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ASTHMA ACROSS THE AGES: ADULTS

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Abbreviations:

ACT, Asthma control test

AERD, aspirin exacerbated respiratory disease

APOEε4, Apolipoprotein E

ATS, American Thoracic society

BHR, bronchial hyperresponsiveness

BMI, body mass index

CI, confidence interval

COPD, chronic obstructive pulmonary disease

CRP, C-reactive protein

CVD, cardiovascular disease

ECRHS, European Community Respiratory Heath Survey

EOA, early onset asthma

FeNO, fractional exhaled nitric oxide

FEV1, forced expiratory volume in 1 second

FVC, forced vital capacity

ICS, inhaled corticosteroid

IL-5, interleukin-5

IL-6, interleukin-6

IL-8, interleukin-8

IL-1β, interleukin-1beta

IFN-γ, interferon gamma

ICS, inhaled corticosteroids

LDL, low density lipoprotein

OR, odds ratio

RHINE, Respiratory Health in Northern Europe study

RNA, ribonucleic acid

SARP, Severe Asthma Research Program

SD, standard deviation

T2, Type 2

TNF-α, tumour necrosis factor alpha

ABSTRACT

Asthma is a common disease affecting approximately 300 million people worldwide, across all age ranges. Despite advances in asthma outcomes of the last few decades, there remains room for improvement in asthma management and for patient outcomes, particularly in older patients. The heterogeneity of asthma is now well recognized, and is known to complicate response to treatment, patient behavior and impact health outcomes. Asthma and its heterogeneity change according to age. Asthma affects people differently across the lifespan. In adults, prevalence is highest among those in middle age, however mortality is greater in the older age group. In this clinical commentary, we describe how age impacts asthma prevalence and incidence, outcomes, disease expression and approach to management in adulthood and in older patients.

INTRODUCTION

Asthma is highly prevalent, and can affect people at all stages of life, from infancy through childhood and adulthood, and into older ages (> 66 years old) (1, 2). Although asthma can cause a negative impact upon a patient's quality of life through loss of work, interruption of daily life activities, emergency room visits and hospitalizations, and potentially death in some, in particular older patients, it is treatable (3, 4). However, there are important differences in the underlying pathophysiology and consequently, presentation of asthma through younger (20-40 years of age) and middle (41-65 years of age) adulthood and in the aged (>66 years of age, "older adults") that must be recognized to decrease its associated morbidity and mortality (Table 1).This article describes our understanding of how aging impacts the epidemiology, exacerbation risk, phenotypes and diagnostic approach to asthma. Key elements include modification of the host response by age, different exposures that might occur at different stages of life, and different comorbidities that may emerge and impact asthma at different ages. This manuscript does not focus upon the effect of aging on the response to asthma therapies, which is reviewed elsewhere (1, 5).

EPIDEMIOLOGY

Prevalence

Asthma prevalence is highest in those 45-64 years of age (Figure 1) (6, 7). There are also significant differences of asthma prevalence with gender across ages. In Australia,

among children (aged 0–14 years), the prevalence was higher for males than females, but among those >15 years old, current asthma was more prevalent in females (10.9%) than in males (8.9%). Among males, the highest prevalence was in those aged 5–9 years (15.1%, CI: 11.0–19.3%), while among females it was highest in those aged >75 years (13.4%, CI: 10.3–16.5%) (7). These trends are similar across nations (1, 6, 8).

Incidence

Although asthma is often considered a disease of childhood onset, it can develop in adulthood, even after the age of 65 years (8). The incidence of asthma in adulthood over a 10-year period was evaluated using data from prospective cohorts, involving eight countries across Europe, and a total population of 23,704 participants. In these studies, asthma incidence varied from 2.9/1,000/year to 8.3/1,000/year (9, 10). The risks for new-onset adult asthma were (asymptomatic) bronchial hyperresponsiveness (BHR), allergic rhinitis (twice as common among participants with incident asthma compared with those without asthma), female gender, respiratory infections in early life, aspirin-exacerbated respiratory disease (AERD), high-risk occupations (less likely in those >65 years of age), environmental pollutants, stressful life events and obesity (11, 12). Although new onset allergic sensitization precipitating asthma is more common in younger adults, it can occur in the aged (12-16).

