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Journal of the Pan African Thoracic Society

Review Article

The reality of managing asthma in sub-Saharan Africa – Priorities and strategies for improving care

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Received : 06 September 2022
Accepted : 21 September 2022
Published : 04 October 2022

DOI
10.25259/JPATS_37_2022

Quick Response Code:

ABSTRACT

Asthma is the most common non-communicable disease in children and remains one of the most common throughout the life course. The great majority of the burden of this disease is seen in low-income and middle-income countries (LMICs), which have disproportionately high asthma-related mortality relative to asthma prevalence. This is particularly true for many countries in sub-Saharan Africa. Although inhaled asthma treatments (particularly those containing inhaled corticosteroids) markedly reduce asthma morbidity and mortality, a substantial proportion of the children, adolescents, and adults with asthma in LMICs do not get to benefit from these, due to poor availability and affordability. In this review, we consider the reality faced by clinicians managing asthma in the primary and secondary care in sub-Saharan Africa and suggest how we might go about making diagnosis and treatment decisions in a range of resource-constrained scenarios. We also provide recommendations for research and policy, to help bridge the gap between current practice in sub-Saharan Africa and Global Initiative for Asthma (GINA) recommended diagnostic processes and treatment for children, adolescents, and adults with asthma.

Keywords: Asthma, Low-middle-income country, Asthma guideline, Global initiative for asthma, Asthma medication

INTRODUCTION

Asthma is the most common non-communicable disease in children and remains one of the most common throughout the life course. The multi-country Global Asthma Network (GAN) Phase I study recently reported that around one in 10 children and one in 15 adults have symptoms of asthma, with a high burden of severe symptoms (approximately 50% of children and adolescents and 40% of adults).[1-3] The Global Burden of Disease study estimated that there were 21.6 million disability-adjusted life years and 461,069 deaths attributable to asthma globally in 2019.[4,5]

The great majority of the burden of this disease is seen in low-income and middle-income countries (LMICs). The World Bank[6] subdivides middle-income countries into lower-middle income and upper-middle income; the lower-middle-income countries, in particular, have shown an increase in the prevalence of asthma symptoms over time and have a disproportionately high asthma-related mortality relative to asthma prevalence.[1,7,8]

Most countries in sub-Saharan Africa (SSA) are categorized by the World Bank as low income or lower-middle income.[6] Health systems in these countries are generally weak, unprepared

to respond to the needs of people with non-communicable diseases, are designed primarily to respond to acute care needs, and are restrained by limited access to effective and affordable asthma care often even the most basic care. There are many challenges in addressing the rising burden of non-communicable diseases, including chronic respiratory diseases like asthma. The global alliance against chronic respiratory diseases (GARDs) has reported that very few patients in low-income and lower-middle-income countries receive adequate diagnostic investigations and treatment for chronic respiratory diseases.[9] In addition to poor access to asthma medicines and diagnostic technologies and the high out-of-pocket expenditure associated with asthma care, there is still limited integration of asthma care into primary care, which is the first point of contact with health care for over 60% of patients.[10,11] Accordingly, children, adolescents, and adults with asthma living in SSA are at a particularly high risk of avoidable morbidity and mortality due to asthma.

There is also the challenge of inadequate human resource capacity to manage asthma. In some SSA countries, the few available health workers have reported low competency in managing patients with chronic respiratory diseases.[12,13] While some progress has been made toward understanding how to integrate non-communicable diseases such as diabetes mellitus and hypertension into primary care, important gaps exist for chronic respiratory diseases such as asthma.[13]

In this review, we discuss the diagnosis and treatment of asthma in children, adolescents, and adults in SSA. We review the literature describing how asthma is diagnosed and treated in SSA and place current practice within the context of African national, regional, and selected international recommendations for asthma diagnosis and treatment from the World Health Organization (WHO), the International Union Against Tuberculosis (TB) and Lung Disease (The Union), and the Global Initiative for Asthma (GINA). We consider the reality faced by clinicians managing asthma in the primary and secondary care settings in SSA and suggest how we might go about making diagnosis and treatment decisions in a range of resource-constrained scenarios. We also provide recommendations for research and policy, to help bridge the gap between current practice in SSA and GINA recommended diagnostic processes and treatment for children, adolescents, and adults with asthma.

HEALTH SYSTEM FACTORS AFFECTING ASTHMA MANAGEMENT IN SSA

Asthma strategies and guidelines in SSA

A national asthma strategy (or national asthma program) is a set of actions agreed upon and enacted by governments to systematically improve asthma outcomes across the population. A comprehensive national asthma strategy requires political commitment at the national government level (including policies, legislation, and funding for capacity building) and can involve the creation of a registry for outcome data, asthma management guidelines, economic analysis and process evaluation, and provision of universal health coverage with essential asthma medicines and support of asthma research.[14,15]

A cross-sectional survey of GAN centers was conducted in 2013–2015 to ascertain which countries have a national asthma strategy.[14] Of the 18 African countries surveyed, only Sudan and Malawi reported having an asthma strategy.[14] GAN also maintains an updated list of national guidelines[16] and documented these in the Global Asthma Report 2014[17] [Table 1].

There are no regional asthma guidelines for SSA. However, guidelines developed for LMICs by the WHO,[18] the Union[19] and Medicines Sans Frontières[20] [Table 2] are relevant in this region and are being used by some SSA countries with context-specific local adaptations.[16] The WHO also publishes a regularly updated Model List of Essential Medicines,[21] which includes one or more asthma medicines from each of the following classes: Short-acting $beta_2$ agonists (SABAs), inhaled corticosteroids (ICSs), ICS plus long-acting $beta_2$-agonist (LABA) combinations, short-acting muscarinic antagonists, and long-acting muscarinic antagonists.

Some SSA countries adopt the GINA strategy report to guide asthma diagnosis and management. GINA was launched in 1993 in collaboration with the National Heart, Lung, and Blood Institute, National Institutes of Health, USA, and WHO.[22] The GINA report[23] is an annually updated global strategy for asthma, underpinned by an ongoing process of reviewing published evidence on asthma management and prevention.[24] This evidence-based strategy can be adapted for local health systems and medicine availability, recognizing the need for asthma care to be tailored to the circumstances of individual countries. However, at present, the recommended GINA approaches to diagnosis and asthma medication [Figures 1-3] cannot be implemented in countries with the most severe resource limitations.

