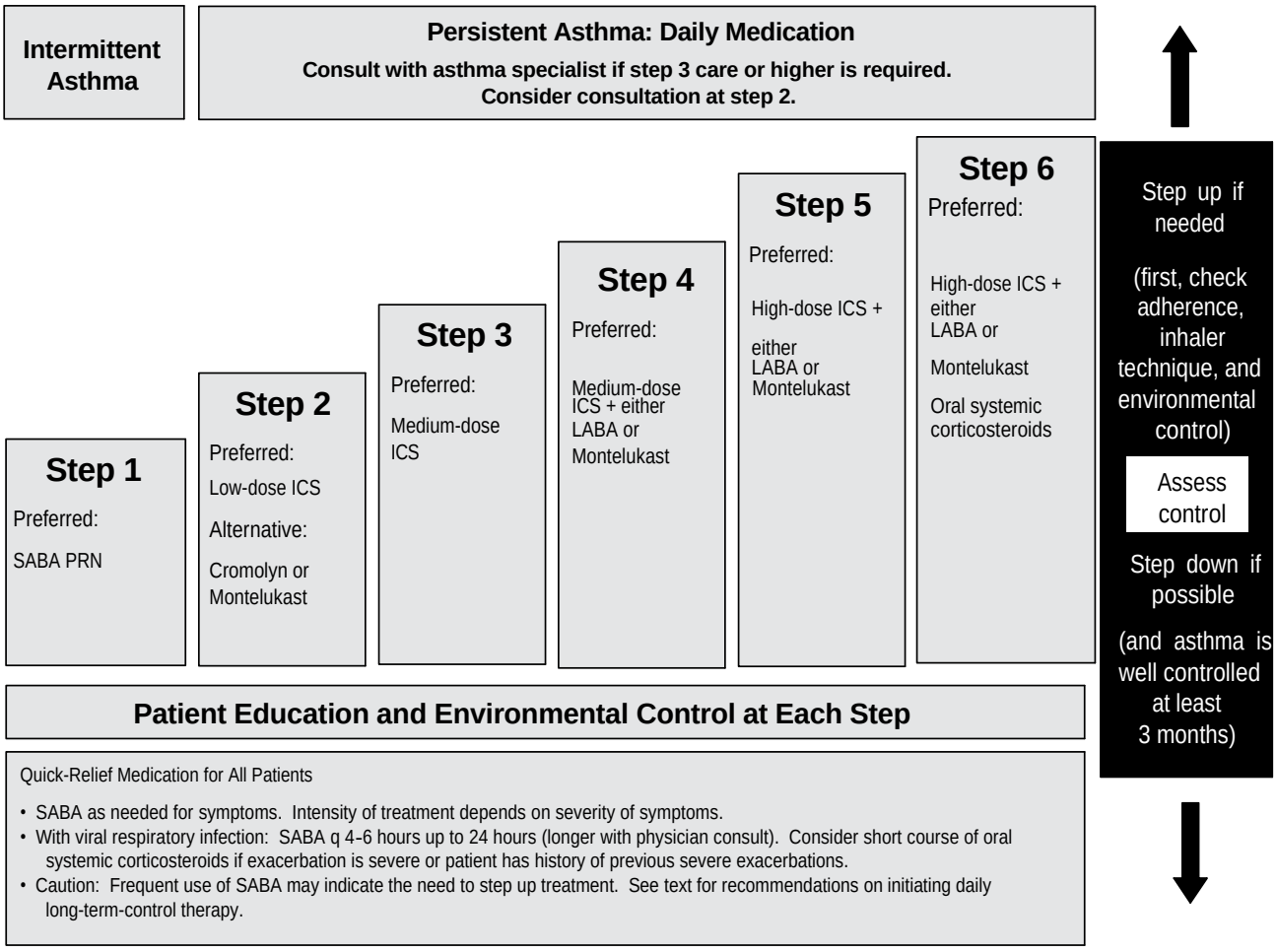
FIGURE 4-1a. STEPWISE APPROACH FOR MANAGING ASTHMA IN CHILDREN 0-4 YEARS OF AGE



Key: **Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy.** ICS, inhaled corticosteroid; LABA, inhaled long-acting beta$_2$-agonist; SABA, inhaled shortacting beta$_2$-agonist

Notes:

The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.

If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.

If clear benefit is not observed within 4-6 weeks and patient/family medication technique and adherence are satisfactory, consider adjusting therapy or alternative diagnosis.

Studies on children 0-4 years of age are limited. Step 2 preferred therapy is based on Evidence A. All other recommendations are based on expert opinion and extrapolation from studies in older children.

Retrieved from Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma (2007)

FIGURE 4-2a. CLASSIFYING ASTHMA SEVERITY AND INITIATING TREATMENT IN CHILDREN 0-4 YEARS OF AGE

Assessing severity and initiating therapy in children who are not currently taking long-term control medication

Components of Severity		Classification of Asthma Severity (0–4 years of age)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	0	1–2x/month	3–4x/month	>1x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year	≥2 exacerbations in 6 months requiring oral systemic corticosteroids, or ≥4 wheezing episodes/1 year lasting >1 day AND risk factors for persistent asthma		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time. → Exacerbations of any severity may occur in patients in any severity category.			
Recommended Step for Initiating Therapy		Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	
(See figure 4–1a for treatment steps.)		In 2–6 weeks, depending on severity, evaluate level of asthma control that is achieved. If no clear benefit is observed in 4–6 weeks, consider adjusting therapy or alternative diagnoses.			

Key: EIB, exercise-induced bronchospasm

Notes

The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.

Level of severity is determined by both impairment and risk. Assess impairment domain by patient's/caregiver's recall of previous 2-4 weeks. Symptom assessment for longer periods should reflect a global assessment such as inquiring whether the patient's asthma is better or worse since the last visit. Assign severity to the most severe category in which any feature occurs.

