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Asthma over the age of 65: All's Well That Ends Well

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Abstract

Asthma in older adults (often classified as those ≥ 65 years of age) is relatively common, underdiagnosed, and sub-optimally treated. It is an important health problem, as the population of the United States continues to age. Unfortunately, asthma morbidity and mortality rates are highest in this age group. Alterations of the innate and adaptive immune responses occur with aging, and contribute to pathophysiologic differences and subsequent treatment challenges. The symptoms of asthma may differ from younger populations, and often include fatigue. There are unique factors that can complicate asthma management among older adults, including comorbidities, menopause, care giver roles, and depression. Pharmacologic therapies are often not as effective as in younger populations, and may have greater side effects. Spirometry, peak flow measurements, and asthma education are typically underutilized, and may contribute to delays in diagnosis as well as worse outcomes. There are specific strategies that health care providers can take to improve the care of older adults with asthma.

Keywords

Asthma; Older Adults; Elderly; Spirometry; Immunosenescence; Depression; Menopause; Education; Asthma COPD Overlap Syndrome (ACOS)

Introduction

To many, there is the belief that asthma occurs in childhood and resolves over time. However, studies show that a significant number of people first develop asthma at a relatively older age, and that it can persist throughout the lifespan. Understanding asthma in older adults is critical to health care providers and researchers, as the number of those above age 65 in the United States is projected to increase to 85 million individuals by the year 2045, a 77% increase since 2015 (Figure 1).¹ Additionally, by 2030, the percent of older adults will increase to 20% of the total population, and therefore those who manage adult

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asthma will likely have many patients above the age of 65. This review covers unique features of asthma in older adults, discusses challenges of diagnostic and management strategies, and highlights areas where further research is needed to address knowledge gaps.

Epidemiology

Accurate data on the prevalence of asthma in older adults can be difficult to obtain. In part, this is due to the fact that many asthma trials specifically exclude individuals above the age of 65. Additionally, in the older adult with respiratory symptoms, often times those with a minimal, remote, or even nonexistent smoking history are misdiagnosed as having COPD rather than asthma,^{2, 3} even though data suggests that approximately 20 pack years are typically required to develop COPD.⁴ A 2015 Centers for Disease Control and Prevention (CDC) survey found that among adults, the prevalence of asthma is highest in those age 45 – 64 years, with 8.4% having a current diagnosis of asthma.⁵ This was the same prevalence as the overall rate for children age 0 – 18. Therefore, asthma remains a common chronic disease across all ages.

Results of the CDC Asthma Call Back Survey (~900,000 individuals) did find that the assumption of asthma typically beginning in childhood is often, but not always, true.⁶ Among all children, asthma incidence was 12.5 per 1000. However, new cases of asthma occurred frequently at any age. In adults over the age of 18 years of age, the greatest incidence rate was in those age 55 – 64 years (4.6 per 1000). In those above the age of 65, the incidence rate was 3.1 per 1000. More recently, Baptist et al. reported in a study in the *Journal* that found that among 180 persistent asthma patients over the age of 55, 46% were diagnosed after the age of 40.⁷ Taken together, these data indicate that asthma is common in those above 65, and that many cases begin later in life.

There appear to be clinical differences between those who develop asthma in childhood, adolescence, or young adult-hood (termed “long standing asthma”, or LSA) and those who develop asthma after the age of 40 (termed “late onset asthma”, or LOA). Those with LOA are more likely to have frequent symptoms, less atopy, and a decreased response to standard inhaled corticosteroids and beta agonists,^{8, 9} though some authors have suggested those with LSA may in fact have worsened outcomes.¹⁰ Recent cluster analyses of older adults has been published, and will help to clarify these issues as well as identify specific phenotypes that may respond preferentially to one treatment over another.^{7, 11}

What does seem clear is that older adults have some of the highest asthma morbidity and mortality rates. For example, as shown in Figure 2, the mortality rate from asthma steadily increases with age. Additionally, studies of severe asthma have shown that older adults may have a more difficult-to-control phenotype than younger populations, with decreased responsiveness to standard medications.^{7, 12, 13} Of those presenting to the emergency department for asthma, adults 65 years have the highest rate who subsequently require hospitalization (approximately 25% admission rate compared to 7.9% for all ages) and longest length of stay.¹⁴ It is important to note that asthma is frequently underdiagnosed, and therefore these numbers may be underestimations.

