



Original Research

Asthma patients' and physicians' perspectives on the burden and management of asthma

Kenneth R. Chapman^a, Li An^b, Sinthia Bosnic-Anticevich^{c,d}, Celeste M. Campomanes^e, Jerónimo Espinosa^f, Priya Jain^{g,1}, Kim L. Lavoie^{h,i}, Jing Li^j, Aman K. Butta^{g,*}^a University of Toronto, Toronto, Canada^b Department of Respiratory and Critical Care Medicine, Beijing Institute of Respiratory Medicine, Beijing Chao-Yang Hospital, Capital Medical University, Beijing, China^c Woolcock Institute of Medical Research, University of Sydney, Sydney, Australia^d Sydney Local Health District, Sydney, Australia^e St Luke's Medical Center, Philippines^f GlaxoSmithKline, San Fernando, Buenos Aires, Argentina^g GlaxoSmithKline, Global Classic and Established Medicines, Singapore^h University of Quebec at Montreal, Montreal, Canadaⁱ Montreal Behavioural Medicine Centre, Centre Intégré Universitaire de Santé et de Services Sociaux Du Nord de L'Île de Montréal (CIUSSS-NIM), Montreal, Canada^j Department of Allergy and Clinical Immunology, Guangzhou Institute of Respiratory Health, Guangzhou, Guangdong, China

ARTICLE INFO

Keywords:

Asthma symptoms
Global cohort
Patient perspectives
Physician perspectives
Guideline adherence
GINA

ABSTRACT

Background: The 2021 Global Initiative for Asthma (GINA) report recommends as-needed inhaled corticosteroid (ICS)/formoterol irrespective of severity, and maintenance and reliever treatment (MART) from GINA Step 3 as part of Treatment Track 1, partly based on the SYGMA studies. We investigated how current clinical practice in Australia, Canada, China and the Philippines relates to latest GINA recommendations.

Methods: Patients and physicians were recruited from online panels between July and August 2020 and invited to complete an online survey. Inclusion criteria: age ≥ 18 years, current/past physician diagnosis of asthma (patients); primary care (Canada also included respirologists/respiratory therapists), treating ≥ 4 patients with asthma per month, ≥ 3 years in clinical practice (physicians).

Results: Overall, 1216/70,183 patients and 803/8376 physicians replied and were eligible for inclusion. Only 8–15% of patients were using MART; 66–81% used regular maintenance therapy with/without an as-needed reliever. Across the four countries, physicians classified 48–63% of their patients as mild (GINA Steps 1–2) and 28–36% as moderate (GINA Steps 3–4). Generally, physicians rated symptom control over exacerbation reduction as their main treatment goal; patients also ranked symptom relief as very important. Approximately 9–29% of patients and 24–45% of physicians were unaware of MART, and among those who prescribed MART, 80–95% prescribed an additional (non-ICS) as-needed reliever.

Interpretation: Most physicians prioritized managing asthma symptoms over exacerbations. A lack of awareness and understanding of MART dosing exists among physicians. Practical strategies are required to implement GINA recommendations effectively in real-world clinical practice and to identify appropriate patients for MART.

1. Introduction

The Global Initiative for Asthma (GINA) 2021 report describes five degrees (steps) of asthma severity and suggests treatment for each of these

steps [1]. Patients at Steps 1 and 2 (mild asthma) are described as experiencing asthma symptoms less than once a day (and less than twice a month for Step 1). GINA 2021 treatment recommendations for adults and adolescents shows two treatment tracks, based on the choice of reliever

Abbreviations: ANOVA, analysis of variance; ICS, inhaled corticosteroid; GINA, Global Initiative for Asthma; LABA, long-acting β_2 -agonist; MART, maintenance and reliever therapy; PRN, as-needed; SABA, short-acting β_2 -agonist; SD, standard deviation; SYGMA, Symbicort Given as Need in Mild Asthma.

All authors contributed equally to this work.

* Corresponding author.

E-mail address: amankapil.x.butta@gsk.com (A.K. Butta).

¹ At the time of the study.

<https://doi.org/10.1016/j.rmed.2021.106524>

Received 29 March 2021; Received in revised form 16 June 2021; Accepted 27 June 2021

Available online 29 June 2021

0954-6111/© 2021 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

(low-dose ICS/formoterol as the recommended reliever for Treatment Track 1 and SABA as the recommended reliever for Treatment Track 2). The proposed initial therapy for patients in Track 1 is as-needed low-dose inhaled corticosteroid (ICS)/formoterol (Steps 1 and 2). Track 2 recommends use of an ICS whenever a SABA is taken (Step 1) or daily low-dose ICS (Step 2) [1]. Patients at GINA Steps 3 and 4 (moderate asthma) are described as experiencing symptoms most days and night-time awakenings once a week or more. For these patients, the preferred daily maintenance regimen is low or medium-dose ICS/formoterol as daily maintenance therapy with additional ICS/formoterol as needed (known as MART [maintenance and as-needed reliever therapy]) in Track 1; or ICS/long-acting β_2 -agonist (LABA) with an as-needed SABA for symptom relief in Track 2 [1].

The recent GINA 2021 report and data that informed these recommendations, most notably from the Symbicort Given as Need in Mild Asthma (SYGMA) trials [2,3], proposes a fundamental shift in our approach to asthma management. GINA reports from 2018 and earlier recommended low-dose ICS with SABA as a reliever from Step 1, with increasing ICS dose and addition of LABAs \pm long-acting muscarinic antagonists with increasing severity, and MART therapy as an option from Step 3 onwards [4,5]. The recommended as-needed ICS/formoterol treatment for patients with mild asthma (Steps 1 and 2) incorporated into GINA recommendations from 2019 represents a significant departure from the long-standing approach of using SABA as a reliever, but also broadens the indication for as-needed ICS/formoterol to include a wider spectrum of patients with asthma [1,6,7].

The SYGMA studies were randomized 52-week, double-blind, clinical trials assessing the effects of as-needed budesonide (ICS)/formoterol compared with twice-daily budesonide plus as-needed terbutaline (SABA) (SYGMA 1 and 2) and as-needed terbutaline alone (SYGMA 1) [2,3]. SYGMA 2 was designed as a superiority trial with exacerbation as the primary endpoint, but so few exacerbations were seen that the study was amended to be a non-inferiority trial [3]. In both SYGMA studies, as-needed budesonide/formoterol was inferior to twice-daily budesonide for symptom control, whilst the impact on exacerbations was non-inferior in SYGMA 2, and indistinguishable between both treatment groups in SYGMA 1. It should be noted that only patients with asthma classified at Step 2 were enrolled in the SYGMA trials [2,3]. An extrapolation of the ICS/formoterol as-needed approach for mild asthma is also seen as part of the MART strategy in moderate asthma. The limitations of this strategy have been reviewed previously and include the failure to achieve control in the majority of MART-treated patients and the development, in one study, of markedly increased eosinophilic airways inflammation [8,9].

We undertook the current study to understand if the GINA recommendation of as-needed controller/reliever therapy across the asthma continuum is consistent with real-world patient and physician perspectives. Given the global nature of the GINA strategy, we undertook the study in countries from a widespread selection of regions across the world with different socioeconomic and healthcare systems to gain insights into how as-needed ICS/formoterol regimens may translate into real-world practice.

2. Materials and methods

2.1. Study design and eligibility criteria

The Asthma Patients' and Physicians' Perspectives on the Burden and Management of Asthma (APPARENT) study was a multinational, cross-sectional online survey of patients and physicians in four countries: Australia, Canada, China, and the Philippines. Patients and physicians were sampled and recruited from high-quality, non-probability panels. Both surveys were fielded between July and August 2020 in local languages, adapted by accredited translators and reviewed to ensure accurate terminology for local healthcare settings was included. In most cases, patients and physicians were initially contacted via email, with surveys completed online. See online Supplementary material for additional details regarding the study design.

Patients were required to be ≥ 18 years with a self-reported history of a past or current diagnosis of asthma made by a physician. The physician survey targeted primary care physicians (general practice, family medicine, and/or internal medicine physicians). In Canada, respirologists and/or respiratory therapists were also included in order to meet the prespecified quota of 200 physicians per country. Physicians were required to be personally responsible for the treatment and management of patients with asthma, to have a minimum of 3 years in clinical practice, and to treat at least four patients with asthma per month on average.