CURRENT STATUS OF ASTHMA DIAGNOSIS IN SSA

Asthma is a clinical diagnosis made by recognizing typical patterns of respiratory symptoms and supported by evidence of variable expiratory airflow limitation.[23]

Underdiagnosis of asthma

Asthma is commonly underdiagnosed in SSA. In a recently reported cross-sectional survey of 519 adults with chronic respiratory symptoms not explained by TB, attending

Table 1: National asthma guidelines and strategies in sub-Saharan Africa.

World Bank income group	Country	National asthma guideline	National asthma strategy
Low	Burkina Faso	?	No
	Burundi	?	?
	Central African Republic	?	?
	Chad	?	?
	Congo, Democratic Republic	?	?
	Eritrea	?	?
	Ethiopia	Yes	?
	The Gambia	Yes International guidelines adopted in addition: WHO-PEN	No
	Guinea	?	?
	Guinea-Bissau	?	?
	Liberia	?	?
	Madagascar	?	?
	Malawi	Yes	Yes
	Mali	No International guideline adopted: WHO-PEN	No
	Mozambique	?	?
	Niger	?	?
	Rwanda	?	?
	Sierra Leone	?	No
	Somalia	?	?
	South Sudan	?	?
	Sudan	?	Yes (adults)
	Togo	?	?
	Uganda	No International guideline adopted: GINA	No
Lower middle	Angola	?	?
	Benin	No International guidelines adopted: WHO-PEN, The Union	No
	Cabo Verde	?	?
	Cameroon	No International guideline adopted: GINA	No
	Comoros	?	?
	Congo, Republic	?	?
	Cote D'Ivoire	?	?
	Eswatini	?	?
	Ghana	No International guideline adopted: WHO-PEN	No
	Kenya	Yes International guideline adopted in addition: WHO	No
	Lesotho	?	?
	Mauritania	?	?
	Nigeria	Yes	No
	Sao Tome and Principe	?	?
	Senegal	No International guideline adopted: GINA	No
	Tanzania	?	?

(Contd...)

Table 1: *(Continued)*.

World Bank income group	Country	National asthma guideline	National asthma strategy
	Zambia	No International guideline adopted: GINA	No
	Zimbabwe	No	No
Upper middle	Botswana	?	?
	Equatorial Guinea	?	?
	Gabon	?	?
	Mauritius	?	?
	Namibia	No	?
	South Africa	Yes	No
High	Seychelles	?	?

?: Unknown status (existence of a national guideline or strategy not verified by Global Asthma Network), GINA: Global Initiative for Asthma strategy report, WHO-PEN: World Health Organization Package of Essential Noncommunicable Disease Interventions for Primary Care,[18] The Union: International Union Against Tuberculosis and Lung Disease guidelines.[19] World Bank income classifications 2021–2022,[6] Global Asthma Network surveys and reports[14,16,17]

hospital clinics in Kenya, Ethiopia, and Sudan, asthma was the diagnosis made in 34% of cases, but a history of wheeze in the past 12 months was reported by 71%.[25] This discrepancy suggests substantial underdiagnosis. In Nigeria, it has been estimated that <50% of people with asthma receive the diagnosis, with children in rural regions at high risk of underdiagnosis.[26] People with chronic respiratory symptoms in SSA often seek help from widely available TB services, but such assessment typically concludes with a diagnosis of "not TB" with few receiving an alternative diagnosis or treatment.[27]

Limited access to diagnostic tests

International guidelines recommend the use of spirometry to demonstrate variable expiratory airflow limitation to support the diagnosis of asthma, if possible, before starting treatment.[23,28] However, in many SSA healthcare facilities, spirometry is absent or not consistently available. Furthermore, where payment is required, may be unaffordable for patients and caregivers. On the other hand, facilities and staff often lack training on how to perform and interpret spirometry accurately.[29-33] In Nigeria, doctors have also reported a lack of access to diagnostic facilities as a major barrier to good asthma practice.[33] In Uganda, spirometry testing is reported to be largely unaffordable, costing the lowest paid government worker a month's salary (a frequently used benchmark metric for affordability).[30]

The use of peak expiratory flow (PEF) meters is proposed in some guidelines as an alternative and usually less costly method for demonstrating variable expiratory airflow limitation.[18,23,28,34] However, even so, they are not available in many countries in SSA. A study of health system preparedness for managing chronic lung diseases in Sudan and Tanzania identified the lack of access to PEF meters for diagnostic purposes as an important barrier to care.[35]

Psychosocial factors contributing to underdiagnosis of asthma

It is also important to recognize that a diagnosis of asthma may not be welcomed by patients and parents of children with asthma, especially where myths and stigma surround the diagnosis.[36] Such obstacles present substantial barriers to effective long-term treatment. For example, in Kenya, studies of children and adults with asthma report reluctance to admit to or accept this diagnosis, even within families.[37]

PRAGMATIC APPROACHES TO THE DIAGNOSIS OF ASTHMA IN RESOURCE-CONSTRAINED SSA SETTINGS

[Table 3] shows three scenarios representing diagnostic options commonly found in resource-constrained SSA settings and suggests a pragmatic approach to asthma diagnosis in each of these scenarios.

Where it is not possible to record any objective measurement of airflow limitation, the diagnosis of asthma is based entirely on clinical assessment in which history forms a major part. This pragmatic syndromic approach comes at the cost of precision. However, the benefits of making a diagnosis based only on history and physical examination likely outweigh the risks in SSA, where the major issues are under-recognition, underdiagnosis, and undertreatment. This is especially so in countries where a diagnosis may open the door to safe and effective inhaled therapies.

PEF meters

When clinical history supports the diagnosis of asthma, but spirometry is not available, the PEF measurement can be used to confirm variable expiratory airflow limitation,

Table 2: Asthma treatment levels recommended in guidelines developed for low-resource settings.

