



# Sex differences in health services and medication use among older adults with asthma

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**ABSTRACT** Sex differences are well documented in chronic disease populations with cardiovascular disease and diabetes. Although recent research has suggested that asthma is more severe in older women compared to men, the extent of this difference remains poorly understood. The objective of this study was to compare rates of asthma-specific health services use (HSU) and medication use, between older women and men with asthma.

This population-based cohort study included 209054 individuals aged  $\geq 66$  years with asthma from health administrative data in Ontario, Canada. The primary exposure was sex. Outcomes included asthma-specific HSU (spirometry, emergency department (ED), hospitalisation, physician office and specialist visits) and medication use (asthma controller and reliever prescriptions). Negative binomial regression models adjusted for age, socioeconomic status and comorbidities were used to ascertain outcomes by sex from 2010 to 2016.

Compared to men, women had lower rates of spirometry (adjusted relative rate (ARR) 0.87, 95% CI 0.85–0.89) and specialist visits for asthma (ARR 0.93, 95% CI 0.90–0.96), but higher rates of asthma-specific ED (ARR 1.43, 95% CI 1.33–1.53) and physician office visits (ARR 1.03, 95% CI 1.01–1.05). Women also had lower asthma controller (ARR 0.98, 95% CI 0.97–0.99) but higher asthma reliever (ARR 1.03, 95% CI 1.02–1.05) prescription fill rates, compared to men.

These findings may indicate poorer disease control, greater asthma severity and poorer access to specialist asthma care in women.



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**Older women with asthma have lower rates of spirometry, asthma specialist visits and asthma controller fill rates, and higher rates of ED visits for asthma, physician office visits for asthma and asthma reliever fill rates, compared to men** <http://bit.ly/33PfMD6>

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## Introduction

Research has demonstrated that sex is an independent predictor of disease among the chronic disease populations with cardiovascular disease and diabetes [1–6]. However, population-based research on sex differences is lacking for respiratory conditions, and in particular for the older subpopulation of people with asthma.

Asthma affects approximately 334 million individuals worldwide [7], with the incidence and prevalence varying by age and sex [8–10]. The burden of asthma is particularly high at age 5–19 years and >60 years, with the former contributing the most to disability and the latter to premature deaths [7].

Sex differences in asthma prevalence, health services use (HSU), morbidity and mortality have been well reported in the literature; however, many studies excluded the older adult population [8, 10]. SCHATZ and CAMARGO JR [10] studied asthma prevalence, healthcare utilisation and medications in those with asthma aged 2–64 years using data from Southern California Kaiser-Permanente Medical Care Program (San Diego, CA, USA). The authors found higher asthma healthcare utilisation in males during childhood and teenage years, but higher utilisation for females among those aged 23–64 years. While girls typically have a lower risk of asthma than boys, women become more susceptible to developing asthma after puberty [8, 10, 11].

Recent research studies in Australia [12] and the USA [13] have shown that asthma is more severe in older women compared to men. Compared to men, older women (aged  $\geq 50$  years) with asthma tend to have more frequent asthma acute HSU [13], a doubled risk of emergency department (ED) visits for asthma [14] and a 1.2-fold increased risk of death, independent of age, comorbidities, demographics, residence and social support [12].

In Canada, the prevalence of asthma is higher in older women than in older men. Among Canadians aged  $\geq 55$  years, asthma is prevalent in about 9% of women compared to 6–7% of men [15]. Similarly, in Ontario, the asthma prevalence is 60% and 33% higher in women than in men for those aged 50–69 years and >70 years, respectively [16].

Despite the growing body of literature on sex differences among older individuals with asthma, few studies have used population-based data. Thus, the objective of this study was to use population-based data from Ontario, Canada, to compare rates of asthma-specific health services and medication use, between older men and women with asthma. Our findings will better the understanding of sex-specific gaps of asthma burden.

## Methods

### *Study design and data sources*

This population-based study used a cohort design with data acquired from Ontario health administrative databases housed at ICES (formerly the Institute for Clinical Evaluative Sciences) in Toronto, Ontario, Canada. In Ontario, there is routine collection of HSU data for research purposes. Using health administrative data allowed us to study HSU over time without selection or response bias. The Ontario Health Insurance Plan (OHIP) claims database captures physician office visits, the National Ambulatory Care Reporting System (NACRS) captures ED visits, the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD) captures hospitalisations, the Ontario Drug Benefit (ODB) database captures prescriptions filled, and the provincial Registered Persons Database (RPDB) provides sociodemographic information.

