



Pediatric Asthma

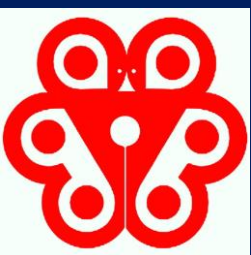
Emergencies

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Pediatric Emergencies, 1/10/1401

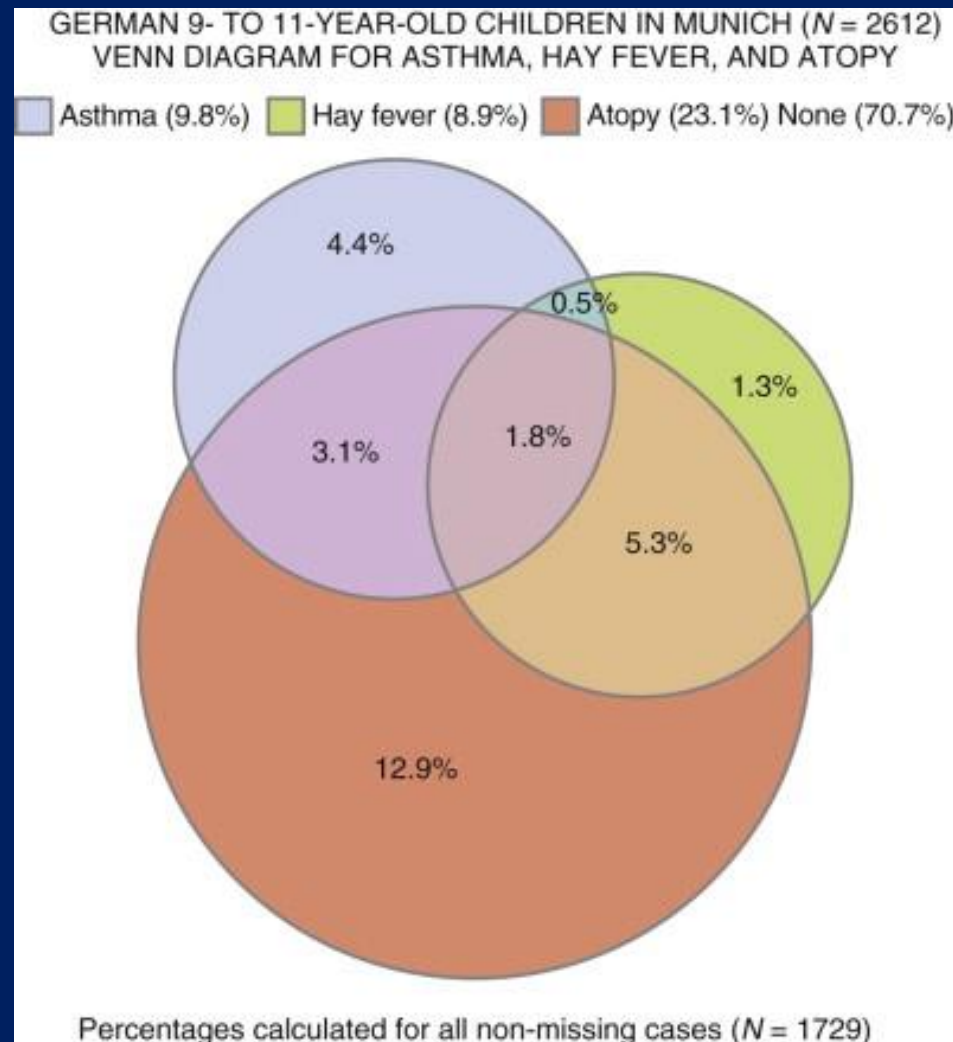
Guilan University of Medical Sciences



Epidemiology of Allergic Diseases

- The **prevalence of asthma and allergies** has *increased* over the last few decades.
- Allergic diseases are **multifactorial**: genetic and **environmental** factors.

The prevalence of asthma, hay fever and atopic sensitization only partially overlaps on a population level.

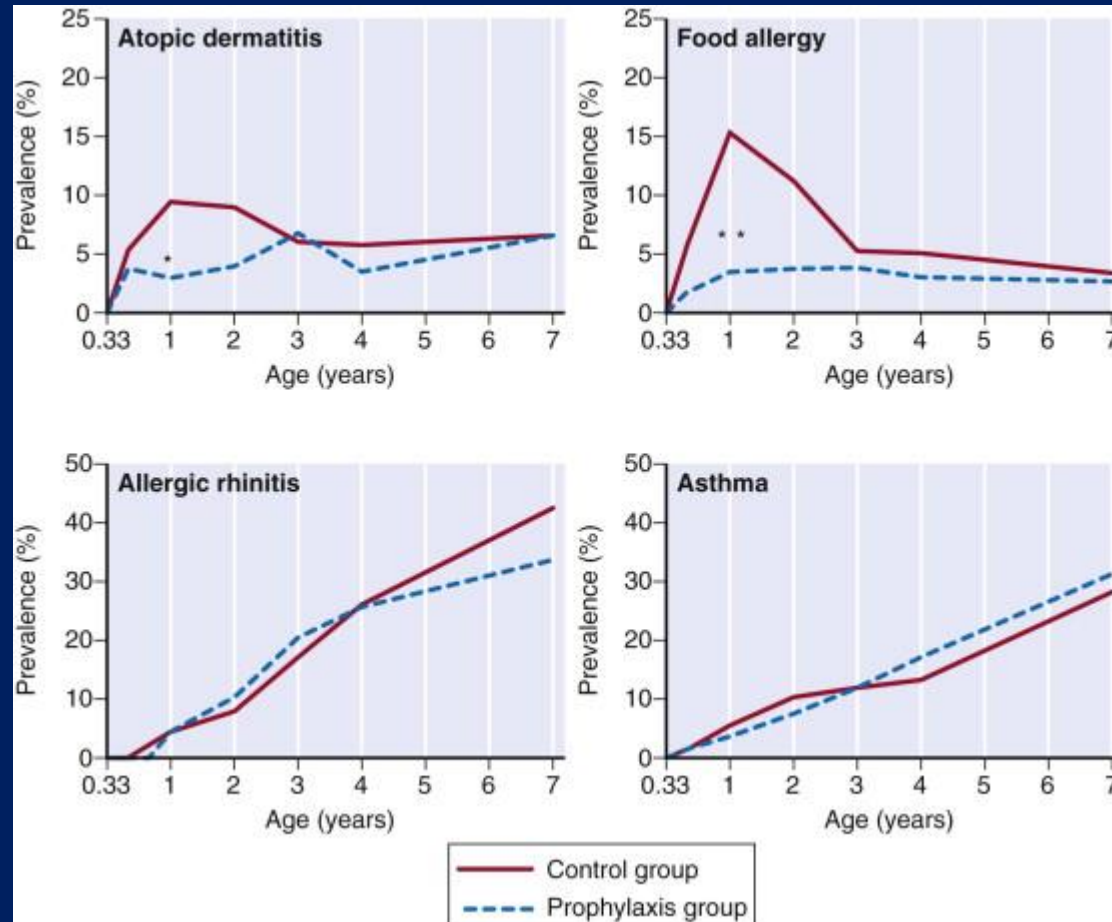


Natural History of Allergic Diseases and Asthma

- The **atopic disorders**
 - atopic dermatitis,
 - food and inhalant allergies,
 - allergic rhinoconjunctivitis
 - and asthma
- **tend to cluster** in
 - individuals,
 - families
 - and locales.

- A developmental '**allergic march**' of childhood
 - **begins with** atopic dermatitis, food allergies and **bronchiolitis episodes** in the first few years of life,
 - and **progresses to** inhalant allergic sensitization, allergic rhinoconjunctivitis and atopic **asthma**.