Immunosenescence

With increasing age, there are alterations in both the innate and adaptive immune responses which likely impact the pathology, and consequently the treatment, of asthma in older adults. Two distinct alterations of aging on the innate and adaptive immune responses have been described and can occur simultaneously. One, “immunosenescence,” is a “blunted” response after a pathogenic threat or tissue injury. However, despite an inability to proliferate, some senescent cells remain alive, functioning at an altered capacity. This results in the second process, “inflammaging,” an increased low-grade basal systemic inflammation (e.g., IL1- β , IL-6 and TNF- α) in the absence of an overt infection.¹⁵ The mechanisms of immunosenescence and inflammaging are the consequence of both “random” (e.g., environmental exposures, accumulation of reactive oxygen species [ROS] from metabolic activity, mutagenesis) and “regulated” (e.g., genetic) events.¹⁶

The possible impacts of immunosenescence and inflammaging on asthma are briefly outlined in Figure 3. Collectively, alterations in innate and adaptive cells likely have several clinical implications including decreasing the response to vaccinations and increasing rates of infections, which in turn may exacerbate asthma, or play a role in the inception of LOA.¹⁷ Furthermore, older patients with asthma may have altered airway and systemic inflammation (i.e. higher neutrophils with increased IL-6, IL-8, C-reactive protein) resembling changes seen in a phenotype of severe asthma in younger patients which is often less responsive to corticosteroid treatment.^{18–20}

Symptoms and Diagnosis

Many of the asthma symptoms common in younger patients (e.g., intermittent chest tightness, nocturnal wheezing and dyspnea) are present in older patients. However, there are important considerations. Older adults frequently note fatigue as a principal symptom, even in the absence of typical asthma manifestations.²¹ Dyspnea is commonly associated with other chronic disorders in older patients (e.g., heart failure, other lung diseases, anemia), therefore asthma as the cause of these symptoms may be overlooked. Furthermore, some older patients may limit their activity to avoid becoming dyspneic, or attribute it to aging itself. Older adults may have a decreased perception of dyspnea even with significant airflow obstruction.^{22, 23} As smoking can induce symptoms of wheeze, cough and sputum production, asthma may be confused with COPD. Prominent gastroesophageal reflux disease (GERD) may present with a chronic cough, hoarseness and wheezing, and therefore needs to be considered in the differential diagnosis of asthma.²⁴

The same objective measures used to diagnose asthma in younger patients are employed in older patients. However, similar to symptoms of asthma in this group, there are age-related factors which must be considered. First, the FEV₁/FVC ratio decreases with aging, and therefore it is essential to use age-adjusted values.^{25, 26} Second, with aging, bronchial hyperresponsiveness (BHR) to methacholine increases;^{27–29} therefore, provocation testing may be less accurate in this age group. Bronchoprovocation challenges may be contraindicated in some older patients with low baseline lung function or cardiac comorbidities. Third, spirometry involves effort dependent maneuvers. Over 80% of older

persons can achieve ATS acceptable results; however, it may be difficult for those who are frail.^{30–36} Poor coordination and muscle weakness in some patients may produce inaccurate readings of peak expiratory flow.^{37, 38} Unfortunately, objective measures of lung function such as spirometry and peak flow measurements are generally underutilized in older patients and contribute to the delay in diagnosis.³⁴

Other tests such as the carbon monoxide diffusing capacity of the lung (DLCO) may help distinguish between asthma and COPD. Chest Computed Tomography (CT) may demonstrate increased wall thickness, and increased air-trapping in older asthmatic patients.³⁹ The use of exhaled nitric oxide (eNO) in older patients is not completely established, and aging itself can increase eNO.^{40, 41} Some studies using eNO as a marker for asthma diagnosis and a measure of control in older patients have shown it to be beneficial,^{42–46} whereas others have not.⁴⁷

Unique factors that can complicate asthma management among older adults – and strategies to address them

Comorbidities

In recent years, there has been a significant increase in the literature demonstrating that comorbidities significantly influence asthma management and control. A 2016 meta-analysis of 11 studies involving 460,000 patients found that asthma patients were more likely to have cardiovascular disease (odds ratio (OR) = 1.9), obesity (OR = 1.51), gut or urinary comorbidities (OR = 1.62), and hypertension (OR = 1.91) compared to those without asthma ($p < 0.0001$ for all comparisons listed).⁴⁸ The National Health and Nutrition Examination Survey (NHANES) revealed that adult asthma patients with comorbidities were more likely to have asthma symptoms, activity limitations, and emergency department visits for asthma compared to asthma patients without comorbidities.⁴⁹ Data specifically looking at adults 65 years has confirmed that in this age group, comorbidities are directly related to asthma hospitalizations and emergency department visits.⁵⁰ As people age, the number of medical conditions and medications to manage these conditions increase. Therefore, the negative impact of comorbidities and asthma management has a greater impact on older adults.

