Research Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2022.45.007167

Over-Prescription of Short-Acting β_2-Agonists in Mexico: Results from the SABINA III Study

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ARTICLE INFO

Received: July 08, 2022

Published: July 18, 2022

Citation: Jose Carlos Herrera-Garcia, Rocio Martina Barriga-Acevedo, Sandra Berenice Saavedra-Sanchez, Guillermo Melendez-Mier, Luis Fernando Tejado-Gallegos, Maarten JHI Beekman. Over-Prescription of Short-Acting β_2-Agonists in Mexico: Results from the SABINA III Study. Biomed J Sci & Tech Res 45(2)-2022. BJSTR. MS.ID.007167.

Keywords: Asthma; Prescription; SABINA; Mexico; Short-acting β_2-agonist

ABSTRACT

Objective: Describe demographic/clinical characteristics and short-acting β_2-agonist (SABA) prescriptions in the Mexican cohort of the SABA use IN Asthma (SABINA) III study.

Methods: Data on patient/disease characteristics and asthma treatments in the year prior to the study visit were collected. Patients (≥12 years) were classified by investigator-defined asthma severity and practice type. Prescription of ≥3 SABA canisters/year was considered over prescription.

Results: Data from 149 asthma patients (mean age: 49.1 years), all of whom were treated by specialists, were analyzed. Most patients were female (79.2%) and had moderate-to-severe asthma (77.2%). Asthma was partly controlled/uncontrolled in 59.7% of patients; 63.1% experienced ≥1 severe exacerbation in the previous year. Overall, 51.7% and 41.6% of patients were prescribed ≥3 and ≥10 SABA canisters, respectively. SABAs were purchased over the counter by 20.8% of patients, of whom 29.0% purchased ≥3 canisters.

Conclusions: SABA over-prescription and over-the-counter purchase was common, highlighting the need for alignment with current recommendations.

Abbreviations: BMI: Body Mass Index; eCRF: Electronic Case Report Form; GINA: Global Initiative for Asthma; HCP: Healthcare Practitioner; ICS: Inhaled Corticosteroid; LABA: Long-Acting β_2-Agonist; OCS: Oral Corticosteroid; OTC: Over-the-Counter; SABA: Short-Acting β_2-agonist; SABINA: SABA use IN Asthma; SD: Standard Deviation

Introduction

Asthma is a chronic disease of the airways that imposes a significant social and economic burden on patients and healthcare systems, affecting approximately 339 million people worldwide [1]. Despite significant advances in asthma care and the availability of updated international and national guidelines on asthma treatment and prevention [2], many patients worldwide may not have benefited from these efforts, especially those living in low- and middle-income countries where access to essential asthma medications remains a challenge [1]. As an upper middle-income country [3], Mexico has an estimated asthma prevalence of 5% [4] that continues to increase, with both underdiagnosis and poor disease control contributing to its impact [1,5]. Studies have shown that asthma in Mexico is associated with a number of factors, such as exposure to traffic-related pollution [6] and an urban lifestyle [7] accompanied by the consumption of a westernized, fat-rich diet [8] and limited physical activity [9]. Notably, the segmentation of the Mexican healthcare system continues to restrict public investment and expenditure and has failed to substantially reduce out-of-pocket expenditure [3].

In addition, human resources and physical infrastructure are in relatively low supply and unequally distributed across the country [3]. Furthermore, the healthcare system faces challenges associated with chronic diseases, such as obesity and diabetes, as well as health inequity[3]. In addition to socioeconomic factors, treatment-related factors, such as overuse of short-acting β_2-agonists (SABAs), often at the expense of regular maintenance therapy with inhaled corticosteroids (ICS), have been associated with poor asthma control across Latin America, including Mexico [10,11]. However, the Global Initiative for Asthma (GINA) no longer recommends as-needed SABAs without concomitant ICSs for patients aged ≥12 years [12].

Considering that medications rank as an important cost driver in asthma management [13], a greater understanding of prescription patterns is an area of growing interest, especially in low- and middle-income countries where improving access to affordable medications represents an unmet need [1]. Therefore, a detailed assessment of both SABA prescription patterns and over-the-counter (OTC) SABA purchases is required to provide clinicians, researchers, and healthcare policymakers with a better understanding on the extent of SABA use to ensure that treatment practices align with the latest evidence-based treatment recommendations, to prioritize healthcare resource expenditure, and to devise public health strategies to improve the quality of care for all patients with asthma.

The SABA use IN Asthma (SABINA) series of studies were undertaken to describe the global extent of SABA use through a series of large observational cohort studies applying a harmonized approach to data collection, evaluation, and interpretation [14]. Findings from SABINA III, conducted across 23 countries in the Asia-Pacific, Africa, the Middle East, Latin America, and in Russia, demonstrated that SABA over-prescription (≥3 canisters) in the previous 12 months was common, occurring in 38.0% of patients, and was associated with poor asthma-related outcomes [15]. Here, we report the results from the Mexican cohort of SABINA to provide real-world evidence on SABA prescriptions and asthma treatment practices in this country. The objectives of this study were to describe the demographics and clinical features of the asthma population by asthma severity, estimate prescriptions of SABA (canisters/year) and ICS (by average daily dose—low, medium, or high) per patient, and describe patients within the different treatment groups.

