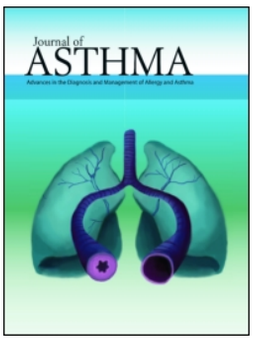

Journal of Asthma

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ijas20

Gender differences in the perception of asthma respiratory symptoms in five Latin American countries

Rodrigo C. Borges, Marcela B. Alith, Oliver A. Nascimento & José R. Jardim

To cite this article: Rodrigo C. Borges, Marcela B. Alith, Oliver A. Nascimento & José R. Jardim (2021): Gender differences in the perception of asthma respiratory symptoms in five Latin American countries, Journal of Asthma, DOI: 10.1080/02770903.2021.1922914

To link to this article: https://doi.org/10.1080/02770903.2021.1922914

JOURNAL OF ASTHMA
https://doi.org/10.1080/02770903.2021.1922914

Gender differences in the perception of asthma respiratory symptoms in five Latin American countries

Rodrigo C. Borges, PT, PhD[a], Marcela B. Alith, PT, PhD[a,b], Oliver A. Nascimento, MD[b,c] and José R. Jardim, MD[b,c]

[a]Hospital Universitário da Universidade de São Paulo (USP), São Paulo, Brazil; [b]Centro de Reabilitação Pulmonar da Escola Paulista de Medicina da Universidade Federal de São Paulo (EPM/Unifesp), São Paulo, Brazil; [c]Respiratory Division of EPM/Unifesp, São Paulo, Brazil

ABSTRACT

Objectives: To determine the differences between sexes in perceptions of asthma symptoms, asthma control, daily activities, and symptom exacerbation in Latin American countries.

Methods: This cross-sectional study was performed using data from the Latin America Asthma Insight and Management (LA-AIM) study ($n = 2167$) carried out in Argentina, Brazil, Mexico, Venezuela, and Puerto Rico. Face-to-face interviews were conducted, and patients orally completed a 53-question survey assessing five main domains of asthma: symptoms, impact on daily activities, disease control, exacerbation, and treatment/medication.

Results: Of the 2167 participants, 762 (35.2%) were males and 1405 (64.8%) were females. Male participants smoked more than females, but history of rhinitis and allergies was more common in females ($p < 0.05$). Women aged 18–40 years had a higher proportion of uncontrolled asthma compared to men of the same age (37.8% and 30.0%, respectively). A higher proportion of symptomatic females reported more frequent symptoms (daytime cough, shortness of breath, breathlessness/wheezing, sputum, tightness in the chest, etc.) than males ($p < 0.05$). Females also experienced more limitations in sports/recreational activities, normal physical exertion, social activities, sleep, and daily activities. Females consulted with health professionals more often than males (67.8% and 59.6%, respectively; $p < 0.05$). Asthma caused a feeling of lack of control over life in 42.6% of females and 31.4% of males.

Conclusion: In Latin America, females report more asthma symptoms, poorer asthma control, more impact on their daily activities, and more visits with health professionals than males.

ARTICLE HISTORY
Received 31 October 2020
Revised 15 April 2021
Accepted 24 April 2021

KEYWORDS
Latin America;
asthma;
signs and symptoms;
quality of life;
activities of daily living;
sex

Introduction

In Latin America, the prevalence and severity of asthma are high, affecting approximately 40 million people (1). The prevalence of "current wheeze" ranged from 8.7% in Mexico to 30.8% in El Salvador, and the prevalence of "ever asthma" ranged from 6.9% in Mexico to 33.1% in Peru (2) among children aged 13–14 years. Urbanization, migration, adoption of a Western lifestyle, and environmental changes (including changes in diet, physical activity, hygiene, and exposure to allergens, irritants, and outdoor and indoor pollutants) influence the variability in asthma prevalence in Latin America (3). Moreover, in these countries, the prevalence of asthma and its associated morbidity is greater than that reported in traditionally high-prevalence countries such as the United States, but it remains neglected as a public health priority (3).

Females experience more asthmatic episodes than males with the same baseline pulmonary function (4). There are multiple reasons for this difference, such as differences in airway physiology and pathology, hormonal interference (5), risk of infectious diseases in childhood (6), and behavioral differences between sexes (7). Although differences have been reported between sexes in some clinical features of asthma (e.g. bronchial reactivity and degree of symptoms), so far, only the impacts of sex and age on different prevalence rates have been established (8).

Some studies carried out in Europe and Asia showed that asthma perception was higher among females and that they experienced more severe symptoms, higher emotional impact (9), and a higher risk of asthma exacerbation (10). Additionally, females reported more visits to emergency health services (11) and lower scores on asthma-related quality-of-life

CONTACT José R. Jardim jardimpneumo@gmail.com Respiratory Division of EPM/Unifesp, Rua Botucatu, 989. Cep, São Paulo 04062-023, Brazil.
Supplemental data for this article can be accessed at publisher's website.

questionnaires (12). In Latin America and Spain, an increased proportion of females is hospitalized due to severe asthma attacks (13). The reasons for the higher rate of hospitalizations in Latin America are not clearly understood, but they may include environmental (14) and genetic factors (15), among others. Complex genetic traits may also be strongly linked with asthma phenotypes (15), as there is a higher degree of genetic admixture in these countries as well as a large variation in environmental exposure. However, detailed information from this region is scarce.

Few studies have investigated the frequency and impact of asthma attacks in Latin America and the intensity of symptoms among males and females (16–18). To the best of our knowledge, the only study in Latin America to report differences in symptoms of asthma between sexes is the one that evaluated the Brazilian components of the multicenter Asthma Insights Management (AIM) study, which showed that females reported feeling more uncomfortable due to their respiratory symptoms (wheezing, number of asthma attacks, and sleep disorders) than males (18). Therefore, the primary objective of the present study was to determine the differences in symptom perception, asthma control, impact on daily activities, and exacerbation between sexes in five Latin American countries of the AIM study. A secondary objective was to identify any differences in symptom perception between both sexes in three different age groups (12–17 years, 17–40 years, and >40 years). The differences in symptom prevalence between sexes may generate different approaches for perception of asthma symptoms, education, and short- and long-term therapies.

Methods

Sample

The current study analyzed data from The Latin America Asthma Insight and Management survey conducted in Argentina, Brazil, Mexico, Venezuela, and Puerto Rico to explore and document patients' perceptions of asthma as well as their knowledge of the disease and its treatment (19). This cross-sectional study was conducted throughout 2011 in all centers and used the same method previously applied in the multicenter AIM study in the United States, Europe, Canada, Asia, and the Pacific Region. The survey was developed by Abt SRBI (New York, NY, USA). As in all other countries in which the AIM questionnaire was applied, all questions were originally drafted in English and translated to the local languages of the five countries; the translated questions were then back-translated to English and compared for meaning against the original English version. For each country, an electronic copy was sent to the centralized professional company in charge of the interviews. A paper copy and an electronic version were provided to each interviewer in each city in which the patients were interviewed. The LA-AIM study was not subject to formal ethics approval or a formal consenting process in any country. The need for full consideration and written informed consent was waived by the Ethics Committee on Clinical Pharmacology at the CIDEA Foundation in Argentina; the Ethics Committee of the Federal University of São Paulo Hospital in São Paulo, Brazil; the Ethics Committee of the Instituto Nacional Enfermedades Repiratorias Ismael Cosio Villegas in Mexico; the Cardio Pulmonary Research Center in Puerto Rico; and the Bioethics Committee for Research at Hospital de Clinicas Caracas, Venezuela.

