New Approaches In Asthma Diagnosis

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Age- and gender-specific incidence of new asthma diagnosis from childhood to late adulthood

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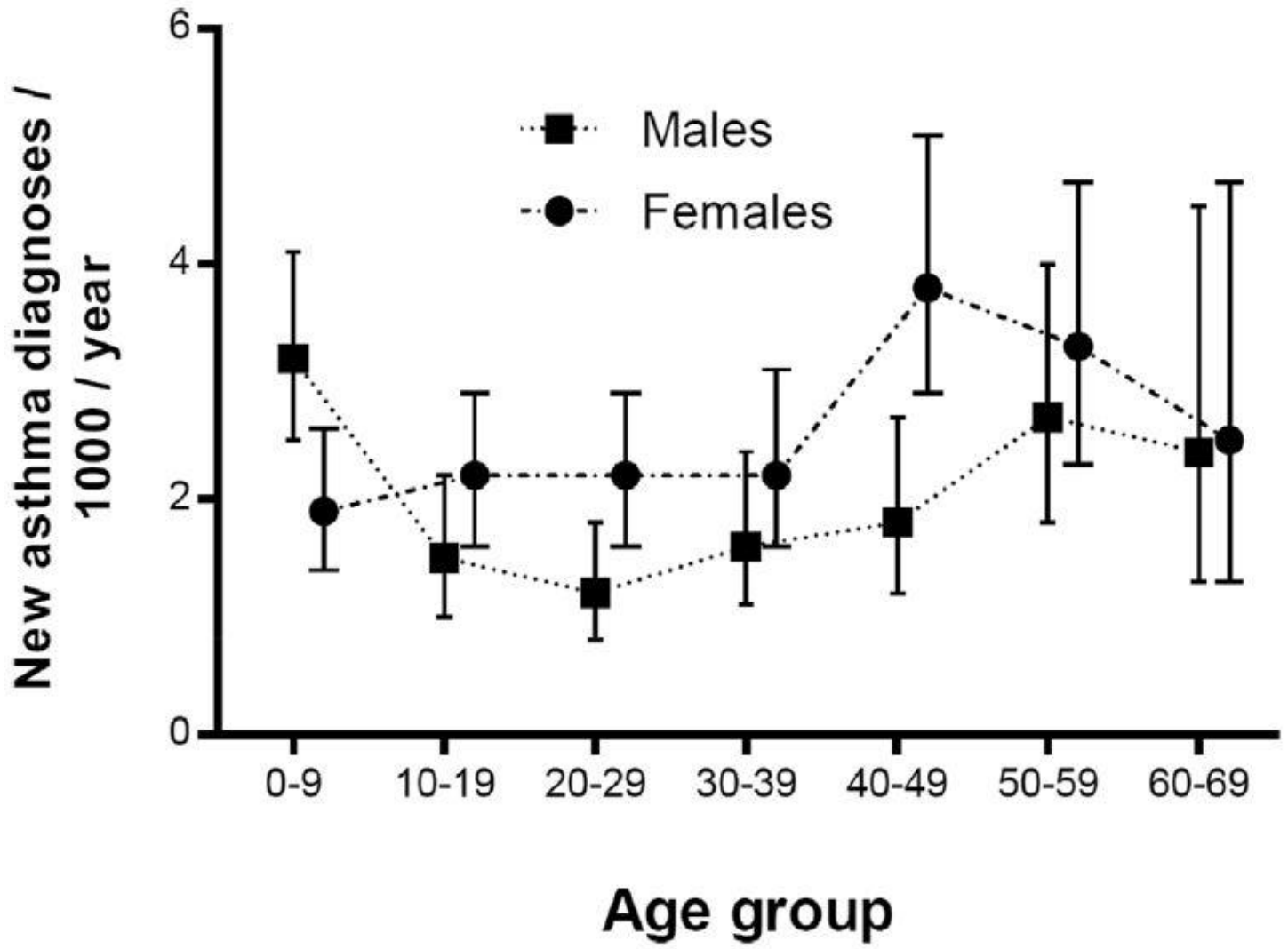
- Asthma with onset in adulthood seems to have poorer prognosis
- Incidence of Asthma diagnosis peaked in Young boys (0-9) and middle-aged women (40-49)
- Prevalence is higher in boys than girls but higher in women than men.
- The gender reversal occurred in adolescence
- Median age at diagnosis was 21 years in men and 29 years in women.
- The proportion of adult-diagnosed asthma were 58.4% in men, and 67.8% in women