At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past 6 months, or ≥4 wheezing episodes in the past year, and who have risk factors for persistent asthma may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

Retrieved from Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma (2007)

FIGURE 4-3a. ASSESSING ASTHMA CONTROL AND ADJUSTING THERAPY IN CHILDREN 0-4 YEARS OF AGE

Components of Control		Classification of Asthma Control (0–4 years of age)		
		Well Controlled	**Not Well Controlled**	**Very Poorly Controlled**
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤1x/month	>1x/month	>1x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year	2–3/year	>3/year
	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.		
Recommended Action for Treatment **(See figure 4–1a for treatment steps.)**		• Maintain current treatment. • Regular followup every 1–6 months. • Consider step down if well controlled for at least 3 months.	• Step up (1 step) and • Reevaluate in 2–6 weeks. • If no clear benefit in 4–6 weeks, consider alternative diagnoses or adjusting therapy. • For side effects, consider alternative treatment options.	• Consider short course of oral systemic corticosteroids, • Step up (1–2 steps), and • Reevaluate in 2 weeks. • If no clear benefit in 4–6 weeks, consider alternative diagnoses or adjusting therapy. • For side effects, consider alternative treatment options.

Key: EIB, exercise-induced bronchospasm

Notes:

The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.

The level of control is based on the most severe impairment or risk category. Assess impairment domain by caregiver's recall of previous 2-4 weeks. Symptom assessment for longer periods should reflect a global assessment such as inquiring whether the patient's asthma is better or worse since the last visit.

At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma control. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate poorer disease control. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have not-well-controlled asthma, even in the absence of impairment levels consistent with not-well-controlled asthma.

Before step up in therapy:

— Review adherence to medications, inhaler technique, and environmental control.

— If alternative treatment option was used in a step, discontinue it and use preferred treatment for that step.

Retrieved from Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma (2007)

FIGURE 4-4b. ESTIMATED COMPARATIVE DAILY DOSAGES FOR INHALED CORTICOSTEROIDS IN CHILDREN

Drug	Low Daily Dose		Medium Daily Dose		High Daily Dose	
	Child 0-4	Child 5-11	Child 0-4	Child 5-11	Child 0-4	Child 5-11
Beclomethasone HFA						
40 or 80 mcg/puff	NA	80-160 mcg	NA	>160-320 mcg	NA	>320 mcg
Budesonide DPI						
90, 180, or 200 mcg/inhalation	NA	180-400 mcg	NA	>400-800 mcg	NA	>800 mcg
Budesonide inhaled						
Inhalation suspension for nebulization (child dose)	0.25-0.5 mg	0.5 mg	>0.5-1.0 mg	1.0 mg	>1.0 mg	2.0 mg
Flunisolide						
250 mcg/puff	NA	500-750 mcg	NA	1,000-1,250 mcg	NA	>1,250 mcg
Flunisolide HFA						
80 mcg/puff	NA	160 mcg	NA	320 mcg	NA	≥640 mcg
Fluticasone						
HFA/MDI: 44, 110, or 220 mcg/puff	176 mcg	88-176 mcg	>176-352 mcg	>176-352 mcg	>352 mcg	>352 mcg
DPI: 50, 100, or 250 mcg/inhalation	NA	100-200 mcg	NA	>200-400 mcg	NA	>400 mcg
Mometasone DPI						
200 mcg/inhalation	NA	NA	NA	NA	NA	NA
Triamcinolone acetonide						
75 mcg/puff	NA	300-600 mcg	NA	>600-900 mcg	NA	>900 mcg

Key: HFA, hydrofluoroalkane; NA, not approved and no data available for this age group

Notes:

The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy. The clinician must monitor the patient's response on several clinical parameters and adjust the dose accordingly. The stepwise approach to therapy emphasizes that once control of asthma is achieved, the dose of medication should be carefully titrated to the minimum dose required to maintain control, thus reducing the potential for adverse effect.

Some doses may be outside package labeling, especially in the high-dose range. Budesonide nebulizer suspension is the only ICS with FDA approved labeling for children <4 years of age.

