REVIEW

Asthma Care in the Elderly: Practical Guidance and Challenges for Clinical Management - A Framework of 5 "Ps"

Jaskiran K Khosa¹, Samuel Louie², Pamela Lobo Moreno¹, Dmitry Abramov¹, Daniel K Rogstad¹, Abdullah Alismail³, Michael J Matus¹, Laren D Tan¹

¹Department of Internal Medicine, Loma Linda University Health, Loma Linda, CA, USA; ²Department of Internal Medicine, University of California, Davis, Sacramento, CA, USA; ³Department of Cardiopulmonary Sciences, Loma Linda University Health, Loma Linda, CA, USA

Correspondence: Laren D Tan, Department of Medicine, Division of Pulmonary, Critical Care, Hyperbaric, Allergy and Sleep Medicine, Loma Linda University Health, 11234 Anderson Street, Suite 6439, Loma Linda, CA, 92354, USA, Tel +1 909-558-8081, Fax +1 909-558-0581, Email LaTan@llu.edu

Abstract: Uncontrolled asthma in the elderly is a public health issue recognized in developed countries such as the United States and among the European Union, both from patient safety and economic perspectives. Variations in the cutoff, which defines elderly age, contribute to epidemiological study difficulties. Nonetheless, the relevance of elderly asthma from a socioeconomic perspective is inarguable. The projected growth of the enlarging geriatric population in the United States portends an impending national health burden that may or may not be preventable with pharmacologic and non-pharmacologic treatments. Asthma in the elderly might be a consequence of uncontrolled disease that is carried throughout a lifetime. Or elderly asthmatics could suffer from uncontrolled asthma, which overlaps with other ailments common with advancing ages that merit consideration, eg, COPD, heart disease, OSA, diabetes mellitus, and other comorbidities. Because of the heterogeneity of asthma phenotypes and other conditions that could mimic the symptoms of elderly asthma, further cohort studies are needed to elucidate the elderly asthmatic pathophysiology and management. More studies to characterize elderly asthma can help address these patients' unmet need for evidence-based guidelines. We introduce the 5 "Ps" (phenotypes, partnership, pharmacology, practice in acute exacerbations, and problems or barriers for the elderly asthmatics) that establish a framework approach for clinical practice.

Keywords: asthma, elderly, uncontrolled asthma

Introduction

Shortness of breath is a frequent complaint of older patients in the primary care setting. However, both dyspnea and cough are common symptoms of both pulmonary and non-pulmonary conditions, and older patients can often have comorbidities that can make the diagnosis more difficult. In addition, the young and the old are affected by different physiologic and pathobiologic manifestations in asthma.¹

What is elderly? What sets the age cut off? Heterogeneity exists in the definition of elderly because of improving life expectancy, Quality of Life (QOL) and level of function within an aged population. Though the age cut off to define the elderly population with asthma has not been firmly established, the American Thoracic Society (ATS) decided that any older adult greater than 65 years of age is elderly.² The World Health Organization (WHO) defines the elderly as an individual 65 years or older, whereas the United Nations (UN) defines the elderly as 60 years or older. While age is a component in determining the elderly, additional factors should also be considered, such as gender, sociodemographic profile, and physiologic measures of aging, including age-related loss of bodily functions, eg, cognition, FEV1, and mobility.

There is a general perception that the elderly are dealt a lower standard of healthcare because of frequent needs for health-care utilization, eg, hospitalizations and poorer outcomes compared to younger populations.³ This is illustrated by

the prevalent use of quality-adjusted life year (QALY) statistics which are index measures calculated by estimating the years of life remaining for a patient following a particular treatment or intervention and weighting each year with a QOL score (on a 0 to 1 scale). ALY discriminates against elderly people by allowing economic evaluations by governments and insurance to justify less coverage of health-care services because of the perceived fewer years of life remaining. The definition of elderly needs to be consistent and agreeable to better design clinical trials to study and produce clinical evidence relevant to the elderly.

Comparable to no other period in history, the current global population trends are skewing towards an enlarging geriatric population above the age of 65 years. By 2050, the proportion of people above the age of 65 years in the United States will exceed 86 million (to account for 25% of the general population). Adults above 85 years of age will be 1 million and the largest growing demographic. WHO estimates that as of 2019, there were 703 million persons aged 65 years or older, and it is projected to double to 1.5 billion by 2050. This has an important bearing with projected increased healthcare resource utilizations, drug costs, asthma-related hospitalizations, and mortality among the growing elderly population worldwide.

The estimated lifetime prevalence of asthma above the age of 65 years old was reported at 10.4% compared to 7.8% among all adults in the United States (US), according to the Center for Disease Control (CDC) National Health Interview Survey. By 2030 it is projected that there will be more than 5 million persons with asthma above the age of 65. The prevalence of asthma in the elderly is reportedly higher in women. Mortality from asthma steadily rises with advancing age. In a large retrospective cohort study of emergency department visits, older asthmatic patients above age 55 had a 5-fold higher risk of overall mortality than younger adults. Helderly patients have the highest reported asthma-related mortality at 51.3 per million persons. Unfortunately, elderly asthmatics likely contribute to a large share of the overall economic burdens and health-care expenditures on the total cost of asthma in the US. Yet, data on the disproportionate cost are limited. According to the Asthma and Allergy Foundation of America, the estimated cost of asthma among all age groups is nearly \$19.7 billion, including nearly \$10 billion in direct costs, such as hospitalizations and \$8 billion in indirect costs, such as lost income from illness or death.

The purpose of this review is to highlight five critical clinical practices for evaluating and treating confirmed elderly asthmatics to provide a framework to help optimize care for this population.

Ist P: Phenotyping Elderly Asthmatics

Asthma among the elderly population is influenced by specific age-related physiologic changes specific to this population. The elderly asthmatic population exhibit more airway obstruction and hyperresponsiveness than younger asthmatic patients. ¹⁴ Age-related decline in lung function can result from reduced lung compliance, decreased lung elastic recoil, increased small airway remodeling with increased central airway thickness, and decreased respiratory muscle strength. ¹⁴ In elderly adults, secondary tracheobronchomalacia or expiratory dynamic airway collapse can also manifest with weakness of the airway walls exacerbated by recurrent airway irritation from long-standing asthma. ¹⁵ Aging is associated with an altered immune response and increased systemic inflammation, colloquially referred to as "inflamm-aging". ¹⁶ These physiologic changes are likely driven by chronic localized and systemic inflammation, causing difficult-to-control symptoms and frequent exacerbations in elderly asthmatic patients.