Asthma remission in adulthood

Asthma can also go into remission in adult life. Westerhof reported that one in 6 patients with adult-onset asthma experience a remission of his or her asthma within the first 5 years of disease onset (17). The Respiratory Health in Northern Europe (RHINE) study reported an overall remission rate of 20.2 per 1,000 person-years among adults aged 26–53 years, meaning that approximately 20% of people experienced a clinical remission of asthma during a 10-year period (18). Similarly, a Swedish study reported a 10-year remission rate of asthma of 14.6% among adults aged 20–69 years (19), and Sozener reported remission in 11.3% of adults (20).

Younger age, younger age of asthma onset, atopy, allergic rhinitis, and fewer comorbidities are linked to a greater possibility of remission (20). Patients with asthma persistence tend to be older, have worse asthma control, require higher doses of inhaled corticosteroids (ICS), have more severe BHR, higher frequency of nasal polyps, and higher levels of blood neutrophils as compared to patients who experience clinical remission. In patients with moderate to severe BHR and nasal polyposis, the chance of remission is close to zero (17, 21, 22).

ASTHMA MORBIDITY AND EXACERBATION RISK THROUGH THE AGES

Asthma morbidity/mortality through the ages

Older adults have high rates of asthma morbidity and mortality when compared to younger adults (3, 4, 6). Adults >65 years of age presenting to the emergency department for asthma had the highest rate of hospitalization (~25% admission rate compared to

7.9% for all ages) and the longest length of stay (24-26)(3, 4, 6). These poorer outcomes in the aged are likely multifactorial and include alteration in lung structure, increased presence of co-morbidities, cognition (discussed below), and alteration of inflammation with aging (discussed below).

Exacerbation risk across the ages

Asthma exacerbations are responsible for a significant disease burden across adult life. There are changes across the age spectrum in the rate and pattern of asthma exacerbations, with the highest rate seen in the oldest age group. In a large population-based study in the UK, the rate of exacerbations was highest in the oldest cohort and lowest in the 5 to 17 years cohort. The exacerbation rate per 10 person-years (95% CI) in adults aged 18 to 54 was 3.22 (3.21 to 3.24), and in adults 55 years and older was 9.40 (9.37 to 9.42). Asthma severity was a common risk factor for asthma exacerbations across the different age ranges. The frequent-exacerbator phenotype was present in 2% of adults with asthma (23, 24).

ASTHMA PHENOTYPES ACROSS ADULTHOOD

Data from large multicenter studies including the Severe Asthma Research Program (SARP) and the Leicester study (UK) have provided important insights into young and middle-aged adult asthma phenotypes (25, 26). Although not designed to target older populations, these studies included some participants up to 80 years old. A smaller cross-sectional cluster study (Detroit, Michigan), recruiting patients (mean age 65.9 years) with asthma has also provided phenotypic data in the aged (27). Despite differences in cohorts

studied, methodology, and numbers of clusters identified, these studies have suggested that adult asthma can be broadly categorized into early-onset (generally prior to 12 years of age) or adult-onset.

Early-onset asthma (EOA)

Early-onset asthma is primarily differentiated into mild allergic and moderate-severe allergic EOA based upon lung function, dosage of controller medications, heath care use for asthma and the need for oral corticosteroid bursts (28). Those subjects in SARP with milder disease were predominantly female and had a BMI 23.6-28kg/m^2 (25). These patients tended to have eosinophilic asthma, although the mild allergic UK cohort also had a higher sputum neutrophil count (26). Data characterizing patients with moderate-severe EOA is less consistent. In SARP, the subjects were more likely to be black males with a slightly earlier age of asthma onset, and a higher BMI (31kg/m^2); despite a baseline FEV1 of 57% predicted, they had good airway reversibility (25). In the UK data, subjects were more likely to be female with a lower BMI ~27.6kg/m^2 (26). This group had higher sputum eosinophils than the milder EOA.