New asthma diagnoses / 1000 / year
6
4
2
0
Males
Females
0-9
10-19
20-29
30-39
40-49
50-59
60-69
Age group

Improving global diagnosis and management of Asthma in children

State of the art review

OPEN ACCESS

Improving the global diagnosis and management of asthma in children

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ABSTRACT

Asthma is the most common chronic condition in children worldwide. It affects daytime activities, sleep and school attendance and causes anxiety to parents, families and other carers. The quality of asthma diagnosis and management globally still needs substantial improvement. From infancy to the teenage years, there are age-specific challenges, including both underdiagnosis and overdiagnosis with stigma-related barriers to treatment in some cultures and in adolescents. Guidelines are increasingly evidence based, but their impact on improving outcomes has been negligible in many parts of the world, often due to lack of implementation. New thinking is needed to enable

a separate clinical entity.[2] The pathophysiology of asthma in all ages of patients was thought to primarily involve bronchial smooth muscle hypertrophy with intermittent smooth muscle spasm.[3 4] With greater knowledge of the underlying immune mechanisms,[5 6] 'asthma' gradually became used as a term for an inflammatory condition with ICS recommended as the first-line controller[7]; but 'asthma' is now no more a diagnosis than 'anaemia' or 'arthritis' and should only be used as an umbrella term to describe a clinical spectrum that includes symptoms of wheeze, breathlessness, chest tightness and cough.[6] Some have questioned whether the term 'asthma' should be abandoned altogether

Age specific challenges to asthma diagnosis and management

- Diagnosis is challenging in the first 3 years of life both identifying whether the child has an airway disease at all and in recognizing the underlying pathophysiology
- Routine measuring blood eosinophil and/or IgE levels, performing skin prick tests and attempting lung function and bronchodilator responsiveness assessments

↓

May not be feasible in some below 3 years age and in resource poor region

↓

Cause Undertreatment and Overtreatment

Age specific challenges to asthma diagnosis and management

- Identification of children whose symptoms will persist needs to be improved
- The Melbourne longitudinal cohort study: “Those with initial severe asthma were more likely have symptoms persisting throughout, with lung function remaining low from study enrolment”
- Among children with mild-to-moderate asthma, 75% have been shown to have abnormal lung growth in childhood, often with a further decline in early adulthood.

Age specific challenges to asthma diagnosis and management

- Teenagers may stop medication due to stigma and embarrassment.
- Barrier to asthma management is more common in teenage boys

Differential Diagnosis and Comorbidities

frontiers in Pediatrics

REVIEW
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Asthma: Differential Diagnosis and Comorbidities

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Childhood asthma remains a multifactorial disease with heterogeneous clinical phenotype and complex genetic inheritance. The primary aim of asthma management is to achieve control of symptoms, in order to reduce the risk of future exacerbations and progressive loss of lung function, which results especially challenging in patients with difficult asthma. When asthma does not respond to maintenance treatment, firstly, the correct diagnosis needs to be confirmed and other diagnosis, such as cystic fibrosis, primary ciliary dyskinesia, immunodeficiency conditions or airway and vascular malformations need to be excluded. If control remains poor after diagnostic

When to look for other diagnosis

- The persistent condition of “problematic respiratory symptoms unresponsive to prescribed asthma therapy” need to motivate a clinical full reassessment to exclude that the patient was wrongly labeled with the diagnosis of asthma.

- All possible condition which might mimic asthma need to be considered.

- Some disease, might also coexist with a diagnosis of Asthma.