### *Study population*

The study cohort included 209 054 Ontario residents aged  $\geq 66$  years with prevalent asthma on 1 April 2010 (which served as baseline). Asthma prevalence was defined using the Ontario Asthma Surveillance Information System (OASIS), which identifies individuals with asthma based on a validated health administrative definition of two or more outpatient visits for asthma in two consecutive years, or one hospitalisation for asthma. This definition has demonstrated a sensitivity of 84% and specificity of 76% in the Ontario adult population [17]. Individuals were excluded from the cohort if they had missing data for age or Ontario residence postal code, or if they did not have a valid Ontario health card number (*i.e.* were uninsured). Participants were followed from baseline until 31 March 2016, death, or they moved outside of Ontario.

### *Exposure and outcome measurement*

The primary exposure was sex, acquired from the RPDB. The primary outcomes were rates of asthma-specific spirometry, ED, hospitalisation, physician office and specialist visits, and prescription fill rates for asthma controller and reliever medications. Rates were derived from outcome counts divided by total follow-up time for each individual. Visit types were identified using International Classification of Disease, 10th Revision (ICD-10) codes and OHIP billing codes. Asthma was defined using ICD-10 codes J45 and J46, and OHIP code 493.

### *Covariates*

Socioeconomic status was measured by proxy using the 2011 Ontario Marginalization Index [18]. The Ontario Marginalization Index uses census data to measure four dimensions of marginalisation (*i.e.* material deprivation, dependency, ethnic concentration and residential instability) at the neighbourhood level. Individuals are assigned a value from 1 (least marginalised) to 5 (most marginalised) for each domain based on their residence location at baseline. Income was also measured by proxy using income quintile (1 to 5), with individuals residing in census divisions with the lowest 20% household income assigned 1, and those in the highest 20% assigned 5. Residence at baseline was measured as “rural” if the individual resided in a community of  $\leq 10\,000$  people, and otherwise as “urban” [19]. Residence at baseline was also measured by local health integration networks (LHINs). LHINs are geographical regions established across Ontario to plan, fund and coordinate local community-based health services [19]. A co-diagnosis of COPD comorbidity was adjusted as a covariate. COPD was defined using a validated health administrative definition of one or more ambulatory care claims for COPD in two consecutive years, or one hospitalisation for COPD [20]. In addition, the number of comorbidities was defined using the Collapsed Aggregated Diagnosis Groups (CADGs) from the Johns Hopkins ACG System Version 10. The CADGs categorise International Classification of Diseases, 9th Revision (ICD-9) and ICD-10 diagnostic codes based on severity and the likelihood of persistence of the respective health condition [21]. The CADGs consist of a series of 12 variables that measure the expected healthcare utilisation of an individual in the 2 years prior to a time point. Other covariates included age at baseline and age at asthma prevalence.

### *Statistical analysis*

Baseline characteristics were described for men and women using frequencies and proportions for categorical variables and means with standard deviations for continuous variables. Differences between men and women on baseline characteristics were compared using a standardised difference score, in order to provide a statistical measure of differences between groups that would not be influenced by the study’s large sample size. Crude yearly rates of HSU and prescriptions filled were calculated and compared between men and women. The majority of asthma controller prescriptions filled were for a 1-month supply, while the majority of asthma reliever prescriptions filled were for  $\leq 1$  month. Multivariate negative binomial regression was used to measure the association between sex and health services and medication outcomes, while adjusting for important confounding variables as outlined. Follow-up time was included as an offset. A rate ratio with 95% confidence interval was produced. In all analyses, a p-value of  $<0.05$  was used to determine statistical significance. All analyses were carried out using SAS Enterprise guide 6.1 (SAS Institute Inc., Cary, NC, USA).

### *Research ethics*

Ethics approval for this study was obtained from the Hospital for Sick Children, in Toronto. Individual participant consent was not required for this study due to exclusive use of large, anonymised population databases.

## **Results**

### *Descriptive statistics*

The study cohort consisted of 209 054 individuals aged  $\geq 66$  years with prevalent asthma who resided in Ontario, of which 131 628 (63%) were women (table 1). Approximately half of the cohort were aged 66–75 years (younger age category) at baseline (1 April 2010) (52% and 54%, for women and men, respectively). The average asthma duration (time from registered asthma onset to study entry) was 12 years for women and 11 years for men. Women and men were both followed for an average of 5 years from baseline to the end of the study (31 March 2016).

