UPDATE ON PEDIATRIC ASTHMA

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PEDIATRIC ALLERGY AND CLINICAL IMMUNOLOGY

ALLENTOWN, PA

CONFLICT OF INTEREST

I have no real or perceived conflict of interests with regards to this topic.

WHAT IS ASTHMA

- Asthma is a heterogeneous disease typically with chronic inflammation. Symptoms of wheezing, SOB, cough, and chest tightness are variable and often present in varying degrees and will vary over time. Airflow limitation is also variable.
- Asthma has phenotypes that are based on demographics, clinical and/or physical characteristics but these phenotypes do not strongly correlate with either pathophysiologic changes or treatment responses

ASTHMA IS A GLOBAL DISEASE

- 334 million people have asthma
- 14% of world's children have asthma symptoms
- 8.6% of young adults (18-45) have asthma symptoms
- 4.5% young adults diagnosed with asthma
- Asthma is the 14th most important disorder in the world based on extent and duration of disability

http://www.globalasthmareport.org/2014/burden/burden.php

CHILDHOOD ASTHMA IS GLOBAL ISSUE

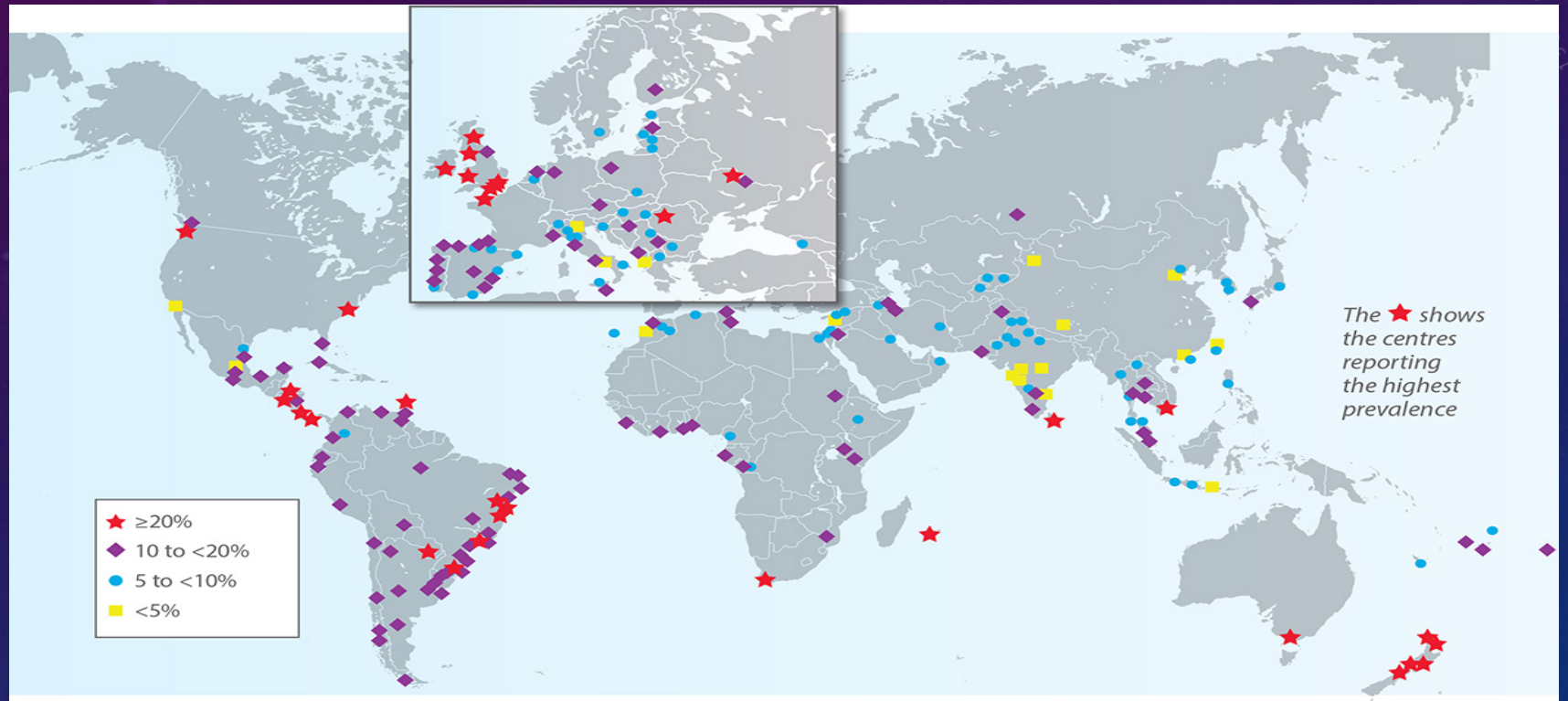


Figure 1: Prevalence of asthma symptoms among 13-14 year olds (ISAAC).

http://www.globalasthmareport.org/2014/burden/burden.php
International Study of Asthma and Allergies in Childhood (ISAAC)

GLOBAL CHILDHOOD ASTHMA IS SEVERE

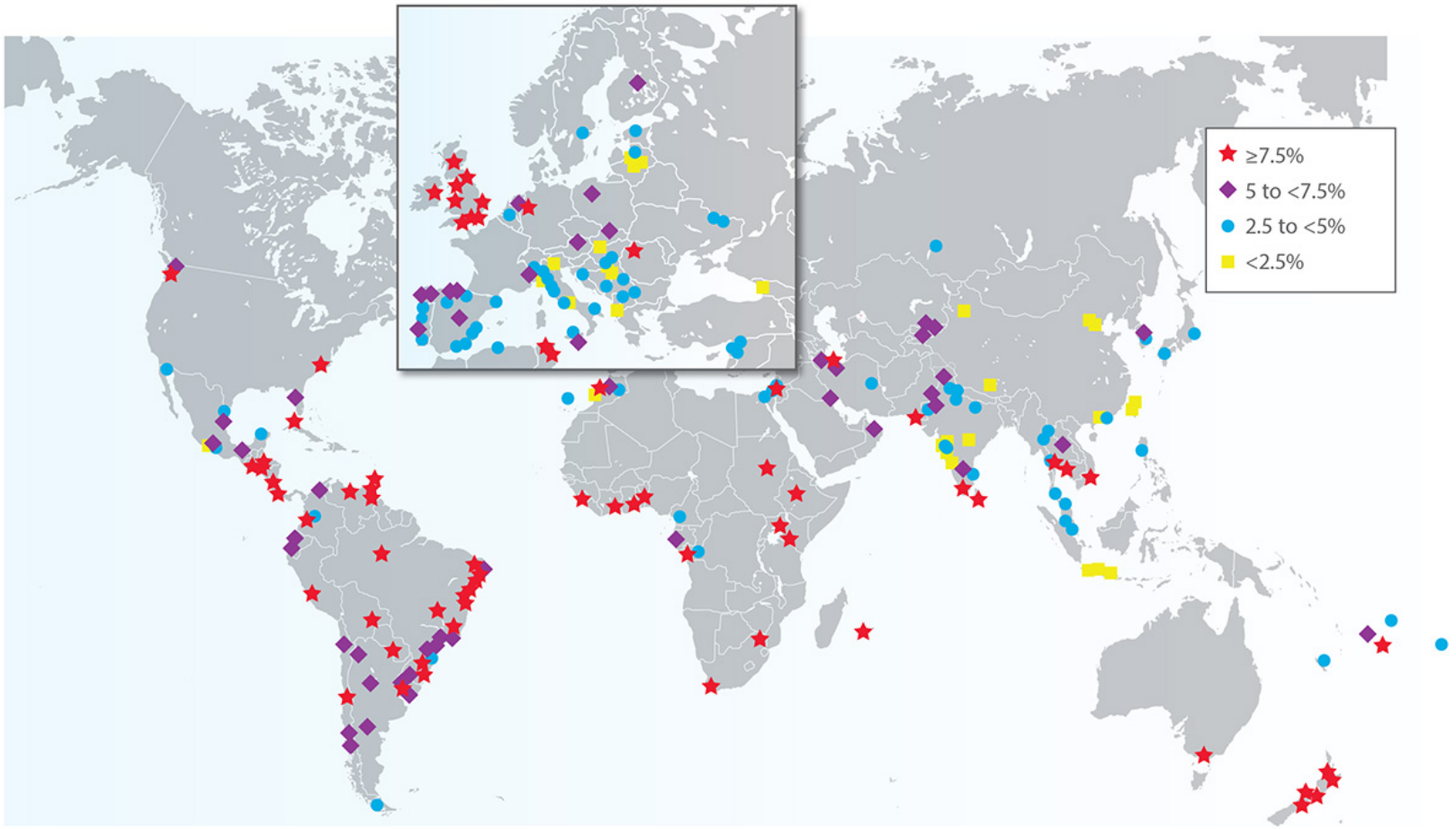
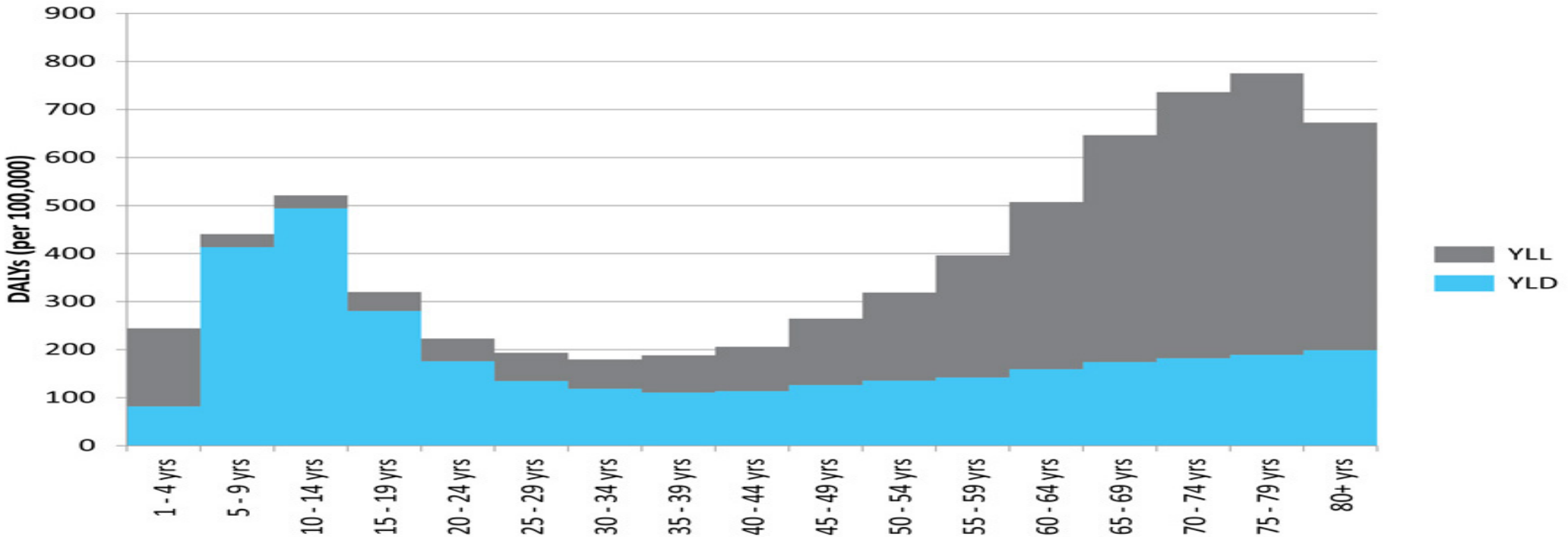