An important question that should always be considered is: are we dealing with asthma or other comorbidities in the elderly patient, or both? The correct diagnosis of asthma is essential in the elderly patient who may be misdiagnosed with concomitant comorbidities such as obstructive lung disease such as COPD or chronic heart disease from atrial fibrillation or heart failure. Obesity is considered a national epidemic, which is true among the elderly, associated with poorer asthma control and higher rates of asthma exacerbations. Sastroesophageal reflux disease increases with age, likely because of reductions in lower esophageal sphincter pressure with age and may contribute to asthma exacerbations. It is also suspected that gut microbiomes promote airway inflammation to contribute to asthma development (see Table 1).

Distinguishing asthma COPD overlap syndrome (ACOS) in the elderly asthmatic is particularly important because ACOS in the elderly is associated with more exacerbations and poorer quality of life (QOL). ¹⁸ Present methodologies for phenotyping the asthmatic subtypes in the elderly are inadequate. However, elderly asthma has been characterized as neutrophilic (variably defined as exceeding 40% to 60% neutrophils in induced sputum samples). ^{20–22} It is postulated that

Table I Mimickers of Asthma in the Elderly

Diagnosis	Symptoms	Tests	Hallmarks that Can Help Distinguish from Asthma
COPD with or without bronchiectasis	Dyspnea, cough, and sputum production	Spirometry, CXR	Smoking history, DLCO, imaging studies (CXR or CT showing emphysema or bullae or a flattened diaphragm)
ACOS	Cough, shortness of breath, wheezing, sputum production	PFT, CT chest, methacholine challenge testing	ACOS patients have lower diffusion capacity and higher blood neutrophil levels ^{67,70,71}
Heart failure	Dyspnea, fatigue, ± cough	BNP, ECHO, CXR	Symptoms of fluid overload: leg edema, orthopnea, PND. Imaging showing pleural effusions or pulmonary edema
Bronchiectasis	Productive cough with exacerbations, fatigue	CT chest, Aspergillus testing, testing for CF, CXR	Productive cough most days of the week. Imaging characteristic
GERD	Dry Cough, heartburn, hoarseness, sore throat, dysphagia, wheezing, abnormal taste, frequent clearing of the throat	EGD, barium swallow, manometry, pH	Association with other laryngeal symptoms, worse in the morning
Hyperventilation/panic disorder	SOB, palpitations, chest tightness, tachypnea	Diagnosis of exclusion	Normal lab and diagnostic tests, history of other mental health conditions like history of anxiety or depression, able to exercise and work without limitations.
ACE-Inhibitor induced cough	Dry Cough	None; diagnosis of exclusion	Dry, "hacking" cough.
Rhinosinusitis	Nasal congestion, runny nose, postnasal drip, and cough	Clinical diagnosis	Frequent history of allergies, recurrent URI symptoms/viral URIs
Vocal Cord Dysfunction	Stridor, wheezing, choking sensation, coughing, wheezing, hoarseness, throat tightness	Laryngoscopy	Sudden onset and inability to speak or ability to speak with a hoarse voice; inhaler typically do not help
Tracheobronchomalacia and EDAC	Wheezing, chronic cough, mucus production	Bronchoscopy, CT chest	Recurrent infections, responsive to positive airway pressure ⁶⁵
Anemia	DOE, fatigue	СВС	Pallor on physical examination, new progressive symptoms, intense fatigue

Abbreviations: ACE-I, Angiotensin-converting enzyme inhibitor; ACOS, asthma chronic obstructive lung disease overlap; ASA, aspirin; BNP, B-natriuretic peptide; CXR, chest radiograph; COPD, chronic obstructive pulmonary disease; CBC, complete blood count; CT, computed tomography; CF, cystic fibrosis; DLCO, diffusion limitation for carbon monoxide; DOE, dyspnea on exertion; ECHO, echocardiogram; EGD, esophagogastroduodenoscopy; EDAC, excessive dynamic airway collapse; GERD, gastroesophageal reflux disease; NSAID, non-steroidal anti-inflammatory drug; PFT, pulmonary function testing; PND, paroxysmal nocturnal; SOB, shortness of breath; URI, upper respiratory tract infection; dyspnea.

age-related microvascular permeability and air trapping from loss of elastic recoil with reduced radial traction in distal airways leads to retention of neutrophils (which have reduced deformability) in the pulmonary microvasculature. Others have postulated that it could also be related to the aging process, the use of corticosteroids, or frequent respiratory infections. 19,71

In contrast to the predominance of neutrophilic asthma, eosinophilic inflammation (T2- pathways) defined at FeNO >50 ppb; sputum eosinophil (2–8%) is also present among the elderly but is considered less frequent. ^{23,24} Evidence has shown that non-atopic asthma predominates among older age groups. ^{11,25} Overlapping of these phenotypes in the individual patient can confound the identification of the dominant asthma phenotype and

endotype. Sub-classification of elderly asthmatics can also be described as "early onset" and "late onset", which is onset of symptoms from childhood or early adulthood as compared to after the age of 40.8 Late onset asthma is associated with more rapid progression in lung function decline, less reversibility, and more severe clinical characteristics. 26,27 Long-standing asthma can also be present in the elderly as they continue to age and has also been reported to accelerate lung function decline.²⁸

As people age, kyphosis with narrowing of the intervertebral disk spaces leads to an increasing vertebral angle which is associated with a significant decline in the fraction of exhaled volume in 1 second (FEV₁) and vital capacity (VC) during spirometry testing.²⁹ With aging, there is a decreased ability to clear mucus from the lungs from reduced cough strength and delayed mucociliary clearance leading to reducing the ability to clear particles in the airways.³⁰ Respiratory muscle age-related decline can lead to an inability to ventilate in the face of increasing demands.²⁹

2nd P: Partnership with the Elderly Asthmatic Patient (See Figure 1)

