Although the symptoms of asthma were 298 per 100,000 in 2017.

These symptoms are triggered by several environmental factors such as allergens, irritants, pollution, weather change, exercise, and viral respiratory infections. Although the symptoms are usually reversible spontaneously or by medications, some patients might experience exacerbations, which could be life-threatening. Exacerbations significantly increase the burden of the disease. The disability-adjusted life years attributed to asthma was 298 per 100,000 in 2017. The
economic burden of asthma includes both direct medical costs (e.g., hospitalizations, emergency department [ED] visits, medical practitioner visits, and medications) and indirect nonmedical costs (e.g., time lost from work, decreased productivity or premature death).[8,9] Several asthma studies showed that direct costs are higher than indirect costs and contribute to 50%–80% of the total costs.[10] In the Middle East and in Africa (MEA), asthma presents a significant burden to the health-care systems and to individuals living with asthma. In a pediatric asthma study in Turkey, hospitalizations and interventions (58.9%) were identified as the main cost factor.[11] However, the economic burden of asthma in the region has not been systematically explored and reported.

The main goal of asthma management is to achieve optimal asthma control and reduce the risk of asthma exacerbations and mortality. Although asthma care has improved over the years, the level of asthma control is not considered optimal in many countries.[12,13] In MEA, asthma control is considered unsatisfactory as more than two-third of the patients have uncontrolled asthma.[14] In an observational cross-sectional study of 939 asthma patients from Turkey, Egypt, Saudi Arabia, Kuwait, and the United Arab Emirates, 44.2% of patients had uncontrolled asthma.[15] In addition, the rate of adherence to asthma medications is poor, with about one-quarter of patient population reporting good medication adherence.[16] A panel of experts met with an aim to address these unmet needs with a focus on the challenges faced by the health-care professionals (HCPs) in diagnosis and treatment and to provide practical recommendations for the management of asthma in MEA, which are presented in this manuscript.

Methodology

The MEA steering committee meeting that convened in January 2021 included a team of 14 members with expertise in the asthma diagnosis and management across MEA (12 pulmonologists: 1 each from Algeria, Kuwait, South Africa, Tunisia, Turkey, and United Arab Emirates and 2 each from Egypt, Lebanon, and Saudi Arabia; one general practitioner from Kenya and 1 family practitioner from Turkey).

The panel of experts discussed the clinical gaps and challenges in the management of asthma and provided practical recommendations based on their clinical experience to improve asthma care in MEA. For the review of evidence and development of recommendations, a literature search was conducted using MEDLINE and EMBASE databases. Several keywords including “asthma,” “management,” “leukotrienes inhibitors,” “long-acting β-agonists,” “inhaled corticosteroids,” “short-acting β-agonists,” “effectiveness,” “survival,” “Middle East,” and “Africa” were used for in-depth literature search on the topic. The results presented in the literature were reviewed, and the recommendations were developed. The opinions and responses were integrated, and a thematic analysis was conducted to methodically categories the region-specific recommendations. This manuscript is an outcome of the expert group discussion with the recommendations for MEA.

Insights of Asthma Management in the Middle East and in Africa

Small regional surveys in patients with asthma in the MEA countries have reported prevalence in the range of 2%–32% [Table 1].[17–23] The Evaluation of Asthma Management in Middle East North Africa Adult population (ESMAA) and SNAPSHOT studies provided an insight into the prevalence and control of asthma across all the assessed Middle Eastern countries and within the Gulf Cooperation Council Countries, with the highest prevalence of controlled asthma reported in Kuwait (42.6%) and Qatar (41.1%).[14,24] In MEA, the ESMAA study reported asthma as being uncontrolled in 41.5% of patients (95% confidence interval [CI]: 40.3%–42.6%), partly controlled in 29.1% (95% CI: 28.1%–30.2%), and controlled in 29.4% (95% CI: 28.4%–30.5%).[14] The SNAPSHOT study reported a significantly lower EuroQol visual analog scale score in patients with asthma as compared to the general population (68.2 ± 22.9 vs. 78.1 ± 17.5; P < 0.0001).[24]