Details on data processing are provided in the online Supplementary material.

This study was approved by the Abt Associates International Review Board (Abt IRB #2059).

2.2. Survey development

The questionnaires developed for this survey to explore the patient and physician perspectives of interest were based on previous similar respiratory questionnaires used in the Global Asthma Physician Survey (GAPS) and the Asia Pacific Survey of Physicians on Asthma and Allergic Rhinitis (ASPAIR). Country-specific feedback was provided to ensure clarity, accurate translation, and applicability to local practices and healthcare settings. A series of bespoke questions were also developed relating to asthma patients' and physicians' perspectives on the burden and management of asthma.

2.3. Statistical analysis

Sample sizes were based on previous research [10] and selected to be sufficient for within-country analyses. For cross-country comparisons, the sample sizes were larger than required.

P-values were determined using Chi-square testing for categorical data and analysis of variance (ANOVA) means testing for continuous data.

As respondents were recruited from high-quality, non-probability panels, formal response rate calculations were not appropriate; cooperation rates are therefore presented. Cooperation rates are defined as the total number of completed surveys divided by the total number of initial web invitations sent minus the number of cases known to be ineligible. Throughout the results section, the proportions of patients or physicians with different responses are presented as ranges indicating the lowest and highest proportions across the four countries.

3. Results

3.1. Study population and cooperation rates

Approximately 13,000–23,000 invitations were sent to patients in Australia, Canada, China, and the Philippines, with approximately 300 surveys completed from each country (e-Table 1). Eligibility was unknown for 12,280–21,447 patients, while 374–1238 were not eligible. Overall patient cooperation rates ranged from 1.4% for the Philippines to 2.4% for Australia (e-Table 1). For the physician survey, approximately 1000–3000 invitations were sent to physicians in each country, with approximately 200 completed surveys returned. Eligibility was unknown for 860–2874 physicians, while 7–99 physicians were not eligible (e-Table 2). Overall physician cooperation rates ranged from 6.5% for Canada to 17.8% for Australia (e-Table 2).

3.2. Sociodemographics

The majority of patients in each country were female; mean (standard deviation [SD]) age ranged from 30.2 (10.4) years for patients in the Philippines to 55.7 (15.2) years for patients in Australia (Table 1). While more than half of patients in China and the Philippines reported a current smoker or vaper in their household, this was reported by only

Table 1
Patient sociodemographic and health characteristics.

	Australia (N = 305)	Canada (N = 308)	China (N = 300)	Philippines (N = 303)	Overall (N = 1216)
Sex, n (%) ^a					
Female	177 (58.0)	202 (65.6)	170 (56.7)	176 (58.1)	725 (59.6)
Age, years, mean (SD)	55.7 (15.2)	49.5 (14.9)	36.6 (8.5)	30.2 (10.4)	43.1 (16.2)
Age category, n (%)					
18–29	16 (5.2)	31 (10.1)	38 (12.7)	172 (56.8)	257 (21.1)
30–39	37 (12.1)	48 (15.6)	185 (61.7)	84 (27.7)	354 (29.1)
40–49	49 (16.1)	69 (22.4)	50 (16.7)	26 (8.6)	194 (16.0)
≥50	203 (66.6)	160 (51.9)	27 (9.0)	21 (6.9)	411 (33.8)
Age at asthma diagnosis, years					
n	292	291	297	271	1151
mean (SD)	29.1 (21.1)	26.6 (19.0)	24.7 (12.5)	13.5 (10.8)	23.7 (17.5)
Education, n (%)					
High school	103 (33.8)	80 (26.0)	8 (2.7)	45 (14.9)	236 (19.4)
College/University	142 (46.6)	190 (61.7)	264 (88.0)	236 (77.9)	832 (68.4)
Post-graduate school	49 (16.1)	32 (10.4)	25 (8.3)	18 (5.9)	124 (10.2)
Smoking status, n (%)					
Current smoker/vaper in household (on daily basis)	67 (22.0)	92 (29.9)	155 (51.7)	169 (55.8)	483 (39.7)
Location of residence, n (%)					
Large city/metro area	60 (19.7)	125 (40.6)	255 (85.0)	122 (40.3)	562 (46.2)
Suburb of large city/metro area	161 (52.8)	81 (26.3)	28 (9.3)	43 (14.2)	313 (25.7)
Household characteristics, mean (SD)					
Household size	2.3 (1.1)	2.5 (1.4)	3.5 (0.9)	5.1 (2.0)	3.3 (1.8)
Individuals with asthma	1.3 (0.5)	1.3 (0.5)	1.2 (0.4)	1.8 (1.0)	1.4 (0.7)
In general, would you say your health is ... ? n (%)					
Excellent	16 (5.2)	10 (3.2)	14 (4.7)	26 (8.6)	66 (5.4)
Very good	65 (21.3)	81 (26.3)	67 (22.3)	59 (19.5)	272 (22.4)
Good	114 (37.4)	118 (38.3)	97 (32.3)	139 (45.9)	468 (38.5)
Fair	81 (26.6)	72 (23.4)	105 (35.0)	64 (21.1)	322 (26.5)
Poor	24 (7.9)	24 (7.8)	16 (5.3)	14 (4.6)	78 (6.4)
Very poor	5 (1.6)	3 (1.0)	1 (0.3)	1 (0.3)	10 (0.8)
Excluding times you had an urgent need due to asthma, have you seen a doctor or health care provider for routine asthma care in the past 12 months? n (%)					
Yes	216 (70.8)	181 (58.8)	278 (92.7)	238 (78.5)	913 (75.1)
In the past 12 months, have you gone to a pharmacy or drug store for advice about treating your asthma? n (%)					
n	305	307	300	303	1215
Yes	61 (20.0)	72 (23.5)	271 (90.3)	227 (74.9)	631 (51.9)

N = total number of patients included in the survey. n = number of patients who responded to the question. ANOVA, analysis of variance; SD, standard deviation.

^a p-value (determined by Chi-square test for categorical data and ANOVA means test for continuous data) did not indicate significant variation ($p \geq 0.05$) between countries; significant variation between countries was observed for all other sociodemographic and health characteristics.

Table 2
Physician sociodemographic characteristics.

	Australia (N = 200)	Canada (N = 202)	China (N = 201)	Philippines (N = 200)	Overall (N = 803)
Sex, n (%)					
Male	134 (67.0)	125 (61.9)	149 (74.1)	70 (35.0)	478 (59.5)
Age, years, mean (SD)					
n	199	202	201	200	802
mean (SD)	48.6 (10.3)	46.6 (10.8)	41.6 (6.4)	48.3 (8.8)	46.2 (9.6)
Years in clinical practice, mean (SD) ^a	19.8 (9.4)	17.3 (9.5)	17.6 (7.2)	17.5 (8.5)	18.0 (8.73)
Age category, n (%)					
n	199	202	201	200	802
25–39	42 (21.0)	65 (32.2)	77 (38.3)	33 (16.5)	217 (27.1)
40–49	69 (34.5)	60 (29.7)	102 (50.7)	84 (42.0)	315 (39.3)
≥50	88 (44.0)	77 (38.1)	22 (10.9)	83 (41.5)	270 (33.7)
Treatment setting, n (%)					
Government sponsored clinic or doctor's office	1 (0.5)	24 (11.9)	18 (9.0)	56 (28.0)	99 (12.3)
Government sponsored hospital or hospital-based facility	3 (1.5)	17 (8.4)	165 (82.1)	23 (11.5)	208 (25.9)
Private clinic or doctor's office	192 (96.0)	150 (74.3)	3 (1.5)	92 (46.0)	437 (54.4)
Location of treatment facility, n (%)					
Large city/metro area	58 (29.0)	98 (48.5)	38 (18.9)	198 (99.0)	392 (48.8)
Suburb of large city/metro area	106 (53.0)	51 (25.2)	29 (14.4)	2 (1.0)	188 (23.4)
Small City	14 (7.0)	29 (14.4)	75 (37.3)	0 (0.0)	118 (14.7)
Town	10 (5.0)	14 (6.9)	41 (20.4)	0 (0.0)	65 (8.1)
Rural area	11 (5.5)	10 (5.0)	18 (9.0)	0 (0.0)	39 (4.9)
Other	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)

N = total number of physicians included in the survey. n = number of physicians who responded to the question.