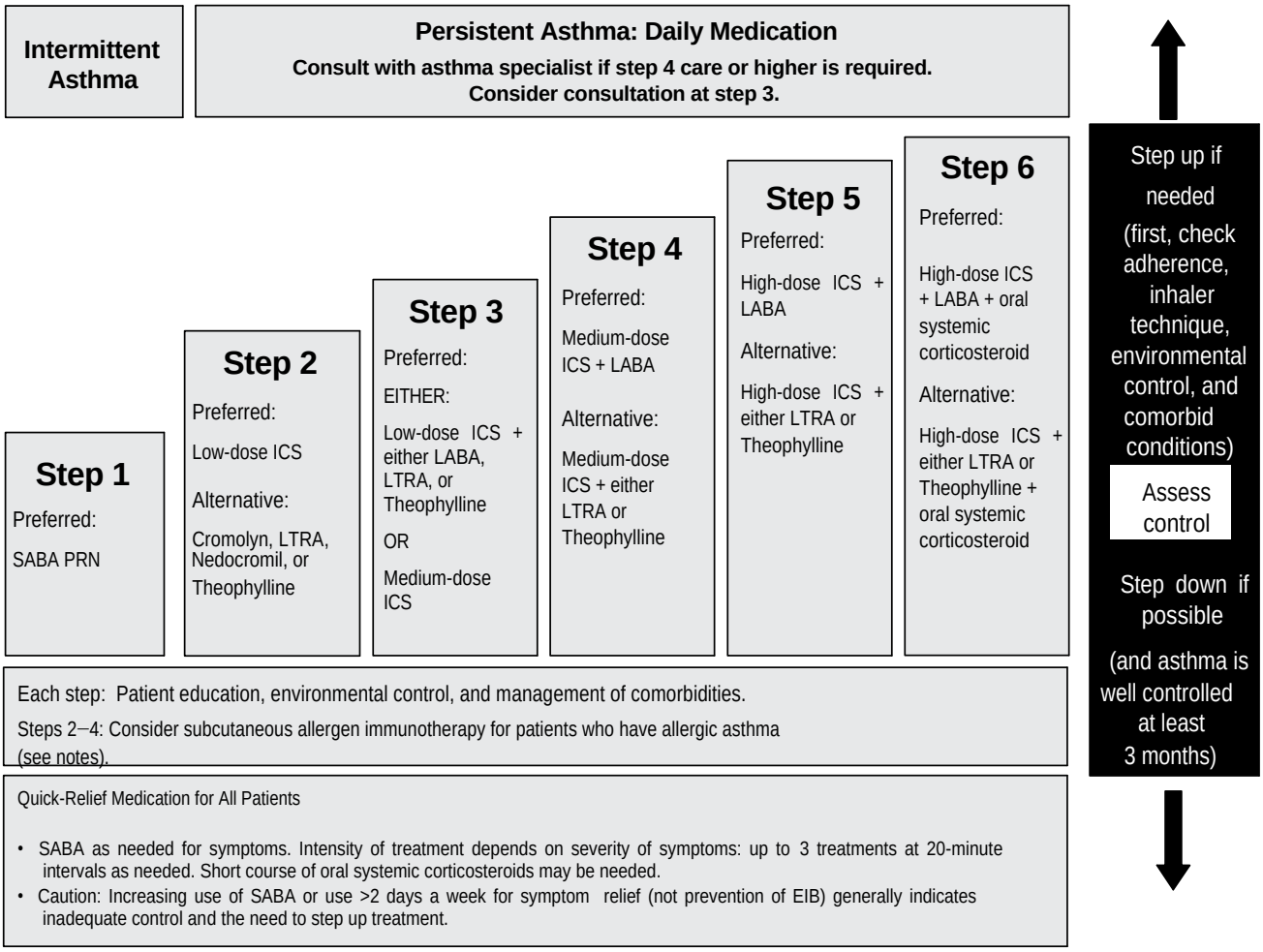
Metered-dose inhaler (MDI) dosages are expressed as the actuator dose (the amount of the drug leaving the actuator and delivered to the patient), which is the labeling required in the United States. This is different from the dosage expressed as the valve dose (the amount of drug leaving the valve, not all of which is available to the patient), which is used in many European countries and in some scientific literature. Dry powder inhaler (DPI) doses are expressed as the amount of drug in the inhaler following activation.

For children <4 years of age: The safety and efficacy of ICSs in children <1 year has not been established. Children <4 years of age generally require delivery of ICS (budesonide and fluticasone HFA) through a face mask that should fit snugly over nose and mouth and avoid nebulizing in the eyes. Wash face after each treatment to prevent local corticosteroid side effects. For budesonide, the dose may be administered 1-3 times daily. Budesonide suspension is compatible with albuterol, ipratropium, and levalbuterol nebulizer solutions in the same nebulizer. Use only jet nebulizers, as ultrasonic nebulizers are ineffective for suspensions.

For fluticasone HFA, the dose should be divided 2 times daily; the low dose for children <4 years is higher than for children 5-11 years of age due to lower dosedelivered with face mask and data on efficacy in young children.

Retrieved from Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma (2007)

FIGURE 4-1b. STEPWISE APPROACH FOR MANAGING ASTHMA IN CHILDREN 5-11 YEARS OF AGE



Key: **Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy.** ICS, inhaled corticosteroid; LABA, inhaled long-acting beta$_2$-agonist, LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

Notes:

The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.

If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.

Theophylline is a less desirable alternative due to the need to monitor serum concentration levels.

Step 1 and step 2 medications are based on Evidence A. Step 3 ICS + adjunctive therapy and ICS are based on Evidence B for efficacy of each treatment and extrapolation from comparator trials in older children and adults—comparator trials are not available for this age group; steps 4-6 are based on expert opinion and extrapolation from studies in older children and adults.

Immunotherapy for steps 2-4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens.
The role of allergy in asthma is greater in children than in adults. Clinicians who administer immunotherapy should be prepared and equipped to identify and treat anaphylaxis that may occur.

Retrieved from Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma (2007)

FIGURE 4-2b. CLASSIFYING ASTHMA SEVERITY AND INITIATING TREATMENT IN CHILDREN 5-11 YEARS OF AGE

Assessing severity and initiating therapy in children who are not currently taking long-term control medication

Components of Severity		Classification of Asthma Severity (5–11 years of age)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC >85%	• FEV_1 = >80% predicted • FEV_1/FVC >80%	• FEV_1 = 60–80% predicted • FEV_1/FVC = 75–80%	• FEV_1 <60% predicted • FEV_1/FVC <75%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. → Frequency and severity may fluctuate over time for patients in any severity category.			
		Relative annual risk of exacerbations may be related to FEV_1.			
Recommended Step for Initiating Therapy (See figure 4–1b for treatment steps.)		Step 1	Step 2	Step 3, medium-dose ICS option and consider short course of oral systemic corticosteroids	Step 3, medium-dose ICS option, or step 4 and consider short course of oral systemic corticosteroids
		In 2–6 weeks, evaluate level of asthma control that is achieved, and adjust therapy accordingly.			

Key: EIB, exercise-induced bronchospasm; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids

Notes

The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.

Level of severity is determined by both impairment and risk. Assess impairment domain by patient's/caregiver's recall of the previous 2-4 weeks and spirometry. Assign severity to the most severe category in which any feature occurs.