Women and men were similar with regard to income quintile and across several dimensions of the Ontario Marginalization Index. However, a greater proportion of women (31%) compared to men (24%) were in the highest quintile of the residential instability dimension, which provides a measure of the proportion of the population that lives alone/in apartment buildings/in non-owned properties, among others. A similar proportion of women (11%) and men (13%) lived in rural areas, while the majority of the population resided in urban locations at baseline.

A lower proportion of women had histories of COPD (57%), diabetes (37%), acute myocardial infarction (7%) and non-lung, non-breast cancer (14%) compared to men (66%, 42%, 13% and 28%, respectively). However, the overall burden of comorbidity, measured through the number of CADGs, was similar between women and men ( $5.6 \pm 2.1$  and  $5.7 \pm 2.1$ ). Approximately one-fifth of women (21%) died during follow-up, compared to one-quarter of men (25%). For both women and men, the most common causes of death were diseases of the circulatory system, neoplasms and diseases of the respiratory system.

TABLE 1 Characteristics of the study population<sup>#</sup> by sex

Characteristic	Women	Men	Standardised difference <sup>¶</sup>
<b>Subjects</b>	131 628	77 426	
<b>Age group at asthma prevalence years</b>			
47–59	43 245 (32.85)	24 712 (31.92)	0.020
60–69	52 023 (39.52)	32 297 (41.71)	0.045
70–99	36 360 (27.62)	20 417 (26.37)	0.028
<b>Age group at baseline<sup>+</sup> years</b>			
66–75	68 022 (51.68)	41 609 (53.74)	0.041
76–85	46 769 (35.53)	28 384 (36.66)	0.024
86–99	16 837 (12.79)	7 433 (9.60)	<b>0.100</b>
<b>Asthma duration years</b>	11.88±5.43	11.41±5.62	0.086
<b>Follow-up time years</b>	5.20±1.60	5.04±1.73	0.097
<b>Income quintile</b>			
1 (lowest)	28 790 (21.87)	14 771 (19.08)	0.069
2	28 197 (21.42)	16 074 (20.76)	0.016
3	25 904 (19.68)	15 527 (20.05)	0.009
4	24 845 (18.88)	15 550 (20.08)	0.031
5 (highest)	23 385 (17.77)	15 227 (19.67)	0.049
Missing	507 (0.39)	277 (0.36)	0.005
<b>Rural</b>			
Yes	15 065 (11.45)	9 951 (12.85)	0.043
No	116 531 (88.53)	67 455 (87.12)	0.043
Missing	32 (0.02)	20 (0.03)	0.001
<b>Ontario Marginalization Index</b>			
Deprivation quintile			
1 (lowest)	24 023 (18.25)	15 166 (19.59)	0.034
2	24 304 (18.46)	15 019 (19.40)	0.024
3	25 673 (19.50)	15 392 (19.88)	0.009
4	26 892 (20.43)	15 418 (19.91)	0.013
5 (highest)	28 941 (21.99)	15 523 (20.05)	0.048
Missing	1 795 (1.36)	908 (1.17)	0.017
Dependency quintile			
1 (lowest)	16 502 (12.54)	10 472 (13.53)	0.029
2	20 221 (15.36)	13 107 (16.93)	0.043
3	22 224 (16.88)	13 891 (17.94)	0.028
4	25 518 (19.39)	15 609 (20.16)	0.019
5 (highest)	45 368 (34.47)	23 439 (30.27)	0.090
Missing	1 795 (1.36)	908 (1.17)	0.017
Ethnic concentration quintile			
1 (lowest)	26 616 (20.22)	15 876 (20.5)	0.007
2	23 409 (17.78)	13 928 (17.99)	0.005
3	23 987 (18.22)	13 710 (17.71)	0.013
4	25 292 (19.21)	14 510 (18.74)	0.012
5 (highest)	30 529 (23.19)	18 494 (23.89)	0.016
Missing	1 795 (1.36)	908 (1.17)	0.017
Residential instability quintile			
1 (lowest)	17 104 (12.99)	12 339 (15.94)	0.084
2	20 979 (15.94)	14 481 (18.70)	0.073
3	24 155 (18.35)	15 385 (19.87)	0.039
4	27 165 (20.64)	15 550 (20.08)	0.014
5 (highest)	40 430 (30.72)	18 763 (24.23)	<b>0.150</b>
Missing	1 795 (1.36)	908 (1.17)	0.017
<b>Prevalence of other health conditions</b>			
COPD	75 507 (57.36)	50 895 (65.73)	<b>0.170</b>
Diabetes	49 022 (37.24)	32 845 (42.42)	<b>0.110</b>
Hypertension	112 497 (85.47)	64 136 (82.84)	0.072
Stroke	39 887 (30.3)	24 054 (31.07)	0.017
Congestive heart failure	34 517 (26.22)	22 578 (29.16)	0.066
Acute myocardial infarction	9 529 (7.24)	9 899 (12.79)	<b>0.190</b>
Lung cancer	4 272 (3.25)	3 315 (4.28)	0.055
Breast cancer	10 435 (7.93)	157 (0.2)	<b>0.400</b>

