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Over-prescription of short-acting β_2-agonists is associated with poor asthma outcomes: results from the African cohort of the SABINA III study

Adel Khattab[a], Ashraf Madkour[a], Anish Ambaram[b], Clifford Smith[c], Chakaya J. Muhwa[d,e], Jared O. Mecha[f], Mohamed Alsayed[g] and Maarten J. H. I. Beekman[h]

[a]Pulmonary Medicine Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt; [b]Department of Pulmonology, Gateway Centre for Respiratory and Gastrointestinal Disease, Durban, South Africa; [c]Morningside Mediclinic, Sandton, Johannesburg, South Africa; [d]Department of Medicine, Therapeutics and Dermatology, Kenyatta University, Nairobi, Kenya; [e]Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, United Kingdom; [f]Department of Clinical Medicine and Therapeutics, University of Nairobi, Nairobi, Kenya; [g]Medicinal Department, AstraZeneca, Dubai, United Arab Emirates; [h]Respiratory & Immunology, AstraZeneca, The Hague, The Netherlands

ABSTRACT

Background: The extent of short-acting β_2-agonist (SABA) overuse in Africa remains poorly documented. As part of the SABA use IN Asthma (SABINA) III study, we assessed SABA prescriptions/clinical outcomes in 3 African countries.

Methods: Data on disease characteristics/asthma treatments were collected from patients ($\geq$12 years) using electronic case report forms. Patients were classified by investigator-defined asthma severity (guided by the 2017 Global Initiative for Asthma) and practice type (primary/specialist care). Multivariable regression models analyzed associations between SABA prescriptions and outcomes.

Results: Data from 1778 patients (mean age, 43.7 years) were analyzed. Most patients were female (62.4%) and had moderate-to-severe asthma (63.3%), with 57.1 and 42.9% of patients treated in specialist and primary care, respectively. Asthma was partly controlled/uncontrolled in 66.2% of patients, with 57.9% experiencing $\geq$1 severe exacerbation in the previous 12 months. Overall, 46.5% of patients were prescribed $\geq$3 SABA canisters in the preceding 12 months (over-prescription); 26.2% were prescribed $\geq$10 canisters. SABAs were purchased over-the-counter by 32.6% of patients, of whom 79.3% had received SABA prescriptions; 71.9% and 40.1% for $\geq$3 and $\geq$10 canisters, respectively. Higher SABA prescriptions (vs. 1–2 canisters) were associated with increased incidence rate of severe exacerbations and lower odds of having at least partly controlled asthma (except 3–5 canisters).

Conclusions: Findings from this African cohort of the SABINA III study indicate that SABA over-prescription and SABA over-the-counter purchase are common and associated with poor asthma-related outcomes. This highlights the need for healthcare providers/policymakers to align clinical practices with the latest treatment recommendations.

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Introduction

Asthma is a serious global health problem[1] estimated to affect approximately 339 million people worldwide[2] and over 119 million people in the African continent[3]. Many patients with asthma require long-term medication daily to control the underlying airway inflammation and prevent symptoms and exacerbations[1,4]. Although inhaled corticosteroids (ICS) are used to treat the underlying airway inflammation, short-acting β_2-agonists (SABAs) provide rapid symptom relief by reducing airway narrowing[1]. However, SABAs have no inherent anti-inflammatory activity[5,6], and their overuse ($\geq$3 canisters/year[7]) is associated with an increased incidence of exacerbations, mortality, and healthcare costs[8–10]. Consequently, owing to safety concerns, the Global Initiative for Asthma (GINA) no longer recommends as-needed SABAs without concomitant ICS for patients aged $\geq$12 years[1].

Despite the availability of effective treatment options[1], asthma remains poorly controlled in a substantial proportion of patients worldwide, with long-term management being insufficient to meet the goals put forward in the GINA recommendations[11]. Therefore, asthma remains a major health problem, particularly in low- and middle-income countries, and represents a greater problem in Africa than originally thought[2] owing to weak healthcare systems, including poor infrastructure; inadequate resources and healthcare provider (HCP) capacity; and low budget allocation[3,12]. In addition, regional factors including diagnostic challenges, low level of awareness of the disease burden, non-availability and unaffordability of ICS, nonadherence to prescribed medications

CONTACT Adel Khattab dr_adkhattab@hotmail.com Pulmonary Medicine Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt
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(when available), lack of patient education, poor communication between HCPs and patients, lower educational levels, and inherent sociocultural misconceptions regarding asthma and its treatment negatively impact asthma management in African countries[3,12,13].

To date, the prevalence of asthma has been reported in only a few parts of Africa, with data indicating a gradual increase in morbidity due to asthma[14]. Furthermore, there is a scarcity of data concerning prescription patterns for asthma medications, in particular the prevalence of SABA use and its consequences, in Africa. Understanding how access to and use of medications impact asthma care, particularly in Africa, where improving access to affordable asthma medication represents an unmet need[2,15], remains of paramount importance. Moreover, an assessment of SABA prescription patterns can help guide policy decisions to align local treatment guidelines with the latest evidence-based treatment recommendations[1] and therefore ensure that patients have sufficient access to essential asthma medications. However, a lack of comprehensive healthcare databases has limited access to patient-level data and evaluation of trends in medication use across the African continent.

The SABA use IN Asthma (SABINA) III study is part of a series of real-world observational studies conducted globally to describe SABA prescription patterns across countries in the Asia Pacific, Africa, the Middle East, Latin America and in Russia using electronic case report forms (eCRFs) to capture patient-level data from HCPs[16]. Here, we report SABA prescription patterns and their association with clinical outcomes in the African cohort (Egypt, South Africa, and Kenya) of the SABINA III study.

Methods

Study design

SABINA III was a cross-sectional, multi-country, multi-centre observational study conducted in 24 countries across 5 continents[16]. The primary objective was to describe SABA prescription patterns in the African cohort of the SABINA III study at an aggregated multi-country level. The secondary objective was to determine the associations between SABA prescriptions and asthma-related health outcomes in this cohort. The methodology for SABINA III has been described previously[7,16]. The study was conducted in accordance with the study protocol, the Declaration of Helsinki, and local ethics committees. Signed informed consent was obtained from all patients or their legal guardians per local ethics review committee regulations.

Study population

Patients aged $\geq$12 years who met the following criteria were eligible for enrollment: a documented physician diagnosis of asthma in their medical records, $\geq$3 prior consultations with their HCP, and medical records containing data for $\geq$12 months before the study visit. 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 investigator's opinion, would limit the patient's ability to participate in the study were excluded. Primary and specialist care study sites were selected using purposive sampling with the aim of obtaining a sample representative of asthma management within each participating country by a national coordinator, who also facilitated the selection of investigators.

Study variables

During the cross-sectional study visit, retrospective data were obtained from existing medical records, and patient data, including an assessment of current asthma symptom control, were collected and entered into an eCRF by the investigator. SABA prescriptions recorded during the 12 months before the study were categorized as 0, 1–2, 3–5, 6–9, 10–12, and $\geq$13 canisters. Over-prescription was defined as a prescription of $\geq$3 SABA canisters in the 12 months prior to the study visit[7]. For consistency, across the whole SABINA program, one SABA canister was assumed to contain 150 inhalations[7]. ICS canister prescriptions in the previous 12 months were recorded and expressed according to the prescribed average daily dose—low, medium, or high (Supplemental Table 1)[17].

Secondary variables included practice type (primary or specialist care), investigator-classified asthma severity (guided by GINA 2017; steps 1–2: mild asthma; steps 3–5: moderate-to-severe asthma)[17], asthma duration, and asthma treatment in the preceding 12 months (SABA monotherapy, SABA in addition to maintenance therapy, ICS, fixed-dose combination of ICS with long-acting β_2-agonists [LABAs], long-term oral corticosteroid [OCS] treatment [any OCS treatment for $>$10 days], OCS burst treatment [defined as a short course of intravenous (IV) corticosteroids or OCS administered for 3–10 days or a single dose of an intramuscular (IM) corticosteroid to treat an exacerbation], and antibiotics prescribed for asthma). In addition, data for SABA purchase over-the-counter [OTC] without a prescription was based on patient recall and obtained directly from patients at the study visit, which was subsequently entered into the eCRF by the investigator.

