

## Clinical Commentary Review

# Impact of Lifestyle Interventions Targeting Healthy Diet, Physical Activity, and Weight Loss on Asthma in Adults: What Is the evidence?

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**Unhealthy lifestyle factors such as poor diet quality, sedentary lifestyle, and obesity are associated with negative health consequences in asthma including poor asthma control, impaired quality of life, and greater health care utilization. Lifestyle modification is the cornerstone of behavioral treatments and has been effective in chronic diseases such as atherothrombotic vascular disease and diabetes. There is a critical need for lifestyle interventions in asthma care that address obesity and its intimately linked risk behaviors in terms of poor diet and physical inactivity. We present in this commentary the promising lifestyle interventions emerging in asthma care that target poor diet, physical inactivity and weight loss, the proposed mechanisms of these lifestyle interventions, and the critical need for guideline-concordant lifestyle interventions in asthma care.** © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017; ■:■-■)

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Asthma prevalence has risen markedly worldwide, affecting an estimated 300 million people currently and projected to increase by 100 million by 2025.<sup>1</sup> Although factors such as genetics and environmental exposures are important contributors to asthma, they cannot account solely for this rapid increase in asthma prevalence. Studies have shown this increase is significantly

associated with environmental changes (eg, urbanization) and unhealthy lifestyle behaviors (eg, poor diet quality, sedentary lifestyle, and obesity).<sup>2-6</sup>

Calorie-excess, nutrient-deficient diets and physical inactivity are associated with poor asthma control, impaired quality of life, and greater health care utilization.<sup>7-13</sup> Obesity, often a result of poor diet and sedentary lifestyle, is not only a risk factor for incident asthma but a disease modifier in pre-existing asthma. Asthma in obese individuals, or “obese asthma,” is a multi-phenotypical disease complex whose exact mechanisms remain elusive, albeit likely multifactorial.<sup>2,4,14</sup> Compared with asthma in normal weight people, asthma in obese individuals is associated with poorer asthma-related quality of life, greater health care utilization, and is more difficult to control partly due to blunted response to standard drug therapy.<sup>7-12</sup> Both epidemiological and *in vitro* cellular studies show that increased body mass index (BMI  $\geq 25$  kg/m<sup>2</sup>) can negatively influence the response to corticosteroids.<sup>15,16</sup>

To address obesity in asthma, interventions targeting obese adults with asthma have been conducted and show improvements in asthma control and asthma-related quality of life.<sup>17</sup> Most of these studies focused on stringent caloric restriction, supervised exercise or bariatric surgery to attain these results. Although short-term efficacy in asthma outcomes were shown, very low calorie diets and supervised exercise are difficult to sustain, and fewer than 2% of individuals eligible for bariatric surgery actually receive it.<sup>18,19</sup> Behavioral medicine has been used to address unhealthy lifestyle behaviors such as poor diet and physical inactivity in other chronic diseases such as hypertension and diabetes.<sup>20,21</sup> These interventions are not only effective in eliciting the desired behavior change but have also shown sustained clinical benefits.<sup>22,23</sup> The need for integrating behavioral medicine in asthma care to specifically address poor diet quality, sedentary lifestyle, and obesity—3 major lifestyle risk factors for asthma morbidity—is imperative, yet minimally met.

Evidence has begun to accrue over the last 2 decades on behavioral interventions promoting dietary change, physical activity and/or weight loss, and their putative mechanisms, in patients with asthma. The scope of this clinical commentary does not entail an exhaustive review of the available literature on lifestyle interventions in asthma, which has been the topic of several recent systematic reviews.<sup>17,24-26</sup> Instead, this commentary will review the most relevant studies of diet and exercise interventions in adult patients with asthma and focus on the need for guideline-concordant lifestyle interventions in pulmonary medicine, specifically asthma. We will emphasize that although lifestyle medicine in pulmonary disease is in its infancy, evidence-based practice and lessons learned from lifestyle interventions in other chronic diseases, such as diabetes and

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**Abbreviations used**

ACQ- Asthma Control Questionnaire  
 AO- Antioxidant  
 AQLQ- Asthma Quality of Life Questionnaire  
 BHR- Bronchial hyperresponsiveness  
 MCID- Minimal clinically important difference  
 RCT- Randomized controlled trial  
 SCFA- Short chain fatty acid

atherothrombotic vascular disease, should impart critical insights for lifestyle interventions in asthma. The overall goal of this commentary is to call for more rigorous research on scalable and sustainable lifestyle interventions specifically addressing unhealthy diet, physical inactivity, and obesity that can effectively improve asthma care, and their underlying physiological mechanisms.

