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Asthma Management: Guideline Updates

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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

Introduction

Morbidity

- Affects 262 million people globally

Mortality

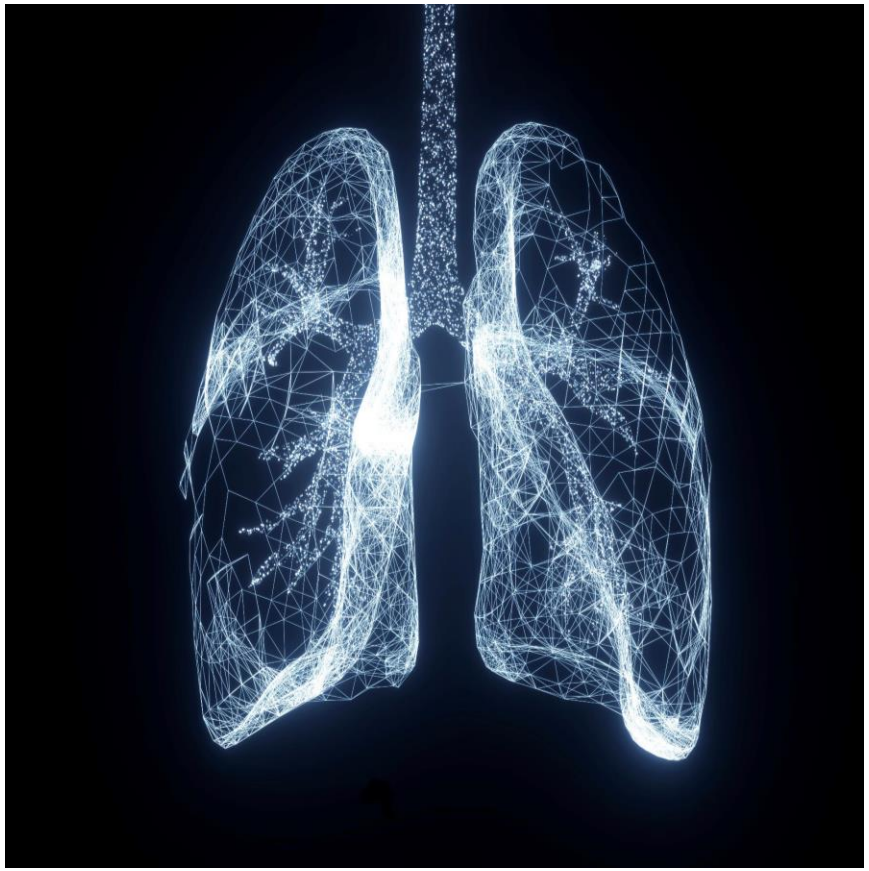
- Global deaths may be as high as 420,000 annually

Impact

- Much of the morbidity and mortality is avoidable with appropriate treatment

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

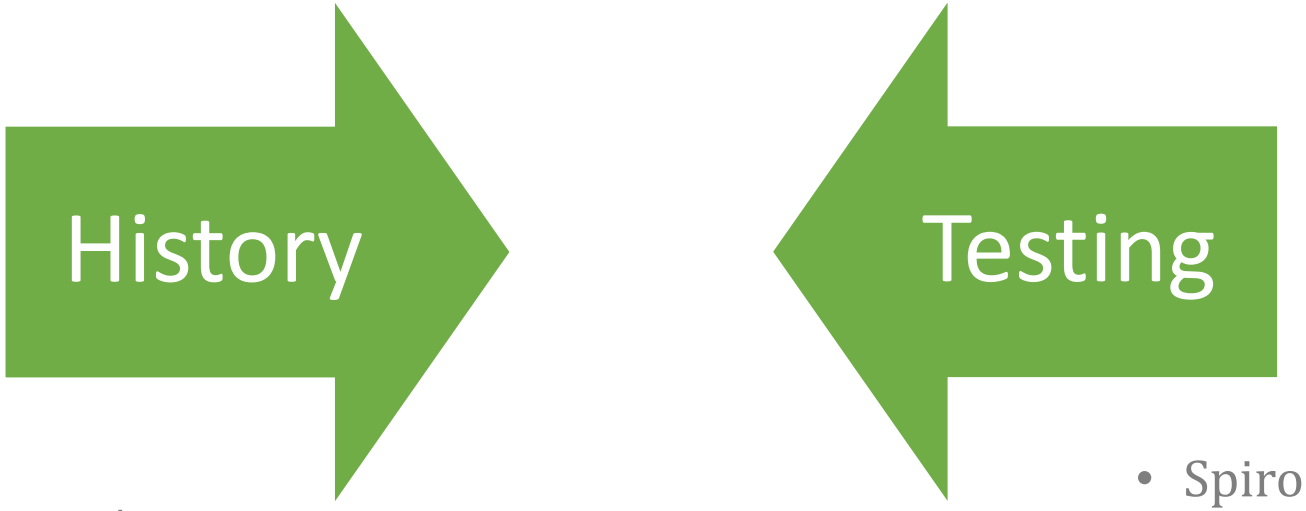
Global Initiative for Asthma. Global strategy for asthma management and prevention https://www.ginasthma.org Accessed 2/8/2022

