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ORIGINAL RESEARCH

Disease Burden, Treatment Patterns and Asthma Control in Adult Patients with Asthma in China: A Real-World Study

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Purpose: To inform better asthma management in China, this study aimed to comprehensively investigate clinical characteristics, treatment patterns, asthma control status, exacerbations, and humanistic burden among adult patients seeking hospital-based asthma care by analyzing data from Adelphi Asthma Disease Specific Program conducted in China.

Patients and Methods: All information was collected on survey date (August–December 2018) from medical records, physicians, or patients, without follow-up being conducted. Results are summarized descriptively for the overall population as well as subgroups defined by GINA 2018 treatment step.

Results: Of the included 765 patients, 46.0%, 40.4%, and 29.2% had undergone lung function, blood eosinophil count, and specific immunoglobulin E/radioallergosorbent testing, and 17.2%, 24.1%, and 58.7% were managed at GINA Steps 1–2, 3, and 4–5, respectively. Asthma was not well controlled in 57.3% of patients based on definitions adapted from the ERS/ATS and 10.7% of patients had experienced ≥1 severe exacerbation in the preceding year. According to patient self-reporting (n=603), the mean (SD) was 0.9 (0.1) for utility on EQ-5D-3L and was 7.8% (10.4%), 36.9% (20.0%), 40.8% (22.2%), and 37.9% (22.3%) for absenteeism, presenteeism, work productivity loss, and activity impairment, respectively, on WPAI. Both asthma control and humanistic burden worsened with progressive GINA treatment steps.

Conclusion: In patients seeking hospital-based asthma care in China, lung function and biomarker tests were underutilized, impairment in productivity and quality of life was observed, and more than half did not achieve well-controlled asthma despite approximately 60% being managed at GINA treatment Steps 4–5. These findings highlight the urgent need for optimizing asthma management in China.

Keywords: asthma control, exacerbation, treatment patterns, health care resource utilization, humanistic burden

Introduction

Asthma is a chronic respiratory disease characterized by chronic airway inflammation and airway remodeling, which causes reversible narrowing of the airways and consequently difficulty in breathing.[1] In 2019, asthma was estimated to affect 262 million people worldwide, equivalent to a prevalence of 3.4%.[2] The prevalence of asthma in China was estimated to be 4.2%, representing 45.7 million patients, according to the national, cross-sectional China Pulmonary Health (CPH) study performed between 2012 and 2015.[3] Asthma is largely underdiagnosed in China. The CPH study found that only 28.8% of asthma patients had ever been physician-diagnosed and 23.4% had ever received a lung function test, most likely due to the low awareness of asthma in both patients and physicians, the limited availability of equipment in primary care, and a lack of well-trained healthcare professionals (HCPs), especially in rural areas.[3,4]

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Sustained asthma control, an essential goal of asthma management,[5,6] can reduce healthcare resource utilization (HCRU) and improve quality of life.[7–9] However, the proportion of Chinese patients with well-controlled asthma has consistently been shown to be unsatisfactory across studies, ranging from 14% to 61% across different definitions of asthma control and disease severity.[10–12]

Given the sub-optimal control, China is faced with a heavy burden from asthma, despite the declining asthma-related mortality recorded in recent years.[13] In the CPH study, 15.5% and 7.2% of asthma patients reported emergency room (ER) visits and hospitalizations, respectively, due to exacerbations within the preceding year.[3] Even in patients with mild asthma, 14.0% visited ER and 3.1% were hospitalized due to exacerbations in the preceding year, according to the Respiratory Disease Specific Program (DSP) conducted in nine major Chinese cities in 2015.[12] Thus, asthma is expected to consume considerable healthcare resources in China given its large asthma population.[3,14] In addition, asthma incurs significant indirect economic impact due to its substantial humanistic burden, especially in patients with uncontrolled asthma.[15–17] Therefore, urgent national actions on improving asthma management in China are imperative, which necessitates a comprehensive understanding of asthma-associated burdens and management landscape.

Asthma treatment, conducted in a stepwise and control-based approach, involves an iterative cycle of control assessment and treatment adjustment.[5,6] Notably, since a single uniform definition of asthma control is still absent, physicians often rely on their own criteria to assess the level of asthma control and consequently may overestimate asthma control compared with patient-perceived asthma control.[18,19] The rate of patient-physician discordance was reported to be around 30%.[20,21] Overestimation of asthma control leads to sub-optimal treatment and worse disease control.[19,20] Therefore, the discordance between physician-perceived and patient-perceived asthma control should be minimized to improve asthma management, but has not been characterized in the Chinese general asthma population. As asthma treatment follows a stepwise approach,[6] understanding the performance of each treatment step is also crucial for optimization of treatment strategies. Nevertheless, very few real-world studies were carried out on this,[22,23] but none in China. With allergy increasingly contributing to asthma pathogenesis in China,[24,25] a further emerging aspect has been building on the important role of biomarkers in asthma management, such as eosinophils and immunoglobulin E (IgE), highlighting the need for a thorough understanding of the use of recommended biomarker tests in China.

To support better decision-making for asthma management in China, this study aimed to comprehensively describe patient characteristics, the use of lung function and biomarker tests, treatment patterns, disease control status from both physician and patient perspectives, HCRU, and humanistic burden in the overall asthma population as well as by treatment step based on a cross-sectional physician and patient survey conducted in China.

Methods

Study Design and Participants

This study analyzed secondary data from Chinese adult patients with physician-confirmed asthma who participated in the Asthma DSP. Detailed methodology for the DSP has been published elsewhere.[26] This cross-sectional physician and patient survey was performed in China from August to December 2018 in a consecutive asthma sample representative of the asthma population receiving routine hospital-based care.

The survey recruited hospital-based respiratory physicians (including chief doctors, vice chief doctors, and doctors in charge) who provided consultation for at least three asthma patients aged ≥18 years per week. Patients aged ≥18 years were eligible to participate if they had physician-confirmed asthma and were not enrolled in a clinical trial for asthma. For the current analysis, patients with physician-confirmed chronic obstructive pulmonary disease (COPD) and asthma-COPD overlap syndrome (ACOS) were excluded.

Participants were recruited from eight cities/provinces, that is, Beijing, Shanghai, Guangdong, Sichuan, Hubei, Shaanxi, Jiangsu, and Liaoning. Cities on the sampling frame list held by the fieldwork partner at the time of data collection were classified into four tiers based on administrative level, city size, population, and economic development level. Tier-1 cities include Beijing, Shanghai, and Guangzhou. Tier-2 cities typically refer to other provincial capitals and major cities. Tier-3 cities are mainly small urban and county-level administrative centers, while tier-4 cities are small- and medium-sized cities and county seats. The cities where the survey was conducted are provided with their tiers in

Supplementary Table 1. A three-tier system is used to classify hospitals in China. Class III hospitals (also known as tertiary hospitals) are equipped with >500 beds and provide a comprehensive medical service at the city, provincial, or national level. Class II hospitals, with a bed capacity between 100 and 500, are often affiliated with a medium-sized city, county, or district. Community health centers (CHCs) are primary hospitals, typically hospitals with ≤100 beds located in towns. The DSP recruited physicians and patients from all three types of hospitals across the eight cities/provinces, which were chosen to give a geographically diverse representation as close as possible to the pragmatically pre-determined set sample size of physicians and hospital class distribution.

