ($P = .0071$), and serum eosinophilic cationic protein of 10 μg/l or greater ($P =$ .0292) were associated with differential response favoring daily ICSs. However, previous exacerbation history, sex, modified asthma predictive index status, serum immunoglobulin E (IgE) levels, and urinary leukotriene E4 (LTE_4) concentrations were not predictive of differential response.

CONCLUSIONS. This study shows that daily ICSs conferred the most protection against symptoms and exacerbations in children with type 2 inflammation evidenced by aeroallergen sensitization and increased blood eosinophil counts. Moreover, clinically accessible biomarkers can be used to predict the medication strategy associated with best response.

REVIEWER COMMENTS. This study demonstrates that phenotype-directed daily ICSs is beneficial in children with type 2 inflammation, even though the risk of dose-dependent reductions in linear growth with daily ICSs may be worse in certain subpopulations. However, more studies need to be done on children who show nontype 2 patterns of inflammation, as these children may have unique inflammatory profiles which may guide treatment selection.

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Should Recommendations About Starting Inhaled Corticosteroid Treatment of Mild Asthma Be Based on Symptom Frequency: A Post-hoc Efficacy Analysis of the START Study

Reddel HK, Busse WW, Pedersen S, et al. *Lancet*. 2017; 389(10065):157–166

PURPOSE OF THE STUDY. The 3-year Steroid Treatment as Regular Therapy (START) study evaluated the symptom-based cutoff of >2 days per week for starting daily inhaled steroid therapy for management of mild asthma.

STUDY POPULATION. Participants ($N = 7138$, ages 4–66 years) were from 32 countries, had mild asthma diagnosed within the past 2 years, and no previous regular corticosteroid therapy.

METHODS. This post-hoc analysis of a randomized control trial comparing once-daily inhaled budesonide ($n =$ 3577, 200 μg for ages <11 years and 400 μg for ages ≥11 years) with placebo ($n = 3561$) was conducted for time to first severe asthma-related event (SARE) (hospital admission, emergency treatment, or death) and change from baseline lung function. Interaction with baseline symptom frequency was investigated.

RESULTS. Baseline days of symptoms per week were 0 to 1 for 2184 participants (31%), 2 for 1914 (27%), and >2 for 3040 (43%). In the budesonide group, time to first SARE was longer for all symptom frequencies (hazard ratios 0.54 [95% CI: 0.34–0.86] for 0 to 1 days/week, 0.60 [0.39–0.93] for 2 days/week, and 0.57 [0.41–0.79] for >2 days/week, $P = .94$). The decline in postbronchodilator lung function was lower after 3 years ($P = .32$).

CONCLUSIONS. In mild, recent-onset asthma, once-daily, low-dose budesonide decreases SARE risk, reduces lung function decline, and improves symptom control similarly for children and adults with symptom frequency of ≤2 days and >2 days per week.

REVIEWER COMMENTS. The occurrence of life-threatening, asthma-related events in some patients with infrequent asthma symptoms encourages consideration of daily inhaled corticosteroid treatment in selected individuals. Data for children are not reported separately, but previous publications of the START study show inclusion of

1897 children ages <11 years and 1148 children ages 11 to 17 years. Inhaled steroid side effects are not reported in this study. A direct comparison of rates of side effects between the low-dose budesonide and placebo groups in children and adults would help to weigh the potential benefits and drawbacks of low-dose daily inhaled corticosteroid treatment in individual patients with infrequent asthma symptoms.

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Oral Corticosteroid Prescribing for Children With Asthma in a Medicaid Managed Care Program

Farber HJ, Silveira EA, Vicere DR, Kothari VD, Giardino AP. *Pediatrics*. 2017;139(5):e20164146

PURPOSE OF THE STUDY. Oral corticosteroids are used for the treatment of moderate to severe exacerbations of asthma, but there is concern about overuse in pediatric populations. This study evaluated prescriptions of oral corticosteroids for children with asthma.

STUDY POPULATION. Children with asthma ages 1 to 18 years with a diagnosis of asthma enrolled in a Medicaid Managed Care Program.

METHODS. Claims data from 2011–2015 from the Texas Childrens' Health Plan were examined.

RESULTS. During the study period, up to 22% of children had an asthma diagnosis and up to 44% of the children had 1 or more prescriptions for oral corticosteroid (OCS) in each year. Children 1–4 years had the highest rate of OCS dispensation. Among those prescribed OCS, <28% had a prescription for an inhaled corticosteroid that same year. Children receiving OCS had more β-agonist prescriptions, emergency department (ED) visits, and hospitalizations compared with those who did not receive OCS. Board-certified pediatricians prescribed OCS less commonly than other primary care providers, but there was a large disparity in the rates of prescription among pediatricians (15% to 86% in 2015). There was no difference in ED visits or hospitalization rates by OCS dispensing quartile among pediatricians.

CONCLUSIONS. OCS dispensation data for children with asthma suggest there is overuse among Medicaid-insured children.

REVIEWER COMMENTS. Overprescription of oral steroids for respiratory symptoms, particularly for children 1–4 years of age, is not surprising, as diagnosing asthma in this age group is challenging due to the inability to perform objective diagnostic evaluation of pulmonary functions. In addition, the low rate of inhaled corticosteroid prescriptions to children with asthma is notable. The study is limited by use of claims data from a low-income population in the Texas Childrens' Health Plan. An editorial in the same issue of the journal (Cabana M. *Pediatrics*. 2017;139[5]: e20170598) highlights possible reasons for overprescription of OCS as (1) regional medical practice culture, (2) regional inhalant environmental allergens and/or irritants affecting asthma morbidity, (3) lack of guidelines or recommendations, or perhaps more importantly, (4) patient or physician barriers to inhaled corticosteroid prescription and use.

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Symptomatic Adrenal Suppression Among Children in Canada

Goldbloom EB, Mokashi A, Cummings EA, et al. *Arch Dis Child*. 2017;102(4):338–339

PURPOSE OF THE STUDY. To determine the national incidence and presenting features of pediatric glucocorticoid-induced symptomatic adrenal suppression (AS) in Canada by using a national pediatric surveillance program.

STUDY POPULATION. Canadian pediatricians and pediatric subspecialists in clinical practice participated in a prospective surveillance through the Canadian Pediatric Surveillance Program, surveying for rare conditions.

METHODS. Over 2500 pediatricians and pediatric subspecialists were surveyed monthly for 2 years through the Canadian Pediatric Surveillance Program either by mail or e-mail. A check-off form asked physicians whether they had identified any new cases of symptomatic adrenal suppression (AS). If a positive response was received, a case report form (CRF) was completed by the responding physician, capturing demographic and medical information. CRFs were reviewed independently by the principal investigators to ensure that there was agreement regarding confirmed cases.

RESULTS. During 2 years of surveillance, 80% of pediatricians participated in the surveillance program. There were 115 cases of symptomatic adrenal suppression (AS) reported, with 46 cases being confirmed. The estimated annual incidence of symptomatic AS is 0.35/100 000 children aged 0–18 years (95% CI 0.26–0.47). More than one-third of the children presented with growth failure, highlighting the importance of growth monitoring in children treated with glucocorticoids (GC). More than one-quarter had nonspecific symptoms such as fatigue, lethargy, nausea, anorexia, vomiting, abdominal pain, and myalgias. Several children exhibited features of Cushing's syndrome. Six children presented with adrenal crisis, one of whom later died. Although GC administration by any route has the potential to result in adrenal suppression, 80% of the children with symptomatic AS were receiving

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