



## Risk factors and clinical outcomes associated with fixed airflow obstruction in older adults with asthma

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### ABSTRACT

**Background:** Asthma in older adults is associated with increased morbidity and mortality compared with asthma in younger patients. Fixed airflow obstruction (FAO) is associated with decreased survival in younger patients, but its significance remains unclear in older adults with asthma.

**Objective:** To identify risk factors and outcomes related to FAO in older adults with asthma.

**Methods:** Subjects older than 55 years with a physician diagnosis of persistent asthma were evaluated. Collected data included participant demographic information, medications, asthma exacerbations, Asthma Control Test (ACT) score, Asthma Quality of Life (AQLQ) score, comorbidities, spirometry, atopic status, and fractional exhaled nitric oxide. Clinical characteristics and outcomes associated with FAO (defined as post-bronchodilator ratio of forced expiratory volume in 1 second to forced vital capacity  $\leq 70\%$ ) were assessed.

**Results:** A total of 186 participants were analyzed (48 men and 138 women, mean age 66 years). FAO was demonstrated in 30% of participants. Using regression analysis, predictors of FAO included advanced age, African American race, male sex, and longer duration of asthma. In outcomes analysis, FAO was associated with worsened ACT and AQLQ scores; however, after controlling for confounding factors, logistic regression showed no association. No significant association was found between FAO and exacerbations, fractional exhaled nitric oxide, atopy, rhinitis, education level, depression, smoking, or body mass index.

**Conclusion:** Risk factors associated with FAO in older adults with asthma include advanced age, African American race, increased asthma duration, and male sex. Unlike younger patients, FAO is not independently associated with worsened asthma control, quality of life, or exacerbations in older patients with asthma.

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### Introduction

Asthma is a chronic disease resulting in episodic airflow obstruction secondary to inflammation and bronchospasm of the respiratory tract. The prevalence of asthma in the United States has continued to escalate, resulting in an increase in health care costs and morbidity and mortality in the affected population.<sup>1</sup> At particular risk is an increasing proportion of older adults with asthma; it is estimated that 1 in 5 patients with asthma will be older than 65 years by 2050, with prevalence increases in the older population continuing to outpace the younger.<sup>2</sup> It has been well documented that morbidity and mortality in older adults with asthma are greater than in the younger population, with a confluence of theorized contributing factors.<sup>3</sup> Patients older than 55 years

have higher rates of emergency department (ED) visits, hospitalization, and asthma-associated health care costs compared with those younger than 55.<sup>4</sup> In fact, persons at least 55 years old have the highest asthma mortality rate compared with all other persons with asthma combined.<sup>5</sup> Despite this, asthma in older adults continues to be an under-recognized and undertreated epidemic.<sup>6</sup>

Although most patients initially demonstrate reversibility with bronchodilators and/or other asthma medications, known as reversible airflow obstruction (RAO), some patients will progress to irreversibility of airflow obstruction, known as fixed airflow obstruction (FAO). The estimated prevalence of FAO has been reported at 8% to 49% in patients with asthma, a wide-ranging estimate.<sup>7,8</sup> In fact, a universal consensus has yet to be established in defining objective measures of FAO.<sup>7,9–19</sup> For this study, the most commonly used and accepted definition of FAO (post-bronchodilator treatment ratio of forced expiratory volume in 1 second [FEV<sub>1</sub>] to forced vital capacity [FVC] < 70%) was used.<sup>12,16,18</sup>

Relatively few studies have been performed to evaluate risk factors for FAO, with significant heterogeneity among inclusion and

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exclusion criteria.<sup>7,9–19</sup> Some proposed risk factors for FAO include adult-onset asthma, older age, African American race, male sex, and a history of smoking based on analyses of patient populations at least 18 years old. Paradoxically, the presence and absence of allergic rhinitis also have been highlighted as risk factors.<sup>7,8,13,14,18</sup> Despite these findings, there have been no prior studies exclusively related to older adults with asthma, the population at greatest risk for morbidity and mortality.<sup>16</sup>

The significance of FAO with regard to clinical outcomes in older adults with asthma also remains unclear. Poorer prognoses have been associated with FAO in younger populations,<sup>9</sup> but no studies have evaluated the significance of FAO in older adults with asthma related to National Institutes of Health (NIH) core asthma outcomes recommendations.<sup>16,20</sup> Currently, it is unknown whether older adults with FAO have poorer outcomes, as seen in younger adults.

