### **COMMENTARY**



# Global Quality Statements on Reliever Use in Asthma in Adults and Children Older than 5 Years of Age

Alan G. Kaplan 👵 · Jaime Correia-de-Sousa · Andrew McIvor on behalf of the Global Policy Steering Group on Improving Asthma Outcomes

Received: November 11, 2020 / Accepted: January 8, 2021 / Published online: February 14, 2021 © The Author(s)

# **ABSTRACT**

Introduction: Widespread misuse of short-acting beta-agonists (SABAs) may contribute to asthmarelated morbidity and mortality. Recognizing this, the Global Initiative for Asthma neither recommends SABA monotherapy nor regards this formulation as a preferred reliever. Many health systems and healthcare professionals (HCPs) experience practical issues in implementing guidelines. Clear quality standards can drive improvements in asthma care and encourage implementation of global and national medical guidelines.

A. G. Kaplan (⊠) Family Physician Airways Group of Canada, Toronto, ON, Canada e-mail: for4kids@gmail.com

### A. G. Kaplan

Department of Family and Community Medicine, University of Toronto, Toronto, ON, Canada

### A. G. Kaplan

Primary Care Respiratory Research, Observational Pragmatic Research Institute, Singapore, Singapore

### J. Correia-de-Sousa

Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, ICVS/3B's - PT Government Associate Laboratory, Campus de Gualtar, Braga, Portugal

#### A. McIvor

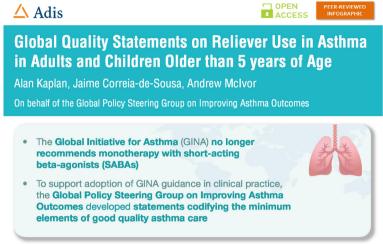
Department of Medicine, T2127, Firestone Institute for Respiratory Health, St Joseph's Healthcare, McMaster University, Hamilton, ON, Canada Methods: A steering group of global asthma experts came together between May and September 2019 to develop quality statements codifying the minimum elements of good quality asthma care. These statements were either evidence based (when robust evidence was available) or reflected a consensus based on clinical expertise and experience of the group.

Results: The quality statements (and associated essential criteria) developed emphasize key elements concerning (1) objective diagnosis specific to individual symptoms, (2) treatment appropriate to the long-term management of asthma as an inflammatory disease, consistent with evidence-based recommendations, (3) controlled dispensing of SABA canisters and monitoring to prevent overuse, (4) regular review of patients after treatment initiation or change, and (5) follow-up of patients in primary care after treatment for an exacerbation in a hospital or an emergency department.

*Conclusions*: The steering group proposes quality statements that national and local clinical groups can implement as quantitative quality standards that are appropriate to their local circumstances, including during the coronavirus disease 2019 (Covid-19) pandemic. By translating these statements into locally relevant quality standards, primary care physicians and HCPs can encourage optimal management and reduce ventable healthcare interactions. The evidencebased evolution of care encapsulated in these statements will further engender high-quality, patient-centered holistic management

addresses asthma as an inflammatory disease. In particular, the statements empower self-management by patients and encourage health-promoting

behaviors, which are essential to reduce exacerbations, the primary goal of asthma management. *Graphic abstract*:







The statements are aimed at empowering self-care and health-promoting behaviors that reduce exacerbations, potentially reducing healthcare system interactions during the Covid-19 pandemic and beyond

This infographic represents the opinions of Alan Kaplan, Jaime Correla-de-Sousa, and Andrew McIvor.
For a full list of declarations, including funding and author disclosure statements, please see the full text online.

**Keywords:** Asthma; Covid-19; Quality standards; Short-acting beta-agonists

# **DIGITAL FEATURES**

This article is published with digital features, including an infographic and summary slide, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.13537163.

## INTRODUCTION

Approximately 339 million people worldwide have asthma, which is the most common chronic respiratory disease [1, 2]. Global prevalence increased by an estimated 12.6% between 1990 and 2015 [1]. While asthma-related mortality has declined in recent decades, an estimated 400,000 people died of asthma in 2015 [1].

### SABA Use as a Marker of Disease Control

Underprescribing of preventer medications and excessive prescribing of short-acting beta-agonists (SABAs) has contributed to asthma-related mortality [3]. For instance, 39% of 189 patients who were prescribed SABAs when they died of asthma received more than 12 short-acting reliever inhalers during the previous year; 4% were prescribed more than 50 reliever inhalers [3]. A study of 93,604 patients with asthma associated high (6.5-12 canister equivalents annually) and excessive (more than 12 annually) SABA use with a higher incidence of asthma-related emergency department (ED) visits or urgent care, hospitalization, and oral corticosteroids use compared with no SABA use [**4**].

All patients with asthma are at risk of exacerbations [5], and SABAs are overused at all stages of severity [6]. A study of 1.06 million patients with asthma from five European countries reported that the prevalence of SABA overuse (three or more canisters per year) ranged from 9% in Italy to 38% in the UK. Outside the UK, rates of SABA overuse were similar in

mild (9%–32%) and moderate-to-severe asthma (8%–31%). In the UK, SABA overuse was more common in moderate-to-severe asthma (58%) than in mild asthma (27%) [6, 7].

Patients use SABAs to alleviate symptoms, without adequate inhaled corticosteroids (ICS) usage [8, 9]. Several factors may contribute to this counterintuitive behavior. For instance, until recently, the Global Initiative for Asthma (GINA) recommended using a SABA bronchodilator alone at step 1 [8]. Patients often overestimate asthma control [8, 10, 11]. A survey of 2003 patients with asthma from four European countries and Canada found that 51% of patients considered their asthma well controlled, despite three or four exacerbations in the previous year. Moreover, 52% and 43% of patients considered their asthma well controlled if they had two urgent doctor visits and one ED visit each year, respectively [10]. Discordance between patients and healthcare professionals (HCPs) could contribute to overreliance on SABAs and underuse of ICS. Use of validated tools to assess control, such as the GINA Assessment of Symptom Control, can increase recognition and appreciation that asthma is inadequately controlled [8].