Other variables included healthcare insurance (not reimbursed [out-of-pocket expenses], partially reimbursed [expenses partially covered by insurance], or fully reimbursed [expenses fully covered by insurance]), education level (primary and secondary school, high school, or university and post-graduate), body mass index (BMI), number of comorbidities, and tobacco smoking status.

Outcomes

Asthma symptom control was evaluated according to the GINA 2017 assessment of asthma control and categorized as well controlled, partly controlled, and uncontrolled[17]. Severe exacerbations in the 12 months before the study visit were based on the American Thoracic Society/European Respiratory Society recommendations[18] and defined as deterioration in asthma resulting in hospitalization or emergency room treatment, or the need for IV corticosteroids or OCS for $\geq$3 days, or a single IM corticosteroid dose.

Statistical analysis

Patient-level analyses are presented as country-aggregated descriptive statistics. The association of SABA prescriptions (3–5, 6–9, 10–12, and ≥13 vs 1–2 canisters) in the previous 12 months with the incidence rate of severe exacerbations and the odds of achieving at least partly controlled asthma (uncontrolled asthma as the reference) was analyzed using negative binomial and logistic regression models, respectively. Patients with 0 SABA prescriptions were excluded as it was not possible to determine the reliever medication used. All regression models used complete-case analyses and were adjusted for prespecified covariates (country, age [continuous variable], sex, and tobacco smoking status) and potential confounders (GINA treatment step, healthcare reimbursement, education level, comorbidities, asthma duration [continuous variable], and BMI [continuous variable]). All statistical tests were 2-sided, at a 5% level of significance, and were performed using the R statistical software (version 3.6.0).

Patient and public involvement

It was not appropriate or possible to involve patients or the public in the design, conduct, reporting, or dissemination plans of our research.

Results

Patient disposition

Of the 1794 patients enrolled, 16 were excluded because their asthma duration was less than 12 months; therefore, 1778 patients were included in the analysis (Supplemental Figure 1). Most patients were recruited from Egypt ($n = 872$; 49.0%), followed by South Africa ($n = 501$; 28.2%) and Kenya ($n = 405$; 22.8%; Supplemental Figure 2). A slightly higher proportion of patients were treated by specialists (57.1%) than by primary care physicians (42.9%; Supplemental Figure 1).

Patient and disease characteristics

Overall, the mean (standard deviation [SD]) age of the patients was 43.7 (16.0) years, with most patients evenly distributed across all age groups. In specialist care, most patients were aged 18–34 years (29.9%), while in primary care most were aged ≥55 years (30.2%). The majority of patients were female (62.4%), classified with moderate-to-severe asthma (GINA steps 3–5; 63.3%), had a BMI of ≥25 kg/m^2 (68.4%), and had never smoked tobacco (80.9%; Table 1). More than one-quarter of patients had received only high school education (28.1%), while 33.7% had obtained university and post-graduate education. Most patients with mild asthma (67.1%) were treated in primary care, while most patients with moderate-to-severe asthma (86.1%) were treated in specialist care. More than half of all patients (53.2%) had no healthcare reimbursement. Overall, nearly half of all patients had ≥1 comorbidity (47.7%). The level of asthma symptom control was assessed as well-controlled in 33.8% of patients, partially controlled in 39.8% of patients, and uncontrolled in 26.4% of patients. Asthma symptom control was generally comparable across asthma severities in patients treated in primary care; however, in specialist care, asthma was well-controlled in a greater percentage of patients with mild asthma than in those with moderate-to-severe asthma (66.2 vs 35.7%; Table 2). Patients reported a mean (SD) of 1.4 (2.4) severe exacerbations, with 57.9 and 16.1% having experienced ≥1 and ≥3 severe asthma exacerbations, respectively, in the previous 12 months. In primary care, a comparable proportion of patients with mild and moderate-to-severe asthma experienced ≥1 severe exacerbation in the previous 12 months (55.6 and 53.2%, respectively). In contrast, in specialist care, a higher proportion of patients with moderate-to-severe asthma than those with mild asthma experienced ≥1 severe exacerbation (62.4 and 46.5%, respectively).

Asthma treatment in the 12 months before the study visit

Overall, 46.5 and 26.2% were prescribed ≥3 and ≥10 SABA canisters, respectively, in the previous 12 months; over one-third of patients (34.3%) were prescribed 0 SABA canisters (Figure 1). Compared with patients with moderate-to-severe asthma, a higher proportion of patients with mild asthma were prescribed ≥3 (69.1 vs. 33.6%) and ≥10 (45.0 vs. 15.3%) SABA canisters, respectively. A higher proportion of patients with mild asthma treated in primary care vs specialist care were prescribed ≥3 (82.9 vs. 19.3%) and ≥10 (54.3 vs. 11.4%) SABA canisters in the preceding 12 months, respectively. Similarly, a higher proportion of patients with moderate-to-severe asthma treated in primary care vs specialist care were prescribed ≥3 (60.2 vs. 26.0%) and ≥10 (43.0 vs. 7.5%) SABA canisters in the 12 months prior, respectively.

Saba monotherapy

Overall, 6.5% of patients were prescribed SABA monotherapy, with a mean (SD) of 6.1 (4.4) canisters in the previous 12 months (Table 3). Among these patients, 66.1% were prescribed ≥3 canisters and 33.0% were prescribed ≥10 canisters in the preceding 12 months. A higher proportion of patients in primary care (12.6%), all of whom had mild asthma, were prescribed SABA monotherapy compared with those treated by specialists (1.8%). SABA monotherapy was prescribed to 18.8 and 12.1% of patients with mild asthma in primary and specialist care, respectively, and to 0.1% of patients with moderate-to-severe asthma in specialist care. Overall, 72.9 and 33.3% of patients were prescribed ≥3 SABA canisters in the previous 12 months in primary and specialist care, respectively.

Saba in addition to maintenance therapy

Most patients (59.3%) were prescribed SABA in addition to maintenance therapy in the previous 12 months, with a mean (SD) of 7.0 (4.8) canisters (Table 3). Overall, 71.3% of

Table 1. Demographics and baseline clinical characteristics of the SABINA III African population by investigator-classified asthma severity and practice type.