Data Collection

The survey date was the date on which physicians and patients completed questionnaires. All information was recorded at the survey date from available medical records, physicians, or patients, without follow-up information being collected (Figure 1). Data were collected by local fieldwork partners and de-identified before receipt by Adelphi. During the period of August to December 2018, each enrolled physician was asked to complete a patient record form (PRF) for their next three (or more) consecutive adult asthma patients at a single point in time. Patient demographics, clinical characteristics, treatment regimens, adherence, comorbidities, disease burden, and symptoms were recorded. The severity of asthma and treatment adherence were evaluated by physicians and were perception-based. Based on clinical judgement, physicians were asked to rate the patient's severity of asthma as mild, moderate or severe. Similarly, physicians were asked to rate the patient's adherence as "not at all adherent", "slightly adherent", "moderately adherent", "very adherent" or "completely adherent" based on the number of times the patient took the prescribed asthma treatment in the last 12 months.

Based on available medical records and physicians' recalled information, asthma control was assessed using a definition adapted from that by the European Respiratory Society (ERS)/American Thoracic Society (ATS).[27] Briefly, uncontrolled asthma was defined as fulfilling one of the following: 1) "not well controlled" according to the 2018 update of the Global Initiative for Asthma (GINA) report or the guidelines of the National Asthma Education and Prevention Program;[28,29] 2) ≥2 bursts of oral corticosteroids (OCS) (≥3 days each in the previous year); 3) ≥1 hospitalization, intensive care unit (ICU) stay or mechanical ventilation in the previous year; and 4) after appropriate bronchodilator withhold forced expiratory volume in one second (FEV_1) <80% predicted (in the presence of reduced FEV_1/forced vital capacity [FVC] ratio below the lower limit of normal).[27] Exacerbation was defined as "a worsening of symptoms beyond normal day-to-day variation". If patients had exacerbation(s), treatment information for the exacerbation(s) was collected (eg, whether exacerbation was treated at an ER, whether OCS was used, etc.).

Current prescription data including inhaled corticosteroid (ICS) daily dosage were retrieved from medical records and used to determine subgroup stratification. The levels of ICS daily dosage were defined based on the criteria in the 2018

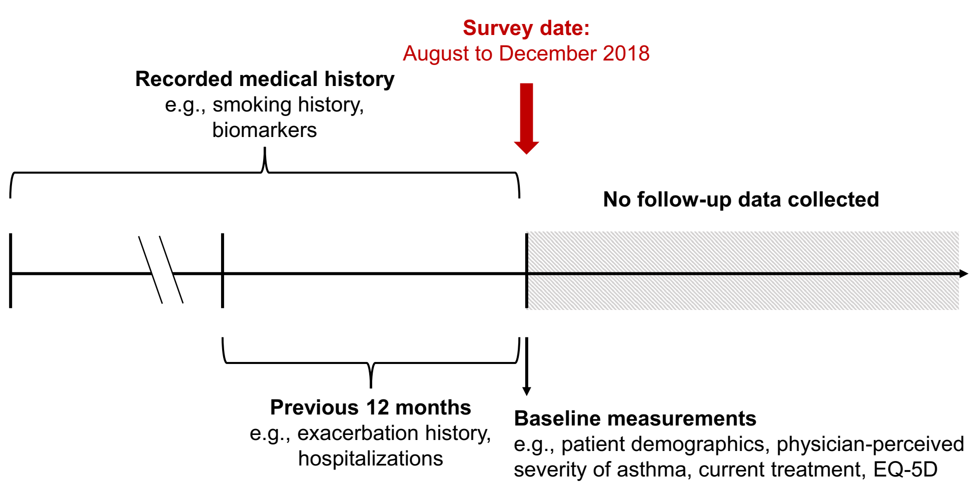

Figure 1 Study schematic diagram. The survey date was the time of survey completion by physicians and patients.

GINA update (low dose, fluticasone propionate 100–250 mcg or equivalent; medium dose, fluticasone propionate >250–500 mcg or equivalent; high dose, fluticasone propionate >500 mcg or equivalent).[28] This analysis used the body mass index (BMI) cut-off points that were designed specifically for Asian and Asian American adults by the Joslin Diabetes Center, Asian American Diabetes Initiative.[30]

Eligible patients were invited by their physicians to voluntarily complete a patient self-completion (PSC) questionnaire, informing on disease burden, frequency of exacerbations (which did not result in HCP visit) and the impact of asthma on work and overall health status. Patients completed three patient-reported outcome (PRO) measures, ie, the Work Productivity and Activity Impairment (WPAI) Questionnaire, the EQ-5D-3L descriptive system, and the EQ-visual analogue scale (EQ-VAS), as part of the questionnaire.[31,32] WPAI yielded four scores including absenteeism, presenteeism, work productivity loss (overall work impairment/absenteeism plus presenteeism), and activity impairment in the seven days before the survey date. EQ-5D-3L assessed the quality of life on a three-point rating scale over each of five dimensions, that is, mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The Chinese-specific tariff was used to calculate the EQ-5D-3L utility scores.[33] EQ-VAS recorded the self-rated health status on a graduated (0–100) scale, with a higher score indicating a better health-related quality of life. The PSC questionnaire was completed by the patient separately from the physician and was linked to the PRF through a unique identifier.

Ethics Approval

The DSP was conducted as a market research survey adhering to the International Chamber of Commerce (ICC)/ European Society for Opinion and Market Research (ESOMAR) International guidelines on observational research and performed in full accordance with the code of conduct outlined in the European Pharmaceutical Market Research Association (EphMRA) International guidelines. For this reason, Institutional Review Board (IRB) approval was not necessary nor sought. In the DSP survey, all participating physicians provided consent; patient consent was not required to complete the PRF given the level of anonymization of data but was obtained from those who agreed to complete the PSC questionnaire. This study utilized existing data collected in the DSP for disease understanding research.

Objectives

The primary objective was to describe patient characteristics, the use of lung function and biomarker tests, treatment patterns, disease control status, HCRU, and symptomatic and humanistic burden of asthma in China.

Statistical Analysis

As the DSP was a non-interventional disease understanding survey, no a priori hypothesis was set. Descriptive analyses were undertaken in the consecutive asthma sample as well as in subgroups stratified by GINA treatment step (Steps 1–2, 3, and 4–5).[28] All the statistical analyses were conducted using the Unicom Intelligence Reporter, version 7.5.[34] Patients with missing values on one variable were excluded from the analysis of that variable only.

Results

In total, 230 hospital-based physicians (26 chief doctors, 94 vice chief doctors, and 110 doctors in charge) across three hospital settings (125 Class III, 65 Class II, and 40 CHC) were enrolled in the DSP and they completed the PRF for 771 adult patients for the consecutive sample. The current study excluded 6 patients with physician-confirmed COPD and ACOS and thus included a total of 765 patients for analysis, with 603 (78.8%) of them having completed the PSC questionnaire. Out of the 765 patients, GINA 2018 treatment steps were calculable in 763: 60 (7.9%), 71 (9.3%), 184 (24.1%), 424 (55.6%), and 24 (3.2%) were prescribed GINA 2018 Step 1, 2, 3, 4, and 5 treatments, respectively.