Figure 2: Prevalence of severe asthma among 13-14 year olds (ISAAC).

http://www.globalasthmareport.org/2014/burden/burden.php
International Study of Asthma and Allergies in Childhood (ISAAC)

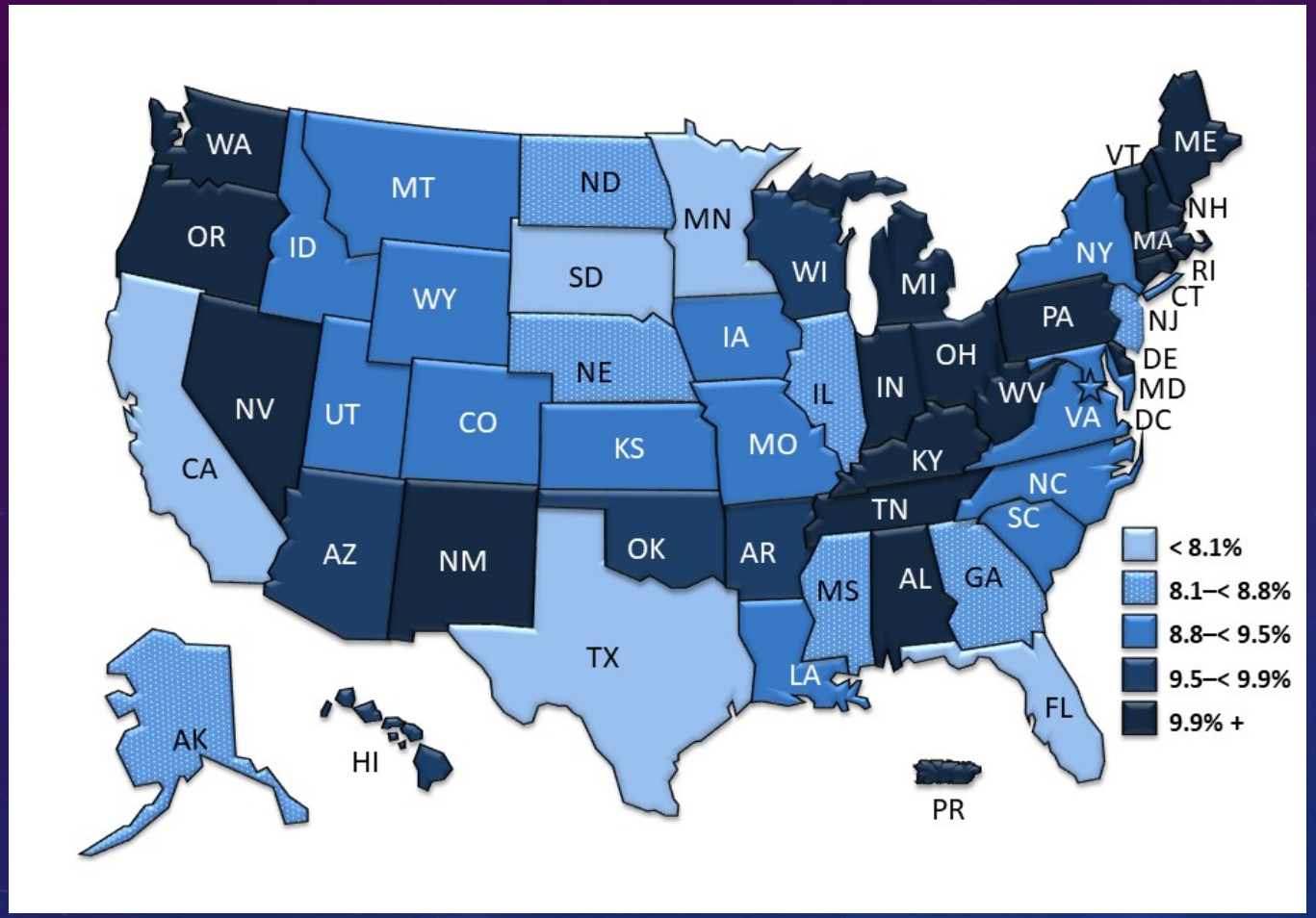
DISABILITY AND DEATH FROM ASTHMA GLOBALLY

Figure 5:
Components of disability adjusted life years (DALYs): years lived with disability (YLD) and years of life lost (YLL) per 100,000 population attributed to asthma by age group. Global population, 2010.



http://www.globalasthmareport.org/2014/burden/burden.php

ASTHMA IN THE UNITED STATES



ADULT SELF-REPORTED CURRENT ASTHMA PREVALENCE (%) BY STATE OR TERRITORY, 2017

Current asthma prevalence among adults varies in states and Puerto Rico, ranging from 7.3% in Texas to 13.2% in New Hampshire.

The median across all states and Puerto Rico was 9.4% with current asthma.

Asthma Prevalence and Health Care Resource Utilization Estimates, United States, 2001-2017
Center for Disease Control; National Asthma Control Program

ASTHMA IS COMMON

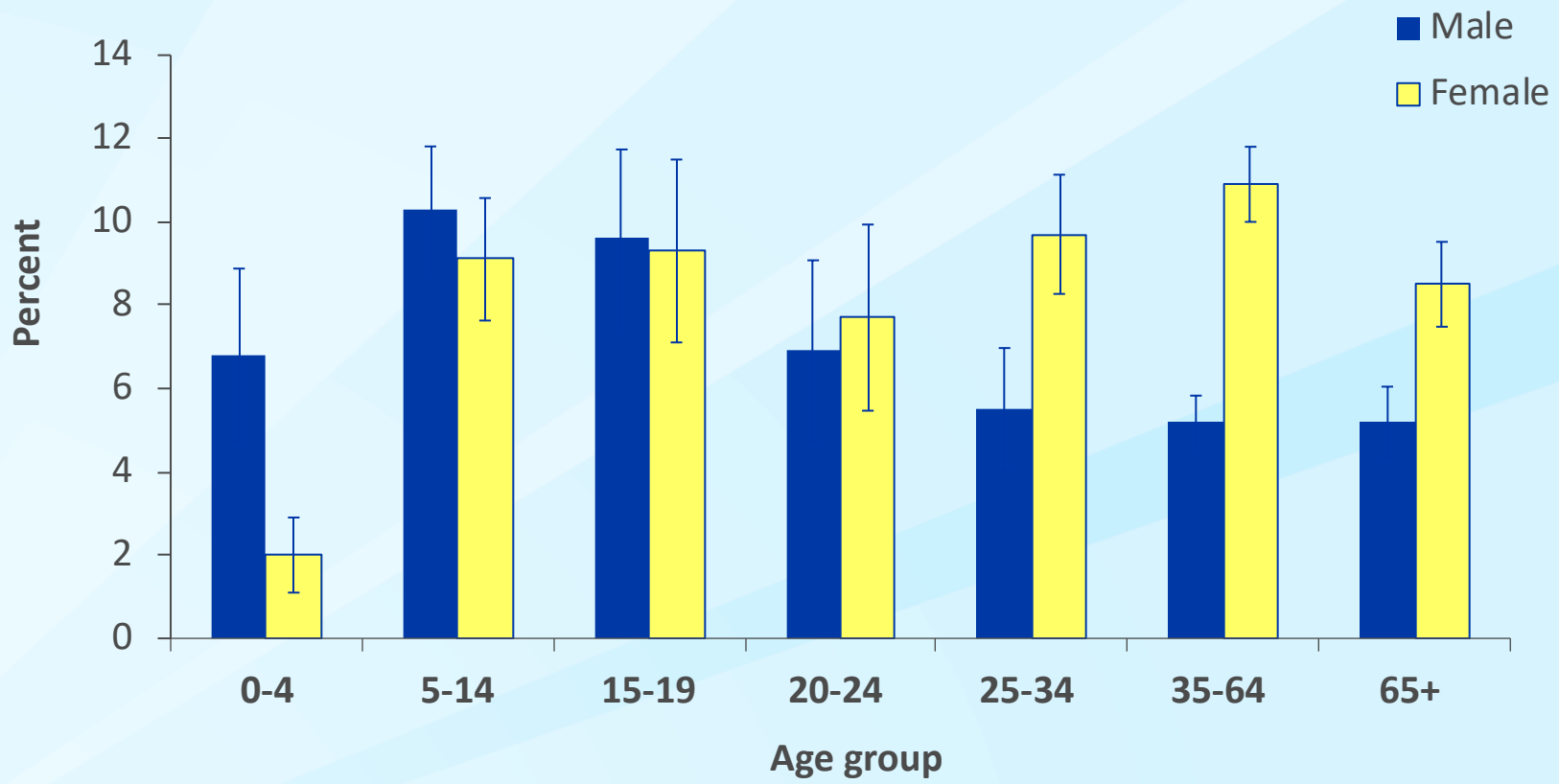
- 1/13 people in the United States have asthma
- 25 million Americans have asthma
- Asthma is the leading chronic disease in children
- In 2017 1/12 children had asthma in the United States
- Currently 5.5 million <18 yrs old have asthma

Asthma Prevalence and Health Care Resource Utilization Estimates, United States
Center for Disease Control; National Asthma Control Program