The goal of this study was to examine clinical characteristics, including risk factors and clinical outcomes, associated with FAO in older adults with asthma.

## Methods

### Participants and Protocol

As part of a blinded, randomized controlled study of older adults with asthma (NCT01979055), participants were recruited from 2 academic institutions in Michigan serving a diverse population of older adults. We recruited subjects older than 55 years with a physician diagnosis of persistent asthma, the age span when asthma mortality rates are the highest.<sup>21</sup> Based on previous data collection from the Centers for Disease Control and Prevention, in addition to other prospective trials, 55 years was used as a threshold for older adults in this study.<sup>22–25</sup> An additional analysis was performed limiting patient age to at least 65 years old and is included in the supplementary materials section. Persistent asthma was defined according to NIH guidelines, including answering yes to the following questions: “Has a doctor or health care provider ever told you that you have asthma?” “Do you still have asthma?” “Do you take any medicine or inhalers for your asthma every day?” Exclusionary criteria included any other significant cardiopulmonary disease (including chronic obstructive pulmonary disease or emphysema), current smokers, a greater than 20 pack-year smoking history (because this level has been associated with the development of chronic obstructive pulmonary disease [COPD]),<sup>26</sup> a lack of telephone access, or significantly impaired cognitive capacity. Computed tomography to assess for emphysematous changes was not performed. Institutional review board approval and written informed consent were obtained.

### Data Collection

#### Demographics

A baseline questionnaire was administered to all study participants. Items assessed included age, sex, race, self-reported ethnicity, education level, asthma medications (including dose and frequency), smoking history, age at diagnosis of asthma, exacerbations during the past year, depression screening, health comorbidities, and body mass index (BMI). To identify depression in patients with asthma, the short-form Geriatric Depression Scale was used; a score higher than 5 is suggestive of depression.<sup>27</sup> To assess education level, participants identified their highest level of completed education. Choices included less than high school, high school completion, 2-year college completion, 4-year college completion, and postgraduate completion. To assess concomitant medical conditions (comorbidities), participants identified the presence or absence of previously diagnosed medical conditions consisting of heart disease, hypertension, stroke, and/or cancer.

### Asthma-related assessments

To assess perceptions of quality of life in patients with asthma, the mini Asthma Quality of Life Questionnaire (AQLQ) was used. The AQLQ is the most commonly used measure of quality of life in those with asthma.<sup>28</sup> Subjective perceptions of asthma control were evaluated using the Asthma Control Test (ACT). A score lower than 20 is suggestive of a patient perception of poor asthma control.<sup>29</sup> Asthma exacerbations were defined as self-reported medical care usage (with asthma as the primary reason) during the previous 12 months for (1) hospitalization, (2) ED visits, (3) unscheduled physician or clinic visits for urgent asthma treatment, and (4) systemic glucocorticoid use; this is consistent with NIH core asthma outcomes.<sup>20</sup> Asthma severity was determined using the NIH National Asthma Education and Prevention Program guidelines.<sup>30</sup> These guidelines, based on asthma medication use, classify asthma severity on a scale of 1 (mild) to 6 (severe; eTable 1).

### Measures of lung function

To assess lung function parameters, a spirometer was used (Model 2001; EasyOne Plus, Zurich, Switzerland) and results were compared with published predicted values at baseline and after combination short-acting  $\beta$ -agonist and anticholinergic administration.<sup>31</sup> The maximal bronchodilator response was determined 10 minutes after inhaling nebulized ipratropium bromide and albuterol (0.5 mg/3 mg per 3 mL) after discontinuation of a short-acting  $\beta$ -agonist for at least 6 hours and a long-acting  $\beta$ -agonist (LABA) for at least 12 hours. FAO was defined as FEV<sub>1</sub>/FVC post-bronchodilator treatment less than 70%, the most commonly used and accepted definition.<sup>12,16,18</sup> Fractional exhaled nitric oxide (FeNO) was measured with a precalibrated nitric oxide monitor (Model 510[k]; Aerocrine AB, Solna, Sweden).