ANOVA, analysis of variance; SD, standard deviation.

^a p-value (determined by Chi-square test for categorical data and ANOVA means test for continuous data) did not indicate significant variation ($p \geq 0.05$) between countries; significant variation between countries was observed for all other sociodemographic characteristics.

29.9% of patients in Canada and 22.0% in Australia (Table 1). Most patients described their current health as either fair or good, with the exception of patients in Canada where the greatest proportion described their health as good or very good (Table 1).

With the exception of the Philippines, the majority of physicians surveyed were male (Table 2). Most physicians practicing in Australia or Canada did so in a private clinic, while most physicians in China reported working in a government-sponsored hospital or hospital-based facility. Treatment setting was varied among physicians in the Philippines (Table 2).

3.3. Asthma status

Most commonly, patients regarded their asthma to be well controlled (41.9–43.7% in Australia, Canada, and China) or somewhat controlled (42.2% in the Philippines) (Fig. 1). Approximately a fifth of patients in Australia (21.0%) and Canada (22.7%) considered their asthma to be completely controlled, whereas <10% of patients in China (8.7%) and the Philippines (8.9%) classed their asthma as completely controlled (Fig. 1).

Despite these perceptions of reasonable control, many patients indicated that their asthma had caused them to experience shortness of breath (≥ 3 times/week: 37.0–47.3%) and night-time awakenings due to

symptoms (≥ 1 time/week: 29.9–60.3%) (Table 3). In addition, rescue inhaler use was generally high (≥ 1 use/day: 22.3–37.5%; 2–3 times per week: 19.2–40.7%).

Physician survey responses indicated that the majority of physicians in all countries (94.5–98.4%) classified the disease severity of their patients as mild, moderate, or severe, with <5% doing so rarely (1.6–4.9%) or never (0.0–1.1%) (Table 3). Physicians classified 48.2–62.9% of their patients as having mild asthma (GINA Steps 1 and 2) with 28.4–36.3% having moderate asthma (GINA Steps 3 and 4) and 10.3–15.9% having severe asthma (GINA Step 5) (Fig. 2).

3.4. MART dosing awareness

A higher proportion of patients indicated that they were aware of MART dosing in China (51.7%) and the Philippines (37.3%) than in Australia and Canada (<20% of patients) (Fig. 3A). In contrast, more than half of all physicians were aware of MART; exceeding 70% in Australia, Canada, and China (Fig. 3B). Despite this relatively high awareness of MART, most physicians indicated that they prescribe a SABA in addition to a MART regimen at least some of the time (Fig. 4). The majority of physicians (73.0–92.0%) indicated that they were aware of as-needed (PRN) dosing for patients with mild asthma (Table 4).

3.5. Current treatment patterns

In Australia, Canada, and China, 46.6–60.0% of patients indicated that they use both a daily maintenance and an as-needed rescue inhaler. In the Philippines, the proportion of patients using only a rescue inhaler (33.7%) was similar to the proportion using both a daily maintenance inhaler and an as-needed rescue inhaler (31.0%) (Table 4). Overall, 66.3–81.3% of patients reported using regular maintenance therapy with or without as-needed reliever therapy; of these, 7.8–14.9% were using MART.

Despite the majority of patients indicating that their doctor or health-care provider had explained to them how to use both their daily maintenance inhaler (87.2–97.3%) and their as-needed reliever inhaler (84.9–98.7%), the proportion of patients who reported using their daily maintenance inhaler for quick relief of symptoms instead of an as-needed reliever varied from 44.0% in Australia to 95.8% in China (Table 4).

For patients with mild asthma (GINA Steps 1 and 2), physicians across each of the countries reported most commonly prescribing SABA alone (31.9–66.5%), followed by daily low-dose ICS with as-needed SABA in Australia, Canada, and the Philippines (13.7–22.3%), and daily low-dose ICS without SABA in China (18.1%) (Table 4). Between 8.8% and 20.9% of physicians reported prescribing a MART regimen for patients with mild asthma (GINA Steps 1 and 2), while 11.5–19.8% reported prescribing MART to patients with moderate asthma (GINA Steps 3 and 4). For patients with moderate asthma (GINA Steps 3 and 4), physicians in Australia and Canada most commonly reported that they would initially prescribe daily low-dose ICS with SABA (41.2% and 29.7%, respectively) or ICS/LABA with SABA (28.6% and 29.7%, respectively). Physicians in China and the Philippines indicated a preference for initial treatment with ICS/LABA and SABA (36.2% and 36.6%, respectively) (Table 4).

3.6. Treatment preferences and aims

For patients with mild asthma (GINA Steps 1 and 2), physicians generally rated symptom control over exacerbation reduction as their main treatment goal (29.3–45.1% vs 9.3–15.4%, respectively); responses were similar for patients at GINA Steps 3 and 4 (24.2–43.6% vs 20.9–30.2%) (Table 5). The only exception to this was in Canada, where a slightly higher proportion of physicians rated exacerbation reduction over symptom control as their main treatment goal (30.2 vs 26.4%) for patients. Across all four countries, physicians ranked symptom severity (29.4–44.1%) over exacerbation risk (18.0–29.2%) as the most important factor when prescribing daily maintenance medication (Table 5). For patients with severe asthma (GINA Step 5), a greater proportion of physicians in Australia,

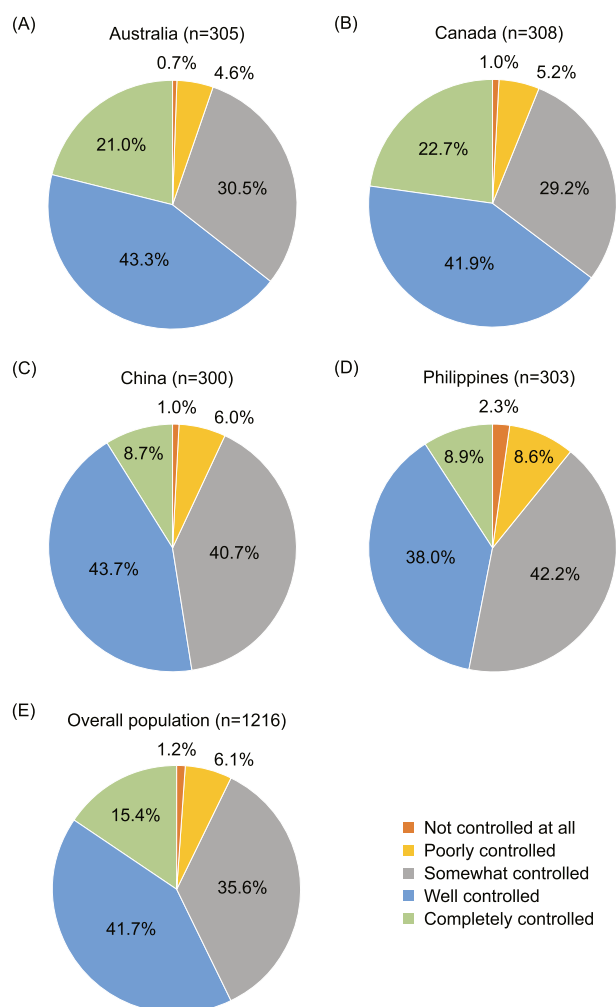


Fig. 1. Patients' perceived level of asthma control. Patient survey question: how would you rate your asthma control during the past 4 weeks? For all data reported here, p-values (determined by Chi-square test) indicated significant variation between countries ($p < 0.05$).

Table 3
Patient asthma status – (A) patient and (B) physician responses.