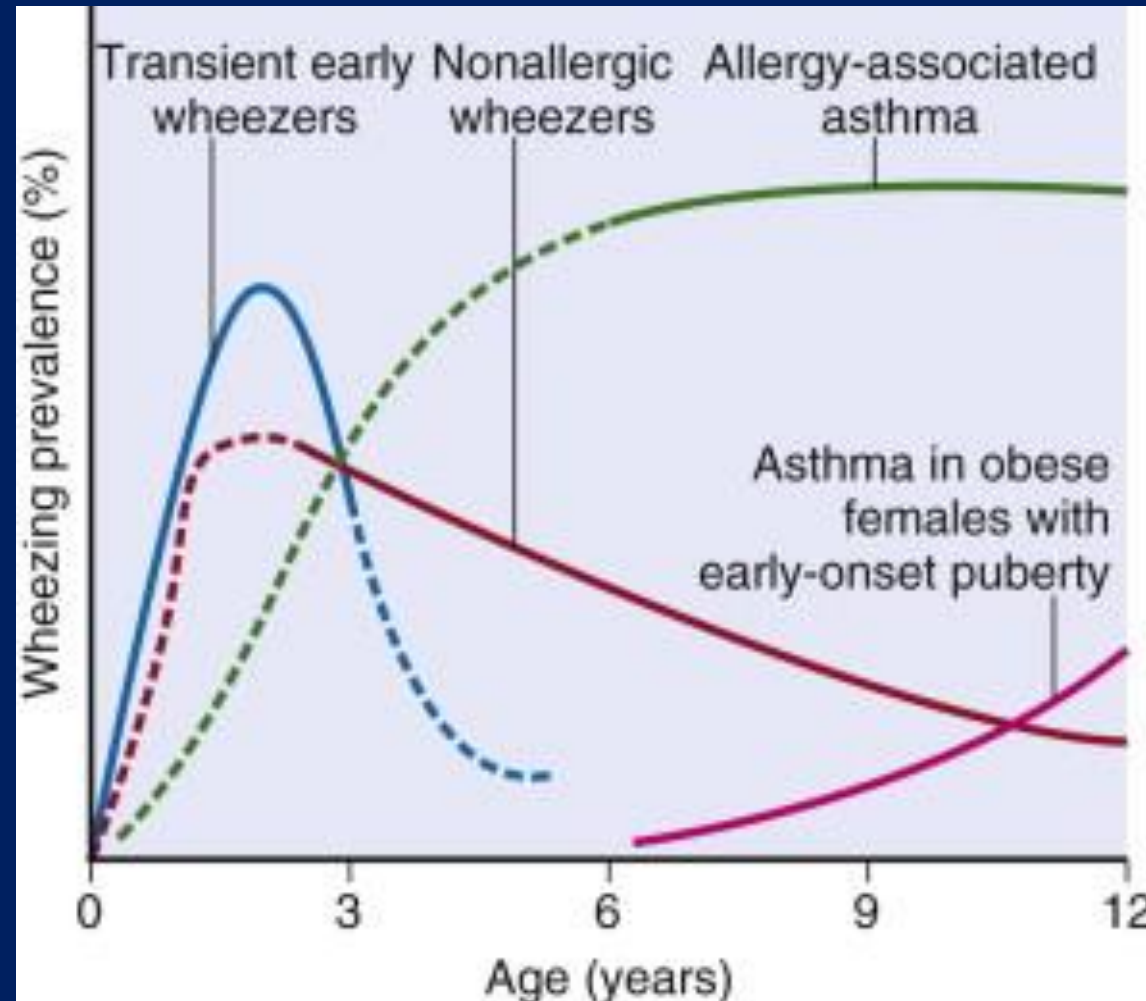
Allergic march of early childhood



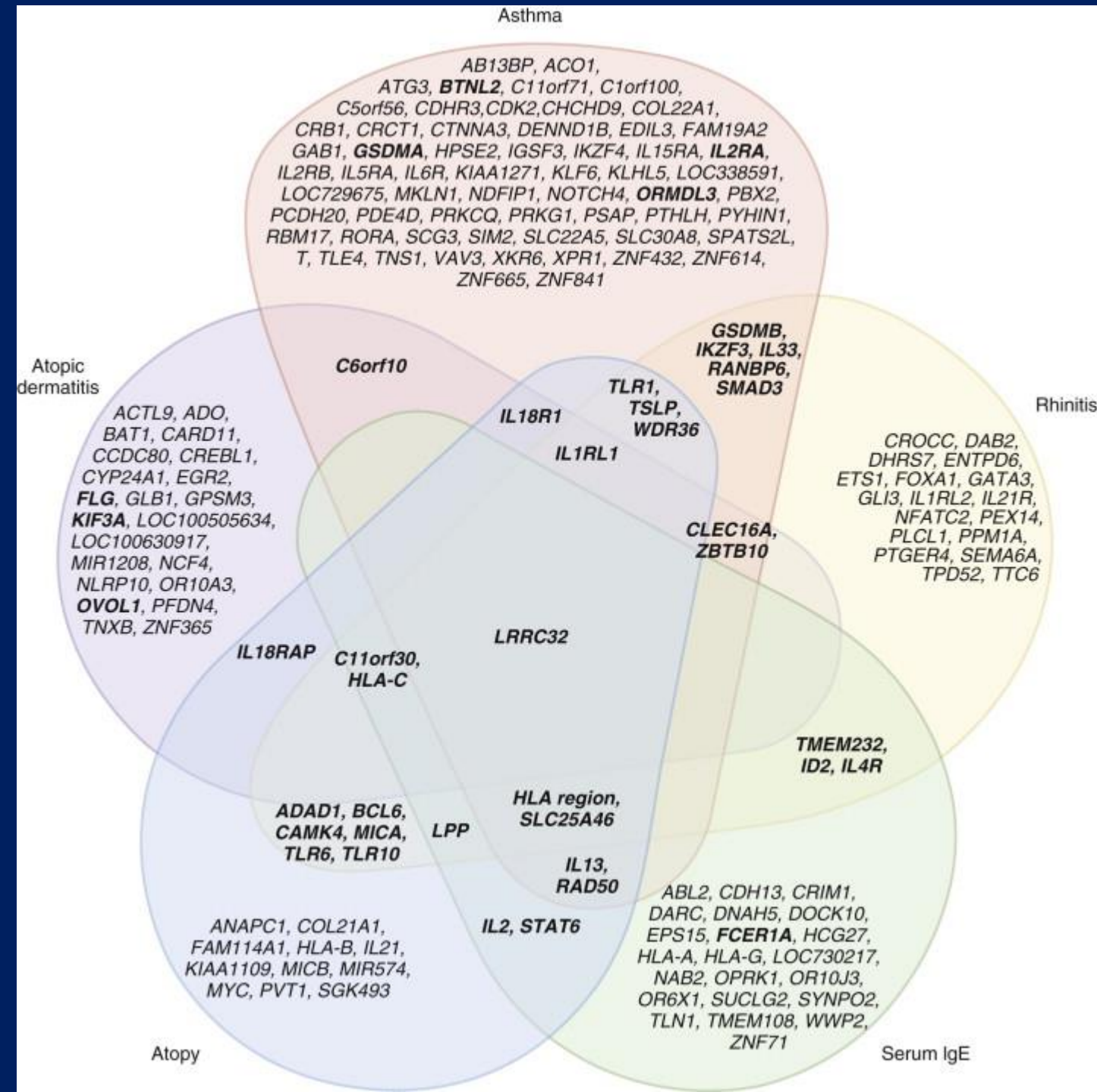
- Although **persistent asthma** commonly begins in the first few years of life, **most infants and toddlers who have recurrent bronchiolitis episodes** do **not** go on to have persistent asthma in later childhood and adulthood.

At least 4 wheezing episodes, plus:	
1 Major criterion	or 2 Minor criteria
Parental asthma	Allergic rhinitis
Eczema	Wheezing apart from colds
Inhalant allergen sensitization	Eosinophils $\geq 4\%$
	Food allergen sensitization

Hypothetical yearly prevalence for recurrent wheezing phenotypes in childhood

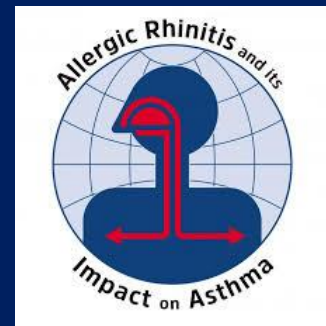


The Genetics of Allergic Disease and Asthma



Chronic Cough

- **Cough** is an important **defense mechanism**.
- Cough is a **common** manifestation of disease in childhood.
- Cough may be classified as **acute** (lasting <3 weeks), **subacute** (lasting 3 to 8 weeks), or **chronic** (lasting >8 weeks).
- The **cause of chronic cough** can be determined in most patients; **specific therapy** based on a systematic evaluation is usually successful.