The Detroit study identified 2 clusters of older patients with EOA; both with high rates of atopic sensitization (74% and 68%) (27). The first had a slightly younger age of asthma onset, a pre-bronchodilator FEV1 of 69.8% predicted, with relatively high rates of fixed airway obstruction (45.7%), and poor disease control (Asthma Control Test [ACT]=17.5). The second was more severe, with a pre-bronchodilator FEV1=37.8% predicted, and even higher rates of fixed airway obstruction (72%) and poorer asthma control

193 (ACT=14.7). Importantly, asthma control in the overall population was low (ACT=17.5)
194 (27). Whether the two groups of early-onset asthma identified in the older population
195 persist from those identified in younger adults requires further research.
196
197 **Adult-onset asthma**
198 Adult-onset asthma can be loosely sub-divided into long-standing asthma developing in
199 the late teens or early 20s, and later onset asthma beginning >40 years of age. A
200 consistent finding of adult-onset asthma is a lower rate of atopy, and a higher BMI and
201 frequency of co-morbidities compared to adults with EOA (15). In SARP, those developing
202 asthma ~42 years of age were mainly females (25). Despite a shorter asthma duration,
203 they had high rates of health care utilization for asthma including oral corticosteroid
204 bursts, which were out of proportion compared to their degree of airflow obstruction. In
205 the UK study however, these subjects with later onset asthma were more likely to be
206 male, have a lower BMI (27 kg/m^2), but they also had high uses of health care resources
207 for asthma (26). This cluster tends to be eosinophil predominant, with higher numbers
208 than with EOA (29). Amelink also reported that in middle-age adult patients with late onset
209 asthma (~41 years of age), those with more severe disease had more nasal symptoms
210 and nasal polyposis, higher blood neutrophil counts and higher sputum eosinophilia than
211 those with less severe disease (29).
212
213 The Detroit aging cohort identified two groups of adult-onset asthma; one with a later
214 onset and the other with longer-standing disease (27). The group with later onset (i.e.,
215 shorter duration of disease) had had a lower FEV1, higher rates of fixed obstruction

(23%), and with a high BMI (32.0 kg/m^2). The longer standing group had a higher FEV1%, and no fixed airway obstruction, and a lower BMI. Data on sputum analysis was not captured.

Progression to COPD/severe asthma

The co-existence of asthma and COPD is common, particularly in older populations. Estimates suggest that this overlap occurs in ~20% of patients with airway disease (30), with a higher prevalence in those >50 years old. In a New Zealand population-based survey, a subgroup of 469 participants >50 years of age underwent complete pulmonary function testing; 96 (20.5%) were defined as having COPD, and 53/96 (55%) exhibited features of both asthma and COPD (31).

Whilst exposure to noxious particles is recognized as the most important risk-factor for the development of COPD, there are other factors. Childhood asthma itself increases the susceptibility to COPD. In a longitudinal analysis of the European Community Respiratory Heath Survey (ECRHS) I and II cohorts both childhood asthma (men OR=10.48 [6.10 to 18.03], p= 0.001, women OR=3.74 [1.55 to 9.02], p=0.003) and paternal asthma were associated with COPD development. The risk increased with the number of childhood disadvantage factors such as maternal asthma, paternal asthma, childhood asthma, respiratory infections and maternal smoking. The OR was 1.7 (95% CI 1.1 to 2.6) and 1.6 (95% CI 1.01 to 2.6) for males and females respectively when one childhood

disadvantage factor was present. This increased to an OR of 6.3 (95% CI 2.4 to 17) for men and 7.2 (95% CI 2.8 to 19) for women when ≥3 factors were present (32).

IMPACT OF AGING ON INFLAMMATION

With increasing age, there are potential alterations of aging on the innate and adaptive immune responses which can occur simultaneously. "Immunosenescence," is a "blunted" response after a pathogenic threat or tissue injury. Despite an inability to proliferate, some senescent cells remain alive, functioning at an altered capacity. This results in "inflammaging," an increased low-grade basal systemic inflammation (e.g., IL1-β, IL-6 and TNF-α) in the absence of an overt infection (33). These immune alterations with aging must be taken into account when measuring inflammatory markers in older adults with asthma. For example, there is an age-related increase in sputum neutrophil counts, regardless of the presence of airway disease (34-36). In adults over the age of 20 years, there appears to be an increase in neutrophil percentage of 0.46% per year (37).