To be eligible for the study, patients must have had their asthma diagnosed by a physician, experienced asthma symptoms, and used asthma medication within the past year. Households with no current patients with asthma or only patients younger than 12 years with asthma were screened out of the survey.

Overall, 51,208 households were screened. Telephone contact was made to determine whether there was anyone with asthma in the house, yielding a sample of at least 400 patients in each country. If more than one eligible patient was present in a household, one of them was randomly selected by the computer-assisted telephone interviewing system. The houses were randomly selected using a national probability sampling.

Patient consent was explicitly obtained before the interview, and respondents were advised that they could refuse to participate at any point during the interview. No identifiable personal information was collected. Patients who agreed to participate in the study were interviewed face to face at their home by a trained professional interviewer. A survey organization based in each targeted country collected the data. Interviewers were native speakers who read the questions and filled out the answers.

The questionnaire consisted of 53 questions, including closed-ended, open-ended, multiple choice, and matrix questions. The questions covered five asthma-related topics: symptoms, impact of asthma on daily activities, patients' perceptions of asthma control, exacerbation, and treatment/medication. Questions about physical and emotional limitations associated with asthma were included to assess the negative physical and emotional impacts of asthma. The questionnaire included questions from the

original LA-AIM study regarding socioeconomic level, education level, asthma-related factors (e.g. smoking, presence of domestic animals, history of rhinitis or allergies, and use of asthma control or rescue medication use), prescription of a written action plan, visits to health-care facilities within the prior 12 months, and limitations to daily activities due to asthma (see Supplementary Material for the questionnaire).

Statistical analysis

In the statistical analysis, categorical variables were presented as absolute numbers and percentages. Sexes in all Latin American countries were analyzed together and also by age group. The chi-squared test was used to compare the overall differences between sexes and the differences between sexes in each age group. A multinomial regression analysis was performed to analyze asthma control; sex and age group were considered independent variables and asthma control the dependent variable. A binary logistic regression analysis was performed to analyze respiratory symptoms, daily activities, and feelings and thoughts (dependent variables) and sex and age group (independent variables). Data analysis was performed using the Statistical Package for the Social Sciences, version 18.0 (SPSS Inc., Chicago, IL, United States), and the level of significance was set at $p < 0.05$.

Table 1. Clinical and demographic characteristics of asthmatic patients in the five countries of Latin America.

Variables	Males ($n = 762$)	Females ($n = 1405$)	p
Age group			
12–17 years, n (%)	194 (25.5)	159 (11.3)	<0.001*
18–40 years, n (%)	323 (42.4)	585 (41.6)	0.735
>40 years, n (%)	245 (32.2)	661 (47.0)	<0.001*
Smoker	137 (18.0)	167 (11.9)	<0.001*
12–17 years, n (%)	38 (19.6)	24 (15.1)	0.270
18–40 years, n (%)	62 (19.2)	70 (12.0)	0.003*
>40 years, n (%)	37 (15.1)	73 (11.0)	0.097
Former smoker	193 (25.3)	286 (20.4)	0.008*
12–17 years, n (%)	30 (15.5)	19 (11.9)	0.342
18–40 years, n (%)	59 (18.3)	105 (17.9)	0.905
>40 years, n (%)	104 (42.4)	162 (24.5)	<0.001*
Nonsmoker	424 (55.6)	940 (66.9)	0.008*
12–17 years, n (%)	122 (62.9)	113 (71.1)	0.105
18–40 years, n (%)	198 (61.3)	406 (69.4)	0.013
>40 years, n (%)	104 (42.4)	421 (63.7)	<0.001*
Pets in the household, n (%)	412 (54.5)	757 (54.0)	0.823
12–17 years, n (%)	112 (57.7)	83 (52.2)	0.364
18–40 years, n (%)	176 (54.7)	299 (51.1)	0.146
>40 years, n (%)	124 (50.8)	375 (56.7)	0.115
History of rhinitis or allergy, n (%)	378 (50.2)	841 (60.2)	<0.001*
12–17 years, n (%)	103 (53.1)	90 (56.6)	0.617
18–40 years, n (%)	161 (49.8)	368 (62.9)	<0.001*
>40 years, n (%)	114 (46.5)	383 (57.9)	0.005*
Level of education			
<4 years of schooling	72 (9.8)	163 (12.0)	0.124
12–17 years, n (%)	17 (8.8)	13 (8.2)	0.844
18–40 years, n (%)	15 (4.6)	26 (4.4)	0.890
>40 years, n (%)	40 (16.3)	124 (18.8)	0.398
≤9 years of schooling	478 (62.7)	867 (61.7)	0.640
12–17 years, n (%)	132 (68.0)	114 (71.7)	0.457
18–40 years, n (%)	204 (63.2)	368 (62.9)	0.940
>40 years, n (%)	142 (58.0)	385 (58.2)	0.938
High school college	185 (24.3)	324 (23.1)	0.523
12–17 years, n (%)	40 (20.6)	28 (17.6)	0.476
18–40 years, n (%)	101 (31.3)	186 (31.8)	0.870
>40 years, n (%)	44 (18.0)	110 (16.6)	0.639

Values are presented as absolute number (percentage). *$p < 0.05$ of the comparison between the sexes.

Results

A total of 2167 asthmatic patients aged ≥12 years were interviewed from a sample of 51,208 households in five Latin American countries, including Argentina ($n = 433$; 19.98%), Brazil ($n = 401$; 18.5%), Mexico ($n = 532$; 24.6%), Puerto Rico ($n = 401$; 18.5%), and Venezuela ($n = 400$; 18.5%). The prevalence of asthma was 3.4% in Argentina, 3.4% in Mexico, 8.8% in Brazil, 16.6% in Venezuela, and 18.3% in Puerto Rico.

Table 1 illustrates the sociodemographic characteristics of study participants according to sex and country. Of those patients, 762 (35.2%) were male (Argentina, $n = 128$; Brazil, $n = 148$; Mexico, $n = 200$; Puerto Rico, $n = 144$; and Venezuela, $n = 142$) and 1405 (64.8%) were female (Argentina, $n = 285$; Brazil, $n = 273$; Mexico, $n = 332$; Puerto Rico, $n = 257$; and Venezuela, $n = 258$). In participants aged 12–17 years, there was a higher proportion of males; this spread was significantly different from that in participants >40 years of age ($p < 0.05$). Education level and the number of pets in the household did not differ significantly between sexes ($p > 0.05$). History of rhinitis or allergies was more prevalent among females (60.2%), especially in participants aged >18 years ($p < 0.05$). Men between the ages of 18 and 40 years smoked more than women in the same age group ($p < 0.05$). A significant difference between sexes was seen in nonsmokers above the age of 40 years, with 63.7% being women ($p < 0.05$).

