

Out of One, Many: Moving beyond a Single Guideline toward Personalized Asthma Care for Obese Children

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Although asthma knowledge and care have improved dramatically since the initial publication of treatment guidelines in 1991, poor asthma control persists in a large number of children in the United States, and the public health burden remains. Although deaths caused by asthma have declined, morbidity resulting from asthma remains significant, and each year more than 50% of children with asthma experience a significant exacerbation necessitating treatment escalation (1). Even among “stable” children with asthma without acute exacerbations, symptoms such as wheezing and cough are common and result in disproportionate healthcare use, missed school/work days, impaired quality of life, and high costs (2, 3).

Asthma in children is clearly a heterogeneous disorder with diverse biological mechanisms underlying clinical phenotypes. The behavioral and environmental factors that contribute to clinical phenotypes and poor asthma control in affected children are likewise complex. For example, limited access to asthma care and poor adherence to asthma controller medication are major causes of preventable disease burden, even in developed countries (4). Exposures to irritants, pollutants, allergens, and tobacco smoke may also disrupt epithelial barrier function and airway innate immune defenses and alter airway tone and caliber independent of asthma severity (5). Comorbid obesity, defined by a body mass index at or above the 95th percentile, also contributes to poorer asthma outcomes in children (6–8), and there is a growing body of literature highlighting multiple mechanisms through which obesity may augment inflammatory

responses in asthma, including increased susceptibility to asthma triggers (9). However, whereas current asthma management guidelines focus a great deal of attention on trigger reduction, obesity is less emphasized and is viewed instead as a complicating or comorbid factor that should be assessed. Clinicians therefore have limited to no guidance regarding the initiation and assessment of asthma treatment in obese children, in part owing to a paucity of literature on the subject.

In this issue of the *AnnalsATS*, Ross and colleagues (pp. 49–58) apply a novel statistical machine learning approach to a large dataset of children with well-phenotyped asthma enrolled in the Childhood Asthma Management Program and the Childhood Asthma Research and Education network (10). The authors identified four phenotypes of asthma in children differentiated by allergic sensitization and body mass. Whereas allergic, nonobese children were more likely to achieve asthma control with the receipt of inhaled corticosteroids, obese children were more likely to achieve asthma control with mast cell stabilization therapy (10). The machine learning approach used to phenotype children is unique from other published approaches, but the results are reassuring in that they confirm phenotypes of obese asthma previously identified by others (namely in adult populations, given fewer studies in children) (11, 12). The results also have biological plausibility and support prior observations of decreased corticosteroid responsiveness in obese patients with asthma (13).

However, potential misdiagnosis of asthma in obese patients remains a concern

in the clinical setting because obese children with asthma may be more likely to experience activity limitation as a result of cardiopulmonary deconditioning and to report nonspecific chest symptoms such as dyspnea, prompting systemic corticosteroid receipt. A primary strength of the study by Ross and colleagues (10) is the inclusion of highly characterized and well-adherent children with documented asthma confirmed by either bronchodilator reversibility testing or bronchial hyperresponsiveness to methacholine who were enrolled in asthma clinical trials. Yet, this same strength is also a potential limitation because the results may not necessarily be generalizable to the real world, where adherence to asthma medications is poor at best and measures of airway physiology can be difficult or even impractical to perform. Also, obesity disproportionately impacts certain ethnic and racial groups, which may not be adequately represented in these prior studies (10).

So, what is the next step for clinicians who manage obese children? Obesity is an epidemic, and nearly 20% of all children in the United States are obese (14). Obesity is also a challenging risk factor to remediate, but nonetheless it is modifiable, given the appropriate interventions. However, many asthma specialty providers are not routinely assessing body mass or providing specific recommendations for weight reduction in children, which may improve not only overall health but also short-term and long-term asthma control (11). For example, researchers in a recent study of children with asthma admitted to a large academic hospital found that obesity was present in

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19.6% of children; yet, body mass index percentile was recorded in only 3.3% of medical records and in only 11% of children with obesity (15). In this same study, only 5.6% of children were given a discharge diagnosis indicating overweight status or obesity, leaving little room for intervention (15). However, the newly released statement from the United States Preventive Services Task Force (June 2017) (16) does offer additional guidance for clinicians and a benchmark for improvement. The task force recommends that 1) all children aged 6 years and older be screened by clinicians for obesity, with body mass indices plotted on appropriate

growth charts for sex and age, and 2) children at or above the 95th percentile be referred for behavioral interventions of at least 26 contact hours, which can improve weight status for up to 12 months with little to no harm (16). Although the report does not specify which clinicians should perform obesity screening, asthma providers may see children with uncontrolled asthma more frequently than primary care providers do and therefore may be in a key position to refer children to existing services.

Nonetheless, there are many remaining questions that must be answered before a “personalized” as opposed to a “one-size-

fits-all” asthma treatment approach can become a reality for obese children. Despite the promise of the phenotypic discoveries of Ross and colleagues (10) and others (12), there is still no universal consensus on what constitutes an asthma “phenotype” in children for the purpose of pharmacotherapy. Prospective clinical trials in obese children are also desperately needed to better understand the treatment needs of these children and how these needs may differ from what is offered in standardized treatment approaches. ■

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