In older adults, comorbidities can impact asthma management in a number of ways. There can be interactions between conditions, similar symptom presentation of asthma and comorbidities, decreased adherence with multiple medications, and conflicting recommendations on care from numerous specialists.⁵¹ In a qualitative study, older adults with asthma and cardiac disease describe having been instructed by their physician to try medications for both conditions simultaneously and/or sequentially during episodes of dyspnea.²¹ Additionally, in patients with multiple comorbidities, asthma may take a ‘back seat’ during a primary care office visit, and be sub-optimally addressed.

To improve the care of older adults with asthma, clinicians should identify, acknowledge, and address comorbidities where appropriate. A recent study by Tay et. al in the *Journal* found that asthma outcomes improved when asthma specialists identified and subsequently treated or referred patients for specific comorbidities (e.g. GERD, sleep apnea, or obesity).⁵²

Additionally, emphasizing to a patient that suboptimal asthma control can make exercise and weight loss problematic may impress upon some the importance of regular asthma care. With improved control, it may be possible for the older adult to reduce the burden of other conditions such as cardiac disease, diabetes, and obesity.

Treatment of co-morbid allergic rhinitis with nasal corticosteroids is a relatively safe approach in older adults, and may be an option to improve asthma control without stepping up controller therapy.⁵³ Specific immunotherapy improves allergic rhinitis in older patients, but risks including anaphylaxis and the use of epinephrine in patients with significant cardiac disease must be considered.⁵⁴ Sublingual immunotherapy has a lower incidence of serious adverse effects and may be an attractive alternative in older adults, though currently most formulations are approved only to the age 65.

Depression

While depression is an asthma comorbidity, it deserves additional mention due to recent literature showing its negative effects on elderly asthmatic patients. Depression is relatively common in adults above the age of 65, affecting up to 20% of older adults in Western countries.⁵⁵ A recent article in the *Journal* demonstrated that older adults with asthma and depression were nearly twice as likely to have poor asthma outcomes across several indicators, including asthma-related ED/urgent care visits, compared with those without depression.⁵⁶ The mechanisms responsible for depression worsening asthma outcomes are not clearly established, and may relate to inflammation, cerebral anatomic changes, autonomic nervous dysfunction, decreased adherence, or ineffective self-management behaviors.⁵⁷

Small trials have shown modest benefit of pharmacotherapy and/or behavioral therapy in the treatment of adults with coexisting asthma and depression, though none were exclusively performed in an older population.^{58–61} Given the prevalence of depression among older adults, its known effects on asthma, and the potential benefit of therapy, asthma providers should consider screening patients for depression (for example, with the Geriatric Depression Scale)⁶² and treat or refer as appropriate.

Menopause and Hormone Replacement Therapy (HRT)

Several studies have documented the effects of hormones such as estrogen and progesterone on airway caliber and asthma exacerbations. A study of 2322 peri-menopausal women found the risk of new-onset asthma was 2.4–3.4 times higher compared to pre-menopausal women,⁶³ and menopause was associated with an accelerated lung function decline.⁶⁴ A separate meta-analysis reported that post-menopausal women on HRT had an increased risk of asthma compared to pre-menopausal women.⁶⁵ Conversely, in women with pre-existing asthma, HRT may improve respiratory symptoms and decrease exacerbations.⁶⁶

Menopause may also increase the number of asthma exacerbations.^{67, 68} There is a spike in exacerbations among asthmatic women that occurs at age 50,⁶⁹ the mean age of menopause in the United States. This may indicate that sex hormones have a protective effect in asthma, or that fluctuations in hormonal levels can be particularly detrimental. Asthma in women that begins after menopause is frequently severe, non-atopic, and often requires oral

corticosteroids for control.^{12, 70} The risks and benefits of HRT must be considered, and the asthma care provider is in a unique position to offer specific information to assist in making decisions about HRT.

Caregiver roles and transportation difficulties

Older adults are ever more frequently taking on greater care giving roles – whether that of a spouse with significant medical problems, a child who is living at home, or a grandchild while the parents work. Being in a stressful caregiver position has been associated with poorer self-reported health, more negative health behaviors, and greater use of health care.⁷¹ It may be beneficial to inquire and acknowledge the challenges that providing care to others entails, and to highlight that to be optimally effective in such a role requires management of one's own health – including asthma.