Challenges and Recommendations for Management of Asthma

The challenges specific to MEA for management of asthma were discussed by the expert panel and recommendations to improve management were framed. Expert panel identified several gaps in the diagnosis and treatment of asthma in the region. Critical challenges for
diagnosis of asthma include lack of awareness about the pathophysiology of the disease and treatment modalities in HCPs and patients, lack of specialized diagnostic facilities, limited access to spirometry, and social stigma associated with asthma. Region-specific factors affecting the asthma control are mentioned in Figure 1.

Poorly controlled asthma is associated with more exacerbations and emergency room visits. Although asthma control is assessed by guideline-defined criteria, patients’ perceptions of control are subjective. One major issue in assessing asthma control is the disconnect between physician-defined or guideline-defined asthma control and patients’ perception of asthma control. Several real-world studies have reported that only about half of the patients meet criteria for well-controlled asthma. In the INSPIRE study, approximately 90% of 3415 patients had an average of 12 periods of asthma exacerbations per year, yet felt their asthma was well controlled. There is also a lack of awareness among patients on the description of controlled asthma. In another study, the percentage of patients with controlled asthma decreased from 58% to 33% after awareness of the definitions for asthma control.

The challenges for management of asthma in MEA are summarized in Table 2. The most common challenges in MEA are overreliance and overuse of short-acting β-agonists (SABAs), underprescription of inhaled corticosteroids (ICS), nonadherence to prescribed medications, and inadequate insurance coverage for its treatment. There are several factors contributing to overreliance of SABAs and underprescription of ICS such as over-the-counter purchase of SABAs, refilling of old prescription without consultation with physicians, using SABAs for rapid symptomatic relief at the time of exacerbations, and lack of knowledge and information about recent guidelines and treatment patterns. There is

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**Table 2: Region-specific challenges and recommendations for optimal management of asthma**

| Challenges | Recommendations |
|------------|----------------|
| Health-care system not well organized | Establish specialized asthma polyclinics with the help from national health authorities across the country |
| Limited pulmonologists treating asthma | Ensure availability of appropriate educational programs to enhance physicians’ and patients’ knowledge in asthma care |
| Guidelines are old and not updated | Moderate/severe asthma patients to be managed by pulmonologists/specialists at the course of their management, while mild cases to be managed by GPs |
| High prevalence of smoking in MEA | Develop a system where patients highly suspicious of having asthma are considered as priority and given an early care (e.g., appointment within 1 week and not exceeding 1 month) |
| Pharmacists may handout asthma medications and even oral corticosteroids without prescriptions | Enhance awareness of GPs on aspects of asthma diagnosis and management, especially the difference between reliever and controller therapies and the importance of maintenance medication for asthma treatment |
| Patients generally buy any medication without prescription | Ensure standardization/harmonization of local guidelines with global guidelines |

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**Figure 1: Factors Responsible for Poor Control of Asthma in the Middle East and Africa Region. SABA = Short-acting β-agonists**

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Contd...
Table 2: Contd...

| Challenges                                                                 | Recommendations                                                                 |
|---------------------------------------------------------------------------|---------------------------------------------------------------------------------|
| An overreliance of ED physicians on SABA as the patients with worsening   | Educate ED physicians on asthma treatments and avoidance of discharging patients on SABA alone |
| symptoms often first go to the ED physicians and receive a prescription of|                                                                                   |
| SABA inhalers                                                              |                                                                                   |
| Use of multiple devices for asthma treatment                               | Asthma patients can be given an option of using smart devices that monitor their peak expiratory flow |
|                                                                            | Specialized asthma centers with a focus on inhaler-use training, treatment adherence, smartphone application use, and transition to biological agents |
|                                                                            | Having one device for reliever and controller medications will help               |
|                                                                            | Use artificial intelligence to identify medications adherence and prevent overuse of SABA |
|                                                                            | Need to include asthma under insurance full coverage                             |
|                                                                            | There is a need to provide good quality asthma care and insurance facilities to all patients in this region |