The Global Initiative for Asthma (GINA) assessment for asthma control in adults and adolescents based on the patients' previous four weeks of symptoms is shown in Figure 1. Overall, females reported more uncontrolled and partially controlled asthma. However, when the analysis accounted for age, females aged 18–40 years had a higher proportion of uncontrolled asthma compared to males (37.8% and 30.0%, respectively; $p < 0.05$). No differences between sexes were observed in the other age groups. The multinomial regression analysis showed that males were 38% less likely to have uncontrolled asthma when compared to females (odds ratio [OR] 0.62; 95% confidence

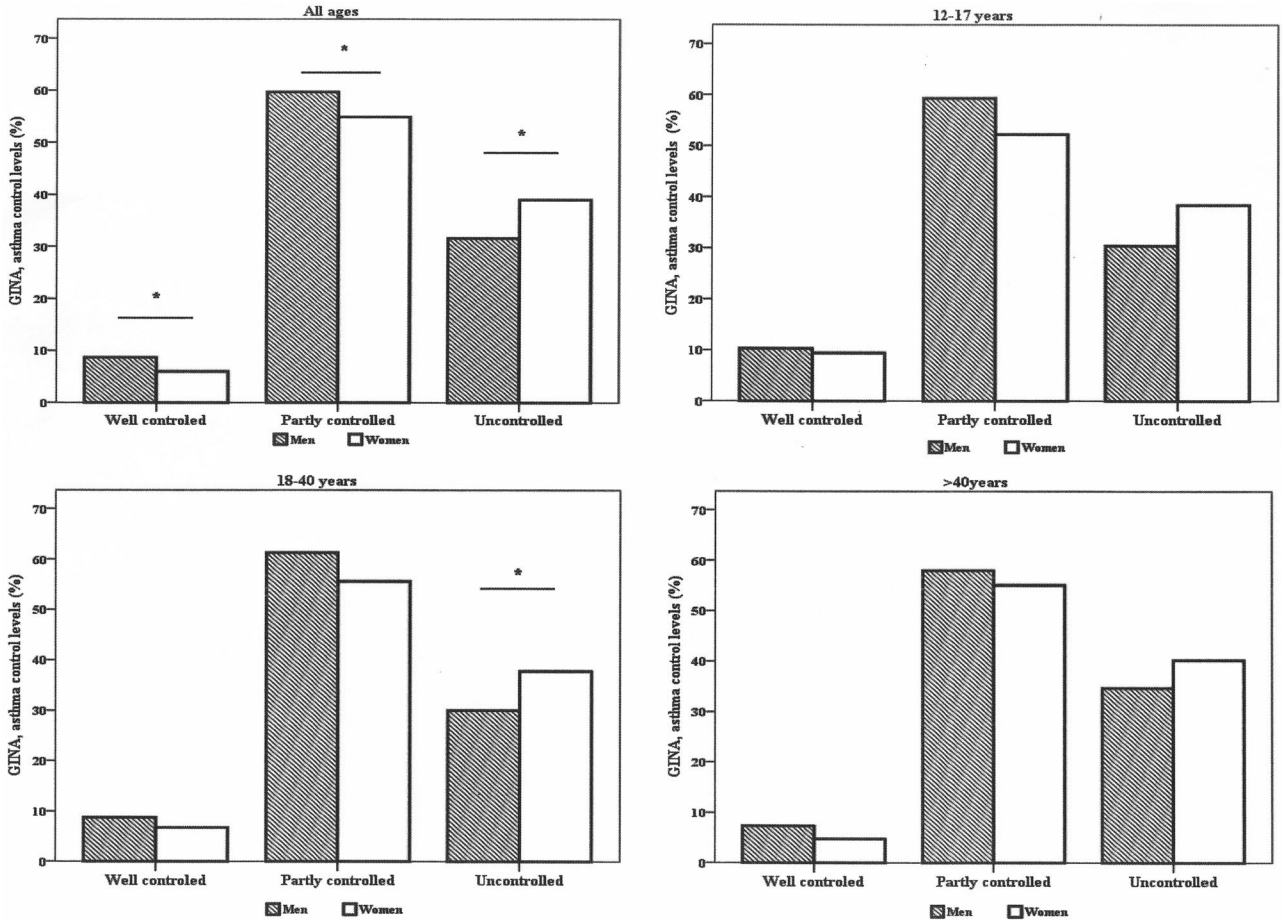

Figure 1. Asthma control in each sex, based on the patient's last 4 weeks symptoms, according to GINA. The data are presented with all participants and also categorized by age group.

interval [CI] 0.43–0.8; $p < 0.05$). Asthmatic patients 12–17 years old were 43% less likely to have uncontrolled asthma than participants over 40 years old (OR 0.57; 95% CI 0.36–0.93; $p < 0.05$).

The proportion of patients with daily respiratory symptoms or with symptoms many days in the worst month over the previous 12 months is shown in Table 2. Across all age groups, females had more respiratory symptoms than males for all assessed items ($p < 0.05$) except waking at night with cough ($p > 0.05$). Women over 40 years of age had a higher proportion of daytime shortness of breath, breathlessness, wheezing, and tightness in the chest when compared to men ($p < 0.05$). In the 18–40 age group, there were differences between sexes for cough, shortness of breath, tightness in the chest during exercise, and waking at night with shortness of breath ($p < 0.05$). The regression analysis showed that the variables "women" and "age over 18 years" were independent factors for reporting symptoms such as daytime cough, shortness of breath, wheezing, tightness in the chest, and cough/shortness of breath/tightness in the chest during exercise ($p < 0.05$) (Table 2).

Females also reported more asthma-related limitations in daily living activities than males for all assessed items ($p < 0.05$). Females reported more limitations in sports and recreation in the age groups of 12–17 and 18–40 years, in normal physical exertion in the age group of 12–17 years, in sleeping in the age group of 18–40 years, and for daily activities in all age groups (Table 3). In the regression analysis, females reported more limitations in daily activities, regardless of age group ($p < 0.05$) (Table 3).

The frequency and proportion of asthmatic patients who strongly agreed and somewhat agreed with any of the following statements: "asthma makes me feel that I have no control over my life"; "I feel incapable because of asthma, compared to my friends"; "asthma affects the way I feel about myself and at least once in my lifetime"; and "I have had such a severe asthma episode that I thought my life was at risk," are shown in Table 4. Females reported stronger agreement with the

Table 2. Respiratory symptoms during the worst month in the past 12 months, by sex in asthmatic patients from five countries of Latin America.