# Fundamental Change in Recommendations

In April 2019, GINA published recommendations that some authors regard as "the most fundamental change in asthma management in 30 years" [12]. GINA no longer recommends SABA monotherapy. To reduce the risk of serious exacerbations and control symptoms, GINA recommends that adults and adolescents with asthma use ICS plus formoterol in a single inhaler, instead of SABA, to alleviate symptoms in mild asthma while simultaneously reducing underlying inflammation. The next step recommends regular daily ICS-containing treatment, but adherence is often challenging [5, 9, 13–17].

In 2017, leading respiratory physicians, academics, and patient group representatives were invited to be part of the Global Policy Steering Group on Improving Asthma Outcomes,

organized and funded by AstraZeneca, to develop initiatives to address inappropriate SABA use and improve asthma management. Quality standards, such as those from the UK, Canada, and Australia [18–20], describe elements of optimal care.

Herein, we describe statements developed by the steering group, which codify the minimum elements of good quality asthma care, in order to encourage national and local clinical groups to reinforce or develop quantitative quality standards appropriate to local circumstances. These statements, aimed at all stakeholders involved in asthma management and treatment, could help address marked differences in the quality of asthma care [2, 21–23].

Coronavirus disease-2019 (Covid-19) emerged during this document's development. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) probably triggers exacerbations, and asthma may be associated with an increased risk of severe disease, hospital admissions, and mortality from Covid-19 [24-26]. ICS, as monotherapy and combined with longacting beta-agonists (LABAs), protect against exacerbations induced by viruses and may, therefore, be beneficial in Covid-19 [27, 28]. Our suggestions are aimed at improving community care, which will reduce avoidable hospital admissions for asthma, and support other recent statements regarding Covid-19 in people with asthma [25, 26, 29]. Many suggestions can be delivered using telemedicine, which can itself improve disease control and quality of life in adults with asthma [30].

## **METHODS**

The quality statements were discussed during a virtual meeting in May 2019. Between May and September 2019, seven members of the steering group from five countries participated in online discussions to reach consensus. Draft statements were presented at the European Respiratory Society Congress in September 2019 and were revised further in 2020 on the basis of additional evidence (including Covid-19). A subgroup finalized statements for diagnosis, prescribing and dispensing, regular asthma

reviews, and post-exacerbation care. Where robust evidence was available, the statements are evidence based. Otherwise, the statements reflect a consensus based on clinical expertise and experience and are aimed at patients, advocacy groups, clinicians, healthcare systems, and payers. This article is based on consensus of a steering group and does not contain any studies with human participants or animals performed by any of the authors.

# **RESULTS**

The finalized quality statements and essential criteria associated with them are summarized in Table 1.

Quality Statement 1: People Suspected of Having Asthma Are Identified and Receive an Objective Diagnosis Specific to Their Individual Symptoms

There is no definitive gold-standard diagnostic test for asthma [31], and symptoms are non-specific [32]. Therefore, asthma is commonly misdiagnosed, especially without objective testing, such as spirometry, which may lead to unnecessary treatment [31, 33, 34]. Underdiagnosis delays appropriate treatment, which increases the likelihood of symptoms, serious exacerbations, and, over time, airway remodeling [31].

GINA includes a diagnostic pathway and criteria that are suitable for most settings [5]. Objective tests can inform the diagnostic pathway. Bronchodilator reversibility and bronchial provocation tests can offer evidence of variable airflow limitation [5]. Spirometry can aid in the differentiation of asthma and other conditions, such as chronic obstructive pulmonary disease (COPD) [33]. Fractional exhaled nitric oxide may predict response to ICS among patients with non-specific respiratory symptoms [35]. Objective tests may not be readily available in primary care [31].

Patients presenting with a history of symptoms indicative of asthma (e.g., wheeze, dyspnea, chest tightness, and cough) [5] require further investigation. Clinicians should be

aware that some common Covid-19 symptoms, particularly dry cough and dyspnea, are characteristic of acute asthma exacerbations and allergic rhinitis [24, 26, 27]. To facilitate social distancing, clinicians should consider telemedicine diagnostic consultations during the Covid-19 pandemic [26, 29, 30, 36], although this will hinder use of objective measures.

Essential criterion: the clinical assessment and investigation of people with indicative symptoms of asthma should focus on making a differential diagnosis.

A primary care physician or respiratory specialist trained in asthma management should make the diagnosis using, where possible (because of social distancing), objective measures. Table 2 summarizes the minimum data set that the subgroup believes is necessary to inform the differential diagnosis. HCPs could consider further testing to determine the phenotype (e.g., eosinophilic-high type 2 inflammation and childhood-onset allergic asthma) or identify triggers (e.g., allergens, air pollution, and occupational exposure) that may be amenable to intervention or behavioral modification [32, 37].

Quality Statement 2: Newly Diagnosed Patients with Asthma Are Treated with Pharmacological and Nonpharmacological Options that Are Appropriate to the Long-Term Management of Asthma as an Inflammatory Disease, In Line with the Latest Evidence-Based Guidelines

Essential criterion: treatment decisions for patients should be based on the latest evidence-based guidelines.