DDx of Chronic Cough in Children

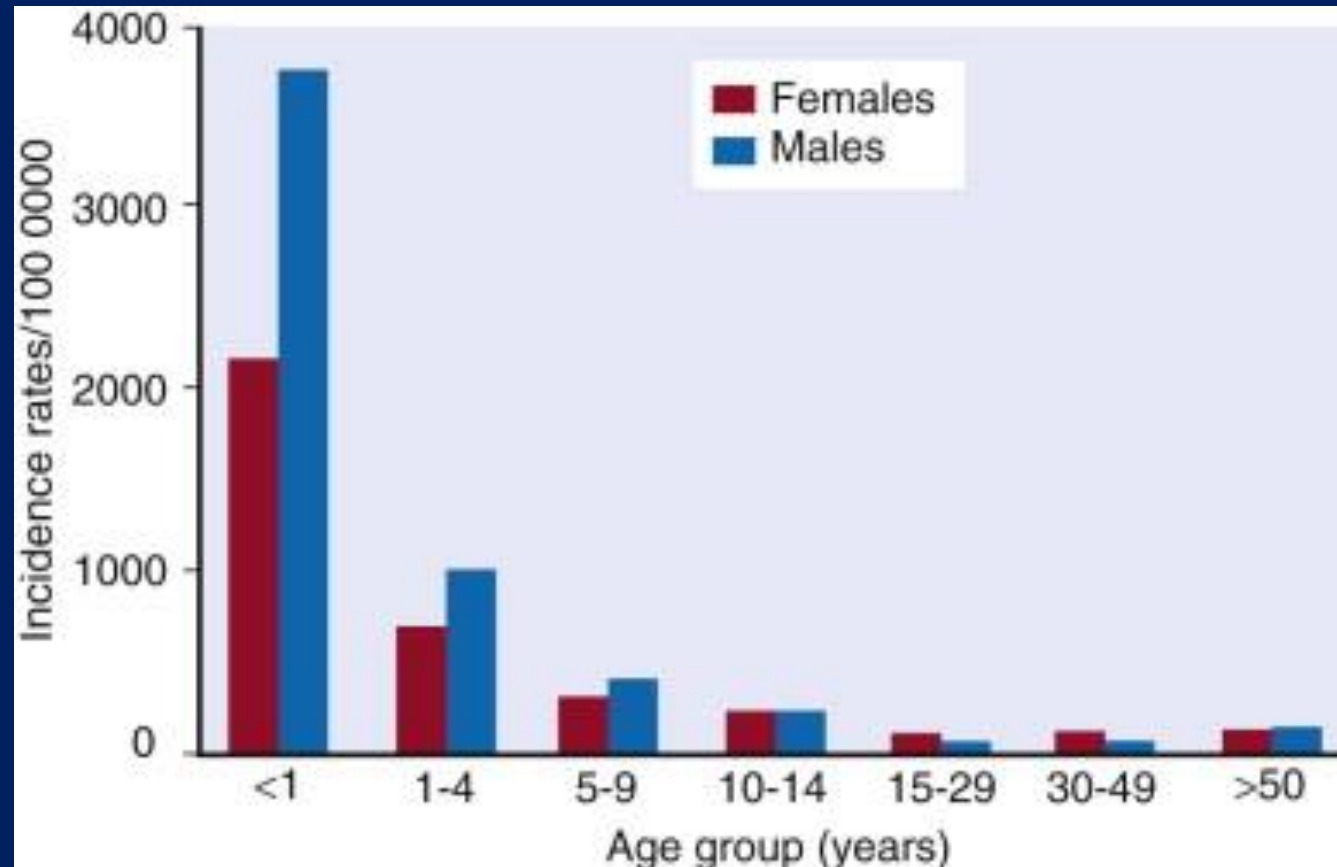
- Congenital anomalies
- Infectious or postinfectious cough
- Rhinitis related
- Gastroesophageal reflux without aspiration
- Aspiration
- Vocal cord dysfunction
- Physical and chemical irritation
- Psychogenic cough
- Habit cough
- Asthma

- **Asthma** is very often associated with chronic cough, but **few children with chronic cough** develop asthma.
- **Cough-variant asthma** is suggested by
 - (1) **airway** obstruction and reversibility,
 - (2) airway hyperresponsiveness and/or
 - (3) clinical improvement after treatment with asthma medications.

- **Gastroesophageal reflux** may
 - *cause or intensify chronic cough* through a vagal reflex or as a result of aspiration of stomach contents.
- **Postinfectious cough**
 - *resolves over time*;
 - the use of oral or inhaled corticosteroids or ipratropium bromide *may shorten its duration*.

Asthma: A Global Concern

Annual incident rates per 100,000 person-years by sex and range for definite + probable asthma cases



GINA Assessment of Asthma Control in Children 5 Years and Younger.

A. SYMPTOM CONTROL

LEVEL OF ASTHMA SYMPTOM CONTROL

In The Past 4 Weeks, Has the Child Had:

Well Controlled

Partly Controlled

Uncontrolled

- Daytime asthma symptoms for more than a few minutes, more than once a week? Yes ☐ No ☐
- Any activity limitation due to asthma? (Runs/plays less than other children, tires easily during walks/playing?) Yes ☐ No ☐
- Reliever medication needed* more than once a week? Yes ☐ No ☐
- Any night waking or night coughing due to asthma? Yes ☐ No ☐

None of these

1-2 of these

3-4 of these

Stepwise approach to long-term management of asthma in children aged 5 years and younger

	STEP-1	STEP-2	STEP-3	STEP-4
PREFERRED CONTROLLER CHOICE		Daily low-dose ICS	Double 'low-dose' ICS	Continue controller & refer for specialist assessment
Other controller options		Leukotriene receptor antagonist (LTRA) intermittent ICS	Low dose ICS + LTRA	Add LTRA Inc. ICS frequency Add intermittent ICS
RELIEVER	As-needed short-acting β_2 -agonist (all children)			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms (Box 6-2)	Symptom pattern consistent with asthma (Box 6-2) and asthma symptoms not well-controlled (Box 6-4), or ≥ 3 exacerbations per year Symptom pattern not consistent with asthma (Box 6-2) but wheezing episodes occur frequently, e.g. every 6–8 weeks Give diagnostic trial for 3 months	Asthma diagnosis, and not well-controlled on low-dose ICS First check diagnosis, inhaler skills, adherence, exposures	Not well-controlled on double ICS

Estimated Comparative Inhaled Corticosteroid Doses

Table 1. Clinically Comparable Doses of Inhaled Corticosteroids

Drug	Comparative Daily Dosages (µg) ^{1,a}					
	Low		Medium		High	
	Child	Adult	Child	Adult	Child	Adult
Beclomethasone dipropionate						
HFA-MDI	80–160	80–240	>160–320	>240–480	>320	>480
Budesonide						
DPI	180–400	200–600	>400–800	>600–1200	>800	>1200
nebules	500	UK	1000	UK	2000	UK
Ciclesonide ^b						
HFA-MDI	80–160	160–320	>160–320	>320–640	>320	>640
Flunisolide						
CFC-MDI	500–750	500–1000	>1000–1250	>1000–2000	>1250	>2000
HFA-MDI	160	320	320	>320–640	≥640	>640
Fluticasone propionate						
HFA-MDI	88–176	88–264	>176–352	264–440	>352	>440
DPI	100–200	100–300	>200–400	300–500	>400	>500
Mometasone furoate ^c DPI	110	220	220–440	440	>440	>440
Triamcinolone acetonide CFC-MDI	300–600	300–750	>600–900	>750–1500	>900	>1500

CFC-MDI = chlorofluorocarbon-propelled metered-dose inhaler; DPI = dry-powder inhaler; HFA-MDI = hydrofluoroalkane-propelled metered-dose inhaler; MDI = metered-dose inhaler; UK = unknown.

^aChild age is 5–11 years.

^bDoses are not from reference 1; rather, data are based on comparative clinical trials with fluticasone propionate and budesonide with ciclesonide.^{2–5}

^cChild doses are not from reference 1; rather, data are based on recent approval in children aged 4–11 years and comparative studies with fluticasone propionate, beclomethasone dipropionate, and budesonide.^{6,7}

Infections and Asthma: Impact on the Natural History of Asthma

- **Wheezing viral respiratory illnesses** are the most common initial presentation of ***childhood asthma***.
- Once asthma is established, **viral infections**, most notably rhinovirus (RV), are the most frequent trigger of ***severe asthma exacerbations***.