At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate greater underlying disease severity. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

Retrieved from Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma (2007)

FIGURE 4-3b. ASSESSING ASTHMA CONTROL AND ADJUSTING THERAPY IN CHILDREN 5-11 YEARS OF AGE

Components of Control		Classification of Asthma Control (5–11 years of age)		
		Well Controlled	**Not Well Controlled**	**Very Poorly Controlled**
Impairment	Symptoms	≤2 days/week but not more than once on each day	>2 days/week or multiple times on ≤2 days/week	Throughout the day
	Nighttime awakenings	≤1x/month	≥2x/month	≥2x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
	Lung function • FEV_1 or peak flow • FEV_1/FVC	 >80% predicted/ personal best >80%	 60–80% predicted/ personal best 75–80%	 <60% predicted/ personal best <75%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year	≥2/year (see note)	
		Consider severity and interval since last exacerbation		
	Reduction in lung growth	Evaluation requires long-term followup.		
	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.		
Recommended Action for Treatment **(See figure 4–1b for treatment steps.)**		• Maintain current step. • Regular followup every 1–6 months. • Consider step down if well controlled for at least 3 months.	• Step up at least 1 step and • Reevaluate in 2–6 weeks. • For side effects: consider alternative treatment options.	• Consider short course of oral systemic corticosteroids, • Step up 1–2 steps, and • Reevaluate in 2 weeks. • For side effects, consider alternative treatment options.

Key: EIB, exercise-induced bronchospasm; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity

Notes:

The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.

The level of control is based on the most severe impairment or risk category. Assess impairment domain by patient's/caregiver's recall of previous 2-4 weeks and by spirometry/or peak flow measures. Symptom assessment for longer periods should reflect a global assessment such as inquiring whether the patient's asthma is better or worse since the last visit.

At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma control. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate poorer disease control. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

Before step up in therapy:

— Review adherence to medications, inhaler technique, environmental control, and comorbid conditions.

— If alternative treatment option was used in a step, discontinue it and use preferred treatment for that step.

Retrieved from Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma (2007)

FIGURE 4-4b. ESTIMATED COMPARATIVE DAILY DOSAGES FOR INHALED CORTICOSTEROIDS IN CHILDREN

Drug	Low Daily Dose		Medium Daily Dose		High Daily Dose	
	Child 0-4	Child 5-11	Child 0-4	Child 5-11	Child 0-4	Child 5-11
Beclomethasone HFA						
40 or 80 mcg/puff	NA	80-160 mcg	NA	>160-320 mcg	NA	>320 mcg
Budesonide DPI						
90, 180, or 200 mcg/inhalation	NA	180-400 mcg	NA	>400-800 mcg	NA	>800 mcg
Budesonide inhaled						
Inhalation suspension for nebulization (child dose)	0.25-0.5 mg	0.5 mg	>0.5-1.0 mg	1.0 mg	>1.0 mg	2.0 mg
Flunisolide						
250 mcg/puff	NA	500-750 mcg	NA	1,000-1,250 mcg	NA	>1,250 mcg
Flunisolide HFA						
80 mcg/puff	NA	160 mcg	NA	320 mcg	NA	≥640 mcg
Fluticasone						
HFA/MDI: 44, 110, or 220 mcg/puff	176 mcg	88-176 mcg	>176-352 mcg	>176-352 mcg	>352 mcg	>352 mcg
DPI: 50, 100, or 250 mcg/inhalation	NA	100-200 mcg	NA	>200-400 mcg	NA	>400 mcg
Mometasone DPI						
200 mcg/inhalation	NA	NA	NA	NA	NA	NA
Triamcinolone acetonide						
75 mcg/puff	NA	300-600 mcg	NA	>600-900 mcg	NA	>900 mcg

Key: HFA, hydrofluoroalkane; NA, not approved and no data available for this age group

Notes:

The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy. The clinician must monitor the patient's response on several clinical parameters and adjust the dose accordingly. The stepwise approach to therapy emphasizes that once control of asthma is achieved, the dose of medication should be carefully titrated to the minimum dose required to maintain control, thus reducing the potential for adverse effect.

Some doses may be outside package labeling, especially in the high-dose range. Budesonide nebulizer suspension is the only ICS with FDA approved labeling for children <4 years of age.

Metered-dose inhaler (MDI) dosages are expressed as the actuator dose (the amount of the drug leaving the actuator and delivered to the patient), which is the labeling required in the United States. This is different from the dosage expressed as the valve dose (the amount of drug leaving the valve, not all of which is available to the patient), which is used in many European countries and in some scientific literature. Dry powder inhaler (DPI) doses are expressed as the amount of drug in the inhaler following activation.

For children <4 years of age: The safety and efficacy of ICSs in children <1 year has not been established. Children <4 years of age generally require delivery of ICS (budesonide and fluticasone HFA) through a face mask that should fit snugly over nose and mouth and avoid nebulizing in the eyes. Wash face after each treatment to prevent local corticosteroid side effects. For budesonide, the dose may be administered 1-3 times daily. Budesonide suspension is compatible with albuterol, ipratropium, and levalbuterol nebulizer solutions in the same nebulizer. Use only jet nebulizers, as ultrasonic nebulizers are ineffective for suspensions.

For fluticasone HFA, the dose should be divided 2 times daily; the low dose for children <4 years is higher than for children 5-11 years of age due to lower dosedelivered with face mask and data on efficacy in young children.