While the immunopathogenesis of asthma is heterogeneous [32], in many patients, airway eosinophilic inflammation and remodeling are the hallmark pathological features [38]. Therefore, asthma treatment should aim at preventing and resolving the underlying inflammation to reduce the risk of serious exacerbations and attempt to prevent long-term airway changes and control symptoms. Adults and adolescents with asthma should use ICS in line with the

latest evidence-based guidelines [5, 12]. ICS reduce the risk of exacerbations, including those requiring hospitalization that are potentially life-threatening, and probably also those associated with SARS-CoV-2 [27, 39–41]. HCPs should consider individualized non-pharmacological options, such as smoking cessation, breathing activities, and practical strategies, to avoid allergens and other triggers [5].

Essential criterion: no patient should be prescribed three or more SABA inhalers per year without undergoing an asthma review with their primary care physician, specialist nurse, or respiratory specialist.

Excessive SABA prescribing is a measure of poor asthma control and an avoidable cause of asthma-related mortality, ED visits or urgent care, hospitalization, and oral corticosteroid use [3–5, 42]. GINA suggests that more than one 200-dose SABA canister a month may be a marker of increased risk of asthma-related mortality [5]. The subgroup agreed that all patients should have an asthma review arranged when their third SABA in 1 year is dispensed.

# Quality Statement 3: Dispensing of SABA Canisters Should Be Controlled and Closely Monitored to Mitigate Against Overuse

Poor adherence to ICS is common (22%–63%) and is associated with adverse outcomes [9, 13–17]. One study found that only 20% of patients used their inhaler correctly at the correct time [16]. Several factors are associated with poor adherence, including young age and adolescence, low educational level, mild asthma, and poor communication with HCPs [13, 17]. Mean adherence to daily controller in people with asthma or COPD increased by 14.5% during the Covid-19 pandemic from 53.7% in the first 7 days of January 2020 to 61.5% during the last 7 days of March 2020 [43].

Adherence and inhaler technique should be assessed at each urgent and routine review (statement 4), with the inhaler choice and training (including demonstrations) individualized for each patient [44]. Reviewing inhaler technique, avoiding (where possible) asthma

Table 1 Summary of quality statements and essential criteria

### Quality statement

# People suspected of having asthma are identified and receive an objective diagnosis specific to their individual symptoms

Newly diagnosed patients with asthma are treated with pharmacological and non-pharmacological options that are appropriate to the long-term management of asthma as an inflammatory disease, in line with the latest evidence-based guidelines

Dispensing of SABA canisters should be controlled and closely monitored to mitigate against overuse

Patients with asthma should be reviewed 3 months after starting or changing treatment. Patients established on treatment should be reviewed regularly (e.g., at least every 12 months)

Patients treated for an asthma exacerbation in hospital or ED should receive an urgent dedicated follow-up by a trained primary care HCP

### **Essential criterion**

The clinical assessment and investigation of people with indicative symptoms of asthma should focus on making a differential diagnosis

Treatment decisions for patients should be based on the latest evidence-based guidelines

No patient should be prescribed three or more SABA inhalers per year without undergoing an asthma review with their primary care physician, specialist nurse, or respiratory specialist

SABAs should be available only when a patient has a valid prescription or a clinical emergency, such as an exacerbation, and should not be prescribed alone. An asthma review (reassessment) should be performed when three or more SABA inhalers are used in 1 year

Any patient collecting three or more SABA inhalers a year from a pharmacist should be referred to their primary care physician, specialist nurse, or respiratory specialist for an asthma review. Where possible, the pharmacist should be informed of any changes to the regimen

All decisions related to ongoing management of patients with asthma should be integrated within a PAAP

All patients should be reviewed in primary care within 2–7 working days of an exacerbation

Patients should be checked by a trained primary care professional or respiratory specialist to ensure that their treatment maintains lung function and prevents exacerbations and to understand why their asthma deteriorated

After an exacerbation, patients should receive, as a minimum, a review of their inhaler technique and current usage of controllers/relievers as well as assessing the need for stepped-up treatment

Each asthma exacerbation should be followed up in primary care after discharge to explore the possible reasons for the attack and to give advice about reducing the risk of exacerbations

ED emergency department, HCP healthcare professional, PAAP personal asthma action plan, SABA short-acting beta-agonist

triggers, ensuring social distancing, and regular handwashing help prevent exacerbations during the Covid-19 pandemic [24].

The high rate of poor adherence to ICS suggests that many patients with asthma rely on SABA monotherapy as their sole treatment [45]. In some parts of the world, such as Australia, SABAs can be bought from community

pharmacists without a prescription [46], which potentially hampers attempts to use ICS alongside bronchodilators to treat the deterioration in asthma control that typically precedes a serious exacerbation.

SABAs may be needed as rescue medication in patients who experience difficulties using a dry-powder inhaler during an acute attack or for

Table 2 Minimum data set needed to inform the differential diagnosis of asthma

When considering a differential diagnosis of asthma, HCPs should record the following in the patient's notes and share with the multidisciplinary team:

Any history of symptoms indicative of asthma

Any history of hospitalization or unscheduled visits to primary or secondary care or both because of acute asthma symptoms

Medication history (including drugs prescribed or bought over the counter for concurrent diseases)

Any family history of asthma, atopy, or allergy

Exposure to smoking (passive and active) and other potential environmental triggers

Lung function tests, such as spirometry (if available), and/or variability in peak expiratory flow

HCP healthcare professional

use with a spacer in an emergency. However, while SABAs alleviate symptoms, they may mask ongoing airway inflammation and their continued use may compromise ICS adherence and possibly promote inflammation when taken regularly by patients not using ICS [9].

The SABA use IN Asthma (SABINA) studies and analysis from the Symbicort Given as Needed in Mild Asthma (SYGMA) 1 trial provide further evidence that overuse of SABA is associated with a significant increase in risk of exacerbations and mortality, and increased healthcare utilization [7, 47, 48]. Elimination of SABA use that is unaccompanied by ICS use is thus crucial to improve asthma outcomes. However, barriers to the complete elimination of SABA reliever use include ingrained SABA reliance behavior among patients and real or perceived affordability of the alternative reliever ICS-formoterol. Additionally, evidence for use of the anti-inflammatory reliever ICS-formoterol in an acute asthma attack setting is limited [49]. The subgroup, therefore, recommends that SABA dispensing should be controlled, closely monitored to identify overuse (three or more canisters per year) as a marker of poor control, and always combined with ICS

[5, 9]. To aid implementation, the subgroup agreed upon two essential criteria.