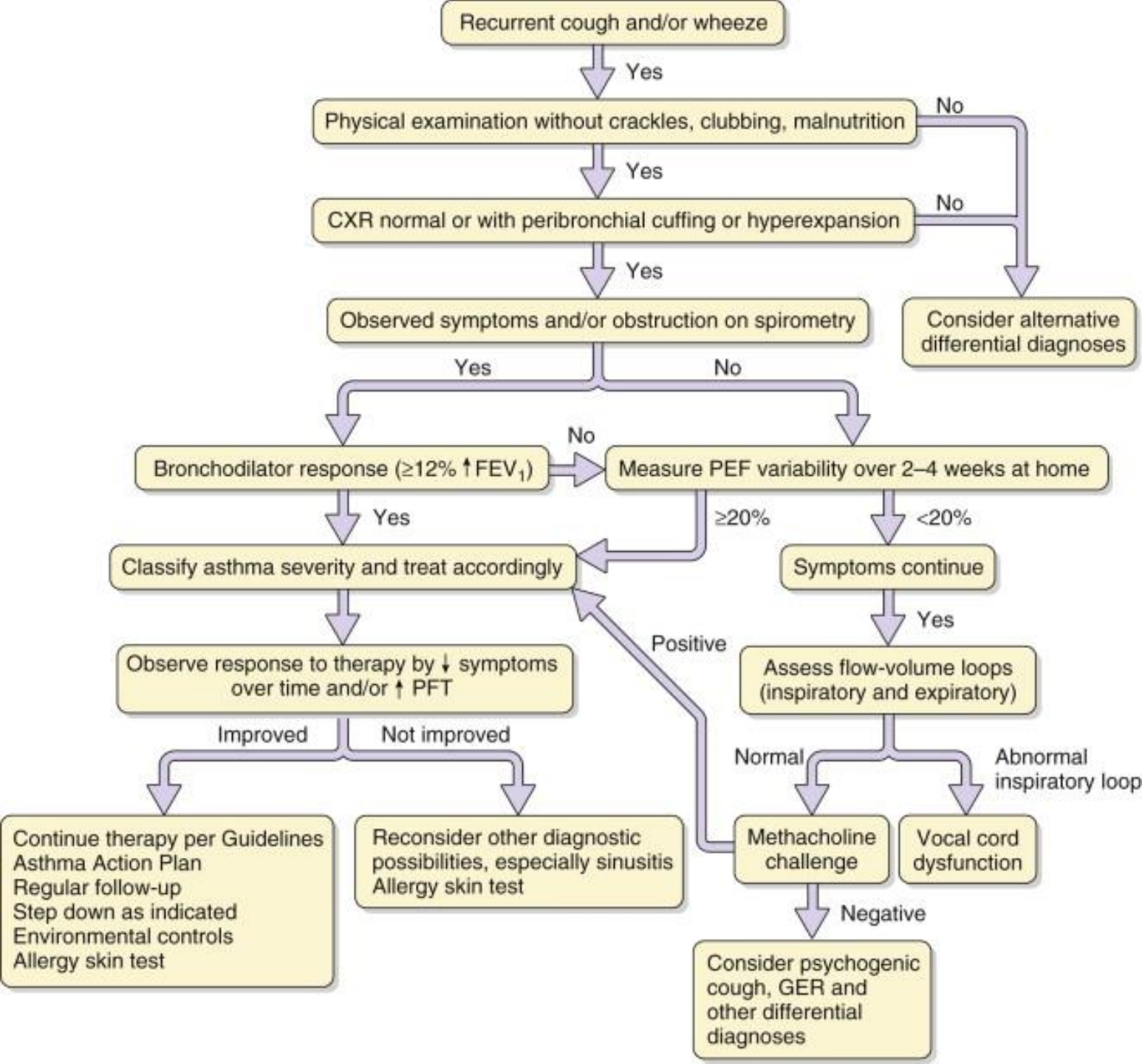
Use of Antibiotics in Asthma

- **Not recommended** the use of antibiotics to treat asthma exacerbations because the majority of the exacerbations have been considered to be triggered by *viral respiratory tract infections*.

Asthma in Older Children: Special Considerations

- Failure of symptoms to respond to β -agonists and oral steroids should prompt consideration that the symptoms are *not caused by asthma* but by another process.
- Consideration of other disorders, particularly sinusitis, is imperative.

- **Pulmonary function measures** may **not accurately reflect asthma severity in children**, who can have an FEV₁ in the normal range even when disease is severe.
- **Asthma** is ***controllable*** in the vast majority of children.
- Even children with **severe asthma** can be expected ***fully to participate in activities.***



Algorithm for establishing diagnosis in children with recurrent cough and wheeze.

From Program NAEaP. Expert Panel Report III: Guidelines for the diagnosis and management of asthma. Bethesda, MD: US Department of Health and Human Services; 2007.

Component of Severity		CLASSIFICATION OF ASTHMA SEVERITY FOR DIFFERENT AGE GROUPS							
		INTERMITTENT		PERSISTENT					
				MILD		MODERATE		SEVERE	
		5–11 Years	≥12 Years	5–11 Years	≥12 Years	5–11 Years	≥12 Years	5–11 Years	≥12 Years
Impairment	Symptoms	≤2 days/week	≤2 days/week	>2 days/week but not daily	>2 days/week but not daily	Daily	Daily	Throughout the day	Throughout the day
	Nighttime awakenings	0	0	1–2×/month	1–2×/month	3–4×/month	3–4×/month	>1×/week	>1×/week
	Short-acting β ₂ -agonist use for symptom control	≤2 days/week	≤2 days/week	>2 days/week but not daily	>2 days/week but not daily	Daily	Daily	Several times per day	Several times per day
	Interference with normal activity	None	None	Minor limitation	Minor limitation	Some limitation	Some limitation	Extremely limited	Extremely limited
	Lung Function	• Normal FEV ₁ between exacerbations • FEV ₁ >80% predicted • FEV ₁ /FVC >85%	• Normal FEV ₁ between exacerbations • FEV ₁ >80% predicted • FEV ₁ /FVC normal	• FEV ₁ ≥80% predicted • FEV ₁ /FVC >80%	• FEV ₁ <80% predicted • FEV ₁ /FVC normal	• FEV ₁ 60–80% predicted • FEV ₁ /FVC = 75–80%	• FEV ₁ >60% but <80% predicted • FEV ₁ /FVC reduced 5%	• FEV ₁ <60% predicted • FEV ₁ /FVC <75%	• FEV ₁ <60% predicted • FEV ₁ /FVC reduced >5%
Risk	Exacerbations (consider frequency and severity)	0–2/year		>2 exacerbations in 1 year					
		Relative annual risk may be related to FEV ₁ Frequency and severity may fluctuate over time Exacerbations of any severity may occur in patients in any severity category							