Guideline	WHO-PEN	MSF	Union
Medication recommendations	Step 1: As-needed inhaled salbutamol Step 2: Regular low-dose inhaled beclometasone (starting dose: adults 100 mcg twice daily; children 100 mcg once or twice daily) plus as-needed inhaled salbutamol Step 3: Regular medium-dose inhaled beclometasone (adults: 200 mcg or 400 mcg twice daily) plus as-needed salbutamol Step 4: Add low-dose oral theophylline Step 5: Add low-dose oral prednisolone (e.g., <10 mg)	Intermittent asthma: As-needed inhaled salbutamol Mild persistent asthma: Regular inhaled beclometasone* plus as-needed inhaled salbutamol Moderate persistent asthma (symptoms daily): Regular inhaled beclometasone* plus inhaled salbutamol 4 times daily Severe persistent asthma: Regular inhaled beclometasone* plus inhaled salbutamol 4–6 times daily	Intermittent asthma: As-needed inhaled salbutamol Mild: HFA beclometasone 100 mcg, 2 puffs/day plus as-needed inhaled salbutamol Moderate: HFA beclometasone 100 mcg, 4 puffs/day plus as-needed inhaled salbutamol Severe: HFA beclometasone 100 mcg, 8 puffs/day plus as-needed inhaled salbutamol
Strengths	Emphasis on inhaled ICS Practical guidance for management with limited resources		
Limitations	Risk of adverse effects with theophylline at step 4 Risk of addition of regular oral prednisolone before other approaches considered	Risks associated with beta$_2$ receptor downregulation with frequent salbutamol dosing in patients with moderate or severe persistent asthma	
		Risk of withholding ICS from patients with intermittent asthma who may benefit	
	Risk of over-reliance on salbutamol Risk of non-adherence to ICS resulting in salbutamol-only treatment ICS-formoterol (or other ICS-LABA combination) is not considered a treatment option at any step Lack of specific pediatric management guidelines		

ICS: Inhaled corticosteroid; GINA: Global Initiative for Asthma; Union: International Union Against Tuberculosis and Lung Disease; MSF: Médecins Sans Frontières; WHO-PEN: World Health Organization Package of Essential Noncommunicable Disease Interventions for Primary Care. *MSF states that doses depend on asthma severity: Children 50–100 mcg twice daily; increase to 200 mcg twice daily if necessary (up to maximum 800 mcg daily). Adults 100–250 mcg twice daily, increase to 500 mcg twice daily if necessary (up to maximum 1500 mcg daily). World Health Organization,[18] Médecins Sans Frontières,[20] International Union Against Tuberculosis and Lung Disease[19]

either as a rapid response to bronchodilator or as within-day variability measured over 2 weeks.

Guidance on using PEF in diagnosis is provided in the GINA strategy report,[23] the WHO Package of Essential Non-communicable Disease Interventions for Primary Care (WHO-PEN),[18] and the European Respiratory Society (ERS) guidelines for the diagnosis of asthma in adults[34] and in children 5–16 years.[28] Training in the use of PEF meters is relatively simple. Such tests should preferably be completed before starting long-term controller treatment.

Based on a Grading of Recommendations, Assessment, Development, and Evaluation analysis, ERS guidelines advise that PEF may be considered in the diagnosis of asthma if no other lung function test is available. However, they suggest that PEF variability should not be considered the primary test for making a diagnosis of asthma (low-quality evidence).[28,34]

Spirometry

In SSA countries where ready access to spirometry is not feasible, we recommend either centralized spirometry offered

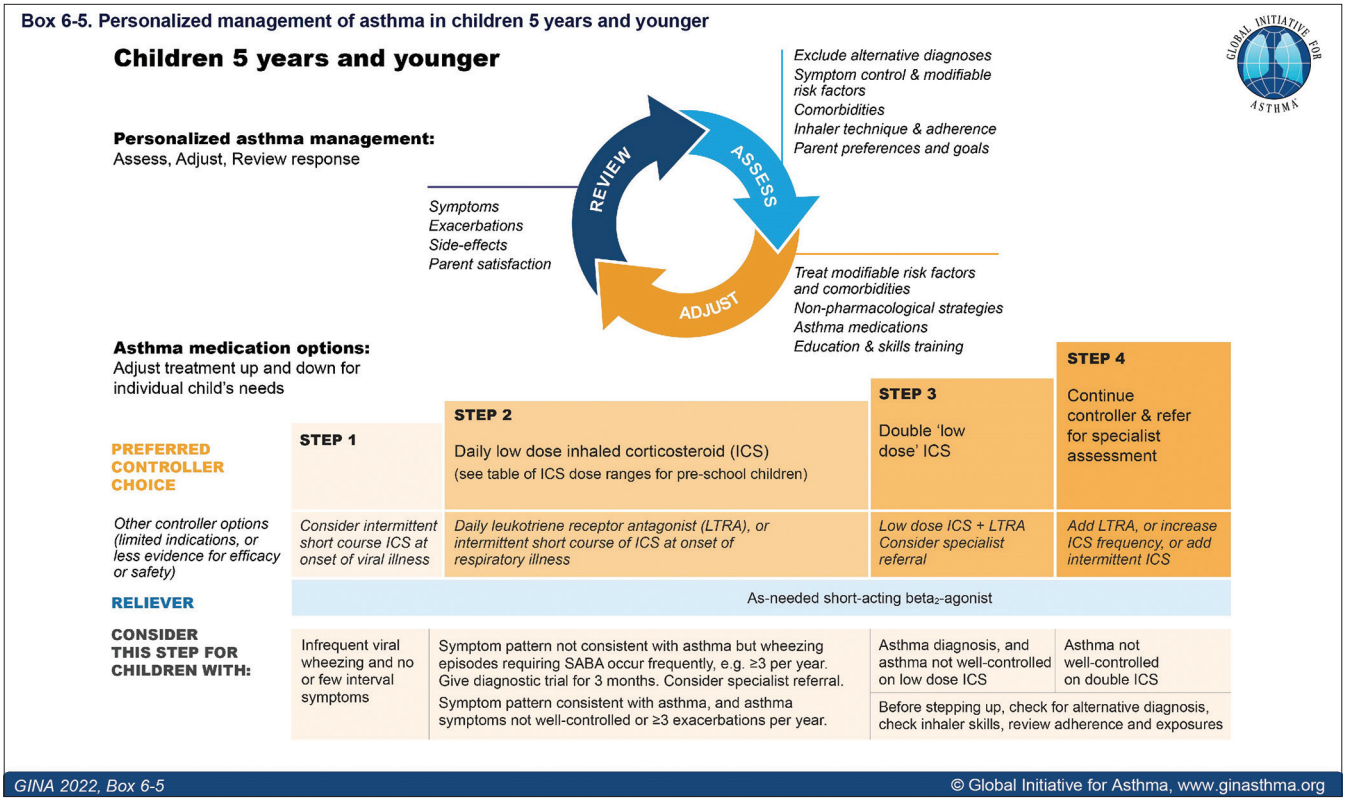

Figure 1: GINA 2022 personalized asthma management for children 5 years and younger. ICS: Inhaled corticosteroids, LTRA: Leukotriene receptor antagonist, SABA: Short-acting beta$_2$ agonist. Source: Boxes 6–5, GINA strategy 2022.[23]

in secondary or tertiary care centers where patients may be referred for spirometry or promoting the use of PEF meters in the primary and secondary care levels.

