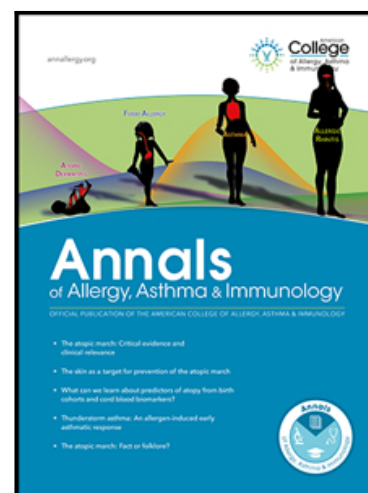


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Seasonal and Regional Variation of Asthma-related Hospitalizations and Mortality among adults in the United States

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Asthma morbidity and mortality is known to exhibit seasonal trends and periodicity. Prior studies done in the US and other countries have suggested seasonal variations in asthma hospitalization but report conflicting results. While most studies note a peak in winter¹⁻³, various trends have been noted in different age categories and regions¹⁻⁵.

We utilized the Nationwide Inpatient Sample (NIS) database to study the seasonal and regional variation of asthma-related hospitalizations among adults in the US. NIS is the largest inpatient database in the

USA sponsored by the Agency for Healthcare Research and Quality⁶. Approximately 8-9 million hospitalizations are sampled each year which, when weighted, represents >35 million hospitalizations annually⁶. International Classification of Diseases ninth revision, Clinical Modification codes (ICD 9-CM) 493.00-493.92 were used to identify all patients discharged with asthma in the first three diagnosis positions between 1 January 2009 and 31 December 2011. Monthly distribution of admission and mortality were stratified per age groups (18-34, 35-64 and ≥65 years) and regions (Northeast, Midwest, West and South). Seasons were classified based on meteorological classification of Northern Hemisphere seasons: Spring (March-May), Summer (June-August), Fall (Sept-Nov), Winter (Dec-Feb). Edwards recognition with estimation of cyclic trend method and Z-test were used to compare the seasonal trend (peak-to-low ratio)⁷. Statistical analysis was conducted using STATA version 13.0 (College Station, TX, USA).

Asthma accounted for a total of 466,256 hospitalizations (weighted= 2,319,799) between 2009-2011. Peak in overall asthma-related hospitalizations were observed during the month of February (peak/low 1.22, 95% CI 1.21-1.22) (Figure 1A and B).

The highest number of hospitalizations were observed in winter months and lowest in summer (8.95 % vs. 6.95 %, $p < 0.001$). Majority of patients receiving care for asthma were in southern region (33.92%), with proportion of admissions from the rest of the regions as: Northeast- 26.20%, Midwest- 22.67%, and West-17.21%. In sub group analysis, this seasonal trend held true even when the hospitalizations were stratified based on regions and age groups. Highest number of hospitalizations were among the age group 35-64 years ($n=1,193,370$), followed by ≥65 years ($n=637,918$) and 18-34 years ($n=488,510$), with peak admissions in the months of January, February and December respectively.

Peak in overall asthma-related mortality was also observed during the month of February (peak/low 1.56, 95% CI 1.46-1.66). However, results varied when stratified based on age groups. For age group 18-34 years ($n=213$), peak in asthma-related mortality was in Nov (Fall) (Peak/low ratio 1.34, 95% CI 1.00-1.98), 35-64 years ($n=2573$) in March (Spring) (peak/low ratio 1.55, 95% CI 1.38-1.74) and ≥65 years ($n=5961$) in February (Winter) (peak/low ratio 1.33, 95% CI 1.24-1.43).