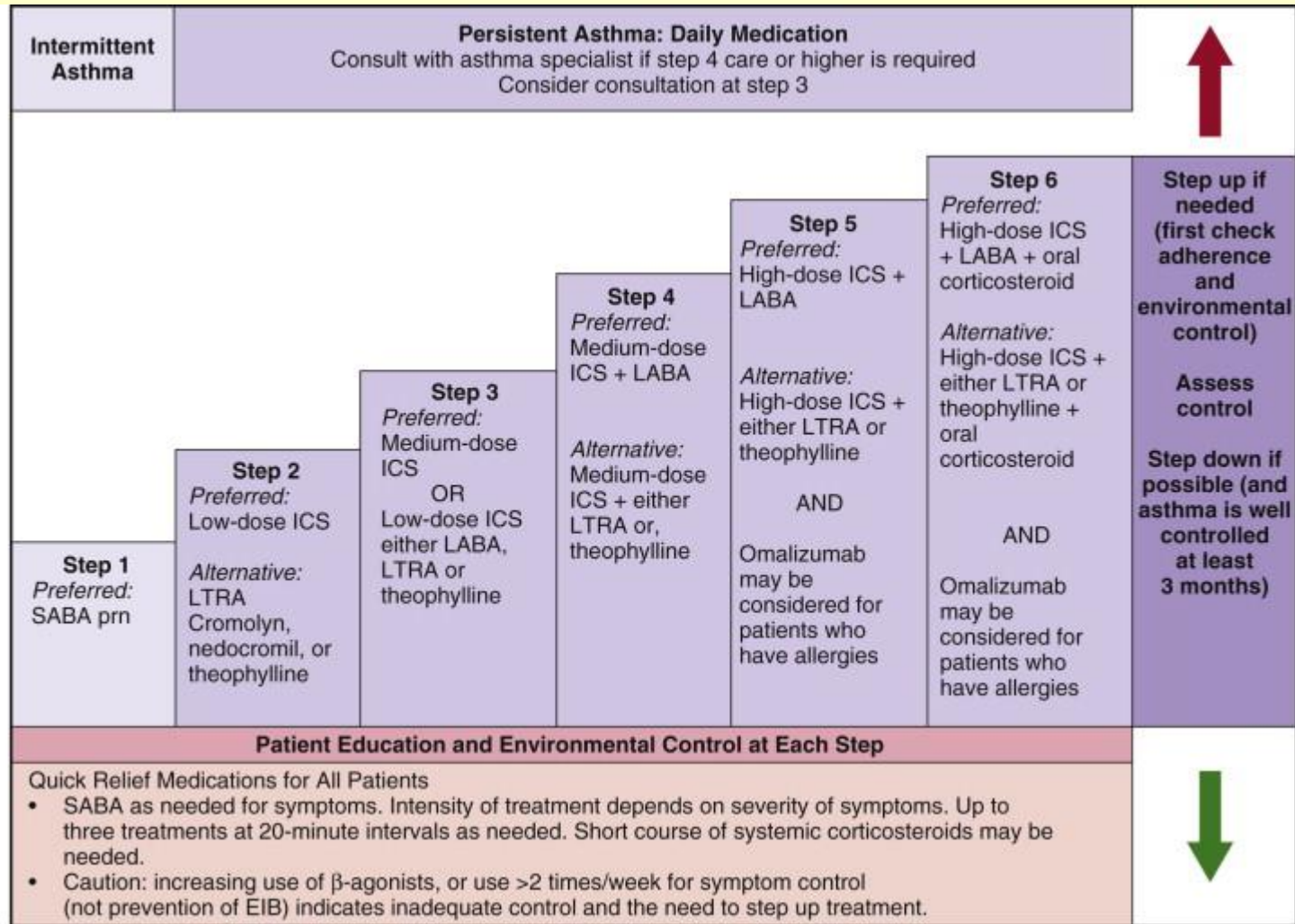
TABLE 34-3

Classification of Asthma Control in Youths ≥12 Years of Age and Adults

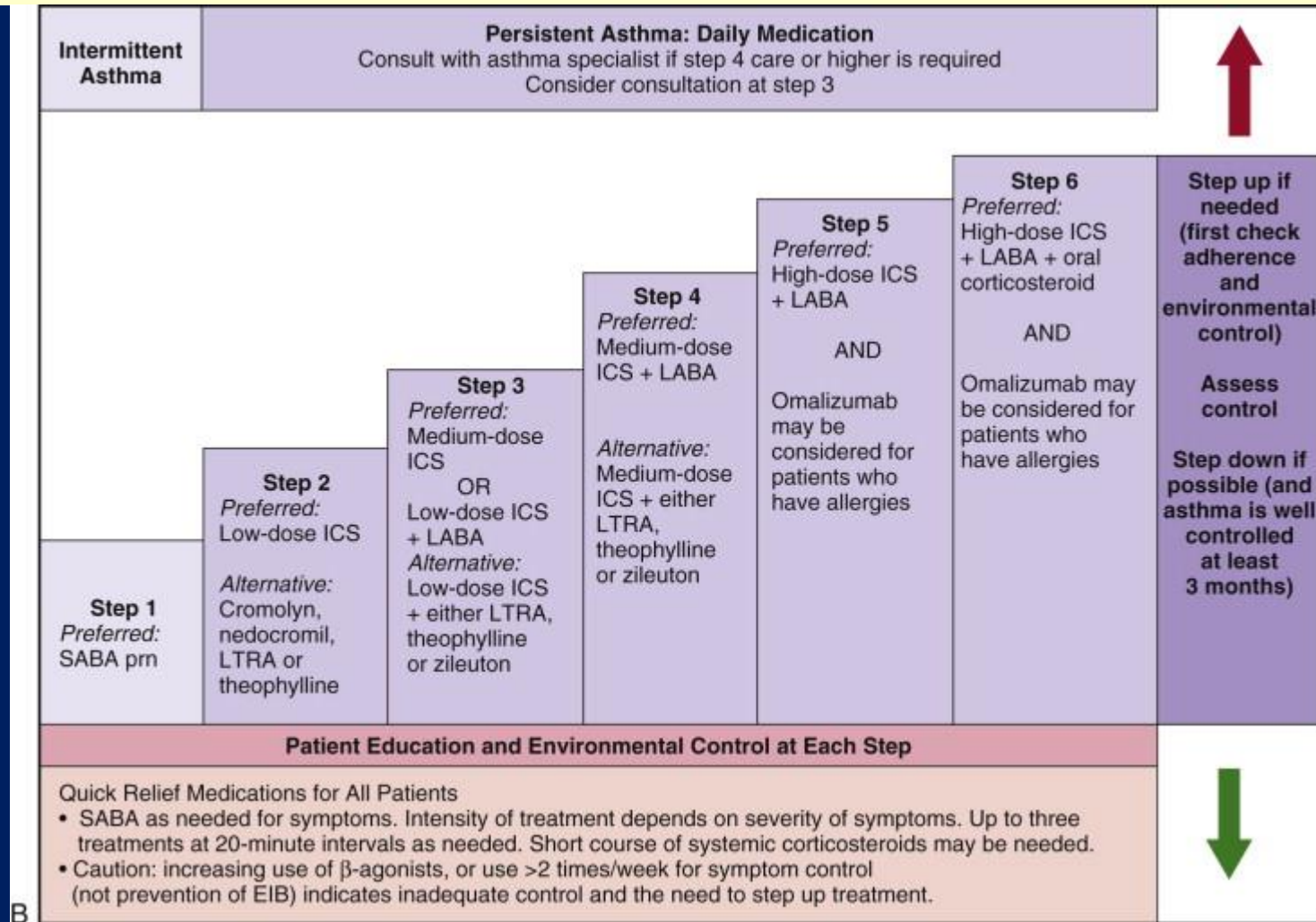
From Program NAEaP. Expert Panel Report III: Guidelines for the diagnosis and management of asthma. Bethesda, MD: US Department of Health and Human Services; 2007.

Component of Control		Classification		
		Well-Controlled	Not Well-Controlled	Very Poorly Controlled
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime Awakenings	≤2/month	1–3/week	≥4/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting β ₂ -agonist use for symptom control	≤2 days/week	>2 days/week	Several times per day
	FEV ₁ or peak flow	>80% predicted/personal best	60–80% predicted/personal best	<60% predicted/personal best
	Validated Questionnaires			
	ATAQ	0	1–2	3–4
	ACQ	≤0.75	≥1.5	N/A
	ACT	≥20	16–19	≤15
Risk	Exacerbations (consider frequency and severity)	0–1/year	2–3/year	>3/year
	Progressive loss of lung function	Evaluation requires long-term follow-up		
	Treatment-related adverse effects	Medication side-effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk		

Stepwise approach for managing children with asthma. 5–11 years of age



Stepwise approach for managing children with asthma. ≥12 years of age



Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction



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

Treatment of modifiable risk factors & comorbidities
Non-pharmacological strategies
Education & skills training
Asthma medications

See 2019 GINA Severe Asthma Pocket Guide for more details about Steps 4–5

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

PREFERRED CONTROLLER
to prevent exacerbations and control symptoms

Other controller options

PREFERRED RELIEVER

Other reliever option

STEP 1
As-needed low dose ICS-formoterol *
Low dose ICS taken whenever SABA is taken †

STEP 2
Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *
Leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †

STEP 3
Low dose ICS-LABA

Medium dose ICS, or low dose ICS+LTRA #

STEP 4
Medium dose ICS-LABA

High dose ICS, add-on tiotropium, or add-on LTRA #

STEP 5
High dose ICS-LABA

Refer for phenotypic assessment ± add-on therapy, e.g. tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R
Add low dose OCS, but consider side-effects