VARIATION IN ASTHMA RATES

- Age
- Gender
- Ethnicity
- Multiple factors

Child and Adult Current Asthma Prevalence by Age and Sex: United States, 2017

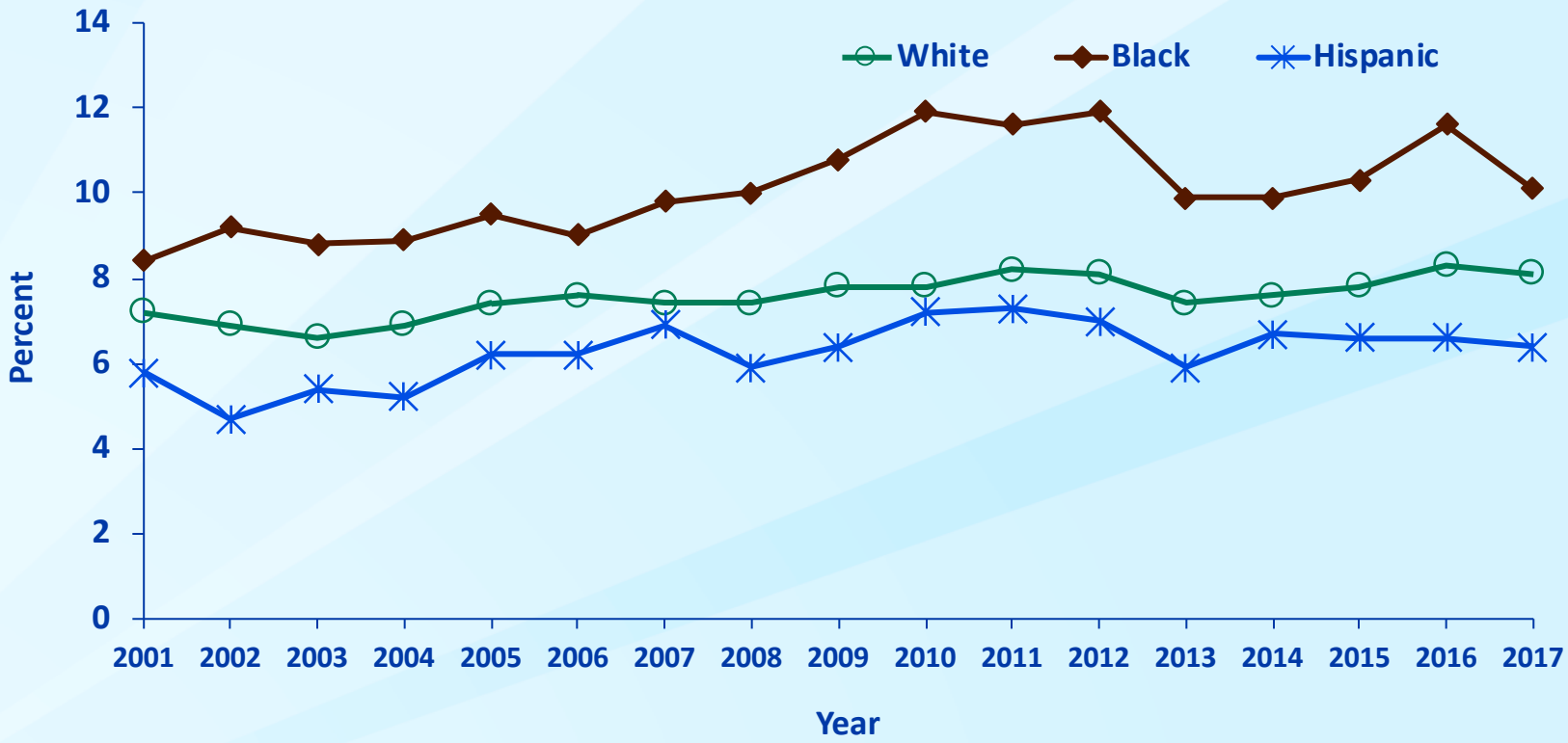


Males and females aged 5-24 years had no difference in percent of current asthma.

Among children 0-4 years, males had a higher percent of asthma and among adults 25 years and older, was higher for women than men.

Asthma Prevalence and Health Care Resource Utilization Estimates, United States, 2001-2017 Center for Disease Control; National Asthma Control Program

Current Asthma Prevalence by Race and Ethnicity: United States, 2001-2017



Blacks are more likely to have asthma than both whites and Hispanics.

Percent of current asthma increased for whites, blacks, and Hispanics from 2001 to 2017.

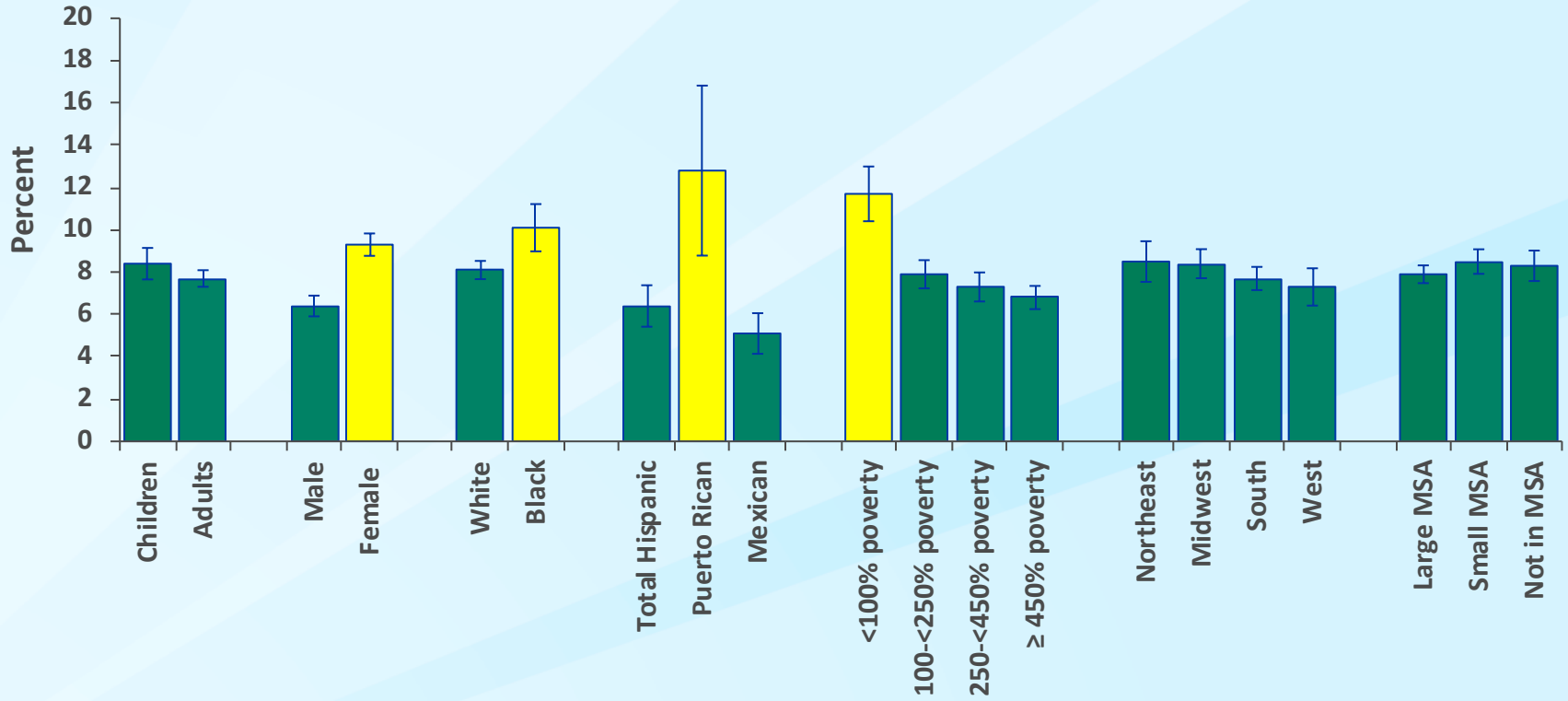
Asthma Prevalence and Health Care Resource Utilization Estimates, United States, 2001-2017 Center for Disease Control; National Asthma Control Program

PEDIATRIC ASTHMA UPDATES
2018 RACE/ETHNICITY BREAKDOWN

- White non-Hispanic: 2 million, 7.7% prevalence
- Black non-Hispanic: 1.4 million, 12.6% prevalence
- Other non-Hispanic: 577 thousand
- Hispanic: 1.5 million, 7.7% prevalence
- Puerto Rican: 253 thousand, 11.3% prevalence
- Mexican: 836 thousand, 6.2 % prevalence

Asthma Prevalence and Health Care Resource Utilization Estimates, United States, Center for Disease Control; National Asthma Control Program

Current Asthma Prevalence by Age Group, Sex, Race and Ethnicity, Poverty Status, Geographic Region, and Place of Residence: United States, 2017



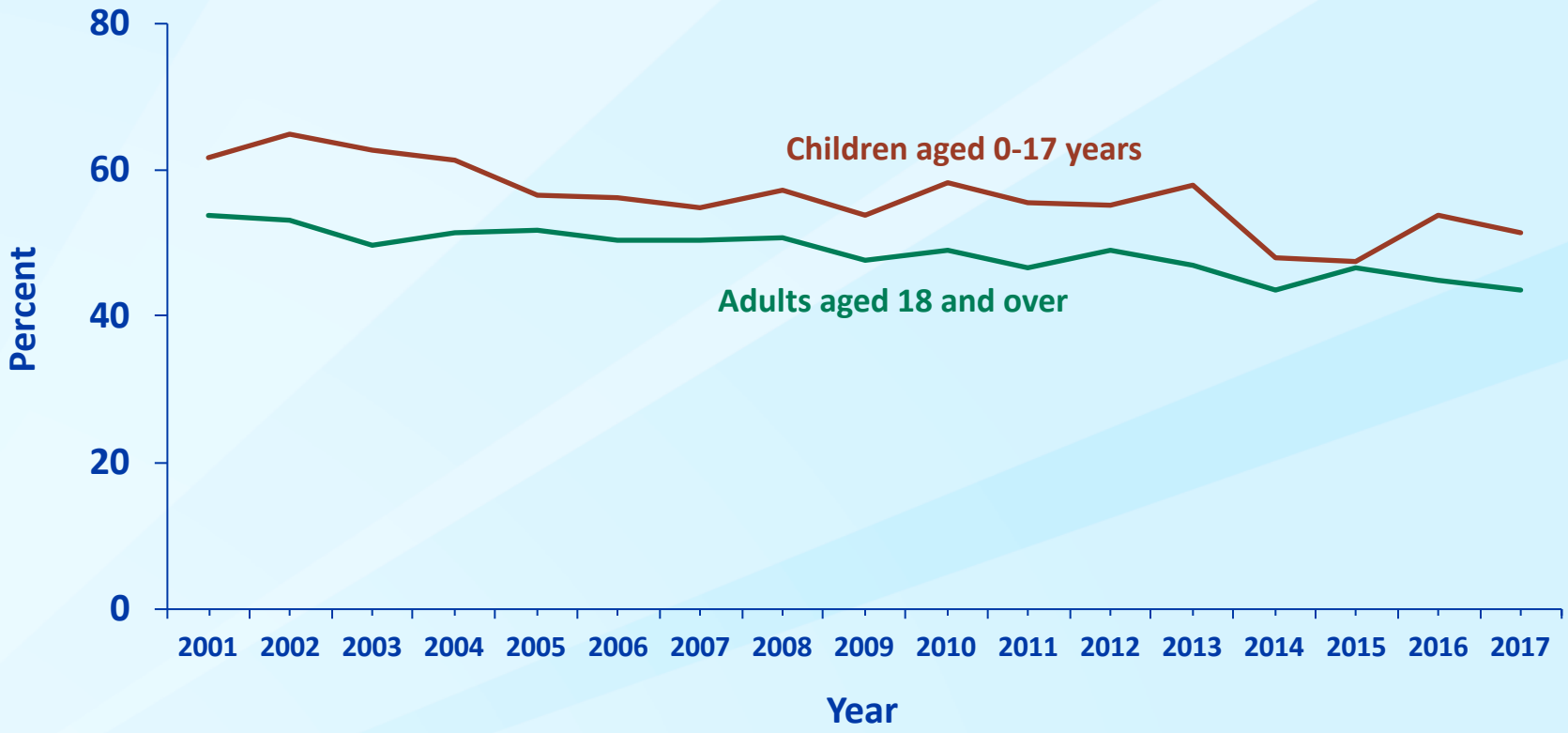
Females, blacks, and Puerto Ricans are more likely to have asthma.