### Atopy

To assess atopic status, participants underwent skin prick testing at baseline evaluation after discontinuation of antihistamine medications for at least 5 days. Atopy was defined by the presence of at least 1 positive skin prick test result, administered with the ComforTen applicator (HollisterStier Allergy, Spokane, Washington), to the tested aeroallergens (house dust mite, mixed grass pollen, mixed tree pollen, mixed weed pollen, mold mix, cockroach, cat dander, dog dander). Positive histamine and negative saline controls also were placed. A positive skin prick test reaction was defined by a wheal at least 3 mm larger than the negative saline control.

### Statistical Analysis

To compare differences between the FAO and RAO groups, 2-sample *t* test and  $\chi^2$  tests were carried out for continuous and dichotomized variables. Logistic regression analysis was conducted to fit the dichotomized response, FAO or RAO, with demographic covariates adjusted as indicated. The estimated odds of FAO compared with the odds of RAO also were calculated and provided. SAS 9.3 (SAS Institute, Cary, North Carolina) was used for the analyses.

## Results

A total of 186 participants were analyzed. The mean age of participants was 66 years (range 58.6–73.4 years) with a 25.8% male and 32.3% African American distribution. The average asthma duration was 32.1 years, and average BMI was 31.2 kg/m<sup>2</sup>. Of the 186 older adults with asthma, 56 (30%) demonstrated FAO according to study criteria. Most participants (*n* = 113; 60.8%) demonstrated atopy, and the mean FeNO value was 28.7 ppb. Participants with RAO demonstrated significant post-treatment improvement in FEV<sub>1</sub>/FVC compared with those with FAO (Table 1).

**Table 1**  
Baseline Participant Data

|                                                | FAO         | RAO         | P value |
|------------------------------------------------|-------------|-------------|---------|
| Participants, n                                | 56          | 130         |         |
| African American, n (%)                        | 55.4 (31)   | 22.3 (29)   | <.0001  |
| Men, n (%)                                     | 37.5 (21)   | 21.5 (28)   | .04     |
| Asthma duration (y), mean (SD)                 | 40.8 (21.3) | 28.4 (19.5) | .0001   |
| Comorbidities <sup>a</sup>                     | 1.1         | 0.8         | .005    |
| Age (y), mean (SD)                             | 67.7 (9.0)  | 65.2 (6.4)  | .07     |
| Smoking duration (pack-years), mean (SD)       | 2.9 (6.2)   | 2.3 (5.4)   | .46     |
| Education level <sup>b</sup>                   | 3.4         | 3.6         | .26     |
| Atopy, n (%)                                   | 62.5 (35)   | 60 (78)     | .75     |
| Rhinitis n (%)                                 | 76.8 (43)   | 72.3 (94)   | .52     |
| Depression, n (%)                              | 23.3 (13)   | 23.9 (31)   | .93     |
| BMI (kg/m <sup>2</sup> )                       | 31.1        | 31.2        | .94     |
| Asthma severity score <sup>c</sup>             | 3.5         | 3.6         | .66     |
| FeNO                                           | 33          | 26.9        | .2      |
| FEV <sub>1</sub> (% predicted), mean (SD)      |             |             |         |
| Pretreatment                                   | 54.5 (16.1) | 77.1 (18.4) | <.0001  |
| Post-treatment                                 | 61.1 (16.3) | 81.8 (16.8) | <.0001  |
| Difference (post minus pre)                    | 6.5 (9.8)   | 4.7 (9.4)   | .22     |
| FEV <sub>1</sub> /FVC (% predicted), mean (SD) |             |             |         |
| Pretreatment                                   | 61.1 (10.6) | 76.1 (6.8)  | <.0001  |
| Post-treatment                                 | 61.1 (8.2)  | 79.4 (5.2)  | <.0001  |
| Difference (post minus pre)                    | 0.007 (9.6) | 3.3 (5.7)   | .02     |

Abbreviations: BMI, body mass index; FAO, fixed airflow obstruction; FeNO, fractional exhaled nitric oxide; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; RAO, reversible airflow obstruction.

<sup>a</sup>Average number of comorbidities including heart disease, hypertension, stroke, and cancer.

<sup>b</sup>1, less high school; 2, high school; 3, 2-year college; 4, 4-year college; 5, postgraduate degree.