Methods

Study Design

The detailed methodology for SABINA III [15] has been published previously. In this observational, cross-sectional study conducted at four sites in Mexico, patients were recruited from August 2019 to January 2020. Retrospective data were obtained from existing medical records, and patient data were collected during a study visit and entered into an electronic case report form (eCRF). The study was conducted in accordance with the study protocol, the Declaration of Helsinki, and local ethics committees, and signed informed consent was obtained from all patients or their legal guardians.

Study Population

Patients aged ≥12 years with a documented diagnosis of asthma, ≥3 consultations with their healthcare practitioner (HCP), and medical records containing data for ≥12 months prior to the study visit were enrolled. Patients with a diagnosis of other chronic respiratory diseases, such as chronic obstructive pulmonary disease, or with an acute or chronic condition that, in the opinion of the investigator, would limit their ability to participate in the study were excluded. Study sites were selected using purposive sampling with the aim of obtaining a sample representative of asthma management within Mexico.

Study Variables

Each patient was categorized by their SABA and ICS prescriptions in the 12 months before the study visit. SABA prescriptions were categorized as 0, 1–2, 3–5, 6–9, 10–12, and ≥13 canisters, with prescription of ≥3 SABA canisters/year being defined as over-prescription [14]. ICS canister prescriptions in the previous 12 months were recorded and categorized according to the prescribed average daily dose (low, medium, or high) [16].

Secondary variables included practice type (primary or specialist care), investigator-classified asthma severity (guided by the GINA 2017 treatment steps: steps 1–2, mild asthma; steps 3–5, moderate-to-severe asthma) [16], time since asthma diagnosis, and prescriptions for asthma medications in the preceding 12 months (SABA monotherapy, SABA in addition to maintenance therapy, ICS, fixed-dose combinations of ICS with long-acting β_2-agonists [LABAs], oral corticosteroid [OCS] burst treatment [defined as a short course of intravenous corticosteroids or OCS administered for 3–10 days or a single dose of an intramuscular corticosteroid to treat an exacerbation], long-term OCS [defined as any OCS treatment for >10 days], and antibiotics). Patients were also asked about pharmacy purchases of OTC SABA without a prescription at the pharmacy in the 12 months prior. Other variables included medication reimbursement status (not reimbursed, partially reimbursed, or fully reimbursed), educational level (primary or secondary school, high school, or university and/or post-graduate), body mass index (BMI), number of comorbid conditions, and smoking status.

Outcomes

Asthma symptom control was evaluated using the GINA 2017 assessment for asthma control [16] and categorized as well controlled, partly controlled, or uncontrolled. Severe exacerbations in the 12 months before the study visit were based on the American Thoracic Society/European Respiratory Society recommendations [17] and defined as a worsening of asthma symptoms requiring hospitalization, an emergency room visit, or the need for intravenous corticosteroids or OCS for ≥3 days or a single dose of an intramuscular corticosteroid.

Statistical Analysis

Descriptive analyses were used to characterize patients according to baseline demographics and clinical characteristics. Continuous variables were summarized by the number of non-missing values, mean, standard deviation (SD), median, and range, whereas categorical variables were summarized by frequency counts and percentages.

Results

Patient Disposition

Of the 150 patients enrolled, one patient was excluded due to an asthma duration of <12 months; therefore, 149 patients were included in the analysis (Supplementary Figure 1). Although the intention was to recruit patients treated in both primary- and specialist-care settings, all patients were recruited by specialists, with most being treated by pulmonologists (94.6%; n=141). However, two patients were erroneously allocated to "primary care." Therefore, data on overall disease characteristics and treatment patterns are reported for 149 patients, whereas data on asthma severity ("mild" vs. "moderate-to-severe") are reported for 147 patients.

Patient Characteristics

Overall, the mean (SD) age of patients was 49.1 (16.3) years, with most patients (55%; n=82) aged 18–54 years (Table 1). Patients with mild asthma were younger than those with moderate-to- severe asthma (mean age, 41.6 years vs. 51.2 years). The majority of patients were female (79.2%; n=118) and had never smoked (79.2%; n=118). The mean (SD) BMI of patients was 28.2 (6.3) kg/m^2, with most (64.4%; n=96) being overweight or obese (BMI ≥25 kg/m^2). The proportion of patients with BMI ≥25 kg/m^2 was higher among those with moderatetosevere asthma than among those with mild asthma (71.1% [n=81] vs. 42.4% [n=14]). More than one-quarter of patients (28.9%; n=43) had received secondary or high school education, while 53% (n=79) had obtained a university and/or post-graduate education. Overall, 55.7% of patients (n=83) had full healthcare reimbursement, while 35.6% of patients (n=53) had no healthcare reimbursement.