The cornerstone in providing care to the elderly asthmatic is nurturing an alliance with the patient and/or caregivers or family members, beginning with a thorough history of asthma to help guide phenotyping and baseline symptoms. Patientcentered asthma care in elderly asthmatics is founded on respect for the individual needs, values and preferences during shared-decision making regarding treatment adjustments to achieve asthma control. As with other asthma groups, key components of partnership with the elderly are clear communication, understanding medications, correct inhaler use, and addressing the patient's and their caregivers' concerns. These barriers include symptom awareness, costs of medications, and difficulty in medical care access, as these were identified when surveying focus groups in older patients with asthma, unlicensed caregivers, and health professionals.³¹

Documenting current symptoms and triggers, confirming correct inhaler use and adherence, accurately recording prior exacerbations, and using systemic corticosteroids is critical when prior authorization is needed in the future for advanced asthma treatments, eg, biologics, pulmonary rehabilitation. Any approach to the elderly patient would be incomplete without discussing goals and patient preferences in advanced care planning.²²

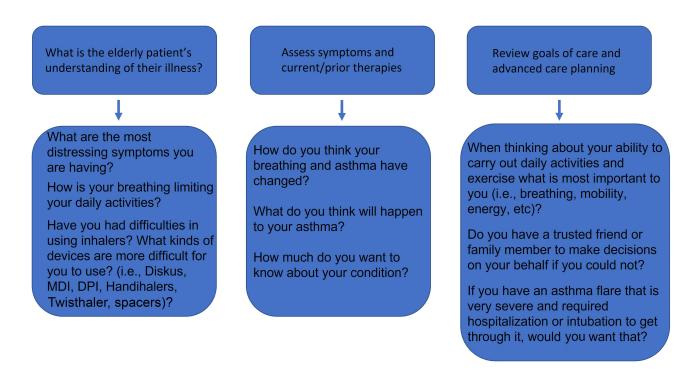


Figure I Discussion points in communicating with elderly patients. Abbreviations: MDI, metered dose inhaler; DPI, dry powdered inhaler.

Why is Shared Decision-Making Critical for Elderly Asthmatic Patients?

Elderly patients with age-related cognitive impairments are coachable on medication regimens but need education in language or graphics that they and their caregivers understand.³² The randomized control trial (SAMBA) embraced a teach-to-goal concept of 391 elderly patients above the age of 60 who were followed on inhaler use with coaching, multilingual asthma educational booklets and reported improved QOL, better asthma control test scores, better medication adherence, better meter dose inhaler (MDI) technique, and fewer asthma-related emergency department visits as compared to the control group without intervention.³³ The SAMBA intervention included 1) screening for barriers to self-management, 2) targeted action and 3) reinforcement overtime at home or in a primary care clinic with follow up via phone at 3 and 6 months and in person follow up at 12 months to assess medication adherence and new problems as reported by the patients. Barriers reported included poor inhaler technique, intermittent inhaled corticosteroids (ICS) use, and cockroach infestations at home.³³ After initial encounters, the patients were explained proper inhaler technique, referred for pest remediation services and educated on roles of the controller and rescue inhalers.

Diminished cognitive function and apraxia (inability to perform a motor activity from thought) in elderly patients with neurologic deficits can make meaningful pulmonary function test (PFT) data difficult or impossible to obtain. Lower scores on the Mini Mental State Examination (overall cognition) and difficulty drawing intersecting pentagons were predictive of spirometry test failure.³⁴ Spirometry in elderly patients may be limited by validated reference values for obstructive and restrictive ventilatory defects especially when stratified by ethnicity (eg, African American/Caucasian/Puerto Rican). The pitfalls include misclassifying a healthy older lung as mildly obstructed or restricted when the lungs have developed physiologic changes and hyperinflation or reduced elastic recoil with reduced vital capacity.

Testing should refer to appropriate reference values for elderly patients, but results can be confusing to interpret.³⁵ The elderly asthmatic may not be able to perform the required maneuvers to fulfill the American Thoracic Society/European Respiratory Society criteria for acceptable and repeatable measurements. Modified standards (such as using the FEV₆) may be prudent here.³⁵

3rd P: Pharmacologic Options

Randomized controlled trial evidence, real-world practice evidence, or treatment guidelines for the elderly asthmatic are wanted. Asthma treatment in elderly patients should be carefully evaluated as there is often polypharmacy. The paucity of original research is the result of age-based exclusion criteria. The mainstay for initial asthma treatments remains inhalation therapy with inhaled corticosteroids with or without an additional controller. The use of inhalers can be problematic if elderly asthmatics suffer from cognitive impairments, visual deficits, arthritis or fine motor skill impairments, or tremors. Inhaler therapy can include breath-activated medication devices, spacer devices to attach to metered dose inhalers, or nebulizers for daily controller use if frailty precludes the ability to generate sufficient inspiratory force (the latter is not currently FDA-approved for older patients with asthma).

Comparison studies of inhaler adherence between younger and older asthmatics (18–35 years of age compared to those above 60 years) showed similar daily compliance. However, older patients with decreased cognition have demonstrated poor inhaler technique, likely due to various cognitive and motor issues. Elderly patients trained on the correct inhaler technique should be continually reassessed during regular follow-up visits to assess asthma control. Studies conducted in Japan and Germany indicate that elderly patients need instructions repeated two to three times in order to master effective inhalation techniques. Choosing the appropriate inhaler device is expected to improve adherence and disease outcomes in elderly patients. However, few reviews compare inhaler device preferences and techniques across elderly adults. Concerns exist that the elderly population are unable to exert sufficient inspiratory flow rates to deagglomerate drugs from excipient lactose inhalers (DPI). However, DPIs may be preferred by older patients over pressurized metered dose inhalers and soft mist inhalers, provided there is sufficient inspiratory airflow. Ease of inhaler handling appears to be the most important factor when surveyed by elderly patients. Ultimately, the best inhaler for the elderly asthmatic is the inhaler that will be used regularly and correctly with objective improvement in symptoms and asthma control.