Continued

TABLE 1 Continued

Characteristic	Women	Men	Standardised difference <sup>¶</sup>
Other cancer	17814 (13.53)	21560 (27.85)	<b>0.360</b>
<b>Number of CADGs</b>	5.62±2.07	5.74±2.07	0.056
<b>Died during follow-up</b>			
Yes	27487 (20.88)	19254 (24.87)	0.095
No	104141 (79.12)	58172 (75.13)	0.095
<b>Cause of death</b>			
Diseases of the circulatory system	7778 (28.3)	5406 (28.08)	0.005
Neoplasms	5938 (21.6)	4849 (25.18)	0.085
Diseases of the respiratory system	5125 (18.65)	3882 (20.16)	0.038
Mental and behavioural disorders	1888 (6.87)	881 (4.58)	0.099
Diseases of the nervous system	996 (3.62)	578 (3.00)	0.035
Other	5490 (19.97)	3455 (17.94)	0.052
Missing	272 (0.99)	203 (1.05)	0.006

Data are presented as n, n (%) or mean±sd, unless otherwise stated. CADGs: Collapsed Aggregated Diagnosis Groups. #: n=209054; ¶: standardised difference of >0.1 generally considered different (shown in bold); \*: 1 April 2010.

**Rates of asthma-specific health services use and prescriptions by sex**

Women had fewer spirometry visits (24.1±64.6 per 100 person-years) and physician office visits (30.4±97.8 per 100 person-years) compared to men (32.4±91.2 and 31.7±107.9 per 100 person-years, respectively) (table 2). Rates of asthma-specific ED visits and hospitalisations were slightly higher among women (0.9±12.1 and 0.8±20.5 per 100 person-years, respectively) compared to men (0.7±6.8 and 0.4±9.7 per 100 person-years, respectively). Rates of asthma-specific specialist visits were similar between women and men (about 10.3±45.0 visits per 100 person-years for both sexes). Women filled fewer asthma controller (3.5±5.1 per person-year) and reliever (1.8±3.8 per person-year) prescriptions compared to men (4.0±6.0 and 2.0±4.8 per person-year, respectively).

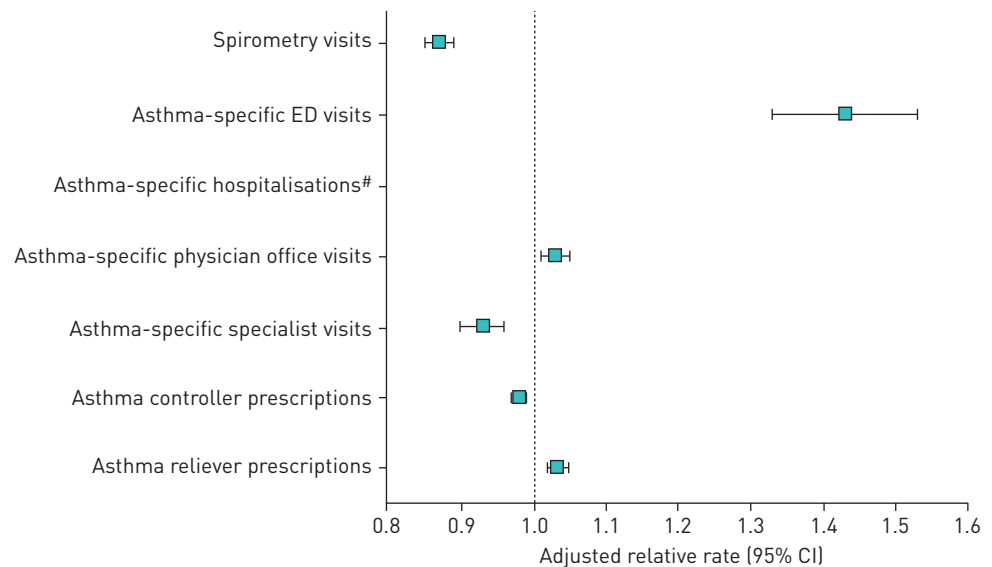
**Adjusted relative rates of asthma-specific health services use and prescriptions by sex**