(A)	Australia (N = 305)	Canada (N = 308)	China (N = 300)	Philippines (N = 303)	Overall (N = 1216)
In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school, or at home? n (%)					
All of the time	7 (2.3)	9 (2.9)	5 (1.7)	10 (3.3)	31 (2.5)
Most of the time	20 (6.6)	27 (8.8)	37 (12.3)	44 (14.5)	128 (10.5)
Some of the time	46 (15.1)	54 (17.5)	168 (56.0)	138 (45.5)	406 (33.4)
A little of the time	84 (27.5)	89 (28.9)	85 (28.3)	95 (31.4)	353 (29.0)
None of the time	148 (48.5)	129 (41.9)	5 (1.7)	16 (5.3)	298 (24.5)
During the past 4 weeks, how often have you had shortness of breath? n (%)					
n	305	307	300	303	1215
More than once a day	49 (16.1)	48 (15.6)	9 (3.0)	33 (10.9)	139 (11.4)
Once a day	29 (9.5)	23 (7.5)	28 (9.3)	31 (10.2)	111 (9.1)
3–6 times per week	35 (11.5)	57 (18.6)	105 (35.0)	56 (18.5)	253 (20.8)
Once or twice per week	135 (44.3)	123 (40.1)	142 (47.3)	151 (49.8)	551 (45.3)
Not at all	57 (18.7)	56 (18.2)	16 (5.3)	32 (10.6)	161 (13.3)
During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness, or pain) wake you up at night or earlier than usual in the morning? n (%)					
n	304	308	300	303	1215
≥4 nights per week	21 (6.9)	17 (5.5)	9 (3.0)	34 (11.2)	81 (6.7)
2–3 nights per week	52 (17.1)	47 (15.3)	98 (32.7)	83 (27.4)	280 (23.0)
Once per week	24 (7.9)	28 (9.1)	74 (24.7)	43 (14.2)	169 (13.9)
Once or twice	83 (27.3)	78 (25.3)	97 (32.3)	99 (32.7)	357 (29.4)
Not at all	124 (40.8)	138 (44.8)	22 (7.3)	44 (14.5)	328 (27.0)
During the past 4 weeks, how often have you used your rescue inhaler/reliever or nebulizer medication? n (%)					
n	304	308	300	303	1215
≥3 times per day	24 (7.9)	29 (9.4)	6 (2.0)	22 (7.3)	81 (6.7)
1–2 times per day	90 (26.9)	80 (26.0)	61 (20.3)	65 (21.5)	296 (24.4)
2–3 times per week	65 (21.4)	59 (19.2)	122 (40.7)	79 (26.1)	325 (26.7)
Once per week or less	71 (23.4)	78 (25.3)	81 (27.0)	109 (36.0)	339 (27.9)
Not at all	54 (17.8)	62 (20.1)	30 (10.0)	28 (9.2)	174 (14.3)
In the past 4 weeks, how often would you say that asthma negatively impacts your daily life? n (%)					
All the time	14 (4.6)	8 (2.6)	8 (2.7)	14 (4.6)	44 (3.6)
Most of the time	19 (6.2)	27 (8.8)	56 (18.7)	81 (26.7)	183 (15.0)
Sometimes	107 (35.1)	109 (35.4)	148 (49.3)	134 (44.2)	498 (41.0)
Rarely	105 (34.4)	113 (36.7)	76 (25.3)	61 (20.1)	355 (29.2)
Never	60 (19.7)	51 (16.6)	12 (4.0)	13 (4.3)	136 (11.2)
(B)	Australia (N = 200)	Canada (N = 202)	China (N = 201)	Philippines (N = 200)	Overall (N = 803)
Do you classify the severity of the asthma in patients you treat? n (%) ^a					
Yes	182 (91.0)	182 (90.1)	189 (94.0)	185 (92.5)	738 (91.9)
How often do you classify your patients as having either mild asthma (GINA Steps 1 and 2), moderate asthma (GINA Steps 3 and 4), or severe asthma (GINA Step 5)? n (%)					
n	182	182	189	185	738
Always	19 (10.4)	33 (18.1)	46 (24.3)	98 (53.0)	196 (26.6)
Often	100 (54.9)	96 (52.7)	106 (56.1)	61 (33.0)	363 (49.2)
Sometimes	53 (29.1)	43 (23.6)	34 (18.0)	23 (12.4)	153 (20.7)
Rarely	8 (4.4)	9 (4.9)	3 (1.6)	3 (1.6)	23 (3.1)
Never	2 (1.1)	1 (0.5)	0 (0.0)	0 (0.0)	3 (0.4)

N = total number of patients/physicians included in the survey. n = number of patients/physicians who responded to the question.

ANOVA, analysis of variance; GINA, Global Initiative for Asthma.

^a p-value (determined by Chi-square test for categorical data and ANOVA means test for continuous data) did not indicate significant variation ($p \geq 0.05$) between countries; significant variation between countries was observed for all other responses.

Canada, and the Philippines ranked exacerbation reduction (29.3–37.9%) over symptom control (21.8–27.1%) as their main treatment goal, while physicians in China still ranked symptom control (58.8%) over exacerbation reduction (27.7%) (Table 5).

Across all countries, approximately 50–90% of patients indicated that it was ‘very important’ that their inhaler treats symptoms such as chest tightness, coughing, and shortness of breath (Table 5). Most patients indicated that if their doctor were to offer them a new inhaler containing a steroid as well as quick relief medicine that they would take it at least as often as they take their current quick relief inhaler (71.5–77.5%) (Table 5).

4. Discussion

Across all four countries included in our survey, physicians ranked

symptom severity over exacerbation risk as the most important factor when prescribing daily maintenance medication. In addition, most physicians prioritized preventing symptoms over reducing the risk of exacerbations as their main treatment goal for both patients with mild (GINA Steps 1–2) and moderate (GINA Steps 3–4) asthma (except in Canada where exacerbation risk reduction was ranked higher for patients with moderate asthma). However, for patients with severe asthma (GINA Step 5), more physicians in Australia, Canada, and the Philippines ranked exacerbation reduction over symptom control as their primary treatment goal. This increasing focus on exacerbation prevention with increasing severity of disease might be expected given the greater likelihood of exacerbations as disease severity increases, but this is likely to be a short-term goal driven by increased hospitalizations and emergency service use rather than a long-term treatment objective. For the majority of

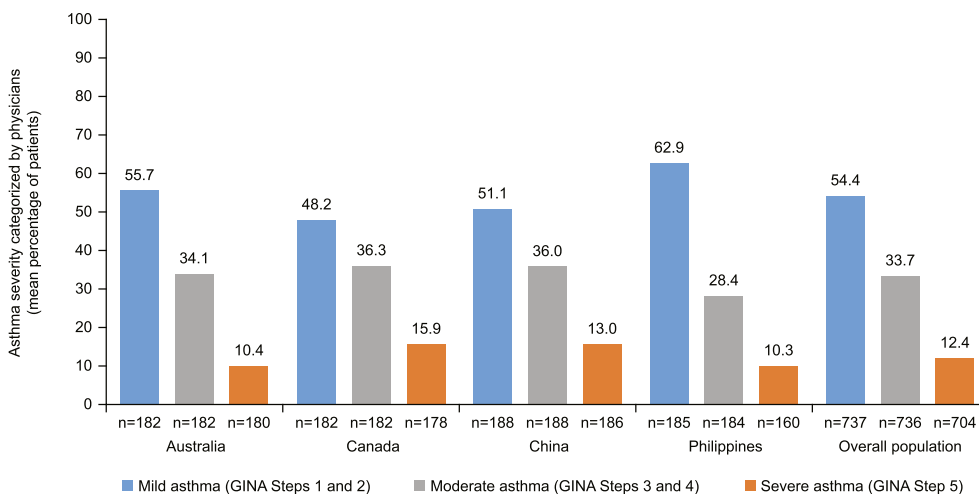


Fig. 2. Physicians' perspectives on the severity of asthma among their patients. Physician survey question: Approximately what percent of your asthma patients have mild asthma (GINA Step 1 and 2)/moderate asthma (GINA Step 3 and 4)/severe asthma (GINA Step 5)? For all data reported here, p-values (determined by ANOVA test) indicated significant variation between countries ($p < 0.05$). ANOVA, analysis of variance; GINA, Global Initiative for Asthma.