People with lower annual household income were more likely to have asthma.

Asthma did not differ by age group, region, or Metropolitan Statistical Area (MSA).

Asthma Prevalence and Health Care Resource Utilization Estimates, United States, 2001-2017 Center for Disease Control; National Asthma Control Program

Asthma Attack Prevalence among Children and Adults with Current Asthma: United States, 2001-2017



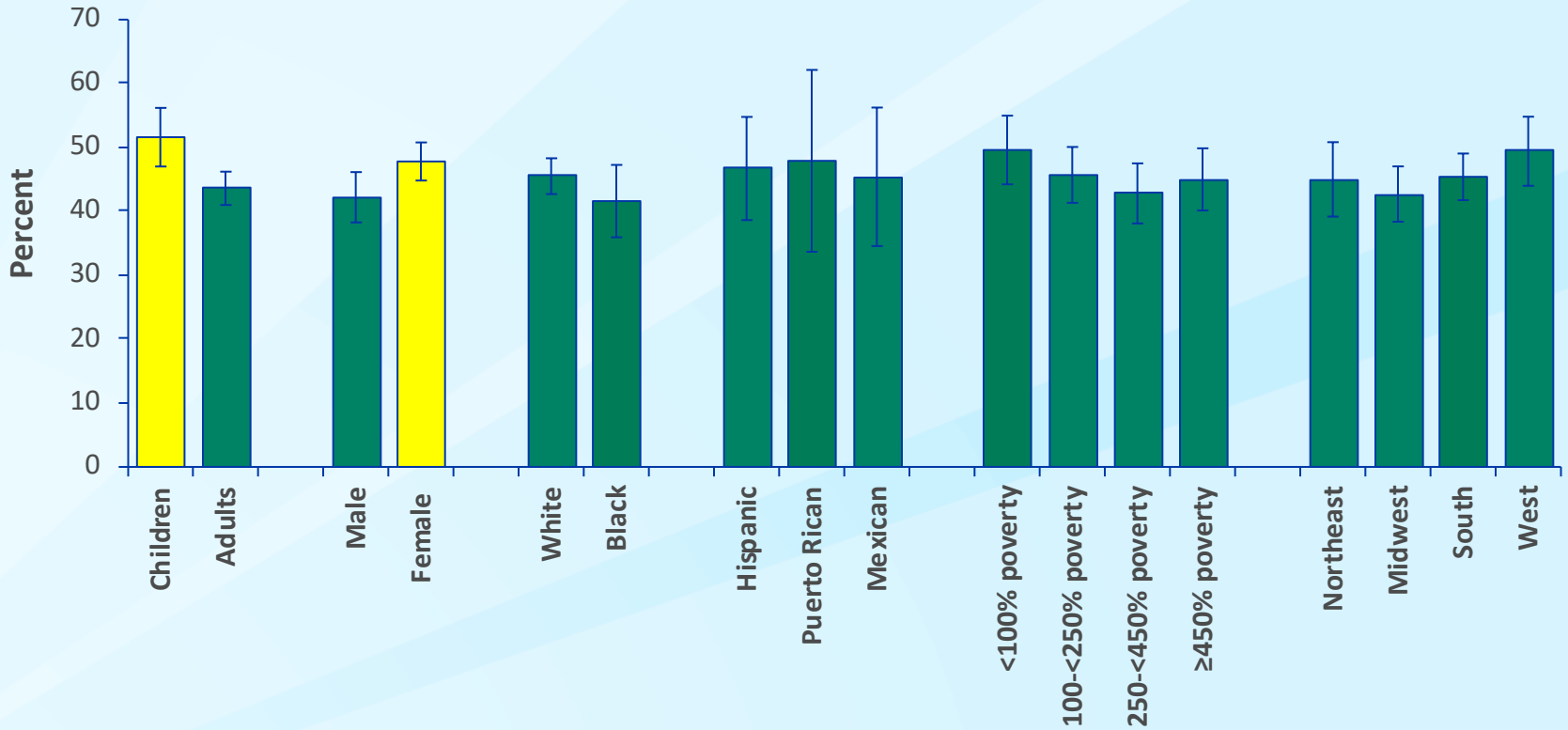
From 2001 to 2017, percent of children and adults with current asthma who had at least one asthma attack in the previous 12 months declined.

For children, asthma attacks declined from 61.7% of children with asthma in 2001 to 51.6% in 2017.

For adults, asthma attacks declined from 53.8% of adults with asthma in 2001 to 43.6% in 2017.

Asthma Prevalence and Health Care Resource Utilization Estimates, United States, 2001-2017 Center for Disease Control; National Asthma Control Program

Asthma Attack Prevalence among Persons with Current Asthma by Age Group, Sex, Race and Ethnicity, Poverty Status, and Geographic Region: Unites States, 2017



In 2017, asthma attacks occurred more often in children and females.
Asthma attack prevalence did not differ by race or ethnicity, poverty level, or census region.

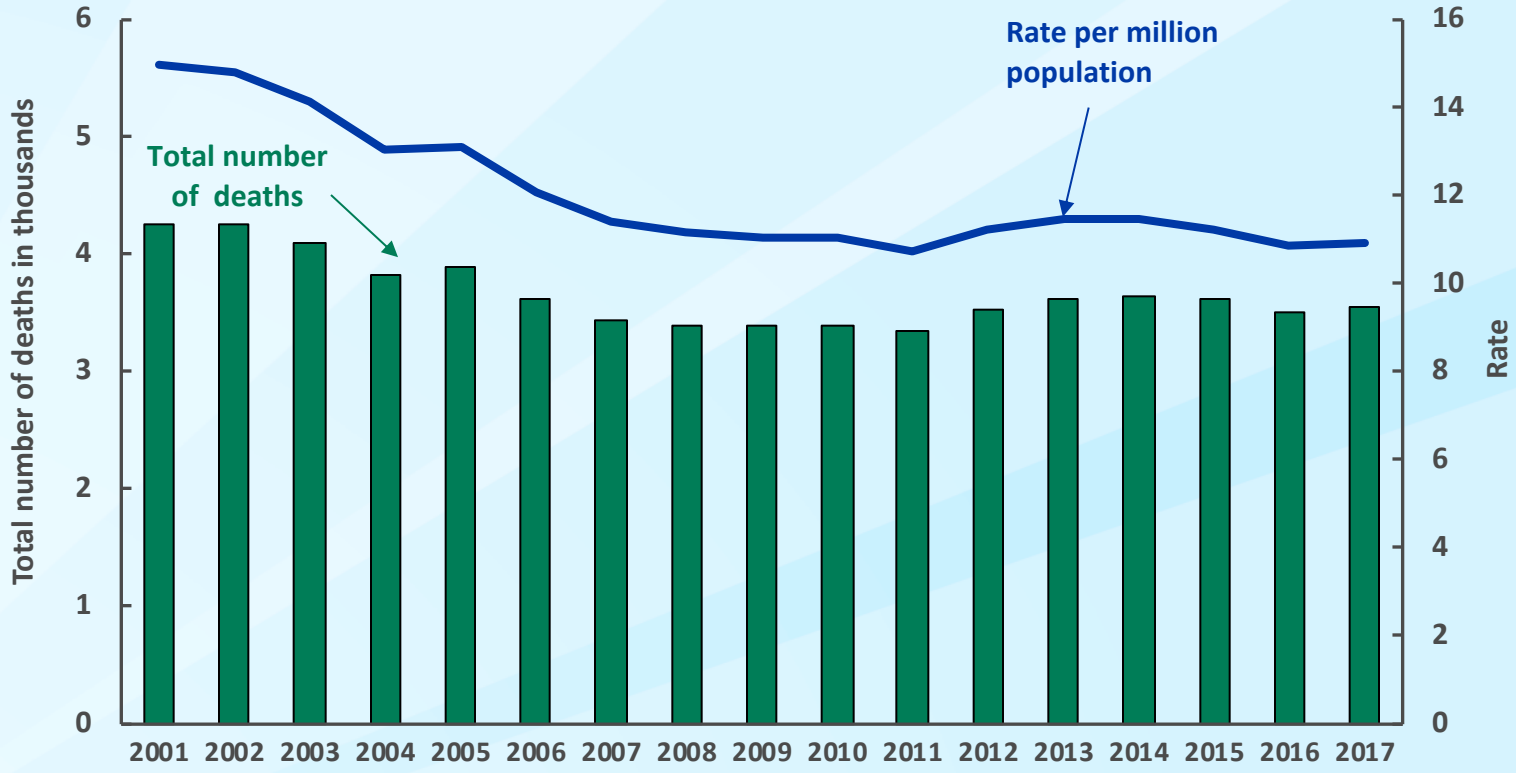
Asthma Prevalence and Health Care Resource Utilization Estimates, United States, 2001-2017 Center for Disease Control; National Asthma Control Program