Induced sputum represents a gold standard test for the measurement of airway inflammation, although it is mainly a research tool. The inflammatory asthma phenotypes and endotypes in older patients have not been as well characterized as in younger adults. However there is emerging evidence that there may be some important inflammatory subsets of older patients with asthma. A T2-ultra high group (diagnosed by elevated sputum RNA-seq) was more prevalent in older adults with asthma. These patients have high levels of sputum eosinophils and neutrophils, elevated FENO, elevated blood

eosinophils (470 cells/μL), low IgE, and respond poorly to corticosteroids (38, 39). Additionally, there appears to be another subset of older patients with asthma with a mixed T1/T2 component, characterized by elevated sputum neutrophils and eosinophils, IL-5, IL-6, IL-8, which was not secondary to the effect of aging (34). Increased sputum neutrophils and IL-6 in the older population was related to decreased asthma control and increased use of health care resources for asthma. There is strong data in studies with patients (~58 years old) with asthma that neutrophilic asthma is associated with increased systemic inflammation, identified by increased CRP (40, 41). Systemic IL-6 is also associated with poorer asthma outcomes (decreased FEV1 and increased exacerbations) (42). In another study comparing asthma, COPD and asthma/COPD overlap patients >55 years old, no statistical differences were seen between sputum neutrophil and eosinophil counts, or serum IL-6 or hsCRP (43). Therefore some older patients with asthma likely have an important systemic inflammatory component of their disease, much like COPD. These similarities also highlight the additional complexities for older people with asthma. The changes in inflammation with aging and obstructive lung disease may be associated with an increased risk of ICS treatment failure with aging, although this requires additional study (44).

IMPACT OF GENDER AND AGING

The relationship between sex hormones, aging and asthma are complex and can impact both early onset and late onset asthma. Menopause may have a protective role in early-onset asthma. Asthma exacerbations are reported in relation to the menstrual cycle, typically in the week preceding the onset of menstruation. The probability of having severe

asthma is higher in males after age 45, but not in females of the same age (45, 46). In the National Inpatient Samples 2011-2012, the risk of asthma-related respiratory failure continued to rise in men after 60, but not in females (46). The underlying mechanisms of these differences are likely multifactorial and include gender differences in asthma symptom perceptions or health-seeking behaviors (47, 48). However, new onset asthma during or after menopause is more likely to be severe and less responsive to anti-inflammatory treatment (49).

Pregnancy

Pregnancy leads to poor asthma control in one third of women (50), increasing the risk of acute attacks (51-54), which may lead to adverse fetal outcomes (51-54). Optimized management of asthma during pregnancy, through appropriate pharmacotherapy and self-management education leads to improved health outcomes for the offspring (51, 52). A personalized approach to managing asthma therapy in pregnancy based on a FeNO guided treatment algorithm compared to symptom-based management, led to a 50% reduction in acute attacks during pregnancy. Additionally, the incidence rate ratio of doctor-diagnosis asthma for the offspring of women treated with a FeNO protocol compared to symptom-based alone, was significantly lower in the former ($p=0.04$) potentially contributing to a primary prevention strategy for reducing the incidence of childhood onset asthma (55).

CONFOUNDING FACTORS ACROSS ADULTHOOD

There are several important co-morbidities, or “treatable traits,” often associated with aging, which increase rates of asthma hospitalizations and emergency room visits (56, 57). McDonald et al reported a cross-sectional study involving 100 patients (recruited from a tertiary care respiratory clinic) with obstructive airway diseases >55 years of age, recruited from a tertiary care respiratory clinic, who underwent a multidimensional assessment to characterize their treatable traits. Those with asthma expressed a mean (SD) of 10.3 (1.9) treatable traits; not different from those with COPD (11.3 (2.8)) and asthma/COPD overlap (43). Subjects undergoing multi-dimensional treatment of their traits, compared to those receiving usual care, had improved asthma outcomes and measures of inflammation (e.g., sputum, systemic) (58). Consequently, a comprehensive and multi-disciplinary approach is necessary for middle-aged and older patients with asthma.

Cardiovascular

Cardiovascular diseases (CVD) are more prevalent in older than younger adults. The presence of CVD worsens asthma outcomes and is more prevalent in patients with asthma, in particular those with severe airway disease (59-61). Conversely, recent studies have suggested that asthma (including late-onset disease) particularly if uncontrolled (62), is an independent risk factor for new-onset CVD (63-65). A decreasing FEV1, may predict future CVD, especially in patients with known obstructive lung disease (66).