Current pharmacotherapy prescribed for elderly asthmatics is extrapolated from clinical trials and expert opinion in much younger asthmatics with eosinophilic and/or Th2-high asthma. Inhaled corticosteroids (ICS) remain the mainstay of initial asthma treatment, but there may be unintended consequences to the elderly asthmatic. Aging can affect the metabolism of drugs because of age-related decline in renal and hepatic metabolism.³⁸ Older patients are less likely to be prescribed ICS after an acute exacerbation requiring hospitalization.³⁹ In one retrospective cohort study, 2495 of 62,654 patients (40%) did not receive ICS, especially among participants above age 80 years as compared to 65 to 70 years.³⁹ This suggests an unresolved conflict exists over what is appropriate inhalation therapy in the elderly asthmatic both during post-acute exacerbation and follow-up asthma control re-evaluation.

Elderly patients receiving higher-dose ICS should be monitored for adverse effects such as increased risks of infection with pneumonia, increased fracture risk, decreased bone mineral density, and retinopathy or cataracts.³⁸ Oral, pharyngeal, and esophageal candidiasis are common adverse effects of ICS; however, little is known about the prevalence in the elderly.⁴⁰ Elderly patients are at risk for other steroid-related complications, including psychologic disorders (eg, insomnia, anxiety, depression, confusion), or drug-induced muscle weakness, myopathies, or easy bruising.³⁸

Short-acting beta-2 receptor agonists (SABA) are commonly prescribed for rescue therapy despite the potential for decreased beta-2 receptor responsiveness in elderly asthmatics.²⁵ This is of concern as recent GINA and National Institute of Health guidelines no longer recommend SABA for rescue, preferring a fixed dose combination of formoterol and a low dose inhaled corticosteroid.^{41–43} Long-acting beta-2 receptor agonists (LABA) and SABA have not specifically been tested in the elderly asthmatic patients. Clinicians should monitor for adverse effects that can be more problematic in elderly asthmatics, such as tremors, tachycardia, and QT prolongation with SABA and LABA.⁴⁴

Long-acting muscarinic antagonists (LAMA) are recommended in Step 5 of the current 2022 Global Strategy for Asthma Management and Prevention guidelines and can be effective in adults with ACOS. However, inhaled muscarinic antagonists can have adverse effects, including urinary outlet obstruction in men and narrow-angle glaucoma. The limitations in generating appropriate inspiratory flow for specific inhaler devices should also be evaluated in selecting individualized therapy for each patient. Annual education and training on correct inhaler techniques have been estimated to improve patient costs per exacerbation by approximately \$1585 and cumulative estimates project up to \$150 million in annual savings. He

Leukotriene receptor antagonists (LTRA) may be beneficial in elderly asthmatics who prefer a pill or those with non-adherence issues or difficulties in using inhalers. ⁶⁸ In addition, LTRAs can be considered in those with poor symptom control despite the correct use of inhalers. Due to the significant adverse effects of theophylline and roflumilast among the elderly, these medications are not considered first-line or FDA approved for asthma and are not discussed in detail here but may be considered on a case-by-case basis.

In addition to pharmacologic interventions, other management strategies are equally essential, including avoidance of known asthma triggers, tobacco smoking cessation, and appropriate vaccinations. Optimization of both non-pharmacologic and pharmacologic interventions tailored to the elderly patient is essential with involvement from advanced practice providers, pharmacists, nurses, respiratory therapists, and the patient's families or caregivers. Pulmonary rehabilitation has been shown as beneficial for asthma of any GINA severity, but studies on elderly patients are lacking. The SABE-Bogota study in Colombia included 2000 patients above the age of 60 and showed the prevalence of ACOS was 16.7%, with sarcopenia at 11.2% compared to elderly patients without ACOS with a prevalence of sarcopenia estimated at 6.96%. This raises the question about the benefits of pulmonary rehabilitation in the elderly as deconditioning is often present and sarcopenia as well for which more research is needed. However, coverage for pulmonary rehabilitation programs and transportation are issues that will also need to be addressed.

Current Biologics

Most younger asthmatics respond well to standard inhaler therapy combining ICS/LABA and do not need the addition of biologics to control their asthma symptoms and reduce exacerbations.¹ Asthmatics, including the elderly, can be considered for biologic therapy if they continue to suffer from poor asthma control despite adhering to high-dose ICS/LABA or require frequent treatment with oral corticosteroids for exacerbations.⁴⁹ For patients who require daily prednisone or those with steroid-related adverse effects that need a steroid-sparing strategy, monoclonal antibodies can

be considered when attempts to withdraw prednisone fail. Patients with severe asthma and evidence of type 2 high-inflammation and/or eosinophilic airway inflammation may benefit from a trial of biologics to improve asthma control and reduce or eliminate oral corticosteroids (OCSs).²⁵

Informing elderly patients and their caregivers about biologic treatments for uncontrolled severe asthma can promote earlier phenotyping and identify specific barriers to biologics, eg, patient preferences or hesitancy, visual or motor impairments or limited support systems if unable to self-administer. None of the biologic therapies for asthma report upper age limits for their use and limited safety data are available for elderly patients.²⁸ High costs or fine motor limitations in self-administration of subcutaneous mediations may pose barriers for older patients.²⁸ Given the costs and potential factors that affect the prescription of biologics, these medications have been typically reserved for the severe asthmatic patients who are not controlled on standard of care therapies (eg, ICS/LABA or require frequent use of oral corticosteroids).²⁸ Specific analyses of costs for inhalation therapy and biologics for the elderly asthmatic are beyond the scope of this paper.

4th P: Practices in Acute Exacerbations

Risk factors predisposing elderly asthmatics to acute exacerbations can include cigarette smoking, obesity, depression, sinusitis, respiratory infections, suboptimal inhaler techniques, or inhaler non-adherence.⁵⁰ Of note, ACOS is a significant factor for exacerbations among the advanced age group above 90 years of age.⁵⁰ It is also likely that lack of access to medications, financial barriers, and poor support systems (such as time-limited oversight or help from home caregivers or home health aides) could contribute to exacerbations among vulnerable elderly in our clinical experience.

There is evidence that most acute asthma exacerbations in children (80–85% in ages 9–11)⁵¹ and adults (57% in ages 19–46)⁵² may be triggered by respiratory viral infections. Overall, rhinovirus is the most common pathogen identified in asthma exacerbations and possibly important in asthma development.^{53,55} Atypical bacterial infections (*M. pneumoniae*, *C. pneumoniae*) may also play a limited role in exacerbations.⁵⁴ Although it may be reasonable to assume these same pathogens are frequently responsible for asthma exacerbations in elderly patients, studies are lacking to provide confidence in this conclusion. A recent systematic review suggests limited evidence for the efficacy of empiric antibiotic therapy given during asthma exacerbation, but the heterogeneity of studies limits the confidence in these conclusions, and they did not include elderly patients.⁵³ While interventions to prevent respiratory viral infections in elderly asthmatic patients (hygiene measures, vaccination when available) are reasonable to promote, empiric antibiotic use during asthma exacerbations is recommended without clear evidence of a concurrent bacterial infection.