Essential criterion: SABAs should be available only when a patient has a valid prescription or a clinical emergency, such as an exacerbation, and should not be prescribed alone. An asthma review (reassessment) should be performed when three or more SABA inhalers are used in 1 year.

Essential criterion: any patient collecting three or more SABA inhalers a year from a pharmacist should be referred to their primary care physician, specialist nurse, or respiratory specialist for an asthma review. Where possible, the pharmacist should be informed of any changes to the regimen.

Quality Statement 4: Patients with Asthma Should Be Reviewed at Least 3 Months After Starting or Changing Treatment. Patients Established on Treatment Should Be Reviewed Regularly (e.g., at Least Every 12 Months)

Patients with asthma experience variable symptoms and airflow limitations that may resolve spontaneously or following treatment. Some patients may be asymptomatic for several weeks or months, but most experience episodic symptomatic worsening, serious exacerbations, or both [5]. Regular monitoring of symptoms and peak flow rate helps identify deteriorating lung function preceding exacerbations. An exacerbation represents, fundamentally, a failure of management. Therefore, several circumstances should trigger an urgent asthma review to determine the reasons for suboptimal control (Table 3; Fig. 1).

HCPs should review patients (using telemedicine where possible during the Covid-19 pandemic) and their personal asthma action plan (PAAP) within 48 h of the exacerbation, but definitely within 7 working days (statement 5). The timing depends on exacerbation severity: the more serious the exacerbation, the more urgent the review.

The subgroup suggests a review 3 months after switching or starting treatment. Patients and, where appropriate, parents and carers should contact their primary care physician, specialist nurse, or respiratory specialist as soon

as possible if control deteriorates or if the patient experiences possible adverse events. HCPs could consider measuring lung function with either peak flow rate or spirometry before changing treatment, 3–6 months later, and then periodically as appropriate [5]. In light of Covid-19 safety protocols, asthma control questionnaires and home peak flow measurements may need to be reconsidered to minimize risk to HCPs and patients.

The subgroup advocates routine review of all patients with asthma at least once a year. The routine review (using telemedicine where possible during the pandemic) should encompass education, training, and support, including comorbidity review and discussion on adherence, trigger advice, smoking status, and inhaler technique. When asthma is stable, HCPs could consider stepping down treatment in line with the GINA guidelines [5]. Patients and, where appropriate, parents and carers should agree on a PAAP with their primary care physician, specialist nurse, or respiratory specialist, which should be reviewed and updated at each urgent or routine review. Table 4 summarizes the minimum elements HCPs should consider during a routine review.

Essential criterion: all decisions related to ongoing management of patients with asthma should be integrated within a PAAP.

The PAAP should provide information about asthma and its treatment in a simple and clear format that is available digitally. The level of detail should be appropriate to the patient's, parent's, or carer's health literacy and life goals. HCPs should review the PAAP during each urgent and routine review with the patient or, where appropriate, the parent or carer and agree on any changes. PAAPs should encompass benefits and side effects of the agreed medicines, known triggers and practical avoidance strategies, when to intensify treatment and seek medical attention, and the implications of different management approaches following an exacerbation and during chronic maintenance therapy (statement 5). The multidisciplinary team should be able to access the PAAP as a patient-held hard copy or electronically.

Quality Statement 5: Patients Treated for an Asthma Exacerbation in Hospital or ED Should Receive an Urgent Dedicated Follow-Up by a Trained Primary Care HCP

An exacerbation represents, fundamentally, a failure of management. The subgroup agreed, therefore, that an exacerbation should trigger an urgent asthma review (using telemedicine where possible during the Covid-19 pandemic) to determine whether the exacerbation is resolving, optimize care, and identify and manage modifiable risk factors (e.g., poor adherence, smoking and other types of air pollution, seasonal allergens). This review, aimed at preventing further exacerbations, should ideally take place within 48 h of the exacerbation (especially if severe) but definitely within 7 working days.

To inform primary care review, the hospital or ED should provide a structured report summarizing the exacerbation's characteristics and any treatment. If the hospital or ED prescribed oral corticosteroids, HCPs should provide clear written instructions regarding the dose and treatment duration. The subgroup agreed upon four essential criteria to support this statement.

Essential criterion: all patients should be reviewed in primary care within 2–7 working days of an exacerbation.

Essential criterion: patients should be checked by a trained primary care professional or respiratory specialist to ensure that their treatment maintains lung function and prevents exacerbations and to understand why their asthma deteriorated.

Follow-up could include a review of current medications, previous exacerbations and comorbidities such as rhinitis, chronic rhinosinusitis, gastroesophageal reflux, obstructive sleep apnea, vocal cord dysfunction, obesity, dysfunctional breathing, anxiety, and depression [50]. One study found that 92% of patients with difficult-to-control asthma had at least one comorbidity [51]. Covid-19 and social isolation may cause psychosocial issues, including anxiety, that may contribute to the presentation [26].