Alternative diagnosis	When to suspect	Useful diagnostic examinations
Cystic fibrosis and bronchiectasis	Daily cough productive of sputum, clubbing, malabsorption and failure to thrive, recurrent chest infections, airways bacterial colonization	Sweat chloride test, Genetic tests, Swab culture, Lung Function tests, Chest CT
Immunodeficiency	Recurrent airway infections, Systemic infections (from a few months of age)	Immunoglobulins and specific tests
Primary ciliary dyskinesia	Neonatal upper airway symptoms, Chronic rhinosinusitis, Recurrent otitis media, Daily wet cough, Laterality defects	Nasal NO, HSVM, EM, Genetic tests, Immunofluorescence, Chest CT
Protracted Bacterial Bronchitis	Cronich wet cough, Poor response to Beta-2 agonists, Good response to prolonged course of antibiotics	Often no need of examinations, Swab culture, Bronchoscopy with BAL
Airway malacia	Monophonic wheeze when the child is active, High risk setting (i.e., pt operated for tracheo-esophageal fistula or vascular ring), Presence of associated stridor	Lung function test (truncated expiratory flow in spirometry), Flexible bronchoscopy, Dynamic CT
Airway foreign body	Abrupt onset of symptoms, History of choking, Unilateral monophonic wheeze, Focal hyperinflation of lung	Bronchoscopy, chest x-ray
Habit cough	Prolonged dry, honking cough; Absence of cough during sleep; Absence of any physical findings	Medical investigations should be avoided
Vocal cord dysfunction	Absence of structural abnormalities, Sudden worsening of "asthma" symptoms, No response to asthma medications	Video of an attack, Laryngoscopy during attack
Bronchiolitis obliterans	History of severe viral respiratory infection in the first 3 years of life	CT scan (characteristic mosaic pattern and air trapping)

CT, computed tomography; EM, eletcron microscopy; HSVM, high speed video microscopy; NO, nitric oxide.

Asthma plus: Co-morbidities

- When symptoms remain uncontrolled despite proper treatment, and all alternate diagnosis have been excluded, possible comorbidities need to be investigated as
  - they maybe coincidental finding
  - or they may contribute directly for the severity of asthma.

- Establishing the real impact and the causative effect of comorbidities on asthma control it is complicated.
- Conditions are listed below:
- Obesity
- GERD
- Food Allergy
- Rhinosinusitis

Obesity

- A risk factor for poor asthma control
- Obese children showed more severe exacerbations (Greater risk of admission to Pediatric ICU)
- Behavioral and weight reduction programs should be offered to Asthmatic obese patients to obtain weight reduction.

Rhinosinusitis

- Chronic Rhinosinusitis is a major disease condition with high morbidity and can influence lower airway disease status in adults
- Based on a cross-sectional Korean study with 17506 participants:
  - CRS as significantly related to asthma
  - CRS without nasal polyps was related to childhood onset asthma
  - CRS with nasal polyps is estimated in 7% of all asthmatics, whereas asthma is reported to occur in 26-48%of patients with CRS with nasal polyps
  - Patients with allergic rhinitis and/or chronic rhinosinusitis report poorer asthma control:
    - More exacerbations
    - More emergency visits
    - More difficulty achieving symptom control

GERD

- Symptoms of GERD is often coexist in children with severe asthma
- Micro-aspiration, acid stimulation of the esophagus and vagus nerve stimulation are the mechanism proposed
- GER can trigger VCD with consequent laryngeal dysfunction mimicking asthma symptom
- it has been proven that GER treatment does not improve asthma control
- symptoms triggered by GER are mimics of asthma symptoms, rather than exacerbating airway inflammation or airway hyper responsiveness.
- Specific examinations assessing for GER in order to exclude this comorbidity
  - impedance-pHmetry
  - and/or gastroesophageal
- A trial of treatment with PPI is recommended as the initial diagnostic step in symptomatic childre

Food Allergy

- There is a higher incidence of food allergy in asthmatic patients admitted to intensive care units
- Sometimes patients with food allergy report bronchospasm caused by ingestion or inhalation of the offending food.
- It is already showed that symptomatic sensitization to foods is associated with asthma and that the risk of asthma morbidity is higher in children with food allergy
- This risk is especially increased in children with high levels of food specific IgEs and multiple or severe food allergy
- Diagnosis of food allergy
  - suggestive clinical history,
  - positive skin prick tests and specific IgE,
  - positive oral food challenge
- Avoidance of offending food

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 *(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

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

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

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)*

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

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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

