

# Epidemiology and Pulmonary Physiology of Severe Asthma



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## KEYWORDS

- Demographics • Phenotype • Health care utilization • Pulmonary function
- Lung elastic recoil • Ventilation heterogeneity • Gas trapping
- Airway hyperresponsiveness

## KEY POINTS

- The definition of severe asthma is still a work in progress.
- The severity of asthma is predictive of higher health care utilization.
- Cluster analysis is useful in characterizing severe asthma phenotypes.
- Airway hyperresponsiveness in severe asthma is a result of abnormal airflow, lung recoil, ventilation, and gas trapping.
- Patients with severe asthma may have a reduced perception of dyspnea.

## INTRODUCTION

Severe asthma is characterized by a complex set of clinical, demographic, and physiologic features. In this article, we review both the epidemiology and pulmonary physiology associated with severe asthma.

## DEMOGRAPHICS OF SEVERE ASTHMA

Asthma has long been recognized as a worldwide noncommunicable disease of importance. Within the population of individuals with asthma, there is a subgroup of individuals at high risk for complications, exacerbations, and a poor quality of life.

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These individuals are classified with severe asthma and they account for 5% to 15% of individuals with asthma in the United States and the world.<sup>1,2</sup> Severe asthma, as defined by the American Thoracic Society and European Respiratory Society (ATS/ERS) clinical practice guidelines, is asthma requiring treatment with high-dose inhaled corticosteroids (ICS) and a second controller during the prior year, and/or oral steroids for at least half of the prior year to prevent symptoms from becoming uncontrolled.<sup>1</sup> Severe asthma also can be described as uncontrolled despite reliance on ICS or frequent oral steroid use.<sup>3</sup> Most of these population numbers are based on questionnaires investigating reported symptoms, particularly the presence of wheezing to assess global asthma burden. Wheezing notoriously overdiagnoses asthma, so may create a slightly higher prevalence than the population truly represents. According to information from the Centers for Disease Control and Prevention (CDC) and Environmental Protection Agency, in 2011, there were 25.9 million individuals in the United States, including 7.1 million children, diagnosed with asthma.<sup>4</sup> In a similar effort in 2013, the CDC found asthma prevalence of 7.3% in America with 8.3% prevalence in children and 7% prevalence in adults. In the black population in the United States there was an almost 50% increase in asthma diagnoses over the past 10 years. Epidemiologic research is ongoing to investigate environmental and social influences on race patterns in asthma prevalence.<sup>5</sup> Evidence also shows that although poverty level does not significantly affect the frequency of asthma attacks among children, adults with incomes less than 250% of the federal poverty level were more likely to report asthma attacks than those with incomes over 450% of the poverty level.<sup>6</sup> Asthma also accounts for a significant number of deaths both in the United States and worldwide. In 2007 alone, there were 3447 deaths in the United States attributed to asthma.<sup>7</sup> Data collected in 2010 as part of the National Hospital Ambulatory Medical Care Survey identified asthma exacerbations as the primary visit diagnosis for more than 15 million office visits and outpatient medical center visits along with 2 million emergency department (ED) visits.<sup>8</sup>

In The Epidemiology and Natural history of asthma: Outcomes and treatment Regimens (TENOR) cohort of patients with severe asthma, gender was distributed differently between older and younger populations.<sup>9</sup> For the adult patients, 71% were women compared with 43% of adolescents and 34% of children. This is similar to the findings of Zein and colleagues,<sup>2</sup> who observed that after adolescence there is a shift from male-predominant severe asthma to female.

## COHORT CHARACTERISTICS OF SEVERE ASTHMA

Over the past 20 years, there have been large cohorts constructed to observe trends in therapies and patient outcomes related to asthma. These were created to better understand high-risk individuals and what traits may contribute to more severe asthma or difficult to control asthma. The 2 largest studies in the United States are the previously mentioned TENOR cohort,<sup>9</sup> and the Severe Asthma Research Program (SARP).<sup>10</sup> In both studies, most patients were enrolled by specialists rather than by identifying asthma based on questionnaires completed by the patient.

The TENOR cohort demonstrated that the presence of a recent exacerbation within 3 months of introduction to the study was the strongest predictor of future asthma exacerbation in individuals older than 12.<sup>9</sup> This remained high when adjusted for patient demographics. Recent exacerbation was defined as an ED visit or overnight hospitalization. Increased risk also remained significant if patients required oral corticosteroids in the 3 months preceding baseline evaluation (**Box 1**). Other factors suggesting high risk included prior pneumonia, intubation, and postbronchodilator

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