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# Sex differences in asthma symptom profiles and control in the American Lung Association Asthma Clinical Research Centers☆

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*Abbreviations:* ACQ, Asthma Control Questionnaire; ALA-ACRC, American Lung Association Asthma Clinical Research Centers; ASUI, Asthma Symptom Utility Index; ATAQ, Asthma Therapy Assessment Questionnaire; BMI, body mass index; $FEV_1$, forced expiratory volume in one second; GERD, gastroesophageal reflux disease; LOCCS, leukotriene or corticosteroid or corticosteroid–salmeterol trial; LODO, Effectiveness of Low Dose Theophylline as Add-On Therapy In Treatment of Asthma; MID, minimal clinically important difference; mini-AQLQ, mini asthma quality of life questionnaire; $PC_{20}$, provocative concentration of methacholine; QOL, quality of life; SABA, short-acting beta-agonist; SARA, Study of Acid Reflux and Asthma; TAPE, Trial of Asthma Patient Education.

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**Summary**
*Objective:* Important differences between men and women with asthma have been demonstrated, with women describing more symptoms and worse asthma-related quality of life (QOL) despite having similar or better pulmonary function. While current guidelines focus heavily on assessing asthma control, they lack information about whether sex-specific approaches to asthma assessment should be considered. We sought to determine if sex differences in asthma control or symptom profiles exist in the well-characterized population of participants in the American Lung Association Asthma Clinical Research Centers (ALA-ACRC) trials.
*Methods:* We reviewed baseline data from four trials published by the ALA-ACRC to evaluate individual item responses to three standardized asthma questionnaires: the Juniper Asthma Control Questionnaire (ACQ), the multi-attribute Asthma Symptom Utility Index (ASUI), and Juniper Mini Asthma Quality of Life Questionnaire (mini-AQLQ).
*Results:* In the poorly-controlled population, women reported similar overall asthma control (mean ACQ 1.9 vs. 1.8; $p = 0.54$), but were more likely to report specific symptoms such as nocturnal awakenings, activity limitations, and shortness of breath on individual item responses. Women reported worse asthma-related QOL on the mini-AQLQ (mean 4.5 vs. 4.9; $p < 0.001$) and more asthma-related symptoms with a lower mean score on the ASUI (0.73 vs. 0.77; $p \leq 0.0001$) and were more likely to report feeling bothered by particular symptoms such as coughing, or environmental triggers.
*Conclusions:* In participants with poorly-controlled asthma, women had outwardly similar asthma control, but had unique symptom profiles on detailed item analyses which were evident on evaluation of three standardized asthma questionnaires.


## Introduction

Population studies reveal sex-related differences in asthma that change with age. In children and early adolescents, asthma is more common in boys [1–3]. After puberty, asthma becomes more common and more severe in women. Women with asthma describe more symptoms and worse quality of life (QOL) than men despite having comparable or better pulmonary function [4–7]. Similarly, women with asthma report greater healthcare utilization [4–6] and more frequent use of short-acting beta-agonists (SABA) [5–7] than men. While the reasons for these observed sex-related differences in asthma morbidity and disease expression have not been fully explained, differences in perception of airflow obstruction [5,8], increased bronchial hyperresponsiveness in women as a result of increased susceptibility to tobacco smoke [9,10], and hormonal influences [11–13] have all been proposed as potential hypotheses.

Sex-specific treatment approaches to asthma care have been developed, and have shown benefit to women when compared to standard nonspecific approaches [14,15]. Despite these findings, current asthma guidelines [16] lack information about whether sex-specific approaches to asthma assessment should be considered. Using detailed evaluation of previously validated questionnaires, we sought to determine if sex differences in asthma control or symptom profiles exist in the population of participants in the American Lung Association Asthma Clinical Research Centers (ALA-ACRC) trials, supporting the need for sex-specific approaches to asthma assessment. Some of the results have been reported previously in the form of an abstract [17]. By examining commonly utilized questionnaires in this manner, the ALA-ACRC data offer a unique approach to the evaluation of the potential influence of sex on the assessment of asthma morbidity and quality of life, and take advantage of a large well-characterized population of participants.

## Methods

### Study design and participants

The ALA-ACRC is a multi-center network of 20 centers dedicated to improving asthma care through clinical