Parameter	All ($N = 1778$)	Primary care ($n = 761$)			Specialists ($n = 1011$)		
		Investigator-classified mild asthma ($n = 510$)	Investigator-classified moderate-to-severe asthma ($n = 250$)	All ($n = 761$)	Investigator-classified mild asthma ($n = 140$)	Investigator-classified moderate-to-severe asthma ($n = 869$)	All ($n = 1011$)
Age (years)							
Mean (SD)	43.7 (16.0)	45.6 (15.1)	46.6 (14.8)	45.9 (15.0)	38.0 (18.9)	42.7 (16.0)	42.0 (16.5)
Median (min–max)	42.0 (12.0–93.0)	45.0 (13.0–87.0)	46.0 (12.0–80.0)	45.0 (12.0–87.0)	37.0 (12.0–93.0)	41.0 (12.0–93.0)	41.0 (12.0–93.0)
Age group (years)							
12–17	76 (4.3)	11 (2.2)	7 (2.8)	18 (2.4)	20 (14.3)	38 (4.4)	58 (5.7)
18–34	455 (25.6)	106 (20.8)	42 (16.8)	148 (19.4)	46 (32.9)	256 (29.5)	302 (29.9)
35–44	420 (23.6)	127 (24.9)	65 (26.0)	193 (25.4)	24 (17.1)	202 (23.2)	227 (22.5)
45–54	355 (20.0)	112 (22.0)	60 (24.0)	172 (22.6)	22 (15.7)	159 (18.3)	182 (18)
≥55	472 (26.5)	154 (30.2)	76 (30.4)	230 (30.2)	28 (20.0)	214 (24.6)	242 (23.9)
Sex							
Female	1109 (62.4)	355 (69.6)	139 (55.6)	494 (64.9)	78 (55.7)	531 (61.1)	611 (60.4)
Male	669 (37.6)	155 (30.4)	111 (44.4)	267 (35.1)	62 (44.3)	338 (38.9)	400 (39.6)
BMI (kg/m^2)							
Mean (SD)	28.2 (6.7)	27.9 (7.3)	29.1 (7.3)	28.3 (7.3)	27.2 (6.0)	28.3 (6.2)	28.2 (6.2)
Median (min–max)	27.2 (13.6–86.7)	26.8 (13.6–57.0)	28.4 (14.3–56.7)	27.2 (13.6–57.0)	26.2 (14.8–46.1)	27.2 (15.2–86.7)	27.2 (14.8–86.7)
BMI group (kg/m^2)							
<18.5	60 (3.4)	30 (5.9)	8 (3.2)	38 (5.0)	6 (4.3)	16 (1.8)	22 (2.2)
≥18.5–24.9	501 (28.2)	159 (31.2)	64 (25.6)	223 (29.3)	47 (33.6)	230 (26.5)	277 (27.4)
≥25–29.9	652 (36.7)	168 (32.9)	80 (32.0)	248 (32.6)	49 (35.0)	349 (40.2)	400 (39.6)
≥30	565 (31.8)	153 (30.0)	98 (39.2)	252 (33.1)	38 (27.1)	274 (31.5)	312 (30.9)
Education level							
Not established	83 (4.7)	10 (2.0)	7 (2.8)	17 (2.2)	3 (2.1)	62 (7.1)	65 (6.4)
Primary school	274 (15.4)	147 (28.8)	29 (11.6)	176 (23.1)	17 (12.1)	81 (9.3)	98 (9.7)
Secondary school	322 (18.1)	113 (22.2)	30 (12.0)	143 (18.8)	25 (17.9)	153 (17.6)	178 (17.6)
High school	499 (28.1)	171 (33.5)	60 (24.0)	232 (30.5)	40 (28.6)	224 (25.8)	264 (26.1)
University and post-graduate education	600 (33.7)	69 (13.5)	124 (49.6)	193 (25.4)	55 (39.3)	349 (40.2)	406 (40.2)
Healthcare insurance/medication funding							
Not reimbursed	946 (53.2)	349 (68.4)	57 (22.8)	406 (53.4)	69 (49.3)	465 (53.6)	535 (53.0)
Partially reimbursed	223 (12.5)	81 (15.9)	29 (11.6)	110 (14.5)	18 (12.9)	95 (10.9)	113 (11.2)
Fully reimbursed	558 (31.4)	74 (14.5)	162 (64.8)	236 (31.0)	53 (37.9)	267 (30.8)	321 (31.8)
Unknown	50 (2.8)	6 (1.2)	2 (0.8)	9 (1.2)	0 (0.0)	41 (4.7)	41 (4.1)
Missing values	1	0	0	0	0	1	1
Total	1777	510	250	761	140	868	1010
Tobacco smoking status history							
Active smoker	158 (8.9)	38 (7.5)	42 (16.8)	81 (10.6)	7 (5.0)	69 (7.9)	76 (7.5)
Former smoker	181 (10.2)	69 (13.5)	35 (14.0)	104 (13.7)	10 (7.1)	66 (7.6)	76 (7.5)
Never smoker	1438 (80.9)	403 (79.0)	173 (69.2)	576 (75.7)	123 (87.9)	733 (84.4)	858 (85.0)
Total	1777	510	250	761	140	868	1010

Abbreviations. BMI, body mass index; max, maximum; min, minimum; SABA, short-acting β_2-agonist; SABINA, SABA use IN Asthma; SD, standard deviation. Data are presented as *n* (%) unless otherwise specified.

patients were prescribed ≥3 SABA canisters and 40.6% were prescribed ≥10 SABA canisters in the 12 months prior. A higher proportion of patients treated in primary care vs specialist care were prescribed SABA in addition to maintenance therapy (75.3 vs. 47.4%). Overall, 87.9 and 61.2% of patients in primary care were prescribed ≥3 and ≥10 canisters, respectively, compared with 51.6 and 16.1% of patients in specialist care.

Saba obtained OTC without prescriptions

Overall, 32.6% of patients purchased SABA OTC, of whom 51.8 and 6.0% purchased ≥3 and ≥10 SABA canisters, respectively (Table 3). Among patients who purchased SABA OTC, 20.7% had no SABA prescriptions and 79.3% had also received SABA prescriptions (Supplemental Figure 3). Of patients with both SABA OTC purchase and SABA prescriptions, 71.9% had received prescriptions for ≥3 SABA canisters and 40.1% had received prescriptions for ≥10 SABA canisters in the previous 12 months. A higher proportion of patients treated in primary care had SABA OTC purchases compared to those treated in specialist care (36.8 vs 29.6%).

Other prescriptions of asthma medication in the 12 months before the study visit

ICS as sole maintenance therapy was prescribed to 28.3% of patients, with a mean (SD) of 10.0 (4.3) ICS canisters in the preceding 12 months (Table 3). Most patients were prescribed medium-dose ICS (60.4%); 28.2 and 11.4% of patients were prescribed low-dose and high-dose ICS, respectively. Over half of patients (53.5%) in primary care were prescribed ICS. In contrast, only 9.5% of patients in specialist care were prescribed ICS. In both primary care and specialist care, ICS was generally prescribed to patients with mild asthma (75.5 and 42.9%, respectively). A higher proportion of patients in primary care vs specialist care were prescribed medium-dose ICS (66.7 vs 33.0%; Table 3).

Table 2. Asthma characteristics of the SABINA III African population according to investigator-classified asthma severity and practice type.

Asthma characteristics	All ($N = 1778$)	Primary care ($n = 761$)			Specialists ($n = 1011$)		
		Investigator-classified mild asthma ($n = 510$)	Investigator-classified moderate-to-severe asthma ($n = 250$)	All ($n = 761$)	Investigator-classified mild asthma ($n = 140$)	Investigator-classified moderate-to-severe asthma ($n = 869$)	All ($n = 1011$)
Asthma duration (years)							
Mean (SD)	14.4 (13.2)	16.5 (12.9)	17.3 (12.6)	16.7 (12.8)	12.5 (13.1)	12.6 (13.3)	12.6 (13.2)
Median (min–max)	10.0 (1.0–85.0)	13.0 (1.0–60.0)	14.0 (1.0–66.0)	13.0 (1.0–66.0)	7.5 (1.0–85.0)	7.0 (1.0–80.0)	7.0 (1.0–85.0)
Number of severe asthma exacerbations 12 months before the study visit							
Mean (SD)	1.4 (2.4)	1.6 (3.3)	1.2 (2.1)	1.5 (2.9)	1.0 (1.4)	1.3 (2.0)	1.3 (1.9)
Number of severe asthma exacerbations 12 months before the study visit by group							
0	749 (42.1)	226 (44.3)	117 (46.8)	343 (45.1)	75 (53.6)	327 (37.6)	403 (39.9)
1	477 (26.8)	100 (19.6)	66 (26.4)	166 (21.8)	31 (22.1)	278 (32.0)	309 (30.6)
2	266 (15.0)	77 (15.1)	38 (15.2)	116 (15.2)	18 (12.9)	131 (15.1)	149 (14.7)
3	119 (6.7)	41 (8.0)	6 (2.4)	47 (6.2)	5 (3.6)	67 (7.7)	72 (7.1)
>3	167 (9.4)	66 (12.9)	23 (9.2)	89 (11.7)	11 (7.9)	66 (7.6)	78 (7.7)
Missing data	0	0	0	0	0	0	0
Total	1778	510	250	761	140	869	1011
GINA classification							
Step 1	146 (8.2)	106 (20.8)	0 (0.0)	106 (13.9)	39 (27.9)	0 (0.0)	39 (3.9)
Step 2	505 (28.5)	404 (79.2)	0 (0.0)	404 (53.2)	101 (72.1)	0 (0.0)	101 (10.0)
Step 3	508 (28.6)	0 (0.0)	96 (38.4)	96 (12.6)	0 (0.0)	411 (47.3)	411 (40.7)
Step 4	500 (28.2)	0 (0.0)	137 (54.8)	137 (18.0)	0 (0.0)	360 (41.4)	360 (35.7)
Step 5	115 (6.5)	0 (0.0)	17 (6.8)	17 (2.2)	0 (0.0)	98 (11.3)	98 (9.7)
Missing data	4	0	0	1	0	0	2
Total	1774	510	250	760	140	869	1009
Level of asthma control							
Well-controlled	593 (33.8)	117 (22.9)	79 (31.6)	196 (25.8)	90 (66.2)	304 (35.7)	394 (39.8)
Partly controlled	700 (39.8)	223 (43.7)	96 (38.4)	320 (42.0)	30 (22.1)	346 (40.6)	377 (38.1)
Uncontrolled	464 (26.4)	170 (33.3)	75 (30.0)	245 (32.2)	16 (11.8)	202 (23.7)	219 (22.1)
Missing data	21	0	0	0	4	17	21
Total	1757	510	250	761	136	852	990
Number of comorbidities							
0	930 (52.3)	289 (56.7)	124 (49.6)	413 (54.3)	79 (56.4)	433 (49.8)	513 (50.7)
1–2	694 (39.0)	177 (34.7)	99 (39.6)	277 (36.4)	51 (36.4)	363 (41.8)	415 (41.0)
3–4	132 (7.4)	35 (6.9)	25 (10.0)	60 (7.9)	8 (5.7)	64 (7.4)	72 (7.1)
≥5	22 (1.2)	9 (1.8)	2 (0.8)	11 (1.4)	2 (1.4)	9 (1.0)	11 (1.1)