<sup>c</sup>National Institutes of Health National Asthma Education and Prevention Program severity score on a scale of 1 (mild) to 6 (most severe).

When limiting the analysis to those at least 65 years old, 97 participants were included. The mean age of participants was 71.3 years with a similar sex, race, asthma duration, and BMI distribution. Of the 97 older adults with asthma, 34 (35%) demonstrated FAO.

#### Risk Factors for FAO

Compared with RAO, stratified group comparison showed a significant association between FAO and African American race, male sex, increased duration of asthma, and increased comorbidities (Table 1). Patient age showed borderline significance ( $P = .07$ ) in association with FAO. After controlling for confounding factors, regression analysis identified independent risk factors associated with FAO that included male sex, increased duration of asthma, older age, and African American race (Table 2). Male sex was recognized as an independent risk factor for the development of FAO, with an almost 4-fold increased risk (odds ratio 3.98). FAO was independently associated with a longer duration of asthma in older adults. For every decade with asthma, the risk for FAO in older adults with asthma increased by 36%. African American race for older adults with asthma was linked with an increased risk of FAO by a factor of more than 4. FAO also was correlated with age. For every decade of life in older adults with asthma, their risk of FAO was increased by 85%. Asthma severity, smoking, atopy, depression, comorbidities,

**Table 2**  
Logistic Regression of Factors Associated With Fixed Airflow Obstruction

|                           | P value | OR   | 95% CI     |
|---------------------------|---------|------|------------|
| Male sex                  | .005    | 3.98 | 1.51–10.54 |
| Asthma duration by decade | .004    | 1.36 | 1.10–1.67  |
| African American race     | .009    | 4.29 | 1.45–12.76 |
| Age (by decade)           | .050    | 1.85 | 1.01–3.40  |

Abbreviations: CI, confidence interval; OR, odds ratio.

**Table 3**  
Outcomes in Older Adults With Asthma\*

|                                         | FAO        | RAO        | P value |
|-----------------------------------------|------------|------------|---------|
| Asthma Control Test score, mean (SD)    | 16.3 (4.7) | 18.2 (4.5) | .01     |
| Asthma quality of Life score, mean (SD) | 4.8 (1.3)  | 5.3 (1.1)  | .008    |
| Asthma exacerbations, n (%)             | 55.4 (31)  | 55.4 (72)  | .997    |
| Hospitalization                         | 14.6 (8)   | 9.2 (12)   | .29     |
| ED visit                                | 23.2 (13)  | 14.6 (19)  | .15     |
| Unscheduled medical visit               | 32.1 (18)  | 34.4 (44)  | .77     |
| Glucocorticoid use                      | 42.9 (24)  | 49.2 (62)  | .43     |

Abbreviations: ED, emergency department; FAO, fixed airflow obstruction; RAO, reversible airflow obstruction.

\*Data presented as % (n) unless otherwise indicated.

education level, rhinitis, and BMI were not independently associated with FAO using regression analysis.

When limiting analysis to those at least 65 years old, stratified group comparison showed a significant association between FAO and African American race, increased duration of asthma, and increased comorbidities (eTable 2). After controlling for confounding factors, regression analysis identified independent risk factors associated with FAO that included increased duration of asthma; male sex and African American race showed borderline significance (eTable 3). For every decade with asthma, the risk for FAO in adults older than 65 years increased by 53% (odds ratio 1.53, 95% confidence interval 1.13–2.08). Asthma severity, smoking, atopy, depression, comorbidities, education level, rhinitis, and BMI were not independently associated with FAO using regression analysis.

#### Clinical Outcomes Associated With FAO

Compared with those with RAO, stratified group comparison showed that those with FAO had lower subjective asthma scores (Table 3). In older adults who demonstrated FAO, ACT scores were lower (16.3 vs 18.2;  $P = .01$ ). In those older adults with FAO, AQLQ scores also were lower (4.8 vs 5.3;  $P = 0.008$ ); these lower AQLQ scores correlated with a perception of a worsened quality of life in participants with FAO. However, after controlling for confounding factors using regression analysis, there was no significant difference between groups (Table 4). Logistic regression did show systemic glucocorticoid use, rhinitis, education level, and BMI as independent risk factors associated with poor perception of asthma control and quality of life. There was no significant difference in clinical outcomes pertaining to exacerbations (hospitalization, ED visits, unscheduled physician or clinic visits for urgent treatment, or systemic glucocorticoid use) between FAO and RAO (Table 3). Logistic regression showed that asthma severity was the only independent risk factor associated with exacerbations in older adults with asthma (odds ratio 1.86, 95% confidence interval 1.36–2.54; eTable 4).