Essential criterion: after an exacerbation, patients should receive, as a minimum, a review of their inhaler technique and current usage of

Table 3 Circumstances that should trigger an urgent asthma review

A patient's asthma symptoms worsen beyond the normal pattern of day-to-day variation despite appropriate use of ICS, LABAs, and other preventer therapies

A patient experiences an asthma exacerbation, especially if the deterioration involves an ED visit or urgent care, hospitalization, nocturnal awakening, difficulty in speaking, or marked impairment in activities of daily living

A patient has not had a routine review in the last 12 months

A patient has been prescribed more than one SABA inhaler in the last 4 months or three or more canisters during the previous year

A patient has been prescribed a new course of oral corticosteroids (e.g., in secondary care)

ED emergency department, ICS inhaled corticosteroids, LABA long-acting beta-agonist, SABA short-acting beta-agonist

controller and reliever inhalers, with an assessment of the need for stepped-up treatment.

The PAAP should include changes to treatment and clear guidance about using controllers and relievers. HCPs should be especially vigilant in "high-risk" patients (e.g., another asthma exacerbation in the previous year, socioeconomic deprivation, poor adherence, incorrect inhaler technique, low lung function, smoking, and blood eosinophilia) [5].

Essential criterion: each asthma exacerbation should be followed up in primary care after discharge to explore the possible reasons for the attack and to give advice about reducing the risk of exacerbations.

# DISCUSSION

Healthcare systems worldwide face different issues when they attempt to optimize asthma management, which Covid-19 may exacerbate. These statements codify the minimum elements

of good quality asthma care that national and local clinical groups can use to develop quantified standards appropriate to each setting, which encourages ownership of the standards. The subgroup hopes that each localized and quantified quality standard will be ambitious yet realistic, practical, and implementable.

Patients often regard asthma as effectively controlled when HCPs would consider there is considerable room for improvement [8, 10, 11]. While the negative effects of SABA over-reliance on patients and health systems are well characterized, entrenched beliefs about necessity and concerns about treatment [52–54] and a psychological reliance on SABA persist [55, 56].

The statements express the necessity of ICS treatment and avoidance of SABA overuse. A meta-analysis of 94 studies of long-term conditions, including asthma, reported that stronger perceptions of treatment necessity (odds ratio [OR] 1.74; 95% CI 1.57, 1.93) and fewer concerns (OR 0.50; 95% CI 0.45, 0.56) were significantly (p < 0.0001) associated with higher adherence [52]. HCPs often experience practical issues in implementing current guidelines [34, 57, 58], including hindrance due to inertia in service structure. These factors reinforce the behaviors that lead to SABA overuse.

Some caveats should be considered. While GINA recommends treatment with daily lowdose ICS or as-needed ICS-formoterol, patients with non-eosinophilic asthma may not respond to ICS therapy [59]. However, recent evidence indicates that as-needed use of low-dose ICS-formoterol in patients with mild asthma reduces the risk of exacerbations irrespective of baseline blood eosinophil count [60]. The subgroup believes these contradictions reiterate that a firm diagnosis is a crucial first step to deciding treatment. Secondly, the evidence base for use of ICS in children younger than 12 years with mild asthma is limited. In a randomized controlled trial of children and adolescents (5–18 years old) with mild asthma, compared with SABA use alone, SABA reliever accompanied by as-needed ICS was more effective at reducing exacerbations [61]. More recently, in a pragmatic trial conducted in African-American children (6-17 years old) in a primary care setting, symptom-based use of ICS and SABA

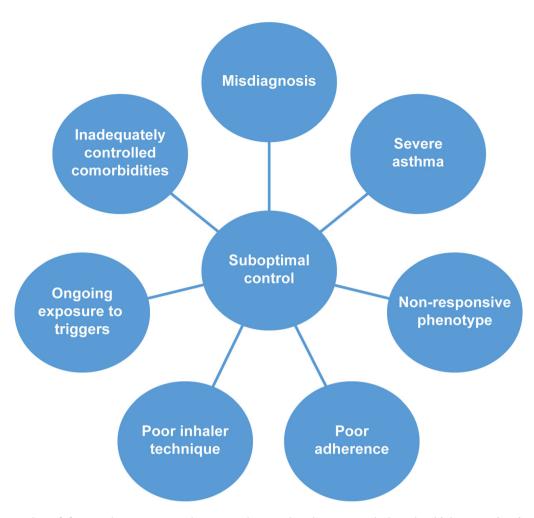


Fig. 1 Examples of factors that may contribute to suboptimal asthma control that should be considered in a post-exacerbation review

reliever resulted in similar asthma control, but lower overall ICS exposure compared with guideline-based treatment of maintenance ICS [62]. Nonetheless, despite gaps in evidence in the pediatric asthma population, GINA recommends use of a dose of ICS with each dose of asneeded SABA as a possible treatment in children with mild asthma based on the inflammatory nature of the disease. While these quality statements are based on clinical experience and evidence-based treatment guidelines, evolving research suggests that other parameters, such as periodic sleep evaluation in patients with asthma [63, 64], may potentially be useful for asthma management. However, further clinical

evidence is needed to fully understand the utility of such procedures.

Overall, these quality statements underscore opportunities to reduce exacerbations and costs associated with healthcare utilization, improve overall asthma control and the quality of life of patients with asthma. While key to these improvements will be changing reliever use behavior in patients, improving other aspects of treatment such as accuracy of diagnosis, inhaler technique, and comorbidity management are all needed to ensure improved clinical outcomes. By translating these statements into locally relevant quantitative quality standards, HCPs (using telemedicine where possible) can encourage health-promoting behaviors.