Abbreviations. GINA, Global Initiative for Asthma; max, maximum; min, minimum; SABA, short-acting β_2-agonist; SABINA, SABA use IN Asthma; SD, standard deviation. Data are presented as *n* (%) unless otherwise specified.

An ICS/LABA fixed-dose combination as maintenance therapy was prescribed to 66.6% of patients, of whom over half (52.2%) were prescribed medium-dose ICS; 34.9 and 12.9% of patients were prescribed low-dose and high-dose ICS, respectively (Table 3). Compared with 91.0% of patients in specialist care who were prescribed an ICS/LABA combination, only 34.2% of patients treated in primary care were prescribed ICS/LABA. Primary care physicians prescribed ICS/LABA for 2.9% of patients with mild asthma (60.0% as low-dose ICS combinations) and for 98.0% of patients with moderate-to-severe asthma (57.2% as medium-dose ICS combinations). Specialists prescribed ICS/LABA for 41.4% of patients with mild asthma (81.0% as low-dose ICS combinations) and for almost all patients (99.0%) with moderate-to-severe asthma (53.3% as medium-dose ICS).

Overall, during the previous 12 months, an OCS burst was prescribed to 34.9% of patients (30.3% in primary care and 38.3% in specialist care). In primary care, a similar proportion of patients with mild (30.4%) and moderate-to-severe asthma (30.1%) were prescribed an OCS burst. However, in specialist care, a higher proportion of patients with moderate-to-severe asthma vs mild asthma were prescribed an OCS burst (40.6 vs. 23.9%; Table 3).

Approximately one-third of all patients (32.7%) were prescribed antibiotics (Table 3). Prescriptions of antibiotics differed between primary care and specialist care providers, with 46.8% of patients in specialist care prescribed antibiotics compared with only 14.5% of patients in primary care.

In addition, in both care modalities, a higher proportion of patients with moderate-to-severe asthma (primary care, 19.8%; specialist care, 50.1%) were prescribed antibiotics compared to those with mild asthma (primary care, 11.8%; specialist care, 27.3%).

Patients prescribed concomitant OCS maintenance treatment and antibiotics for asthma

Overall, only 0.6% of patients ($n = 10$) were prescribed concomitant OCS maintenance treatment and antibiotics for asthma. Of these patients, the majority (80%) were treated by specialists. The demographics, baseline clinical characteristics and asthma characteristics of patients prescribed OCS maintenance treatment and antibiotics is presented in Supplemental Tables 2 and 3. All patients prescribed concomitant OCS maintenance treatment and antibiotics were also prescribed SABA in addition to maintenance therapy, with 70% of these patients receiving prescriptions for ≥3 canisters in the previous 12 months (Supplemental Table 4). In addition, 90% of patients prescribed concomitant OCS maintenance treatment and antibiotics were prescribed ICS/

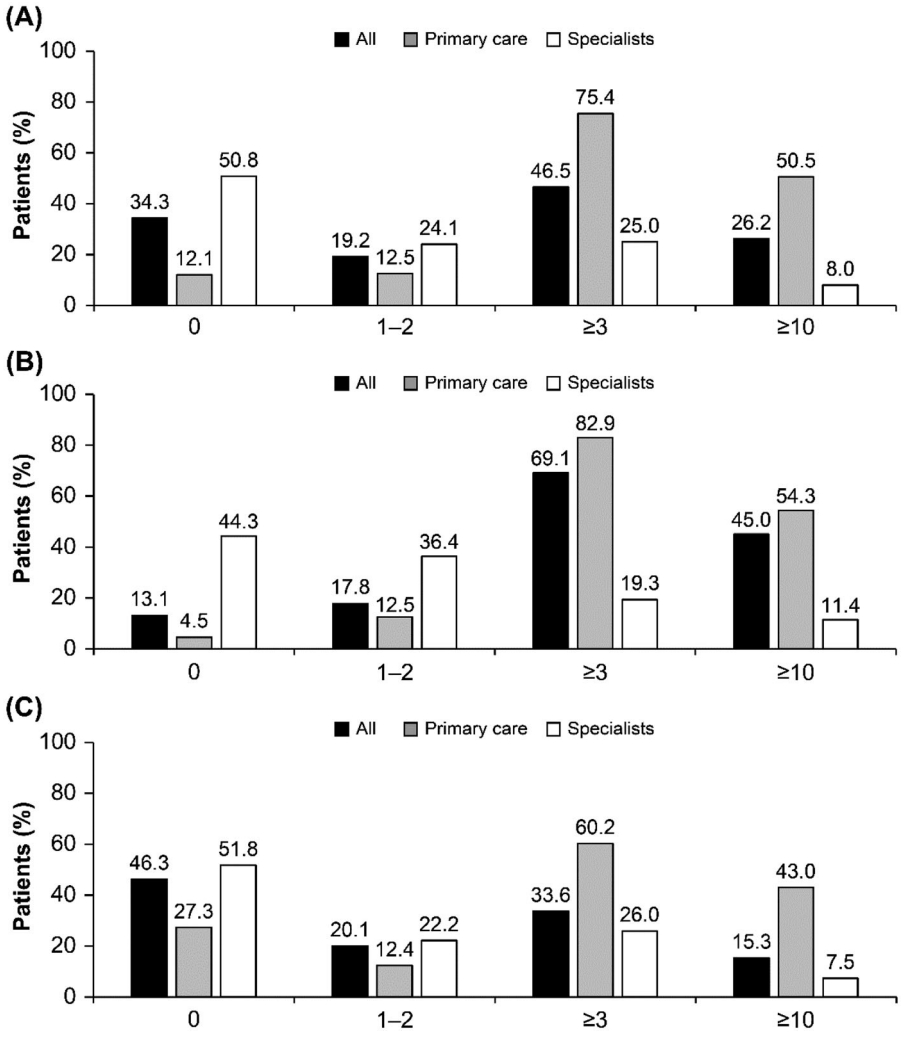

Figure 1. Proportion of patients (%) receiving SABA prescriptions in the 12 months before the study visit according to investigator-classified asthma severity and practice type in the SABINA III African cohort ($N = 1778$): (A) all patients, (B) mild asthma, and (C) moderate-to-severe asthma. *Patients without SABA prescriptions did not report which reliever they were using. Abbreviations. SABA, short-acting β_2-agonist; SABINA, SABA use IN asthma.