There are potential mechanisms to explain the link between asthma and CVD. Increasing systemic IL-6 is associated with the presence of CVD with poorer outcomes (67-69). A subset of older patients with asthma appear to have a strong IL-6 component (34). Frequent oral corticosteroid use can also worsen CVD. A recent study suggested that in adults >70 years, who had the Apolipoprotein E (APOEε4) allele (associated with CVD and atherosclerosis (70), had a greater decline in FEV1 and FEV1/FVC (71). APOE deficient antigen sensitized and challenged mice developed airway hyperresponsiveness and mucous cell metaplasia (72, 73). The APOEε4 allele is associated with an increased innate response, thereby altering systemic and potentially airway inflammation (72, 74). Moreover, eosinophils promote thrombus growth and are able to be activated by oxidized LDL to activate macrophages from M2 to M1 (71).

Obesity

Older persons with asthma, compared to aged matched without asthma, are more likely to be obese, with increased abdominal adipose tissue (75, 76). The relationship between obesity, aging and asthma outcomes is likely multifactorial. Two studies of older patients with asthma reported that with increased BMI, there was a significant loss of asthma control (77, 78). However, when analysis was adjusted for depression and lower income in one of the studies, the relationship between obesity and asthma outcomes was lost, suggesting a complex relationship between these factors in the aged (78).

There are many reasons why obese patients with asthma have poorer outcomes; however, whether aging affects these mechanisms is not clear. Obesity is associated

with increased systemic T1 inflammation (i.e., TNF-α, IL-1β, IL-6), released from activated adipocytes and adipose tissue-resident cells, which "spill over" into the lungs (79, 80). Elevated sputum NLRP3, IL-1β and neutrophils are increased in obese patients with asthma, and after consumption of saturated fatty acids (80, 81). The relationship between obesity and neutrophilic asthma in females, may only be important for patients under <50 years of age, suggesting that sex hormones are an important component with obesity (82).

Physical inactivity

Physical inactivity is an important modifiable risk-factor associated with poor outcomes in the general population, including increased mortality (83). Physical inactivity is observed at higher rates in asthma compared to non-asthma control populations. The populations at higher risk of physical inactivity in asthma are females and older people (84). This is important as increased physical activity in asthma is associated with improved outcomes. In a cross-sectional study that evaluated physical activity in severe asthma, median age 59 (range 43 to 68), steps per day were strongly and independently associated with better exercise capacity (coefficient, 0.0169; 95% CI, 0.008-0.025; P < .001) (85). A systematic review reported in patients with asthma over different severities, similar results (84). Improving physical activity in asthma, and particularly in older people with asthma is a priority.

Depression

Depression is highly prevalent in female patients with asthma, particularly in the aged (57, 75, 86, 87). The impact of depression on asthma morbidity is substantial in this age group, associated with poor asthma control, more severe airway obstruction, poorer quality of life, and increased health care utilization (87-89). There are several mechanisms by which depression can exacerbate asthma, and whether these mechanisms differ with age is not clear at the present. The severity of depression has been associated with increased systemic T1 inflammation (i.e., IL-1β, IL-6, TNF-α) and markers of inflammation (i.e., CRP) (90, 91), often seen in patients with a more "neutrophilic" asthma. In other chronic diseases such as rheumatoid arthritis, coronary disease, and atherosclerosis, depression increases systemic inflammation (92-95) and peripheral neutrophilia (96). Although not specifically targeting older patients, in a study of 24 participants with asthma (mean age 44.45 years), depression was associated with increased sputum and serum IL-1β and IFN-γ, which were inversely associated with impaired bronchodilator response (97). Lower adherence to ICS in older patients with asthma was strongly associated depressive symptoms (98).

Chronic rhinosinusitis and nasal polyposis

Nasal polyposis is typically a disease of adult life. Up to 10% of the population report nasal polyposis (99) whereas imaging studies identify a prevalence of between 3% and 6.4% when using objective criteria (100). Nasal polyposis is a risk factor for adult-onset asthma (101), difficult-to-control asthma, asthma exacerbations, and increased mortality (102). Analyses identify both eosinophilic and noneosinophilic types of nasal polyposis

(103, 104), with noneosinophilic forms having a better surgical outcomes (104). Aspirin sensitivity is also associated with nasal polyposis and asthma, and is termed AERD, with a prevalence of 9.6%, increasing to 40% in patients with allergic fungal sinusitis (105). Therapeutic options for chronic rhinosinusitis with nasal polyposis include intranasal corticosteroid use, systemic corticosteroids, sinonasal surgery (106) and T2-directed monoclonal antibody therapy such as dupilumab (107).