Risk Factors

- Family history
- Allergies
- Exposure to cigarette smoke
- Air pollution
- Obesity
- Occupational exposures

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

Asthma Diagnosis



- History of variable symptoms
- Physical Exam

- Spirometry
  - FEV_1
  - FVC
  - PEF

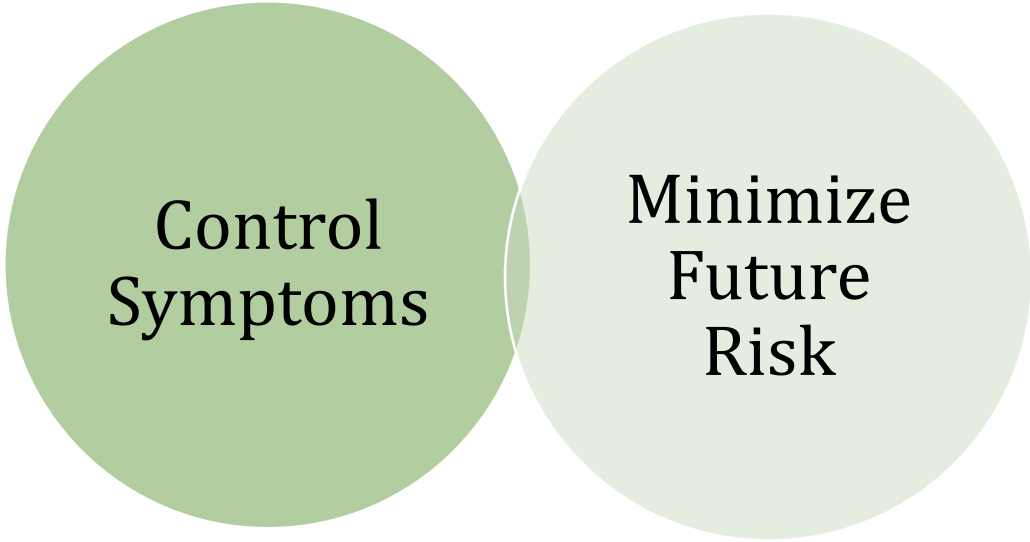
FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; PEF: Peak Expiratory Flow

Global Initiative for Asthma. Global strategy for asthma management and prevention https://www.ginasthma.org 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



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

Asthma Treatment Guidelines

GINA 2021

Presenting Symptoms	Initial Treatment
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

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

- Initial treatment options for ADULTS and adolescents
- **SABA monotherapy NOT recommended in Adults/Adolescents**