Transportation can also be problematic for many older adults. Loss of driving privileges can make follow-up care difficult. The asthma provider can help work with senior service agencies, case managers, or social workers to document the need for follow-up care, and may also try to schedule visits on the same day as other medical appointments.⁷²

Complementary and Alternative Medicine

The use of complementary and alternative medicine (CAM) to manage asthma symptoms is between 20 – 30%.⁷³ An analysis of over 7000 adults above the age of 55 from the Asthma Call Back Survey found that this number was even higher at 39%.⁷⁴ The most frequent modalities included breathing exercises, vitamins, and herbal therapy. Other research has shown that older adults with asthma rarely, if ever, discuss CAM with their physician.²¹ Therefore, the provider caring for the older adult with asthma should inquire about CAM usage, discuss potential risks/benefits of such therapies as compared to traditional medicine, and discuss how CAM can be used in conjunction with traditional therapies.

Financial concerns—The current rate among adults over the age of 65 living in poverty is approximately 10%, and this number is expected to rise in the upcoming years.⁷⁵ Poverty has numerous detrimental effects on health, such as the inability to afford insurance copays, increased exposure to pollution and/or environmental triggers, and increased psychological stress which worsens asthma. Patients living in poverty often feel ashamed, and few bring up the inability to pay with their provider.⁷⁶ Tangible steps that providers can use include empathetic questions on the ability to afford medications while on a fixed income, prescribing medications with the lowest copay, provision of list of financial resources, and referral to social work when appropriate.⁷⁷

Pharmacologic challenges/strategies

Much of the recommendations for asthma management in older patients is based upon therapeutic studies mostly in patients primarily <60 years of age,⁷⁸ and a recent ATS workshop report on management of asthma in the elderly specifically noted difficulties in making concrete pharmacologic recommendations.⁷⁹ There are several important challenges, both in relationship to potential age-related responses to therapies, and decreases in

cognitive and physical functioning. For example, older patients with decreased cognitive function had poorer inhaler technique.⁸⁰ To improve medication delivery and adherence, older patients can be prescribed breath-activated medication devices,⁸¹ spacers to attach to metered dose inhalers (MDI) or medications which can be delivered by nebulizer (including corticosteroids for daily controller use, although this is not currently an FDA indication for patients with asthma over 12 years of age), or an Ellipta™ DPI device.⁸² Furthermore, like treatment of other medical conditions in geriatric medicine, there are issues of polypharmacy, drug-drug interactions and cost of medications which can significantly impact optimal treatment. The following sections will address issues of rescue and controller asthma therapies in the aged.

Rescue medications

Although not recently investigated, the literature suggests that older patients may have a more pronounced bronchodilator response to anti-cholinergic compared to beta₂ agonist therapy.^{83, 84} With aging, there may be a decline in beta₂-receptor density, responsiveness and affinity.^{85, 86} Older patients may be more sensitive to adverse effects of beta₂-agonists, particularly those with unstable cardiovascular disorders.^{87, 88} Research in adults comparing albuterol to levalbuterol has demonstrated a similar rate of side effects (including headache, tremor, hyperglycemia and tachycardia), though studies in an predominantly elderly population are lacking.^{89, 90} Although more likely with oral agents, cognitive impairment, falls, symptomatic urinary outlet obstruction and closed angle glaucoma are potential risks of high doses of inhaled anti-cholinergics.⁹¹

Controller therapies

Inhaled corticosteroids (ICS) are important controller therapies in patients with persistent asthma, yet appear to be underutilized in older patients.⁹²⁻⁹⁴ There are possible reasons for their underuse in this age group, including concerns for adverse effects of higher doses and under-diagnosis of asthma in older adults. Older patients, in particular women, receiving higher dose ICS (e.g., >1000mcg/day budesonide equivalent) should be monitored closely for decreased bone mineral density and increased fracture risk.⁹⁵⁻⁹⁸ Older patients should be given an ICS with a lower bioavailability and at the lowest dose to control their disease, with consideration of step-down therapy if he/she is well controlled for at least three months. To decrease the effects of corticosteroids on bone resorption, patients should be encouraged to exercise (if possible), avoid excess alcohol intake, and use daily supplemental calcium with vitamin D. Observational studies in the elderly have suggested that ICS have a small, but significant risk of subcapsular and nuclear cataracts^{99, 100} and a small risk for developing glaucoma; however, further studies are needed.¹⁰¹

In regard to the effectiveness, data suggests that ICS therapy is less effective in older adults compared to younger age groups. Th-17 mediated asthma, marked by neutrophilic inflammation, has been recognized to be less responsive to ICS therapy, and is likely more common among older asthmatics.¹⁰² Additionally, some older patients with asthma may have a component of fixed airway obstruction.¹⁰³ A large, retrospective review of 10 landmark asthma trials in patients with mild-moderate disease on ICS therapy, found an age-related increase in treatment failures.¹⁰⁴ In this analysis, the number of patients receiving

inhaled corticosteroids was significantly higher than all other therapies suggesting that it may have been underpowered to detect a similarly increased failures with other controller medications.