Patient Demographics and Clinical Characteristics

Patient demographic and clinical characteristics are summarized in Table 1. The mean age (standard deviation [SD]) was 44.4 (13.8) years and 51.8% were female, with 23.5%, 32.0%, 24.3%, and 20.1% from Tier-1, −2, −3, and −4 cities, respectively. Nearly half of patients (49.2%, 376/765) were recruited from Class III hospitals. Most patients were never smokers (69.2%, 528/765) and had a BMI between 18.5 kg/m^2 and <27 kg/m^2 (90.9%, 687/756). Physician-perceived

Table 1 Physician-Recorded Patient Demographics and Clinical Characteristics

Characteristics	Total (N=765)	GINA 1–2 (N=131)	GINA 3 (N=184)	GINA 4–5 (N=448)
Age, years				
Mean ± SD	44.4 ± 13.8	48.5 ± 14.3	43.8 ± 12.7	43.4 ± 13.9
Sex, n (%)	n=764	n=130	n=184	n=448
Male	368 (48.2)	71 (54.6)	87 (47.3)	210 (46.9)
Female	396 (51.8)	59 (45.4)	97 (52.7)	238 (53.1)
Smoking history, n (%)	n=763	n=130	n=184	n=447
Current smoker	46 (6.0)	16 (12.3)	6 (3.3)	24 (5.4)
Ex-smoker	173 (22.7)	35 (26.9)	39 (21.2)	99 (22.1)
Never smoked	528 (69.2)	76 (58.5)	138 (75.0)	312 (69.8)
Do not know	16 (2.1)	3 (2.3)	1 (0.5)	12 (2.7)
BMI, n (%)	n=756	n=127	n=182	n=438
<18.5 kg/m^2	46 (6.1)	12 (9.4)	10 (5.5)	23 (5.3)
18.5–22.9 kg/m^2	382 (50.5)	67 (52.8)	85 (46.7)	235 (53.7)
23.0–26.9 kg/m^2	305 (40.3)	44 (34.6)	83 (45.6)	166 (37.9)
≥27.0 kg/m^2	23 (3.0)	4 (3.1)	4 (2.2)	14 (3.2)
City tier, n (%)				
Tier 1	180 (23.5)	54 (41.2)	27 (14.7)	97 (21.7)
Tier 2	245 (32.0)	20 (15.3)	63 (34.2)	162 (36.2)
Tier 3	186 (24.3)	39 (29.8)	48 (26.1)	99 (22.1)
Tier 4	154 (20.1)	18 (13.7)	46 (25.0)	90 (20.1)
Hospital type, n (%)				
CHC	195 (25.5)	60 (45.8)	29 (15.8)	104 (23.2)
Class II hospital	194 (25.4)	26 (19.9)	46 (25.0)	122 (27.2)
Class III hospital	376 (49.2)	45 (34.4)	109 (59.2)	222 (49.6)
Physician-perceived severity of asthma, n (%)	n=764	n=131	n=184	n=447
Mild	421 (55.1)	82 (62.6)	110 (59.8)	228 (51.0)
Moderate	319 (41.8)	48 (36.6)	69 (37.5)	201 (45.0)
Severe	24 (3.1)	1 (0.8)	5 (2.7)	18 (4.0)
Most common comorbidities, n (%)	n=764	n=130	n=184	n=448
Allergic rhinitis	412 (53.9)	76 (58.5)	83 (45.1)	253 (56.5)
Hypertension	143 (18.7)	35 (26.9)	33 (17.9)	75 (16.7)
CRSsNP	85 (11.1)	9 (6.9)	19 (10.3)	57 (12.7)
Diabetes	69 (9.0)	9 (6.9)	14 (7.6)	45 (10.0)
Elevated cholesterol / hyperlipidemia	58 (7.6)	14 (10.8)	16 (8.7)	28 (6.3)
Arthritis	40 (5.3)	7 (5.4)	10 (5.4)	23 (5.1)
Pre-bronchodilator FEV$_1$ predicted score measurement captured, n (%)				
Ever tested	352 (46.0)	56 (42.7)	60 (32.6)	236 (52.7)
Tested in the last 12 months	183 (52.0)	30 (53.6)	31 (51.7)	122 (51.7)
Most recent pre-bronchodilator FEV$_1$ predicted score in the last 12 months, n (%)	n=183	n=30	n=31	n=122
<30%	1 (0.5)	0	0	1 (0.8)
30–49%	21 (11.5)	5 (16.7)	1 (3.2)	15 (12.3)
50–79%	152 (83.1)	22 (73.3)	29 (93.5)	101 (82.8)
≥80%	9 (4.9)	3 (10.0)	1 (3.2)	5 (4.1)

(*Continued*)

Table 1 (Continued).

Characteristics	Total (N=765)	GINA 1–2 (N=131)	GINA 3 (N=184)	GINA 4–5 (N=448)
Blood eosinophil count				
Ever tested, n (%)	309 (40.4)	45 (34.4)	67 (36.4)	196 (43.8)
Tested in the last 12 months	256 (82.8)	35 (77.8)	51 (76.1)	170 (86.7)
Most recent blood eosinophil count	n=143[a]	n=22	n=32	n=89
Geometric mean (log SD), cells/μL	219 (2)	350 (1)	258 (1)	184 (2)
Specific IgE test/RAST				
Test taken, n (%)	223 (29.2)	15 (11.5)	59 (32.1)	149 (33.3)
Most recent specific IgE test/RAST result	n=211[a]	n=14	n=56	n=141
Normal IgE, n (%)	37 (17.5)	4 (28.6)	9 (16.7)	24 (17.0)
Elevated IgE, n (%)	174 (82.5)	10 (71.4)	47 (83.9)	117 (83.0)

Notes: [a]Some patients may have had test results recorded but the exact values were not available at the time of PRF completion.
Abbreviations: BMI, body mass index; CHC, community health center; CRSsNP, chronic rhinosinusitis without nasal polyps; FEV_1, forced expiratory volume in one second; GINA, Global Initiative for Asthma; IgE, allergen-specific immunoglobulin E; RAST, radioallergosorbent test; SD, standard deviation.

asthma severity was mild, moderate, and severe in 55.1% (421/764), 41.8% (319/764), and 3.1% (24/764) of patients, respectively. Only 46.0% (352/765) of patients had ever had a recorded pre-bronchodilator FEV_1 % predicted measurement and in those with records, only 52.0% (183/352) had this measured in the last 12 months. Among those with records in the last 12 months, 83.1% (152) had FEV_1 % predicted values between 50% and 79%. Blood eosinophil count (BEC) data were available in 40.4% (309/765) of patients and in those with records, 82.8% (256/309) had this measured in the last 12 months. The geometric mean (log SD) for the most recent BEC value was 219 (2) cells/μL. Only 29.2% (223/765) of patients had ever undergone a specific IgE or radioallergosorbent test (RAST), and for those with a test value recorded, specific IgE levels above the upper limit of normal were evident in 82.5% (174/211) of patients.