Table 1: Sociodemographics of the SABINA III Mexico cohort by investigator-classified asthma severity.

Parameter	All (N=149)*	Specialists (n=147)	
		Investigator classified mild asthma (n=33)	Investigator classified moderate-to-severe asthma (n=114)
Age (years)			
Mean (SD)	49.1 (16.3)	41.6 (18.8)	51.2 (15.1)
Median (min–max)	49.0 (13.0–87.0)	38.0 (13.0–83.0)	52.0 (13.0–87.0)
Age group (years)			
12–17	5 (3.4)	4 (12.1)	1 (0.9)
18–54	82 (55)	21 (63.6)	60 (52.6)
≥55	62 (41.6)	8 (24.2)	53 (46.5)
Sex			
Female	118 (79.2)	26 (78.8)	90 (78.9)
Male	31 (20.8)	7 (21.2)	24 (21.1)

BMI (kg/m²)			
Mean (SD)	28.2 (6.3)	26.5 (6.8)	28.7 (6.0)
Median (min–max)	26.4 (16.4–48.7)	24.3 (16.4–46.4)	27.3 (16.6–48.7)
BMI group (kg/m²)			
<18.5	4 (2.7)	3 (9.1)	1 (0.9)
18.5–24.9	49 (32.9)	16 (48.5)	32 (28.1)
25–29.9	46 (30.9)	6 (18.2)	40 (35.1)
≥30	50 (33.6)	8 (24.2)	41 (36)
Education level			
Not established	6 (4)	2 (6.1)	3 (2.6)
Primary school	21 (14.1)	3 (9.1)	17 (14.9)
Secondary school	18 (12.1)	5 (15.2)	13 (11.4)
High school	25 (16.8)	3 (9.1)	22 (19.3)
University and/or post-graduate education	79 (53)	20 (60.6)	59 (51.8)
Healthcare insurance/medication funding			
Not reimbursed	53 (35.6)	11 (33.3)	40 (35.1)
Partially reimbursed	10 (6.7)	4 (12.1)	6 (5.3)
Fully reimbursed	83 (55.7)	18 (54.5)	65 (57)
Unknown	3 (2)	0 (0)	3 (2.6)
Smoking status			
Active smoker	5 (3.4)	1 (3)	4 (3.5)
Former smoker	26 (17.4)	4 (12.1)	22 (19.3)
Never smoker	118 (79.2)	28 (84.8)	88 (77.2)

*Two patients were erroneously classified under primary care.

Data are presented as n (%) unless otherwise specified.

BMI: body mass index; max: maximum; min: minimum; SABA: short-acting β2-agonist; SABINA: SABA use IN Asthma; SD: standard deviation

Disease Characteristics

Patients had a mean (SD) asthma duration of 13.9 (15.1) years (Table 2). Overall, 22.8% of patients (n=34) had investigator-classified mild asthma (GINA steps 1–2) and 77.2% (n=115) had moderate-to-severe asthma (GINA steps 3–5); the majority of patients were at GINA step 4 (51.0%; n=76). A comparable proportion of patients reported having no comorbidities and ≥1 comorbidity (48.3% [n=72] and 51.7% [n=77], respectively). However, a higher proportion of patients with moderate-to-severe asthma reported having ≥1 comorbidity compared with those with mild asthma (54.4% [n=62] vs. 39.4% [n=13]). Patients reported a mean (SD) of 1.3 (1.7) severe exacerbations in the previous 12 months, with 63.1% (n=94) and 15.4% (n=23) of patients experiencing ≥1 and ≥3 severe exacerbations, respectively. The level of asthma control was assessed as well-controlled in 40.3% of patients (n=60), partly controlled in 25.5% of patients (n=38), and uncontrolled in 34.2% of patients (n=51). More patients with mild asthma reported having well-controlled asthma compared with those with moderate-to-severe asthma (54.5% [n=18] vs. 36.0% [n=41]), whereas a higher proportion of patients with moderate-to-severe asthma reported having uncontrolled asthma compared with those with mild asthma (37.7% [n=43] vs. 24.2% [n=8]).

Table 2: Asthma characteristics of the SABINA III Mexico cohort according to investigator-classified asthma.