Asthma is Deadly

- 10 deaths/million (3,564 people) in 2017
- Adults have a 4X greater risk of death than children
  - 13.3/million versus 2.8/million
- Adult women have greater risk than adult men
- Boys have greater risk than girls
- Non-Hispanic blacks have 3X greater risk of death than other ethnic groups

www.cdc.gov/asthma/asthma_stats/asthma_underlying_death.html

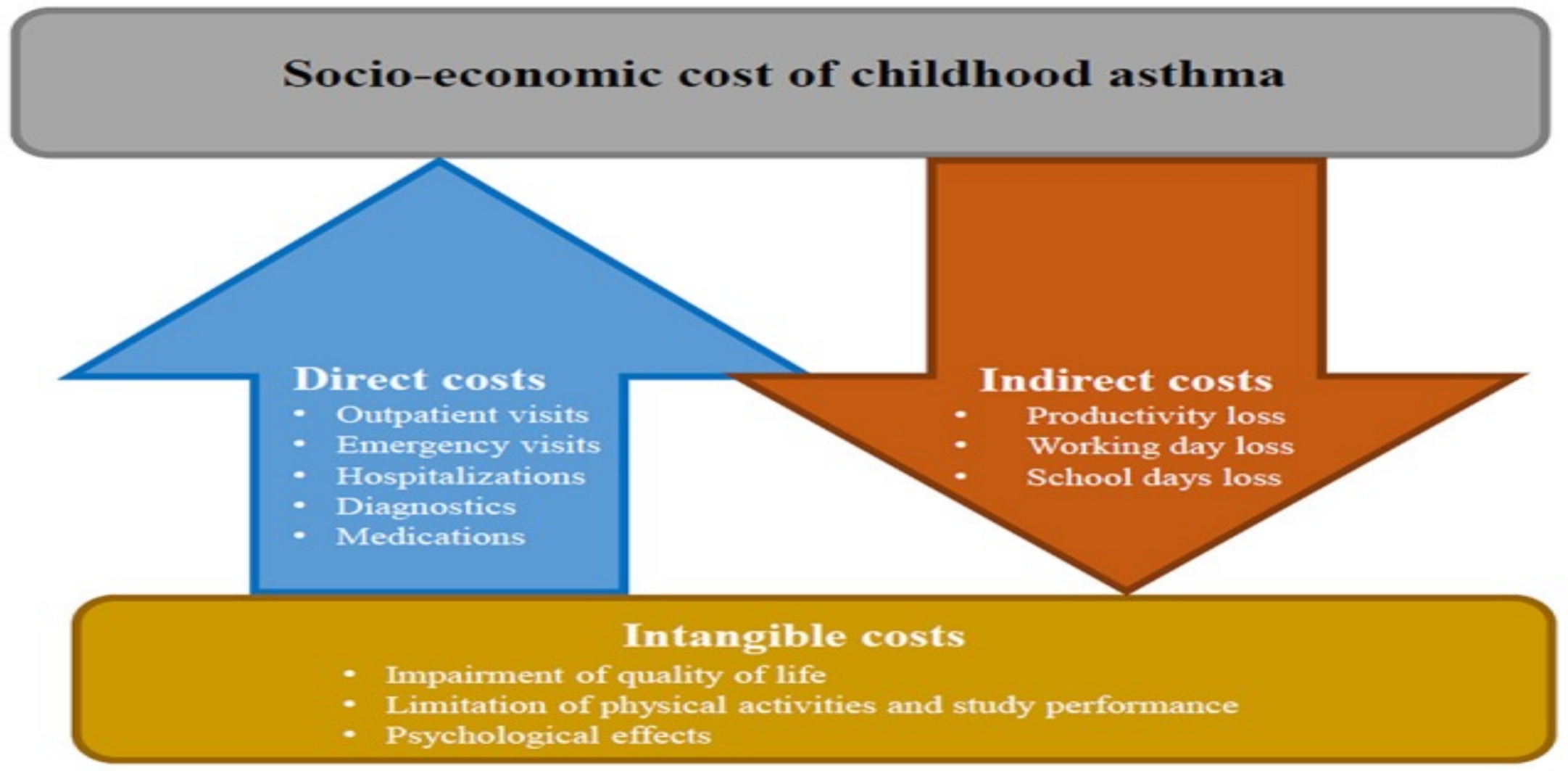
Asthma Deaths:
United States, 2001–2017



The rate of asthma deaths declined from 15.0 per million population in 2001 to 11.2 deaths per million population in 2008. Rates gradually peaked between 2011 and 2014 but not significant.

Asthma Prevalence and Health Care Resource Utilization Estimates, United States, 2001-2017Center for Disease Control; National Asthma Control Program

ASTHMA IS COSTLY



SEVERE UNCONTROLLED ASTHMA SIGNIFICANTLY IMPACTED QUALITY OF LIFE

- 97 percent report that their asthma limits their everyday tasks
- 93 percent said their asthma negatively affects their physical health
- 83 percent said asthma affects their personal relationships with family, spouses/partners, friends, co-workers
- 78 percent said asthma was always in the back of their mind
- 76 percent said they feel frustrated by their asthma
- 71 percent said asthma negatively affects their emotional health
- 55 percent had symptoms more than once a day
- 48 percent used their quick-relief inhaler more than once a day
- 41 percent said they believe their asthma is so severe that there are no medicines that can make it better

WHAT'S NEW FOR 2020

- COVID-19
- Use of ICS in mild intermittent asthma (based on GINA)
- Increased number of biologics approved in pediatrics
- Consideration of what level to start treatment for 6 yrs and up
- Consideration of treating children <5 yrs of age with recurrent wheezing
- Potential avoidance of montelukast (GINA)
- Updates to assessing severity of exacerbations in young children

Global Initiative for Asthma (GINA)

What's new in GINA 2020?

GINA Global Strategy for Asthma Management and Prevention

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COVID 19 AND ASTHMA

COVID-19 and asthma *(as at April 3, 2020)*

- Advise patients with asthma to continue taking their prescribed asthma medications, particularly *inhaled corticosteroids* (ICS), and oral corticosteroids (OCS) if prescribed
  - Asthma medications should be continued as usual. Stopping ICS often leads to potentially dangerous worsening of asthma
  - For patients with severe asthma: continue biologic therapy, and do not suddenly stop OCS if prescribed
- Make sure that all patients have a *written asthma action plan* with instructions about:
  - Increasing controller and reliever medication when asthma worsens
  - Taking a short course of OCS for severe asthma exacerbations
  - When to seek medical help
  - See the GINA 2020 report for more information about treatment options for asthma action plans.
- *Avoid nebulizers* where possible
  - Nebulizers increase the risk of disseminating virus to other patients AND to health care professionals
  - Pressurized metered dose inhaler via a spacer is the preferred treatment during severe exacerbations, with a mouthpiece or tightly fitting face mask if required

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COVID-19 and asthma *(as at March 30, 2020)*

- *Avoid spirometry* in patients with confirmed/suspected COVID-19
  - Spirometry can disseminate viral particles and expose staff and patients to risk of infection
  - While community transmission of the virus is occurring in your region, postpone spirometry and peak flow measurement within health care facilities unless there is an urgent need
  - Follow contact and droplet precautions
- *Follow strict infection control procedures* if aerosol-generating procedures are needed
  - For example: nebulization, oxygen therapy (including with nasal prongs), sputum induction, manual ventilation, non-invasive ventilation and intubation
  - World Health Organization (WHO) infection control recommendations are found here: www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125
- *Follow local health advice* about hygiene strategies and use of personal protective equipment, as new information becomes available in your country or region

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Other resources for COVID-19 *(as at March 30, 2020)*

- Information for health professionals
  - World Health Organization (WHO) recommendations for infection control www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125
  - Centers for Disease Control and Prevention (CDC) www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html,
- Information for patients
  - CDC: https://www.cdc.gov/coronavirus/2019-ncov/index.html.
- Information for health systems
  - www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance
- Follow local health advice about hygiene strategies and use of personal protective equipment as new information becomes available in your country or region

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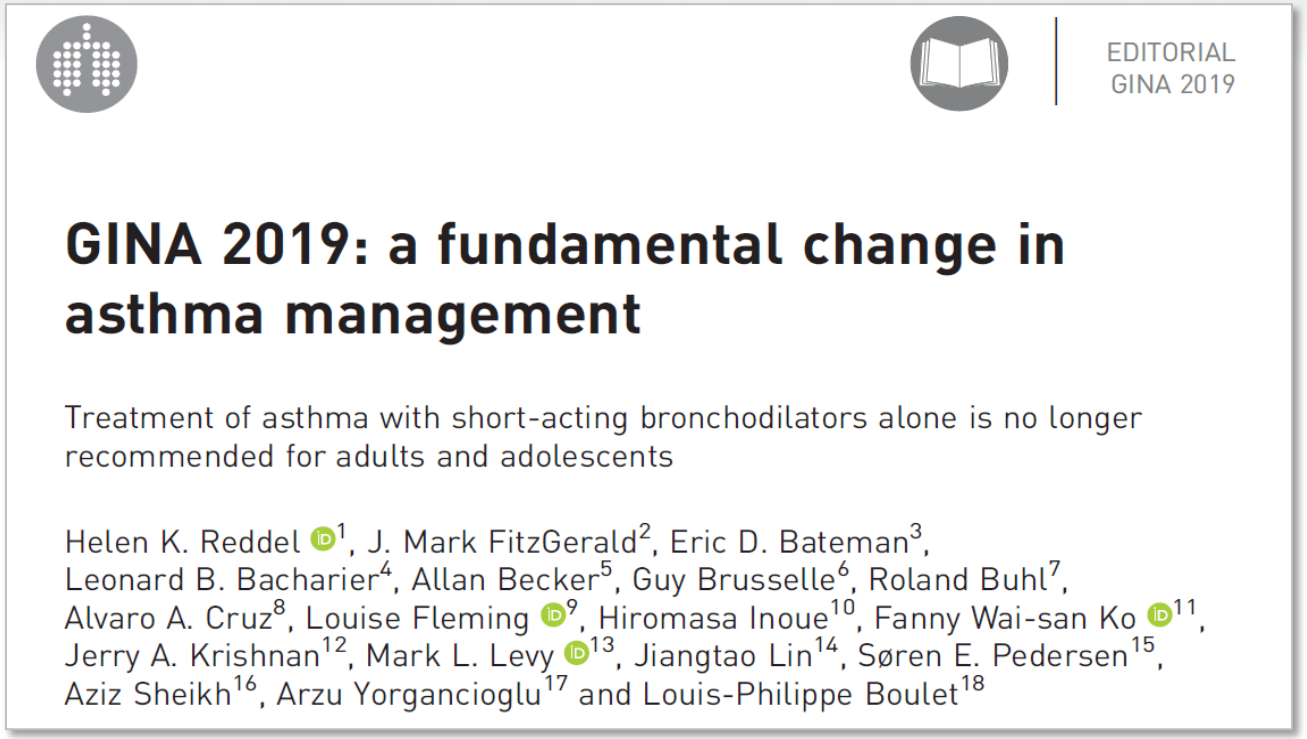
POTENTIAL INCREASING ROLE OF ICS

A reminder – the key change in GINA 2019



EDITORIAL
GINA 2019

GINA 2019: a fundamental change in asthma management

Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents

Helen K. Reddel[1], J. Mark FitzGerald[2], Eric D. Bateman[3], Leonard B. Bacharier[4], Allan Becker[5], Guy Brusselle[6], Roland Buhl[7], Alvaro A. Cruz[8], Louise Fleming[9], Hiromasa Inoue[10], Fanny Wai-san Ko[11], Jerry A. Krishnan[12], Mark L. Levy[13], Jiangtao Lin[14], Søren E. Pedersen[15], Aziz Sheikh[16], Arzu Yorgancioglu[17] and Louis-Philippe Boulet[18]

@ERSpublications
GINA no longer recommends treating adults/adolescents with asthma with short-acting bronchodilators alone. Instead, they should receive symptom-driven (in mild asthma) or a daily corticosteroid-containing inhaler, to reduce risk of severe exacerbations. http://bit.ly/310LLzE

Cite this article as: Reddel HK, FitzGerald JM, Bateman ED, *et al.* GINA 2019: a fundamental change in asthma management. *Eur Respir J* 2019; 53: 1901046 [https://doi.org/10.1183/13993003.01046-2019].