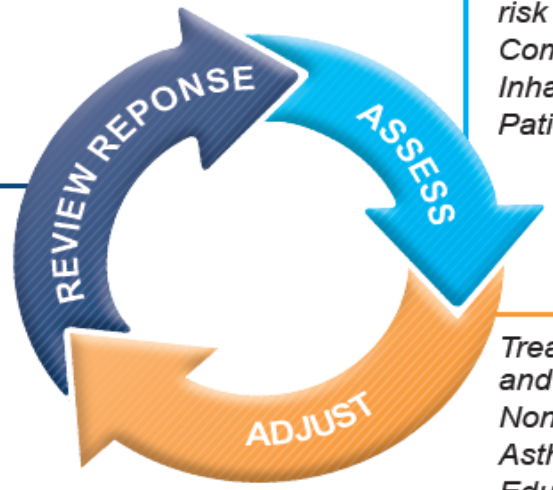
The main GINA treatment figure

- 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

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)*				

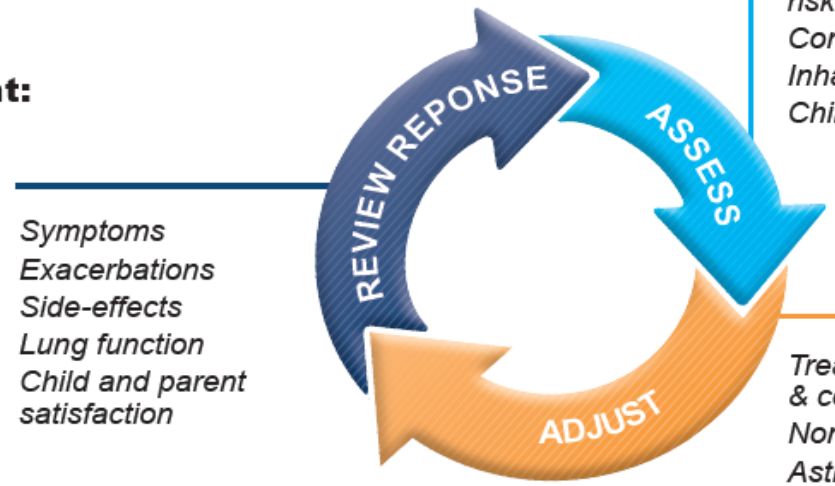
* *Data only with budesonide-formoterol (bud-form)*
† *Separate or combination ICS and SABA inhalers*

‡ *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*

Box 3-5B

Children 6-11 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
Child and parent preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Child and parent satisfaction