LABA fixed-dose combination, with only 10% receiving an OCS burst prescription.

Association of SABA prescriptions with asthma-related health outcomes

In prespecified regression analyses (Supplemental Figure 4), higher SABA prescriptions (3–5, 6–9, 10–12, and ≥13 vs. 1–2 canisters) in the previous 12 months were associated with an increase in the incidence rate of severe exacerbations, although not statistically significant for all SABA prescription categories (Figure 2(A)). Compared with patients prescribed 1–2 SABA canisters, no increase in the incidence rate of severe exacerbations was observed in patients prescribed 3–5 (adjusted incidence rate ratio [IRR], 1.02; 95% confidence interval [CI], 0.80–1.31; *p*-value, .870) and 6–9 (IRR, 1.01; 95% CI, 0.79–1.30; *p*-value, .914) SABA canisters. However, the prescription of 10–12 SABA canisters (vs 1–2 canisters) was associated with a significant 28.0% increase in severe exacerbations (IRR, 1.28; 95% CI, 1.04–1.59; *p*-value, .029). Although the prescription of ≥13 canisters (vs. 1–2 canisters) was associated with a 78.0% increase in the incidence rate of severe exacerbations, this did not reach statistical significance (IRR, 1.78; 95% CI, 0.98–3.37; *p*-value, .059).

Additionally, the odds of having at least partly controlled asthma decreased with higher SABA prescriptions, with the exception of patients prescribed 3–5 SABA canisters (odds ratio [OR], 1.27; 95% CI, 0.79–2.08; *p*-value, .337; Figure 2(B)). The prescription of 6–9 and 10–12 SABA canisters (vs 1–2 canisters) was associated with 42.0% (OR, 0.58; 95% CI, 0.37–0.90; *p*-value, .014) and 38.0% (OR, 0.62; 95% CI, 0.41–0.92; *p*-value, .020) significantly lower odds of having at least partly controlled asthma, respectively. Despite 54.0% lower odds of having at least partly controlled asthma, this association was not significant for prescription of ≥13 canisters (vs. 1–2 canisters; OR, 0.46; 95% CI, 0.14–1.57; *p*-value, .202).

Comparison of results between SABINA Africa and SABINA III

A comparison of data on sociodemographic and disease characteristics, asthma treatments, and asthma-related

Table 3. Asthma treatments prescribed and SABA canisters purchased OTC in the 12 months before the study visit by patients in the SABINA III African cohort.

	All ($N = 1778$)	Primary care ($n = 761$)			Specialists ($n = 1011$)		
		Investigator-classified mild asthma ($n = 510$)	Investigator-classified moderate-to-severe asthma ($n = 250$)	All ($n = 761$)	Investigator-classified mild asthma ($n = 140$)	Investigator-classified moderate-to-severe asthma ($n = 869$)	All ($n = 1011$)
Patients prescribed SABA monotherapy							
Yes	115 (6.5)	96 (18.8)	0 (0.0)	96 (12.6)	17 (12.1)	1 (0.1)	18 (1.8)
Number of canisters or inhalers per patient prescribed 12 months before the study visit							
Number of patients	115	96	NA	96	17	1	18
Mean (SD)	6.1 (4.4)	6.5 (4.3)	NA	6.5 (4.3)	4.1 (4.8)	6.0 (NA)	4.2 (4.7)
Median (min–max)	6.0 (1.0–14.0)	6.0 (1.0–14.0)	NA	6.0 (1.0–14.0)	1.0 (1.0–12.0)	6.0 (6.0–6.0)	1.0 (1.0–12.0)
Number of canisters or inhalers (as categories) per patient prescribed 12 months before the study visit							
1–2	39 (33.9)	26 (27.1)	NA	26 (27.1)	12 (70.6)	0 (0.0)	12 (66.7)
3–5	12 (10.4)	12 (12.5)	NA	12 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)
6–9	26 (22.6)	24 (25.0)	NA	24 (25.0)	1 (5.9)	1 (100.0)	2 (11.1)
10–12	37 (32.2)	33 (34.4)	NA	33 (34.4)	4 (23.5)	0 (0.0)	4 (22.2)
≥13	1 (0.9)	1 (1.0)	NA	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing data	0	0	NA	0	0	0	0
Total	115	96	NA	96	17	1	18
Patients prescribed SABA in addition to maintenance therapy							
Yes	1054 (59.3)	391 (76.7)	182 (72.8)	573 (75.3)	61 (43.6)	418 (48.1)	479 (47.4)
Number of canisters or inhalers per patient prescribed 12 months before the study visit							
Number of patients	1053	391	181	572	61	418	479
Mean (SD)	7.0 (4.8)	9.2 (3.9)	8.8 (4.9)	9.1 (4.2)	4.0 (4.2)	4.6 (4.1)	4.5 (4.1)
Median (min–max)	6.0 (1.0–30.0)	12.0 (1.0–24.0)	12.0 (1.0–30.0)	12.0 (1.0–30.0)	2.0 (1.0–12.0)	3.0 (1.0–24.0)	3.0 (1.0–24.0)
Missing data	1 (0.1)	0 (0.0)	1 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
Number of canisters or inhalers (as categories) per patient prescribed 12 months before the study visit							
1–2	302 (28.7)	38 (9.7)	31 (17.1)	69 (12.1)	39 (63.9)	193 (46.2)	232 (48.4)
3–5	135 (12.8)	37 (9.5)	8 (4.4)	45 (7.9)	6 (9.8)	84 (20.1)	90 (18.8)
6–9	189 (17.9)	73 (18.7)	35 (19.3)	108 (18.9)	4 (6.6)	76 (18.2)	80 (16.7)
10–12	411 (39.0)	239 (61.1)	104 (57.5)	343 (60.0)	12 (19.7)	56 (13.4)	68 (14.2)
≥13	16 (1.5)	4 (1.0)	3 (1.7)	7 (1.2)	0 (0.0)	9 (2.2)	9 (1.9)
Missing data	1	0	1	1	0	0	0
Total	1053	391	181	572	61	418	479
Patients purchased SABA without a prescription 12 months before the study visit							
Yes	579 (32.6)	201 (39.4)	78 (31.2)	280 (36.8)	33 (23.6)	265 (30.6)	298 (29.6)
Unknown	33 (1.9)	0 (0.0)	4 (1.6)	4 (0.5)	1 (0.7)	28 (3.2)	29 (2.9)
Missing data	3	0	0	0	0	3	3
Total	1775	510	250	761	140	866	1008
Number of canisters or inhalers (as categories) per patient obtained without a prescription 12 months before the study visit							
1–2	274 (47.3)	85 (42.3)	27 (34.6)	113 (40.4)	22 (66.7)	139 (52.5)	161 (54.0)
3–5	212 (36.6)	86 (42.8)	40 (51.3)	126 (45.0)	5 (15.2)	80 (30.2)	85 (28.5)
6–9	53 (9.2)	16 (8.0)	8 (10.3)	24 (8.6)	3 (9.1)	26 (9.8)	29 (9.7)
10–12	23 (4.0)	9 (4.5)	2 (2.6)	11 (3.9)	2 (6.1)	10 (3.8)	12 (4.0)
≥13	12 (2.1)	4 (2.0)	1 (1.3)	5 (1.8)	1 (3.0)	6 (2.3)	7 (2.3)
NA[a]	5 (0.9)	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)	4 (1.5)	4 (1.3)
Patients prescribed ICS							
Yes	504 (28.3)	385 (75.5)	22 (8.8)	407 (53.5)	60 (42.9)	36 (4.1)	96 (9.5)
Total prescribed daily ICS dose							
Low dose	141 (28.2)	78 (20.4)	6 (27.3)	84 (20.7)	43 (72.9)	14 (40.0)	57 (60.6)
Medium dose	302 (60.4)	256 (66.8)	14 (63.6)	270 (66.7)	15 (25.4)	16 (45.7)	31 (33.0)
High dose	57 (11.4)	49 (12.8)	2 (9.1)	51 (12.6)	1 (1.7)	5 (14.3)	6 (6.4)
Missing values	4	2	0	2	1	1	2
Total	500	383	22	405	59	35	94
Number of canisters or inhalers per patient prescribed 12 months before the study visit							
Number of patients	503	385	22	407	59	36	95
Mean (SD)	10.0 (4.3)	10.7 (3.7)	10.5 (5.5)	10.7 (3.8)	7.6 (5.7)	6.8 (4.4)	7.3 (5.2)
Median (min–max)	12.0 (1.0–36.0)	12.0 (1.0–36.0)	12.0 (1.0–24.0)	12.0 (1.0–36.0)	6.0 (1.0–30.0)	5.5 (1.0–12.0)	6.0 (1.0–30.0)
Missing values	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.0)
Patients prescribed ICS/LABA (fixed-dose combination)							
Yes	1180 (66.6)	15 (2.9)	244 (98.0)	260 (34.2)	58 (41.4)	855 (99.0)	915 (91.0)
Missing values	6	0	1	1	0	5	5
Total	1772	510	249	760	140	864	1006
Total prescribed daily ICS dose							
Low dose	410 (34.9)	9 (60.0)	76 (31.3)	85 (32.8)	47 (81.0)	276 (32.5)	325 (35.7)
Medium dose	613 (52.2)	5 (33.3)	139 (57.2)	145 (56.0)	11 (19.0)	453 (53.3)	464 (51.0)