Multiple medications for other co-morbidities

Older people with multiple morbidities may experience adverse effects from medication interactions (108). In older people with multiple comorbidities and polypharmacy there is an increased risk of adverse drug effects that relate not only to drug – drug interactions (eg. statins and macrolides) but also drug-disease interactions (e.g beta blockers in asthma). In addition to drug interactions other factors related to multiple medications impact asthma in older individuals. A prospective, multicenter Korean study reported that fewer medications for comorbidities predicted improved-asthma control in patients with asthma (OR = 0.863, P = 0.004) (109) . Furthermore, the use of more medications to treat comorbid conditions is associated with an increase in suboptimal treatment adherence (110).

Smoking

Smoking is a particularly important risk-factor for patients with asthma irrespective of age, but there are some populations more likely to smoke. Smoking prevalence in patients with asthma overall is similar to that of the general population (approximately 15%) (111, 112).

Adults with late-onset asthma have higher smoking rates compared to those with early onset (113).

Smoking significantly complicates asthma. It is associated with higher treatment requirements for ICS with reduced responsiveness (114), accelerated lung function decline (115), and increased risk of severe attacks (111, 116). Smoking cessation is a priority and strategies should be personalized to the asthma population taking into account the age of the patient (112).

Cognition and asthma self-management

Asthma self-management, including adherence to controller medications, correct use of inhaler devices, trigger avoidance, use of asthma action plans, and peak flow monitoring, are important determinants of asthma control. Unfortunately, studies have consistently reported that less than half of adult asthma patients are adherent to these key self-management behaviors and that low adherence is associated with worse disease outcomes (117, 118). Older adults with asthma face even greater barriers and appear to have lower rates of adherence to self-management compared to younger individuals (119).

Two factors that can negatively impact asthma self-management in older adults are low health literature and impaired cognitive function (120, 121). Health literacy is defined as the ability to gather, process and understand the health information needed to make health care-related decisions. Low health literacy is more prevalent among adults >65

439 years of age (affecting up to 60% of individuals) and has been associated with lower
440 adherence to asthma medication as well as worse asthma control and poorer quality of
441 life (121-123). Similarly, age-related cognitive decline (particularly memory problems and
442 decreased executive function) is related to decreased ability to self-manage asthma
443 (124). Difficulties remembering health care provider instructions for self-management,
444 problems handling complex medication regimens (common among older patients), and
445 challenges managing acute attacks are some of the barriers to effective self-management
446 faced by asthma patients with cognitive decline. Moreover, illness beliefs (e.g.,
447 conceptualizing asthma as an acute illness only present when having symptoms) and
448 concerns about medications (e.g., ICS cause dependence or are toxic) are strong
449 predictors of lower adherence to asthma medications and may explain, in part, the
450 relationship between low health literacy and cognitive problems with self-management
451 (125, 126). This knowledge has led to the development of effective comprehensive
452 personalized asthma self-management interventions for older asthmatics targeting these
453 beliefs and other key barriers to asthma control (127).
454
455 **Inhaler device selection**
456 Inhaled medication is the cornerstone of asthma pharmacotherapy. Unfortunately
457 suboptimal use of inhaler therapy is frequently observed in people with asthma, and age
458 significantly compounds this issue. In a group of patients with airway disease (aged 55-
459 87 years of age), 48.5% had inadequate inhaler technique and 50% were using several
460 different types of inhalation device, termed inhaler device polypharmacy (43). Older
461 patients with decreased cognition and health literacy are at particular risk of poor inhaler

technique (128, 129). Factors that should be considered when prescribing inhaled medications include efficacy, safety and proficiency. In addition to adherence, cost and patient preference the assessment of proficiency should incorporate age related factors such as peak inspiratory flow rate, manual dexterity, coordination and handling capacity and comorbidities that affect device use such as cognitive and vision impairment (130, 131). Figure 2 highlights the difficulties faced by older people and presents an algorithm for device selection.