Additional reasons for exacerbations in the elderly could be because of the health-care disparities notable in this population, as disparities have been described in younger asthmatics. Important determinants of health may be attributable to physiologic and social factors. The US CHRONICLE study for Asthma/COPD. Among 1884 enrolled patients, the majority were female (69%), White (75%) and diagnosed with asthma as adults (60%). Female, Black, Hispanic, and younger patients had higher annual exacerbations that were statistically significant versus male, white, non-Hispanic, and older patients, respectively. Black, Hispanics, and younger patients aged 18–49 years had higher asthma hospitalizations. In addition, female and Black patients had poorer symptom control and poorer health-related quality of life (HRQoL).

Elderly patients with asthma exacerbations prompt a very low threshold for referral to an emergency department. Mortality is higher after hospitalization in this group with comorbid conditions, as evidenced by a 5-year study of 1063 patients in the United Kingdom and National Health Service with 250,043 asthma admissions.⁵⁸ In this study, critical care admissions were associated with a high rate of death than out of ICU level of care; secondary co-morbidities that were associated with mortality after hospitalization included in order of prevalence: cardiac arrest (unspecified), anoxic brain injury (not classified), ischemic heart disease, acute lower respiratory infections or pneumonia, sepsis, COPD exacerbations and heart failure.⁵⁸ Characteristics of other diseases that could mimic clinical signs and symptoms of asthma in the elderly are described in Table 1.

In acute exacerbations, treatment with systemic glucocorticoids can cause steroid-related complications such as acute delirium, increase the risk for bone fractures, pneumonia, hyperglycemia, and electrolyte disturbances that can exacerbate morbidity related to the exacerbation itself.^{59,60} Primary care specialists and subspecialists can discuss goals of care with

Khosa et al Dovepress

the elderly asthmatic, caregivers and families, including mechanical ventilation after endotracheal intubation for status asthmatic and near-fatal asthma.

5th P: Problems for Elderly Asthmatics (Barriers Not Otherwise Discussed)

Age-related changes in HRQoL experiences are variable such that significant constitutional heterogeneity exists among older patients from very "fit" to very "frail".⁶¹ Overall, frailty in gross and fine motor skills can affect asthma severity in elderly patients who struggle with hand eye coordination deficits possibly leading to ineffective use of prescribed inhalers. Neurocognitive impairments and decreased memory can affect the elderly in regular medication adherence, especially in the setting of polypharmacy.⁴⁰ Studies have shown that among elderly asthmatics keeping inhalers in the same location with use as part of a daily routine at a specific time of day was more likely to maintain adherence compared to other strategies (such as alarms, reminders, and medication lists).⁶² Smart inhalers are available today for any asthma patient, including the elderly but costs may be a limiting factor. Digihaler is the first and only smart inhaler system with built-in sensors that automatically records the patient's inhalation of drug(s).⁶³ More studies are needed for smart inhalers and ease of use for elderly patients, especially in special circumstances such as weak fine motor skills, neuromuscular weakness (for example, sequelae of cerebrovascular accidents), or peripheral neuropathy in use of conventional inhalers that require manual dexterity and grip strength.

Elderly asthmatics face challenges in multiple domains for basic medical services, including transportation to clinic appointments, access to telemedicine services, and disparities in the affordability of medications. Asthma in the elderly

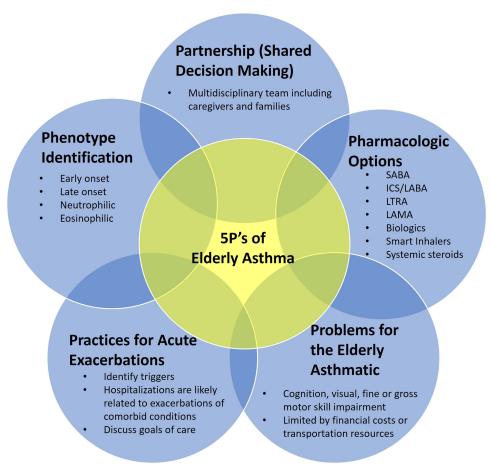


Figure 2 Key Principles ("5 Ps") in Approaching Asthma in the Elderly.

Abbreviations: SABA, short acting-beta agonist; ICS, inhaled corticosteroid; LABA, long acting-beta agonist, LTRA, leukotriene receptor antagonists; LAMA, long-acting muscarinic antagonists.

contributes to diminished quality of life (QOL), characterized by limited activities, the loss of the ability to function independently, and social isolation.¹⁰ Uncontrolled asthma progression diminishes QOL, limits daily activities and restricts the independence and social well-being of the elderly.²⁰ These sequelae can then contribute to repeated hospitalization, which is further associated with the deteriorated condition, making treatment more difficult in a vicious cycle.¹⁰ Moreover, the deleterious effects of uncontrolled asthma in the elderly patient should include an evaluation of mental health as these patients report symptoms of depression, anxiety and post-traumatic stress disorder.

Psychosocial complications associated with depression and anxiety also impact caregivers who witness uncontrolled symptoms in loved ones as they age.⁶⁴ Therefore, elderly asthmatics benefit from early referral to a multidisciplinary team with social work/case managers who can liaison with available community resources such as adult senior centers, home health services and drug affordability programs.⁶⁹

Conclusion

The principles described here in the "5P's" can guide primary care providers, pulmonologists, asthmatologists and respiratory care providers in a practical approach to help control symptoms and prevent exacerbations (see Figure 2). Asthma in the elderly can be more challenging to manage with coexistent comorbid conditions or age-related decline in cognitive, motor, or visual deficits. Despite age-related changes in cognition, motor skills and polypharmacy, evidence suggests elderly patients can be trained for proper inhaler techniques over the course of two or three educational discussions. Education to the patient and families or caregivers regarding disease process and proper inhaler use, as well as identifying alarm signs and exacerbations, is key to reducing emergency department visits, improving medication adherence, and overall reducing mortality. The goals of the patients and their families should be reviewed (especially during hospitalizations with a discussion of preferences for or against invasive ventilation or non-invasive ventilation in acute exacerbations). Many questions remain in elderly asthma treatment, especially in advanced dementia or end-stage co-morbidities (eg, heart failure, COPD). Elderly patients were not included in clinical trials and evidence informing the guidelines from which we extrapolate current therapies such as inhalers and oral medications. Novel therapies such as biologics can be considered in refractory or severe diseases for elderly patients, but more studies are necessary for this population. Future directions should also focus on the elderly population for individuals 85 years or older for whom management guidelines remain especially scarce.