AAP=Asthma action plan, ED=Emergency department, GPs=General physicians, ICS=Intranasal corticosteroids, LABA=Long-acting β-agonists, MEA=Middle East and Africa, SABA=Short-acting β-agonists

Action Plan for Management of Asthma in the Middle East and in Africa

Asthma is a variable condition with symptoms and signs that are often not present during a routine health-care appointment, leading to difficulties in diagnosis. Optimal diagnosis is the cornerstone for ensuring patient-centric tailored treatment; however, misdiagnosis of asthma is a major challenge, especially in low-and middle-income countries. A national household survey from Saudi Arabia estimated the self-reported clinical diagnosis of asthma to be 4.05%. Evidence from the ESMAA study reported that diagnosis at least 5 years earlier was significantly associated with uncontrolled asthma ($P < 0.001$).

Comprehensive history taking, physical examination, and demonstration of variable airflow limitation by spirometry or peak flow measurement form the essential elements of asthma diagnostic process [Figure 2].

There are challenges for the implementation of guideline recommendations in all asthma management facilities due to the paucity of testing for airway obstruction, time limitations, and cost of introducing techniques such as fractional exhaled nitric oxide. In addition, fear of social stigma associated with asthma is a common deterrent among patients to accept a definite diagnosis. Experts opined that, in MEA, patients prefer using SABA inhalers for respiratory symptoms, which, in most countries, are available as over-the-counter medications. This causes underutilization of asthma clinics leading to missed diagnosis and increased risk of exacerbations, thereby increasing the severity of asthma.

Asthma guideline strategies focus on symptom control, risk reduction, minimizing medications side effects, and control of morbidities. Asthma control is based on assessing asthma symptoms, use of reliever medications, and impact on daily activities. The clinical status of a patient is described as controlled, partly controlled, or uncontrolled depending on the symptoms during the prior 4 weeks. The optimal control of asthma is freedom from troublesome respiratory symptoms during both day and night, needing minimal or no reliever medications (no more than two puffs SABA/week), maintaining daily activity, and maintaining normal or the best possible lung function. A composite measure of the diagnostic tests is required for the comprehensive assessment of asthma control. Several tools such as the GINA asthma symptoms assessment, the asthma control questionnaire, and asthma control test have brought forth validated control ‘scores’ that can be used in the treatment decisions.

Asthma has long-term sequelae even in patients with mild-or-moderate disease and may experience airway...
In other studies, ICS with long-acting β-agonists (LABAs) prevented exacerbations and loss of lung function but were less effective at mitigating mortality. Thus, uncontrolled asthma has a major impact on the quality of life.\(^{[1,25,45,46]}\)

### Multidisciplinary Approach to Asthma Management

Educing HCPs and increasing awareness of patients are critical to achieve optimal asthma control.\(^{[53]}\) HCPs are recommended to be made aware of the recent local and global guidelines for the management of asthma. The guidelines developed by the Saudi Initiative for Asthma (SINA) recommend a well-structured asthma education program with the goal for enhanced patient-health-care worker partnership, better understanding of clinical presentation and methods of diagnosis, and ability to differentiate between “reliever” and “controller” medications and their appropriate indications to improve quality of life and reduce cost and optimal utilization of health-care resources.\(^{[53]}\) Several studies have shown improvement in asthma control with patient education about the disease, use of asthma management devices, lifestyle modifications, and routine consultation with the physicians.\(^{[1,25,45,46]}\)

The factors responsible for good adherence are higher age, presence of medical insurance coverage, smoking status history, level and frequency of exacerbations, high level of asthma control, and quality of life (mental or physical). Thus, increasing ICS prescription and bringing asthma into mainstream insurance coverage seem to be the foremost for improving the adherence of patients.\(^{[47,48]}\)

Another vital element of effective management of asthma is a written asthma action plan. This personalized plan can act as a guide for self-medication and primary caregivers during the episodes of exacerbations. Several digital platforms are now available to aid self-management of asthma and aid HCPs track patients’ exacerbation episodes.\(^{[46-48]}\) It is also important to review the action plan during regular consultation with HCPs to keep the plan updated as per the recent assessments.