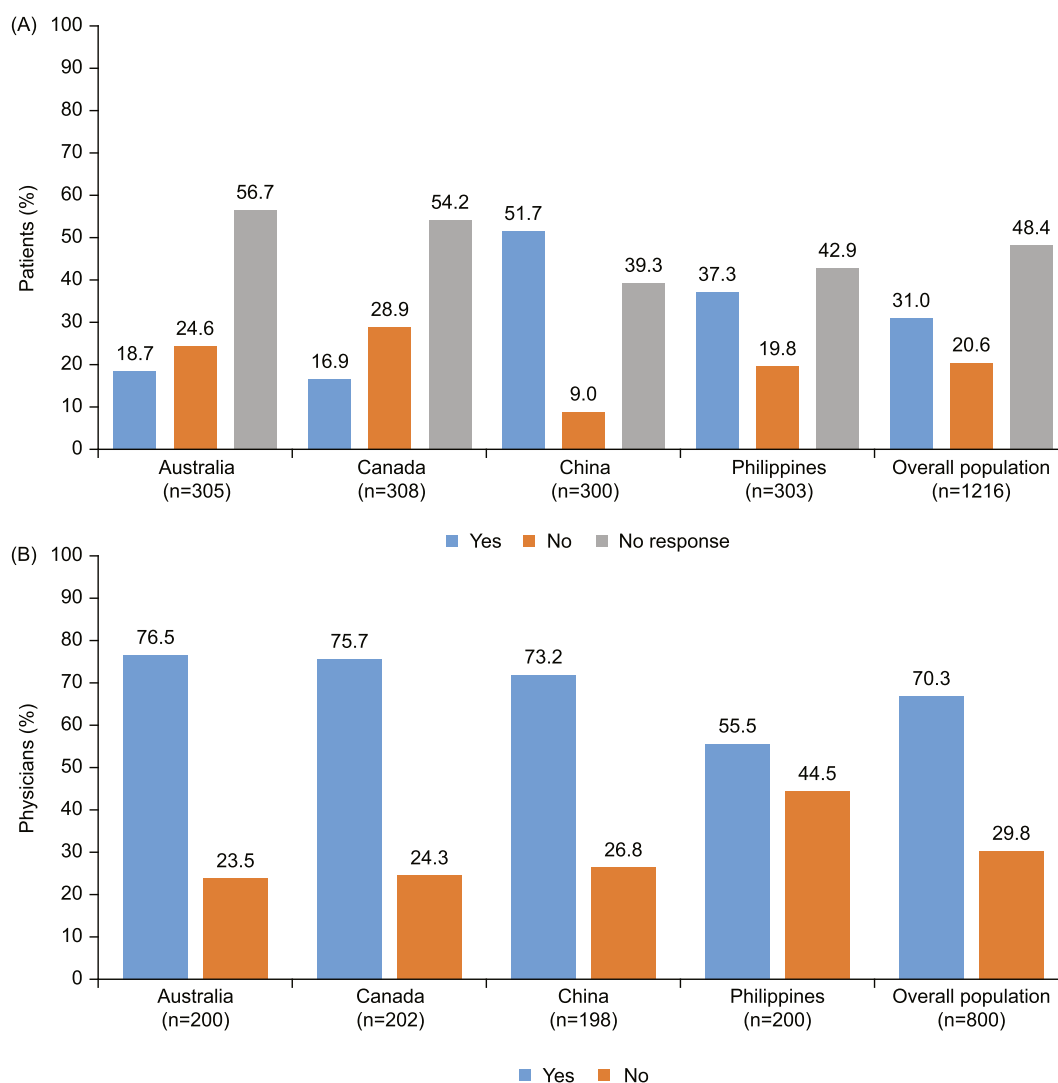


Fig. 3. Patient (A) and physician (B) awareness of MART. Patient survey question (A): Some inhalers can be used as a combination asthma controller/maintenance inhaler and as a rescue inhaler/reliever as needed, in one inhaler. This approach is called MART dosing ... Are you aware of this approach for treating asthma? Physician survey question (B): Are you aware of the MART dosing approach for asthma? For all data reported here, p-values (determined by Chi-square test) indicated significant variation between countries ($p < 0.05$). MART, maintenance and reliever therapy.

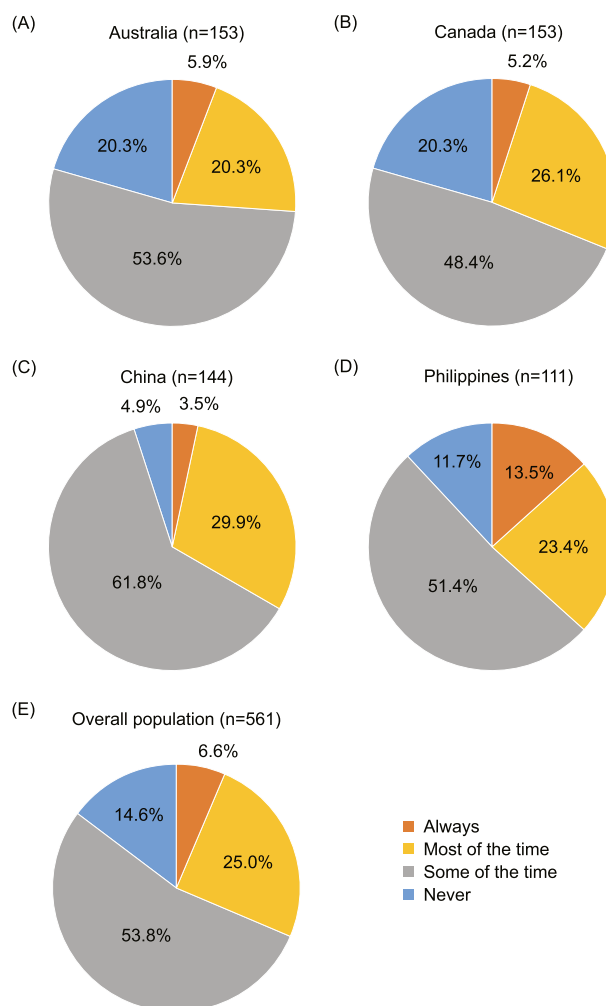


Fig. 4. Frequency of prescribing SABA when using MART, as reported by physicians. Physician survey question: When you prescribe ICS/LABA as MART for asthma, how often do you also prescribe a short-acting β_2 -agonist or a short-acting bronchodilator as a reliever? For all data reported here, p-values (determined by Chi-square test) indicated significant variation between countries ($p < 0.05$). MART, maintenance and reliever therapy; SABA, short-acting β_2 -agonist.

patients with mild or moderate disease, the focus is on symptom control, a priority shared by their physicians. The high ranking of symptom relief by physicians is aligned with the control-based management approach recommended by the GINA report [1], which highlights that in many patients managed in primary care, achieving symptom control is also a good guide to reduced risk of exacerbations. In addition, the ranking of symptom relief as the main patient goal indicates that relieving suffering is the priority for patients with asthma.

Approximately 45–65% of patients surveyed considered their asthma to be completely controlled or well controlled; aligning with current estimates from the literature that approximately 40–60% of patients with asthma are not well controlled, and supporting the representative nature of the patient sample [11–13]. However, the frequent use of rescue inhalers and high symptom burden observed indicates that the patients in this study may have overestimated their level of asthma control. This is consistent with findings from several other studies that indicated patients perceive their asthma control to be better than it actually is [14–16], possibly due to a lack of understanding by the patient of the severity of the disease [17]. Improved communication between patients and physicians and increased expectations of what can be achieved with asthma treatments may improve management and outcomes.

More than 90% of physicians reported that they classify the severity of asthma in their patients. For patients with moderate asthma, physicians most frequently reported prescribing an ICS/LABA regimen (50–80%), in accordance with current international recommendations [1]. However, for

patients with mild asthma, most physicians reported using as-needed SABA only (30–70%) or low-dose ICS plus as-needed SABA (10–20%), despite the recommended shift to as-needed ICS/formoterol in recently updated global recommendations [1]. This continuing use of separate controller and reliever inhalers, with controller used to suppress the need for reliever, suggests that real-world clinical practice takes some time to evolve and adopt new recommendations. However, this approach is also consistent with the finding in the SYGMA 1 study that regular low-dose ICS with separate SABA use provided superior control of symptoms compared with as-needed ICS/formoterol [2].