(*continued*)

Table 3. Continued.

	All ($N = 1778$)	Primary care ($n = 761$)			Specialists ($n = 1011$)		
		Investigator-classified mild asthma ($n = 510$)	Investigator-classified moderate-to-severe asthma ($n = 250$)	All ($n = 761$)	Investigator-classified mild asthma ($n = 140$)	Investigator-classified moderate-to-severe asthma ($n = 869$)	All ($n = 1011$)
High dose	151 (12.9)	1 (6.7)	28 (11.5)	29 (11.2)	0 (0.0)	121 (14.2)	121 (13.3)
Missing values	6	0	1	1	0	5	5
Total	1174	15	243	259	58	850	910
Patients prescribed OCS burst/short course							
Yes	617 (34.9)	155 (30.4)	75 (30.1)	230 (30.3)	33 (23.9)	350 (40.6)	384 (38.3)
Missing values	9	0	1	1	2	6	8
Total	1769	510	249	760	138	863	1003
Patients prescribed OCS maintenance treatment							
Yes	106 (6.0)	46 (9.0)	17 (6.8)	63 (8.3)	2 (1.4)	41 (4.7)	43 (4.3)
Missing values	9	0	1	1	2	5	8
Total	1769	510	249	760	138	864	1003
Patients prescribed antibiotics (prescribed for asthma)							
Yes	573 (32.7)	60 (11.8)	49 (19.8)	110 (14.5)	38 (27.3)	424 (50.1)	462 (46.8)
Missing values	28	2	2	4	1	23	24
Total	1750	508	248	757	139	846	987

[a]"NA" could be selected in the eCRF when patients purchased non-canister forms of SABA (e.g. oral or nebulized SABA) without a prescription.
Abbreviations. eCRF, electronic case report form; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; max, maximum; min, minimum; NA, not applicable; OCS, oral corticosteroid; OTC, over the counter; SABA, short-acting β_2-agonist; SABINA, SABA use IN Asthma; SD, standard deviation.
Data are presented as *n* (%) unless otherwise specified.

clinical outcomes in the previous 12 months between the SABINA Africa and the overall SABINA III population is summarized in Supplemental Table 5. The key differences are highlighted in the Discussion section.

Discussion

Asthma is an increasing health problem in Africa that has received relatively little attention[3]. Overall, there is a paucity of large-scale clinical trials from Africa, with most studies conducted in South African and Nigerian populations[3]. Furthermore, significant gaps remain in the current knowledge of asthma management in Africa. Therefore, the results from the African cohort of the SABINA III study in 1778 patients with asthma provide valuable real-world evidence on asthma management practices in this region. Notably, while the majority of patients were prescribed maintenance therapy in the form of either ICS or ICS/LABA fixed-dose combinations, SABA over-prescription was common, with 46.5% of patients overall being prescribed $\geq$3 SABA canisters in the preceding12 months, which was associated with poor asthma-related health outcomes in terms of an increased incidence of severe exacerbations (statistically significant for 10–12 canisters) and poor asthma control (statistically significant for 6–9 and 10–12 canisters).

Overall, the baseline patient and disease characteristics in this study were generally consistent with those observed in the SABINA III population[16]. However, compared with the overall population (mean age, 49.4 years)[16], patients in this African cohort were younger (mean age, 43.7 years). This finding may be explained in part by the reported increase in asthma prevalence among children in Africa[3] and the fact that Africa has one of the world's youngest populations[19,20]. Although the mean BMI of this African cohort (28.2 kg/m^2) was comparable to previous reports from this continent[13,21], most patients (68.4%) had a BMI of $\geq$25 kg/m^2. This finding is likely attributable to the fact that 62.4% of patients in this African cohort were female and is in line with the SABINA III population, where 68.1% of patients were female and 65.6% had a BMI of $\geq$25 kg/m^2; based on previous research, older females with high BMI represent a distinct cluster of asthma patients[22,23]. Importantly, and in contrast to the SABINA III population[16], the African cohort had a relatively balanced distribution of patients treated in primary and specialist care (42.9 and 57.1%, respectively vs. 17.2 and 82.3%, respectively), thereby providing an understanding of how asthma is currently being managed and treated in Africa. Thus, compared with the overall SABINA III population, a lower percentage of patients from this African cohort had moderate-to-severe asthma (63.3 vs 76.%, respectively)[16]. Overall, the majority of patients in this study had received secondary school education or higher (79.9%). Although this was substantially higher than that previously documented in Africa, where less than 50% of patients had reported secondary school education or higher[21,24], these findings were comparable with the overall SABINA III population (76%)[16].

Of concern, a high proportion of patients in this African cohort were prescribed SABA treatments, both SABA monotherapy and SABA with maintenance therapy. Indeed, compared with the SABINA III population[16], a higher proportion of patients in this study were prescribed $\geq$3 SABA canisters as monotherapy (66.1 vs. 53.6%) or in addition to maintenance therapy (71.3 vs. 61.7%), in the previous 12 months, which is regarded as over-prescription. Worryingly, 33.0 and 40.6% of patients receiving SABA as monotherapy or with maintenance treatment, respectively, were prescribed $\geq$10 canisters in the preceding 12 months. Although more apparent in primary care, these trends were observed in both primary and specialist care. Such findings suggest an urgent