When limiting the analysis to those at least 65 years old, similar findings were demonstrated. Compared with those with RAO, stratified group comparison showed that those with FAO had lower subjective asthma quality-of-life scores, but not asthma control (eTable 5). However, after controlling for confounding factors using regression analysis, there was no significant difference between groups (eTable 6). Logistic regression did show systemic glucocorticoid use was an independent risk factor associated with poor perception of asthma quality of life. There was no significant difference in clinical outcomes pertaining to exacerbations (hospitalization, ED visits, unscheduled physician or clinic visits for urgent treatment, or systemic glucocorticoid use) between FAO and RAO.

**Table 4**  
Linear Regression of Predictors of ACT and AQLQ Scores

|                                             | $\beta$ | 95% CI         | P value |
|---------------------------------------------|---------|----------------|---------|
| <b>ACT</b>                                  |         |                |         |
| Race                                        | −2.37   | −4.0 to −0.78  | .004    |
| Systemic glucocorticoid use                 | −1.89   | −3.16 to −0.62 | .004    |
| Rhinitis                                    | −1.92   | −3.33 to −0.51 | .008    |
| Education level                             | 0.65    | 0.06–1.24      | .03     |
| Fixed airflow obstruction                   | 0.04    | −1.61 to 1.69  | .96     |
| Sex                                         | −0.43   | −1.90 to 1.04  | .57     |
| Age                                         | −0.07   | −0.97 to 0.83  | .87     |
| Asthma severity score <sup>a</sup>          | −0.47   | −1.0 to 0.06   | .09     |
| Asthma duration                             | −0.05   | −0.38 to 0.28  | .75     |
| Atopy                                       | 0.66    | −0.65 to 1.97  | .33     |
| Depression                                  | −0.63   | −2.10 to 0.84  | .4      |
| BMI                                         | −0.05   | −0.13 to 0.03  | .31     |
| Comorbidities <sup>b</sup>                  | −0.47   | −1.37 to 0.43  | .31     |
| Fractional exhaled nitric oxide             | −0.01   | −0.03 to 0.01  | .21     |
| FEV <sub>1</sub> pretreatment (% predicted) | 0.03    | −0.01 to 0.07  | .09     |
| <b>AQLQ</b>                                 |         |                |         |
| Race                                        | −0.86   | −1.25 to −0.47 | .0001   |
| Systemic glucocorticoid use                 | −0.49   | −0.80 to −0.18 | .002    |
| Rhinitis                                    | −0.56   | −0.89 to −0.23 | .001    |
| BMI                                         | −0.02   | −0.04 to 0.01  | .03     |
| Asthma severity score <sup>a</sup>          | −0.14   | −0.28 to −0.01 | .04     |
| Education level                             | 0.15    | 0.01–0.29      | .05     |
| Fixed airflow obstruction                   | −0.17   | −0.56 to 0.22  | .41     |
| Sex                                         | −0.31   | −0.66 to 0.04  | .09     |
| Age                                         | 0.06    | −0.16 to 0.28  | .6      |
| Asthma duration                             | 0.02    | −0.06 to 0.10  | .57     |
| Atopy                                       | 0.01    | −0.30 to 0.32  | .95     |
| Depression                                  | −0.14   | −0.49 to 0.21  | .45     |
| Comorbidities <sup>2</sup>                  | −0.08   | −0.30 to 0.14  | .47     |
| Fractional exhaled nitric oxide             | −0.002  | −0.01 to 0.01  | .51     |
| FEV <sub>1</sub> pretreatment (% predicted) | 0.005   | −0.01 to 0.02  | .28     |

Abbreviations: ACT, asthma control test; AQLQ, asthma quality of life questionnaire; BMI, body mass index; CI, confidence interval; FEV<sub>1</sub>, forced expiratory volume in 1 second.

<sup>a</sup>National Institutes of Health National Asthma Education and Prevention Program severity score on a scale of 1 (mild) to 6 (most severe).