Maintenance OCS is not a preferred option at Step 5 because of serious side-effects

* Off-label; data only with budesonide-formoterol (bud-form)
† Off-label; separate or combination ICS and SABA inhalers

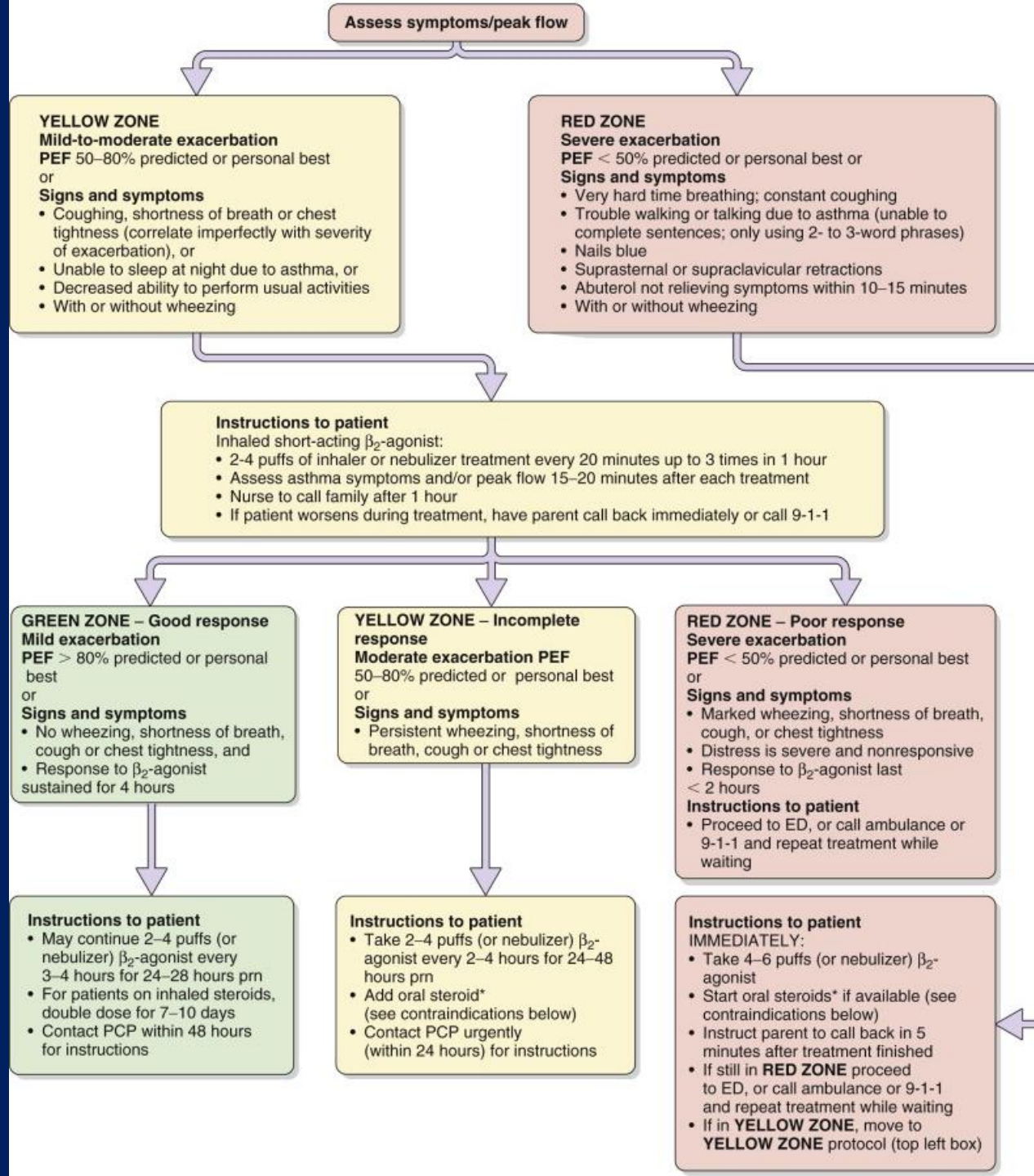
‡ Low-dose ICS-form is the reliever for patients prescribed bud-form or BDP-form maintenance and reliever therapy
Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV₁ >70% predicted

A holistic approach – not just symptom control

ICS-containing controller is recommended across all severities to reduce exacerbation risk

“Preferred” and “other” options are provided at each step, based on evidence

SABA is not a preferred reliever because of the risks of SABA-only treatment, including if adherence is poor



Algorithm for treatment of acute asthma symptoms

Refractory Childhood Asthma: Assessment and Management

- Problematic, **severe asthma** comprises
 - **wrong diagnosis** ('not asthma at all'),
 - asthma with **co-morbidities** ('asthma plus'),
 - **difficult asthma** (need to get the basic steps of asthma management correct) **50%!!!**
 - **true severe, therapy-resistant asthma** **5-10%!!!**

- More than 50% of children referred to tertiary centers with problematic severe asthma in fact will be **well controlled if basic management is optimal**; they do not require therapy with 'beyond guidelines' medications.
- There is little or no evidence base for '**beyond guidelines**' therapy in *children who fail standard therapies* including omalizumab.

TABLE 37-3
Differential Diagnoses of Severe Asthma

Class of Diagnosis	Examples
Local immunodeficiency	Cystic fibrosis, primary ciliary dyskinesia, persistent bacterial bronchitis
Systemic immunodeficiency	Any, including B cell and T cell dysfunction
Intraluminal bronchial obstruction	Foreign body, carcinoid, other tumor
Intramural bronchial obstruction	Bronchomalacia, complete cartilage rings, intramural tumor
Extraluminal bronchial obstruction	Vascular ring, pulmonary artery sling, congenital lung cyst, enlarged lymph nodes due to tumor or tuberculosis, other mediastinal masses
Direct aspiration	Bulbar or pseudobulbar palsy; laryngeal cleft
Aspiration by direct contamination	H-type fistula
Aspiration secondary to reflux	Any cause of gastroesophageal reflux, including hiatus hernia and esophageal dysmotility
Complications of prematurity	Bronchomalacia, structuring secondary to intubation, vocal cord palsy secondary to surgery for patent arterial duct
Congenital heart disease	Bronchial compression from enlarged cardiac chambers or great vessels; pulmonary edema
Interstitial lung disease	Any not presenting with neonatal respiratory failure
Dysfunctional breathing	Vocal cord dysfunction, hyperventilation syndromes

B. FUTURE RISK FOR POOR ASTHMA OUTCOMES

Risk Factors for Asthma Exacerbations within the Next Few Months

- Uncontrolled asthma symptoms
- One or more severe exacerbation in previous year
- The start of the child's usual 'flare-up' season (especially if fall/autumn)
- Exposures: tobacco smoke; indoor or outdoor air pollution; indoor allergens (e.g. house dust mite, cockroach, pets, mold), especially in combination with viral infection
- Major psychological or socioeconomic problems for child or family
- Poor adherence with controller medication, or incorrect inhaler technique

Risk Factors for Fixed Airflow Limitation

- Severe asthma with several hospitalizations
- History of bronchiolitis

Risk Factors for Medication Side-Effects

- Systemic: Frequent courses of OCS; high-dose and/or potent ICS
- Local: moderate/high-dose or potent ICS; incorrect inhaler technique; failure to protect skin or eyes when using ICS by nebulizer or spacer with face mask