We observed a significant seasonal variation in asthma-related hospitalizations, which is in line with previous studies. Prior studies from UK, Spain, Canada, Malta and USA have demonstrated a winter/fall predominance of asthma hospitalization and mortality^{1,2,5}. Although our study also found a higher incidence of asthma exacerbation requiring hospitalization during winter months, there was a significant discrepancy in mortality peaks across different age groups. For older patient population, winter was the season for highest hospitalization and mortality of disease, whereas; for younger adults, highest mortality was observed in spring/fall. Although higher asthma related hospitalizations were observed in the age group of 35-64 years as compared to other age groups, highest mortality was observed in the elder population. This study also supports the hypothesis of asthma disease process not varying according to different regions of the country, but mostly depending on the seasonality of the regions. Hence, a relative change in seasonal conditions might play a bigger role than absolute weather conditions itself.

The exact cause of seasonality in asthma is not clearly understood with previous reports suggesting multiple hypotheses. Effect of aero allergens, aggressive environmental triggers may have higher impact on younger individuals causing exacerbations during spring/fall¹. While no reliable relationship to pollen counts affecting the disease severity during spring/fall has been established, other climatic changes may

still play a role. Cold-induced activation of sympathetic nervous system in experimental studies associated with sympathetic surge causing increased cardiovascular events and further exacerbating once stable asthma may account for exacerbations seen in winter for the elderly population⁸. Viral infections, such as rhino virus and influenza being higher in fall/winter has been regarded as another important factor and a significant association have been described between these and incidence of asthma hospitalizations^{5, 9-10}. A more potent effect of these infections in the elderly verses the younger population might as well be responsible for the differences in trends seen.

Acknowledging the seasonal variability in hospitalization and mortality has a great potential to improve the quality of care and patient outcomes in asthma management. Discrepancy in mortality across ages might relate to different triggers and mechanisms associated with exacerbations for different age groups. A better understanding of these trends and determinants of variations may aid in formulating necessary measures for improving the quality of life of asthmatic patients and at the same time decreasing economic burden to our health care system.

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Figure 1A and B. Seasonal variation of asthma-related hospitalizations and mortality in US.

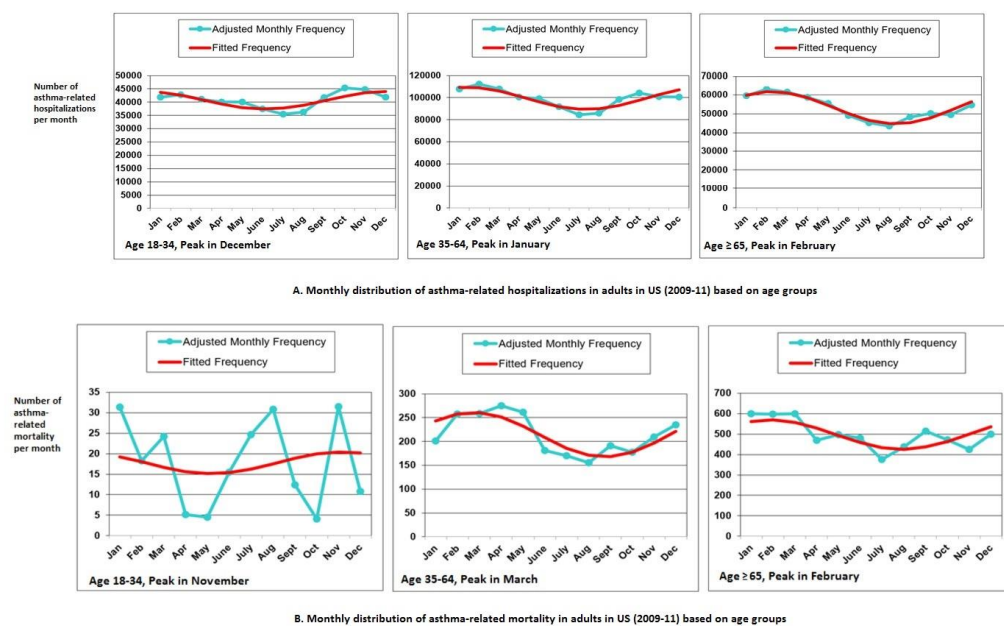


Figure 1A and B. Seasonal variation of asthma-related hospitalizations and mortality in US.