Despite these findings, ICS use reduces hospital admissions and mortality in older adults,¹⁰⁵ but similar to younger patients with asthma, there are likely specific disease phenotypes which responds better to corticosteroid therapy. The use of ultra-fine particle ICS medications may be beneficial in older asthmatics, who are reported to have more small airway involvement,¹⁰⁶ but this has not been formally evaluated. Despite this data, ICS therapy is still currently the preferred medication for older patients with persistent disease.

The safety of long acting beta-agonist (LABA) use in older patients, particular those with underlying cardiovascular disease, has been most studied in COPD. Studies specifically focused on the safety of this class of drugs in the elderly asthma patients are lacking; however, the boxed warning for use of LABAs as monotherapy applies to all patients with asthma. A recent large FDA-mandated study demonstrated the safety of LABAs as add-on therapy in asthma, and included 11% of individuals ≥ 64 years. While no increased evidence of adverse events was found in older adults, the study was not adequately powered for that subpopulation.¹⁰⁷ Long acting muscarinic antagonists have been shown to be efficacious as add-on therapy in asthmatics up to age 75 years.^{108, 109} Their use in older patients with asthma requires further study, particularly if this age group has a preferential bronchodilator response to anti-cholinergics.

The use of oral controller asthma therapies for older patients is attractive in that it would likely increase compliance due to its ease of use. There are a few studies examining the efficacy of leukotriene receptor antagonists (LTRAs) in older patients. Although significant improvement in asthma indices was observed in older patients receiving LTRAs, it was less pronounced than in younger patients¹¹⁰ and in older patients treated with ICS therapy.^{111, 112} The use of methylxanthines (e.g. theophylline) in older adults, is limited by its relatively weak bronchodilator properties, along with its many side effects and drug interactions.¹¹³

Injectable biologics offer a potentially easier administration and effective medication for older patients with asthma. Most studies of anti-IgE (omalizumab) treatment in older patients with asthma have demonstrated clinical improvement in asthma symptoms and exacerbations, though the response may be less than in younger patients.^{114–117} Analysis from data collected from 2 randomized clinical trials investigating the use of reslizumab (an anti-IL-5 monoclonal antibody) demonstrate a reduction in asthma exacerbations and improved lung function in patients with LOA.,¹¹⁸

Nonpharmacologic treatments

A recent review in the *Journal* discussed the current state of nonpharmacologic treatment for severe asthma. While this review was not focused on older adults, it reported that both pulmonary rehabilitation and breathing techniques may be helpful in a subset of patients without causing harm.¹¹⁹ Among older adults, there are limited studies that appear to

support these techniques.^{120, 121} Additionally, older patients with asthma have been shown to have a poorer understanding of their medication use and self-management.¹²² Asthma educational strategies appear beneficial in older adults, although these strategies are frequently underutilized in this population.^{123, 124} For example, a 6-session randomized controlled trial of a self-regulation behavioral intervention demonstrated an improvement in health care utilization, asthma control and quality of life compared to the control group.¹²⁵

Asthma COPD Overlap (ACO)

A specific entity in the differential diagnosis that deserves mention is Asthma COPD Overlap (ACO), which has also been referred to as Asthma COPD Overlap Syndrome (ACOS). A recent workshop by the NIH and American Thoracic Society described this disorder as a condition in which patients with asthma have features of COPD, or patients with COPD have features of asthma.¹²⁶ Patients with ACO appear to have more hospitalizations, worse quality of life, and greater symptom burden than those with asthma or COPD alone.^{127, 128} Although precise definition, diagnosis, testing, and treatment options for ACO are still being established, what is most germane to this review is that a majority of ACO patients will likely be above the age of 50. As the NIH workshop participants note, at this time there is not a single, universal definition of ACO for diagnosis and treatment, but several research themes are emerging. Unquestionably, older adults with asthma will play an important role in future investigations of ACO.¹²⁶

Conclusion

Asthma among older adults is a common disorder, and as the population of the United States grows older, it will be encountered by anyone who manages adult asthma. As demonstrated in Tables 1 and 2, there are unique features related to diagnosis, medication, and non-pharmaceutical concerns that must be identified and properly managed in order to provide optimal care. As further research is performed in older adults with asthma, important medical discoveries will ensure that management in the golden years is truly golden.