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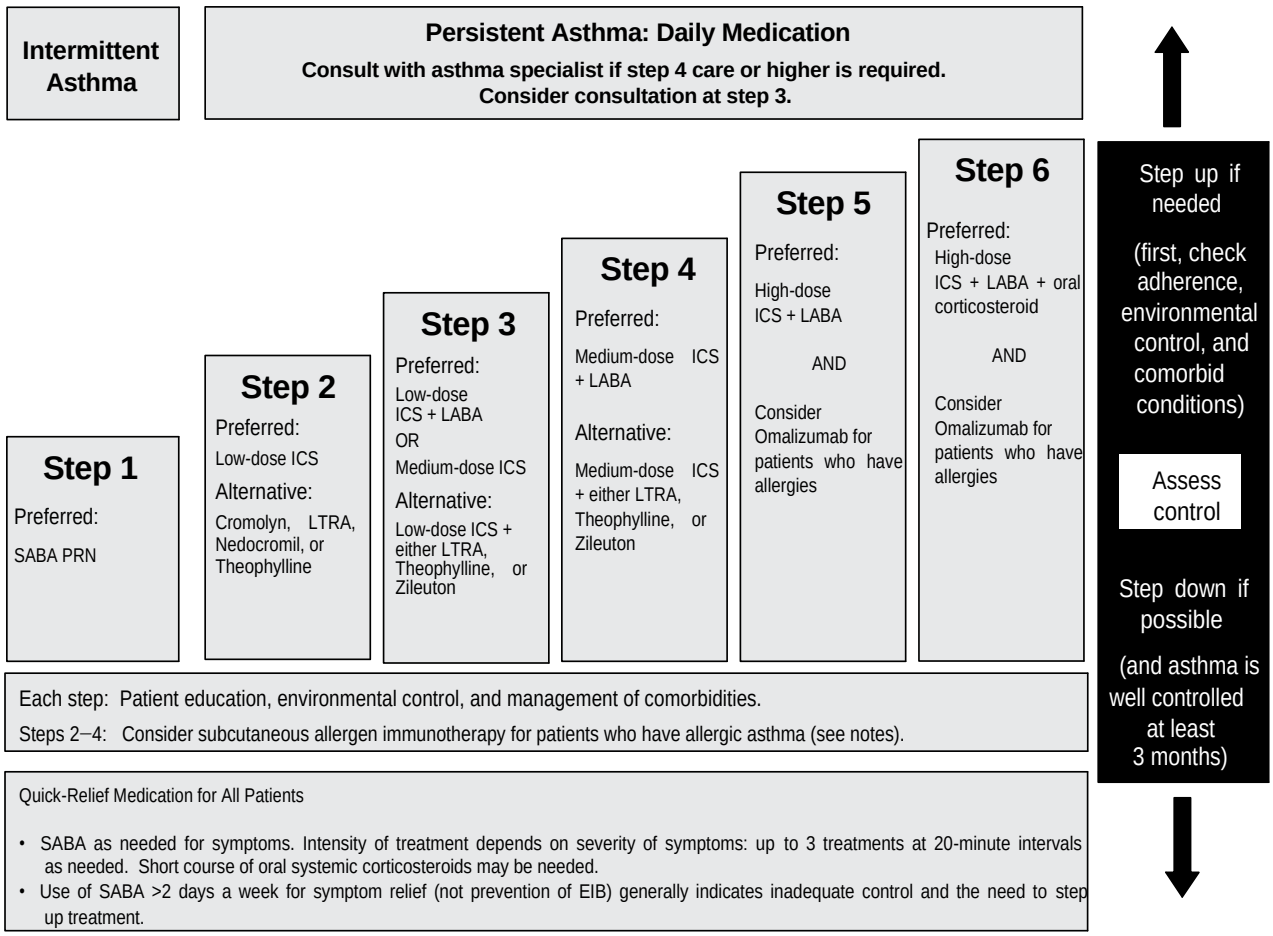
FIGURE 4-5. STEPWISE APPROACH FOR MANAGING ASTHMA IN YOUTHS ≥12 YEARS OF AGE AND ADULTS



— Key: **Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy.** EIB, exercise-induced bronchospasm; ICS, inhaled corticosteroid; LABA, long -acting inhaled beta $_2$ agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

Notes:

The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.

If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.

Zileuton is a less desirable alternative due to limited studies as adjunctive therapy and the need to monitor liver function. Theophylline requires monitoring of serum concentration levels.

In step 6, before oral systemic corticosteroids are introduced, a trial of high-dose ICS + LABA + either LTRA, theophylline, or zileuton may be considered, although this approach has not been studied in clinical trials.

Step 1, 2, and 3 preferred therapies are based on Evidence A; step 3 alternative therapy is based on Evidence A for LTRA, Evidence B for theophylline, and Evidence D for zileuton. Step 4 preferred therapy is based on Evidence B, and alternative therapy is based on Evidence B for LTRA and theophylline and Evidence D for zileuton. Step 5 preferred therapy is based on Evidence B. Step 6 preferred therapy is based on (EPR 2 1997) and Evidence B for omalizumab.

Immunotherapy for steps 2-4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens. The role of allergy in asthma is greater in children than in adults.

Clinicians who administer immunotherapy or omalizumab should be prepared and equipped to identify and treat anaphylaxis that may occur.

Retrieved from Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma (2007)

FIGURE 4-6. CLASSIFYING ASTHMA SEVERITY AND INITIATING TREATMENT IN YOUTHS ≥12 YEARS OF AGE AND ADULTS

— **Assessing severity and initiating treatment for patients who are not currently taking long-term control medications**

Components of Severity		Classification of Asthma Severity ≥12 years of age			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily, and not more than 1x on any day	Daily	Several times per day
Normal FEV $_1$/FVC: 8–19 yr 85%; 20–39 yr 80%; 40–59 yr 75%; 60–80 yr 70%	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note)		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV_1.			
Recommended Step for Initiating Treatment		Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	Step 4 or 5 and consider short course of oral systemic corticosteroids
(See figure 4–5 for treatment steps.)		In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			

—

Key: FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICU, intensive care unit

Notes:

The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.