Variables	Males ($n = 762$)	Females ($n = 1405$)	Odds ratio (CI-95%)	p
Daytime cough, n (%)	284 (37.3)	597 (42.5)*	1.205 (1.001–1.450)	0.049[&]
12–17 years, n (%)	80 (41.2)	61 (38.5)	0.887 (0.578–1.362)	0.584
18–40 years, n (%)	103 (31.9)	217 (37.1)	1.259 (0.944–1.680)	0.116
>40 years, n (%)	101 (41.2)	319 (48.3)	1.330 (0.989–1.789)	0.060
Daytime shortness of breath, n (%)	240 (31.5)	572 (40.7)*	1.403 (1.160–1.697)	<0.001[&]
12–17 years, n (%)	61 (31.4)	48 (30.2)	0.943 (0.599–1.485)	0.800
18–40 years, n (%)	86 (26.6)	225 (38.5)*	1.722 (1.279–2.330)	<0.001[&]
>40 years, n (%)	93 (38.0)	299 (45.2)*	1.330 (1.000–1.822)	0.050[&]
Breathlessness/wheezing, n (%)	210 (27.6)	509 (36.2)*	1.404 (1.154–1.709)	<0.001[&]
12–17 years, n (%)	54 (27.8)	41 (25.8)	0.901 (0.561–1.447)	0.666
18–40 years, n (%)	80 (24.8)	196 (33.5)*	1.530 (1.128–2.077)	0.006[&]
>40 years, n (%)	76 (31.0)	272 (41.1)*	1.555 (1.138–2.124)	0.006[&]
Cough with sputum, n (%)	176 (23.1)	382 (27.2)*	1.168 (0.947–1.442)	0.147
12–17 years, n (%)	44 (22.7)	35 (22.0)	0.962 (0.582–1.592)	0.881
18–40 years, n (%)	62 (19.2)	134 (22.9)	1.251 (0.893–1.753)	0.194
>40 years, n (%)	70 (28.6)	213 (32.2)	1.189 (0.862–1.640)	0.292
Tightness in the chest, n (%)	211 (27.7)	503 (35.8)*	1.397 (1.147–1700)	<0.001[&]
12–17 years, n (%)	57 (29.4)	46 (28.9)	0.978 (0.617–1.552)	0.926
18–40 years, n (%)	78 (24.1)	193 (33.0)*	1.546 (1.137–2.103)	0.005[&]
>40 years, n (%)	76 (31.0)	264 (39.9)*	1.479 (1.082–2.021)	0.014[&]
Cough/shortness of breath/ tightness in the chest during exercise, n (%)	180 (23.6)	415 (29.5)*	1.310 (1.065–1.612)	0.011[&]
12–17 years, n (%)	52 (26.8)	40 (25.2)	0.918 (0.569–1.482)	0.726
18–40 years, n (%)	61 (18.9)	151 (25.8)*	1.494 (1.069–2.088)	0.019[&]
>40 years, n (%)	67 (27.3)	224 (33.9)	1.362 (0.985–1.883)	0.062
Waking at night with shortness of breath, n (%)	217 (28.5)	497 (35.4)*	1.330 (1.094–1.618)	0.004[&]
12–17 years, n (%)	58 (29.9)	49 (30.8)	1.045 (0.662–1.648)	0.851
18–40 years, n (%)	77 (23.8)	195 (33.3)*	1.597 (1.174–2.174)	0.003[&]
>40 years, n (%)	82 (33.5)	253 (38.3)	1.233 (0.906–1.678)	0.184
Waking at night with a cough, n (%)	240 (31.5)	491 (34.9)	1.123 (0.926–1.361)	0.239
12–17 years, n (%)	63 (32.5)	49 (30.8)	0.926 (0.590–1.454)	0.739
18–40 years, n (%)	90 (27.9)	181 (30.9)	1.160 (0.859–1.565)	0.332
>40 years, n (%)	87 (35.5)	261 (39.5)	1.185 (0.874–1.607)	0.275

The values are presented as absolute number and percentage of patients who answered that they had symptoms every day or most days. *$p < 0.05$ of the comparison between the sexes using the chi square test. [&]$p < 0.05$ in the logistic regression analysis and sex and age groups as an independent variable and symptom as a dependent variable. Males were the reference for analysis.

Table 3. Asthma-related limitation in activities of daily living, by sex in asthmatic patients from five countries of Latin America.

Variables	Males ($n = 762$)	Females ($n = 1405$)	Odds ratio (CI-95%)	p
Sports/recreation, n (%)	149 (19.6)	362 (25.8)*	1.378 (1.104–1.720)	0.005[&]
12–17 years, n (%)	37 (19.1)	47 (29.6)*	1.781 (1.086–2.919)	0.022[&]
18–40 years, n (%)	44 (13.6)	111 (19.0)*	1.485 (1.016–2.170)	0.041[&]
>40 years, n (%)	68 (27.8)	204 (30.9)	1.162 (0.840–1.608)	0.365
Normal physical exertion, n (%)	119 (15.6)	341 (24.3)*	1.549 (1.220–1967)	<0.001[&]
12–17 years, n (%)	20 (10.3)	36 (22.6)*	2.546 (1.407–4.609)	0.002[&]
18–40 years, n (%)	33 (10.2)	84 (14.4)	1.473 (0.961–2.260)	0.076
>40 years, n (%)	66 (26.9)	221 (33.4)	1.362 (0.984–1.886)	0.062
Social activities, n (%)	66 (8.7)	196 (14.0)*	1.520 (1.125–2.055)	0.006[&]
12–17 years, n (%)	11 (5.7)	18 (11.3)	2.124 (0.972–4.640)	0.059
18–40 years, n (%)	18 (5.6)	52 (8.9)	1.653 (0.950–2.877)	0.075
>40years, n (%)	37 (15.1)	126 (19.1)	1.324 (0.888–1.975)	0.169
Sleep, n (%)	130 (17.1)	345 (24.6)*	1.474 (1.172–1.853)	0.001[&]
12–17 years, n (%)	27 (13.9)	32 (20.1)	1.558 (0.889–2.733)	0.122
18–40 years, n (%)	48 (14.9)	125 (21.4)*	1.557 (1.081–2.242)	0.017[&]
>40 years, n (%)	55 (22.4)	188 (28.4)	1.373 (0.973–1.938)	0.071
Daily activities, n (%)	75 (9.8)	252 (17.9)*	1.750 (1.322–2.318)	<0.001[&]
12–17 years, n (%)	9 (4.6)	20 (12.6)	2.958 (1.307–6.694)	0.009[&]
18–40 years, n (%)	26 (8.0)	72 (12.3)	1.603 (1.001–2.567)	0.049[&]
>40 years, n (%)	40 (16.3)	160 (24.2)	1.637 (1.116–2.400)	0.012[&]

The values are presented as absolute number and percentage of patients who answered they had a lot of limitations in activities of daily living. *$p < 0.05$ of the comparison between the sexes using the chi square test. [&]$p < 0.05$ in the logistic regression analysis and sex and age groups as an independent variable and activities of daily living as a dependent variable. Men were the reference for analysis.

Table 4. Frequency and proportion of asthmatic patients who strongly agreed or somewhat agreed with any of the statements below, by sex.