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Background to changes in 2019 - the risks of 'mild' asthma

- Patients with apparently mild asthma are at risk of serious adverse events
  - 30–37% of adults with acute asthma
  - 16% of patients with near-fatal asthma
  - 15–20% of adults dying of asthma

  } had symptoms less than weekly in previous 3 months *(Dusser, Allergy 2007)*

- Exacerbation triggers are variable (viruses, pollens, pollution, poor adherence)
- Inhaled SABA has been first-line treatment for asthma for 50 years
  - This dates from an era when asthma was thought to be a disease of bronchoconstriction
  - Patient satisfaction with, and reliance on, SABA treatment is reinforced by its rapid relief of symptoms, its prominence in ED and hospital management of exacerbations, and low cost
  - Patients commonly believe that *"My reliever gives me control over my asthma"*, so they often don't see the need for additional treatment

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Background to changes in 2019 - the risks of SABA-only treatment

- Regular or frequent use of SABA is associated with adverse effects
  - β-receptor downregulation, decreased bronchoprotection, rebound hyperresponsiveness, decreased bronchodilator response *(Hancox, Respir Med 2000)*
  - Increased allergic response, and increased eosinophilic airway inflammation *(Aldridge, AJRCCM 2000)*
- Higher use of SABA is associated with adverse clinical outcomes
  - Dispensing of ≥3 canisters per year (average 1.7 puffs/day) is associated with higher risk of emergency department presentations *(Stanford, AAAI 2012)*
  - Dispensing of ≥12 canisters per year is associated with higher risk of death *(Suissa, AJRCCM 1994)*

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The 12-year history behind changes in GINA 2019

- Since 2007, GINA has been actively seeking interventions for mild asthma
  - to reduce the risk of asthma-related exacerbations and death
  - to provide consistent messaging about the goals of asthma treatment, including prevention of exacerbations, across the spectrum of asthma severity
  - to avoid establishing patient reliance on SABA early in the course of the disease
- GINA emphasized poor adherence as a modifiable risk factor for exacerbations
  - When the reliever is SABA, poor adherence with maintenance controller exposes the patient to risks of SABA-only treatment
- GINA members repeatedly sought funding for RCTs of as-needed ICS-formoterol for risk reduction in mild asthma
  - Eventually culminated in 2014 with the initiation of the SYGMA studies, published in 2018 *(O'Byrne NEJMed 2018; Bateman NEJMed 2018)*

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GINA 2019 – landmark changes in asthma management

- For safety, GINA no longer recommends SABA-only treatment for Step 1
  - This decision was based on evidence that SABA-only treatment increases the risk of severe exacerbations, and that adding any ICS significantly reduces the risk
- GINA now recommends that all adults and adolescents with asthma should receive ICS-containing controller treatment, to reduce the risk of serious exacerbations
  - The ICS can be delivered by regular daily treatment or, in mild asthma, by as-needed low dose ICS-formoterol
- This is a population-level risk reduction strategy
  - Other examples: statins, anti-hypertensives
  - Individual patients may not necessarily experience (or be aware of) short-term clinical benefit
  - The aim is to reduce the probability of serious adverse outcomes at a population level

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The main GINA treatment figure

- Personalized asthma management: Assess – Adjust – Review response
  - NOT just medications, NOT one-size-fits-all
- No changes from 2019 in preferred and 'other' treatment options
  - Additional supporting evidence for recommendations in Steps 1 and 2
  - Some formatting changes for clarity
- Separate figures for adults/adolescents, children 6–11 years and children ≤5 years
  - For children ≤5 years, see Chapter 6 of main GINA report

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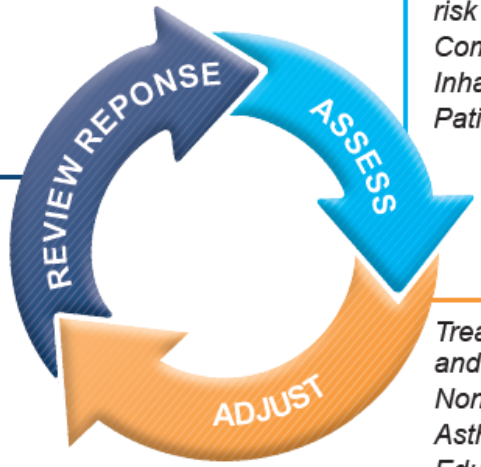
Box 3-5A

Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (including lung function)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down or up)
Education & skills training

Asthma medication options:
Adjust treatment up and down for individual patient needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	As-needed low dose ICS-formoterol *	Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *	Low dose ICS-LABA	Medium dose ICS-LABA	High dose ICS-LABA Refer for phenotypic assessment ± add-on therapy, e.g.tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R
Other controller options	*Low dose ICS taken whenever SABA is taken †*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †*	*Medium dose ICS, or low dose ICS+LTRA #*	*High dose ICS, add-on tiotropium, or add-on LTRA #*	*Add low dose OCS, but consider side-effects*
PREFERRED RELIEVER	As-needed low dose ICS-formoterol *		As-needed low dose ICS-formoterol for patients prescribed maintenance and reliever therapy‡		
Other reliever option	*As-needed short-acting β_2-agonist (SABA)*				

* *Data only with budesonide-formoterol (bud-form)*
† *Separate or combination ICS and SABA inhalers*
‡ *Low-dose ICS-form is the reliever only for patients prescribed bud-form or BDP-form maintenance and reliever therapy*
\# *Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV1 >70% predicted*

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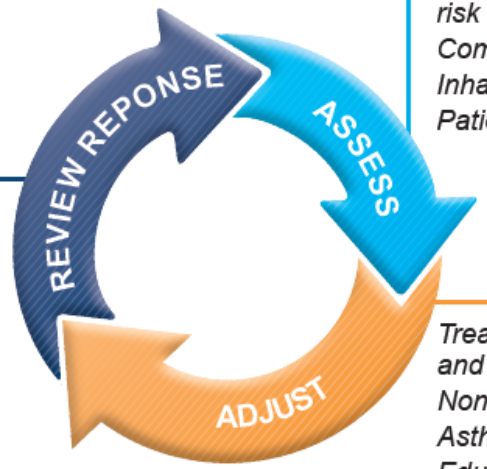
Box 3-5A

Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response



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ICS-formoterol is the preferred reliever for patients prescribed maintenance and reliever therapy. For other ICS-LABAs, the reliever is SABA

Asthma medication options:
Adjust treatment up and down for individual patient needs

	STEP 1	STEP 2	STEP 3		
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	As-needed low dose ICS-formoterol *	Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *	Low dose ICS-LABA		e.g.tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R
Other controller options	*Low dose ICS taken whenever SABA is taken †*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †*	*Medium dose ICS, or low dose ICS+LTRA #*	*High dose ICS, add-on tiotropium, or add-on LTRA #*	*Add low dose OCS, but consider side-effects*
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\# *Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV1 >70% predicted*

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Additional supporting evidence

- Two additional RCTs of as-needed low dose budesonide-formoterol in mild asthma
  - 12-month studies, open-label, no twice-daily placebo, i.e. the way it would be used in real life
  - Novel START *(Beasley et al, NEJM 2019, n=668)* and PRACTICAL *(Hardy et al, Lancet 2019, independent study, n=885)*
  - Significant reduction in severe exacerbations vs SABA alone, and vs maintenance ICS, with small or no difference in symptom control, and lower average ICS dose
  - Patients in RCTs of this regimen in mild asthma now total n=9,565
- Both of these studies included inflammatory markers
  - FeNO was significantly reduced by as-needed ICS-formoterol (with average 3-5 doses per week)
  - Reduction in risk of severe exacerbations with as-needed ICS-formoterol was independent of baseline characteristics, including blood eosinophils and exhaled nitric oxide
- An additional RCT of taking ICS whenever SABA is taken (separate inhalers)
  - ASIST, in African-American children 6-17 years with mild asthma, compared with physician-adjusted treatment *(Sumino et al, JACI in Pract 2019, n=206)*
  - No difference in outcomes but significantly less dosage of inhaled corticosteroids

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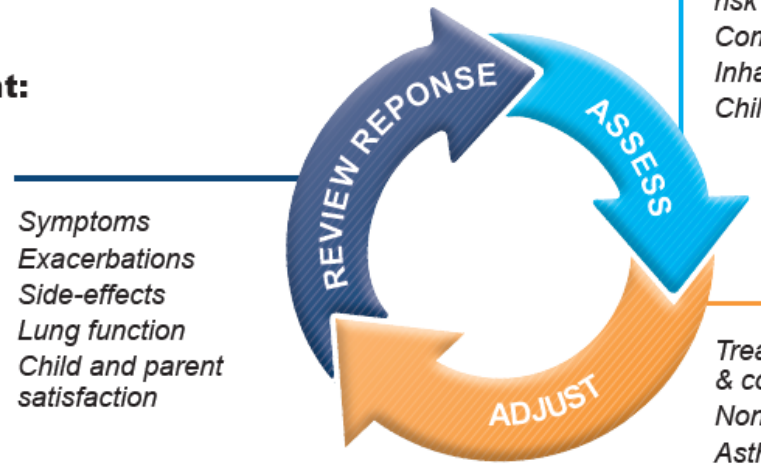
Box 3-5B

Children 6-11 years

Personalized asthma management:
Assess, Adjust, Review response



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Asthma medications (adjust down or up)
Education & skills training

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms		Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)	Low dose ICS-LABA or medium dose ICS	Medium dose ICS-LABA Refer for expert advice	Refer for phenotypic assessment ± add-on therapy, e.g. anti-IgE
Other controller options	*Low dose ICS taken whenever SABA taken*; or daily low dose ICS*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken**	*Low dose ICS + LTRA*	*High dose ICS-LABA, or add-on tiotropium, or add-on LTRA*	*Add-on anti-IL5, or add-on low dose OCS, but consider side-effects*
RELIEVER	*As-needed short-acting β_2-agonist (SABA)*				

* *Separate ICS and SABA inhalers*

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CURRENT APPROVED ICS MEDICATIONS FOR CHILDREN IN USA

- Beclomethasone HFA: 5 yrs and up
- Budesonide DPI: 6 yrs and up
- Budesonide suspension: 1 year and up
- Ciclesonide HFA: 12 yrs and up
- Fluticasone propionate: 4 yrs and up
- Fluticasone propionate DPI: 4 years and up
- Fluticasone furoate DPI: 5 yrs and up
- Mometasone HFA: 5 years and up
- Mometasone DPI: 4 years and up