Asthma characteristics	All (N=149)*	Specialists (n=147)	
		Investigator-classified mild asthma (n=33)	Investigator-classified moderate-to-severe asthma (n=114)
Asthma duration (years)			
Mean (SD)	13.9 (15.1)	14.4 (15.3)	13.9 (15.2)
Median (min–max)	7.0 (1.0–65.0)	7.0 (1.0–60.0)	7.0 (1.0–65.0)
Number of severe asthma exacerbations in the past 12 months			

Mean (SD)	1.3 (1.7)	1.0 (1.3)	1.4 (1.9)
Number of severe asthma exacerbations in the past 12 months by group			
0	55 (36.9)	14 (42.4)	41 (36)
1	48 (32.2)	12 (36.4)	34 (29.8)
2	23 (15.4)	3 (9.1)	20 (17.5)
3	13 (8.7)	3 (9.1)	10 (8.8)
>3	10 (6.7)	1 (3)	9 (7.9)
GINA classification			
Step 1	25 (16.8)	25 (75.8)	0 (0)
Step 2	9 (6)	8 (24.2)	0 (0)
Step 3	26 (17.4)	0 (0)	26 (22.8)
Step 4	76 (51)	0 (0)	75 (65.8)
Step 5	13 (8.7)	0 (0)	13 (11.4)
Level of asthma control			
Well controlled	60 (40.3)	18 (54.5)	41 (36)
Partly controlled	38 (25.5)	7 (21.2)	30 (26.3)
Uncontrolled	51 (34.2)	8 (24.2)	43 (37.7)
Number of comorbidities			
0	72 (48.3)	20 (60.6)	52 (45.6)
1–2	70 (47)	10 (30.3)	58 (50.9)
3–4	7 (4.7)	3 (9.1)	4 (3.5)
≥5	NA	NA	NA

*Two patients were erroneously classified under primary care.

Data are presented as n (%) unless otherwise specified.

GINA: Global Initiative for Asthma; max: maximum; min: minimum; NA: not applicable; SABA: short-acting β2-agonist; SABINA: SABA use IN Asthma; SD: standard deviation.

Asthma Treatment in the 12 Months before the Study Visit

Overall, 51.7% of patients (n=77) were prescribed ≥3 SABA canisters, defined as over-prescription, and 41.6% of patients (n=62) were prescribed ≥10 SABA canisters in the preceding 12 months (Figure 1). Approximately one-third of all patients (32.2%; n=48) were prescribed 0 SABA canisters.

A comparable proportion of patients with mild asthma and moderate-to-severe asthma were prescribed ≥3 SABA canisters in the previous 12 months (52.9% [n=18] and 51.3% [n=59], respectively). However, a higher proportion of patients with moderate-to-severe asthma were prescribed ≥10 SABA canisters 12 months prior (44.3% [n=51] vs. 32.4% [n=11]).

	All	Mild asthma	Moderate-to-severe asthma
0*	32.2	11.8	38.3
1–2	16.1	35.3	10.4
3–5	7.4	11.8	6.1
6–9	2.7	8.8	0.9
10–12	40.3	32.4	42.6
≥ 13	1.3	0	1.7

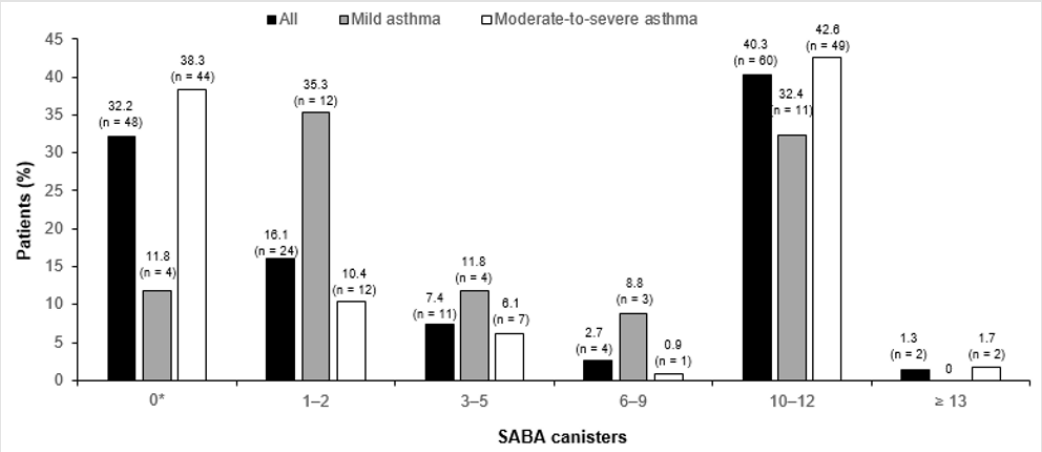


Figure 1: Proportion of patients receiving SABA prescriptions in the 12 months before the study visit according to investigator classified asthma severity in the SABINA III Mexico cohort (N=149).

*Patients without SABA prescriptions did not report what reliever they were using.

SABA: short-acting β_2-agonist; SABINA: SABA use IN Asthma

Prescriptions and Purchase of SABA

SABA Monotherapy: Overall, 8.7% of patients (n=13), all of whom were categorized with mild asthma, were prescribed SABA monotherapy in the previous 12 months, with a mean (SD) of 7.0 (4.7) canisters (Table 3A). Of these patients, 69.2% (n=9) were prescribed ≥3 SABA canisters in the 12 months prior. Moreover, 46.2% (n=6) were prescribed ≥10 SABA canisters in the previous 12 months.