Where spirometry is available, it should be used as part of the diagnostic workup, as per the guidance in the GINA strategy report (2022).[23] It is important to note that in patients with long-standing asthma, especially those with a history of severe exacerbations, airflow limitation may become persistent (i.e., with less likelihood of demonstrating a significant bronchodilator response).

CURRENT STATUS OF ASTHMA TREATMENT IN SSA

Like underdiagnosis, undertreatment of asthma is a global problem and particularly common in SSA. A study done in Nigeria found that only 11% of people with asthma used an ICS, and asthma symptoms were controlled in only 6.2%.[38] The burden of asthma was high in this study, with three-quarters of respondents reporting absenteeism from school or work due to asthma in the preceding year.[38] Furthermore, a prospective cohort study in Uganda reported that only 33% of participants with asthma had controlled asthma, of which 33% were on inhaled controller medications, and 60% had one or more asthma exacerbations each year.[39] A hospital-based study in Uganda found that, in children aged <5 years with asthma symptoms, over 90% were rather diagnosed with pneumonia and treated with antibiotics, thus missing opportunities to address the correct chronic disease.[40]

In Kenya, only about 60% of people with asthma diagnosis had received asthma medications, and these were usually limited to oral salbutamol or oral prednisolone, with inhaled treatment only deemed necessary for those with the most severe disease.[41] In some countries, including Kenya, there is a preference for oral medications over inhaled medications and fear of ICS.[37] An audit-based study in South Africa found that only 31.5% of children with asthma had well-controlled asthma and 17.6% had been admitted to hospital in the previous year.[42]

Lack of access (availability and affordability) to purpose-designed spacers or pediatric doses of asthma medicines is also a challenge for clinicians managing asthma in LMICs.[43]

PRAGMATIC APPROACHES TO THE TREATMENT OF ASTHMA IN RESOURCE-CONSTRAINED SSA SETTINGS

[Table 3] includes scenarios for medical treatment options commonly encountered in resource-constrained SSA settings

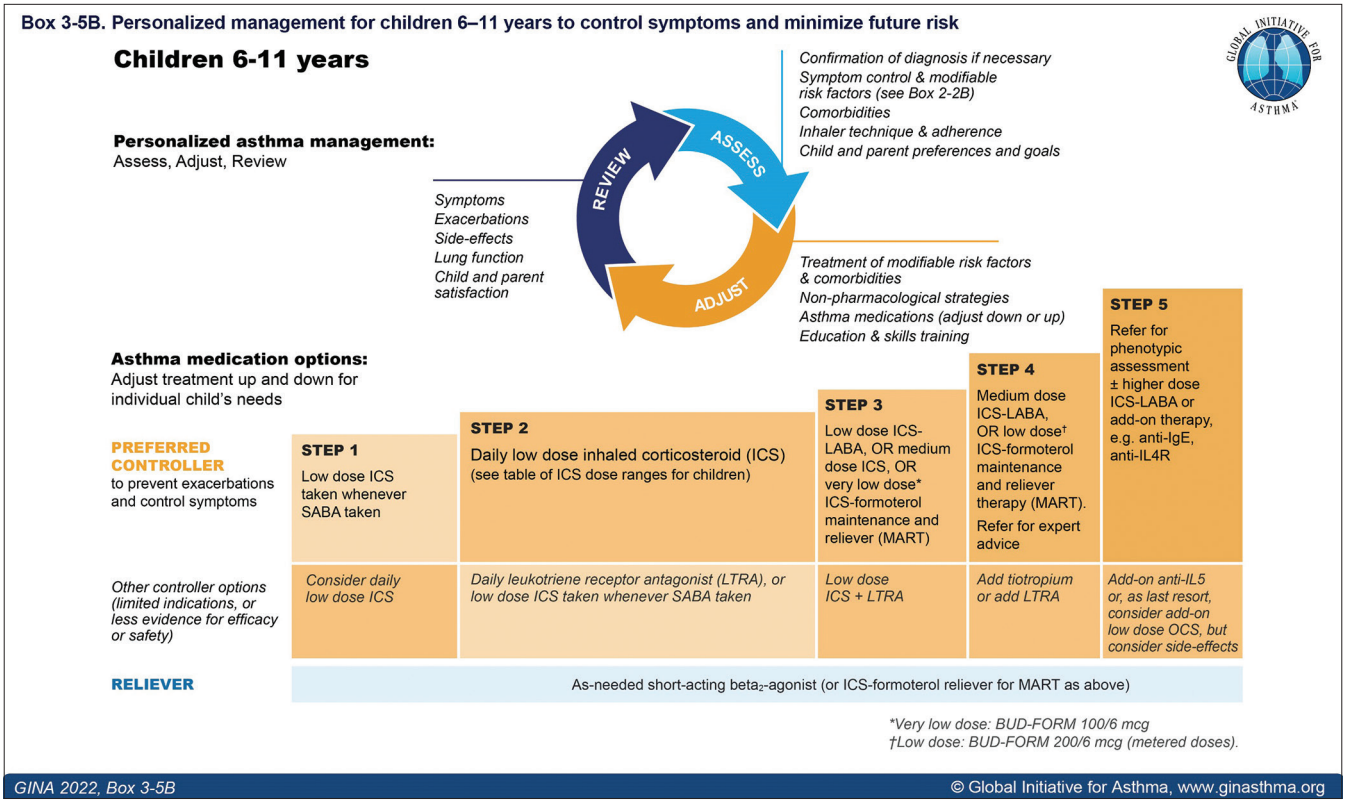

Figure 2: GINA 2022 personalized asthma management for children 6–11 years. BUD-FORM: Budesonide-formoterol, ICS: Inhaled corticosteroid, LABA: Long-acting beta$_2$ agonist, LTRA: Leukotriene receptor antagonist, MART: Maintenance and reliever therapy with ICS-formoterol, OCS: Oral corticosteroid, SABA: Short-acting beta$_2$ agonist. Source: Box 3-5B, GINA strategy 2022.[23] For initial asthma treatment in children aged 6–11 years, Boxes 3–4C and 3–4D in GINA strategy 2022. For low, medium, and high ICS doses in children, Boxes 3–6 in GINA strategy 2022.

and makes pragmatic suggestions on how to approach asthma management within these constraints.