DIFFERENCES IN DIAGNOSTIC APPROACH ACROSS ADULTHOOD

Asthma symptoms

Many of the asthma symptoms in younger adults (i.e., episodic wheezing, shortness of breath, cough and chest tightness) are characteristic of those in older adults. However, in older patients, dyspnea is a common symptom of other disorders including cardiac disease, anemia or other lung diseases, therefore asthma as an etiology of these symptoms may be overlooked. Additionally, some older patients may limit their activity to avoid getting dyspneic. Older patients often have a decreased perception of asthma symptoms despite significant airway obstruction (132).

Lung Function testing

There are age-related factors which must be considered when interpreting lung function measurements. Changes in the structure of the aging lung decrease the FEV_1/FVC ratio; age-adjusted values are recommended to avoid over-diagnosis of obstruction (133).

Aging increases BHR to methacholine (134), therefore, provocation testing may be over-interpreted. Although >80% of older persons can achieve ATS acceptable results to perform spirometry, it may be difficult for those who are frail (135). Poor coordination and muscle weakness in some patients may produce inaccurate readings of peak expiratory flow (136).

CONCLUSION

Asthma is a common condition which affects individuals across the lifespan. Despite improvement in outcomes for people with asthma over the last few decades, outcomes for remain poor, particularly for certain age groups including older people. The impacts of asthma in adulthood vary according to age, and include pathophysiological and biological changes, self-management and behavioral traits and increasing prevalence and severity of comorbidity that are impacted by advancing age. Life events such as pregnancy and behaviors like smoking are some of the features that affect individuals with asthma during younger age. Recognizing the needs of individuals with asthma according to their life stage will enable a more personalized approach patient care and improve patient outcomes.

506 **Table 1: Impact of asthma risk factors across adulthood**

	AGE (Yrs)			
	20-40	**41-65**	**66-75**	**>75**
Airway caliber			Age-related airflow limitation confounds diagnosis, Lung aging, Reduced FEV1 response to treatment	Age-related airflow limitation confounds diagnosis, Lung aging, Reduced FEV1 response to treatment
Airway inflammation	T2 asthma is prevalent Neutrophilic asthma ~10%	Late onset eosinophilic asthma develops, Age related increase in airway neutrophils	Inflammaging and reduced corticosteroid response Increase in airway neutrophils	Inflammaging and reduced corticosteroid response Increased airway neutrophils
Triggers	Occupational exposures	Occupational exposures		
Comorbidities	Allergic rhinitis Obesity	Nasal polyps Obesity	Comorbidity prevalence increases Obesity	Comorbidity prevalence Increases Obesity
Life events	Occupation relevant Pregnancy can worsen asthma Menstrual Cycle and perimenstrual exacerbations	Occupation relevant Menopause: variable effects possible Menstrual Cycle and perimenstrual exacerbations	Retirement+	Social Isolation
Treatment			Reduced response to corticosteroids Medication polypharmacy -drug-drug interactions	Cognitive impairment limits inhaler device choice, and adherence Medication polypharmacy - drug-drug interactions

Self Management	Adherence	Adherence	Adherence Increased age related factors affecting inhaler technique(Fig 2)	Adherence Increased age related factors affecting inhaler technique(Fig 2) Cognitive impairment

+ Retirement is expected to be associated with reduced occupational triggers, and retirees report reduced perception of asthma triggers (137).