Statements	Males ($n = 762$)	Females ($n = 1405$)	Odds ratio (CI-95%)	p
Asthma causes me to feel that I have no control over my life, n (%)	239 (31.4)	599 (42.6)*	1.516 (1.254–1.833)	<0.001[&]
12–17 years, n (%)	54 (27.8)	53 (33.3)	1.296 (0.822–2.044)	0.264
18–40 years, n (%)	94 (29.1)	232 (39.7)*	1.601 (1.196–2.143)	0.002[&]
>40 years, n (%)	91 (37.1)	314 (47.5)*	1.531 (1.134–2.069)	0.005[&]
I feel incapable because of asthma, compared with my friends, n (%)	177 (23.2)	427 (30.4)*	1.395 (1.134–1.716)	0.002[&]
12–17 years, n (%)	38 (19.6)	48 (30.2)*	1.775 (1.087–2.899)	0.002[&]
18–40 years, n (%)	71 (22.0)	168 (28.7)*	1.430 (1.040–1.966)	0.028[&]
>40 years, n (%)	68 (27.8)	211 (31.9)	1.220 (0.883–1.687)	0.228
Asthma affects the way I feel about myself, n (%)	236 (31.0)	591 (42.1)*	1.490 (1.231–1.803)	<0.001[&]
12–17 years, n (%)	52 (26.8)	53 (33.3)	1.365 (0.864–2.158)	0.182
18–40 years, n (%)	85 (26.3)	218 (37.3)*	1.663 (1.233–2.243)	0.001[&]
>40 years, n (%)	99 (40.4)	320 (48.4)*	1.384 (1.028–1.863)	0.03[2&]
At least once in my lifetime, I have had such a severe asthma episode that I thought my life was at risk – (yes) n (%)	302 (39.6)	647 (46.0)*	1.257 (1.047–1.510)	0.014[&]
12–17 years, n (%)	81 (41.8)	66 (41.5)	0.999 (0.647–1.515)	0.963
18–40 years, n (%)	115 (35.6)	245 (41.9)	1.303 (0.984–1.726)	0.064
>40 years, n (%)	106 (43.3)	336 (50.8)	1.356 (1.009–1.821)	0.043[&]

Values are presented as absolute number and (percentage) for sexes. *$p < 0.05$ of the comparison between the sexes using the chi square test. [&]$p < 0.05$ in the logistic regression analysis and gender and age groups as an independent variable and feelings or thoughts as a dependent variable. Males were the reference for analysis.

statement "asthma makes me feel I am not in control of my life" (42.6% for females vs 31.4% for males; $p < 0.05$). Females also reported stronger agreement than males with all other statements ($p < 0.05$). These findings were confirmed in the regression analysis (Table 4).

In participants aged >40 years, men responded that their health was "excellent," "very good," or "good" in 52.2% of cases, compared with 39.0% of women ($p < 0.001$). The other age groups reported no differences between sexes. Overall, 28% of females reported that their health limited the type or amount of work they could do, while 20% of males reported the same ($p = 0.003$). However, when divided by age group, there was no difference between sexes ($p > 0.05$). There was a significant difference ($p < 0.001$) in the number of days females stayed at home in the previous 12 months due to illness (3 [1–8] days) when compared to males (5 [2–14] days). These differences between sexes remained when compared by age group. A higher proportion of females (67.8%) reported visits to doctors or other health professionals in the previous 12 months due to asthma exacerbation, worsening of symptoms, or sudden and severe asthma episodes compared to males (59.6%). Differences were observed in the two age groups older than 18 years. The proportion of females who were hospitalized for asthma in the previous 12 months was higher in all age groups ($p < 0.05$). There was no difference between sexes and age groups in the frequency of being admitted to the ICU ($p > 0.05$).

Discussion

This study demonstrated that females with asthma in Latin America experience greater impacts on asthma control, respiratory symptoms, daily activities, and feelings and thoughts caused by the disease when compared to men. Differences in respiratory symptoms became more evident after 18 years of age, with a higher proportion of uncontrolled asthma in women aged 18–40 years. In addition, women of all age groups consulted more health professionals and doctors and were more often hospitalized for asthma in the previous 12 months than males. These differences have been the subjects of several studies that investigated physiological, psychological, and environmental mechanisms related to asthma.

Asthma in Latin American countries is an important cause of morbidity and consumes a significant portion of health resources (20). It poses enormous challenges for health policy makers, health service providers, and researchers with respect to responding to and alleviating the growing burden of disability caused by the disease, especially among females. Nevertheless, data quantifying the impact of asthma upon the population and health resources in Latin American countries are still scarce. To our knowledge, this is the first multicenter study carried out in Latin America with the aim of evaluating differences in the impacts of asthma between sexes in different age groups.

Uncontrolled asthma prevalence was higher in females than in males. Many explanations for the sex-specific differences observed in asthma control can be considered. Females with poorly controlled asthma have reported more gastroesophageal reflux disease and rhinosinusitis and are more likely to associate their asthma symptoms with allergies (21). In our study, 60.2% of females reported a history of rhinitis or allergies, compared to 50.2% of males ($p < 0.05$). These findings are similar to those from other studies, in which females with asthma were more likely to report allergic co-morbidities or rhinosinusitis and seemed to be more susceptible than males to environmental triggers (4,21,22). Furthermore, females exhibited increased bronchial hyperresponsiveness as a result of increased susceptibility to tobacco smoke, contributing to increased sensitivity to environmental triggers (23,24). Although the prevalence of smoking in our study was lower in females, in two other studies, female smokers were 2.2 times more likely to carry a diagnosis of asthma and report more asthma symptoms such as wheezing (25,26). These conditions could potentially worsen asthma control and symptoms in the present study or, perhaps more importantly, result in symptoms that mimic those of asthma and potentially influence responses to the questionnaires.

Female participants experienced more severe respiratory symptoms in our study, such as daytime shortness of breath, cough with sputum, breathlessness/wheezing, tightness in the chest, and symptoms during exercise. Previously, females have been shown to report more asthma symptoms when analyzed using standardized questionnaires (27). In addition, they reported more serious complaints regarding the frequency and intensity of symptoms as well as limitations in activities (28). In another study of 914 patients with asthma aged 3–55 years, females also reported more symptoms than males, and increasing age was an independent factor for worsening symptoms (29). We found similar results—women above 40 years of age reported more daytime shortness of breath on a daily or near-daily basis than those between 12 and 17 years of age (45.2% and 30.2%, respectively). It is possible that older patients are less responsive to drug therapies, such as inhaled corticosteroids, and therefore experience more frequent exacerbation of symptoms (30). Another aspect that may influence symptoms is lower adherence to therapeutic protocols. One previous study found that low adherence to inhaled corticosteroid therapy led to poor asthma-related outcomes and caused asthma-related hospitalizations (31). It is estimated that 60% of asthma-related hospitalizations could be attributed to poor adherence to inhaled corticosteroid therapy (30). Based on these findings, it appears that symptoms differ between males and females and are also age-dependent in asthmatic patients in Latin America.

The perception of asthmatic symptoms is highly subjective and may vary widely. Causes for the differences between sexes may be due to underlying mechanisms of the disease in each sex or due to general differences in overall perceptions of disease symptoms. For example, one study found that compared to females, males reported lower perceptions of the degree of obstruction and chest discomfort for similar levels of airway obstruction; the same study also found that men may not seek the appropriate care for the same degree of tightness (28). Other authors claim that factors such as puberty, pregnancy, menopause, hormonal contraceptives or replacement therapy, and hormonal variation during the menstrual cycle are associated with changes in asthma severity in females (12,32). Furthermore, sex hormones alter the function of epithelial cells in the airway—the progesterone receptor is expressed in the airway epithelium and may impact mucociliary clearance during the menstrual cycle (33,34). Additionally, markers of inflammation (e.g. exhaled nitric oxide, sputum eosinophils, and serum leukotrienes) are higher in females with severe asthma symptoms, emphasizing the possibility that an increased inflammatory response is responsible for the worsening of asthma, coinciding with physiological hormonal fluctuations (35,36). Another hypothesis is that the anatomical differences between males and females explain the differences in symptom perception between sexes. Enright et al. (37) proposed that height is correlated with airway size such that women, who tend to have shorter statures than men, have smaller airway diameters and therefore higher airway reactivity. These factors may all contribute to the different perceptions of asthma symptoms between sexes.