The results of the multivariable negative binomial regression revealed that women had a 13% lower rate of spirometry (adjusted relative rate (ARR) 0.87, 95% CI 0.85–0.89) and a 43% higher rate of ED visits for asthma (ARR 1.43, 95% CI 1.33–1.53) (figure 1). Women also had a higher rate of physician office visits for asthma (ARR 1.03, 95% CI 1.01–1.05) and a lower rate of specialist visits for asthma (ARR 0.93, 95% CI 0.90–0.96). The negative binomial regression model for hospitalisations did not converge (logistic regression results are presented in the online supplementary material). With regard to medication use, women had a lower fill rate of asthma controller prescriptions (ARR 0.98, 95% CI 0.97–0.99) and a higher fill rate of asthma reliever prescriptions (ARR 1.03, 95% CI 1.02–1.05) compared to men. The multivariate regression models were adjusted for age at baseline, age at asthma prevalence, CADGs, Ontario

TABLE 2 Mean rates of asthma-specific health services use (HSU) and prescriptions by sex

Outcome	Women	Men	Standardised difference <sup>#</sup>
<b>Subjects</b>	131628	77426	
<b>Asthma-specific HSU per 100 person-years</b>			
Spirometry visits	24.1±64.6	32.4±91.2	<b>0.105</b>
Asthma-specific ED visits	0.9±12.1	0.7±6.8	0.025
Asthma-specific hospitalisations	0.8±20.5	0.4±9.7	0.029
Asthma-specific physician office visits	30.4±97.8	31.7±107.9	0.012
Asthma-specific specialist visits	10.3±45.0	10.4±47.2	0.003
<b>Asthma-specific medication use per person-year</b>			
Asthma controller prescriptions	3.5±5.1	4.0±6.0	0.088
Asthma reliever prescriptions	1.8±3.8	2.0±4.8	0.046

Data are presented as n or mean±sd, unless otherwise stated. #: standardised difference of >0.1 generally considered different (shown in bold).



**FIGURE 1** Forest plot for adjusted relative rates of asthma-specific health services use and prescriptions for women *versus* men. The multivariate negative binomial regression models were adjusted for age at baseline, age at asthma prevalence, Collapsed Aggregated Diagnosis Groups, Ontario Marginalization Index, local health integration networks, rurality and COPD; offset by  $\log(\text{years observed})$ . Data are shown for the study population ( $n=209\,054$ ). ED: emergency department. #: the negative binomial regression model did not converge.

Marginalization Index, LHINs, rurality and COPD. The unadjusted and adjusted relative rates are presented in the online supplementary material.

## Discussion

Recent research studies have suggested that asthma is more severe in older women compared to men [12–14]. However, the extent of this difference remains poorly understood. Using health administrative data from Ontario, our study was one of the largest population-based cohort studies to examine sex differences in older adults with asthma. In this study, we found that, compared to men, older women with asthma had lower rates of spirometry and specialist visits for asthma, and higher rates of ED and physician office visits for asthma. We also found that women had a lower asthma controller prescription fill rate and a higher asthma reliever prescription fill rate, compared to men. These differences may suggest poorer disease control, higher asthma severity and poorer access to specialist asthma care in older women. These results are consistent with the limited published literature.

Previous research has suggested that, while men and women may perceive asthma symptoms similarly, their approach to managing asthma symptoms and healthcare-seeking behaviour may differ [10]. Women tend to have an altered perception of breathlessness [14]. EBIHARA *et al.* [22] found that older individuals (64% female) had a decreased perception of airflow obstruction and this was associated with greater medication costs, hospitalisations and mortality, compared to those with a better perception of dyspnoea. To overcome the decreased perception of breathlessness, the National Institutes of Health (NIH) asthma guidelines recommend periodic assessment of asthma control with spirometry [14, 23]. However, similar to our observation, SIKJÆR *et al.* [24] found that significantly fewer women than men had undergone pulmonary function testing, based on an Internet-based questionnaire administered to a random sample of the Danish population. The lower use of spirometry to measure and monitor lung function may be due to either provider or patient behaviours. Therefore, it is important to increase awareness of the importance of monitoring asthma control, such as with spirometry, among both providers and individuals with asthma, to ensure patients receive the best asthma care.