1392 Adv Ther (2021) 38:1382–1396

 Table 4
 Minimum elements that healthcare professionals

 should consider during each routine review

Record significant asthma-related medical events and risk factors, including exacerbations, symptoms, nocturnal awakenings, and comorbidities

Review medications for asthma (e.g., number of canisters and frequency of use of SABAs, LABAs, and ICS), and comorbidities and concurrent medications that might influence control (e.g., non-steroidal anti-inflammatory drugs, including those purchased over the counter); sources of information include self-report, prescriptions issued, and drugs dispensed by a pharmacist

Assess adherence based on patient, parent, or carer report, and patterns of drugs dispensed (e.g., medication possession ratio or proportion of days covered)

Assess barriers and facilitators to appropriate use of ICS, including cost, understanding of asthma pathogenesis and treatment, and concerns about adverse events

Assess inhaler technique against a device-specific checklist

Confirm patient and household smoking habits and offer smoking cessation services and support when relevant

Assess potential allergens, occupational agents, and environmental or occupational factors that may trigger asthma symptoms and exacerbations; where practical, discuss avoidance strategies

Review comorbidities and use of other medications that may jeopardize a patient's asthma control

Provide or review an agreed upon PAAP to help patients recognize when their asthma is poorly controlled despite adequate compliance and inhaler technique

ICS inhaled corticosteroids, LABA long-acting beta-agonist, PAAP personal asthma action plan, SABA short-acting beta-agonist

including appropriate ICS use and patient-centered holistic management that addresses asthma as an inflammatory disease. The statements empower self-care and health-promoting behaviors that reduce exacerbations, which is the primary goal of asthma management, and reduce healthcare system interactions during the Covid-19 pandemic and beyond.

### **ACKNOWLEDGEMENTS**

This article is presented on behalf of the Global Policy Steering Group on Improving Asthma Outcomes. The steering group was formed in 2018 and comprises leading healthcare professionals, patient group representatives, and acarepresentatives demic in the asthma community, brought together by AstraZeneca (no compensation was involved) to advance the debate and action on national-level initiatives that improve asthma outcomes and to provide international leadership, clarity, and momentum behind best practice policies and their implementation. Members of this steering group are as follows: Jaime Correia de Sousa, Community Health, Life and Health Sciences Research Institute, School of Medicine, University of Minho, Braga, Portugal and International Primary Care Respiratory Group; Alvaro A. Cruz, ProAR Foundation and Federal University of Bahia, Brazil; John L Faul, Connolly Hospital Blanchardstown, Ireland; Santiago Quirce, Spanish Society of Allergology Clinical Immunology, Hospital La Paz Institute for Health Research (IdiPAZ), Madrid, Spain; Alan Kaplan, University of Toronto, Toronto, Ontario, Canada, Family Physician Airways Group of Canada and International Primary Care Respiratory Group and the Observational and Pragmatic Research Institute in Singapore; Peter Kardos, Centre for Allergy, Respiratory and Sleep Medicine at Red Cross Maingau Hospital, Frankfurt, Germany; Mark L Levy, Locum general practitioner, London, UK; Vince Mak, Imperial College Healthcare NHS Trust, London, UK; Guy B. Marks, South Western Sydney

Clinical School, University of New South Wales, Sydney, Australia; Andrew McIvor, Firestone Institute for Respiratory Health, St. Joseph's Healthcare and McMaster University, Hamilton, Ontario, Canada; Otto Spranger, European Lung Foundation and Global Allergy and Asthma Patient Platform, Vienna, Austria; Luigi Visintin, European Lung Foundation and FederASMA e Allergie ONLUS, Prato, Italy.

*Funding.* AstraZeneca funded the journal's Rapid Service Fees for publication of this manuscript and the open access fees.

Medical Writing, Editorial, and Other Assistance. Mark Greener, on behalf of ENGINE MHP, and Michelle Rebello, of CACTUS Life Sciences provided medical writing assistance, funded by AstraZeneca. ENGINE MHP provided a 'secretariat' role to the Steering Group, funded by AstraZeneca.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

**Disclosures.** Alan G. Kaplan is a member of an advisory board or speaker's bureau for AstraZeneca, Behring, Boehringer Ingelheim, Covis. Grifols. GlaxoSmithKline. Pfizer. Purdue. Novartis, Novo Nordisk, Sanofi, Talecris, and Trudell. Jaime Correia-de-Sousa participated in advisory boards with Boehringer Ingelheim, GlaxoSmithKline, and AstraZeneca, received grants and personal fees from GlaxoSmithKline, grants from AstraZeneca, and speaker's fees from Mundipharma, outside the submitted work. Andrew McIvor has received honoraria for attending advisory boards, providing continuing medical education, and participating in clinical trials as an investigator AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Pfizer, Merck, and Novartis. All authors are part of the Global Policy Steering Group on Improving Asthma Outcomes Steering Group which was brought together by AstraZeneca (no compensation was involved) to

advance the debate and action on national-level initiatives that improve asthma outcomes and to provide international leadership, clarity, and momentum behind best practice policies and their implementation. While AstraZeneca paid for medical writing support, the final decision for content inclusion and submission of the manuscript rested with authors.

Compliance with Ethics Guidelines. This article is based on consensus of a steering group and does not contain any studies with human participants or animals performed by any of the authors.

**Data** Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Open Access. This article is licensed under a Creative Commons Attribution-Non-Commercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view of this licence, visit http:// creativecommons.org/licenses/by-nc/4.0/.

## REFERENCES

Soriano J, Abajobir A, Abate K, et al. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Respir Med. 2017;5:691–706.