<sup>b</sup>Comorbidities including heart disease, hypertension, stroke, and cancer.

## Discussion

Our findings identified the prevalence of FAO in older adults with asthma at a rate of 30% compared with previously reported incidence rates for all age groups at 8% to 49%.<sup>8</sup> Using regression analysis, in older adults, FAO was associated with older age, male sex, African American race, and a longer duration of asthma. No significant association was found between FAO and asthma severity, smoking, atopy, or FeNO, which is disparate from previous studies of younger populations.<sup>8–19</sup> In addition, no association was found between FAO and BMI or education levels.

Compared with those with RAO, there was no difference in exacerbations (hospitalization, ED visits, unscheduled physician or clinic visits for urgent treatment, or systemic glucocorticoid use) in those with FAO; this lack of association differs from that seen in younger patients with FAO.<sup>9</sup> A similar discordance was recently demonstrated when assessing obesity and asthma morbidity in older vs younger patients with asthma.<sup>32</sup> Although bivariate group comparison did show differences in subjective asthma scores, after controlling for confounding factors, ACT and AQLQ scores were not significantly different. Asthma severity, rhinitis, education level, and BMI were identified as independent predictors of worsened outcomes in older patients with asthma, which are consistent with prior reports.<sup>1,3,33,34</sup> Although depression did not affect outcomes in our study, it has been noted to do so in older adults with asthma.<sup>35,36</sup>

To our knowledge, this is the first study to evaluate predictors and outcomes associated with FAO in older adults diagnosed with persistent asthma, the population with the highest asthma morbidity and mortality. Previous studies have demonstrated an

association between FAO and potentially poorer health care outcomes in younger populations with asthma.<sup>9,16</sup> However, in our study of older adults with asthma, lung function assessments (FEV<sub>1</sub>, FeNO, FAO) did not play a role in predicting ACT score, AQLQ score, or asthma exacerbations. In fact, compared with younger patients, lung function optimization might be a misguided goal for older populations with asthma. Other investigators have demonstrated no advantage in asthma outcomes with the use of peak flow monitoring in older adults with asthma.<sup>37</sup> Therefore, health care providers should focus on other previously established risk factors, including asthma severity (determined by medication use, not lung function test results), systemic corticosteroid use, socioeconomic status with education as a proxy, depression, and BMI to improve outcomes for older adults.<sup>3,32–36,38</sup>

Limitations of the study include a patient population limited to the Midwestern United States; exclusion of participants with prior diagnoses of COPD and emphysema, which has the potential for excluding those with the asthma COPD overlap syndrome; and baseline data obtained at a single visit, nonreflective of the potential fluctuating nature of asthma. Although the study had potential for misdiagnosis of asthma by health care providers, asthma was defined using commonly accepted criteria for diagnosis.<sup>37,39</sup> Asthma severity could have been misclassified based on the criteria of asthma medication use, but other large-scale studies have used asthma medications to classify asthma severity.<sup>35,40</sup> In addition, although characteristic associations were identified in this study, causality cannot be inferred in a cross-sectional study. Although the study might have been underpowered to find differences in asthma exacerbations, this is unlikely, because the *P* value was .997, and the specific components of asthma exacerbations were equally split between the 2 groups. Although the demographic of patients at least 55 years old is broad, future studies are required to further analyze select patient populations, including those categorized as the “very old” (>80 years) and those with asthma COPD overlap syndrome.<sup>41</sup>

Despite these limitations, the results suggest that independent risk factors associated with FAO in older adults with asthma include male sex, older age, African American race, and increased duration of asthma. Unlike younger patients, our results suggest that FAO is not implicated in poorer asthma outcomes in older adults, placing less emphasis on lung function maximization for optimal care outcomes in this population. Asthma is a complex disease, and further isolation of germane risk factors is paramount for optimal evaluation, diagnosis, management, and counseling related to the treatment of older adults with asthma.