When considering the applicability of the SYGMA trial data to support the use of as-needed ICS/formoterol in mild asthma [2,3], it is worth noting that, based on physician estimates of asthma severity in this real-world survey, approximately half of patients would not have been eligible for entry into these trials based on asthma severity alone. The high rates of smoking/vaping observed in some countries also would have made many of these patients in this real-world survey ineligible for entry into the SYGMA trials. These differences highlight the challenges of translating results from controlled clinical trials to real-world clinical practice.

The implementation of the recommendation for as-needed ICS/formoterol in real-world settings merits assessment for both patients with mild asthma and patients receiving ICS/formoterol as part of MART. For patients with mild asthma, the recommendation in the GINA report for as-needed ICS/formoterol is based on its non-inferiority in reducing the rate of exacerbations compared with ICS maintenance therapy [2,3]. However, our

Table 4
Current medication regimens and prescribing behavior – (A) patient and (B) physician responses.

(A)	Australia (N = 305)	Canada (N = 308)	China (N = 300)	Philippines (N = 303)	Overall (N = 1216)
Thinking about your asthma medication, do you use a controller/maintenance inhaler, a rescue inhaler/reliever, both a controller/maintenance inhaler and rescue inhaler/reliever, or one inhaler that is for both control and rescue? n (%)					
n	305	307	300	303	1215
Only use a controller/maintenance inhaler	61 (20.0)	55 (17.9)	18 (6.0)	62 (20.5)	196 (16.1)
Only use a rescue inhaler/reliever (eg, blue inhaler) for quick relief of symptoms	57 (18.7)	85 (27.7)	62 (20.7)	102 (33.7)	306 (25.2)
Use both a controller/daily inhaler and a rescue inhaler/reliever (eg, blue inhaler) as needed	157 (51.5)	143 (46.6)	180 (60.0)	94 (31.0)	574 (47.2)
Use one inhaler for both daily use and as a rescue inhaler/reliever (eg, blue inhaler) as needed	30 (9.8)	24 (7.8)	40 (13.3)	45 (14.9)	139 (11.4)
How often do you use a regular controller/maintenance inhaler? n (%)					
n	248	222	238	201	909
Twice a day or more	98 (39.5)	83 (37.4)	24 (10.1)	33 (16.4)	238 (26.2)
Once a day	93 (37.5)	76 (34.2)	51 (21.4)	45 (22.4)	265 (29.2)
Several times a week	32 (12.9)	29 (13.1)	106 (44.5)	51 (25.4)	218 (24.0)
Once a week	6 (2.4)	10 (4.5)	30 (12.6)	37 (18.4)	83 (9.1)
Less than once a week	19 (7.7)	24 (10.8)	27 (11.3)	35 (17.4)	105 (11.6)
Has your doctor or healthcare provider explained the purpose of a controller/maintenance inhaler? n (%)					
Yes	266 (87.2)	276 (89.6)	292 (97.3)	281 (92.7)	1115 (91.7)
How often do you use a quick relief rescue inhaler/reliever (eg, blue inhaler)? n (%)					
n	244	252	282	241	1019
Twice a day or more	54 (22.1)	40 (15.9)	15 (5.3)	18 (7.5)	127 (12.5)
Once a day	33 (13.5)	26 (10.3)	53 (18.8)	42 (17.4)	154 (15.1)
Several times a week	54 (22.1)	54 (21.4)	101 (35.8)	71 (29.5)	280 (27.5)
Once a week	36 (14.8)	35 (13.9)	59 (20.9)	54 (22.4)	184 (18.1)
Less than once a week	67 (27.5)	97 (38.5)	54 (19.1)	56 (23.2)	274 (26.9)
Have you ever used your controller/maintenance inhaler for quick relief of symptoms instead of a rescue inhaler/reliever (eg, blue inhaler)? n (%)					
n	248	222	238	201	909
Yes	109 (44.0)	101 (45.5)	228 (95.8)	177 (88.1)	615 (67.7)
Has your doctor or healthcare provider explained the purpose of a rescue/reliever (blue) inhaler? n (%)					
n	305	307	300	303	1215
Yes	259 (84.9)	272 (88.6)	296 (98.7)	287 (94.7)	1114 (91.7)
(B)					
	Australia (N = 200)	Canada (N = 202)	China (N = 201)	Philippines (N = 200)	Overall (N = 803)
Please think about your typical treatment approach for patients with mild asthma (GINA Steps 1 and 2). What treatment option might you consider initially? n (%)					
n	182	182	188	184	736
Inhaled SABA only (eg, salbutamol)	121 (66.5)	82 (45.1)	60 (31.9)	86 (46.7)	349 (47.4)
Low-dose ICS without inhaled SABA therapy	11 (6.0)	14 (7.7)	34 (18.1)	14 (7.6)	73 (9.9)
Low-dose ICS with inhaled SABA therapy	25 (13.7)	36 (19.8)	29 (15.4)	41 (22.3)	131 (17.8)
ICS/formoterol fixed-dose combination as needed (MART)	16 (8.8)	38 (20.9)	25 (13.3)	17 (9.2)	96 (13.0)
ICS/LABA fixed-dose combination with inhaled SABA	4 (2.2)	4 (2.2)	11 (5.9)	6 (3.3)	25 (3.4)
ICS/LABA fixed-dose combination without inhaled SABA	5 (2.7)	7 (3.8)	12 (6.4)	18 (9.8)	42 (5.7)
Theophylline	0 (0.0)	0 (0.0)	17 (9.0)	0 (0.0)	17 (2.3)
Not receiving any prescribed therapy	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.1)
Other	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	2 (0.3)
Please think about your typical treatment approach for patients with moderate asthma (GINA Steps 3 and 4). What treatment option might you consider initially? n (%)					
n	182	182	188	183	735
Inhaled SABA only (eg, salbutamol)	7 (3.8)	4 (2.2)	3 (1.6)	8 (4.4)	22 (3.0)
Low-dose ICS without inhaled SABA therapy	7 (3.8)	9 (4.9)	4 (2.1)	5 (2.7)	25 (3.4)
Low-dose ICS with inhaled SABA therapy	75 (41.2)	54 (29.7)	34 (18.1)	49 (26.8)	212 (28.8)
ICS/formoterol fixed-dose combination as needed (MART)	21 (11.5)	36 (19.8)	35 (18.6)	27 (14.8)	119 (16.2)
ICS/LABA fixed-dose combination with inhaled SABA	52 (28.6)	54 (29.7)	68 (36.2)	67 (36.6)	241 (32.8)
ICS/LABA fixed-dose combination without inhaled SABA	20 (11.0)	25 (13.7)	38 (20.2)	24 (13.1)	107 (14.6)
Theophylline	0 (0.0)	0 (0.0)	5 (2.7)	0 (0.0)	5 (0.7)
Other	0 (0.0)	0 (0.0)	1 (0.5)	2 (1.1)	3 (0.4)
Refused	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.1)
Are you aware of the PRN dosing approach for mild asthma (GINA Steps 1 and 2)? n (%)					
Yes	164 (82.0)	170 (84.2)	185 (92.0)	146 (73.0)	665 (82.8)

For all data reported here, p-values (determined by Chi-square test) indicated significant variation between countries ($p < 0.05$).

N = total number of patients/physicians included in the survey. n = number of patients/physicians who responded to the question.

ICS, inhaled corticosteroids; LABA, long-acting β_2 -agonist; MART, maintenance and reliever therapy; PRN, as-needed; SABA, short-acting β_2 -agonist.

survey suggests that both physicians and patients consider symptom control over exacerbation risk reduction to be their primary goal in treating mild asthma in the real-world setting. Thus, there may be a need to develop practical strategies to support physicians in identifying those with mild asthma who are most likely to benefit from ICS/formoterol rather than trying to apply the same general approach to all those classified as having mild disease. With regards to the use of as-needed ICS/formoterol within the MART regimen, our results indicate that while most physicians reported they

were aware of MART, prescribing rates for MART and patient-reported use of MART were low, with daily maintenance ICS or ICS/LABA plus SABA being the most widely used regimen in all countries. These findings suggest a lack of patient and physician awareness and understanding of the clinical benefits of MART. An increase in the provision of effective and consistent education for both patients and physicians on the benefits and use of as-needed ICS/formoterol, including its use as part of the MART regimen, may serve to address current gaps and improve asthma management overall.

