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

GC by inhaler alone or inhaler in combination with other routes. Nearly two-thirds of the children had asthma, and another 15% had asthma plus another condition being treated with GC. Almost one-third of the children were treated with ICS alone. The most commonly used ICS was fluticasone, with most children receiving doses of ~500 μg/day.

CONCLUSIONS. The estimated incidence of symptomatic AS in the pediatric population is small, but it is potentially much higher in at-risk groups (children treated with GC). The close monitoring of growth and asking about nonspecific symptoms such as fatigue, nausea, and myalgia may help with earlier detection. To reduce the risk of AS, physicians must be aware that AS can occur, evaluate GC doses frequently, and use the lowest effective dose.

REVIEWER COMMENTS. This study is a good reminder that we must be aware of the risk of adrenal suppression in children treated with glucocorticoids. Although inhaled corticosteroids have dramatically improved asthma care, the close monitoring of growth and attention to nonspecific or vague symptoms suggesting AS is essential. Our goal for asthma treatment is to use the least amount possible to keep asthma in control.

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Tiotropium Add-on Therapy in Adolescents With Moderate Asthma: A 1-Year Randomized Controlled Trial

Hamelmann E, Bateman ED, Vogelberg C, et al. *J Allergy Clin Immunol*. 2016;138(2):441–450.e8

PURPOSE OF THE STUDY. Phase II studies in children and adolescents have demonstrated that tiotropium is an effective add-on to inhaled corticosteroid (ICS) maintenance therapy. This study sought to assess the safety and efficacy of once-daily tiotropium Respimat added to ICS in a phase III trial in adolescents with moderate symptomatic asthma.

STUDY POPULATION. Eligible patients were aged 12–17 years with histories of asthma of >3 months and who were symptomatic at screening, as defined by the 7-question Asthma Control Questionnaire (ACQ-7). Patients were required to have been receiving ICS +/− long-acting β agonist (LABA) or leukotriene receptor antagonist (LTRA), FEV1 60% to 90% of predicted normal, at least 12% reversibility after albuterol, FEV1 variability within 30% between screening and randomization, and no history of smoking or other lung disease.

METHODS. In this 48-week, double-blind, placebo-controlled, parallel-group study, 398 patients were randomized to receive 5 mcg or 2.5 mcg of tiotropium or placebo via a Respimat device once daily as an add-on to usual ICS, with or without LTRA. LABA use was not permitted. The primary efficacy end point was change from baseline in FEV1 within 3 hours after dosing at week 24. Blinded efficacy and safety monitoring continued to week 48. Secondary end points included trough FEV1, area under the curve (AUC) for FEV1 within 3 hours after dosing, various other pulmonary function measures after 24 weeks of treatment, time to first asthma exacerbation, asthma control (ACQ-6 and ACQ-7), and quality of life as evidenced with the Asthma Quality of Life Questionnaire with Standard Activities (ACLQ).

RESULTS. Both active treatment doses resulted in significantly greater improvement in the FEV1 primary end point versus the placebo ($P < .001$ for 5 mcg, $P < .01$ for 2.5 mcg). Trough FEV1 improved significantly only for the 5-mcg dose versus the placebo ($P < .03$). Also significant were changes in FEV1 AUC for both 5-mcg ($P < .001$) and 2.5-mcg ($P < .008$) doses. Trends for improvement in asthma control and health-related quality of life were observed over the 48-week course but were not statistically significant. No significant side effects occurred with use of either active dose.

CONCLUSIONS. Once-daily tiotropium significantly improved lung function and was safe and well tolerated as an add-on to maintenance ICS in adolescents with moderate symptomatic asthma, especially at the 5 mcg dose. This finding adds to the growing body of evidence supporting the inclusion of tiotropium as an option in step therapy for uncontrolled asthma in adolescents.

REVIEWER COMMENTS. The authors point out that there is considerable heterogeneity in individuals' responses to LABAs and long-acting anticholinergics, and there are no clinical markers we can employ to choose 1 agent versus the other. So, we are not in the "either or" circumstance, at least not yet, in the adolescent population. Given current evidence, tiotropium could be considered as a treatment option for adolescents with moderate persistent disease, in combination with ICS +/− LTRA.

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Real-life Effectiveness of Omalizumab in Severe Allergic Asthma Above the Recommended Dosing Range Criteria

Hew M, Gillman A, Sutherland M, et al. *Clin Exp Allergy*. 2016;46(11):1407–1415

PURPOSE OF THE STUDY. To determine if omalizumab (anti-IgE) above the standard dosing ranges can be beneficial in severe asthmatics and compare responses to patients who are within normal dosing ranges.

Symptomatic Adrenal Suppression Among Children in Canada

Mary V. Lasley

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