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U.S. Population above 65 years

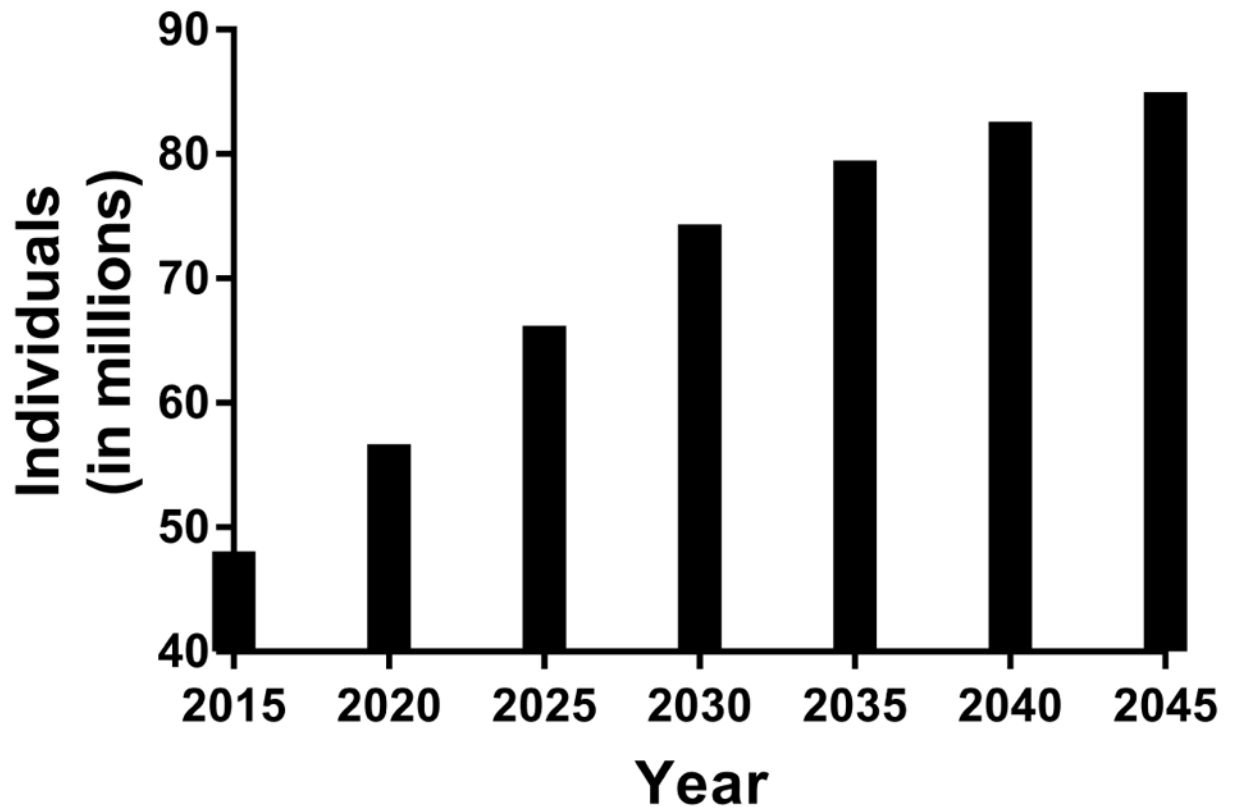


Figure 1. Projected U.S. population 65 years. Projections based on 2015 analysis of U.S Census data by Population Reference Bureau