Disclosure

The authors report no conflicts of interest in this work.

References

- 1. Tan LD, Nguyen N, Alismail A, Castro M. Management of uncontrolled asthma: a framework for novel and legacy biologic treatments. *J Asthma Allergy*. 2022;29(15):875–883. doi:10.2147/JAA.S369836
- 2. Skloot GS, Busse PJ, Braman SS, et al.; ATS ad hoc Committee on Asthma in the Elderly. An official American Thoracic Society workshop report: evaluation and management of asthma in the elderly. Ann Am Thorac Soc. 2016;13(11):2064–2077. doi:10.1513/AnnalsATS.201608-658ST
- 3. Ben-Harush A, Shiovitz-Ezra S, Doron I, et al. Ageism among physicians, nurses, and social workers: findings from a qualitative study. *Eur J Ageing*. 2016;14(1):39–48. doi:10.1007/s10433-016-0389-9
- Salomon JA. Quality adjusted life years. In: Quah SR, editor. International Encyclopedia of Public Health (Second Edition). Academic Press; 2017:224–228.
- 5. Yaghoubi M, Adibi A, Safari A, FitzGerald JM, Sadatsafavi M. The projected economic and health burden of uncontrolled asthma in the United States. *Am J Respir Crit Care Med.* 2019;200(9):1102–1112. doi:10.1164/rccm.201901-0016OC
- Tsuchiya A. QALYs and ageism: philosophical theories and age weighting. Health Econ. 2000;9(1):57–68. doi:10.1002/(SICI)1099-1050(200001)
 57::AID-HEC484>3.0.CO;2-N
- 7. Kaur BP, Lahewala S, Arora S, et al. Asthma: hospitalization trends and predictors of in-hospital mortality and hospitalization Costs in the USA (2001-2010). Int Arch Allergy Immunol. 2015;168(2):71–78. doi:10.1159/000441687
- 8. Hanania NA, King MJ, Braman SS. Asthma in elderly workshop participants. Asthma in the elderly: current understanding and future research needs--a report of a National Institute on Aging (NIA) workshop. *J Allergy Clin Immunol*. 2011;128(3 Suppl):S4–24. doi:10.1016/j. iaci.2011.06.048
- 9. Oraka E, Kim HJ, King ME, Callahan DB. Asthma prevalence among US elderly by age groups: age still matters. *J Asthma*. 2012;49(6):593–599. doi:10.3109/02770903.2012.684252
- 10. Zhang Y, Huang L. Characteristics of older adult hospitalized patients with bronchial asthma: a retrospective study. *Allergy Asthma Clin Immunol*. 2021;17(1):122. doi:10.1186/s13223-021-00628-0

Khosa et al Dovepress

11. Tsai C, Lee W, Hanania NA. Age-Related differences in clinical outcomes for acute asthma in the United States, 2006-2008. *J Allergy Clin Immunol*. 2012;129:1252–1258.e1. doi:10.1016/j.jaci.2012.01.061