Patients managed at GINA Steps 1–2 had a mean age (SD) of 48.5 (14.3), while those managed at GINA Steps 3 or 4–5 had a mean age (SD) of 43.8 (12.7) and 43.4 (13.9), respectively. A higher proportion of patients managed at GINA Steps 1–2 had a smoking history (39.2%, 51/130) and were treated at CHCs (45.8%, 60/131), compared with those managed at GINA Step 3 (24.5% [45/184] and 15.8% [29/184]) or at Steps 4–5 (27.5% [123/447] and 23.2% [104/448]) (Table 1). More patients managed at GINA Steps 4–5 had spirometry (52.7% [236/448]), BEC test (43.8% [196/448]) and specific IgE test/RAST (33.3% [149/448]) ever undertaken compared respectively with those managed at Steps 1–2 (42.8% [56/131], 34.4% [45/131] and 11.5% [15/131]) or at Step 3 (32.6% [60/184], 36.4% [67/184] and 32.1% [59/184]).

Treatment Patterns

In the GINA Steps 1–2 group, 45.8% (60/131) were prescribed a short-acting beta-2 agonist (SABA) only, followed by a leukotriene receptor antagonist (LTRA) only (29.0% [38/131]) and ICS only (22.1% [29/131]) (Figure 2). In the GINA Step 3 group, 91.8% (169/184) were prescribed the combination of ICS and a long-acting beta-2 agonist (LABA) only, followed by ICS plus LTRA (3.8% [7/184]) (Figure 2). In the GINA Steps 4–5 group, the most prescribed regimen was ICS/LABA plus LTRA (48.2% [216/448]), followed by ICS/LABA only (34.4% [154/448]) and ICS/LABA plus a long-acting muscarinic antagonist (LAMA; 6.7% [30/448]) (Figure 2). Notably, 5.4% (24/448) of patients from the GINA Steps 4–5 group were prescribed OCS-containing maintenance treatments (Figure 2).

The mean number (SD) of currently prescribed asthma maintenance treatments was 1.3 (0.7), increasing from 0.5 (0.5) for Steps 1–2, to 1.1 (0.3) for Step 3, and to 1.7 (0.6) for Steps 4–5 (Table 2). The mean treatment duration (SD) of current medications was 20.7 (29.7) months and did not vary much by GINA treatment step (Table 2).

An ICS total daily dose was recorded for 105 patients managed at GINA Step 3 and 298 patients managed at GINA Steps 4–5 (Table 2). In the ICS-treated patients managed at GINA Steps 4–5, 195 (65.4%) and 52 (17.4%) patients

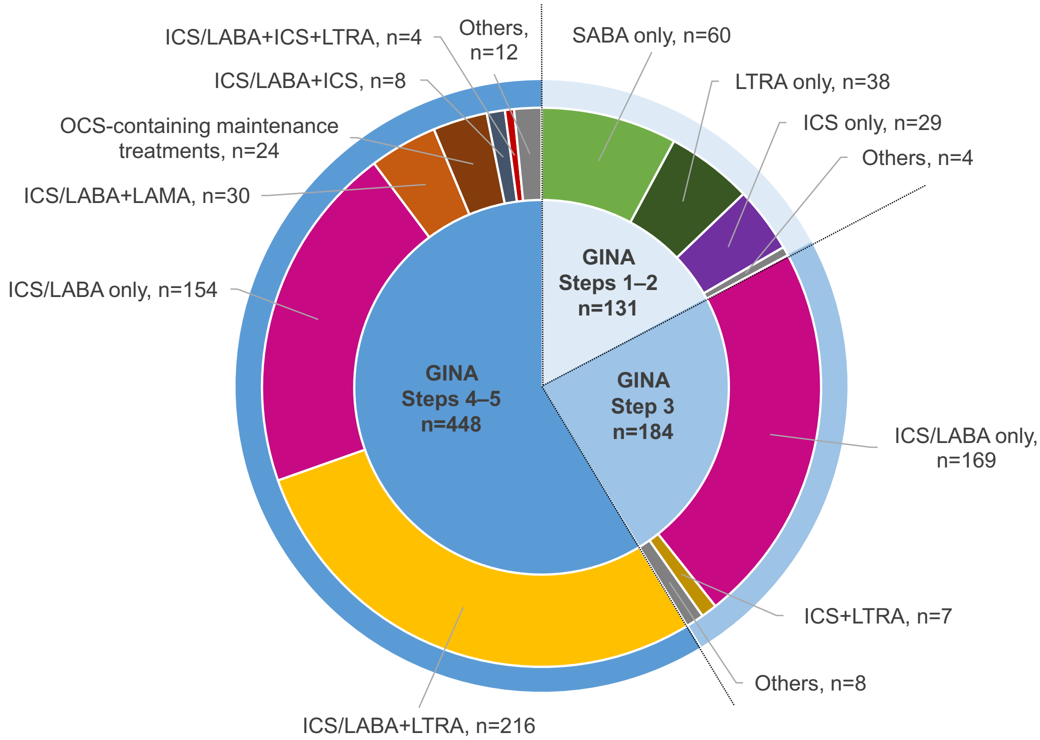

Figure 2 Currently prescribed asthma treatments.
Abbreviations: GINA, Global Initiative for Asthma; ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroid; SABA, short-acting beta-agonist.

received a medium and high daily dose, respectively. The mean number (SD) of OCS bursts in the last 12 months was 0.3 (1.1) and did not vary much by GINA treatment step.

Among patients who had inhaler device types recorded, almost all (97.8% [486/497]) were using dry powder inhalers, 9.7% (48/497) were using soft mist inhalers, and none were using metered-dose inhalers. Physicians perceived 39.8% (304/763), 44.4% (339/763), and 5.4% (41/763) of patients to be moderately, very, and completely adherent to prescribed

Table 2 Physician-Recorded Current Asthma Treatments

	Total (N=765)	GINA 1–2 (N=131)	GINA 3 (N=184)	GINA 4–5 (N=448)
Number of currently prescribed maintenance treatments				
Mean ± SD	1.3±0.7	0.5±0.5	1.1±0.3	1.7±0.6
Duration of prescribed treatments	n=758	n=129	n=183	n=444
Mean ± SD, months	20.7±29.7	17.9±31.4	21.5±19.9	21.2±32.5
ICS total daily dosage[a], n (%)	n=403	–	n=105	n=298
Low	156 (38.7)	–	105 (100.0)	51 (17.1)
Medium	195 (48.4)	–	–	195 (65.4)
High	52 (12.9)	–	–	52 (17.4)
Inhaler device type, n (%)	n=497	n=23	n=147	n=327
Dry powder inhaler	486 (97.8)	19 (82.6)	140 (95.2)	327 (100.0)
Soft mist inhaler	48 (9.7)	4 (17.4)	7 (4.8)	37 (11.3)
Metered-dose inhalers	0	0	0	0

(*Continued*)

Table 2 (Continued).