U.S. Asthma Mortality rate

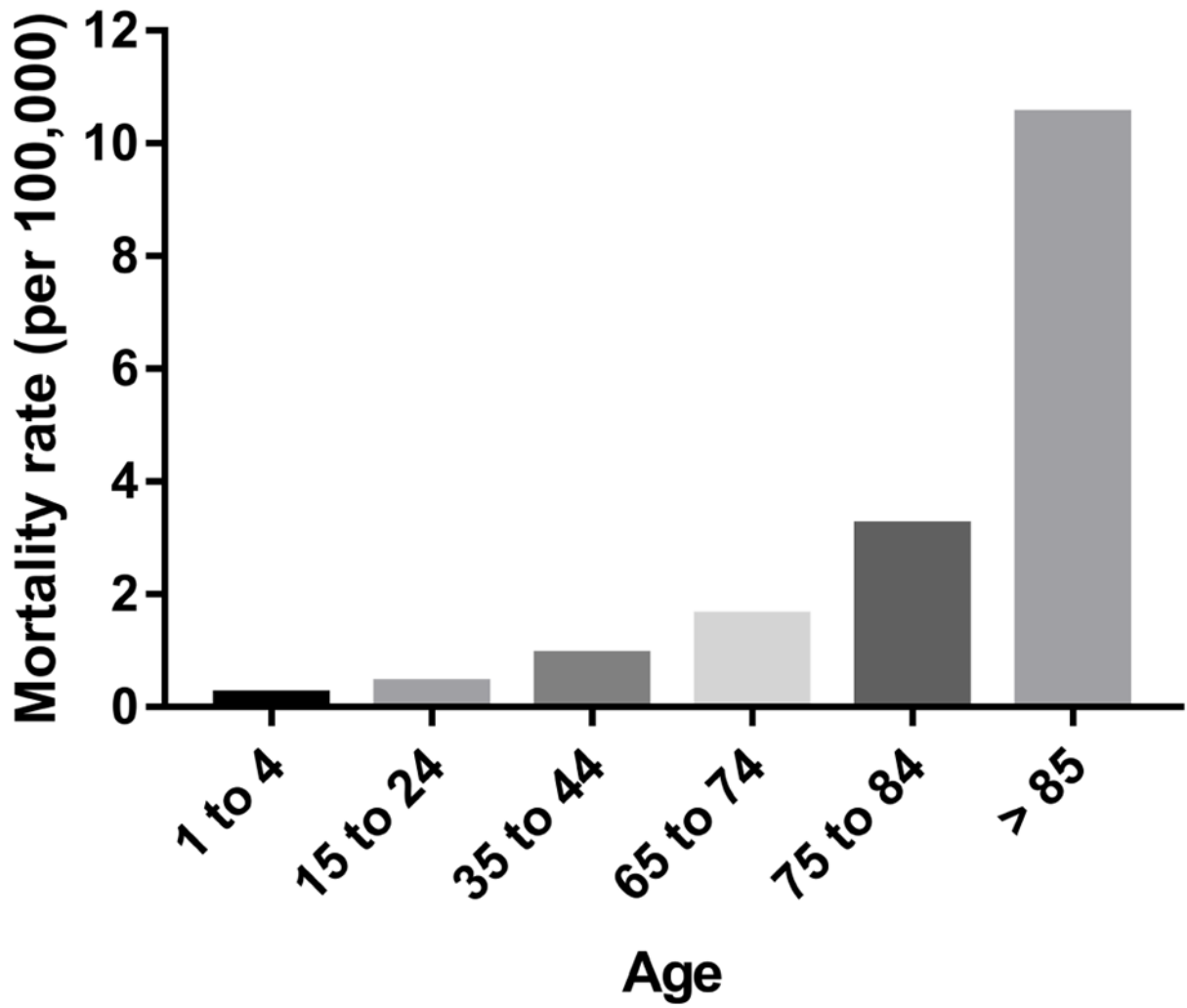


Figure 2. Mortality rates for asthma among different age groups (young children, adolescents, young adults, and older/very old adults). Adapted from: Kochanek KD, Murphy SL, Xu JQ, Tejada-Vera B. Deaths: Final data for 2014. National vital statistics reports; vol 65 no 4. Hyattsville, MD: National Center for Health Statistics. 2016