- Global Asthma Network. The global asthma report. 2018. http://www.globalasthmareport.org/Global% 20Asthma%20Report%202018.pdf. Accessed April 2020.
- Royal College of Physicians. Why asthma still kills: the National Review of Asthma Deaths (NRAD) confidential enquiry report. 2014. http://www.rcplondon.ac.uk/projects/outputs/why-asthmastill-kills. Accessed April 2020.
- Silver HS, Blanchette CM, Kamble S, et al. Relationship between short-acting β2-adrenergic agonist use and healthcare costs. Am J Manag Care. 2011;17:19–27.
- Global Initiative for Asthma. Global strategy for asthma management and prevention. 2020. http:// ginasthma.org/gina-reports. Accessed April 2020.
- Janson C, Menzies-Gow A, Nan C, et al. SABINA: an overview of short-acting β2-agonist use in asthma in European countries. Adv Ther. 2020;37:1124–35.
- Bloom CI, Cabrera C, Arnetorp S, et al. Asthma-related health outcomes associated with short-acting β2-agonist inhaler use: an observational UK study as part of the SABINA global program. Adv Ther. 2020;37:4190–208.
- 8. O'Byrne PM, Jenkins C, Bateman ED. The paradoxes of asthma management: time for a new approach? Eur Respir J. 2017;50:1701103.
- 9. Martin MJ, Harrison TW. Is it time to move away from short-acting beta-agonists in asthma management? Eur Respir J. 2019;53:1802223.
- Sastre J, Fabbri LM, Price D, et al. Insights, attitudes, and perceptions about asthma and its treatment: a multinational survey of patients from Europe and Canada. World Allergy Organ J. 2016;9:13.
- 11. Price D, Fletcher M, van der Molen T. Asthma control and management in 8,000 European patients: the REcognise Asthma and LInk to Symptoms and Experience (REALISE) survey. NPJ Prim Care Respir Med. 2014;24:14009.
- Reddel HK, FitzGerald JM, Bateman ED, et al. GINA 2019: a fundamental change in asthma management. Eur Respir J. 2019;53:1901046.
- 13. Bårnes CB, Ulrik CS. Asthma and adherence to inhaled corticosteroids: current status and future perspectives. Respir Care. 2015;60:455–68.
- Williams LK, Pladevall M, Xi H, et al. Relationship between adherence to inhaled corticosteroids and poor outcomes among adults with asthma. J Allergy Clin Immunol. 2004;114:1288–93.

- 15. Dima AL, van Ganse E, Stadler G, et al. Does adherence to inhaled corticosteroids predict asthma-related outcomes over time? A cohort study. Eur Respir J. 2019;54:1900901.
- 16. Sulaiman I, Seheult J, MacHale E, et al. Irregular and ineffective: a quantitative observational study of the time and technique of inhaler use. J Allergy Clin Immunol. 2016;4:900–9.e2.
- 17. Kaplan A, Price D. Treatment adherence in adolescents with asthma. J Asthma Allergy. 2020;13: 39–49.
- 18. National Institute for Health and Care Excellence. Asthma quality standard [QS25]. 2018. http://www.nice.org.uk/guidance/qs25. Accessed April 2020.
- 19. Health Quality Ontario. Asthma in children and adolescents. 2020. http://www.hqontario.ca/eviden ce-to-improve-care/quality-standards/view-all-qual ity-standards/asthma-in-children-and-adolescents. Accessed April 2020.
- Department of Health Western Australia. Asthma model of care. 2012. http://www.health.wa.gov.au/ ~/media/Files/Corporate/general%20documents/ Health%20Networks/Respiratory/Asthma-Modelof-Care.pdf.
- 21. Price C, Agarwal G, Chan D, et al. Large care gaps in primary care management of asthma: a longitudinal practice audit. BMJ Open. 2019;9:e022506.
- 22. Levy ML, Garnett F, Kuku A, et al. A review of asthma care in 50 general practices in Bedfordshire, United Kingdom. NPJ Prim Care Respir Med. 2018;28:29.
- 23. Sheikh A, Steiner MFC, Cezard G, et al. Ethnic variations in asthma hospital admission, readmission and death: a retrospective, national cohort study of 4.62 million people in Scotland. BMC Med. 2016;14:3.
- 24. Abrams EM, 't Jong GW, Yang CL. Asthma and COVID-19. CMAJ. 2020;192:E551.
- 25. Licskai C, Yang CL, Ducharme FM, et al. Key highlights from the Canadian Thoracic Society's position statement on the optimization of asthma management during the COVID-19 pandemic. Chest. 2020;158:1335–7.
- Beaney T, Salman D, Samee T, et al. Assessment and management of adults with asthma during the covid-19 pandemic. BMJ. 2020;369:m2092.
- Scadding GK, Hellings PW, Bachert C, et al. Allergic respiratory disease care in the COVID-19 era: a EUFOREA statement. World Allergy Organ J. 2020;13:100124.

- 28. Reddel HK, Jenkins C, Quirce S, et al. Effect of different asthma treatments on risk of cold-related exacerbations. Eur Respir J. 2011;38:584–93.
- Levin M, Morais-Almeida M, Ansotegui IJ, et al. Acute asthma management during SARS-CoV2pandemic 2020. World Allergy Organ J. 2020;13: 100125.
- 30. Chongmelaxme B, Lee S, Dhippayom T, et al. The effects of telemedicine on asthma control and patients' quality of life in adults: a systematic review and meta-analysis. J Allergy Clin Immunol Pract. 2019;7(199–216):e11.
- 31. Kavanagh J, Jackson DJ, Kent BD. Over- and underdiagnosis in asthma. Breathe. 2019;15:e20–7.
- 32. Papi A, Brightling C, Pedersen SE, et al. Asthma. Lancet. 2018;391:783–800.
- 33. Heffler E, Crimi C, Mancuso S, et al. Misdiagnosis of asthma and COPD and underuse of spirometry in primary care unselected patients. Respir Med. 2018;142:48–52.
- 34. Gagné ME, Boulet L-P. Implementation of asthma clinical practice guidelines in primary care: a cross-sectional study based on the Knowledge-to-Action Cycle. J Asthma. 2018;55:310–7.
- 35. Price DB, Buhl R, Chan A, et al. Fractional exhaled nitric oxide as a predictor of response to inhaled corticosteroids in patients with non-specific respiratory symptoms and insignificant bronchodilator reversibility: a randomised controlled trial. Lancet Respir Med. 2018;6:29–39.
- 36. Rabuñal R, Suarez-Gil R, Golpe R, et al. Usefulness of a telemedicine tool TELEA in the management of the COVID-19 pandemic. Telemed J E Health. 2020;26:1332–5.
- 37. Cai Y, Zijlema WL, Doiron D, et al. Ambient air pollution, traffic noise and adult asthma prevalence: a BioSHaRE approach. Eur Respir J. 2017;49: 1502127.
- 38. Saglani S, Lloyd CM. Novel concepts in airway inflammation and remodelling in asthma. Eur Respir J. 2015;46:1796–804.
- Loymans RJB, Gemperli A, Cohen J, et al. Comparative effectiveness of long term drug treatment strategies to prevent asthma exacerbations: network meta-analysis. BMJ. 2014;348:g3009.
- 40. Suissa S, Ernst P, Benayoun S, et al. Low-dose inhaled corticosteroids and the prevention of death from asthma. N Engl J Med. 2000;343:332–6.