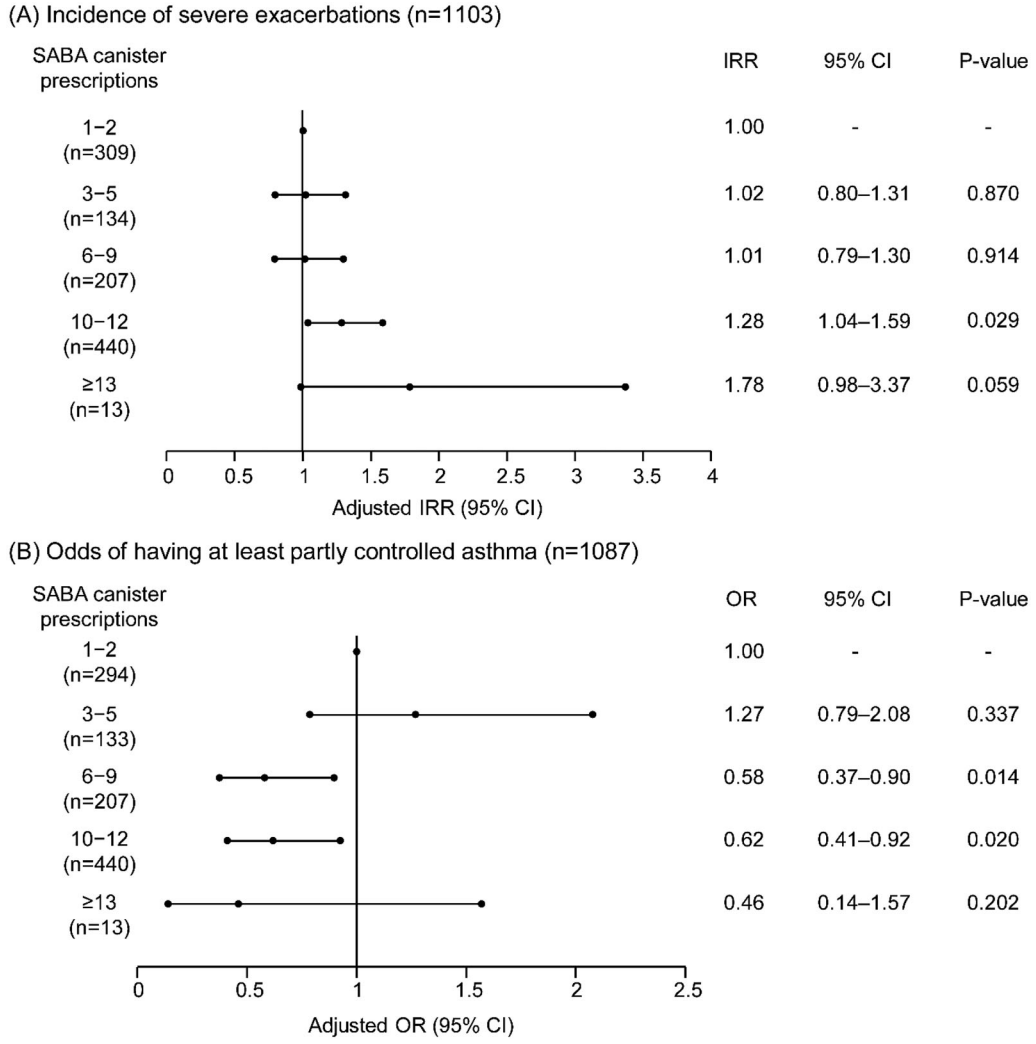

Figure 2. Association of SABA prescriptions with (A) severe exacerbations in the 12 months before the study visit and (B) level of asthma control assessed during the study visit in the SABINA III African cohort. Abbreviations. BMI, body mass index; CI, confidence interval; GINA, global initiative for asthma; IRR, incidence rate ratio; OR, odds ratio; SABA, short-acting β_2-agonist; SABINA, SABA use IN asthma. Based on the covariable significance in the models, IRRs are corrected by country, age, sex, BMI, tobacco smoking history, GINA step, healthcare insurance, prescriber type, comorbidity, asthma duration, and education level. ORs are corrected by country, age, sex, BMI, asthma duration, tobacco smoking history, comorbidity, GINA step, healthcare insurance, prescriber type, and education level.

need for educational initiatives targeted at both primary care physicians and specialists to align clinical practices in Africa with current treatment recommendations. This is of critical importance since many African countries have no standard protocols for the diagnosis and management of asthma in place, and where available, such guidelines are rarely widely disseminated and implemented[3]. Indeed, it has been highlighted that educating both HCPs and patients is essential to address the current challenges posed by asthma in Africa[25]. A lack of full healthcare reimbursement may also have contributed to SABA over-prescription in this African cohort. In contrast to both the SABINA III study[16], where 47.2% of patients had full healthcare reimbursement, and the ESMAA (Assessment of Asthma Control in Adult Asthma Population in the Middle East and North Africa) study, which included 3 African countries (Algeria, Egypt, and Tunisia), and reported that the majority of patients had medical insurance coverage, ranging from 52.5% (in Egypt) to 87.2% (in Algeria)[13], only 31.4% of patients in this African cohort were fully reimbursed. Notably, the proportion of patients with no healthcare reimbursement in this African cohort was ~2-fold higher than that observed in the SABINA III population (53.2 vs. 27.3%), despite patients reporting comparable levels of education. Although higher education is associated with increased rates of healthcare insurance coverage[26], factors such as high premiums, limited understanding of entitlements, or insufficient healthcare benefits[27] may have prevented patients in this African cohort from applying or receiving healthcare reimbursement. Consequently, there is a need to transform the way in which healthcare delivery is funded across Africa by moving away from out-of-pocket expenses[27], strengthening/pooling resources, providing support through existing legislation, enacting new laws or policies, and ensuring harmonization across different government departments[28]. This is of particular importance since a lack of healthcare insurance has been linked to consistently poorer quality of asthma care, including a lower likelihood of receiving ICS[29].

Crucially, not all SABAs were obtained with prescriptions., Indeed, despite the fact that over three-quarters of patients

(79.3%) had already been prescribed SABA, approximately one-third of patients (32.6%) in this African cohort purchased SABA OTC, which was considerably higher than the 18% observed in the overall SABINA III population[16]. This highlights patients' over-reliance on SABA therapy and willingness to self-manage their worsening of asthma symptoms[30–32]. However, this is a matter of grave concern since SABA purchase has been associated with low rates of consultation with family practitioners and specialists; low use of prescription-only medication, particularly ICS; and undertreatment of asthma[33–35]. Overall, these findings provide valuable insights into how patients in this African cohort self-manage their asthma; it would appear to be common practice for them to purchase SABA from a private pharmacy, which may further contribute to poor asthma control. Moreover, the high cost of ICS-containing combination inhalers compared with single SABA inhalers in African countries[36–38] may have further contributed to out-of-pocket spending for OTC SABA purchase. Indeed, studies have consistently demonstrated that affordability of internationally recommended treatments for asthma in low-and middle-income countries, including Africa, remains a major challenge[36–38]. Consequently, there is an urgent need to implement policies that regulate the purchase of SABA without prescription while ensuring that patients have access to affordable care and asthma medications, including adequate provision for maintenance therapy.

To our knowledge, this is the first study to assess the association between SABA prescription patterns and asthma-related health outcomes in an African population. Overall, our findings revealed that higher SABA prescriptions showed a significant association with an increase in the incidence rate of severe exacerbations (10–12 canisters) and lower odds of achieving at least partly controlled asthma (6–9 and 10–12 canisters). Although these associations were not statistically significant for all the SABA categories analyzed, most likely due to the small patient numbers in some of the subgroups, the results were generally consistent with those reported in the SABINA I and II studies (conducted in the United Kingdom[8] and Sweden[9]) the SABINA III study[16], and other studies that have established a link between high SABA use and an increased risk of exacerbations and poor asthma control[39–41].

Most patients in this African cohort were prescribed maintenance medication in the form of either ICS (28.3% of patients) or fixed-dose combination ICS/LABA (66.6% of patients). These findings were expected given the higher proportion of patients with moderate-to-severe asthma (63.3%). Likewise, the proportion of patients prescribed ICS (28.3%) was comparable to the percentage of patients at GINA step 2 (28.5%). Overall, a higher proportion of patients in primary care compared with specialist care were prescribed ICS (53.5 vs. 9.5%), which was in line with the proportion of GINA step 2-treated patients in both care modalities (53.2 vs. 10%). Nevertheless, the majority of patients in this African cohort who were prescribed ICS (GINA step 2) received prescriptions for medium-dose ICS (60.4%) instead of the recommended low-dose ICS[1]. This trend was particularly apparent among patients treated by primary care physicians, where 66.7% were prescribed medium-dose ICS. This finding, which could be explained by the fact that primary care physicians are often not familiar with GINA[42], indicates that prescribing practices in this cohort of patients did not always conform to internationally recommended guidelines[1] and are in line with previous reports from Africa that have documented poor awareness of international guidelines and a low level of participation at update trainings on asthma management[43–45]. This nonadherence to international asthma management guidelines underscores the urgent need for extensive asthma campaigns to popularize the use of guidelines among physicians and the importance of continuing medical education in Africa. Fortunately, the National Asthma Education Programme (NAEP), whose mission is to provide asthma education to healthcare professionals, patients, and the lay public and whose benchmark asthma education course is the only accredited asthma course in South Africa, is expanding its footprint across South Africa and the African continent[46].