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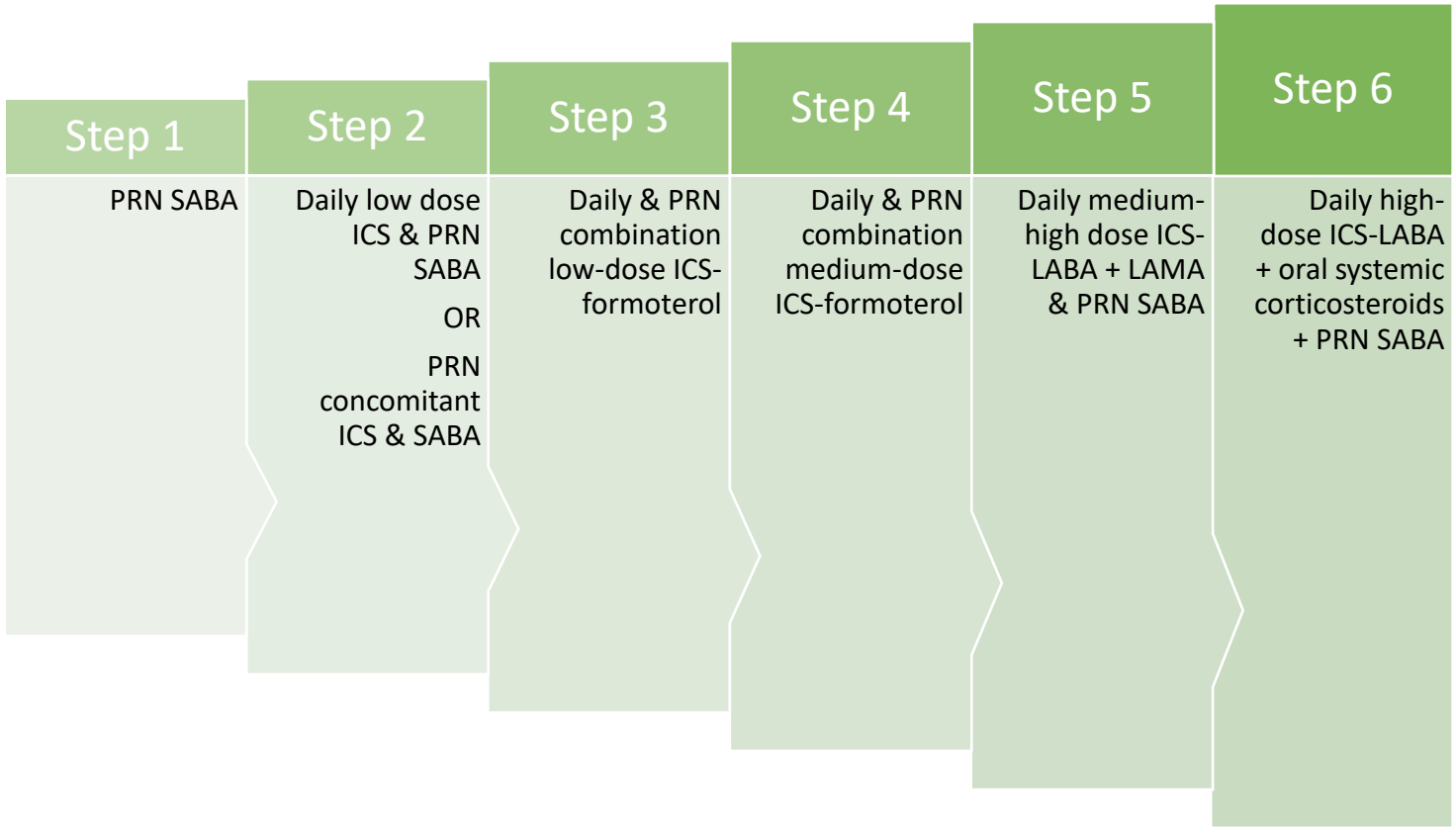
Asthma Treatment Guidelines