Table 5
Treatment goals and preferences – (A) patient and (B) physician responses.

	Australia (N = 305)	Canada (N = 308)	China (N = 300)	Philippines (N = 303)	Overall (N = 1216)
Would you prefer ... ? n (%)					
n	173	167	118	130	588
An inhaler that you take every day to prevent asthma symptoms	109 (63.0)	75 (44.9)	62 (52.5)	65 (50.0)	311 (52.9)
An inhaler that you use only after asthma symptoms appear	62 (35.8)	90 (53.9)	56 (47.5)	64 (49.2)	272 (46.3)
Other	2 (1.2)	2 (1.2)	0 (0.0)	1 (0.9)	5 (0.9)
I would rather use my daily controller/maintenance inhaler than have to remember to take my inhaler as needed when I get symptomatic? n (%)					
n	132	107	91	88	418
Strongly agree	57 (43.2)	33 (30.8)	40 (44.0)	34 (38.6)	164 (39.2)
Somewhat agree	49 (37.1)	42 (39.3)	40 (44.0)	33 (37.5)	164 (39.2)
Somewhat disagree	22 (16.7)	18 (16.8)	10 (11.0)	18 (20.5)	68 (16.3)
Strongly disagree	4 (3.0)	14 (13.1)	1 (1.1)	3 (3.4)	22 (5.3)
If your doctor gave you a new quick relief inhaler that contained steroid as well as quick relief medicine, would you use the new inhaler? n (%)					
n	173	167	118	130	588
More often than your current quick relief inhaler	17 (9.8)	25 (15.0)	27 (22.9)	32 (24.6)	101 (17.2)
About as often as your current quick relief inhaler	117 (67.6)	98 (58.7)	61 (51.7)	61 (46.9)	337 (57.3)
Less often than your current quick relief inhaler	39 (22.5)	44 (26.3)	30 (25.4)	37 (28.5)	150 (25.5)
How important is it that your inhaler treats chest tightness? n (%)					
n	173	167	118	130	588
Very important	128 (74.0)	115 (68.9)	62 (52.5)	112 (86.2)	417 (70.9)
Somewhat important	30 (17.3)	39 (23.4)	40 (33.9)	15 (11.5)	124 (21.1)
Slightly important	9 (5.2)	9 (5.4)	13 (11.0)	2 (1.5)	33 (5.6)
Not at all important	6 (3.5)	4 (2.4)	3 (2.5)	1 (0.8)	14 (2.4)
How important is it that your inhaler treats shortness of breath? n (%)					
n	173	167	118	130	588
Very important	149 (86.1)	142 (85.0)	82 (69.5)	118 (90.8)	491 (83.5)
Somewhat important	15 (8.7)	16 (9.6)	31 (26.3)	9 (6.9)	71 (12.1)
Slightly important	3 (1.7)	7 (4.2)	5 (4.2)	1 (0.8)	16 (2.7)
Not at all important	6 (3.5)	2 (1.2)	0 (0.0)	2 (1.5)	10 (1.7)
How important is it that your inhaler treats coughing? n (%)					
n	173	167	118	130	588
Very important	107 (61.8)	92 (55.1)	56 (47.5)	98 (75.4)	353 (60.0)
Somewhat important	44 (25.4)	51 (30.5)	49 (41.5)	26 (20.0)	170 (28.9)
Slightly important	16 (9.2)	19 (11.4)	12 (10.2)	5 (3.8)	52 (8.8)
Not at all important	6 (3.5)	5 (3.0)	1 (0.8)	1 (0.8)	13 (2.2)
	Australia (N = 200)	Canada (N = 202)	China (N = 201)	Philippines (N = 200)	Overall (N = 803)
What are the goals that you aim to attain in your patients with mild asthma (GINA Steps 1 and 2)? n (%)					
n	182	182	188	184	736
Rank symptom control as 1	81 (44.5)	82 (45.1)	70 (37.2)	54 (29.3)	287 (39.0)
Rank exacerbation reduction as 1	17 (9.3)	28 (15.4)	21 (11.2)	19 (10.3)	85 (11.5)
Rank overall asthma control as 1	84 (46.2)	72 (39.6)	97 (51.6)	111 (60.3)	364 (49.5)
What are the goals that you aim to attain in your patients with moderate asthma (GINA Steps 3 and 4)? n (%)					
n	182	182	188	182	734
Rank symptom control as 1	55 (30.2)	48 (26.4)	82 (43.6)	44 (24.2)	229 (31.2)
Rank exacerbation reduction as 1	40 (22.0)	55 (30.2)	51 (27.1)	38 (20.9)	184 (25.1)
Rank overall asthma control as 1	87 (47.8)	79 (43.4)	55 (29.3)	100 (54.9)	321 (43.7)
What are the goals that you aim to attain in your patients with severe asthma (GINA Step 5)? n (%)					
n	176	174	177	140	667
Rank symptom control as 1	44 (25.0)	38 (21.8)	104 (58.8)	38 (27.1)	224 (33.6)
Rank exacerbation reduction as 1	57 (32.4)	66 (37.9)	49 (27.7)	41 (29.3)	213 (31.9)
Rank overall asthma control as 1	75 (42.6)	70 (40.2)	24 (13.6)	61 (43.6)	230 (34.5)
What is THE MOST important factor to you when prescribing controller/maintenance medications? n (%)					
n	153	153	144	111	561
Patients with poorer asthma control (eg, lower scores on the Asthma Control Test)	33 (21.6)	30 (19.6)	31 (21.5)	23 (20.7)	117 (20.9)
Symptom severity	52 (34.0)	45 (29.4)	45 (31.3)	49 (44.1)	191 (34.0)
Patients who exacerbate or are at risk of exacerbation	37 (24.2)	38 (24.8)	42 (29.2)	20 (18.0)	137 (24.4)
Patients with poor adherence	12 (7.8)	14 (9.2)	12 (8.3)	6 (5.4)	44 (7.8)
Other ^a	19 (12.4)	26 (17.0)	14 (9.7)	13 (11.7)	72 (12.8)

For all data reported here, p-values (determined by Chi-square test) indicated significant variation between countries ($p < 0.05$).

N = total number of patients/physicians included in the survey. n = number of patients/physicians who responded to the question.

^a Including: patients with lots of comorbidities, patients with more severe lung function, patient inhaler preference, cost to the patient, flexibility to change ICS dose, patient age.

Most of the trends we observed in this study were similar across the four countries, including the significant proportion of patients with moderate or severe asthma (not represented in the SYGMA trials), the physician ranking of symptom severity over exacerbation prevention as the most important factor when prescribing daily maintenance medication, and the relatively low levels of awareness and understanding of MART. Some findings did vary slightly more across countries as may be expected owing to differences

in population characteristics and variation in country-specific guidelines [18–22]. The cooperation rates seen in the study were deemed acceptable by data collection specialists given the lack of available response rate information for studies from these countries. There are inherent limitations associated with the data collection methods used in this study; data likely lack representativeness due to the highly specific populations targeted and there are physician/patient biases and selection bias associated with the use

of surveys and recruitment from non-probability panels. The fact that most patients responding to the survey were women, in line with real-world asthma prevalence [23], suggests that the survey sample may be partly representative of the asthma population.

Another limitation is the large proportion of respondents who did not respond to certain questions; we have indicated in the data tables where this is the case. Additionally, we did not collect additional information on the physician, and thus estimated parameters are not available by physician type. Finally, due to the nature of this study, we were not able to match physician and patient responses.

5. Conclusions

Most physicians focus on the prevention of asthma symptoms over exacerbations; a perspective shared by the majority of patients. The preferred symptom reliever suggested by the GINA report is ICS/formoterol. Despite the recommendation for treatment with as-needed ICS/formoterol to achieve symptom control for patients across the asthma severity spectrum (and as part of MART for patients at Steps 3 or higher) [1], there appears to be limited implementation and understanding of MART. There is therefore a need for improved education on treatment strategies, particularly treatment regimens involving as-needed ICS/formoterol.

Declaration of competing interest

Guarantor statement: Dr Aman Butta and Professor Kenneth Chapman take responsibility of the integrity of the work as a whole.