With respect to daily activities, females experienced more asthma-related limitations than males during normal physical exertion, sports, daily and social activities, and sleeping ($p < 0.05$). Asthma limits patients physically, emotionally, and socially. It interferes with children's schoolwork and recreation and negatively affects their social development (38). It impedes performance at work and in carrying out domestic responsibilities (39). In the elderly, asthma can threaten functional status, therefore contributing to the loss of autonomy (40).

In our study, a higher proportion of females reported that they felt as if they had no control over

their lives due to asthma and that the disease affected the way they felt about themselves. There is a negative correlation between dyspnea and social desirability in males, but the correlation is positive in females (41). This could be explained by differences in social and cultural standards between sexes. When males get sick, social and professional factors can lead them to underestimate the severity of their disease. Conversely, females do not experience the same cultural constraints and do not feel embarrassed to report symptoms or seek social support (42). Moreover, compared to males, females reported higher levels of pain and reported using a greater range of coping strategies (i.e. seeking social support, problem solving, and palliative behaviors) (43). However, it is important to note that these potential explanations are speculative with respect to our results.

Over the 12 months prior to the study period, females reported more episodes of asthmatic symptom exacerbation, visits to medical facilities, and hospitalizations than males. Previous studies have also reported that females went more to emergency departments and health services and received more medications than males (44,45). Females with asthma are 2–3 times more likely to be hospitalized for asthma than males and have longer hospital stays (10,46,47). Females admitted to the emergency room with severe asthma attacks were hospitalized more frequently than males, despite better pulmonary function and better oxygen levels. The difference in females' hospitalization rate does not seem to be related to the lower use of medication (48,49). Furthermore, after hospitalization, more than 50% of females report persistent dyspnea (50). Therefore, the differences in females' perception of symptoms result in lower disease control, over-treatment, and increased use of health systems.

Based on the results of our study, it is plausible that different public policies could be implemented for asthmatic patients in Latin America in order to maximize symptom control and the long-term impact of the disease, especially among female patients and the elderly. Disease education seems to be crucial, since only 40% of patients are compliant with long-term therapies for asthma (51). Studies in Brazil and Chile demonstrated that education on the self-management of asthma medication led to improved disease control (52,53). Clark et al. (54,55) showed that asthma management improved asthma-related quality of life in women and resulted in decreased use of rescue inhalers when compared to usual care. Older patients require special attention given their increased risk of mortality and lower rates of medication adherence. In this setting, family members and caregivers should be included in the design of asthma self-management plans.

The present study has some limitations. Five Latin American countries were included; this may not represent the whole population of asthmatic patients in the region. However, data retrieved from the five countries yielded similar conclusions to studies in other countries. Furthermore, patients' demographic locations within the five countries were not reported; therefore, we were unable to assess whether living in economically disadvantaged regions may influence asthma control.

Additionally, questionnaires for participants aged 12–17 years were completed by their parents, which may have resulted in some information bias and could not be statistically controlled. However, the study's large sample size reduced the chance of random error or bias. The chance of bias from the interviewers was also reduced by the questionnaire's use of open, closed, and matrix questions.

Environmental and occupational exposures impair control of asthma, though this study did not quantify these variables. For example, the use of disinfectants is associated with worse asthma control among healthcare professionals (56). However, this study included patients of all ages above 12 years, rendering it nearly impossible to track these exposures and avoid bias.

In this study of 51,208 households, the overall prevalence of asthma was approximately 4%. This prevalence is smaller than those observed in European countries (1) but similar to those found in other studies using the same method, such as India and Asia-Pacific countries (in which the prevalence is 6%) (57,58). Additionally, inclusion criteria for the present study included a medical diagnosis of asthma and the use of medication over the previous year, which may have restricted the sample.

The study population consisted of almost twice as many females as males, which may lead some to question the results obtained. The chi-squared test was used to compare the groups. The principle of this test is to compare proportions, such as possible divergences between observed and expected frequencies of an event, without requiring the same number of participants in each group. All conditions required by the test were respected: the groups were independent, the items in each group were randomly selected, the observations were frequencies or counts, each observation belonged to only one category, and the sample was relatively large. Our study followed the same statistical test and analyzed a similar population of women (63%) used by other authors without incurring

an analysis bias (21). In addition, a regression analysis was included in the study to ensure the results and avoid any bias. Finally, we did not analyze data regarding lung function tested by spirometry. However, the medical diagnosis of asthma based on symptoms has been largely used in epidemiological studies (59).