Response	Cell Type	Age-Associated Changes
Innate	Neutrophils	<ul style="list-style-type: none"> • ↑ number of cells in BALF and neutrophil elastase in non-asthmatics¹²⁹ • ↑ number of cells in sputum of older vs younger patients with asthma^{18,130,20} • ↑ numbers of sputum neutrophil mediators in older patients with asthma (IL-8, MMP-9)^{18,20} • ↓ chemotaxis¹³¹ • ↓ secretion of neutrophil extracellular traps (NETs), which normally function to immobilize bacteria¹³² • ↓ phagocytosis^{133,134} • ↑ basal production of ROS and neutrophil elastase (damages local tissues)^{131,135,136} • ↓ production of ROS in response to bacterial infection^{135,137}
	Eosinophils	<ul style="list-style-type: none"> • ↓ degranulation of peripheral cells in response to IL-5 in older patients with asthma¹³⁸ • ↑ peripheral number of cells associated with development of BHR and aging in men (Normative Aging study)¹³⁹
	Dendritic Cells	<ul style="list-style-type: none"> • ↑ IL-6 and TNF-α expression and ↓ IFN-γ^{140,141} • ↓ phagocytosis¹⁴² • ↓ Toll-like receptor function (TLR)¹⁴³ • ↓ migration¹⁴⁴
	Macrophages	<ul style="list-style-type: none"> • ↓ phagocytosis^{145,134} • ↓ TLR expression¹⁴⁶ • ↑ TNF-α, IL-8 expression¹⁴⁷
	Epithelial Cells	<ul style="list-style-type: none"> • ↓ ciliary beat frequency^{147,149} • ↓ barrier function due to loss of tight cellular junctions¹⁵⁰
Adaptive	B-Lymphocytes	<ul style="list-style-type: none"> • ↓ ability to produce specific, long-lasting and diverse antibodies to antigens (e.g., vaccination, infection)¹⁵¹ • ↓ naïve cells produced by the bone marrow¹⁵² • ↓ Total IgE^{153,154} • ↓ Antigen-specific IgE (however, antigen sensitization in older patients with asthma not uncommon, but its effect on asthma not clear)^{155,156}
	T-Lymphocytes	<ul style="list-style-type: none"> • ↓ naïve T-cells as thymus involutes¹⁵⁷ • ↑ number of circulating T-cells due to increase number of memory T-cells¹⁵⁸ • ↓ expression of CD154 (CD40L), decreasing B-cell activation and antibody class switching^{159,160} • ↑ survival of memory CD8+ cells, possibly due to chronic Cytomegalovirus (CMV) stimulation^{161,162}. (Inverted CD4:CD8 ratio in older adults with asthma, associated with decreased asthma control [preliminary data P. Busse])
	Th17 Cells	<ul style="list-style-type: none"> • ↑ number with aging¹⁶³ • ↑ number in BALF of LOA animal model^{20,164}

Figure 3.

Impacts of immunosenescence and inflammaging on asthma. A list of corresponding citations is available online.

Table 1

Important non-medication considerations for older 357 adults with asthma

Item	Possible solution
Symptoms of asthma are often similar to other age groups, but differences do exist	Ask about non-traditional asthma symptoms, such as fatigue
Older adults may have a decreased perception of dyspnea	Consider use of a peak flow meter to assist in assessment of airflow obstruction
Bronchial hyper-responsiveness to methacholine increases with age	Interpret results with caution, and consider a higher threshold for an abnormal test
Older adults with decreased cognition have poor inhaler technique	Consider breath-activated devices, spacers, and nebulizers
Comorbidities are common among older adults, and can negatively impact asthma	Identify, acknowledge, and address comorbidities where appropriate
Depression is especially problematic asthma management for older adults	Consider screening, treatment and/or referral for depression
Menopause is often associated with asthma exacerbations	The risks and benefits of hormone replacement therapy should be carefully considered in difficult to control asthma
Older adults frequently have caregiver roles for their spouse, children, or grandchildren	Acknowledge the challenges, and stress that to be optimally effective you must take care of your own health
Transportation can be problematic	Work with senior service agencies and social workers; schedule multiple appointments on the same day
Frequent use of complementary and alternative medicine (CAM) for asthma	Discuss risks and benefits of such therapies with your patient; consider how breathing exercises and asthma education can be incorporated
Poverty is a growing problem among older adults, and can adversely affect health	Use empathetic communication to discuss financial issues; prescribe medications with the lowest copay; refer to appropriate financial services

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Table 2

Medication considerations in older 360 adults with asthma

Medication	Consideration
Short acting beta agonists	<ul style="list-style-type: none"> Decline in β-2 receptors density and responsiveness Older adults are more sensitive to adverse effects
Short acting muscarinic antagonists	<ul style="list-style-type: none"> May have a more pronounced response than beta agonists as a rescue medication Watch for anticholinergic side effects (i.e. falls, urinary symptoms, cognitive impairment)
Inhaled corticosteroids	<ul style="list-style-type: none"> Preferred controller therapy yet underutilized Monitor for osteoporosis, cataracts, and glaucoma Less effective than in younger populations
Long acting beta agonists	<ul style="list-style-type: none"> Should not be used as monotherapy in asthma Most safety data from COPD trials
Long acting muscarinic antagonists	<ul style="list-style-type: none"> Have been shown to be effective as an add-on therapy for older adults More data needed, given older adults potential preferential bronchodilator response to anticholinergic therapy
Leukotriene receptor antagonists	<ul style="list-style-type: none"> Show some benefit, but less effective than in younger populations
Specific immunotherapy	<ul style="list-style-type: none"> Shows benefit in older adults Must consider risks/benefits of anaphylaxis and epinephrine use in patients with cardiac disease
Omalizumab	<ul style="list-style-type: none"> Show some benefit, but less effective than in younger populations