Researchers in the USA have found that asthma specialists provide more thorough care than primary care physicians [25]. Individuals treated by an asthma specialist were more likely to own and use a steroid inhaler and peak flow meter daily [25]. Asthma specialists also provided more information on preventing and controlling asthma attacks [25]. However, we found that women had lower rates of specialist visits for asthma compared to men. Among the cardiovascular disease population, a lower referral rate to cardiac rehabilitation has been widely reported among women [26]. Our findings may indicate a similar lower referral rate to specialist asthma care in older women with asthma. Improving access to asthma specialist

care among older women with asthma may lead to improved asthma disease management and reduced asthma morbidity.

In this study, higher rates of ED and physician office visits for asthma were observed among older women, compared to men. ANTONICELLI *et al.* [27] found that HSU was positively associated with asthma severity. Therefore, these findings may indicate greater asthma severity among women. The trend of greater asthma morbidity in older women is also observed in other developed countries such as Australia and the USA [12, 14]. Researchers have suggested that there are multiple factors at play: biological, lifestyle, societal, environmental, diagnostic, disease management, comorbidities (*e.g.* COPD) and access to care. The extra burden may be due to sex-specific differences in biological and physiological features, such as greater fluctuations in hormone levels [28, 29], generally lower IgE levels [30], greater prevalence of atopy [28], smaller lung size and airway calibre [8, 31] and thus expedited declines in airway capacity [28] in older women. Increased asthma HSU in older women may be related to the menopause, which increases the risk of asthma attacks [32, 33]. It may also be related to poor asthma control [28], such as improper use of respiratory inhalers [34] and a lower asthma controller prescription rate [11, 35].

We found that women had a lower asthma controller prescription fill rate and a higher asthma reliever prescription fill rate, compared to men. In a national population-based study in South Korea, similar to our observation, CHOI *et al.* [35] found that the inhaled corticosteroid prescription rate among individuals with asthma was lower among females and those aged >90 years. Underutilisation of controller medications among older adults with asthma may lead to preventable HSU [36]. Additionally, since asthma reliever medications are used to rapidly treat asthma symptoms, a higher asthma reliever prescription fill rate among older women may indicate more poorly controlled asthma [36].

The descriptive mean rates showed no difference in the outcomes between women and men except for spirometry visit rates. However, when adjusted for the confounders, all rates indicated statistically significant differences. Specifically, women had a statistically higher relative rate for ED visits, physician office visits and reliever medications filled, but lower relative rate for spirometry visits, specialist visits and controller medications filled. This suggested that negative confounding influenced the unadjusted observed rates.

Strengths of this study include the use of health administrative data to collect information about asthma-specific HSU and prescriptions in Ontario. This data source allowed us to study longitudinal HSU without selection or response bias, and may allow us to generalise our results to other populations of older individuals with asthma. However, using health administrative data, we were limited in our ability to adjust for important lifestyle factors that could confound the relationship between men and women and HSU, such as smoking, body mass index and health-seeking behaviours. Using this data source, we were also limited in our ability to examine prescriptions written and prescriptions taken. Furthermore, our ability to identify individuals with asthma was limited by the sensitivity and specificity of our asthma definition. It is possible that individuals in our study cohort were misclassified as individuals with asthma.

Our findings may help inform the future development of prevention and management initiatives that aim to decrease the risk of poor health outcomes and thereby improve the quality of life in older women living with asthma. A better understanding about the sex-specific risk factors for asthma morbidity in older women, particularly the high-utilisation group, would also facilitate targeted monitoring in the future.

### Conclusion

Older women with asthma had lower rates of spirometry, asthma specialist visits and asthma controller fill rates, and higher rates of ED visits for asthma, physician office visits for asthma and asthma reliever fill rates, compared to men. These differences may indicate poorer disease control, greater asthma severity and poorer access to specialist asthma care in women. Future research should aim to identify factors that explain these sex differences, to ensure optimal asthma care for all.

Conflict of interest: None declared.

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