Treatment of modifiable risk factors & comorbidities
Non-pharmacological strategies
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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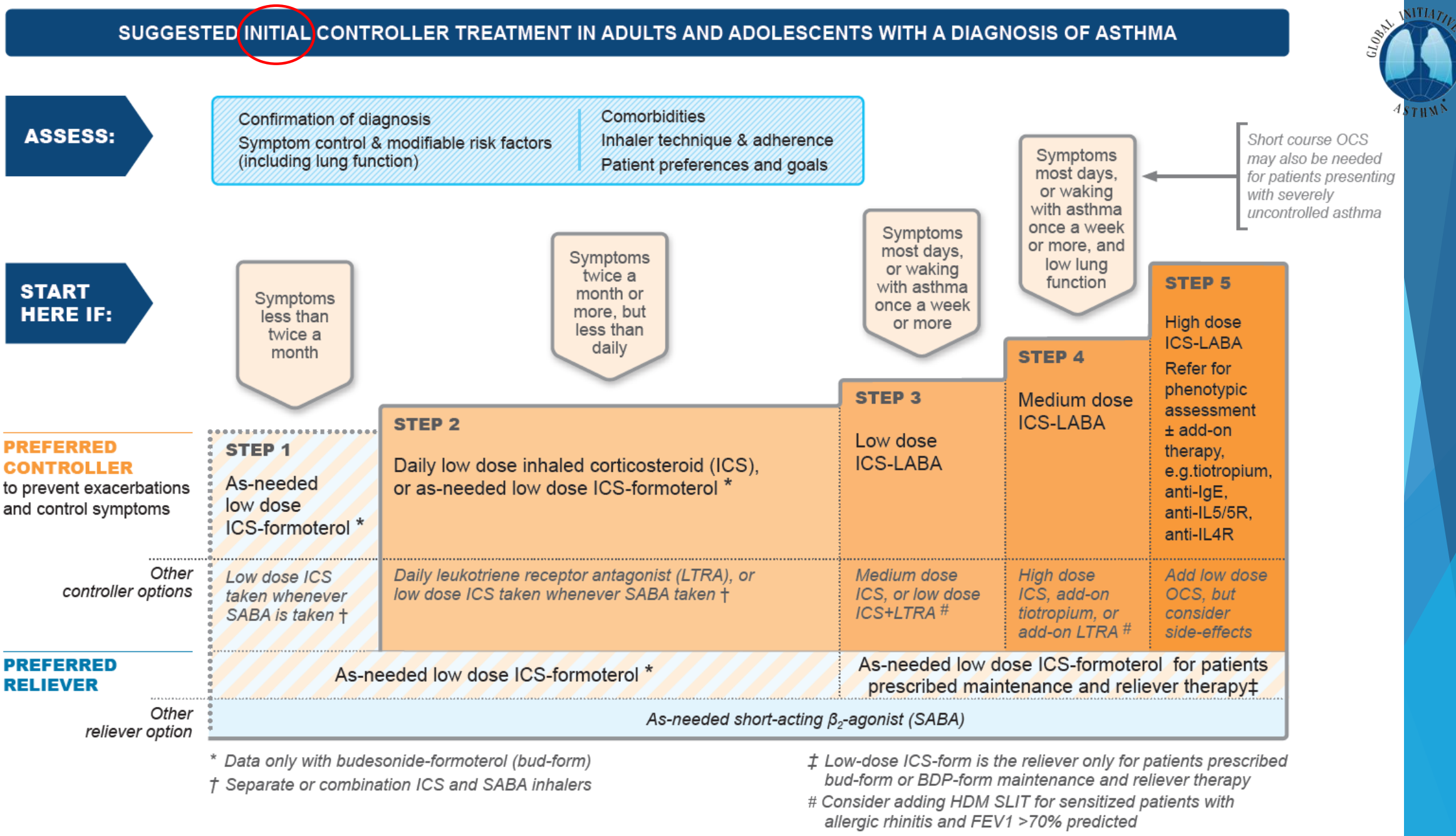
SUGGESTED INITIAL CONTROLLER TREATMENT IN ADULTS AND ADOLESCENTS WITH A DIAGNOSIS OF ASTHMA



