

## Original Article

# The Dietary Inflammatory Index and Current Wheeze Among Children and Adults in the United States

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**What is already known about this topic?** Dietary patterns are associated with asthma and lung function, likely through proinflammatory pathways.

**What does this article add to our knowledge?** An overall proinflammatory diet, assessed by the Dietary Inflammatory Index (DII), increases the risk of current wheeze in adults and in children with high fractional exhaled nitric oxide. Moreover, the DII is associated with decreased forced expiratory volume in 1 second and forced vital capacity in adults without wheezing.

**How does this study impact current management guidelines?** A diet with higher proinflammatory components and lower anti-inflammatory components may have detrimental effects on asthma symptoms in adults and atopic children in the United States. Our findings further support studies of whole-diet interventions to reduce asthma burden.

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Conflicts of interest: N. Shivappa and M. D. Wirth are employees of Connecting Health Innovations LLC (CHI). J. R. Hébert owns controlling interest in CHI, a company planning to license the right to his invention of the dietary inflammatory index (DII) from the University of South Carolina to develop computer and smart phone applications for patient counseling and dietary intervention in clinical settings. J. C. Celedón received materials from Merck (inhaled steroids) and Pharmavite (vitamin D and placebo tablets), to provide medications at no cost to participants in 2 NIH-funded studies, unrelated to the current work. The rest of the authors declare that they have no relevant conflicts of interest.

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**BACKGROUND:** A proinflammatory diet may increase allergic airway inflammation by affecting innate and adaptive immune responses.

**OBJECTIVE:** In this study, we examine the relation between the diet's inflammatory potential, measured by the Dietary Inflammatory Index (DII), and current asthma, current wheeze, and lung function in U.S. children and adults.

**METHODS:** We analyzed data from 8,175 children (aged 6-17 years) and 22,294 adults (aged 18-79 years) who participated in the 2007-2012 National Health and Nutrition Examination Survey. The DII was calculated by nutrient intake based on 24-hour dietary recalls, and normalized as per 1,000 calories of food consumed to account for total energy intake. Multivariable regression models were used for the analysis of the DII and current asthma, current wheeze, and lung function measures. **RESULTS:** Higher DII (a proinflammatory diet) was associated with current wheeze among adults (eg, odds ratio [OR] for quartile 4 vs 1, OR = 1.41, 95% confidence interval [CI] = 1.17-1.70;  $P_{\text{trend}} < .01$ ) and among children with high fractional exhaled nitric oxide (a marker of eosinophilic airway inflammation; OR = 2.38, 95% CI = 1.13-5.02;  $P_{\text{trend}} = .05$ ). The DII also was associated with decreased forced expiratory volume in 1 second and forced vital capacity in adults without asthma or wheezing. The DII was not associated with lung function in children or current asthma in either age group. **CONCLUSIONS:** Our findings suggest that a proinflammatory diet, assessed by the DII, increases the odds of current wheeze in adults and children with allergic (atopic) wheeze. These results further support testing dietary interventions as part of the management of asthma. © 2018 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2018; ■■■-■)

**Key words:** Dietary Inflammatory Index; Asthma; Wheezing; Lung function; NHANES

**Abbreviations used**

<i>BDR</i> - Bronchodilator response ( $[\text{post-bronchodilator FEV}_1 - \text{pre-bronchodilator FEV}_1] / \text{pre-bronchodilator FEV}_1 \times 100$ )
<i>BMI</i> - Body mass index (weight [kg]/height [m] <sup>2</sup> )
<i>CDC</i> - Centers for Disease Control and Prevention
<i>COPD</i> - chronic obstructive pulmonary disease
<i>CRP</i> - C-reactive protein
<i>DII</i> - Dietary inflammatory index
<i>FeNO</i> - Fractional exhaled nitric oxide
<i>FEV<sub>1</sub></i> - Forced expiratory volume in 1 second
<i>FVC</i> - Forced vital capacity
<i>NHANES</i> - National Health and Nutrition Examination Survey
<i>PUFA</i> - Polyunsaturated fatty acid
<i>SCFA</i> - Short chain fatty acid

Asthma is a chronic inflammatory airway disease that affects approximately 330 million people worldwide.<sup>1</sup> Temporal changes in environment and lifestyle, including diet, may partly explain the “asthma epidemic” in industrialized countries.<sup>2,3</sup> Whereas a Mediterranean diet (characterized by high intake of fruits, vegetables, and omega-3 polyunsaturated fatty acids [PUFAs]) has been associated with lower risk of asthma and wheeze,<sup>4</sup> a Westernized diet (characterized by low intake of fiber but high intake of saturated fats) has been associated with increased risk of asthma and wheeze.<sup>5</sup>