	Total (N=765)	GINA 1–2 (N=131)	GINA 3 (N=184)	GINA 4–5 (N=448)
Number of OCS bursts in the last 12 months	n=763	n=130	n=184	n=447
Mean ± SD	0.3±1.1	0.5±1.2	0.2±0.8	0.4±1.2
Physician-perceived adherence to prescribed treatments, n (%)	n=763	n=130	n=184	n=447
Not adherent at all	3 (0.4)	1 (0.8)	0	2 (0.4)
Slightly adherent	76 (10.0)	12 (9.2)	17 (9.2)	47 (10.5)
Moderately adherent	304 (39.8)	61 (46.9)	50 (27.2)	193 (43.2)
Very adherent	339 (44.4)	51 (39.2)	95 (51.6)	191 (42.7)
Completely adherent	41 (5.4)	5 (3.9)	22 (12.0)	14 (3.1)

Notes: [a]Data on daily dosage were retrieved from available medical records and categorized based on cut-offs defined by the 2018 GINA update.
Abbreviations: GINA, Global Initiative for Asthma; ICS, inhaled corticosteroid; OCS, oral corticosteroid; SD, standard deviation.

treatments, respectively (Table 2). The proportion of patients who were perceived to be very or completely adherent was numerically higher in those managed at GINA Step 3 (63.6%, 117/184) than in those managed at Steps 1–2 (43.1%, 56/130) and Steps 4–5 (45.9%, 205/447) (Table 2).

Asthma Control, Exacerbations, and HCRU

Asthma was not well controlled in 57.3% (438/765) of patients (Table 3). The proportion of patients with uncontrolled asthma increased with GINA treatment step, from 45.0% (59/131) in Steps 1–2 to 50.5% (93/184) in Step 3 and to 63.8%

Table 3 Physician-Recorded Asthma Control and Physician- and Patient-Reported Exacerbations

	Total (N=765)	GINA 1–2 (N=131)	GINA 3 (N=184)	GINA 4–5 (N=448)
Physician-recorded asthma control				
Asthma control based on the adapted ERS/ATS taskforce definition, n (%)				
Well-controlled	327 (42.7)	72 (55.0)	91 (49.5)	162 (36.2)
Not well-controlled	438 (57.3)	59 (45.0)	93 (50.5)	286 (63.8)
Physicians' satisfaction with current asthma control, n (%)	n=762	n=130	n=184	n=446
Satisfied	447 (58.7)	74 (56.9)	110 (59.8)	262 (58.7)
Dissatisfied but I know this is the best Possible control that can be Realistically achieved for this patient	201 (26.4)	33 (25.4)	39 (21.2)	129 (28.9)
Dissatisfied and I know better control Can be achieved for this patient	114 (14.9)	23 (17.7)	35 (19.0)	55 (12.3)
Physician-recorded severe exacerbations in the last 12 months				
Number of severe exacerbations[a], n (%)				
0 exacerbation	700 (91.5)	122 (93.1)	176 (95.7)	400 (89.3)
1 exacerbation	44 (5.8)	6 (4.6)	6 (3.3)	32 (7.1)
≥2 exacerbations	21 (2.7)	3 (2.3)	2 (1.1)	16 (3.6)
Exacerbations leading to ER visit, n (%)				
0 exacerbation	749 (97.9)	128 (97.7)	181 (98.4)	438 (97.8)
1 exacerbation	14 (1.8)	2 (1.5)	3 (1.6)	9 (2.0)
≥2 exacerbations	2 (0.3)	1 (0.8)	0	1 (0.2)

(*Continued*)

Table 3 (Continued).

	Total (N=765)	GINA 1–2 (N=131)	GINA 3 (N=184)	GINA 4–5 (N=448)
Exacerbations leading to overnight hospitalization, n (%)				
0 exacerbation	726 (94.9)	128 (97.7)	178 (96.7)	418 (93.3)
1 exacerbation	30 (3.9)	1 (0.8)	5 (2.7)	24 (5.4)
≥2 exacerbations	9 (1.2)	2 (1.5)	1 (0.5)	6 (1.3)
Exacerbations leading to OCS course, n (%)				
0 exacerbation	714 (93.3)	122 (93.1)	179 (97.3)	411 (91.7)
1 exacerbation	40 (5.2)	7 (5.3)	5 (2.7)	28 (6.3)
≥2 exacerbations	11 (1.4)	2 (1.5)	0	9 (2.0)
Patient-reported exacerbations in the last four weeks				
Number of flare-ups which did not result in HCP visit, n (%)	n=602	n=96	n=146	n=359
Not at all	143 (23.8)	15 (15.6)	54 (37.0)	74 (20.6)
Less than once a week	250 (41.5)	40 (41.7)	49 (33.6)	160 (44.6)
Once or twice a week	150 (24.9)	28 (29.1)	32 (21.9)	90 (25.1)
3 to 6 times a week	41 (6.8)	10 (10.4)	6 (4.1)	25 (7.0)
Everyday	10 (1.7)	1 (1.0)	3 (2.1)	6 (1.7)
Do not know	8 (1.3)	2 (2.1)	2 (1.4)	4 (1.1)

Notes: [a]Severe exacerbation was defined as exacerbation that results in an acute OCS treatment, ER visit, or overnight hospitalization.
Abbreviations: ATS, American Thoracic Society; ER, emergency room; ERS, European Respiratory Society; GINA, Global Initiative for Asthma; HCP, healthcare professional; n, number of patients who had a physician-recorded answer or responded to the question; N, total number of patients included in the survey; OCS, oral corticosteroid.

(286/448) in Steps 4–5. Physicians were satisfied with the current asthma control in 58.7% (447/762) of patients. In 14.9% (114/762) of patients, physicians were dissatisfied with their asthma control and thought that better control could be achieved (Table 3).

In the last 12 months, 8.5% (65/765) of patients were reported by physicians to experience at least one severe exacerbation, with the GINA Steps 4–5 group seeing the highest proportion of 10.7% (48/448) (Table 3). Additionally, 33.4% (201/602) of patients reported having at least one flare-up per week which did not result in HCP visits in the last four weeks (Table 3).

Patients visited HCPs for an average (SD) of 4.6 (3.3) times in the previous 12 months. Furthermore, 6.1% (47/765) of patients experienced at least one ER visit or overnight hospitalization due to asthma and hospitalized patients spent an average (SD) of 9.6 (6.0) nights in hospital (Table 4). The proportion of patients who experienced at least one asthma-

Table 4 Physician-Recorded Healthcare Resource Utilization Due to Asthma in the Last 12 Months, per Patient

	Total (N=765)	GINA 1–2 (N=131)	GINA 3 (N=184)	GINA 4–5 (N=448)
HCP visits, mean ± SD	4.6±3.3	5.0±4.0	4.3± 2.9	4.6± 3.2
Hospitalizations (including ER visits and overnight hospitalizations) **n (%)**				
0	718 (93.9)	126 (96.2)	177 (96.2)	413 (92.2)
1	33 (4.3)	3 (2.3)	5 (2.7)	25 (5.6)
≥2	14 (1.8)	2 (1.5)	2 (1.1)	10 (2.2)
ER visits (no overnight), mean ± SD	0.02±0.17	0.03±0.21	0.02±0.13	0.02±0.17
Overnight hospitalizations, mean ± SD	0.07±0.31	0.05±0.32	0.04±0.22	0.08±0.33
Number of in-patient nights at hospital	n=37	n=4	n=5	n=28
Mean ± SD	9.6±6.0	13.5±12.5	8.6±3.1	9.2±5.1

Abbreviations: ER, emergency room; GINA, Global Initiative for Asthma; HCP, healthcare professional; SD, standard deviation.

related ER visit or overnight hospitalization was 7.8% (35/448) in the GINA Steps 4–5 group, higher than 3.8% (5/131) in the GINA Steps 1–2 group and 3.8% (7/184) in the GINA Step 3 group, respectively (Table 4).