## Supplementary Data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.anai.2017.10.004>.

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## Supplementary Data

**eTable 1**

Asthma Severity Scoring Based on National Institutes of Health National Asthma Education and Prevention Program Asthma Medication Use

| Severity score | Asthma medication                                                   |
|----------------|---------------------------------------------------------------------|
| 1              | SABA                                                                |
| 2              | low-dose ICS or cromolyn or montelukast                             |
| 3              | medium-dose ICS                                                     |
| 4              | medium-dose ICS + LABA or montelukast                               |
| 5              | high-dose ICS + LABA or montelukast                                 |
| 6              | high-dose ICS + LABA or montelukast + oral systemic glucocorticoids |

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting  $\beta$ -agonist; SABA, short-acting  $\beta$ -agonist.

**eTable 2**

Baseline Participant Data for Patients at Least 65 Years Old

|                                           | FAO         | RAO         | P value |
|-------------------------------------------|-------------|-------------|---------|
| Participants, n                           | 34          | 63          |         |
| African American, n (%)                   | 44.1 (15)   | 20.6 (13)   | .01     |
| Asthma duration (y), mean (SD)            | 43.7 (20.9) | 30.6 (20.5) | .004    |
| Comorbidities <sup>a</sup>                | 1.1         | 0.8         | .04     |
| Men                                       | 32.4 (11)   | 20.6 (13)   | .2      |
| Age (y), mean (SD)                        | 72.9 (7.7)  | 70.4 (5.1)  | .1      |
| Smoking duration (pack-years), mean (SD)  | 3.2 (6.3)   | 2.8 (6.2)   | .77     |
| Education level <sup>b</sup>              | 3.7         | 3.7         | .93     |
| Atopy, n (%)                              | 64.7 (22)   | 63.5 (40)   | .91     |
| Rhinitis, n (%)                           | 85.3 (29)   | 73 (46)     | .17     |
| Depression, n (%)                         | 20.6 (7)    | 22.2 (14)   | .85     |
| BMI (kg/m <sup>2</sup> )                  | 30.4        | 31.5        | .55     |
| Asthma severity score <sup>c</sup>        | 3.4         | 3.6         | .35     |
| FeNO (ppb)                                | 37.6        | 28.2        | .18     |
| FEV <sub>1</sub> (% predicted), mean (SD) |             |             |         |
| Pretreatment                              | 56.9 (15.6) | 78.6 (21.2) | <.0001  |
| Post-treatment                            | 61.6 (15.6) | 83.3 (19.2) | <.0001  |
| FEV <sub>1</sub> /FVC, mean (SD)          |             |             |         |
| Pretreatment                              | 60.4 (9.9)  | 75.8 (7.4)  | <.0001  |
| Post-treatment                            | 60.8 (9.1)  | 79.3 (5.2)  | <.0001  |

Abbreviations: BMI, body mass index; FAO, fixed airflow obstruction; FeNO, fractional exhaled nitric oxide; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; RAO, reversible airflow obstruction.

<sup>a</sup>Average number of comorbidities including heart disease, hypertension, stroke, and cancer.

<sup>b</sup>1, less than high school; 2, high school; 3, 2-year college; 4, 4-year college; 5, post-graduate degree.

<sup>c</sup>National Institutes of Health National Asthma Education and Prevention Program severity score on a scale of 1 (mild) to 6 (most severe).

**eTable 3**

Logistic Regression of Factors Associated With Fixed Airflow Obstruction in Patients at Least 65 Years Old

|                           | P value | OR   | 95% CI     |
|---------------------------|---------|------|------------|
| Asthma duration by decade | .006    | 1.53 | 1.13–2.08  |
| Male sex                  | .08     | 3.69 | 0.84–16.13 |
| African American race     | .08     | 4.54 | 0.83–24.93 |
| Age (by decade)           | .34     | 1.72 | 0.57–5.21  |

Abbreviations: CI, confidence interval; OR, odds ratio.