Dietary components can modulate immunity by regulating T-helper (Th)2 (proallergic) immune responses that lead to airway inflammation.<sup>6</sup> Dietary lipids can contribute to allergic diseases (such as atopic asthma) by enhancing inflammation,<sup>7</sup> whereas vitamin C and vitamin E have shown anti-inflammatory effects and potentially beneficial effects on asthma symptoms.<sup>8</sup> We previously reported that frequent consumption of vegetables and grains, coupled with less frequent consumption of dairy products and sweets, was associated with lower risk of asthma<sup>9</sup> but better lung function (higher forced expiratory volume in 1 second [FEV<sub>1</sub>] and forced vital capacity [FVC])<sup>10</sup> in Puerto Rican children, a finding that may be mediated by IL-17F-dependent inflammatory pathways.<sup>9,10</sup>

Recent studies of diet and chronic diseases have focused on dietary patterns, as the combined and interacting effects of dietary components may have greater effects on disease pathogenesis than individual nutrients. The Dietary Inflammatory Index (DII) is a score that categorizes an individual’s diet on a continuum from the most anti-inflammatory to the most proinflammatory. The DII was developed and validated to account for the whole diet of an individual, and not individual nutrients or food items.<sup>11,12</sup> A higher DII score, which reflects a proinflammatory diet, was recently associated with asthma and lower FEV<sub>1</sub> in a small case-control study of adults.<sup>13</sup>

We hypothesized that a proinflammatory diet is associated with increased asthma or wheeze, and worsened lung function. To test this hypothesis, we examined the relation between DII score and current asthma, current wheeze, and lung function in a large representative sample of U.S. children and adults. Because the proinflammatory effects of diet may vary by allergic status, we also examined whether the estimated effects of the DII on asthma or lung function are modified by the level of fractional exhaled nitric oxide (FeNO, a marker of eosinophilic airway inflammation).

**METHODS****Subject recruitment and study procedures**

The National Health and Nutrition Examination Survey (NHANES) is a cross-sectional nationwide survey designed to assess the health and nutritional status of the noninstitutionalized U.S. population. Study participants were selected by using stratified multistage probability sampling. By design, persons 60 years and older and ethnic minorities (African Americans and Hispanics) were oversampled to increase the statistical power for data analysis, and to represent the U.S. population across all ages. Both children (aged 6–17 years) and adults (aged 18–79 years) who participated in the 2007–2008, 2009–2010, and 2011–2012 NHANES cycles were included in this analysis. The NHANES interview includes questions on demographic, socioeconomic, dietary, and health-related factors. The examination component consists of medical and physiological measurements, as well as laboratory tests administered by highly trained medical personnel. NHANES was approved by the Institutional Review Board of the National Center for Health Statistics of the U.S. Centers for Disease Control and Prevention (CDC). Informed consent was obtained from all participants. A proxy provided information for survey participants who were less than 16 years of age and for subjects who could not answer the questions by themselves.

Survey participants aged 6 to 79 years were eligible for spirometry, except for those who were on supplemental oxygen or had painful ear infections, current chest pain or a physical problem with forceful expiration, surgery (of the eye, chest, or the abdomen) in the prior 3 months, heart disease, history of an aneurysm or a detached retina, hemoptysis, or history of a collapsed lung or tuberculosis exposure. Eligible participants performed spirometry following American Thoracic Society recommendations.<sup>14</sup> The best FEV<sub>1</sub> and FVC were selected for analysis. Participants whose baseline FEV<sub>1</sub>/FVC ratio was below the lower limit of normal<sup>15,16</sup> and/or whose baseline FEV<sub>1</sub> was below 70% of the predicted value for their demographic characteristics underwent a repeat spirometry, 15 minutes after inhalation of albuterol. Participants were excluded from bronchodilator administration if they had recently used a short-acting inhaled  $\beta_2$ -agonist or had a previous adverse reaction to albuterol; had a history of congenital heart disease, hypertension, major arrhythmia, or an implanted defibrillator; or were pregnant or breastfeeding. Percent predicted FEV<sub>1</sub>, FVC, and FEV<sub>1</sub>/FVC in children and adults were calculated using Global Lung Initiative equations that account for age, sex, race/ethnicity, and height.<sup>17</sup> FeNO was measured using the Aerocrine NIOX MINO, a portable, hand-held nitric oxide analyzer (Aerocrine AB, Solna, Sweden). The NHANES protocol required 2 valid FeNO measurements that were reproducible. High FeNO was defined as  $\geq 20$  ppb in children and  $\geq 25$  ppb in adults.<sup>18</sup> Further details of the methods, protocols, and definitions used in NHANES can be found at <http://www.cdc.gov/nchs/nhanes.htm>.

**The dietary inflammatory index**

The development and validation of the DII has previously been reported.<sup>11,12</sup> Peer-reviewed literature published between 1950 and 2010 was evaluated, and 1943 articles linked to 45 individual nutrients, foods, or flavonoid intake parameters were identified. Points were assigned to each of these parameters according to whether they: (1) increased (+1), decreased (−1), or had no (0) effect on the 4 established proinflammatory biomarkers: IL-1 $\beta$ , IL-6, TNF- $\alpha$ , and C-reactive protein (CRP); or (2) decreased (+1), increased (−1), or had no (0) effect on the 2 established anti-inflammatory biomarkers:

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