APPROVED COMBINATION MEDICATIONS AND ANTICHOLINERGICS FOR CHILDREN IN USA

- Formoterol/budesonide HFA: 6 yrs and up
- Salmeterol/fluticasone propionate DPI: 4 yrs and up
- Salmeterol/fluticasone propionate HFA: 12 yrs and up
- Formoterol/mometasone HFA: 5 yrs and up
- Tiotropium inhalation 1.25mcg: 6 yrs and up

APPROVED BIOLOGICS IN ASTHMA FOR CHILDREN IN USA

- Omalizumab (anti-IgE): 6 yrs and up
- Mepolizumab (anti-IL5): 6 yrs and up
- Dupilumab (anti-IL4/IL 13): 6 yrs and up ONLY FOR ATOPIC DERMATITIS
- Biologics are considered for moderate to severe asthma and are prescribed after referral to specialist for phenotypic markers

Low, medium and high doses of different ICS

- NOT a table of equivalence
  - Suggested total daily doses for ‘low’, ‘medium’ and ‘high’ dose treatment options
  - Based on available studies (very few) and product information
  - Does NOT imply potency equivalence
- Doses may be country-specific depending on local availability, regulatory labelling and clinical guidelines
- Clinical relevance
  - Low dose ICS provides most of the clinical benefit of ICS for most patients with asthma
  - However, ICS responsiveness varies between patients, so some patients may need medium dose ICS if their asthma is uncontrolled despite good adherence and correct technique
  - High dose ICS (in combination with LABA or separately) is needed by very few patients
    - Its long-term use is associated with an increased risk of local and systemic side-effects, which must be balanced against the potential benefits

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Low, medium and high ICS doses: adults/adolescents

Adults and adolescents (12 years and older)			
Inhaled corticosteroid	**Total daily ICS dose (mcg)**		
	Low	**Medium**	**High**
Beclometasone dipropionate (pMDI, standard particle, HFA)	200-500	>500-1000	>1000
Beclometasone dipropionate (pMDI, extrafine particle*, HFA)	100–200	>200–400	>400
Budesonide (DPI)	200–400	>400–800	>800
Ciclesonide (pMDI, extrafine particle*, HFA)	80–160	>160–320	>320
Fluticasone furoate (DPI)	100		200
Fluticasone propionate (DPI)	100–250	>250–500	>500
Fluticasone propionate (pMDI, standard particle, HFA)	100–250	>250–500	>500
Mometasone furoate (DPI)	200		400
Mometasone furoate (pMDI, standard particle, HFA)	200-400		>400

This is NOT a table of equivalence. These are suggested total daily doses for the 'low', 'medium' and 'high' dose treatment options with different ICS.

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; pMDI: pressurized metered dose inhaler (non-CFC); * see product information

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Low, medium and high ICS doses: children 6-11 years

Children 6–11 years			
Inhaled corticosteroid	Total daily ICS dose (mcg)		
	Low	Medium	High
Beclometasone dipropionate (pMDI, standard particle, HFA)	100–200	>200–400	>400
Beclometasone dipropionate (pMDI, extrafine particle*, HFA)	50-100	>100-200	>200
Budesonide (DPI)	100–200	>200–400	>400
Budesonide (nebules)	250–500	>500–1000	>1000
Ciclesonide (pMDI, extrafine particle*, HFA)	80	>80-160	>160
Fluticasone furoate (DPI)	50		n.a.
Fluticasone propionate (DPI)	50-100	>100-200	>200
Fluticasone propionate (pMDI, standard particle, HFA)	50-100	>100-200	>200
Mometasone furoate (pMDI, standard particle, HFA)	100		200

This is NOT a table of equivalence. These are suggested total daily doses for the 'low', 'medium' and 'high' dose treatment options with different ICS.

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; pMDI: pressurized metered dose inhaler (non-CFC); * see product information

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Low, medium and high ICS doses: children 5 years and younger

Inhaled corticosteroid	Low total daily dose (mcg) (age-group with adequate safety and effectiveness data)
BDP (pMDI, standard particle, HFA)	100 (ages 5 years and older)
BDP (pMDI, extrafine particle, HFA)	50 (ages 5 years and older)
Budesonide nebulized	500 (ages 1 year and older)
Fluticasone propionate (pMDI, standard particle, HFA)	50 (ages 4 years and older)
Fluticasone furoate (DPI)	Not sufficiently studied in children 5 years and younger)
Mometasone furoate (pMDI, standard particle, HFA)	100 (ages 5 years and older)
Ciclesonide (pMDI, extrafine particle, HFA)	Not sufficiently studied in children 5 years and younger

This is NOT a table of equivalence. These are suggested total daily doses for the 'low' dose treatment options with different ICS.

BDP: beclometasone dipropionate; DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; pMDI: pressurized metered dose inhaler (non-CFC)

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Initial asthma treatment – where to start?

- Should all patients start at Step 1?

- Table about initial treatment since 2014, but not widely known
  - → New figures created (two versions)

Box 3-4, GINA 2019

Box 3-4. Initial asthma treatment - recommended options for adults and adolescents

Presenting symptoms	Preferred INITIAL treatment
All patients	**SABA-only treatment (without ICS) is not recommended**
Infrequent asthma symptoms, e.g. less than twice a month	• As-needed low dose ICS-formoterol (Evidence B) Other options include taking ICS whenever SABA is taken, in combination or separate inhalers (Evidence B)
Asthma symptoms or need for reliever twice a month or more	• Low dose ICS** with as-needed SABA (Evidence A), or • As-needed low dose ICS-formoterol (Evidence A) Other options include LTRA (less effective than ICS, Evidence A), or taking ICS whenever SABA is taken either in combination or separate inhalers (Evidence B). Consider likely adherence with controller if reliever is SABA.
Troublesome asthma symptoms most days; or waking due to asthma once a week or more, especially if any risk factors exist (Box 2-2B)	• Low dose ICS-LABA† as maintenance and reliever therapy with ICS-formoterol# (Evidence A) or as conventional maintenance treatment with as-needed SABA (Evidence A), OR • Medium dose ICS† with as-needed SABA (Evidence A)
Initial asthma presentation is with severely uncontrolled asthma, or with an acute exacerbation	• Short course of oral corticosteroids AND start regular controller treatment with high-dose ICS (Evidence A), or medium-dose ICS-LABA# (Evidence D)
Before starting initial controller treatment	
• Record evidence for the diagnosis of asthma, if possible • Record the patient's level of symptom control and risk factors, including lung function (Box 2-2, p17) • Consider factors influencing choice between available treatment options (Box 3-3, p27) • Ensure that the patient can use the inhaler correctly • Schedule an appointment for a follow-up visit	
After starting initial controller treatment	
• Review patient's response (Box 2-2, p.31) after 2–3 months, or earlier depending on clinical urgency • See Box 3-5 for recommendations for ongoing treatment and other key management issues • Step down treatment once good control has been maintained for 3 months (Box 3-7, p.56).	

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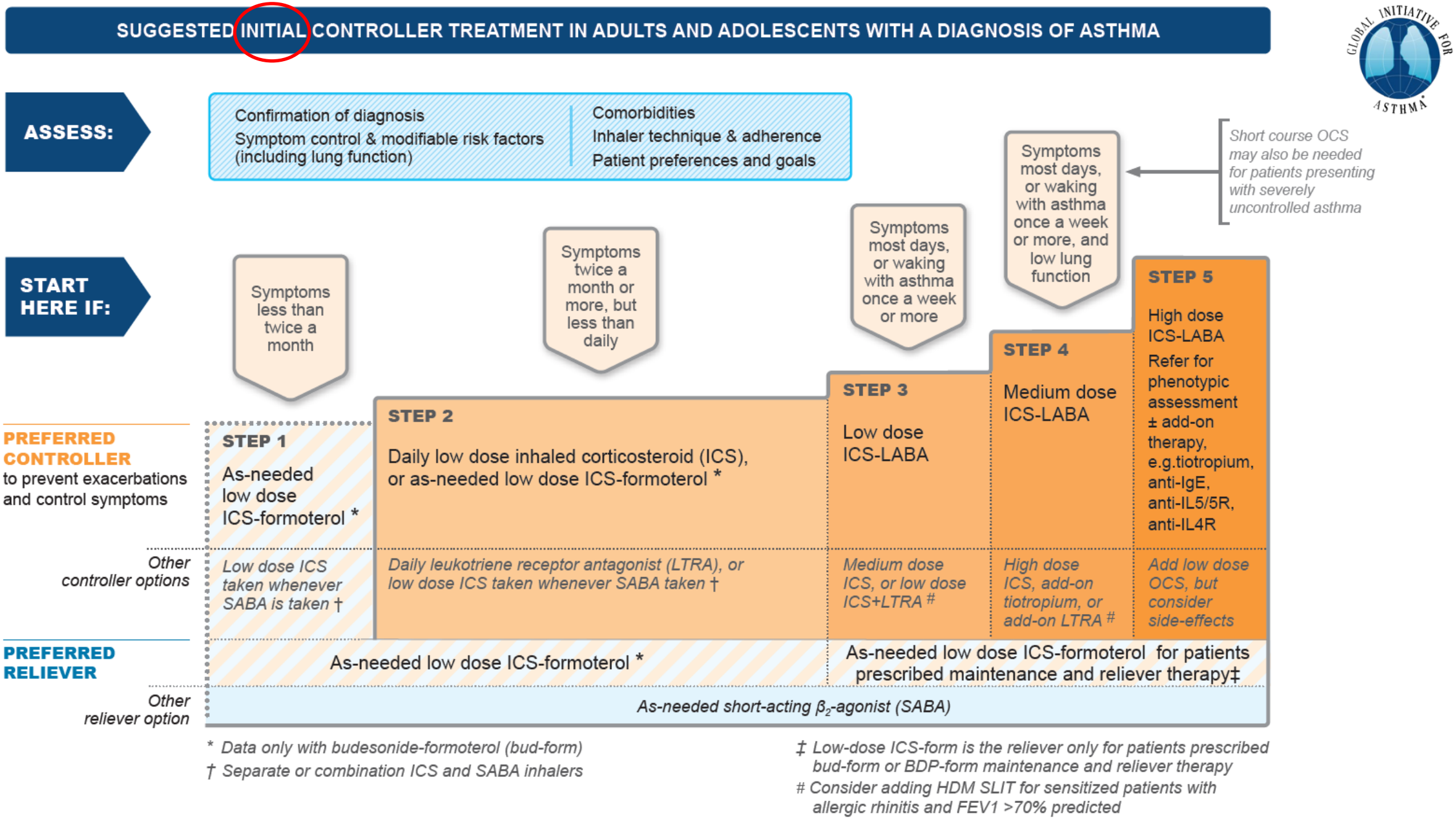
SUGGESTED INITIAL CONTROLLER TREATMENT IN ADULTS AND ADOLESCENTS WITH A DIAGNOSIS OF ASTHMA



* Data only with budesonide-formoterol (bud-form)

