

PRACTICE OPTIONS FROM BEYOND OUR PAGES

Could We Discontinue All Asthma Medications in a Third of Adult Asthmatics?

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Practice Options from Beyond Our Pages focuses on identifying, critiquing, and placing into context research studies published in other journals that have the potential to change our clinical practices. It is written by Allergy-Immunology Fellows partnered with faculty members, and does not require an invitation for submission. This feature is coordinated by Editorial Board members Matthew Rank, MD and Julie Wang, MD.

REFERENCE

Aaron SD, Vandemheen KL, FitzGerald JM, Ainslie M, Gupta S, Lemi re C, et al, for the Canadian Respiratory Research Network. Reevaluation of diagnosis in adults with physician-diagnosed asthma. *JAMA* 2017;317:269-79.

BACKGROUND

Asthma guidelines recommend diagnosing asthma via a history and objective airflow limitation. Once asthma is controlled for 3 months, it is recommended to attempt to step down controller medications. Despite this, asthma is frequently diagnosed based on symptoms, response to therapy, and physical examination alone. Asthma overdiagnosis has been found in previous studies,¹⁻³ and may expose patients to excess cost, medications, and possible harm. This prospective study was performed to determine the percentage of newly diagnosed patients with asthma (<5 years), who had asthma based on objective measurements at the time of the study.

METHODS

A total of 16,931 people were randomly contacted by telephone, surrounding the 10 largest Canadian metropolitan areas. Of them, 16,230 were excluded because of not having asthma diagnosed, being <18, contraindications to bronchial provocation challenges, long-term prednisone use, having asthma for >5 years, not completing the questionnaire, or smoking >10 pack years.

Of the remaining 701 people, 88 withdrew because of lack of follow-up, not having reproducible spirometry, or being deemed unsafe for methacholine challenge. Therefore, 613 participants were reported.

At visit 1, participants completed the Asthma Quality of Life Questionnaire (AQLQ) and underwent pre- and post-albuterol (short-acting bronchodilator, 400 µg) spirometry. Asthma was

confirmed if patients met American Thoracic Society criteria, of forced expiratory volume in 1 second (FEV1) increasing by 12% and 200 mL after SABA. If not reversible, patients proceeded to the second visit for the bronchial provocation challenge using methacholine.

At visit 2, participants with a 20% decrease in their FEV1, with a concentration of ≤8 mg/mL of methacholine, were diagnosed with asthma. Participants with a nondiagnostic challenge were instructed to decrease their controller dosage by half or stop anti-leukotriene medications. At visit 3, they underwent a repeat methacholine challenge. If normal, then all controller medications were stopped, and at visit 4, a final challenge was performed. If still nondiagnostic while on no medications, participants were deemed not to have asthma. Participants were then referred to a pulmonologist, to determine an alternative diagnosis for their respiratory symptoms. Two independent pulmonologists reviewed those decisions. Patients who had no evidence of asthma were then monitored for the next 12 months, while on no controller medications. Methacholine challenges were then performed at 6 and 12 months to rule out asthma.

RESULTS

Thirty-three percent of the enrolled participants (203/613) had asthma ruled out. At the end of the study, 231 had negative methacholine challenges, while off all controller medications. Subsequently, 28 of these participants were confirmed to have asthma in the 12-month follow-up period.

Using multivariate logistic regression analysis, characteristics that differentiated asthmatics from nonasthmatics were established. Wheezing, chest tightness, dyspnea, lower forced vital capacity and FEV1 on spirometry, and lower total and component AQLQ scores were found to be noted more often in patients with asthma.

Those who had asthma were more likely to have had spirometry performed (55.6%) than those who had asthma ruled out (43.8%; absolute difference, 11.8%; 95% confidence interval, 2.1% to 21.5%).

The main alternative diagnoses, after asthma exclusion, are listed in Table I. Note that 12 participants (2%) had serious cardiopulmonary conditions, which required intervention.