Conclusion

This study revealed that Latin American females with asthma experience a greater impact on respiratory symptoms, disease control, daily activities, and feelings and thoughts related to the disease when compared to males. In addition, symptoms increased with advancing age, corresponding with a higher proportion of uncontrolled asthma and a greater need for health services. Understanding sex-specific differences in response to disease and symptoms may result in changes to strategies for the management and treatment of females with asthma in Latin America.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. Masoli M, Fabian D, Holt S, Beasley R, Global Initiative for Asthma (GINA) Program. The global burden of asthma: executive summary of the GINA Dissemination Committee report. Allergy. 2004;59(5):469–478. doi:10.1111/j.1398-9995.2004.00526.x.
2. Mallol J, Solé D, Baeza-Bacab M, Aguirre-Camposano V, Soto-Quiros M, Baena-Cagnani C, Latin American ISAAC Group. Regional variation in asthma symptom prevalence in Latin American children. J Asthma. 2010; 47(6):644–650. doi:10.3109/02770901003686480.
3. Cooper PJ, Rodrigues LC, Cruz AA, Barreto ML. Asthma in Latin America: a public heath challenge and research opportunity. Allergy. 2009;64(1):5–17. doi:10.1111/j.1398-9995.2008.01902.x.
4. Zein JG, Erzurum SC. Asthma is different in women. Curr Allergy Asthma Rep. 2015;15(6):28. doi:10.1007/s11882-015-0528-y.
5. Osman M. Therapeutic implications of sex differences in asthma and atopy. Arch Dis Child. 2003;88(7):587–590. doi:10.1136/adc.88.7.587.
6. Burgess JA, Abramson MJ, Gurrin LC, Byrnes GB, Matheson MC, May CL, Giles GG, Johns DP, Hopper JL, Walters EH, et al. Childhood infections and the risk of asthma: a longitudinal study over 37 years. Chest. 2012;142(3):647–654. doi:10.1378/chest.11-1432.
7. Redline S, Gold D. Challenges in interpreting gender differences in asthma. Am J Respir Crit Care Med. 1994;150(5):1219–1221. doi:10.1164/ajrccm.150.5.7952543.
8. Pignataro FS, Bonini M, Forgione A, Melandri S, Usmani OS. Asthma and gender: the female lung. Pharmacol Res. 2017;119:384–390. doi:10.1016/j.phrs.2017.02.017.
9. Colombo D, Zagni E, Ferri F, Canonica GW, the PROXIMA Study Centers. Gender differences in asthma perception and its impact on quality of life: a post hoc analysis of the PROXIMA (Patient Reported Outcomes and Xolair® In the Management of Asthma) study. Allergy Asthma Clin Immunol. 2019;15(1):65. doi:10.1186/s13223-019-0380-z.
10. Hsiao HP, Lin MC, Wu CC, Wang CC, Wang TN. Sex-specific asthma phenotypes, inflammatory patterns, and asthma control in a cluster analysis. J Allergy Clin Immunol Pract. 2019;7(2):556–567.e15. doi:10.1016/j.jaip.2018.08.008.
11. Selberg S, Hedman L, Jansson SA, Backman H, Stridsman C. Asthma control and acute healthcare visits among young adults with asthma-a population-based study. J Adv Nurs. 2019;75(12):3525–3534. doi:10.1111/jan.14174.
12. Zein JG, Denson JL, Wechsler ME. Asthma over the adult life course: gender and hormonal influences. Clin Chest Med. 2019;40(1):149–161. doi:10.1016/j.ccm.2018.10.009.
13. Rodrigo GJ, Plaza V, Bellido-Casado J, Neffen H, Bazús MT, Levy G, Armengol J. The study of severe asthma in Latin America and Spain (1994-2004): characteristics of patients hospitalized with acute severe asthma. J Bras Pneumol. 2009;35(7):635–644. doi:10.1590/s18063713200900070004.
14. Escamilla-Nuñez M-C, Barraza-Villarreal A, Hernandez-Cadena L, Moreno-Macias H, Ramirez-Aguilar M, Sienra-Monge J-J, Cortez-Lugo M, Texcalac J-L, del Rio-Navarro B, Romieu I, et al. Traffic-related air pollution and respiratory symptoms among asthmatic children, resident in Mexico City: the EVA cohort study. Respir Res. 2008;9(1):74. doi:10.1186/1465-9921-9-74.
15. Moffatt MF, Kabesch M, Liang L, Dixon AL, Strachan D, Heath S, Depner M, von Berg A, Bufe A, Rietschel E, et al. Genetic variants regulating ORMDL3 expression contribute to the risk of childhood asthma. Nature. 2007;448(7152):470–473. doi:10.1038/nature06014.
16. Boechat JL, Rios JL, Sant'Anna CC, França AT. Prevalence and severity of asthma symptoms in school-age children in the city of Duque de Caxias, Rio de Janeiro, Brazil. J Bras Pneumol. 2005;31(2):111–117. doi:10.1590/S1806-37132005000200005.
17. Muino A, Menezes AM, Reichert FF, Duquia RP, Chatkin M. Wheezing phenotypes from birth to adolescence: a cohort study in Pelotas, Brazil, 1993-2004. J Bras Pneumol. 2008;34(6):347–355. doi:10.1590/S1806-37132008000600003.
18. Zillmer LR, Gazzotti MR, Nascimento OA, Montealegre F, Fish J, Jardim JR. Gender differences in the perception of asthma and respiratory symptoms in a population sample of asthma patients in four Brazilian cities. J Bras Pneumol. 2014;40(6):591–598. doi:10.1590/S1806-37132014000600002.
19. Maspero JF, Jardim JR, Aranda A, Tassinari CP, Gonzalez-Diaz SN, Sansores RH, Moreno-Cantu JJ,

Fish JE. Insights, attitudes, and perceptions about asthma and its treatment: findings from a multinational survey of patients from Latin America. World Allergy Organ J. 2013;6(1):19. doi:10.1186/1939-4551-6-19.
20. Franco R, Santos AC, do Nascimento HF, Souza-Machado C, Ponte E, Souza-Machado A, Loureiro S, Barreto ML, Rodrigues LC, Cruz AA. Cost-effectiveness analysis of a state funded programme for control of severe asthma. BMC Public Health. 2007;7(1):82. doi:10.1186/1471-2458-7-82.
21. McCallister JW, Holbrook JT, Wei CY, Parsons JP, Benninger CG, Dixon AE, Gerald LB, Mastronarde JG. American Lung Association Asthma Clinical Research Centers. Sex differences in asthma symptom profiles and control in the American Lung Association Asthma Clinical Research Centers. Respir Med. 2013;107(10):1491–1500. Oct doi:10.1016/j.rmed.2013.07.024.
22. Temprano J, Mannino DM. The effect of sex on asthma control from the National Asthma Survey. J Allergy Clin Immunol. 2009; 123(4):854–860. doi:10.1016/j.jaci.2008.12.009.
23. Leynaert B, Bousquet J, Henry C, Liard R, Neukirch F. Is bronchial hyperresponsiveness more frequent in women than in men? A population-based study. Am J Respir Crit Care Med. 1997;156(5):1413–1420. doi:10.1164/ajrccm.156.5.9701060.
24. Paoletti P, Carrozzi L, Viegi G, Modena P, Ballerin L, Di Pede F, Grado L, Baldacci S, Pedreschi M, Vellutini M. Distribution of bronchial responsiveness in a general population: effect of sex, age, smoking, and level of pulmonary function. Am J Respir Crit Care Med. 1995;151(6):1770–1777. doi:10.1164/ajrccm.151.6.7767519.
25. Syamlal G, Mazurek JM, Dube SR. Gender differences in smoking among U.S. working adults. Am J Prev Med. 2014;47(4):467–475. doi:10.1016/j.amepre.2014.06.013.
26. Bjerg A, Ekerljung L, Eriksson J, Ólafsdóttir IS, Middelveld R, Franklin KA, Forsberg B, Larsson K, Lötvall J, Torén K, et al. Higher risk of wheeze in female than male smokers. Results from the Swedish GA 2 LEN study. PLoS One. 2013;8(1):e54137. doi:10.1371/journal.pone.0054137.
27. Lee JH, Haselkorn T, Chipps BE, Miller DP, Wenzel SE. Tenor study group. Gender differences in IgE-mediated allergic asthma in the epidemiology and natural history of asthma: outcomes and treatment regimens (TENOR) study. J Asthma. 2006;43:179–184. doi:10.1080/02770900600566405.
28. Cydulka RK, Emerman CL, Rowe BH, Clark S, Woodruff PG, Singh AK, Camargo CA. Differences between men and women in reporting of symptoms during an asthma exacerbation. Ann Emerg Med. 2001;38(2):123–128. doi:10.1067/mem.2001.114305.
29. Osborne ML, Vollmer WM, Linton KL, Buist AS. Characteristics of patients with asthma within a large HMO: a comparison by age and gender. Am J Respir Crit Care Med. 1998;157(1):123–128. doi:10.1164/ajrccm.157.1.9612063.
30. Banerji A, Clark S, Afilalo M, Blanda MP, Cydulka RK, Camargo CA. Prospective multicenter study of acute asthma in younger versus older adults presenting to the emergency department. J Am Geriatr Soc. 2006;54(1):48–55. doi:10.1111/j.1532-5415.2005.00563.x.
31. Williams LK, Pladevall M, Xi H, Peterson EL, Joseph C, Lafata JE, Ownby DR, Johnson CC. Relationship between adherence to inhaled corticosteroids and poor outcomes among adults with asthma. J Allergy Clin Immunol. 2004;114(6):1288–1293. doi:10.1016/j.jaci.2004.09.028.
32. Shah R, Newcomb DC. Sex bias in asthma prevalence and pathogenesis. Front Immunol. 2018;9:2997. doi:10.3389/fimmu.2018.02997.
33. Jain R, Ray JM, Pan JH, Brody SL. Sex hormone-dependent regulation of cilia beat frequency in airway epithelium. Am J Respir Cell Mol Biol. 2012;46(4):446–453. doi:10.1165/rcmb.2011-0107OC.
34. Fuseini H, Newcomb DC. Mechanisms driving gender differences in asthma. Curr Allergy Asthma Rep. 2017;17(3):19. doi:10.1007/s11882-017-0686-1.
35. Skobeloff EM, Spivey WH, Silverman R, Eskin BA, Harchelroad F, Alessi TV. The effect of the menstrual cycle on asthma presentations in the emergency department. Arch Intern Med. 1996;156(16):1837–1840. doi:10.1001/archinte.1996.00440150091010.
36. Nakasato H, Ohrui T, Sekizawa K, Matsui T, Yamaya M, Tamura G, Sasaki H. Prevention of severe premenstrual asthma attacks by leukotriene receptor antagonist. J Allergy Clin Immunol. 1999;104(3):585–588. doi:10.1016/S0091-6749(99)70327-1.
37. Enright PL, Lebowitz MD, Cockroft DW. Physiologic measures: pulmonary function tests. Asthma outcome. Am J Respir Crit Care Med. 1994;149(2_pt_2):S9–S18. discussion S19-S20. doi:10.1164/ajrccm/149.2_Pt_2.S9.
38. Hill RA, Standen PJ, Tattersfield AE. Asthma, wheezing, and school absence in primary schools. Arch Dis Child. 1989;64(2):246–251. doi:10.1136/adc.64.2.246.
39. Williams SJ. Chronic respiratory illness and disability: a critical review of the psychosocial literature. Soc Sci Med. 1989;28(8):791–803. doi:10.1016/0277-9536(89)90108-1.
40. Burrows B, Barbee RA, Cline MG, Knudson RJ, Lebowitz MD. Characteristics of asthma among elderly adults in a sample of the general population. Chest. 1991;100(4):935–942. doi:10.1378/chest.100.4.935.
41. Nowobilski R, Furgał M, Polczyk R, de Barbaro B, Szczeklik A. Gender gap in psychogenic factors may affect perception of asthma symptoms. J Investig Allergol Clin Immunol. 2011;21(3):193–198.
42. Macintyre S, Ford G, Hunt K. Do women 'over-report' morbidity? Men's and women's responses to structured prompting on a standard question on long standing illness. Soc Sci Med. 1999;48(1):89–98. doi:10.1016/S0277-9536(98)00292-5.
43. Unruh AM, Ritchie J, Merskey H. Does gender affect appraisal of pain and pain coping strategies?Clin J Pain. 1999;15(1):31–40. doi:10.1097/00002508-199903000-00006.
44. Gender disparities in clinical decision making. Council on Ethical and Judicial Affairs, American Medical Association [see comments]. JAMA. 1991;266:559–562.
45. Verbrugge LM, Steiner RP. Physician treatment of men and women patients: sex bias or appropriate care?