Saba in Addition to Maintenance Therapy: Overall, 59.1% of patients (n=88) were prescribed SABA in addition to any maintenance therapy, with a mean (SD) of 8.7 (4.8) canisters in the previous 12 months (Table 3B). Among these patients, 77.3% (n=68) and 63.6% (n=56) were prescribed ≥3 and ≥10 SABA canisters, respectively, in the preceding 12 months. Compared with patients with mild asthma, a higher proportion of patients with moderate-to-severe asthma were prescribed ≥3 (82.9% [n=58] vs. 50.0% [n=8]) and ≥10 (72.9% [n=51] vs. 25.0% [n=4]) SABA canisters.

OTC SABA Purchase: Approximately one-fifth of all patients (20.8%; n=31) purchased SABA OTC, of whom 71% (n=22) purchased 1-2 canisters and 29.0% (n=9) purchased ≥3 canisters (Table 3C).

Table 3: Patients in the SABINA III Mexico cohort who (A) received prescriptions for SABA monotherapy, (B) received prescriptions for SABA in addition to maintenance therapy, and (C) purchased SABA without a prescription in the 12 months before the study visit.

	All (N=149)*	Specialists (n=147)	
		Investigator-classified mild asthma (n=33)	Investigator-classified moderate-to-severe asthma (n=114)
(A) Prescriptions for SABA monotherapy			
Patients who were prescribed SABA monotherapy			
Yes	13 (8.7)	13 (39.4)	0 (0)
No	136 (91.3)	20 (60.6)	114 (100)

Number of canisters or inhalers per patient prescribed 12 months before the study visit			
Number of patients	13	13	NA
Mean (SD)	7.0 (4.7)	7.0 (4.7)	NA
Median (min–max)	6.0 (2.0–12.0)	6.0 (2.0–12.0)	NA
Number of canisters or inhalers (as categories) per patient prescribed 12 months before the study visit			
1–2	4 (30.8)	4 (30.8)	NA
3–5	2 (15.4)	2 (15.4)	NA
6–9	1 (7.7)	1 (7.7)	NA
10–12	6 (46.2)	6 (46.2)	NA
≥13	NA	NA	NA
(B) Prescription for SABA in addition to maintenance therapy			
Patients who were prescribed SABA in addition to maintenance therapy			
Yes	88 (59.1)	16 (48.5)	70 (61.4)
No	61 (40.9)	17 (51.5)	44 (38.6)
Number of canisters or inhalers per patient prescribed 12 months before the study visit			
Number of patients	88	16	70
Mean (SD)	8.7 (4.8)	4.9 (4.5)	9.6 (4.5)
Median (min–max)	12.0 (1.0–18.0)	2.5 (1.0–12.0)	12.0 (1.0–18.0)
Number of canisters or inhalers (as categories) per patient prescribed 12 months before the study visit			
1–2	20 (22.7)	8 (50)	12 (17.1)
3–5	9 (10.2)	2 (12.5)	6 (8.6)
6–9	3 (3.4)	2 (12.5)	1 (1.4)
10–12	54 (61.4)	4 (25)	49 (70)
≥13	2 (2.3)	0 (0)	2 (2.9)
(C) SABA purchase without prescriptions			
Patients who purchased SABA OTC without a prescription 12 months before the study visit			
Yes	31 (20.8)	8 (24.2)	23 (20.2)
No	116 (77.9)	25 (75.8)	89 (78.1)
Unknown	2 (1.3)	0 (0)	2 (1.8)
Number of canisters or inhalers (as categories) per patient obtained without a prescription 12 months before the study visit			
1–2	22 (71)	5 (62.5)	17 (73.9)
3–5	6 (19.4)	2 (25)	4 (17.4)
6–9	1 (3.2)	0 (0)	1 (4.3)
10–12	2 (6.5)	1 (12.5)	1 (4.3)
≥13	NA	NA	NA
NA**	NA	NA	NA

*Two patients were erroneously classified under primary care.

**"NA" could be selected in the eCRF when patients purchased non-canister forms of SABA (e.g., oral or nebulized SABA) without a prescription.

Data are presented as n (%) unless otherwise specified.

eCRF: electronic case report form; max: maximum; min: minimum; NA: not applicable; OTC: over-the-counter; SABA: short-acting β_2-agonist; SABINA: SABA use IN Asthma; SD: standard deviation.

Prescriptions for other Asthma Treatments

Overall, 17.4% of all patients (n=26) were prescribed maintenance therapy in the form of ICS, with a mean (SD) of 9.6 (4.1) canisters in the previous 12 months (Table 4A). Two-thirds of these patients (66.7%; n=16) were prescribed medium-dose ICS. Most patients (77.9%; n=116) were prescribed an ICS/LABA fixed-dose combination as maintenance therapy, with 63.8% (n=74) prescribed medium-dose ICS (Table 4B). The majority of patients with moderate-to-severe asthma (99.1%; n=113) were prescribed

ICS/LABA fixed-dose combination. Overall, in the preceding 12 months, 39.6% of patients (n=59) were prescribed an OCS burst (Table 4C). Compared with patients with mild asthma, a higher proportion of patients with moderate-to-severe asthma were prescribed an OCS burst (44.7% [n=51] vs. 21.2% [n=7]). A small percentage of patients (4.7%; n=7), all of whom had moderate-to-severe asthma, were prescribed antibiotics (Table 4D).