All patients

We suggest that all patients, regardless of what asthma medicines are available, should receive asthma education and an action plan (written or pictorial) including advice about when to seek emergency treatment. This should be tailored to the individual patient's circumstances and the health services they might access in the event of an exacerbation. Patients receiving any inhaled medications should be taught how to use the inhaler, and the technique should be checked at each visit to a healthcare center. Individual asthma education for self-management or parental management can be delivered by doctors, trained allied health professionals such as nurses, or trained lay health workers.[44,45]

Oral salbutamol, theophylline, and prednisolone

Oral salbutamol, theophylline, and prednisolone are widely available and affordable. In some countries, these are the only available medicines for the maintenance treatment of asthma and emergency management of asthma exacerbations. This limited range of treatment options is common in SSA and represents the lowest quality of asthma care as it is associated with a high risk of serious side effects. GINA does not recommend the use of oral salbutamol or theophylline where inhaled therapy is available.[23] While acknowledging that clinicians in some contexts are constrained to work with this restricted formulary, all involved in health care in SSA are urged to work toward the phasing out these asthma treatments and their replacement with inhaled therapies both for relief and as maintenance treatment, on the basis that these are both safer and considerably more effective.

For patients living in remote areas, it is particularly important that action plans make provision for potentially life-saving management in the event of a severe asthma attack. This may include an emergency supply of oral prednisolone (a single dose or short course) to be taken according to written instructions when symptoms worsen. It is important to note that an inhaled SABA kept at home for emergencies (even if unaffordable for day-to-day use) together with a short course of oral prednisolone may be lifesaving.

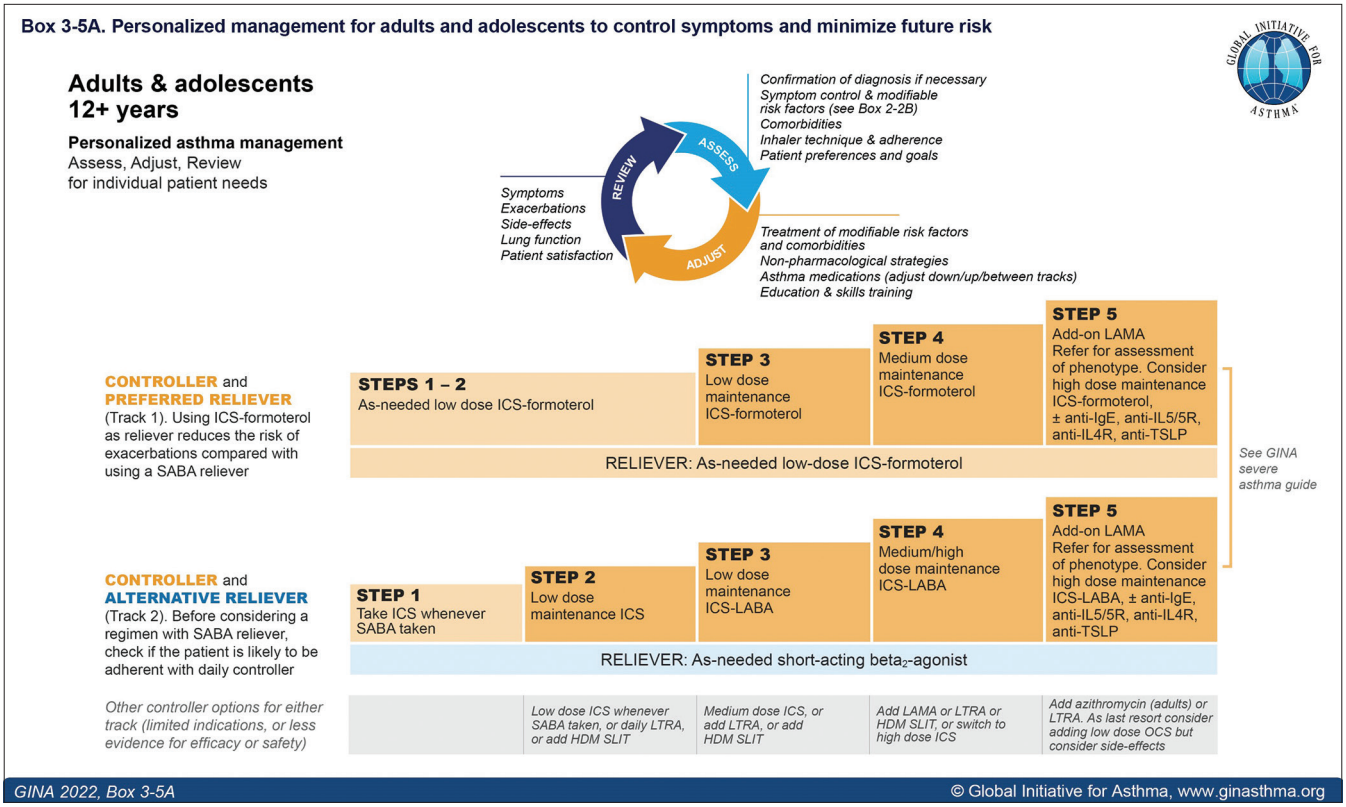

Figure 3: GINA 2022 personalized asthma management for adults and adolescents. HDM: House dust mite, ICS: Inhaled corticosteroid, LABA: Long-acting beta2-agonist, LAMA: Long-acting muscarinic antagonist, LTRA: Leukotriene receptor antagonist, OCS: oral corticosteroid, SABA: Short-acting beta$_2$ agonist, SLIT: Sublingual immunotherapy. Source: Box 3-5A in GINA strategy 2022.[23] For recommendations about initial asthma treatment in adults and adolescents, Boxes 3-4A and 3-4B in GINA strategy 2022. For low, medium, and high ICS doses for adults and adolescents, Boxes 3-6 in GINA strategy 2022.

In some regions, daily or alternate-day oral prednisolone is the only option for controlling symptoms and limiting exacerbations. However, clinicians and patients need to acknowledge and be alert to the high risk of adverse effects of long-term use of this treatment.[46]

Inhaled SABA

Inhaled SABA (usually salbutamol) offers a considerable advantage over oral bronchodilators both in terms of effectiveness and safety, and used as needed should be preferred to oral bronchodilators. As with all inhaled therapies, it is important that careful attention is given to ensuring that the patient can use the inhaler effectively. A spacer device that may improve delivery can be made at little cost from disposable plastic drink bottles and this has been noted to be as equally effective.[47] The use of SABA alone to manage asthma is intended only for settings in which ICS cannot be obtained. On grounds of safety, GINA recommends against the use of as-needed SABA without the concurrent use of an ICS, since the addition of a reliever combined or taken concurrently with an ICS is associated with a large reduction in severe exacerbations and potentially asthma mortality.[23]

ICS and ICS-formoterol

Where ICS is available, it is important that this is offered to all patients with asthma, in line with GINA 2022 recommendations and based on evidence that it substantially reduces asthma mortality and morbidity.[23]

Where appropriate ICS-formoterol combinations are available and affordable, we recommend using ICS-formoterol according to GINA 2022 "Track 1" for adolescents/adults.[23] Formoterol is a rapid-onset LABA. While several ICS-LABA combinations have been developed, ICS-formoterol, used either as-needed only (for patients with mild asthma) or as both maintenance and reliever therapy ("MART"), is the preferred option for managing asthma of all severities, based on published evidence.[23] The budesonide-formoterol combination can be used as needed for symptom relief in either of these regimens, with safety and efficacy demonstrated for formoterol up to a total daily dose (maintenance plus as-needed doses) of 72 mcg (54 mcg delivered dose).