### Overreliance on Short-Acting β-Agonists in Asthma Management

For decades, the standard therapy for mild asthma has been as-needed SABA (GINA step 1) and low-dose ICS with as-needed SABA for symptomatic relief (GINA step 2).\(^{[1]}\) The overreliance of patients on SABAs stems from the rapid relief after inhalation;\(^{[59]}\) however, SABAs lack anti-inflammatory properties resulting in worse long-term outcomes and higher risk of asthma exacerbations and death compared with the outcomes when appropriate dose of ICS and other controllers are used.\(^{[50-52]}\) Regular use of SABA has also been associated with an increase in lung hyper-responsiveness, leading to increased sensitivity to asthma trigger factors.\(^{[53]}\) A population-based health data analysis from Canada reported a higher incidence of visits to ED (odds ratio [OR], 1.25; 95% CI: 1.18–1.33), hospitalization (OR, 1.45; 95% CI: 1.26–1.66), and use of oral corticosteroids (relative risk, 1.06; 95% CI: 1.04–1.08) with overuse of SABA.\(^{[54]}\)

In an ED setting, SABA overreliance is also associated with transient lactic acidosis, tachycardia, arrhythmias, QTc interval prolongation, hypokalemia, hypomagnesaemia, muscle tremors and cramps, and anxiety. Suboptimal prescription of controller medications and overreliance on SABAs has contributed to asthma-related mortality.\(^{[55-57]}\) According to a European survey-based study, approximately 39% of patients who received more than 12 canisters of SABA inhalers during the previous year died of asthma.\(^{[58]}\)

On the other hand, results of randomized controlled trials and observational studies report a significant reduction in the risk of severe exacerbations and asthma-related deaths with the use of ICS in mild asthma.\(^{[51,52,59,60]}\) In one study, ICS reduced the risk of asthma exacerbations by 60% and increased the days with controlled asthma by 50%.\(^{[59]}\) In other studies, ICS with long-acting β-agonists (LABAs) prevented exacerbations and loss of lung function but were less effective at mitigating symptoms than regular ICS maintenance therapy.\(^{[59,61,62]}\)

**The efficacy and safety of budesonide/formoterol as reliever therapy in patients with asthma were evaluated in two randomized, double-blind, placebo-controlled trials.**\(^{[61,62]}\) The outcomes of these trials indicated that as-needed budesonide-formoterol combination was superior to as-needed SABA and provided a noninferior...
effect on annual rate of exacerbation reduction, with a less exposure to ICS, though was lower in controlling symptoms when compared with a maintenance ICS regimen. Similarly, the Novel START (Novel Symbicort Turbuhaler Asthma Reliever Therapy) trial demonstrated the external validity of the pervious findings.\cite{63} In PRACTICAL study, the incidence of severe exacerbations was lower with as-needed budesonide–formoterol than with maintenance budesonide plus terbutaline as needed.\cite{64}

Therefore, it is recommended to optimize the use of ICS and SABA. The suboptimal use of ICS and overuse of SABA need to be discouraged. Patients requiring more than three canisters of SABAs per year are recommended to undergo detailed clinical assessment.\cite{1,58} It is recommended to use as-needed low-dose ICS and formoterol as the preferred rescue option when ICS/formoterol combination is used for the management of asthma or one of the options for mild cases.\cite{58} When ICS is combined with LABAs other than formoterol, SABA is the recommended option as a reliever.\cite{1}