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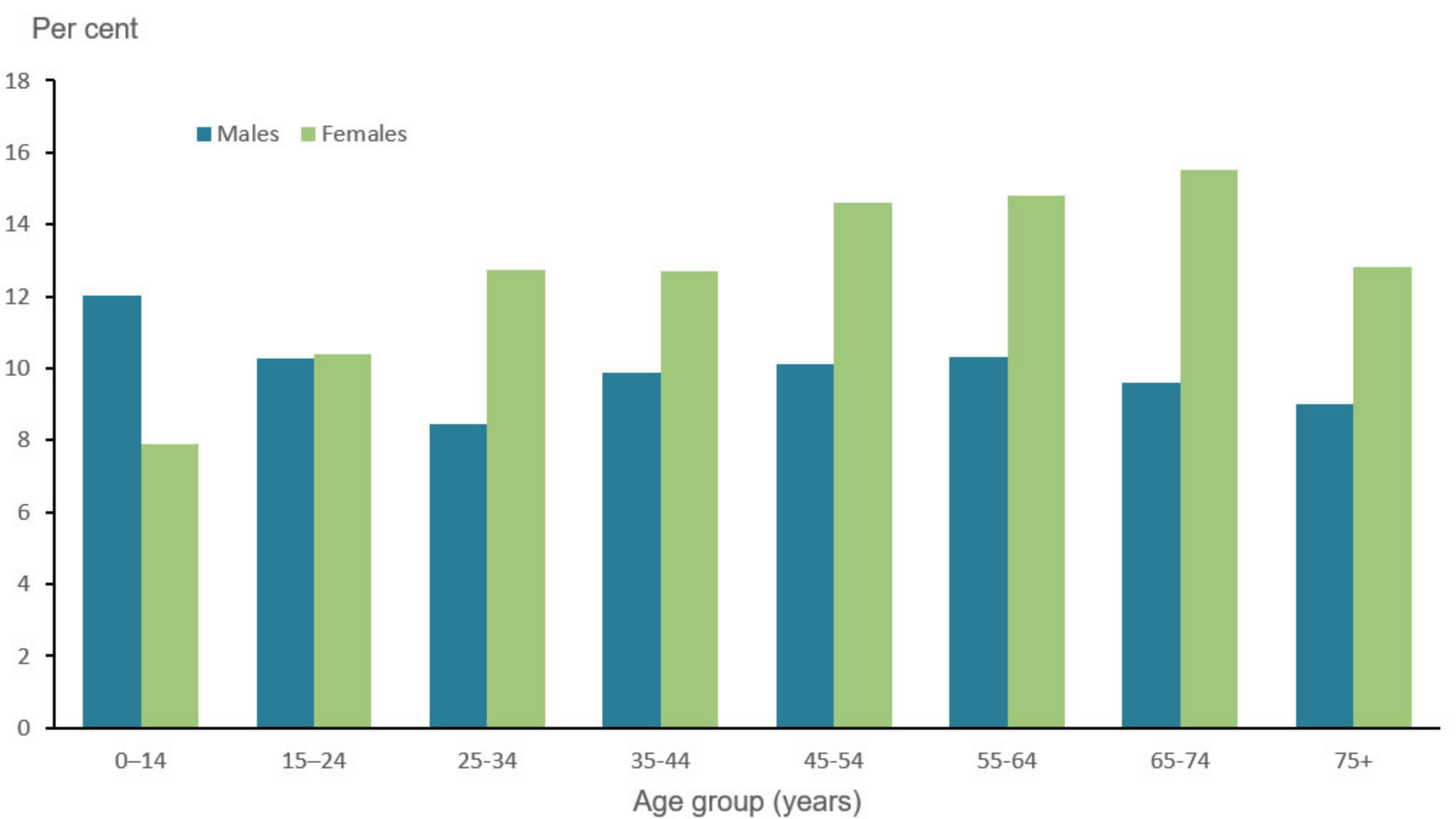
Figure Legends:

Figure 1: Prevalence of asthma, by age and sex, 2017–18. Refers to people who self-reported that they were diagnosed by a doctor or nurse as having asthma (current and long-term). Source: Australian Institute of Health and Welfare.

Figure 2: Challenges with the use of inhalation therapy in elderly patients with asthma, and an algorithm for appropriate inhaler device selection. HCP, health care professional. (Re-used with permission (130)).


Per cent
18
16
14
12
10
8
6
4
2
0
Males
Females
0–14
15–24
25-34
35-44
45-54
55-64
65-74
75+
Age group (years)

Difficulties faced by elderly patients

- Cognitive impairment and dementia
- Worsening hypoxia or hypercapnia from COPD or COPD exacerbations
- Neuromuscular conditions (eg, Parkinson's disease or complications after a stroke)
- Altered metabolism and increased risk of side effects
- Increased number of critical errors
- Loss of physical hand and finger muscle strength
- Arthritis or joint pain
- Comorbidities and complexity of accompanying medication regimens

Proposed algorithm for inhaler selection in the elderly

1. **Patient ability to use device:** cognitive function, manual dexterity, hand strength
2. **Medication availability/cost/ reimbursement**
3. **Device considerations/ patient preference:** eg, time required to administer and clean, portability, convenience
4. **Educational session:** HCP demonstrates correct technique and assesses patient technique after training; device gets prescribed for a trial period
5. **Therapeutic assessment:** review adherence/ therapeutic impact; assess technique; shared decison-making regarding changes to therapy (re-assess step 2–5)