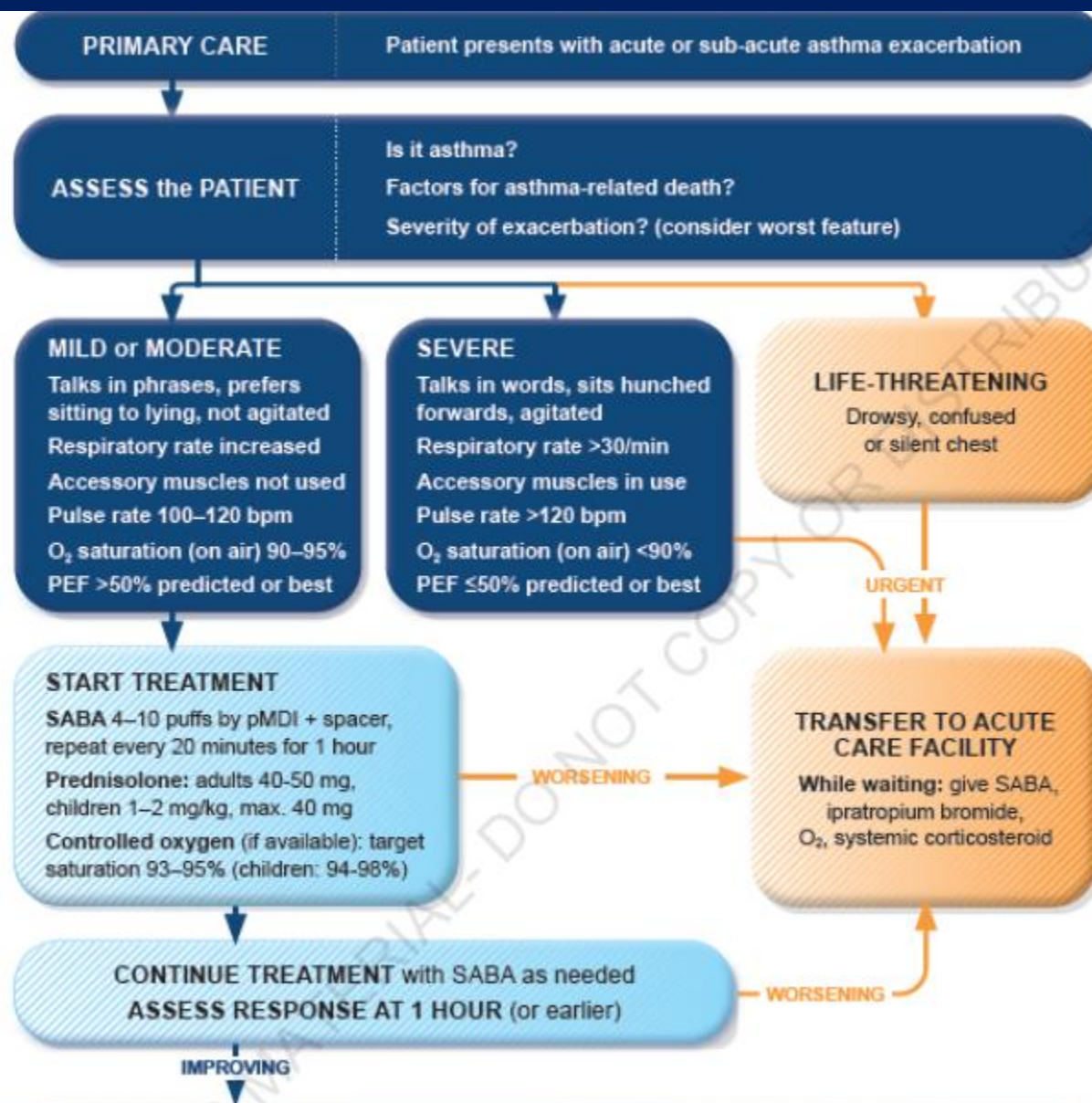
It's Time to Start Phenotyping Our Patients with Asthma

Box 1

Clinical variables and biomarkers used to phenotype pediatric asthma

- Aeroallergen skin prick testing/ImmunoCAP
- Total IgE
- Blood eosinophil count
- F_ENO
- Spirometry with bronchodilator response
- Rhinitis symptoms
- Demographic features including race and body mass index

Box 4-3. Management of asthma exacerbations in primary care (adults, adolescents, children 6–11 years)



SABA 4–10 puffs by pMDI + spacer, repeat every 20 minutes for 1 hour
Prednisolone: adults 40–50 mg, children 1–2 mg/kg, max. 40 mg
Controlled oxygen (if available): target saturation 93–95% (children: 94–98%)

WORSENING

TRANSFER TO ACUTE CARE FACILITY

While waiting: give SABA, ipratropium bromide, O₂, systemic corticosteroid

CONTINUE TREATMENT with SABA as needed
ASSESS RESPONSE AT 1 HOUR (or earlier)

WORSENING

IMPROVING

ASSESS FOR DISCHARGE

Symptoms improved, not needing SABA
PEF improving, and >60–80% of personal best or predicted
Oxygen saturation >94% room air
Resources at home adequate