## WHAT DO WE KNOW ABOUT LIFESTYLE INTERVENTIONS IN ASTHMA?

### Dietary pattern changes in asthma

Healthy dietary patterns rather than specific foods or nutrients have received growing attention in nutrition research and practice guidelines for chronic disease prevention and control, such as in cardiovascular disease where there is robust evidence for dietary pattern interventions.<sup>27</sup> Yet, this is only a nascent field in asthma.<sup>28</sup> Three pilot randomized controlled trials (RCTs) to date have investigated the effect of dietary patterns in adult asthma (Table I). Wood et al<sup>29</sup> compared a high- versus low-antioxidant (AO) diet for 14 days in adults with stable asthma; then participants went on to receive placebo or tomato extract for 14 weeks. Despite its shortcomings (eg, short duration and high attrition at 42%), it was the first study to provide evidence that a low AO diet could lead to a reduction in forced expiratory volume in 1 second (FEV<sub>1</sub>;  $P = .01$ ) and forced vital capacity (FVC;  $P = .02$ ) and a 2.26 greater risk of having an asthma exacerbation. The authors concluded that a whole-food approach, rich in fruit and vegetables, could be more important than an isolated AO supplementation in the management of asthma. Sexton et al examined 2 interventions promoting Mediterranean diet with dietitian counseling over 3 months compared with an end-of-trial offering of a single dietitian counseling session, recipes, and free food in 38 adults with symptomatic asthma. The trial showed the feasibility of improving Mediterranean diet scores (6.62 vs 0.44;  $P < .001$ ) and clinically significant changes (MCID  $\geq 0.5$ ) in several subdomains of Asthma Quality of Life Questionnaire (AQLQ) (symptoms, emotional, and environmental) yet this did not reach statistical significance for either intervention.<sup>30</sup> Ma et al conducted a pilot RCT of a 6-month behavioral intervention specifically promoting the dietary approaches to stop hypertension (DASH) diet in patients with uncontrolled persistent asthma. This study was designed for weight maintenance and produced greater improvements in diet quality (net increase in DASH score = 0.8), asthma control (net decrease in Asthma Control Questionnaire [ACQ] = -0.2), and asthma-related quality of life (net increase in AQLQ overall = 0.4) compared with usual care control.<sup>31</sup> These findings suggest that improved diet quality following a healthy dietary pattern intervention may

have therapeutic benefits for adult patients with uncontrolled asthma.

Diet quality may affect asthma control through improved physiological responses to medications and metabolomic effects. A high-fat meal reduces bronchodilator responsiveness in patients with asthma.<sup>32</sup> The underlying mechanisms behind this are unknown, though may be related to increased airway inflammation after a high-fat meal.<sup>32</sup> Regardless of the cellular mechanism, this prior work suggests that improving diet quality (lower fat content) may enhance the responsiveness to  $\beta$ -agonist medication. The metabolomic effects of diet quality relate to circulating short chain fatty acids (SCFAs). SCFAs promote dendritic cell hematopoiesis and impair the ability to promote Th2 effector cells, thus inhibiting allergic inflammation in a mouse model of asthma.<sup>33</sup> Further, SCFAs decrease allergic effector T-cell responses, promote formation of T regulatory cells,<sup>34,35</sup> and reduce nuclear factor kappa-light-chain-enhancer of activated B-cell activation in macrophages.<sup>36</sup> These studies link diet quality to SCFAs and altered innate and adaptive immune responses. This may suggest an important link between diet quality and asthma.

### Physical activity and asthma

Several population-based studies show individuals with asthma engage in less physical activity and are more sedentary than their counterparts without asthma.<sup>7,37-39</sup> A worsening of asthma symptoms during exercise or a restriction of physical activity leading to deconditioning have been identified as reasons for these low levels of physical activity among adults with asthma.<sup>40-42</sup> Low levels of physical activity have been associated with negative health consequences including greater asthma symptoms, poorer asthma control, and asthma-related quality of life.

Physical activity interventions in adults with asthma have focused primarily on improving physical fitness, lung function, asthma control, and airway inflammation through aerobic exercise training. The results of these studies have varied and are difficult to compare because of differences in study design and study protocols. The study protocols include various types of aerobic exercise such as walking, running, jogging, weight training, or a combination of these.<sup>7</sup> Seven RCTs published to date have examined the effects of physical activity alone in adults with asthma (Table II).<sup>43-49</sup> These studies consistently found improvements in asthma-related quality of life, asthma symptoms, and exercise capacity (see Table II for effect size). Although these studies are promising, they have included small groups of patients attending structured training sessions at a gym in academic centers or led by physiotherapists, which are poorly generalizable to a real-world setting.

How physical activity can impact asthma is poorly understood. Changes in airway inflammation have been assessed in 4 of these interventions, and all but one found significant decreases in fractionated exhaled nitric oxide.<sup>44,47-49</sup> Three of these studies examined sputum cell counts; 2 found a decrease in total cells and eosinophils in individuals with asthma post-exercise training, whereas the other study found no changes in sputum cell differentials.<sup>47-49</sup> Murine models support these findings of reduced eosinophilic airway inflammation postexercise. Ovalbumin-sensitized mice have a significant reduction in eosinophils in bronchoalveolar lavage after 45 minutes of exercise on a treadmill at a moderate intensity.<sup>50</sup> This appears to be

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