- 12. Safiri S, Karamzad N, Kaufman JS, et al. Prevalence, Deaths and Disability-Adjusted-Life-Years (DALYs) Due to Type 2 Diabetes and Its Attributable Risk Factors in 204 Countries and Territories, 1990-2019: results From the Global Burden of Disease Study 2019. Front Endocrinol. 2022;13:838027. doi:10.3389/fendo.2022.838027
- 13. Dunn RM, Busse PJ, Wechsler ME. Asthma in the elderly and late-onset adult asthma. Allergy. 2018;73(2):284-294. doi:10.1111/all.13258
- Boulet LP, Robitaille C, Deschesnes F, Villeneuve H, Boulay ME. Comparative clinical, physiological, and inflammatory characteristics of elderly subjects with or without asthma and young subjects with asthma. Chest. 2017;152(6):1203–1213. doi:10.1016/j.chest.2017.09.019
- Malenfant JH, Batsis JA. Obesity in the geriatric population a global health perspective. J Glob Health Rep. 2019;3:e2019045. doi:10.29392/joghr.3.e2019045
- Wardzyńska A, Pawełczyk M, Rywaniak J, Makowska J, Jamroz-Brzeska J, Kowalski ML. Circulating miRNA expression in asthmatics is age-related and associated with clinical asthma parameters, respiratory function and systemic inflammation. Respir Res. 2021;22(1):177. doi:10.1186/s12931-021-01769-x
- 17. Gibson PG, Simpson JL. The overlap syndrome of asthma and COPD: what are its features and how important is it?". *Thorax*. 2009;64:728–735. doi:10.1136/thx.2008.108027
- 18. Gherasim A, Dao A, Bernstein JA. Confounders of severe asthma: diagnoses to consider when asthma symptoms persist despite optimal therapy. *World Allergy Organ J.* 2018;11(29):29. doi:10.1186/s40413-018-0207-2
- 19. Maykut RJ, Kianifard F, Geba GP. Response of older patients with IgE-mediated asthma to omalizumab: a pooled analysis. *J Asthma*. 2008;45 (3):173–181. doi:10.1080/02770900701247277
- 20. Israel E, Reddel HK. Severe and difficult-to-treat asthma in adults. N Eng J Med. 2017;377:965-976. doi:10.1056/NEJMra1608969
- 21. Schleich F, Graff S, Guissard F, et al. Asthma in elderly is characterized by increased sputum neutrophils, lower airway caliber variability and air trapping. *Respir Res.* 2021;22(1):15. doi:10.1186/s12931-021-01619-w
- 22. Incalzi RA, Bellia V, Catalano F, et al. Evaluation of health outcomes in elderly patients with asthma and COPD using disease-specific and generic instruments: the salute respiratoria nell'Anziano. *Chest.* 2001;120(3):734–742. doi:10.1378/chest.120.3.734
- 23. Battaglia S, Benfante A, Spatafora M, Scichilone N. Asthma in the elderly: a different disease? *Breathe*. 2016;12(1):18–28. doi:10.1183/20734735.002816
- 24. Khatri SB, Iaccarino JM, Barochia A, et al.; American Thoracic Society Assembly on Allergy, Immunology, and Inflammation. Use of fractional exhaled nitric oxide to guide the treatment of asthma: an official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med.* 2021;204(10):e97–e109. doi:10.1164/rccm.202109-2093ST
- 25. Agondi RC, Andrade MC, Takejima P, Aun MV, Kalil J, Giavina-Bianchi P. Atopy is associated with age at asthma onset in elderly patients. *J Allergy Clin Immunol Pract.* 2018;6(3):865–871. doi:10.1016/j.jaip.2017.10.028
- Cuttitta G, Cibella F, Bellia V, et al. Changes in FVC during methacholine-induced bronchoconstriction in elderly patients with asthma: bronchial hyperresponsiveness and aging. Chest. 2001;119(6):1685–1690. doi:10.1378/chest.119.6.1685
- 27. Sears MR. Lung function decline in asthma. Eur Resp J. 2007;30(3):411-413. doi:10.1183/09031936.00080007
- 28. Yawn BP, Han MK. Practical considerations for the diagnosis and management of asthma in older Adults. *Mayo Clin Proc.* 2017;92 (11):1697–1705. doi:10.1016/j.mayocp.2017.08.005
- 29. Lowery EM, Brubaker AL, Kuhlmann E, Kovacs EJ. The aging lung. Clin Interv Aging. 2013;8:1489-1496. doi:10.2147/CIA.S51152
- 30. Proença de Oliveira-Maul J, Barbosa de Carvalho H, Goto DM. Aging, diabetes, and hypertension are associated with decreased nasal mucociliary clearance. *Chest.* 2013;143(4):1091–1097. doi:10.1378/chest.12-1183
- 31. Cortes T, Lee A, Boal J, Mion L, Butler A. Using focus groups to identify asthma care and education issues for elderly urban-dwelling minority individuals. *Appl Nurs Res.* 2004;17(3):207–212. doi:10.1016/j.apnr.2004.06.002
- 32. Enright PL, McClelland RL, Newman AB, Gottlieb DJ, Lebowitz MD. Underdiagnosis and undertreatment of asthma in the elderly. Cardiovascular Health Study Research Group. *Chest.* 1999;116(3):603–613. doi:10.1378/chest.116.3.603
- 33. Federman AD, O'Conor R, Mindlis I, et al. Effect of a self-management support intervention on asthma outcomes in older adults: the SAMBA Study Randomized Clinical Trial. *JAMA Intern Med.* 2019;179(8):1113–1121. doi:10.1001/jamainternmed.2019.1201
- 34. Allen SC, Baxter M. A comparison of four tests of cognition as predictors of inability to perform spirometry in old age. *Age Ageing*. 2009;38 (5):537–541. doi:10.1093/ageing/afp104
- 35. Ruppel GL, Enright PL. Pulmonary function testing. Respir Care. 2012;57(1):165-175. doi:10.4187/respcare.01640
- 36. Baptist AP, Busse PJ. Asthma over the age of 65: all's well that ends well. J Allergy Clin Immunol Pract. 2018;6(3):764–773. doi:10.1016/j. jaip.2018.02.007
- 37. Ruessel K, Luecke E, Schreiber J. Inhaler devices in a geriatric patient population: a prospective cross-sectional study on patient preferences. Patient Prefer Adherence. 2020;7(14):1811–1822. doi:10.2147/PPA.S262057
- 38. Battaglia S, Cardillo I, Lavorini F, Spatafora M, Scichilone N. Safety considerations of inhaled corticosteroids in the elderly. *Drugs Aging*. 2014;31 (11):787–796. doi:10.1007/s40266-014-0213-1
- 39. Sin DD, Tu JV. Underuse of inhaled steroid therapy in elderly patients with asthma. Chest. 2001;119(3):720-725. doi:10.1378/chest.119.3.720
- 40. Scichilone N, Ventura MT, Bonini M, et al. Choosing wisely: practical considerations on treatment efficacy and safety of asthma in the elderly. *Clin Mol Allergy*. 2015;13(7). doi:10.1186/s12948-015-0016-x
- 41. Chapman KR, Barnes NC, Greening AP, Jones PW, Pedersen S. Single maintenance and reliever therapy (SMART) of asthma: a critical appraisal. *Thorax*. 2010;65(8):747–752. doi:10.1136/thx.2009.128504
- 42. Beasley R, Harrison T, Peterson S, et al. Evaluation of budesonide-formoterol for maintenance and reliever therapy among patients with poorly controlled asthma: a systematic review and meta-analysis. *JAMA Netw Open.* 2022;5(3):e220615. doi:10.1001/jamanetworkopen.2022.0615
- 43. 2020 Focused updates to the asthma management guidelines: a report from the national asthma education and prevention program coordinating committee expert panel working group. National Heart Lung and Blood Institute, US Department of Health and Human Services; 2020. Available from: https://www.nhlbi.nih.gov/resources/2020-focused-updates-asthma-management-guidelines. Accessed December 23, 2022.
- 44. Balkrishnan R, Christensen DB, Bowton DL. Self-reported health status, prophylactic medication use, and healthcare costs in older adults with asthma. *J Am Geriatr Soc.* 2002;50(5):924–929. doi:10.1046/j.1532-5415.2002.50221.x

45. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention; 2022. Available from: www.ginasthma.org. Accessed December 23, 2022.