Level of severity is determined by assessment of both impairment and risk. Assess impairment domain by patient's/caregiver's recall of previous 2-4 weeks and spirometry. Assign severity to the most severe category in which any feature occurs.

At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate greater underlying disease severity. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

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FIGURE 4-7. ASSESSING ASTHMA CONTROL AND ADJUSTING THERAPY IN YOUTHS ≥12 YEARS OF AGE AND ADULTS

Components of Control		Classification of Asthma Control (≥12 years of age)		
		Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤2x/month	1–3x/week	≥4x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤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 ACQ ACT	 0 ≤0.75* ≥20	 1-2 ≥1.5 16–19	 3-4 N/A ≤15
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year	≥2/year (see note)	
		Consider severity and interval since last exacerbation		
	Progressive loss of lung function	Evaluation requires long-term followup care		
	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.		
Recommended Action for Treatment (see figure 4–5 for treatment steps)		• Maintain current step. • Regular followups every 1–6 months to maintain control. • Consider step down if well controlled for at least 3 months.	• Step up 1 step and • Reevaluate in 2–6 weeks. • For side effects, consider alternative treatment options.	• Consider short course of oral systemic corticosteroids, • Step up 1–2 steps, and • Reevaluate in 2 weeks. • For side effects, consider alternative treatment options.

— *ACQ values of 0.76-1.4 are indeterminate regarding well-controlled asthma.
— Key: EIB, exercise-induced bronchospasm; ICU, intensive care unit

Notes:

The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.

The level of control is based on the most severe impairment or risk category. Assess impairment domain by patient's recall of previous 2-4 weeks and by spirometry/or peak flow measures. Symptom assessment for longer periods should reflect a global assessment, such as inquiring whether the patient's asthma is better or worse since the last visit.

At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma control. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate poorer disease control. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have not-well-controlled asthma, even in the absence of impairment levels consistent with not-well-controlled asthma.

Validated Questionnaires for the impairment domain (the questionnaires do not assess lung function or the risk domain)

ATAQ = Asthma Therapy Assessment Questionnaire© (See sample in "Component 1: Measures of Asthma Assessment and Monitoring.")

ACQ = Asthma Control Questionnaire© (user package may be obtained at www.qoltech.co.uk or juniper@qoltech.co.uk)

ACT = Asthma Control Test™ (See sample in "Component 1: Measures of Asthma Assessment and Monitoring.")

Minimal Important Difference: 1.0 for the ATAQ; 0.5 for the ACQ; not determined for the ACT.

Before step up in therapy:

— Review adherence to medication, inhaler technique, environmental control, and comorbid conditions.
— If an alternative treatment option was used in a step, discontinue and use the preferred treatment for that step.

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FIGURE 4-8b. ESTIMATED COMPARATIVE DAILY DOSAGES FOR INHALED CORTICOSTEROIDS FOR YOUTHS ≥12 YEARS OF AGE AND ADULTS

Drug	Low Daily Dose Adult	Medium Daily Dose Adult	High Daily Dose Adult
Beclomethasone HFA 40 or 80 mcg/puff	80-240 mcg	>240-480 mcg	>480 mcg
Budesonide DPI 90, 180, or 200 mcg/inhalation	180-600 mcg	>600-1,200 mcg	>1,200 mcg
Flunisolide 250 mcg/puff	500-1,000 mcg	>1,000-2,000 mcg	>2,000 mcg
Flunisolide HFA 80 mcg/puff	320 mcg	>320-640 mcg	>640 mcg
Fluticasone			
HFA/MDI: 44, 110, or 220 mcg/puff	88-264 mcg	>264-440 mcg	>440 mcg
DPI: 50, 100, or 250 mcg/inhalation	100-300 mcg	>300-500 mcg	>500 mcg
Mometasone DPI 200 mcg/inhalation	200 mcg	400 mcg	>400 mcg
Triamcinolone acetonide 75 mcg/puff	300-750 mcg	>750-1,500 mcg	>1,500 mcg

Key: DPI, dry powder inhaler; HFA, hydrofluoroalkane; MDI, metered-dose inhaler

Notes:

The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy. The clinician must monitor the patient's response on several clinical parameters and adjust the dose accordingly. The stepwise approach to therapy emphasizes that once control of asthma is achieved, the dose of medication should be carefully titrated to the minimum dose required to maintain control, thus reducing the potential for adverse effect.

Some doses may be outside package labeling, especially in the high-dose range.

MDI dosages are expressed as the actuator dose (the amount of the drug leaving the actuator and delivered to the patient), which is the labeling required in the United States. This is different from the dosage expressed as the valve dose (the amount of drug leaving the valve, not all of which is available to the patient), which is used in many European countries and in some scientific literature. DPI doses are expressed as the amount of drug in the inhaler following activation.

Comparative dosages are based on published comparative clinical trials (Adams et al. 2005; Barnes et al. 1998; Kelly 1998; Lasserson et al. 2005; Pedersen and O'Byrne 1997). The rationale for some key comparisons is summarized as follows:

— The high dose is the dose that appears likely to be the threshold beyond which significant hypothalamic-pituitary-adrenal (HPA) axis suppression is produced, and, by extrapolation, the risk is increased for other clinically significant systemic effects if used for prolonged periods of time (Martin et al. 2002; Szefler et al. 2002).

— The low- and medium-doses reflect findings from dose-ranging studies in which incremental efficacy within the low- to medium-dose ranges was established without increased systemic effect as measured by overnight cortisol excretion. The studies demonstrated a relatively flat dose-response curve for efficacy at the medium-dose range; that is, increasing the dose of high-dose range did not significantly increase efficacy but did increase systemic effect (Adams et al. 2001; Martin et al. 2002; Szefler et al. 2002).