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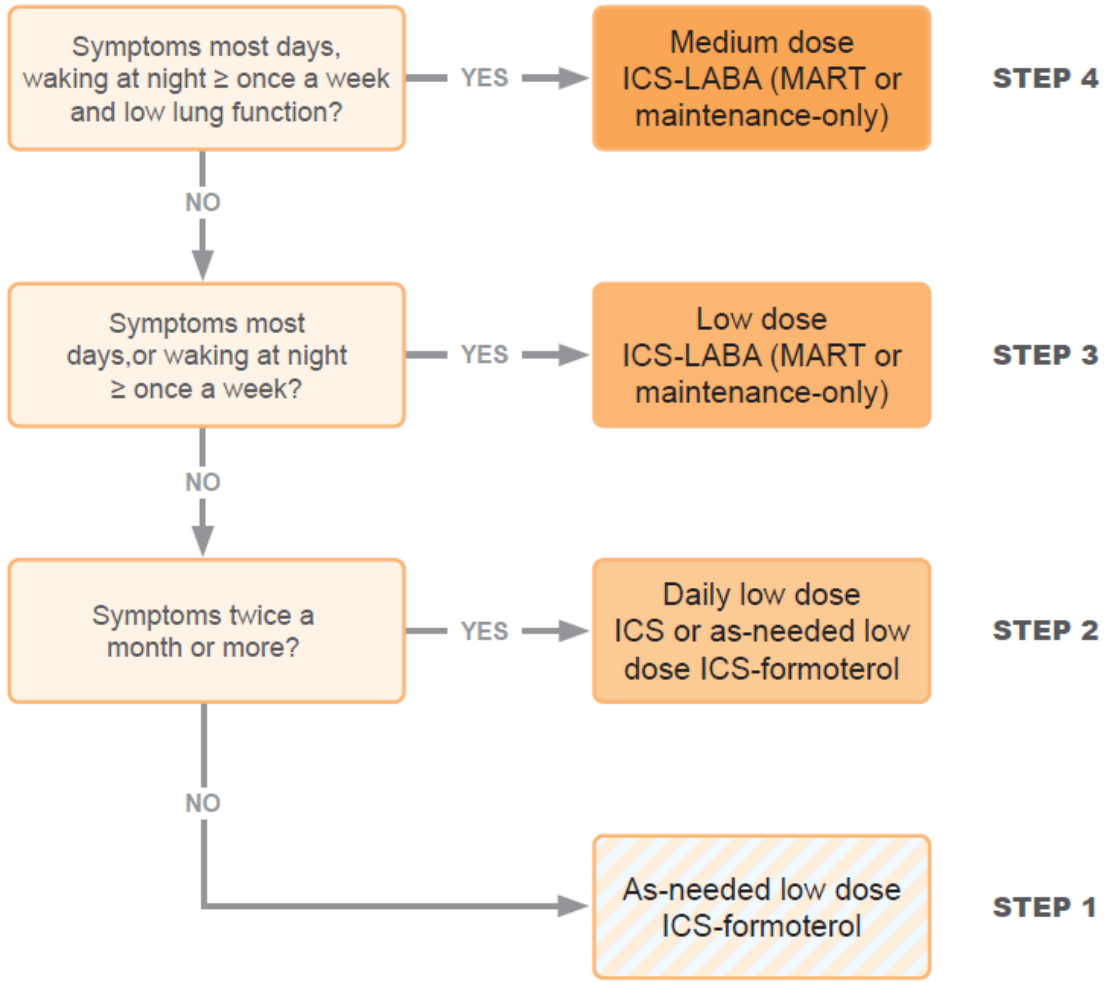
SUGGESTED INITIAL CONTROLLER TREATMENT IN ADULTS AND ADOLESCENTS WITH A DIAGNOSIS OF ASTHMA

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

- Freque
  - Hig

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

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

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

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

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)

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section **3** (including inhaler technique, adherence, comorbidities)

6b Consider *add-on biologic Type 2* targeted treatments

- Consider add-on Type 2-targeted biologic for patients with exacerbations or poor symptom control on high dose ICS-LABA, who:
  - have eosinophilic or allergic biomarkers, or
  - need maintenance OCS
- Consider **local payer eligibility criteria** and **predictors of response** when choosing between available therapies
- Also consider cost, dosing frequency, route (SC or IV), patient preference

Which biologic is appropriate to start first?

Anti-IgE

*Is the patient eligible for **anti-IgE** for severe allergic asthma?*

- Sensitization on skin prick testing or specific IgE
- Total serum IgE and weight within dosage range
- Exacerbations in last year

What factors may predict good asthma response to anti-IgE?

- Blood eosinophils ≥260/µl ++
- FeNO ≥20 ppb +
- Allergen-driven symptoms +
- Childhood-onset asthma +

no / *no*

Anti-IL5 / Anti-IL5R

*Is the patient eligible for **anti-IL5 / anti-IL5R** for severe eosinophilic asthma?*

- Exacerbations in last year
- Blood eosinophils ≥300/µl

What factors may predict good asthma response to anti-IL5/5R?

- Higher blood eosinophils +++
- More exacerbations in previous year +++
- Adult-onset of asthma ++
- Nasal polyposis ++

no / *no*

Anti-IL4R

*Is the patient eligible for **anti-IL4R***

… for severe eosinophilic asthma?

- Exacerbations in last year
- Blood eosinophils ≥150/µl or FeNO ≥25 ppb

… or because of need for maintenance OCS?

What factors may predict good asthma response to anti-IL4R?

- Higher blood eosinophils +++
- Higher FeNO +++

Anti-IL4R may also be used to treat

- Moderate/severe atopic dermatitis
- Nasal polyposis

Eligible for none?