Overall, an OCS burst was prescribed to 34.9% of patients, potentially indicating OCS burst–treated exacerbations in these patients. A greater percentage of patients in specialist care (38.3%) compared with primary care (30.3%) were prescribed an OCS burst, likely reflective of the greater number of patients with moderate-to-severe asthma under specialist care. Interestingly, 32.7% of patients were prescribed antibiotics, with this occurring in a higher proportion of patients in specialist care compared to those in primary care (46.8 vs. 14.5%). The high rates of antibiotic prescriptions issued by specialists in this African cohort are consistent with the results of a study from Uganda which reported that more than half of all patients with asthma treated in chest and emergency units of a tertiary healthcare facility received antibiotics[44]. This suggests a lack of understanding of the mechanisms underlying antimicrobial resistance[47] and unfamiliarity with asthma management guidelines that do not support the routine use of antibiotics in the treatment of acute asthma exacerbations unless there is strong evidence of lung infection[1]. Moreover, antibiotics can increase the cost of prescription, may cause adverse effects[48] and could delay the use of appropriate therapy. Thus, the extent of antibiotic use in this study represents a serious concern underscoring the need for targeted interventions, such as antimicrobial stewardship programs (ASPs), to tackle antibiotic resistance. Although there is a paucity of data on the implementation of ASPs in African countries[49], the World Health Organization provides a practical toolkit for implementing antimicrobial stewardship in healthcare facilities to help low- and middle-income countries optimize antibiotic use[50]. This toolkit focuses on improving awareness and understanding of antimicrobial resistance, strengthening knowledge and evidence base through surveillance, promoting sanitation and hygiene to prevent infections, and providing guidance to HCPs to change their antibiotic prescribing behavior[50]. In South Africa, implementation of a pharmacist-led stewardship program across a diverse group of 47 urban and rural private hospitals demonstrated that it was possible to substantially

reduce antibiotic use despite limited resources and no prior stewardship experience[51].

Of key importance, only one-third of patients (33.8%) in the current study had well-controlled asthma. While the level of asthma control was less than what is typically observed, with results from the Asthma Insight and Management (AIM) study reporting that globally, a median of 67.0% (range, 27.0 – 88.0%) of patients perceived their asthma as completely controlled and/or well-controlled[52], this finding is aligned with previous reports from Africa[21,24]. For example, the ESMAA, reported that asthma was only controlled in 29.4% of 7179 evaluable patients[13]. Furthermore, the level of asthma control in this African cohort was poor when compared with that of the SABINA III population (the proportion of patients with well-controlled asthma was 43.3%)[16]. Consequently, the burden of asthma in these three African countries was high, with 57.9% of patients experiencing at least 1 severe asthma exacerbation in the previous year. Therefore, the levels of asthma control in Africa remain below recommended standards and have contributed to the disease burden[3]. Of note, a high percentage of patients with mild asthma, across both primary and specialist care, experienced ≥1 severe exacerbation in the previous 12 months (55.6 and 46.5%, respectively). This could be due in part to a substantial proportion of patients with partly controlled/uncontrolled asthma (77 and 33.9%, respectively). However, consistent with previously published reports[53–55], these results demonstrate that many patients with mild asthma experience suboptimal symptom control[54] and are at risk of exacerbations. Such findings indicate potential under-estimation of asthma severity and over-estimation of disease control in patients with milder disease or the under-treatment of patients with "mild" asthma resulting in poor symptom control[1,56]. However, to overcome this, a number of unique challenges faced by African countries will need to be overcome, including those arising from limited healthcare facilities and health planning; a lack of trained staff, diagnostic apparatus, and organized health promotion programs; the high cost and unavailability of essential asthma medications and devices; and a lack of patient self-monitoring equipment and educational materials, all of which have previously hindered efforts at improving asthma management[3,12,13,57]. In addition, due consideration will need to be given to underlying risk factors, such as the rapid rate of urbanization, which has been linked to the increase in the burden of asthma across Africa[3,58]. Crucially, inherent socio-cultural misconceptions will need to be addressed in order to enhance understanding of asthma and improve acceptance and use of asthma medications among patients[3,59].

Our study is not without limitations. Prescription data may not always reflect actual medication use or adherence and therefore SABA use may have been over-estimated or under-estimated. Owing to its observational nature, the study may also be prone to bias, e.g. therapies may be differently prescribed depending on disease severity[60]. Indeed, 2.9 and 41.4% of patients classified as having mild asthma in primary and specialist care, respectively, had ICS/LABA prescriptions, suggesting differences in local treatment practices compared with GINA recommendations. Patient-reported data on SABA OTC purchase may have been subject to recall and non-response bias[60,61]. In addition, due to the small sample size for some SABA prescription categories, our results should be generalized with caution across these three African countries. Furthermore, disease severity was based on the GINA 2017 recommendations (in place at the time this study was conceived and implemented), where as-needed SABA was the preferred treatment option for patients at GINA step 1[17], which may have accounted for some of the high levels of SABA prescription observed in this study. Consequently, GINA step 1-treated patients who were prescribed ≥3 SABA/year would have been classified by investigators as having mild asthma if their symptoms were adequately controlled. Notably, this study was not designed to examine the impact of patient demographics or baseline clinical characteristics on SABA prescription patterns, although, such an analysis may be the subject of future research. Additionally, only the number of comorbidities (categorized as 0, 1–2, 3–4 and ≥5) were recorded in the eCRF, while data on the type and rate of comorbidities, were not captured. Finally, although data from a large patient population were analyzed, only 3 countries from Africa were included in the study. Therefore, results should be interpreted in the context of country-specific clinical practices and regulations and not generalized to the African continent as a whole. However, aggregated data from these 3 African countries enabled a detailed analysis of asthma treatment in a large patient population and an assessment of trends in SABA prescriptions and their impact on patient health in Africa. Taken together, these findings highlight that a concerted effort is required by national governments, HCPs, and patients to reduce the current burden of asthma and by healthcare policymakers to regulate SABA purchase without prescription in Africa so that clinical practices are aligned with current treatment recommendations. The future publication of individual country data from Egypt, South Africa and Kenya will provide further valuable real-world insights into asthma treatment practices at a country level.

Conclusions

The results from the African cohort of the SABINA III study in over 1700 patients with asthma demonstrated that approximately 1 out of every 2 patients was prescribed SABA in excess of treatment recommendations (≥3 canisters in the previous 12 months). In addition, of the 32.6% of patients who purchased SABA OTC, just over 50.0% purchased ≥3 canisters in the preceding 12 months, with almost 80.0% already receiving prescriptions for SABA canisters. With some exceptions, higher SABA prescriptions (vs. 1–2 canisters) were associated with poor asthma-related outcomes. These findings from the African cohort of the SABINA III study highlight that SABA over-prescription remains a major public health concern, necessitating that HCPs and policymakers urgently work together to improve asthma care and education and ensure that clinical practices are aligned with the latest evidence-based treatment recommendations.

Transparency

Declaration of funding

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 and funded medical writing support.

Declaration of financial/other relationships

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Author contributions

All authors contributed to data collection, data analysis, data interpretation, and writing. The study was designed by M.J.H.I.B.

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Data availability statement

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.

ORCID

Adel Khattab http://orcid.org/0000-0002-4253-0662

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