— The dose for budesonide DPI is based on recently available comparative data with other medications. These new data, including meta-analyses, show that budesonide DPI is comparable to approximately twice the microgram dose of fluticasone MDI or DPI (Adams et al. 2005; Barnes et al. 1998; Nielsen and Dahl 2000).

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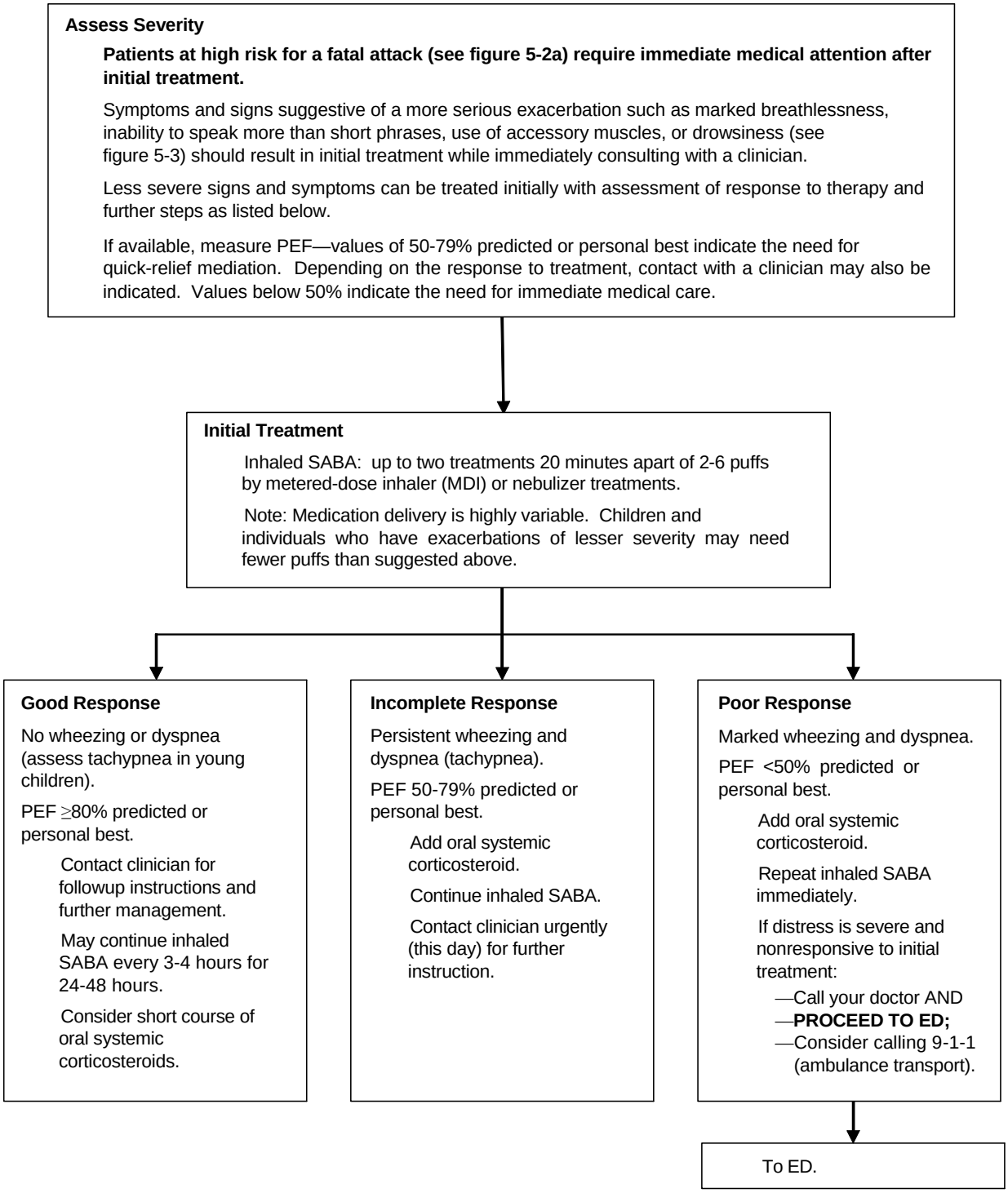
FIGURE 5-4. MANAGEMENT OF ASTHMA EXACERBATIONS: HOME TREATMENT



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Key: ED, emergency department; MDI, metered-dose inhaler; PEF, peak expiratory flow; SABA, short-acting beta$_2$-agonist (quick-relief inhaler)

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FIGURE 5-3. FORMAL EVALUATION OF ASTHMA EXACERBATION SEVERITY IN THE URGENT OR EMERGENCY CARE SETTING

	Mild	Moderate	Severe	Subset: Respiratory Arrest Imminent
Symptoms				
Breathlessness	While walking Can lie down	While at rest (infant—softer, shorter cry, difficulty feeding) Prefers sitting	While at rest (infant—stops feeding) Sits upright	
Talks in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy or confused
Signs				
Respiratory rate	Increased	Increased Guide to rates of breathing in awake children: *Age* <2 months 2-12 months 1-5 years 6-8 years	Often >30/minute *Normal rate* <60/minute <50/minute <40/minute <30/minute	
Use of accessory muscles; suprasternal retractions	Usually not	Commonly	Usually	Paradoxical thoracoabdominal movement
Wheeze	Moderate, often only end expiratory	Loud; throughout exhalation	Usually loud; throughout inhalation and exhalation	Absence of wheeze
Pulse/minute	<100	100-120 Guide to normal pulse rates in children:: *Age* 2-12 months 1-2 years 2-8 years	>120 *Normal rate* <160/minute <120/minute <110/minute	Bradycardia
Pulsus paradoxus	Absent <10 mmHg	May be present 10-25 mmHg	Often present >25 mmHg (adult) 20-40 mmHg (child)	Absence suggests respiratory muscle fatigue
Functional Assessment				
PEF percent predicted or percent personal best	≥70 percent	Approx. 40-69 percent or response lasts <2 hours	<40 percent	<25 percent Note: PEF testing may not be needed in very severe attacks
PaO_2 (on air)	Normal (test not usually necessary)	≥60 mmHg (test not usually necessary)	<60 mmHg: possible cyanosis	
and/or PCO_2	<42 mmHg (test not usually necessary)	<42 mmHg (test not usually necessary)	≥42 mmHg: possible respiratory failure (See pages 393-394, 399.)	
SaO_2 percent (on air) at sea level	>95 percent (test not usually necessary)	90-95 percent (test not usually necessary)	<90 percent	
	Hypercapnia (hypoventilation) develops more readily in young children than in adults and adolescents.			