† Separate or combination ICS and SABA inhalers

‡ Low-dose ICS-form is the reliever only for patients prescribed bud-form or BDP-form maintenance and reliever therapy

Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV1 >70% predicted

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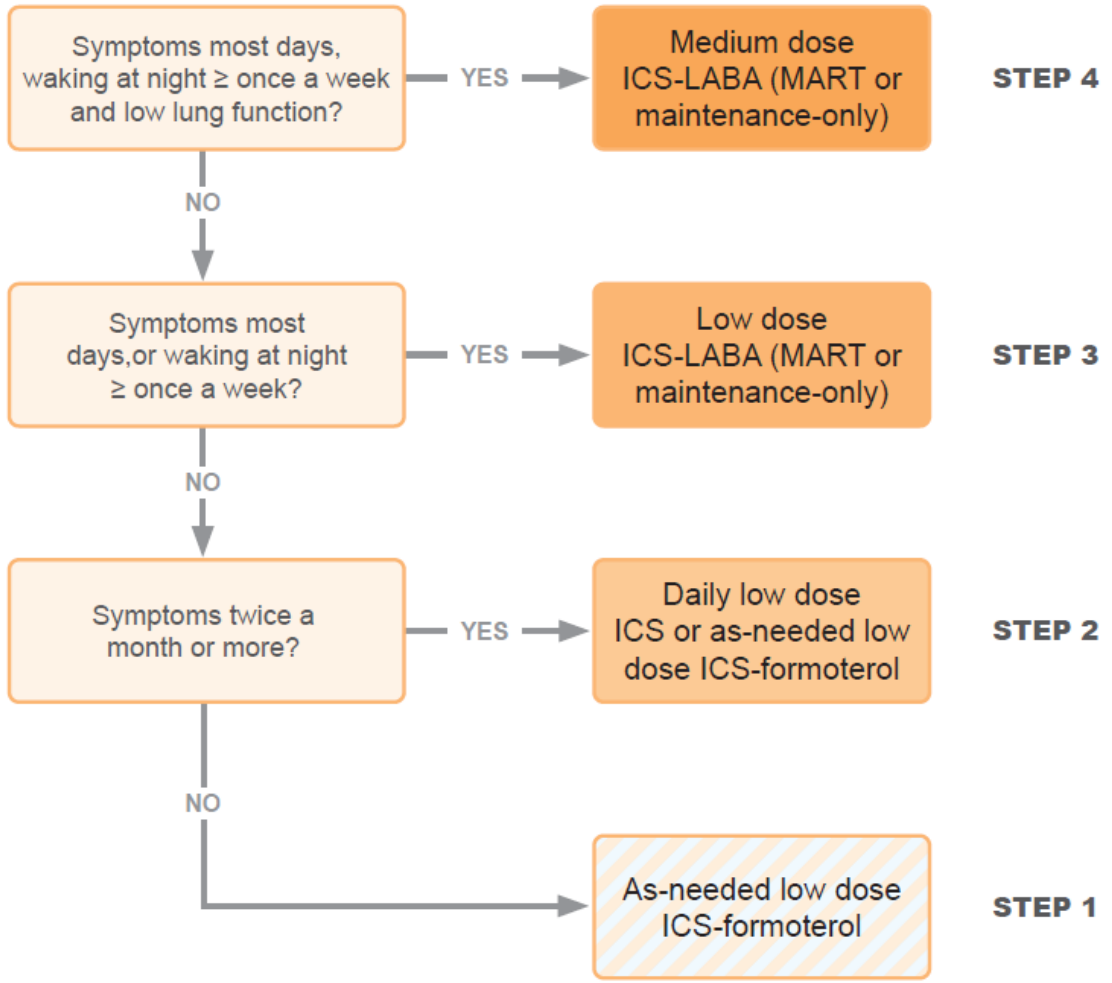
SUGGESTED INITIAL CONTROLLER TREATMENT IN ADULTS AND ADOLESCENTS WITH A DIAGNOSIS OF ASTHMA

FIRST ASSESS:

- Confirmation of diagnosis
- Symptom control & modifiable risk factors (including lung function)
- Comorbidities
- Inhaler technique & adherence
- Patient preferences & goals



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SUGGESTED INITIAL CONTROLLER TREATMENT IN CHILDREN 6-11 YEARS WITH A DIAGNOSIS OF ASTHMA

ASSESS:

- Confirmation of diagnosis
- Symptom control & modifiable risk factors (including lung function)
- Comorbidities
- Inhaler technique & adherence
- Child and parent preferences and goals

START HERE IF:

Symptoms less than twice a month	Symptoms twice a month or more, but less than daily	Symptoms most days, or waking with asthma once a week or more	Symptoms most days, or waking with asthma once a week or more, and low lung function

Short course OCS may also be needed for patients presenting with severely uncontrolled asthma

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms		Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)	Low dose ICS-LABA or medium dose ICS	Medium dose ICS-LABA Refer for expert advice	Refer for phenotypic assessment ± add-on therapy, e.g. anti-IgE
Other controller options	*Low dose ICS taken whenever SABA taken*; or daily low dose ICS*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken**	*Low dose ICS + LTRA*	*High dose ICS-LABA, or add-on tiotropium, or add-on LTRA*	*Add-on anti-IL5, or add-on low dose OCS, but consider side-effects*
RELIEVER	*As-needed short-acting β_2-agonist (SABA)*				

* *Separate ICS and SABA inhalers*

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SUGGESTED INITIAL CONTROLLER TREATMENT IN CHILDREN 6-11 YEARS WITH A DIAGNOSIS OF ASTHMA

FIRST ASSESS:

- Confirmation of diagnosis
- Symptom control & modifiable risk factors (including lung function)
- Comorbidities
- Inhaler technique & adherence
- Child and parent preferences and goals

IF: / **START WITH:**

Symptoms most days, waking at night ≥ once a week and low lung function? — YES → Medium dose ICS-LABA or refer for expert advice — **STEP 4**

Short course OCS may also be needed for patients presenting with severely uncontrolled asthma

NO

Symptoms most days,or waking at night ≥ once a week? — YES → Low dose ICS-LABA or medium dose ICS — **STEP 3**

NO

Symptoms twice a month or more? — YES → Daily low dose ICS — **STEP 2**

NO

As-needed SABA — **STEP 1**

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Assessment of symptom control

- Frequency of SABA use is included in symptom control assessment
  - Higher SABA use is associated with worse outcomes, even in patients taking ICS

Box 2-2. GINA assessment of asthma control in adults, adolescents and children 6–11 years

A. Asthma symptom control		Level of asthma symptom control		
In the past 4 weeks, has the patient had:		**Well controlled**	**Partly controlled**	**Uncontrolled**
• Daytime asthma symptoms more than twice/week?	Yes☐ No☐	None of these	1–2 of these	3–4 of these
• Any night waking due to asthma?	Yes☐ No☐			
• Reliever (SABA) for symptoms more than twice/week?*	Yes☐ No☐			
• Any activity limitation due to asthma?	Yes☐ No☐			

- Our current view is that frequency of ICS-formoterol use should not be included in symptom control assessment, particularly in patients not taking maintenance ICS
  - The as-needed ICS-formoterol is providing the patient's controller therapy
  - Further data awaited: this issue will be reviewed again next year

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KEY POINTS ABOUT WHEEZING AND ASTHMA IN CHILDREN <5 YRS

- Recurrent wheezing with URTI in children <5 yrs is common but deciding whether it is asthma is difficult
- Previous classification of symptom-based (episodic wheeze or multi-trigger wheeze) or temporal-based (transient, persistent and late-onset wheeze) do not identify stable phenotypes and clinical usefulness is unclear
- A probability approach of symptoms during and between viral infections is likely more useful in predicting asthma

SYMPTOM-BASED PROBABILITY OF ASTHMA IN CHILDREN <5 YRS

- Few have asthma
  - Symptoms of cough, wheeze, heavy breathing for <10 days during URTI
  - 2-3 episodes/year
  - No symptoms between episodes
- Some have asthma
  - Symptoms of cough, wheeze, heavy breathing for >10 days during URTI
  - >3 episodes/yr, severe episodes and/or night worsening
  - Occasional cough, wheeze between episodes
- Most have asthma
  - Symptoms >10 days during URTI
  - >3 episodes/yr, severe episodes and/or night worsening
  - Symptoms between episodes of cough, wheeze, heavy breathing while laughing, playing
  - Allergic sensitization, atopic dermatitis, food allergy and/or family history of asthma
- Therapeutic trial with low dose ICS for 2-3 months associated with improvement in symptoms followed by worsening after discontinuation is a strong predictor for asthma

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MAJOR CHANGE IN MEDICATION RECOMMENDATIONS IS CONCERN FOR ADDING OR CONTINUING MONTELUKAST

Adverse effects with montelukast

- FDA boxed warning in March 2020 about risk of serious neuropsychiatric events, including suicidality, with montelukast
  - Includes suicidality in adults and adolescents
  - Nightmares and behavioral problems in children
- Before prescribing montelukast, health professionals should consider its benefits and risks, and patients should be counselled about the risk of neuropsychiatric events

FDA requires Boxed Warning about serious mental health side effects for asthma and allergy drug montelukast (Singulair); advises restricting use for allergic rhinitis

Risks may include suicidal thoughts or actions

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CHANGES IN ASSESSING SEVERITY OF EXACERBATION IN CHILDREN <5 YRS OF AGE

- Altered consciousness: No (mild); Yes (severe)
- Oximetry: >95% (mild); <92% (severe)
- Speech: sentences (mild); words (severe)
- Heart rate: <100 bpm 9mild); >180bpm 1-3 yrs or >150 bpm 4-5 yrs (severe)
- RR: ≤ 40/minute (mild); >40/minute (severe)
- Central cyanosis: absent (mild); present (severe)
- Wheeze intensity: variable (mild); silent chest (severe)
- Sub-glottic/sub-sternal retractions removed as too subjective

GINA methodology – additional details

- The GINA report is a global strategy document
  - Regulatory approvals and submissions differ from country to country
  - Many recommendations are 'off-label' in various countries, particularly for paediatrics
  - → The term 'off-label' is no longer used in the GINA report or slides
- For new therapies
  - Regulatory agencies often receive more safety data than are in peer-reviewed literature
  - → GINA makes recommendations based on the best available evidence, after approval by at least one major regulatory agency (e.g. EMA, FDA)
- For existing medications with evidence for new regimens or populations
  - If satisfied with evidence for safety and effectiveness, GINA may consider making recommendations that are not covered by a regulatory indication in any country at the time
  - Examples: long-term macrolides for moderate-severe asthma (2018); as-needed ICS-formoterol, or taking ICS whenever SABA is taken, for mild asthma (2019)
- When assessing and treating patients
  - Use your own professional judgment
  - Take into account local and national guidelines and payer eligibility criteria, and licensed drug doses

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THANK YOU & QUESTIONS

My Happy Place!