Med Care. 1981;19(6):609–632. doi:10.1097/00005650-198106000-00005.
46. Dodge RR, Burrows B. The prevalence and incidence of asthma and asthma-like symptoms in a general population sample. Am Rev Respir Dis. 1980;122:567–575. doi:10.1164/arrd.1980.122.4.567.
47. Skobeloff EM, Spivey WH, St. Clair SS, Schoffstall JM. The influence of age and sex on asthma admissions. JAMA. 1992;268(24):3437–3440. doi:10.1001/jama.1992.03490240045034.
48. Schatz M, Clark S, Camargo CA. Sex differences in the presentation and course of asthma hospitalizations. Chest. 2006;129(1):50–55. doi:10.1378/chest.129.1.50.
49. Awadh N, Chu S, Grunfeld A, Simpson K, FitzGerald JM. Comparison of males and females presenting with acute asthma to the emergency department. Respir Med. 1996;90(8):485–489. doi:10.1016/S0954-6111(96)90176-6.
50. Singh AK, Cydulka RK, Stahmer SA, Woodruff PG, Camargo CA.Jr. Sex differences among adults presenting to the emergency department with acute asthma. Multicenter Asthma Research Collaboration Investigators. Arch Intern Med. 1999;159(11):1237–1243. doi:10.1001/archinte.159.11.1237.
51. Pazitková TV, Martínez VTP, Martínez LB. Relación entre la severidad de las manifestaciones de asma bronquial y el cumplimiento del tratamiento intercrisis Relation between the severity of bronchial asthma manifestations and the fulfilment of the inter-crisis treatment. Rev Cubana Med Gen Integr. 2011;27(3):294–306.
52. Dalcin PT, Grutcki DM, Laporte PP, Lima PB, Viana VP, Konzen GL, Menegotto SM, Fonseca MA, Pereira RP. Impact of a short-term educational intervention on adherence to asthma treatment and on asthma control. J Bras Pneumol. 2011;37(1):19–27. doi:10.1590/S1806-37132011000100005.
53. Henríquez MT, Ceruti D E. Education in asthmatic children controlled at Roberto del Rio Hospital: impact on knowledge, adhesion and disease control. Rev Chil Enferm Respir. 2013;29(2):70–74. doi:10.4067/S0717-73482013000200002.
54. Clark NM, Gong ZM, Wang SJ, Lin X, Bria WF, Johnson TR. A randomized trial of a selfregulation intervention for women with asthma. Chest. 2007;132(1):88–97. doi:10.1378/chest.06-2539.
55. Clark NM, Gong ZM, Wang SJ, Valerio MA, Bria WF, Johnson TR. From the female perspective: long-term effects on quality of life of a program for women with asthma. Gend Med. 2010;7(2):125–136. doi:10.1016/j.genm.2010.04.005.
56. Dumas O, Wiley AS, Quinot C, Varraso R, Zock JP, Henneberger PK, Speizer FE, Le Moual N, Camargo CA.Jr. Occupational exposure to disinfectants and asthma control in US nurses. Eur Respir J. 2017;50(4):1700237. doi:10.1183/13993003.00237-2017.
57. Gold LS, Thompson P, Salvi S, Faruqi RA, Sullivan SD. Level of asthma control and health care utilization in Asia-Pacific countries. Respir Med. 2014;108(2):271–277. doi:10.1016/j.rmed.2013.12.004.
58. Salvi SS, Apte KK, Dhar R, Shetty P, Faruqi RA, Thompson PJ, Guleria R. Asthma insights and management in India: lessons learnt from the Asia Pacific - asthma insights and management (AP-AIM) study. J Assoc Physicians India. 2015;63(9):36–43.
59. Global Initiative for Asthma. Global strategy for asthma management and prevention (upadated 2020). 2020 [acessed 2020 Sept 01]. www.ginasthma.org.