NAEPP 2020

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

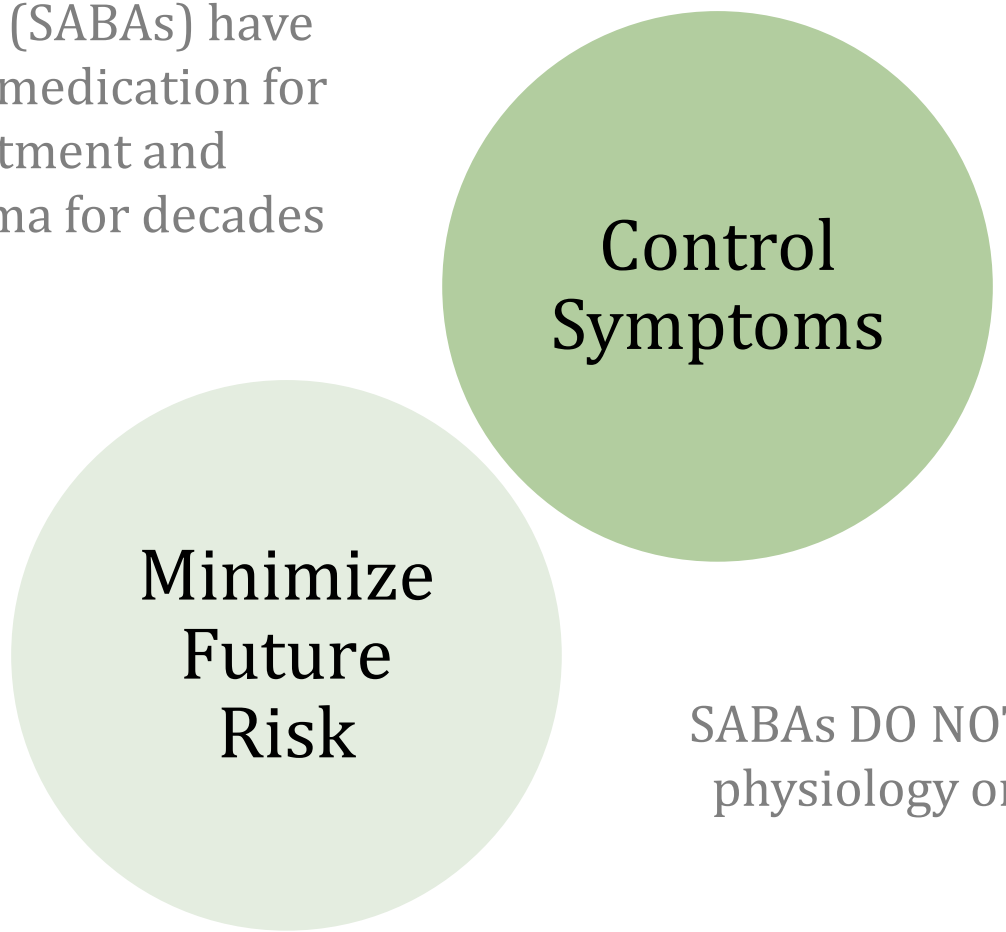


PRN, as needed; SABA, Short-acting beta agonist; ICS, Inhaled corticosteroid; LABA, Long-acting beta agonist; LAMA, Long-acting muscarinic antagonist

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



SABAs work quickly to control current symptoms

SABAs DO NOT address underlying physiology or prevent future risk

Global Initiative for Asthma. Global strategy for asthma management and prevention https://www.ginasthma.org 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.

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.

Nwaru BI, et al.: Results

	0-2 SABA canisters	3-5 SABA canisters	6-10 SABA canisters	≥ 11 SABA canisters
Subjects	254,500	76,619	27,065	7,140
Any exacerbation	32,653 (12.8%)	13,071 (17.1%)	5,754 (21.3%)	2,049 (28.7%)
Hospitalization rate Asthma main cause per 1000 person-years (95% CI)	1.0 (0.9-1.1)	2.8 (2.4-3.1)	6.1 (5.2-7.1)	17.9 (14.8-21.0)

More than 2 canisters per year defined as SABA overuse

As SABA utilization increases, exacerbation and hospitalization rates also increase

SABA, Short-acting beta agonist; CI, Confidence interval

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].

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, asthma-related 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 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].

Nwaru BI, et al.: Results

Treatment Step	Risk of asthma exacerbation	
	0-2 SABA canisters	3+ SABA canisters
Step 1	1.00	1.18 (1.14-1.21)
Step 2	1.00	1.28 (1.25-1.32)
Step 3	1.00	1.41 (1.38-1.44)
Step 4	1.00	1.46 (1.42-1.50)

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

Utilization of ≥3 SABA canisters during baseline year resulted in increased risk of exacerbations regardless of asthma severity

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 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, et al.

SYGMA 1

- 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

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.