Symptomatic and Humanistic Burden

Among 757 patients with available data, the most frequent physician-recorded symptoms that occurred among patients in the last four weeks included shortness of breath during exertion (58.8%), productive cough (55.4%), shortness of breath when exposed to trigger factors (49.3%), dry cough (44.9%), and wheezing (42.3%) (Figure 3A). In the last four weeks, all these symptoms occurred more commonly among the GINA Step 3 and 4–5 groups than among the GINA Steps 1–2 group (Figure 3A). These five symptoms were also reported by physicians to be the most troublesome symptom in the last 12 months among the GINA Step 3 and 4–5 groups (Figure 3B).

Physicians reported that 5%–13% of patients were frequently or constantly affected by asthma in terms of impact on getting up and ready for the day (10.3%, 79/765), personal relationships (4.8%, 37/765), leisure/personal time (5.8%, 48/764), work (6.7%, 51/762), and sleep (12.8%, 98/765) (Figure 4A). Patients managed at GINA Step 3 and Steps 4–5 were more likely affected in getting up and ready for the day and work, while patients managed at GINA Steps 1–2 were more likely affected in personal relationships, leisure/personal time, and sleep (Figure 4A).

As assessed by the WPAI questionnaire, the patient-reported mean (SD) was 7.8% (10.4%) for absenteeism, 36.9% (20.0%) for presenteeism, 40.8% (22.2%) for work productivity loss, and 37.9% (22.3%) for activity impairment, with all except activity impairment increasing with GINA treatment step (Figure 4B). The mean (SD) utility (EQ-5D-3L) was 0.9 (0.1) and the mean EQ-VAS score (SD) was 79 (8.7). By either measurement, the three subgroups by GINA treatment

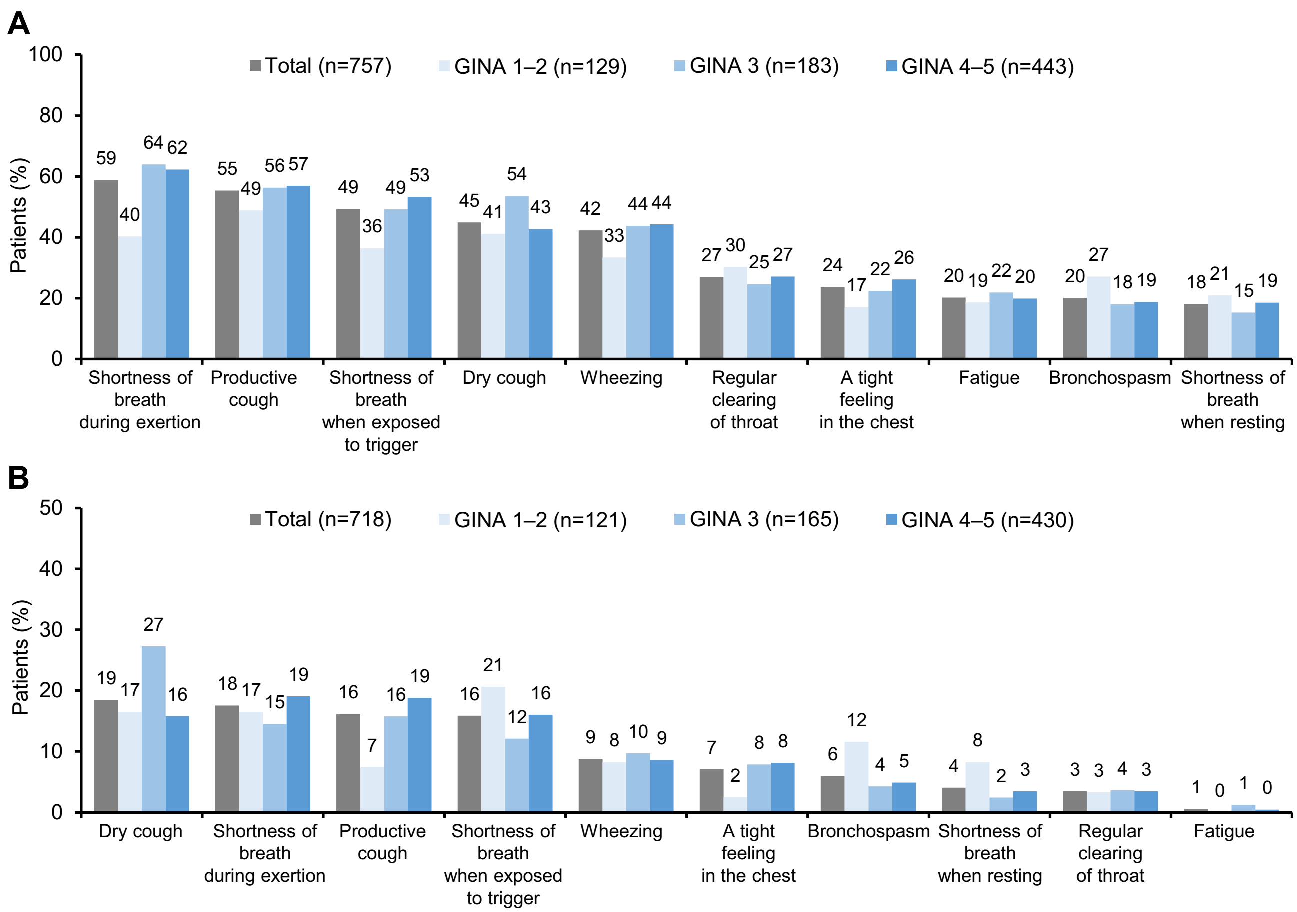

Figure 3 Physician-recorded symptomatic burden of asthma. (**A**) Most common symptoms in the last four weeks (multiple choices available) and (**B**) the most troublesome symptom in the last 12 months (single choice).
Abbreviation: GINA, Global Initiative for Asthma.