Table 4: Patients in the SABINA III Mexico cohort who received prescriptions for (A) ICS, (B) ICS/LABA (fixed-dose combination), (C) OCS burst/short course, and (D) antibiotics in the 12 months before the study visit.

	All (N=149)*	Specialists (n=147)	
		Investigator-classified mild asthma (n=33)	Investigator-classified moderate-to-severe asthma (n=114)
(A) Patients who were prescribed ICS			
Yes	26 (17.4)	7 (21.2)	17 (14.9)
No	123 (82.6)	26 (78.8)	97 (85.1)
Total prescribed daily ICS dose			
Low dose	7 (29.2)	3 (50)	4 (23.5)
Medium dose	16 (66.7)	3 (50)	12 (70.6)
High dose	1 (4.2)	0 (0)	1 (5.9)
Missing values	2	1	0
Total	24	6	17
Number of canisters or inhalers per patient prescribed 12 months before the study visit			
Number of patients	25	7	17
Mean (SD)	9.6 (4.1)	9.0 (3.9)	9.6 (4.4)
Median (min–max)	12.0 (1.0–12.0)	12.0 (3.0–12.0)	12.0 (1.0–12.0)
Missing values	1	0	0
(B) Patients who were prescribed ICS/LABA (fixed-dose combination)			
Yes	116 (77.9)	3 (9.1)	113 (99.1)
No	33 (22.1)	30 (90.9)	1 (0.9)
Total prescribed daily ICS dose			
Low dose	35 (30.2)	1 (33.3)	34 (30.1)
Medium dose	74 (63.8)	2 (66.7)	72 (63.7)
High dose	7 (6)	0 (0)	7 (6.2)
(C) Patients who were prescribed OCS burst/short course			
Yes	59 (39.6)	7 (21.2)	51 (44.7)
No	90 (60.4)	26 (78.8)	63 (55.3)
(D) Patients who were prescribed antibiotics for asthma			
Yes	7 (4.7)	0 (0)	7 (6.1)
No	141 (95.3)	32 (100)	107 (93.9)
Missing values	1	1	0
Total	148	32	114

*Two patients were erroneously classified under primary care.

Data are presented as n (%) unless otherwise specified.

ICS: inhaled corticosteroid; LABA: long-acting β2-agonist; max: maximum; min: minimum; OCS: oral corticosteroid; SABA: short-acting β2-agonist; SABINA: SABA use IN Asthma; SD: standard deviation.

Discussion

The findings from the Mexican cohort of the SABINA III study highlight that asthma continues to impose a considerable healthcare and socioeconomic burden on this patient population. Although most patients were prescribed maintenance therapy (ICS and ICS/LABA fixed-dose combinations), more than half of all patients (51.7%) received ≥3 SABA canister prescriptions in the previous 12 months.

In general, the overall demographic and lifestyle characteristics of the SABINA Mexico population were comparable with that of the SABINA III [15] population, although 79.2% of patients in the Mexican cohort were female, which was higher than that observed in the SABINA III [15] population. Notably, approximately two-thirds of patients in the Mexican cohort (64.4%) were classified as overweight or obese (BMI ≥25 kg/m^2); this finding is not entirely unexpected as the rates of obesity in Mexico have increased dramatically over the past 30 years, with Mexico now ranking second in the world for the overall prevalence of obesity, second only to the United States [3]. Even though all study sites were intended to be representative of healthcare practices across Mexico, their selection was likely restricted due to inherent challenges commonly encountered in conducting clinical trials at a primary care level [18]. Therefore, all patients were treated by specialists, with the majority having moderate-to-severe asthma (77.2%). Consequently, this cohort of patients from Mexico likely represents a "better case scenario," given that all patients received specialist care.

Over-prescription of SABA medication was common in the Mexican cohort, with 69.2% and 77.3% of patients prescribed ≥3 SABA canisters as monotherapy or in addition to maintenance therapy, respectively, in the preceding 12 months. Therefore, a higher proportion of patients from Mexico were prescribed ≥3 SABA canisters as monotherapy and in addition to maintenance therapy compared with the overall SABINA III population, where this was reported in 53.6% and 61.7% of patients, respectively [15]. Moreover, SABA over-prescription might have been higher if primary care physicians, who may be less familiar with treatment recommendations, had participated in this study. Although findings from this study are based on a small number of patients, they are consistent with those of previous studies from Latin America, including Mexico, that have reported an over-reliance on SABAs among patients with asthma [10,11], reinforcing the urgent need for routine monitoring of SABA prescription patterns to promptly identify patients at increased risk of exacerbations [19]. The SABA prescription patterns observed in this patient cohort from Mexico may also be attributed to prescribing habits, such as automatic prescription refills, which may have resulted in a high and unnecessary number of dispensed canisters. This clearly demonstrates the need to reduce inappropriate prescribing of SABA; in this regard, it has been suggested that the use of electronic alerts integrated within electronic health records and delivered as part of a multicomponent intervention may prove to be a useful tool to reduce SABA over-prescription [20].