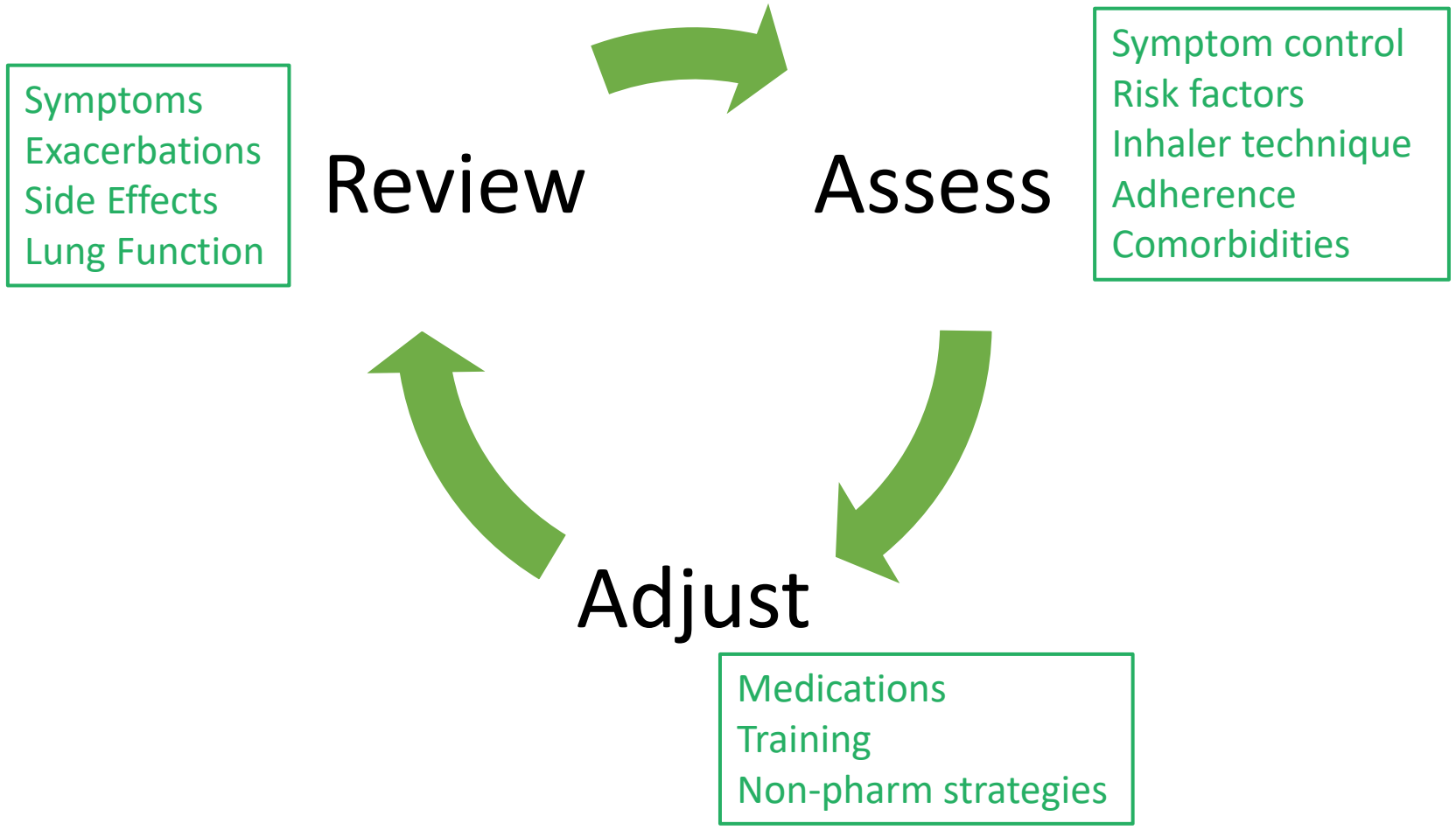
Bateman ED, et al.

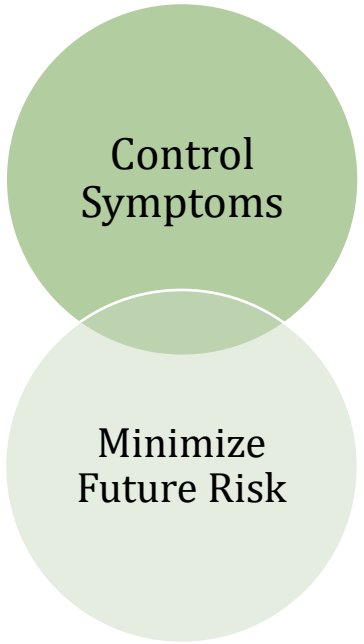
SYGMA 2

- 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

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.

Treatment Principles





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- The Global Asthma Report 2018. Asthma Mortality. globalasthmareport.org/burden/mortality.php Accessed 3/1/2022
- American Lung Association. Asthma Risk Factors. www.lung.org/lung-health-diseases/lung-disease-lookup/asthma/asthma-symptoms-causes-risk-factors/asthma-risk-factors. 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.

Thank you