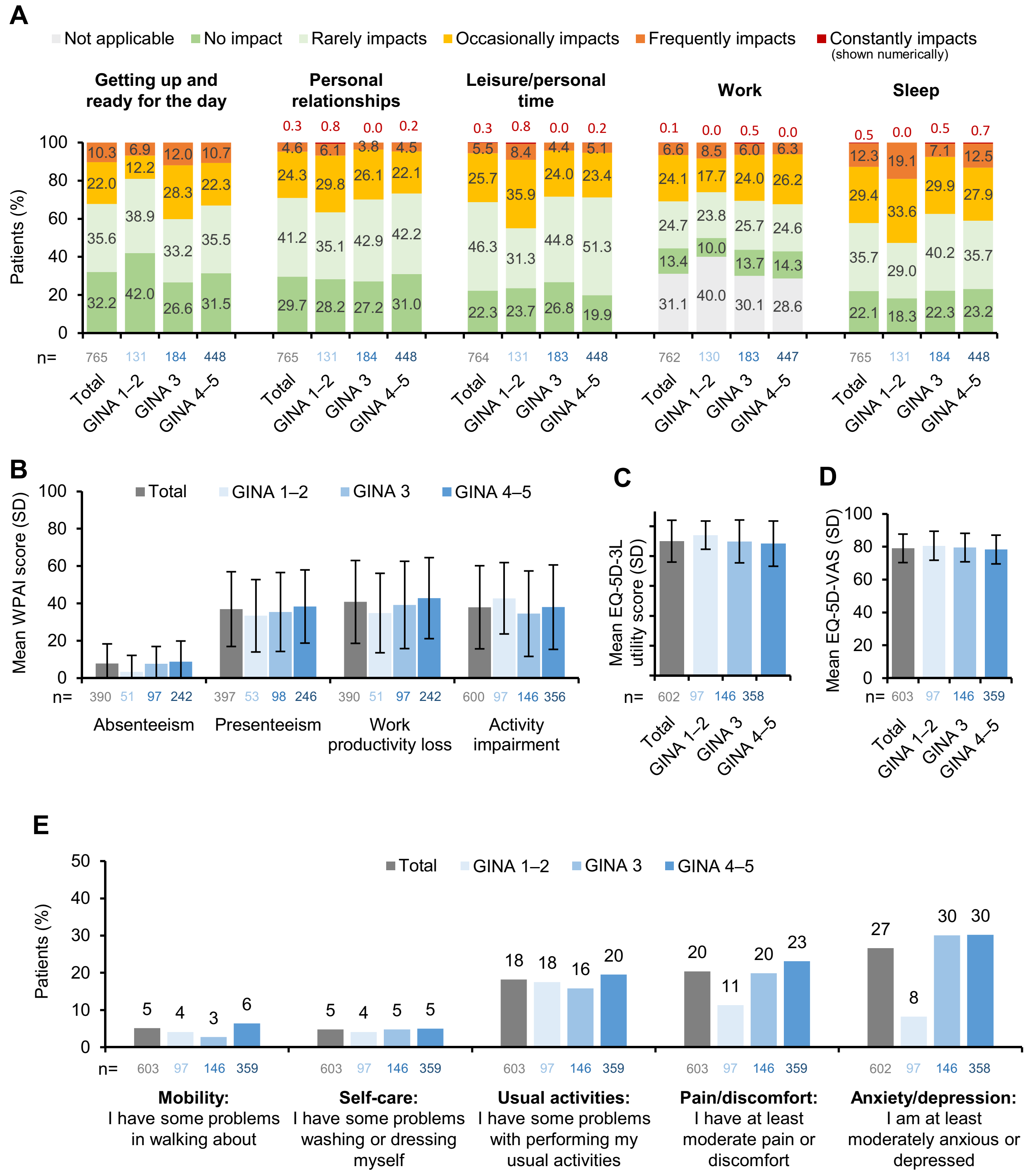

Figure 4 Physician-recorded and patient-reported humanistic burden of asthma. (**A**) Physician-recorded impact of asthma on patients' daily activities in the last four weeks; (**B**) patient-reported work productivity and activity impairment, (**C**) patient-reported EQ-5D-3L utility score, (**D**) patient-reported EQ-VAS, and (**E**) results for each dimension from EQ-5D-3L assessment.

Abbreviations: GINA, Global Initiative for Asthma; SD, standard deviation; VAS, visual analogue scale; WAPI, Work Productivity and Activity Impairment.

step were similar in mean utility score (Figure 4C and 4D). According to EQ-5D-3L, 18.2% (110/603), 20.4% (123/603), and 26.5% (160/603) of patients had at least some problems with performing usual activities, moderate/extreme pain or discomfort, and moderate/extreme anxiety or depression, respectively (Figure 4E). The GINA Step 3 and 4–5 groups had slightly more patients experiencing moderate/extreme pain or discomfort as well as anxiety or depression, compared with the GINA Steps 1–2 group (Figure 4E).

Discussion

Our study comprehensively examined the clinical characteristics, lung function and biomarker tests, treatment patterns, disease control status, HCRU, and symptomatic and humanistic burden in a large asthma sample representative of the real-world Chinese population receiving routine asthma care from hospitals. The study revealed that across the spectrum of GINA 2018 steps, largely resembling the treatment steps in the most recent Chinese guidelines (2020), there was a high proportion of patients whose asthma was uncontrolled and a substantial HCRU burden related to asthma along with heavy symptomatic and humanistic burdens, highlighting the urgent need for the establishment of a national framework to optimize asthma management, regardless of GINA step treatment. Commensurate with this, the study identified the infrequent use of lung function and biomarker tests, objective measures that aid the correct diagnosis and inform about management.

Although spirometry testing is recommended for the diagnosis and assessment of asthma,[5,6] fewer than half of patients in our study had ever had a recorded pre-bronchodilator FEV_1 result, consistent with the infrequent use of lung function tests previously reported in everyday non-specialist clinical use and the diagnosing of asthma in China.[3,12,35,36] In the absence of spirometry testing, although other objective methods such as peak expiratory flow may be used, the diagnosis of asthma might be solely based on symptoms or treatment response, leading to potential misdiagnosis. The underuse of lung function measurements may result from the limited availability of spirometers in primary and secondary hospitals, physicians' low awareness of spirometry's importance, and a lack of trained technicians. According to a study in Hunan province, only 1.6% of CHCs and 39.0% of Class II hospitals were equipped with spirometers, compared with 100% availability in Class III hospitals.[37] This reflects both the expense of purchasing spirometers and the need for training to use and maintain calibration.[35,37] The low awareness of spirometry's importance and the perceived low cost-effectiveness of pulmonary function testing among physicians further limit the ambition to incorporate lung function measures into everyday practice, a situation compounded by unreliable reporting due to undertraining among technicians, which limits the utilization rate of spirometers in clinical practice, especially in community care.[37,38]

Biomarker measurement is recommended for asthma management. Specifically, allergy tests are recommended in the initial evaluation of asthma and elevated BEC is considered a risk factor for exacerbations.[5,6] Phenotyping based on those biomarkers can guide biologic treatment decisions.[5] However, our study found that both BEC testing and specific IgE testing (or RAST) were underutilized, as only 40.4% and 29.2% of total patients, and 43.8% and 33.3% of patients managed at GINA Steps 4–5, had ever undergone these two tests, respectively. The underutilization of these tests may be attributed to the absence of specific recommendations for allergy-related testing in the then-latest local guidelines.[39] Furthermore, although BEC testing was recommended to assess the efficacy of anti-inflammatory treatments,[39] such a practice might not be well implemented at the time of the study (2018). The recommendation for biomarker tests is further reinforced in the 2020 Chinese guidelines and the latest GINA updates, both of which recommend BEC and IgE measurements to inform biomarker-guided treatment and treatment de-escalation.[5,6]

Our study suggests that the utilization rate of specific IgE testing, although still not ideal, appeared to be improving. The proportion of patients who had ever undergone a specific IgE test (or RAST) was 29.2% in this study, much higher than 12% reported by another nationwide cross-sectional study conducted between 2012 and 2013.[10] Allergic asthma is estimated to constitute 60%–80% of asthma cases worldwide.[25] Over 80% of patients with their most recent specific IgE test/RAST results recorded in our study had an elevated specific IgE level, indicating the same dominance of allergic phenotype in Chinese adult patients with asthma, although the elevated IgE levels might be partly attributed to the co-existing allergic rhinitis, which was present in more than half of the included patients.