- 41. Suissa S, Ernst P, Kezouh A. Regular use of inhaled corticosteroids and the long term prevention of hospitalisation for asthma. Thorax. 2002;57:880–4.
- 42. Kaplan A. SABA overuse. J Lung Pulm Respir Res. 2019;6:101–2.
- 43. Kaye L, Theye B, Smeenk I, et al. Changes in medication adherence among patients with asthma and COPD during the COVID-19 pandemic. J Allergy Clin Immunol Pract. 2020;8:2384–5.
- 44. Kaplan A, Price D. Matching inhaler devices with patients: the role of the primary care physician. Can Respir J. 2018;2018:9473051.
- 45. Kaplan A, Mitchell P, Cave A, et al. Effective asthma management: is it time to let the AIR out of SABA? J Clin Med. 2020;9:921.
- Azzi EA, Kritikos V, Peters MJ, et al. Understanding reliever overuse in patients purchasing over-thecounter short-acting beta<sub>2</sub> agonists: an Australian community pharmacy-based survey. BMJ Open. 2019;9:e028995.
- 47. Nwaru BI, Ekström M, Hasvold P, et al. Overuse of short-acting β2-agonists in asthma is associated with increased risk of exacerbation and mortality: a nationwide cohort study of the global SABINA programme. Eur Respir J. 2020;55:1901872.
- 48. O'Byrne PM, FitzGerald JM, Bateman ED, et al. Effect of a single day of increased as-needed budesonide–formoterol use on short-term risk of severe exacerbations in patients with mild asthma: a post-hoc analysis of the SYGMA 1 study. Lancet Respir Med. 2020;S2213-2600(20)30416–21.
- 49. Balanag VM, Yunus F, Yang PC, et al. Efficacy and safety of budesonide/formoterol compared with salbutamol in the treatment of acute asthma. Pulm Pharmacol Ther. 2006;19:139–47.
- 50. Tay TR, Hew M. Comorbid, "treatable traits" in difficult asthma: current evidence and clinical evaluation. Allergy. 2018;73:1369–82.
- 51. Hekking P-P, Amelink M, Wener RR, et al. Comorbidities in difficult-to-control asthma. J Allergy Clin Immunol Pract. 2018;6:108–13.
- 52. Horne R, Chapman SCE, Parham R, et al. Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: a meta-analytic review of the necessity-concerns framework. PLoS One. 2013;8:e80633.
- 53. Østrem A, Horne R. Reducing asthma attacks: consider patients' beliefs. NPJ Prim Care Respir Med. 2015;25:15021.

- 54. Horne R. Compliance, adherence, and concordance: implications for asthma treatment. Chest. 2006;130:65S-72S.
- 55. Gerald JK, Carr TF, Wei CY, et al. Albuterol overuse: a marker of psychological distress? J Allergy Clin Immunol Pract. 2015;3:957–62.
- 56. Yang JF, Chaudhuri R, Thomson NC, et al. Insights into frequent asthma exacerbations from a primary care perspective and the implications of UK National Review of Asthma Deaths recommendations. NPJ Prim Care Respir Med. 2018;28:35.
- 57. Lingner H, Burger B, Kardos P, et al. What patients really think about asthma guidelines: barriers to guideline implementation from the patients' perspective. BMC Pulm Med. 2017;17:13.
- 58. Aït-Khaled N, Enarson DA, Bencharif N, et al. Implementation of asthma guidelines in health centres of several developing countries. Int J Tuberc Lung Dis. 2006;10:104–9.
- 59. Lazarus SC, Krishnan JA, King TS, et al. Mometasone or tiotropium in mild asthma with a low sputum eosinophil level. N Engl J Med. 2019;380: 2009–19.

- 60. Pavord ID, Holliday M, Reddel HK, et al. Predictive value of blood eosinophils and exhaled nitric oxide in adults with mild asthma: a prespecified subgroup analysis of an open-label, parallel-group, randomised controlled trial. Lancet Respir Med. 2020;8:671–80.
- 61. Martinez FD, Chinchilli VM, Morgan WJ, et al. Use of beclomethasone dipropionate as rescue treatment for children with mild persistent asthma (TREXA): a randomised, double-blind, placebocontrolled trial. Lancet. 2011;377:650–7.
- 62. Sumino K, Bacharier LB, Taylor J, et al. A pragmatic trial of symptom-based inhaled corticosteroid use in African-American children with mild asthma. J Allergy Clin Immunol Pract. 2020;8:176–85.e2.
- 63. Kavanagh J, Jackson DJ, Kent BD. Sleep and asthma. Curr Opin Pulm Med. 2018;24:569–73.
- 64. Luyster FS, Teodorescu M, Bleecker E, et al. Sleep quality and asthma control and quality of life in non-severe and severe asthma. Sleep Breath. 2012;16:1129–37.