There is now a large body of evidence, primarily from high-income countries, supporting the use of MART

Table 3: Pragmatic approaches to diagnosis and treatment of asthma in resource-constrained settings.*

Pragmatic approach	Notes
Diagnosis of asthma	
Scenario 1. No diagnostic technologies are currently available	
Clinical diagnosis based on: 1. Recognizing typical symptoms (cough, wheeze, and dyspnea) that fluctuate over time and increase with exposure to triggers (e.g., respiratory infections, allergens, exercise, cold air, or air pollution) 2. Recognizing symptoms that raise the suspicion of alternative diagnoses, particularly TB and HIV-AIDS (e.g., fever, weight loss, malaise, and chronic sputum production) 3. Considering factors that increase the probability that the respiratory symptoms are caused by asthma (e.g., history of childhood eczema, family history of allergies and/or asthma, and>3 episodes/year requiring health-care visits) 4. Observing short-term (minutes) resolution of symptoms in response to an inhaled bronchodilator (e.g., salbutamol) and/or long-term control of symptoms with a treatment trial of ICS-containing therapy.	If no improvement with recommended asthma treatment, or if symptoms are not typical of asthma, assess for alternative diagnoses or refer to a higher level of care. In children aged≤5 years, differential diagnosis is broad, including viral infections presenting with asthma-like symptoms. The probability of asthma is highest in those: • Presenting with>3 episodes of wheezing per year • With symptoms that persist>10 days after an acute respiratory tract infection • Who remain symptomatic between flare-ups • With a personal or family history of atopy. Where there are no diagnostics clinicians should advocate for access to peak flow meters (primary care level) and spirometers (secondary/tertiary care level)
Scenario 2. PEF but not spirometry is currently available	
Method 1.Bronchodilator response: Measure PEF before and 15 min after giving 2 puffs (200 mcg) of salbutamol. Improvement in PEF≥20% increases likelihood of a diagnosis of asthma (compared with COPD and other diagnoses).[18] Method 2. PEF variability:[34] Monitor over 2 weeks. Variation of>20% in adults or>12% in children supports asthma diagnosis. Method 3. Therapeutic trial:[23] Document symptoms and PEF. Treat with regular ICS and as-needed SABA for 4 weeks (with a 1-week course of oral corticosteroids if necessary). PEF improvement>20% from baseline supports diagnosis of asthma.	These tests should be completed before starting long-term controller treatment. Interpret lack of significant bronchodilator response with caution; most patients with asthma show<20% increase in PEF after salbutamol.[18] PEF variability over 2 weeks can confirm the diagnosis of asthma or identify the need for further investigation. The absence of variable expiratory flow measured by PEF does not rule out the diagnosis of asthma.[23,34] Guidance available in: • GINA strategy report[23] • WHO-PEN[18] • ERS guidelines[28,34]
Scenario 3. Spirometry available	
Make diagnosis based on history of variable respiratory symptoms, confirmed expiratory airflow limitation and confirmed variability in lung function: 1. Identify expiratory airflow limitation: reduced FEV_1 (<LLN or<80% predicted) and FEV_1/FVC<LLN or<0.8 2. Identify excessive variability in expiratory airflow: Measure FEV_1 before and 10–15 minutes after inhalation of 400 mcg salbutamol. In adults, adolescents, and children with variable respiratory symptoms, FEV_1 increases by≥12% and≥200 mL confirms the diagnosis of asthma.	Other methods include measuring FEV_1:[23] •Before and after a therapeutic trial •Before and after challenge tests •Between visits over time. Guidance (including other methods) is available in GINA strategy report.[23] Bronchodilator response<12% does not exclude asthma.
Treatment of asthma	
All settings Provide all patients with asthma education and an asthma action plan (written or pictorial). Clinicians should advocate for access to affordable inhaled asthma medications for children, adolescents, and adults and skills training for health professionals and lay workers.	
Scenario 1. Only oral salbutamol, theophylline, and prednisolone are currently available**	
Acute care pragmatic approaches: 1. Provide oral prednisolone (course or single dose) for emergency use, with instructions on asthma action plan. 2. Use ICS in preference to oral bronchodilators to manage symptoms Maintenance treatment pragmatic approaches: 1. Oral salbutamol to control symptoms if no inhaled bronchodilator is available. Titrate to individual lowest beneficial dose to minimize adverse effects.	These approaches are not best practices but represent a necessary compromise where inhaled SABA and ICS are not available. The best and safest approach is to reserve oral prednisolone for the treatment of exacerbations and avoid regular use. However, maintenance of oral prednisolone might be necessary if it is the only option for controlling symptoms and limiting exacerbations.

(Contd...)

Table 3: *(Continued)*.

