



Alison Sutton, Pharm.D., BCACP Asthma Management: Guideline Updates



Objectives

- 1. Define asthma
- 2. Discuss diagnosis and treatment goals of asthma
- 3. Discuss updated GINA and NAEPP guidelines
- 4. Discuss impact of overutilization of short-acting beta agonists on exacerbations, hospitalizations, and mortality
- 5. Discuss impact of studies on medications recommended for mild asthma



Global Heath Metrics. Asthma-Level 3 cause. <u>www.thelancet.com/pb-assets/Lancet/gbd/summaries/diseases/asthma.pdf</u>. Accessed 3/1/2022 The Global Asthma Report 2018. Asthma Mortality. <u>globalasthmareport.org/burden/mortality.php</u> Accessed 3/1/2022

Asthma Overview



Characterized by **chronic airway inflammation**

Symptoms include wheeze, shortness of breath, chest tightness, and cough

Symptoms are often **variable** with periods of symptom worsening

Risk Factors



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American Lung Association. Asthma Risk Factors. <u>www.lung.org/lung-health-diseases/lung-disease-</u>lookup/asthma/asthma-symptoms-causes-risk-factors/asthma-risk-factors. Accessed March 1, 2022.



FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; PEF: Peak Expiratory Flow

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Global Initiative for Asthma. Global strategy for asthma management and prevention <u>https://www.ginasthma.org</u> Accessed 2/8/2022

Asthma Treatment Goals

- Both current symptoms and future risks should be managed
- Treatment should be individualized based on adherence, patient preferences, symptom frequency at initial presentation, comorbidities



Asthma Treatment Guidelines

Presenting Symptoms	Initial Treatment Preferred Option Alternate Option
Infrequent symptoms	PRN low dose ICS-formoterol Low dose ICS PRN taken with SABA
Symptoms twice a month or more	PRN low dose ICS-formoterol Low dose ICS with PRN SABA
Troublesome symptoms most days AND/OR Waking due to symptoms once a week or more	Low dose ICS-formoterol maintenance and reliever Low dose ICS-LABA with PRN SABA
Initial presentation is acute exacerbation or severely uncontrolled	Medium dose ICS-formoterol maintenance and reliever High dose ICS (or medium dose ICS-LABA) with PRN SABA

GINA 2021

• Initial treatment options for ADULTS and adolescents

• SABA monotherapy NOT recommended in Adults/Adolescents

PRN, as needed; SABA, Short-acting beta agonist; ICS, Inhaled corticosteroid; LABA, Long-acting beta agonist

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NAEPP 2020

Asthma Treatment Guidelines

- Stepwise approach to treatment in 12 & older
- Alternatives for each step can be found in full guidelines
- SABA monotherapy recommended for "Intermittent Asthma" only

1	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
	PRN SABA	Daily low dose ICS & PRN SABA OR PRN concomitant ICS & SABA	Daily & PRN combination low-dose ICS- formoterol	Daily & PRN combination medium-dose ICS-formoterol	Daily medium- high dose ICS- LABA + LAMA & PRN SABA	Daily high- dose ICS-LABA + oral systemic corticosteroids + PRN SABA

PRN, as needed; SABA, Short-acting beta agonist; ICS, Inhaled corticosteroid; LABA, Long-acting beta agonist; LAMA, Long-acting muscarinic antagonist

2020 Focused Updates To the Asthma Management Guidelines. Accessed March 1, 2020. www.nhlbi.nih.gov/sites/default/files/publications/AsthmaManagementGuidelinesReport-2-4-21.pdf

Role of Short-Acting Beta Agonists

Short-Acting Beta Agonists (SABAs) have been a mainstay of reliever medication for all steps of asthma treatment and monotherapy for mild asthma for decades



Global Initiative for Asthma. Global strategy for asthma management and prevention <u>https://www.ginasthma.org</u> Accessed 2/8/2022

Select Clinical Trials

Study	Study Design	Results
Nwaru BI, et al.	Retrospective cohort n = 365,324	Higher SABA use was associated with increased exacerbation and mortality risks.
O'Byrne P, et al.	Double-blind RCT n = 3836	In patients with mild asthma, as-needed budesonide–formoterol provided superior asthma-symptom control to as-needed terbutaline but was inferior to budesonide maintenance therapy. Exacerbation rates with the two budesonide-containing regimens were similar and were lower than the rate with terbutaline.
Bateman ED, et al.	Double-blind RCT n = 4215	In patients with mild asthma, budesonide–formoterol used as needed was noninferior to twice-daily budesonide with respect to the rate of severe asthma exacerbations during 52 weeks of treatment but was inferior in controlling symptoms.