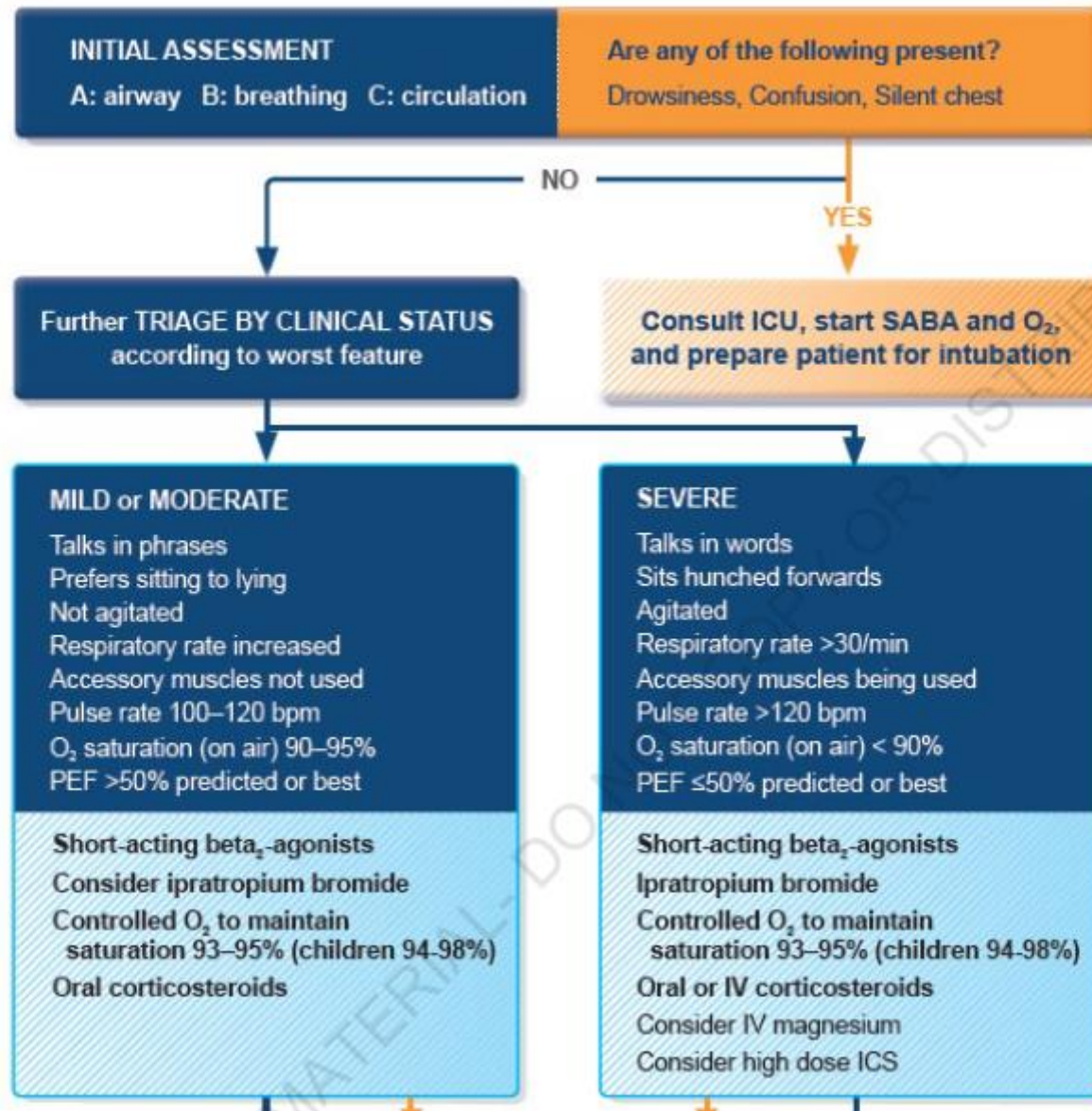
ARRANGE at DISCHARGE

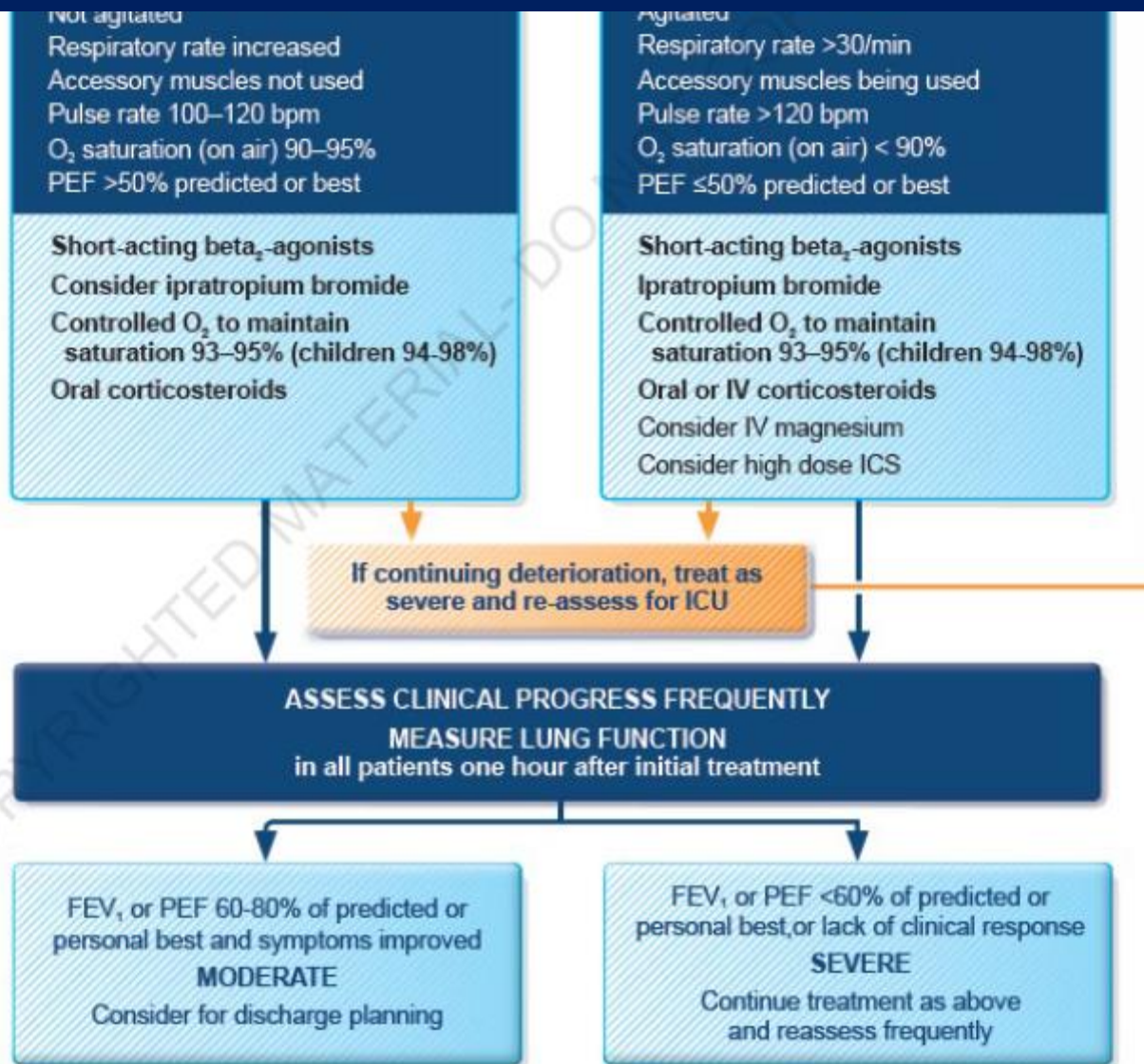
Reliever: continue as needed
Controller: start, or step up. Check inhaler technique, adherence
Prednisolone: continue, usually for 5–7 days (3–5 days for children)
Follow up: within 2–7 days (1–2 days for children)

FOLLOW UP

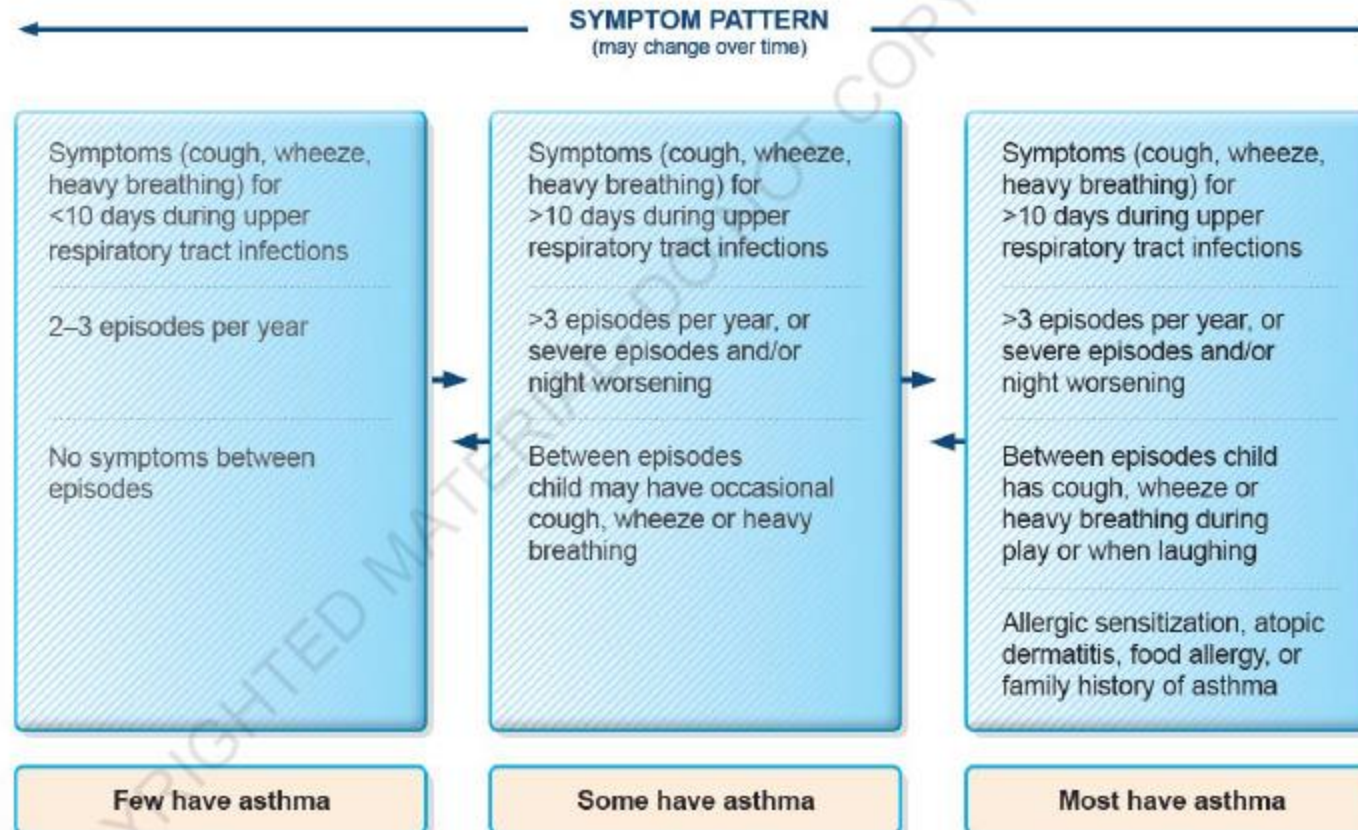
Review symptoms and signs: Is the exacerbation resolving? Should prednisone be continued?
Reliever: reduce to as-needed. **Controller:** continue higher dose for short term (1–2 weeks) or long term (3 months), depending on background to exacerbation
Risk factors: check and correct modifiable risk factors that may have contributed to exacerbation, including inhaler technique and adherence. Refer if >1–2 exacerbations in a year.
Action plan: Is it understood? Was it used appropriately? Does it need modification?

Box 4-4. Management of asthma exacerbations in acute care facility, e.g. emergency department





Box 6-1. Probability of asthma diagnosis in children 5 years and younger



Box 6-8. Management of acute asthma or wheezing in children 5 years and younger