Unregulated access to SABAs was also common, with more than one-fifth of patients (20.8%) purchasing SABA OTC; this was comparable with the SABINA III study (18.0%). Among patients who purchased SABA OTC, 29.0% purchased ≥3 SABA canisters in the previous 12 months. These findings, although based on small patient numbers, are concerning because many patients who purchased SABA OTC likely did so in addition to their SABA prescriptions. However, these data provide valuable insights into patients' beliefs and attitudes toward asthma management and are in alignment with previous research from Latin America, including Mexico, which reported that approximately half of the patients with asthma use quick-relief medication daily, believing that it is acceptable to do so [11]. As SABA purchases have been associated with infrequent physician consultations and undertreatment of asthma [21], these findings emphasize the urgent need for policymakers to regulate the availability of SABAs without prescription, while ensuring improved access to affordable medications to improve overall asthma management.

In general, most patients (77.9%) were prescribed maintenance medication in the form of a fixed-dose combination of ICS/LABA, which was in alignment with the fact that 77.2% of patients had moderate-to-severe asthma (GINA steps 3–5). However, patients were prescribed a mean of 9.6 ICS canisters in the preceding 12 months. This quantity suggests underuse, as one canister per month is considered good clinical practice, although in some cases, a single ICS inhaler provides a 2-month supply. The observation that prescriptions for maintenance medication did not conform to internationally recommended guidelines may also potentially indicate the risk of polypharmacy among patients in Mexico. Indeed, polypharmacy, or the use of multiple medications to treat patients with multimorbidities, or one or more medicinal agents to treat a single condition, is a common practice in Mexico and an area of concern as it is associated with chronic disease, suboptimal treatment outcomes, and increased adverse events due to drug-drug interactions [22,23].

Despite all patients being treated by specialists, the level of asthma control in SABINA Mexico was poor, with 59.7% of patients having partly controlled/uncontrolled asthma, which translated to a high disease burden, with 63.1% of patients experiencing ≥1 severe exacerbation in the preceding 12 months. In line with other studies [11,24], our findings may be attributed to SABA over-reliance and ICS underuse, particularly as previous research has demonstrated that patients from Latin American countries, including Mexico, have concerns about ICS use, do not have a clear understanding of adequate asthma control or how to measure control, and have low expectations on the benefits of successful asthma management, all of which translate to low treatment adherence [11].

The high disease burden observed in this Mexican cohort may also be explained by a lack of healthcare insurance and access to essential medications. Indeed, inadequate healthcare insurance coverage in patients with asthma has been associated with increased emergency room visits [25] and poor quality of care, including

a lower likelihood of receiving ICS [26]. In line with estimates that more than half of the Mexican population is not covered by healthcare insurance [27], only 62.4% of patients from this Mexican cohort received partial or full healthcare reimbursement, while 35.6% received no healthcare reimbursement. Given that poor asthma control remains a major clinical challenge in Mexico, asthma advocacy programs can impact asthma care positively by improving access to treatment, raising awareness of disease and its effective management, and ensuring integration of the patient perspective into policy decisions [1].

In 2017, asthma experts from Mexico presented at the Senators' Chamber of the Mexican Republic and underscored the importance of asthma as a public health concern, which necessitates a wider basic catalog of asthma medications and well-trained physicians [1]. The findings from this Mexican cohort further emphasize this point and highlight the need for political commitment supported by appropriate policies to improve overall disease management by establishing educational programs targeted at both patients and HCPs; providing additional education for specialists; regulating SABA OTC purchase while ensuring access to quality care and affordable medications, including adequate provision for ICS-containing medications; and prioritizing the implementation of current evidence-based recommendations. Following the historic 2019 updates in the GINA report on asthma management and prevention [12], a panel of experts in Mexico have now recommended that all patients with asthma receive anti-inflammatory treatment [28]. An effective strategy proposed by these experts was the use of low-dose ICS with a fast-acting β_2-agonist as the preferred reliever for patients with intermittent symptoms and for those with persistent symptoms as a daily controller treatment and as-needed reliever medication [28]. This anti-inflammatory reliever approach represents a viable asthma management strategy, as ICS and fast-acting β_2-agonists are available across most low-income settings [29]. However, as the current Mexican asthma guidelines [30] have not adopted these updated treatment recommendations, immediate action should be taken to ensure alignment with GINA.

Limitations

This study has several limitations. Prescription data were considered a surrogate for medication usage and do not reflect actual SABA administration or provide information on medication adherence, potentially contributing to an under-estimation or over-estimation of SABA use. As this analysis was limited to 149 patients, all of whom were recruited by specialists, the study population is not representative of the overall national asthma population. Therefore, additional studies are required to gain a more comprehensive understanding of treatment patterns in both primary and specialist care. Moreover, the greater number of patients with moderate-to-severe asthma recruited into the study may influence the generalizability of the results.