For patients who were managed at GINA Steps 4–5 and receiving ICS/LABA in this study, LTRA was more frequently prescribed as an add-on than LAMA (48.2% versus 6.7%). This large usage difference might be attributed to two key factors, ie, the high proportion (56.5%) of patients with concomitant allergic rhinitis and no approved single-inhaler therapy of ICS/LABA/LAMA in China at that time. Asthma patients with concomitant allergic rhinitis were more likely to be prescribed LTRA, which has been recommended by local clinical guidance as a first-line treatment for such patients since 2013.[39,40] Furthermore, since there was no approved single-inhaler therapy for ICS/LABA/LAMA in 2018, the addition of LAMA to ICS/LABA would necessitate a separate inhaler. Such a prescription, however, was anticipated to be discouraged compared with LTRA oral formulations due to treatment inconvenience and the associated higher costs.

Our study found that although physicians were satisfied with the current asthma control in 58.7% of patients, only 42.7% of patients had well-controlled asthma based on the adapted ERS/ATS definition. Similarly, the 2015 DSP in Chinese patients with mild asthma reported that 75.0% of patients were perceived by physicians to have well or completely controlled asthma but only 14.2% of those patients achieved well-controlled asthma according to the 2016 GINA criteria.[12] The discrepancy in our study could be partly explained by the differences between the adapted ERS/ATS definition and that in the 2016 Chinese guidelines.[27,39] The 2016 Chinese guidelines recommended assessing the symptom control in the past four weeks, while the adapted ERS/ATS definition also requires no frequent severe or serious exacerbations in the previous year and no airflow limitations.[27,39] The likelihood of these discrepancies arising would be lessened by the consistent use of validated PRO instruments alongside the measurement of a disease activity biomarker in routine asthma management. A clinical trial from China has shown that ACT-guided treatment improves the level of asthma control compared with usual care.[41]

Despite the high treatment intensity, patients managed at GINA Steps 4–5 in our study appeared to have suboptimal disease control, as indicated by the high proportion of patients (63.8%) with not well-controlled asthma and the frequent occurrence of severe exacerbations (10.7%) in the preceding year. These findings suggest that a considerable proportion of patients could not achieve asthma control with treatments available at the time of the survey and should have required more effective treatment options. Fortunately, the treatment landscape is changing for patients with severe asthma. The add-on use of targeted biologics is recommended at GINA Step 5 in the recent guidelines for asthma which cannot be controlled with preferred treatments at GINA Step 4 and requires treatment escalation.[6] To the best of our knowledge, China currently has two approved biologics for asthma (omalizumab for moderate-to-severe allergic asthma [approved 2017] and mepolizumab for severe asthma with an eosinophilic phenotype [approved January 2024]),[42,43] and some others are under regulatory review. Besides, mepolizumab is also licensed for eosinophilic granulomatosis with polyangiitis in China,[42] a disease in which severe asthma is a common comorbidity.[44] Clinical studies have demonstrated that biologics can significantly reduce the risk of exacerbations and the use of OCS and improve the quality of life in patients with severe asthma,[45] but further research in China is warranted because there still lack real-world data on the effectiveness and safety of these biologics in Chinese patients.

Our study is the first, to our knowledge, to report WPAI results in a representative sample of the asthma population seeking hospital-based care in China. The previous study reporting WPAI in Chinese asthma patients included only patients with severe asthma from two provinces.[11] Our study showed a high overall work productivity impairment (40.8%) in asthma patients. Asthma increases the risk of depression and anxiety.[46] A cross-sectional study from a Chinese tertiary center conducted in 2012 reported that 11.9% and 13.4% of asthma patients had anxiety symptoms (Self Rating Anxiety Scale) and depression (Self Rating Depression Scale), respectively.[47] In contrast, 20% and 27% of patients in our study had pain/discomfort and anxiety/depression (EQ-5D-3L), respectively. Our study's identification of a significant humanistic burden further highlights the imperative for improved asthma control in China.

Our study indicates that asthma management needs to be further optimized in China given the high proportion of patients with uncontrolled asthma, the considerable HCRU burden, and impairment of productivity. First, in addition to the development of portable and easy-to-use spirometers,[48] proper training is needed for both physicians and technicians to improve the frequency and quality of spirometry testing in non-specialist respiratory care,[49,50] and in support of diagnosis, differential diagnosis, and management of asthma.[5,6] Second, further efforts are needed to raise awareness among physicians of the up-to-date guideline recommendations, with the adoption of standardized asthma control questionnaires and biomarker measurements to guide management. Third, although asthma management needs to be improved across the spectrum of GINA steps, special efforts are required to improve disease control in those who are managed at later GINA Steps given the substantially higher proportions of patients with not well-controlled asthma in these subgroups.

Our study adds valuable insights into asthma management in China. In particular, parallel data collection from both patients and their physicians provides a holistic view of asthma-related burdens. However, this study has some limitations. Firstly, the participating patients might not reflect the general asthma population in China, since only patients who sought hospital-based asthma care were recruited. Secondly, while minimal inclusion criteria governed the selection of the participating physicians, participation would have been influenced by the willingness to complete the survey and by pragmatic geographical considerations. The non-random, convenience sampling could lead to sampling bias, and thus affect the generalizability of the study findings. Thirdly, no audit of medical records was conducted, which may have led to some missing data, particularly on lung function and biomarker tests. Lastly, recall bias might have affected responses from both physicians and patients.

Conclusion

Our study demonstrated that in patients seeking hospital-based asthma care in China, there is a high disease burden with lung function and biomarker tests underutilized. For management of asthma, approximately 60% received GINA 2018 Steps 4–5 therapy, but asthma was still uncontrolled in more than half of patients. Furthermore, a small but still significant proportion of patients were hospitalized due to asthma and thus incurred a considerable HCRU burden, and impairment of productivity and quality of life were also observed. These findings highlight the urgent need for optimizing asthma management in China, thus reducing disease burden, HCRU burden, and healthcare costs therein.

Abbreviations

ATS, American Thoracic Society; BEC, blood eosinophil count; BMI, body mass index; CHC, community health centers; COPD, chronic obstructive pulmonary disease; CPH, China Pulmonary Health; CRSsNP, chronic rhinosinusitis without nasal polyps; DSP, Respiratory Disease Specific Program; EQ-VAS, EQ-visual analogue scale; ER, emergency room; ERS, European Respiratory Society; FeNO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in one second; GINA, Global Initiative for Asthma; HCP, healthcare professional; HCRU, healthcare resource utilization; ICS, inhaled corticosteroid; ICU, intensive care unit; IgE, immunoglobulin E; LABA, long-acting beta-2 agonist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroid; PRF, patient record form; PRO, patient-reported outcome; PSC, patient self-completion; RAST, radioallergosorbent test; SABA, short-acting beta-agonist; SD, standard deviation; WPAI, Work Productivity and Activity Impairment.

Data Sharing Statement

The datasets used and/or analyzed during the current study were made fully available to all authors but are not publicly available and remain the intellectual property of Adelphi Real World. Requests to access to the data can be made by contacting the corresponding author.

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V.B., R.AC., Z.T., P.H., A.R., and T.Y. are employees of GSK. V.B., R.AC., Z.T., P.H., and A.R. hold GSK stocks and shares. J.S. was an employee of Adelphi Real World at the time the study was conducted, and A.H. and M.S. are employees of Adelphi Real World. The authors report no other conflicts of interest in this work.

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