**Impact of Short-Acting β-Agonists Overreliance on Asthma Guidelines Updated in 2021**

In clinical practice, asthma severity is assessed retrospectively based on the treatment step required to control symptoms and exacerbations.\cite{1,65-67} Prior to classifying asthma severity, it is essential to ensure that control is achieved and maintained while using the minimal level of medications over a few months.\cite{1} Since asthma severity level could change over months or years, asthma severity level can be classified as follows: Mild asthma is controlled asthma at step 1 or 2, moderate asthma is controlled asthma at step 3, and severe asthma is that requires treatment at step 4 or 5.\cite{1} Recent guideline updates addressed the issues related to SABA overreliance and underutilization of anti-inflammatory therapy, especially in mild asthma. SABA is no longer recommended on an as-needed basis for mild asthma.\cite{32,66,69} The recent GINA updates have recommended two tracks for asthma management based on the prescribed reliever therapy.\cite{1} Track 1 [Figure 3.1] is based on utilizing as-needed anti-inflammatory reliever therapy with low-dose ICS-formoterol combination for mild asthma (step 1–2). For moderate-to-severe asthma (step 3–5), ICS-formoterol is used as maintenance and reliever therapy (MART). For Track 2 [Figure 3.1], SABA is utilized as a reliever therapy on an as-needed basis. Step 1 requires ICS whenever SABA is needed, step 2 requires low-dose ICS, step 3 requires low-dose maintenance ICS in combination with LABA, and step 4 requires medium-to-high-dose maintenance ICS in combination with LABA. Uncontrolled patients at step 4 in both tracks may require additional therapy such as long-acting anti-muscarinic agent (LAMA). Biologics are considered for uncontrolled patients with moderate-to-severe asthma based on phenotype.

The expert panel recommends adapting the GINA strategies at country and regional levels. One of the examples of successful customization of these strategies is the SINA guidelines introduced by the Saudi Thoracic Society in 2009.\cite{70} The latest update by SINA-2021 has adopted a simple and friendly algorithm [Figure 3.2] which is similar to GINA for recommending avoidance of overreliance on SABA alone for mild cases. The preferred option for step 1 is as-needed low-dose ICS-formoterol combination or adding low-dose ICS when SABA is used. For step 2, low-dose ICS is used for compliant patients, otherwise as-needed low-dose ICS. For step 3, low-dose maintenance ICS in combination with LABA either as MART approach when formoterol is used or as a regular proactive regular dosing with other combination. For step 4, further escalation to medium-high-dose ICS is done with LABA. The once-a-day combination of ICS/LABA is also available that has an adherence advantage over twice-a-day combination.\cite{50,76} Uncontrolled patients at step 4 may require additional therapy such as LAMA. Biologics are considered for uncontrolled patients with moderate-to-severe asthma based on phenotype.

**Short-Acting β-Agonists Alone-free Clinical Practice**

Despite strong evidence suggesting an association of asthma exacerbations, increased risk of hospitalizations and ED visits, the inappropriate use of SABA is still prevalent. Besides safety issues, inappropriate use of SABA has been shown to be associated with a 6% increase in total asthma-related costs in the immediate 3-month period, and 5% and 6% increase in outpatient services and medications costs, respectively.\cite{58} With the recent recommendations to avoid prescribing SABA alone in the management of mild asthma (step 1) and the observed practice of discharging patients from EDs with SABA alone, the expert panel recommends SABA-alone-free clinical practice. Patients with mild asthma are at risk of exacerbations as the triggers for exacerbations include environmental exposures (smoke, air pollution, or allergens), poor adherence to controller medications, prior history of exacerbations, and high SABA use.\cite{60} However, in an ED setting, patients are often administered SABA inhalers for rapid relief of asthma exacerbations.\cite{77-79} As per the recent GINA guidelines, while discharging patients from acute care centers, ICS-containing controller medications should be prescribed. If the patients are on
Besides ED, there are other avenues of inappropriate SABA use. In the United Kingdom, an asthma-related outpatient visit to a general practitioner in the previous year was associated with a higher likelihood of inappropriate SABA use. On the other hand, visiting a specialist and the use of ICS in the previous year were associated with lower likelihood of inappropriate use of SABA. Some patient-related factors also contribute to the overuse of SABA and suboptimal use of ICS. A qualitative study in six countries in Europe and the United States showed that patients have a strong preference to SABA relievers because of their convenience of use prompted by symptoms and effectiveness in quickly alleviating asthma symptoms, allowing patients an uninterrupted routine. Conversely, patients do not perceive the benefits of ICS-based maintenance therapy, as they are not overtly apparent. Female patients having received pulmonary function tests and visited a specialist and those who are from higher socio-economic strata and have higher continuity of care were observed to be at lower risk of inappropriate SABA use.

