

# All-Cause Mortality in Asthma

## The Importance of Age, Comorbidity, and Socioeconomic Status

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Most studies investigating the increased health burden suffered by patients with asthma investigate health care use events or deaths specifically resulting from asthma exacerbations. In this issue of *AnnalsATS*, To and colleagues (pp. 1210–1217) employed a more comprehensive approach (1). To understand the full contribution of asthma to risk of death over time in a patient population, the authors contend we must not only measure asthma-specific mortality but also look at all-cause mortality among patients with asthma. The authors used an unusual opportunity to investigate this question, given that their home province of Ontario in Canada has a well-documented universal single-payer health care system that covers all physician and hospital services.

The authors found that although all-cause and asthma-specific mortality decreased in their province from 1999 to 2008, the all-cause mortality rate stayed consistently higher in the population with asthma than in the general population. This suggests that in the general population of Ontario, patients with asthma are dying earlier from nonasthma causes than patients who do not have asthma. That patients with asthma are dying from other causes is not surprising, as the overall asthma-specific mortality rate is relatively low compared with that of other chronic diseases. However, the finding that patients with asthma are dying at higher rates than the general population deserves thoughtful consideration. It is also conceivable that in many cases, asthma may be an insidious direct or indirect contributor to death

that may not be indicated on death certificates, in which case the estimates provided by To and colleagues are likely conservative.

It has previously been shown that asthma mortality rates increase with advancing age (2). There may be several reasons for this observation: Adult-onset asthma tends to be more severe on average than asthma that first manifests at an early age (3), and patients with asthma tend to develop cardiovascular disease, chronic obstructive pulmonary disease (COPD), and other important comorbid conditions as they age. Indeed, the importance of comorbid diseases has been an area of recent interest with regard to heightened risk for mortality (4) and poor health outcomes (5, 6) in patients with COPD, but it has been less comprehensively studied in populations with asthma. The report by To and colleagues highlights the importance of further investigation in this area.

A particularly interesting phenotype is the asthma/COPD overlap syndrome. It is also possible that some patients with COPD are misclassified as having asthma, but it has been shown that those who have a codiagnosis of asthma and COPD have greater risk for exacerbations and hospitalizations than if they have either diagnosis alone (7, 8). As a matter of fact, in the current study, the highest mortality rate ratio between the asthma and general population was for COPD-specific mortality, suggesting a codiagnosis of COPD as a partial explanation for some of the increased risk for death observed.

The results of this article highlight the importance of better understanding this subgroup of people with heightened risk for poor outcomes and the characteristics that may put them at risk, whether extrinsic (indoor or outdoor pollutants, smoking or secondhand smoke exposure, occupational exposures), intrinsic (inflammatory or immunologic abnormalities or a robust allergic immune response), or a combination.

The authors report that although all-cause mortality in the population with asthma has declined across all age groups for men, mortality rates for women have not shown a similar decline (overall mortality rate for women increased from 766.1 per 100,000 in 1999 to 769.4 per 100,000 in 2008). This disparity is greater in people younger than 60 years, as seen in the 20–39-year age group, which experienced a slight rise in mortality rates during this period (61.4 per 100,000 in 1999 compared with 63.7 in 2008). Although the analysis by To and colleagues does not suggest a clear etiology for this sex disparity, it is consistent with data from the Centers for Disease Control and Prevention showing that all-cause mortality (without regard for asthma) has declined faster in men compared with in women, leading to a decline in the male-to-female ratio of deaths since the early 1980s (9).

Particularly interesting findings are the observed higher mortality rate for patients with asthma who have a lower socioeconomic status and the lack of decrease in all-cause mortality over time among those with lower socioeconomic status. A possible reason is that progress

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in asthma treatment has reduced overall mortality rates but may not be equally accessible to those with the lowest socioeconomic status. Further, there may be underlying factors or exposures such as smoking, pollution exposure, and poor dietary patterns, which often cluster in populations with lower socioeconomic status (10, 11) and predispose individuals to asthma as well as other conditions that subsequently lead to increased risk for death.

In addition, it is recognized that African Americans suffer higher asthma prevalence as well as higher asthma mortality rates than whites (11, 12). Often it is difficult to untangle the contribution of race or socioeconomic status to health outcomes. Whether racial health disparities

are contributing to some of the observed differences in all-cause mortality remains unclear in the current analysis. Furthermore, as smoking has been linked to the development of asthma and is associated with the development of other chronic conditions, such as COPD, heart disease, cancer, and obesity, understanding the differences in smoking patterns by race and socioeconomic status may shed insight on the observed differences in mortality rates.

Last, we note that the case definition of asthma used by To and coworkers, requiring either two outpatient health care encounters in two consecutive years or one hospitalization for asthma, likely preselects patients with asthma who are requiring health care visits for their

asthma and perhaps excludes those with milder disease and lower mortality rates.

Despite some of the inherent limitations of the current study, To and coworkers illustrate that patients with asthma have higher all-cause mortality than people in the general population of Ontario and that individuals with lower socioeconomic status continue to be at increased risk. A better understanding of the factors that lead to this increased mortality risk is needed, and incorporation of all-cause mortality as an outcome in future asthma studies should be considered. ■

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