Pragmatic approach	Notes
2. Low dose of prednisolone daily or every alternate day if necessary to control symptoms and limit exacerbations. 3. Oral theophylline if it is the only bronchodilator treatment option available. If blood level monitoring is not possible, the safest option may be to avoid exceeding the lowest age-appropriate dose. Titrate to individual lowest beneficial dose to minimize adverse effects.	Frequent or long-term prednisolone is associated with adverse effects – monitor and discuss with patient or caregiver. Maintenance of prednisolone is rarely warranted in children. Oral salbutamol and oral theophylline have systemic adverse effects and do not address underlying airway inflammation, so patient remains at risk of exacerbations and asthma death. Salbutamol is preferable to theophylline if inhaled bronchodilator therapy is not available. Theophylline has a narrow therapeutic window. Ideally, blood levels should be monitored, but this approach is extremely unlikely to be available in resource-limited settings. Concurrent use of theophylline and salbutamol is unlikely to achieve sufficient additional benefit to offset adverse effects.
Scenario 2. Inhaled SABA available but not ICS**	
Provide training in correct inhaler technique. If inadequate symptom control, a trial of daily oral theophylline, taken in addition to as-needed inhaled salbutamol, is preferable to resort to regular prednisolone. If inhaled SABA can be obtained but is unaffordable for day-to-day use, provide one inhaler for emergencies and usage instructions (with oral prednisolone) in asthma action plan.	Train patient in correct inhaler technique. Use spacer with pMDI (can be made from plastic drink bottle). In patients using as-needed SABA, oral salbutamol or oral theophylline are generally unlikely to provide additional benefit. The GINA recommendation against the use of as-needed SABA without ICS is based on the very large reduction in severe exacerbations and asthma mortality seen with ICS-containing treatment, compared with SABA-only treatment.[23]
Scenario 3. ICS but not ICS-formoterol available**	
Train patient in correct inhaler technique. Where ICS (but not ICS-formoterol) is available and affordable, use ICS according to GINA 2022 "Track 2" for adolescents/adults, to avoid SABA-only treatment:[23] • For patients who do not need maintenance ICS treatment, instruct patients to take a dose of ICS each time they use SABA for symptom relief. • For patients who need maintenance treatment, use ICS regularly, with SABA taken as needed for symptom relief.	In patients prescribed maintenance ICS, use strategies to encourage adherence.
Scenario 4. ICS-formoterol is available*	
Train patient in correct inhaler technique Recommended treatment options: • As-needed-only low dose ICS-formoterol for patients with mild asthma • MART with low-dose ICS-formoterol as both maintenance and reliever treatment for patients with moderate asthma: patient takes regular daily dose (e.g., 1 inhalation twice daily) plus extra doses as needed for symptom relief. Double the number of maintenance inhalations for patients with severe asthma.	ICS-formoterol, either as-needed only (mild asthma) or as MART is the preferred option for managing asthma of all severities, based on evidence. For budesonide-formoterol combination, safety and efficacy have been demonstrated for formoterol up to a total daily dose (maintenance plus as-needed doses) of 72 mcg (54 mcg delivered dose) on individual days.

COPD: Chronic obstructive pulmonary disease, ERS: European Respiratory Society, FEV_1: Forced expiratory volume in 1 s, FEV_1/FVC: Ratio of forced expiratory volume in 1 s to forced vital capacity; ICS: Inhaled corticosteroids; GINA: Global Initiative for Asthma, LLN: Lower limit of normal, MART: Maintenance and reliever therapy, PEF: Peak expiratory flow, SABA: Short-acting $beta_2$ agonists, WHO-PEN: WHO-PEN: World Health Organization Package of Essential Noncommunicable Disease Interventions for Primary Care. ∗Based on evidence where available and the experience of the authors. ** "Available" means both obtainable in the country and accessible/affordable

with ICS-formoterol in adolescents and adults,[48,49] and one large study in children.[50] MART with budesonide-formoterol and beclometasone-formoterol is approved by regulators in many countries. More recently, the SYGMA 1&2,[51-53] PRACTICAL,[54] and Novel START[55] trials have demonstrated that mild asthma in adolescents and adults can

be managed effectively with just "as-needed" budesonide-formoterol ICS, with particularly large reductions in severe exacerbations and emergency visits/hospitalizations compared with inhaled SABA alone.[56] In that study, as-needed-only low-dose budesonide-formoterol also reduced need for emergency department visits and hospitalization, compared with maintenance ICS plus as-needed SABA.[56]

In addition to its demonstrated efficacy[56] and excellent safety profile,[57,58] the use of ICS-formoterol to manage asthma across all severity levels may have special advantage for countries of SSA: Even among patients with mild asthma, the reduction in exacerbations, compared with SABA only[51-56] or maintenance ICS plus as-needed SABA,[56] would reduce the burden of acute asthma on health services. This strategy ensures that all patients receive doses of ICS. In settings where access to care is limited, even symptom prompted the use of ICS-containing medications is likely to be beneficial. The simplicity of a single inhaler for both symptom relief and (where required) maintenance treatment might make it easier for patients to use their medicines correctly. Even in well-resourced health systems, where patients have access to self-management education provided by health professionals, the historical approach that begins with SABA, along with the later addition of daily maintenance treatment, commonly confuses patients about the roles and correct use (timing and technique) of multiple inhalers. The use of a single ICS-formoterol inhaler also simplifies the process of stepping up and down between treatment levels, as it does not involve adding a second inhaler device when initiating maintenance treatment or when increasing or decreasing maintenance treatment. For some health services, this strategy may simplify drug procurement by reducing the requirement for a wider variety of products.

APPROACHES TO STRENGTHENING HEALTH SYSTEMS FOR ASTHMA CARE IN RESOURCE-CONSTRAINED SSA COUNTRIES

Current initiatives supporting improvement in asthma care in SSA

The WHO has a strong mandate to reduce the burden of chronic respiratory diseases in LMICs.[8] Its current (13th) General Programme of Work sets out clear frameworks for patient-centered health services to deliver care across disease types and settings.[59] The WHO considers integrated care for chronic respiratory diseases to be central to meeting these objectives. Strategies developed by the WHO to address lung health in LMICs include the Practical Approach to Lung Health (PAL)[60] and WHO-PEN[18] disease interventions to provide protocols for the diagnosis and treatment, both acute and long term, of asthma and COPD in resource-constrained settings.

GARDs focus on the needs of LMICs and vulnerable populations. It supports the WHO to establish and strengthen national policies and tailored initiatives for the prevention and control of chronic respiratory diseases.[61] GARD goals for LMICs are to improve diagnosis, acknowledging that a syndromic approach to diagnosis will be necessary for most countries, and secure accessible and affordable treatment for all patients. The current GARD activities include demonstration projects in South Africa and Mozambique.[62,63]

GINA has made a considerable effort, particularly over recent years, to maximize the relevance of the GINA recommendations to resource-constrained settings in LMICs (and under-resourced settings within high-income countries).[23] Sections of the strategy have been expanded to address the needs of patients living in these resource-constrained settings. GINA activities include publishing articles on the implementation of the GINA strategy in the context of LMICs,[7,64-66] World Asthma Day advocacy efforts to shine a spotlight on the needs of patients with asthma around the world, including in LMICs,[67] and promoting management of asthma in LMICs as a key topic for research.[68] An important aspect of all these efforts is to ensure patients with asthma, wherever they may be and are provided with care that meets a basic quality standard as outlined in the GINA strategy.