Nevertheless, to the best of our knowledge, this is the first study specifically designed to examine the extent of SABA prescriptions and asthma treatment practices in Mexico, which may have important public health and policy implications. Moreover, centralized eCRFs can be a reliable source of real-world data, allowing policymakers and clinicians to consider the necessary targeted changes in clinical practice to improve outcomes for patients with asthma in Mexico.

Conclusion

Results from the Mexican cohort of SABINA III reveal concerning SABA prescription practices; despite specialist care, approximately one in every two patients were over-prescribed SABAs (≥3 canisters) and approximately four in every 10 patients were prescribed ≥10 canisters in the preceding 12 months. In addition, unregulated access to SABA was common, with 20.8% of patients purchasing SABAs OTC, of whom 29.0% purchased ≥3 SABA canisters in the previous 12 months. Taken together, these findings highlight that SABA over-prescription is a major public health concern in Mexico, requiring HCPs and policymakers to prioritize the alignment of clinical practices with the latest evidence-based recommendations to improve long-term treatment outcomes for patients with asthma.

Acknowledgments

AstraZeneca funded all the SABINA studies and was involved in designing the study, developing the study protocol, conducting the study, and performing the analyses. AstraZeneca was given the opportunity to review the manuscript before submission. Medical writing and editorial support were provided by Cactus Life Sciences (part of Cactus Communications, Mumbai, India) in accordance with Good Publication Practice (GPP3) guidelines (http://www.ismpp.org/gpp3) and fully funded by AstraZeneca.

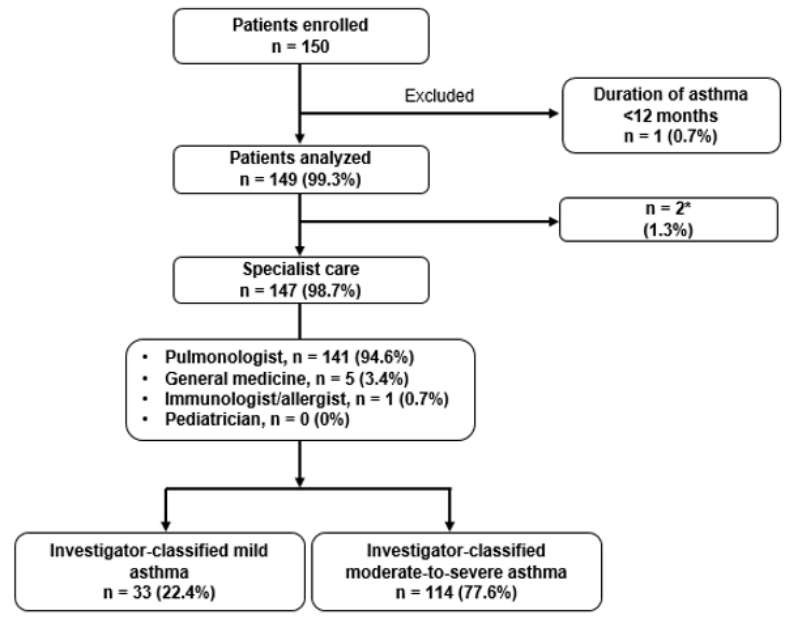
Data Availability Statement

The data underlying the findings described in this manuscript may be obtained in accordance with AstraZeneca's data sharing policy described at https://astrazenecagrouptrials.pharmacm.com/ST/Submission/Disclosure.

Author Disclosure:

Jose Carlos Herrera-Garcia has participated in clinical studies funded by AstraZeneca, Novartis, GSK, and Boehringer Ingelheim. He has also served as a speaker at international congresses and as Principal Editor at the Intech Open Library. Rocio Martina Barriga-Acevedo has participated in clinical trials for AstraZeneca, GlaxoSmithKline, Novartis, and Chiesi. Sandra Berenice Saavedra-Sanchez has participated as an investigator, co-investigator, and study coordinator in various studies with AstraZeneca, Pfizer, Novartis, Sanofi, and Bristol Myers Squibb. Guillermo

Melendez-Mier has participated in clinical trials for AstraZeneca, GlaxoSmithKline, Eli Lilly, Pfizer, MSD, and Takeda. He has also served as a journal reviewer. Luis Fernando Tejado-Gallegos is an employee of AstraZeneca. Maarten J.H.I. Beekman was an employee of AstraZeneca at the time this study was conducted.



*Two patients were erroneously classified under primary care.

SABA: short-acting β2-agonist; SABINA: SABA use IN Asthma.

Supplementary Figure 1: Patient disposition in the SABINA III Mexico cohort (N=149) by investigator-classified asthma severity.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2022.45.007167

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Submission Link: https://biomedres.us/submit-manuscript.php