Discouraging SABA overreliance requires a fundamental shift in the practice of recommending SABA alone for patients with milder forms of asthma to recommending as-needed low-dose ICS-formoterol or ICS controller medications with SABA. Collaborative efforts involving patients, caregivers, and policy makers are needed to encourage SABA alone-free clinical practice. The need is to identify practitioners and patients who are at risk of inappropriate use of SABA. Awareness programs to enhance understanding of the latest guideline recommendations among general physicians and ED care providers may help in eliminating SABA monotherapy prescription practice. The use of upcoming tools such as the SABA Reliance Questionnaire may help physicians to assess patients’ beliefs about SABA. It can also initiate a dialogue between patients and providers and may alleviate SABA monotherapy and overuse.

**Conclusion**

- We recommend adapting the GINA strategies...

...to tailor the treatment approach based on individual patient needs.

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**Figure 3: 1: Approach for Management of Asthma in Adults and Adolescents as per GINA Guidelines.**

ICS = Inhaled corticosteroid, IgE = Immunoglobulin E, IL = Interleukin, LABA = Long-acting bronchodilator, LAMA = Long-acting muscarinic antagonist, LTRA = Leukotriene receptor antagonist, OCS = Oral corticosteroid, SABA = Short-acting beta-agonist

**Figure 3: 2: Approach for Management of Asthma in Adults and Adolescents as per SINA Guidelines.**

ICS = Inhaled corticosteroid, IgE = Immunoglobulin E, IL = Interleukin, LABA = Long-acting bronchodilator, LAMA = Long-acting muscarinic antagonist, LTRA = Leukotriene receptor antagonist, SABA = Short-acting beta-agonist
at country and regional levels, which essentially involves the following algorithm

- Avoidance of overreliance on SABA alone for mild cases
- Step 1: Low-dose ICS-formoterol combination or adding low-dose ICS when SABA is used
- Step 2: Low-dose ICS for compliant patients, otherwise as-needed low-dose ICS
- Step 3: Low-dose maintenance ICS in combination with LABA either as MART approach when formoterol is used or as a regular proactive regular dosing with other combination
- Step 4: Further escalation to medium-to-high-dose ICS with LABA.

This calls for fundamental shift in prescription practices in ED as well as in general practice settings. Considering the adverse effects of SABA’s overreliance, the MEA experts recommend stringent regulations overprescription of SABA monotherapy. Over-the-counter availability of SABA should be discouraged and patients on SABA need to be monitored at regular intervals.

It is imperative to drive awareness of the adverse effects of SABA overreliance and exacerbation risks due to inadequate use of ICS among the treating physicians. Various patient-reported tools can help identify the overuse of SABA among patients with asthma.

In addition, patient awareness interventions should focus on differentiating in perceived symptomatic relief versus clinical control of asthma. Platforms such as social media, scientific societies, and patient advocacy groups could be utilized to educate the physicians, patients, and policymakers. Medical insurance coverage of asthma medications will help improve compliance. Furthermore, dissemination of simple tools for assessment and flowchart-based algorithms for management and referral of patients could play a key role in lowering the clinical and financial burden of asthma in the region.

Generation and publication of local epidemiological data and current treatment practices can provide further insights and help in the development of robust regional treatment guidelines. The current manuscript identified the challenges and presents consensus recommendations for specialists as well as general practitioners for the management of asthma in MEA.

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Conflicts of interest
There are no conflicts of interest.

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