**eTable 4**Logistic Regression of Predictors of Asthma Exacerbations<sup>a</sup>

|                                             | OR   | 95% CI    | P value |
|---------------------------------------------|------|-----------|---------|
| Asthma severity score <sup>b</sup>          | 1.86 | 1.36–2.54 | <.001   |
| Fixed airflow obstruction                   | 0.78 | 0.30–1.99 | .6      |
| Sex                                         | 0.47 | 0.21–1.07 | .07     |
| Race                                        | 1.39 | 0.55–3.53 | .49     |
| Age (decade)                                | 0.61 | 0.37–1.02 | .06     |
| Smoking duration                            | 1.04 | 0.97–1.11 | .27     |
| Asthma duration                             | 1.04 | 0.86–1.25 | .69     |
| Atopy                                       | 0.88 | 0.42–1.86 | .74     |
| Rhinitis                                    | 1.44 | 0.65–3.23 | .37     |
| Depression                                  | 0.63 | 0.27–1.45 | .28     |
| BMI                                         | 1.04 | 0.98–1.09 | .17     |
| Comorbidities <sup>c</sup>                  | 0.76 | 0.46–1.25 | .27     |
| Education level                             | 1.01 | 0.73–1.40 | .93     |
| FEV <sub>1</sub> pretreatment (% predicted) | 0.99 | 0.97–1.01 | .32     |
| FeNO (ppb)                                  | 0.99 | 0.99–1.01 | .88     |

Abbreviations: BMI, body mass index; CI, confidence interval; FeNO, fractional exhaled nitric oxide; FEV<sub>1</sub>, forced expiratory volume in 1 second; OR, odds ratio.

<sup>a</sup>Hospitalization, emergency department visit, oral glucocorticoid use, or unscheduled visit for asthma during the past 12 months.

<sup>b</sup>National Institutes of Health National Asthma Education and Prevention Program severity score on a scale of 1 (mild) to 6 (most severe).

<sup>c</sup>Comorbidities including heart disease, hypertension, stroke, and cancer.

**eTable 5**Outcomes in Older Adults With Asthma ( $\geq 65$  years old)

|                              | FAO  | RAO  | P value          |
|------------------------------|------|------|------------------|
| Asthma Quality of Life score | 4.9  | 5.4  | .05              |
| Asthma Control Test score    | 16.9 | 18.2 | .19              |
| Exacerbations, %             | 47.1 | 49.2 | .84              |
| Hospitalization, %           | 6.1  | 9.5  | .56 <sup>a</sup> |
| ED visit, %                  | 14.7 | 9.5  | .44 <sup>a</sup> |
| Unscheduled medical visit, % | 23.5 | 30.2 | .49              |
| Glucocorticoid use, %        | 35.3 | 45   | .36              |

Abbreviations: ED, emergency visit; FAO, fixed airflow obstruction; RAO, reversible airflow obstruction.

<sup>a</sup>The  $\chi^2$  test might not be a valid test because of the small sample.

**eTable 6**Linear Regression of Predictors of Asthma Quality of Life Questionnaire score ( $\geq 65$  Years Old)

|                                             | $\beta$ | 95% CI         | P value |
|---------------------------------------------|---------|----------------|---------|
| Systemic glucocorticoid use                 | −0.48   | −0.92 to −0.04 | .04     |
| Race                                        | −0.45   | −1.05 to 0.15  | .14     |
| Rhinitis                                    | −0.46   | −0.98 to 0.06  | .09     |
| BMI                                         | −0.02   | −0.05 to 0.01  | .18     |
| Asthma severity score <sup>a</sup>          | −0.11   | −0.28 to 0.06  | .2      |
| Education level                             | 0.16    | −0.04 to 0.36  | .12     |
| Fixed airflow obstruction                   | −0.166  | −0.71 to 0.37  | .55     |
| Sex                                         | −0.498  | −1.04 to 0.04  | .07     |
| Age                                         | −0.03   | −0.41 to 0.35  | .9      |
| Asthma duration                             | −0.02   | −0.13 to 0.09  | .78     |
| Atopy                                       | −0.122  | −0.60 to 0.36  | .62     |
| Depression                                  | −0.07   | −0.58 to 0.44  | .79     |
| Comorbidities <sup>b</sup>                  | −0.01   | −0.35 to 0.33  | .96     |
| FeNO                                        | −0.01   | −0.02 to 0.00  | .18     |
| FEV <sub>1</sub> pretreatment (% predicted) | 0.01    | −0.00 to 0.02  | .17     |

Abbreviations: BMI, body mass index; CI, confidence interval; FeNO, fractional exhaled nitric oxide; FEV<sub>1</sub>, forced expiratory volume in 1 second.

<sup>a</sup>National Institutes of Health National Asthma Education and Prevention Program severity score on a scale of 1 (mild) to 6 (most severe).

<sup>b</sup>Comorbidities including heart disease, hypertension, stroke, and cancer.