- 46. Maricoto T, Marques-Gomes J, Correia-de-Sousa J, Taborda-Barata L. Inhaler review in older adults with asthma or COPD: a cost-effectiveness study and a perspective in Portugal. *J Am Geriatr Soc.* 2019;67(7):1430–1436. doi:10.1111/jgs.15834
- 47. Zampogna E, Paneroni M, Cherubino F, et al. Effectiveness of a pulmonary rehabilitation program on persistent asthma stratified for severity. Respir Care. 2019;64(12):1523–1530. doi:10.4187/respcare.06761
- 48. Borda MG, Celis-Preciado CA, Pérez-Zepeda MU, Ríos-Zuluaga JD. Cano-Gutiérrez CA Sarcopenia in the elderly with history of COPD/Asthma. Results of the SABE-Bogotá Study. Rev Esp Geriatr Gerontol. 2017;52(6):313–316. doi:10.1016/j.regg.2016.07.003
- 49. Nanda A, Baptist AP, Divekar R, et al. Asthma in the older adult. J Asthma. 2020;57(3):241-252. doi:10.1080/02770903.2019.1565828
- 50. Sohn KH, Song WJ, Park JS, et al.; Elderly Asthma Cohort in Korea Group. Risk factors for acute exacerbations in elderly asthma: what makes asthma in older adults distinctive? *Allergy Asthma Immunol Res.* 2020;12(3):443–453. doi:10.4168/aair.2020.12.3.443
- 51. Johnston SL, Pattemore PK, Sanderson G, et al. Community study of role of viral infections in exacerbations of asthma in 9-11 year old children. *BMJ*. 1995;310(6989):1225–1229. doi:10.1136/bmj.310.6989.1225
- 52. Nicholson KG, Kent J, Ireland DC. Respiratory viruses and exacerbations of asthma in adults. BMJ. 1993;307(6910):982–986. doi:10.1136/bmj.307.6910.982
- 53. Normansell R, Sayer B, Waterson S, Dennett EJ, Del Forno M, Dunleavy A. Antibiotics for exacerbations of asthma. *Cochrane Database Syst Rev.* 2018;6(6):CD002741. doi:10.1002/14651858.CD002741.pub2
- 54. Singh AM, Busse WW. Asthma exacerbations. 2: aetiology. Thorax. 2006;61(9):809-816. doi:10.1136/thx.2005.045179
- 55. Busse WW, Lemanske RF, Gern JE. Role of viral respiratory infections in asthma and asthma exacerbations. *Lancet*. 2010;376(9743):826–834. doi:10.1016/S0140-6736(10)61380-3
- 56. Lugogo N, Judson E, Haight E, et al. Severe asthma exacerbation rates are increased among female, Black, Hispanic, and younger adult patients: results from the US CHRONICLE study. *J Asthma*. 2022;9:1–14. doi:10.1080/02770903.2022.2102036
- 57. Menzies-Gow AN, McBrien C, Unni B, et al. Real world biologic use and switch patterns in severe asthma: data from the international severe asthma registry and the US CHRONICLE study. *J Asthma Allergy*. 2022;13(15):63–78. doi:10.2147/JAA.S328653
- 58. Watson L, Turk F, James P, et al. Factors associated with mortality after an asthma admission: a national United Kingdom database analysis. *Respir Med.* 2007;101(8):1659–1664. doi:10.1016/j.rmed.2007.03.006
- 59. Louie S. The perils of prednisone. Consultant. 2020;60(9):12-16. doi:10.25270/con.2020.09.00001
- 60. Newnham DM. Asthma medications and their potential adverse effects in the elderly: recommendations for prescribing. *Drug Saf.* 2001;24 (14):1065–1080. doi:10.2165/00002018-200124140-00005
- 61. Figueiredo RG, Pinheiro GP, Arata V, et al. Impact of frailty in elderly patients with moderate to severe asthma. *PLoS One*. 2022;17(7):e0270921. doi:10.1371/journal.pone.0270921
- Brooks TL, Leventhal H, Wolf MS, et al. Federman AD Strategies used by older adults with asthma for adherence to inhaled corticosteroids. J Gen Intern Med. 2014;29(11):1506–1512. doi:10.1007/s11606-014-2940-8
- 63. Hoyte FCL, Mosnaim GS, Rogers L, et al. Effectiveness of a digital inhaler system for patients with asthma: a 12-week, open-label, randomized study (CONNECT1). J Allergy Clin Immunol Pract. 2022;10(10):2579–2587. doi:10.1016/j.jaip.2022.08.023
- 64. Urso DL. Asthma in the elderly. Curr Gerontol Geriatr Res. 2009;2009:858415. doi:10.1155/2009/858415
- 65. Dal negro RW, Tognella S, Guerriero M, Micheletto C. Prevalence of tracheobronchomalacia and excessive dynamic airway collapse in bronchial asthma of different severity. *Multidiscip Respir Med.* 2013;8(1):32. doi:10.1186/2049-6958-8-32
- 66. Schleich F, Graff S, Guissard F, et al. Asthma in elderly is characterized by increased sputum neutrophils, lower airway caliber variability and air trapping. *Respir Res.* 2021;22:15.
- 67. Postma DS, Rabe KF. The asthma-COPD overlap syndrome. N Engl J Med. 2015;373(13):1241–1249. doi:10.1056/NEJMra1411863
- 68. Bellanti JA, Settipane RA. Atopy, asthma, and the elderly: a paradigm for personalized therapy. *Allergy Asthma Proc.* 2017;38(3):167–169. doi:10.2500/aap.2017.38.4056
- 69. Gibson PG, McDonald VM, Marks GB. Asthma in older adults. Lancet. 2010;376(9743):803-813. doi:10.1016/S0140-6736(10)61087-2
- 70. Tommola M, Ilmarinen P, Tuomisto LE, et al. Differences between asthma-COPD overlap syndrome and adult-onset asthma. Eur Respir J. 2017;49 (5):1602383. doi:10.1183/13993003.02383-2016
- 71. Crisford H, Sapey E, Rogers GB, et al. Neutrophils in asthma: the good, the bad and the bacteria. *Thorax*. 2021;76(8):835–844. doi:10.1136/thoraxjnl-2020-215986

Journal of Asthma and Allergy

Dovepress

Publish your work in this journal

The Journal of Asthma and Allergy is an international, peer-reviewed open-access journal publishing original research, reports, editorials and commentaries on the following topics: Asthma; Pulmonary physiology; Asthma related clinical health; Clinical immunology and the immunological basis of disease; Pharmacological interventions and new therapies. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/journal-of-asthma-and-allergy-journal