Clinical Pearl: Max dose of Budesonide/Formoterol is 4 puffs daily (18mcg formoterol) regardless of dosing regimen per labeling. Max 12 puffs daily (54 mcg formoterol) per guidelines.

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 [https://doi.org/10.1183/13993003.01872-2019].

O'Byrne P, FitzGerald M, Bateman E, Barnes P. Inhaled combined budesonide-formoterol as needed in mild asthma. N Engl J Med. 2018;378:1865-76.

Bateman ED, Reddel HK, O'Byrne PM, et al. As-needed budesonide-formoterol versus maintenance budesonide in mild asthma. N Engl J Med 2018;378:1877-87.

Clinical Pharmacology [database on]ine]. Tampa, FL: Gold Standard, Inc.; 2022. URL: http://www.clinicalpharmacology.com. Updated May 2021. © 2020 Envolve. Confidential and Proprietary.

Nwaru BI, et al.: Results

Association between baseline SABA use and mortality				
Overall mortality		Asthma-related mortality	Respiratory-related mortality	
0-2 canisters	1.00	1.00	1.00	
3-5 canisters	1.26 (1.14-1.38)	1.70 (0.49-5.88)	1.26 (0.73-2.17)	
6-10 canisters 1.66 (1.48-1.87)		4.70 (1.47-15.04)	2.87 (1.67-4.92)	
≥11 canisters	2.33 (2.01-2.71)	31.72 (11.88-84.70)	6.33 (3.56-11.26)	

Increased utilization of SABA resulted in increased risk of overall mortality, asthmarelated mortality, and respiratory-related mortality

Hazard Ratio adjusted for treatment step, Charlson Comorbidity Index, sex, and age.

Nwaru BI, Ekström M, Hasvold P, et al. Overuse of short-acting β 2-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 [https://doi.org/10.1183/13993003.01872-2019].

Nwaru BI, et al.: Results

Risk of asthma exacerbation			
Treatment Step	0-2 SABA canisters	3+ SABA canisters	
Step 1	1.00	1.18 (1.14-1.21)	Utilization of ≥3 SABA
Step 2	1.00	1.28 (1.25-1.32)	canisters during baseline year
Step 3	1.00	1.41 (1.38-1.44)	exacerbations regardless of
Step 4	1.00	1.46 (1.42-1.50)	asthma severity

Hazard Ratio adjusted for age at asthma diagnosis, sex, treatment step, and comorbidity

Study Limitations:

SABA overuse not correlated with adjustment of maintenance asthma medication

Asthma diagnosis inferred from pharmacy claims

Nwaru BI, Ekström M, Hasvold P, et al. Overuse of short-acting β 2-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 [https://doi.org/10.1183/13993003.01872-2019].

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SYGMA 1

O'Byrne P, et al.

- Double-blind RCT comparing:
 - SABA PRN
 - Budesonide-Formoterol PRN
 - Budesonide + SABA PRN
- Primary End Point
 - Superiority of Budesonide-Formoterol PRN compared to SABA PRN in terms of asthma symptom control

Results:

- PRN Budesonide-formoterol SUPERIOR to PRN SABA for symptom control
- PRN Budesonide-formoterol INFERIOR to Budesonide maintenance for symptom control
- PRN Budesonide-formoterol & Budesonide maintenance SUPERIOR to PRN SABA for severe exacerbations

SYGMA 2

Bateman ED, et al.

- Double-blind RCT comparing:
 - Budesonide-Formoterol PRN
 - Budesonide + SABA PRN
- Primary End Point:
 - Non-inferiority of Budesonide-Formoterol PRN to Budesonide maintenance in terms of severe exacerbations

- Results:
 - PRN Budesonide-formoterol NON-INFERIOR to Budesonide maintenance for severe exacerbations
 - PRN Budesonide-formoterol INFERIOR to Budesonide maintenance for symptom control

Treatment Principles

Symptoms Exacerbations Side Effects Lung Function

Review

Assess

Medications

Non-pharm strategies

Training

Adjust

Symptom control Risk factors Inhaler technique Adherence Comorbidities Control Symptoms

Minimize Future Risk

Global Initiative for Asthma. Global strategy for asthma management and prevention <u>https://www.ginasthma.org</u> Accessed 2/8/2022

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- The Global Asthma Report 2018. Asthma Mortality. <u>globalasthmareport.org/burden/mortality.php</u> Accessed 3/1/2022
- American Lung Association. Asthma Risk Factors. <u>www.lung.org/lung-health-diseases/lung-disease-lookup/asthma/asthma-symptoms-causes-risk-factors/asthma-risk-factors</u>. Accessed March 1, 2022.
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- O'Byrne P, FitzGerald M, Bateman E, Barnes P. Inhaled combined budesonide–formoterol as needed in mild asthma. N Engl J Med. 2018;378:1865–76.



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