Of the 22 patients who were diagnosed with asthma during the 12-month follow-up, 16 were asymptomatic and 6 had symptoms requiring asthma treatment including 1 patient who

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TABLE I. Alternative diagnoses to asthma

Pulmonologist diagnosis	No. of participants
Asymptomatic w/o medications	61
Nose/sinus	
Allergic/nonallergic rhinitis	54
Gastrointestinal	
GERD	18
Psychiatric	
Anxiety	8
Deconditioning	
Obesity	7
Serious potentially life-threatening diagnoses	
Cardiovascular	
Ischemic heart disease	4
Pulmonary hypertension	1
Airway/pulmonary	
Bronchiectasis	2
Subglottic stenosis	2
Sarcoidosis	1
Interstitial lung disease	1
Tracheobronchomalacia	1

GERD, Gastroesophageal reflux disease.

needed oral steroids. Therefore, only 7 of 613 (1.1%) had worsening of asthma during this diagnostic evaluation.

CRITICAL APPRAISAL

This study's strengths include employing a prospective design, recruiting a large number of potential participants, from a representative pool of the population, who underwent objective measures of asthma with expert review, and employed appropriate intervals for follow-up visits.

A major limitation is the exclusion of asthmatics diagnosed more than 5 years before the study inception. The study authors use this rationale to "evaluate contemporary diagnostic practices." Studies on the natural history of asthma found that asthma remission may occur in the second decade of life, but is highly unusual in patients between the ages of 30 and 60.¹ Patients in this age range make up a large group of current asthmatics, and were likely diagnosed more than 5 years before this study, making them ineligible for consideration. Although this study's findings are applicable to newly diagnosed asthmatics, it cannot draw the conclusion that 33% of total asthmatics in the USA or Canada are misdiagnosed. Furthermore, many patients in the 18 to 29 age range may have relapsing-remitting disease, such that they may not have had objective findings of asthma during the time the patients were evaluated and followed.

Other limitations include that participants were likely to have less severe asthma, as several steroid dependent asthmatics were

excluded. Candidates who declined participation may have done so because of the severity of their asthma. Thus the actual percentage of misdiagnosed asthma could be lower than the quoted 33%. Conversely, relying on the provocation challenge, with a specificity of 80%, could have led to overdiagnosis of asthma that would decrease the number of patients found to be asthma free. A follow-up period longer than 12 months would increase confidence in the findings, as asthma is an episodic disorder, shown by 22 patients being reclassified as asthmatic in the follow-up.

This is the first prospective study concerning asthma over-diagnosis. Previous retrospective studies have been performed. An analysis, of children aged 6 to 18, done in 4 academic primary health care centers in the Netherlands found that only 16% were diagnosed with asthma via spirometry. By the record review, it was estimated that 53% were misdiagnosed.² Another retrospective study looked at patients >15 years old, referred to an allergy clinic, with a possible diagnoses of asthma with normal spirometry. Only 49% of patients had a positive methacholine challenge test.³ The current study is consistent with these past studies using more rigorous evaluation methods.

RECOMMENDATION

This study shows that asthma should be diagnosed using objective measures of airflow limitation or bronchial hyper-responsiveness. Clinicians should not rely on symptoms alone as asthma rescue inhalers have been shown to have a strong placebo effect.⁴ Patients with nonreversible spirometry should have it repeated or referred for bronchial challenge testing. Patients who have stable asthma for a 3-month period, especially those who were initially diagnosed without using objective measures, should have their asthma controller medications tapered. This study likely overestimates the percentage of misdiagnosed asthma, but does show that asthma medications could be safely stopped in a significant percentage of current patients. However, in a more general asthma population encountered in clinical practice, that proportion is likely to be less than the 33% quoted. This is due to the fact that many patients will have been diagnosed with asthma for >5 years, and will have more severe asthma than those included in this study.

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