Return to section **6a**

Choose one if eligible; trial for at least 4 months and assess response

Good asthma response?

yes — Good response to T2-targeted therapy

unclear — Extend trial to 6-12 months

no

STOP add-on

Consider switching to a different Type 2-targeted therapy, if eligible

no — Little/no response to T2-targeted therapy

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Patients with features of asthma and COPD

- Also called ‘asthma-COPD overlap’ or ‘asthma+COPD’
  - NOT a single disease, but a descriptive label for patients commonly seen in clinical practice
- Asthma and COPD are heterogeneous and overlapping conditions
  - The definitions of asthma and COPD are not mutually exclusive
  - Each includes several phenotypes that are likely to have different underlying mechanisms
  - There is increasing interest in the potential for precision treatment
- However, the labels ‘asthma’ and ‘COPD’ are still clinically important, as evidence supports safety-based differences in treatment recommendations
  - Asthma: never treat with bronchodilators alone (risk of death, hospitalization, severe exacerbations)
  - COPD: start treatment with LABA and/or LAMA without ICS
  - Patients with diagnoses of both asthma and COPD are more likely to die or be hospitalized if treated with LABA vs ICS-LABA *(Gershon et al, JAMA 2014; Kendzerska et al, Annals ATS 2019)*
  - High dose ICS may be needed for severe asthma, but should not be used in COPD (risk of pneumonia)
- Chapter 5 has been rewritten for clinical utility, focusing on clinical recognition and safe initial treatment

Patients with features of asthma and COPD

CLINICAL PHENOTYPE - ADULTS WITH CHRONIC RESPIRATORY SYMPTOMS (dyspnea, cough, chest tightness, wheeze)

HIGHLY LIKELY TO BE ASTHMA
if several of the following features
TREAT AS ASTHMA

HISTORY
- Symptoms vary over time and in intensity
  - Triggers may include laughter, exercise, allergens, seasonal
  - Onset before age 40 years
  - Symptoms improve spontaneously or with bronchodilators (minutes) or ICS (days to weeks)
- Current asthma diagnosis, or asthma diagnosis in childhood

LUNG FUNCTION
- Variable expiratory airflow limitation
- Persistent airflow limitation may be present

FEATURES OF BOTH ASTHMA + COPD
TREAT AS ASTHMA

HISTORY
- Symptoms intermittent or episodic
  - May have started before or after age 40
- May have a history of smoking and/or other toxic exposures, or history of low birth weight or respiratory illness such as tuberculosis
- Any of asthma features at left (e.g. common triggers; symptoms improve spontaneously or with bronchodilators or ICS; current asthma diagnosis or asthma diagnosis in childhood)

LUNG FUNCTION
- Persistent expiratory airflow limitation
- With or without bronchodilator reversibility

LIKELY TO BE COPD
if several of the following features
TREAT AS COPD

HISTORY
- Dyspnea persistent (most days)
  - Onset after age 40 years
  - Limitation of physical activity
  - May have been preceded by cough/sputum
  - Bronchodilator provides only limited relief
- History of smoking and/or other toxic exposure, or history of low birth weight or respiratory illness such as tuberculosis
- No past or current diagnosis of asthma

LUNG FUNCTION
- Persistent expiratory airflow limitation
- With or without bronchodilator reversibility

INITIAL PHARMACOLOGICAL TREATMENT (as well as treating comorbidities and risk factors. See Box 3-5A)

- **ICS-CONTAINING TREATMENT IS ESSENTIAL to reduce risk of severe exacerbations and death.** See Box 3-5A
  - As-needed low dose ICS-formoterol may be used as reliever. See Box 3-5A
- **DO NOT GIVE LABA and/or LAMA without ICS**
- Avoid maintenance OCS

- **ICS-CONTAINING TREATMENT IS ESSENTIAL to reduce risk of severe exacerbations and death.** See Box 3-5A
- Add-on LABA and/or LAMA usually also needed
- Additional COPD treatments as per GOLD
- **DO NOT GIVE LABA and/or LAMA without ICS**
- Avoid maintenance OCS

- **TREAT AS COPD (see GOLD report)**
  - Initially LAMA and/or LABA
  - Add ICS as per GOLD for patients with hospitalizations, ≥2 exacerbations/year requiring OCS, or blood eosinophils ≥300/µl
- Avoid high dose ICS, avoid maintenance OCS
- Reliever containing ICS is not recommended

REVIEW PATIENT AFTER 2-3 MONTHS. REFER FOR EXPERT ADVICE IF DIAGNOSTIC UNCERTAINTY OR INADEQUATE RESPONSE

Question?