Regional initiatives in SSA include Practical Approach to Care Kit (PACK) developed by the Knowledge Translation Unit of the University of Cape Town Lung Institute.[69-73]

Strengthening asthma education for health professionals

Training health workers to conduct high-quality spirometry are an important priority in SSA. The Pan African Thoracic Society (PATS) has a program to provide training and education on spirometry, but there remain challenges to be overcome.[29]

In some SSA countries where ICS is available, ongoing prescribing of oral salbutamol, theophylline, and prednisolone, or sole prescription of inhaled salbutamol, may be influenced by patient preference in populations with low health literacy, or lack of access to ongoing medical education on evidence-based asthma management. A similar problem has been documented in India, where primary care physicians' lack of awareness of the importance of ICS treatment in asthma management is one of the main reasons why, even when ICS is available, many people with asthma do not use it.[66]

Therefore, we recommend that regular and updated asthma education for doctors and other health care workers be prioritized, as well as considering patient asthma education delivered by non-health professionals, especially in rural settings.

Enabling effective asthma care delivered by non-physician health workers

The GINA report[23] cites several studies showing the effectiveness of asthma education provided by nurses, pharmacists, and lay health workers.[74-79]

Nurse-led asthma care has been shown to markedly reduce asthma exacerbations among adults in rural Cameroon.[80] Studies in Malawi have demonstrated that asthma symptoms and exacerbations can be reduced by clinical assessment, optimization of inhaled treatment, and individualized asthma education delivered by trained non-physicians,[45] and that this education is well received by parents.[44]

RESEARCH RECOMMENDATIONS

With the notable exception of selected South African settings, research into the diagnosis and management of asthma in SSA is extremely limited.[69-73] There is only limited evidence about the implementation of the WHO-PEN asthma guidelines in SSA[81] and no clinical trial evidence from these countries on the recommended GINA approach of using ICS-formoterol as reliever (Track 1).[23] There is an urgent need to change this situation, because only relevant, locally generated evidence can inform changes to policy and increase investment into programs for the treatment of children, adolescents, and adults with asthma in SSA.

We suggest the following major priorities for asthma research in SSA:

- Baseline data – Collect and maintain accurate, regularly updated data on the prevalence of asthma, burden of symptoms, exacerbations, health system resource utilization, and the availability and affordability of the WHO essential asthma medicines and technology. These data are necessary to identify and address needs and measure progress (or lack of it) so that policy and decision makers can be held to account
- Local clinical trials – Design and conduct a clinical trial in SSA to evaluate the clinical effects and cost-effectiveness of the GINA track 1 approach (ICS-formoterol across all levels of asthma severity), compared with the current standard of care. This evidence is needed to inform changes to treatment recommendations (and investment in their implementation)
- **I**mplementation strategies – Design and conduct implementation studies to improve access to diagnosis and acceptance of appropriate treatments. This approach might involve operationalizing the GINA recommendations in a range of health systems, with consideration of local issues including human resource capacity strengthening, medicine management and supply, and data capture systems to document effectiveness and impact on patient outcomes. We recommend strong involvement of service users (patients and caregivers) in the research process to maximize understanding of what works, why, and how
- Delivery models – Further evaluate models for delivery of asthma care within different health systems in SSA using an integrated care approach that empowers all categories of the primary health-care personnel, including non-physicians, to diagnose and manage asthma, such as those developed for the PACK[69-73]
- Community attitudes and knowledge – Develop and evaluate innovative tools that will improve community acceptance of asthma and its management.

Substantial strengthening of research capability in SSA is needed to enable this research. It is imperative that adequate opportunities are created for this research to be led and delivered by appropriately skilled and experienced African investigators. A successful model to achieve this is the PATS Methods in Epidemiological, Clinical, and Operational Research (PATS MECOR), which offers training and networking opportunities for clinicians from SSA who are interested in research.[7,82-84]

Policy recommendations for SSA healthcare systems

We make the following recommendations for policy and decision-makers:

- Develop national asthma strategies based on relevant evidence
- Develop evidence-based national asthma management guidelines (or adapt guidelines from elsewhere that can be implemented nationally at all levels of care)
- Develop evidence-based regional asthma management guidelines that can provide the basis for national guidelines where individual countries lack resources to develop these
- Ensure WHO essential medicines and devices for the treatment of asthma are made available and affordable to all children, adolescents, and adults
- Improve access to diagnostic tools to facilitate diagnosis of asthma in children, adolescents, and adults
- Support community-based programs that improve asthma literacy
- Reorient health systems to integrate asthma care into primary health care and improve human resource capacity through training, mentorship, and supervision programs.

CONCLUSION

There are well-established evidence-based strategies for the management of asthma, including GINA which, if fully implemented, would have a substantial impact on the global burden of avoidable asthma morbidity and mortality.

The reality of managing asthma in SSA is commonly very different: Limited by substantial resource constraints affecting access to care, diagnostics, and treatments. In this review, we have acknowledged this reality and provided some pragmatic suggestions for how to best manage children, adolescents, and adults with asthma under these resource-constrained conditions.

However, clinicians and policymakers must *not* accept these constraints as inevitable and permanent. Instead, we must develop and implement research and policy recommendations that will improve asthma care in SSA, including making WHO Essential Medicines available to all.

Acknowledgments

We thank Jenni Harman for her editorial assistance and GINA for supporting this work.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Financial support and sponsorship

Global Initiative for Asthma (GINA).

Conflicts of interest

KM has reported advisory board fees from AstraZeneca; RM has received advisory board and honoraria and investigator initiated research from AstraZeneca and honoraria from MSD; HR reports research grants for investigator-initiated studies from AstraZeneca, GSK, and Novartis, and honoraria for participating in advisory boards or consulting for AstraZeneca, Chiesi, GlaxoSmithKline, Novartis, and Sanofi; and for providing independent medical education at symposia funded by AstraZeneca, Boehringer Ingelheim, Chiesi, Getz, GlaxoSmithKline, Sanofi, and Teva. AAY is a member of the GINA board, EDB has received honoraria for lectures from AstraZeneca, Boehringer Ingelheim, Cipla, Chiesi, Hikma pharma, Menarini, Novartis, Orion, Regeneron, and Sanofi Genzyme, and consulting fees from AstraZeneca, Novartis, Regeneron, and Sanofi Genzyme in the past 3 years.

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How to cite this article: Mortimer K, Masekela R, Ozoh OB, Bateman ED, Nantanda R, Yorgancıoğlu AA, *et al*. The reality of managing asthma in sub-Saharan Africa – Priorities and strategies for improving care. J Pan Afr Thorac Soc 2022;3:105-20.