Data availability: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Funding sources: This study was funded by GlaxoSmithKline (GSK study 212911).

Conflicts of Interest: KRC has received research grant funding, speaker fees, and consulting fees from AstraZeneca, Grifols, GSK, Novartis, and Sanofi, Regeneron; speaker fees and consulting fees from Boehringer Ingelheim and Teva; consulting fees from CSL Behring and Takeda; LA and JL have no conflicts of interest to disclose; SB-A has received consulting fees, honorarium, and research funding from Teva, AstraZeneca, Boehringer Ingelheim, GSK, and Mylan; CMC has received honorarium from AstraZeneca, Novartis, Boehringer Ingelheim, UAP, and OEP; KL has received consulting fees/speaker fees from GSK, Boehringer Ingelheim, Janssen, Bausch, Astellas, Novartis, AstraZeneca, and Sojceci Inc. JE, PJ and AKB are employees of and own stocks/shares in GSK.

Acknowledgements: Editorial support in the form of preparation of the first draft based on input from all authors, and collation and incorporation of author feedback to develop subsequent drafts, was provided by Rebecca Dawson, PhD, and Chloe Stevenson, MSci, of Fishawack Indicia Ltd, UK, part of Fishawack Health, and was funded by GSK.

Relvar, BREO, Advair, Seretide, Flovent, Ventolin and Flixotide are owned by or licensed to the GSK Group of Companies. Symbicort and Pulmicort are trademarks of AstraZeneca. Zenhale is a trademark of Merck. Alvesco is a trademark of Covis Pharma. Fostair is a trademark of Chiesi Farmaceutici. Flutiform is a trademark of Napp Pharmaceuticals.

Role of the sponsor: This study was funded by GSK (study number 212911). The funders of the study had a role in the study design, data analysis, data interpretation, and writing of the report.

Prior abstract(s) publication: Data from this study were submitted in abstract form and presented as e-Posters at the American Thoracic Society 2021 congress (May 14–19, 2021) and the European Academy of Allergy and Clinical Immunology (EAACI) 2021 congress (July 10–12, 2021).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rmed.2021.106524>.

References

- [1] GINA, Global Initiative for Asthma - global strategy for asthma management and prevention, 2021. <https://ginasthma.org/>. (Accessed 21 May 2021).
- [2] P.M. O'Byrne, J.M. FitzGerald, E.D. Bateman, P.J. Barnes, N. Zhong, C. Keen, C. Jorup, R. Lamarca, S. Ivanov, H.K. Reddel, Inhaled combined budesonide-formoterol as needed in mild asthma, *N. Engl. J. Med.* 378 (20) (2018) 1865–1876.
- [3] E.D. Bateman, H.K. Reddel, P.M. O'Byrne, P.J. Barnes, N. Zhong, C. Keen, C. Jorup, R. Lamarca, A. Siwek-Posluszna, J.M. FitzGerald, As-needed budesonide-formoterol versus maintenance budesonide in mild asthma, *N. Engl. J. Med.* 378 (20) (2018) 1877–1887.
- [4] GINA, Global Initiative for Asthma - global strategy for asthma management and prevention, 2017. <https://ginasthma.org/>. (Accessed 21 May 2021).
- [5] GINA, Global Initiative for Asthma - global strategy for asthma management and prevention, 2018. <https://ginasthma.org/>. (Accessed 21 May 2021).
- [6] GINA, Global Initiative for Asthma - global strategy for asthma management and prevention, 2019. <https://ginasthma.org/>. (Accessed 21 May 2021).
- [7] GINA, Global Initiative for Asthma - Global Strategy for Asthma Management and Prevention, 2020. <https://ginasthma.org/>. (Accessed 21 May 2021).
- [8] K.R. Chapman, N.C. Barnes, A.P. Greening, P.W. Jones, S. Pedersen, Single maintenance and reliever therapy (SMART) of asthma: a critical appraisal, *Thorax* 65 (8) (2010) 747–752.
- [9] I.D. Pavord, P.K. Jeffery, Y. Qiu, J. Zhu, D. Parker, A. Carlshheimer, I. Naya, N. C. Barnes, Airway inflammation in patients with asthma with high-fixed or low-fixed plus as-needed budesonide/formoterol, *J. Allergy Clin. Immunol.* 123 (5) (2009) 1083–1089, 1089.e1-7.
- [10] K.R. Chapman, D. Hinds, P. Piazza, C. Raherison, M. Gibbs, T. Greulich, K. Gaalswyk, J. Lin, M. Adachi, K.J. Davis, Physician perspectives on the burden and management of asthma in six countries: the Global Asthma Physician Survey (GAPS), *BMC Pulm. Med.* 17 (1) (2017) 153.
- [11] J. Vietri, K. Burslem, J. Su, Poor asthma control among US workers: health-related quality of life, work impairment, and health care use, *J. Occup. Environ. Med.* 56 (4) (2014) 425–430.
- [12] M. Mintz, A.W. Gilseman, C.L. Bui, R. Ziemiecki, R.H. Stanford, W. Lincourt, H. Ortega, Assessment of asthma control in primary care, *Curr. Med. Res. Opin.* 25 (10) (2009) 2523–2531.
- [13] D. Price, M. Fletcher, T. van der Molen, Asthma control and management in 8,000 European patients: the REcognise Asthma and Link to Symptoms and Experience (REALISE) survey, *NPJ Prim. Care. Respir. Med.* 24 (2014) 14009.
- [14] V. Kritikos, D. Price, A. Papi, A. Infantino, B. Ställberg, D. Ryan, F. Lavorini, H. Chrystyn, J. Haughney, K. Lisspers, K. Gruffydd-Jones, M. Román Rodríguez, S. Höegh Henriksen, T. van der Molen, V. Carter, S. Bosnic-Anticevich, A multinational observational study identifying primary care patients at risk of overestimation of asthma control, *NPJ Prim. Care. Respir. Med.* 29 (1) (2019) 43.
- [15] K.R. Chapman, P. Ernst, A. Grenville, P. Dewland, S. Zimmerman, Control of asthma in Canada: failure to achieve guideline targets, *Canc. Res. J.* 8 (2001), 245261.
- [16] M. Fletcher, D. Hiles, E. Luck, P242 Patients overestimate their degree of asthma control despite the presence of symptoms: a UK survey, *Thorax* 67 (Suppl 2) (2012). A170-A170.
- [17] K.F. Rabe, P.A. Vermeire, J.B. Soriano, W.C. Maier, Clinical management of asthma in 1999: the asthma insights and reality in europe (AIRE) study, *Eur. Respir. J.* 16 (5) (2000) 802–807.
- [18] National Asthma Council, Australian asthma handbook, 2020. www.assthmehandbook.org.au. (Accessed 6 January 2021).
- [19] M.D. Loughheed, C. Lemiere, F.M. Ducharme, C. Liciskai, S.D. Dell, B.H. Rowe, M. Fitzgerald, R. Leigh, W. Watson, L.P. Boulet, A. Canadian Thoracic Society Asthma Clinical, Canadian Thoracic Society 2012 guideline update: diagnosis and management of asthma in preschoolers, children and adults, *Canc. Res. J.* 19 (2) (2012) 127–164.
- [20] Philippine College of Chest Physicians Council on Asthma, Philippine consensus report on asthma diagnosis and management 2019. <http://philchest.org/wp-content/uploads/2020/07/PCRAM-11082019.pdf>. (Accessed 6 January 2021).
- [21] Asthma workgroup and Chinese thoracic society and Chinese society of general practitioners, Chinese guideline for the prevention and management of bronchial asthma (primary health care version), *J. Thorac. Dis.* 5 (5) (2013) 667–677.
- [22] J. Lin, B. Xing, P. Chen, M. Huang, X. Zhou, C. Wu, D. Yang, K. Yin, S. Cai, X. Cheng, C. Hao, C. Wang, C. Liu, A. China Asthma, Chinese expert consensus-based guideline on assessment and management of asthma exacerbation, *J. Thorac. Dis.* 11 (12) (2019) 4918–4935.
- [23] H. Fuseini, D.C. Newcomb, Mechanisms driving gender differences in Asthma, *Curr. Allergy Asthma Rep.* 17 (3) (2017) 19.