Key: PaO_2, arterial oxygen pressure; PCO_2, partial pressure of carbon dioxide; PEF, peak expiratory flow; SaO_2, oxygen saturation

Notes:

The presence of several parameters, but not necessarily all, indicates the general classification of the exacerbation.

Many of these parameters have not been systematically studied, especially as they correlate with each other. Thus, they serve only as general guides (Cham et al. 2002; Chey et al. 1999; Gorelick et al. 2004b; Karras et al. 2000; Kelly et al. 2002b and 2004; Keogh et al. 2001; McCarren et al. 2000; Rodrigo and Rodrigo 1998b; Rodrigo et al. 2004; Smith et al. 2002).

The emotional impact of asthma symptoms on the patient and family is variable but must be recognized and addressed and can affect approaches to treatment and followup (Ritz et al. 2000; Strunk and Mrazek 1986; von Leupoldt and Dahme 2005).

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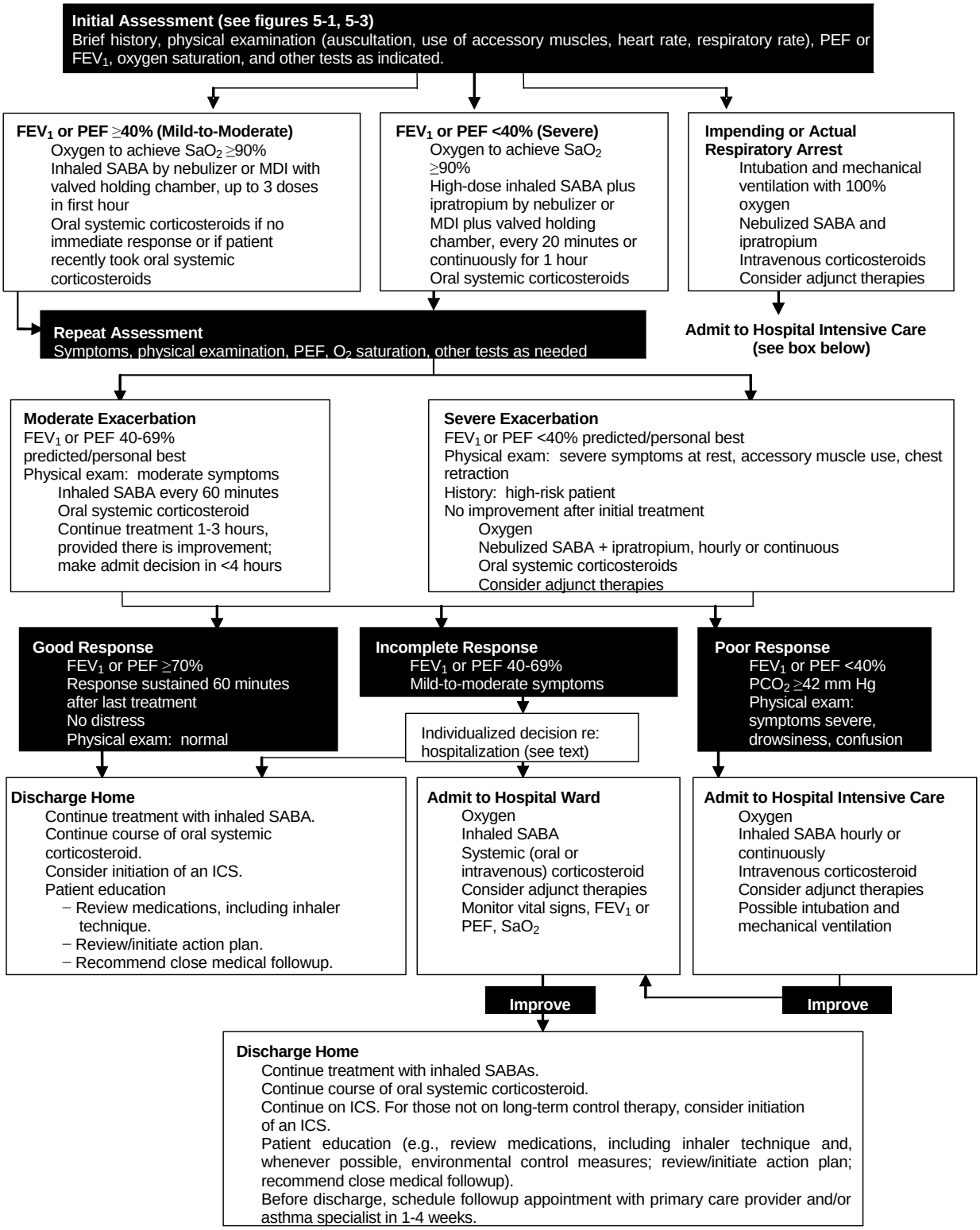
FIGURE 5-6. MANAGEMENT OF ASTHMA EXACERBATIONS: EMERGENCY DEPARTMENT AND HOSPITAL-BASED CARE



Key: FEV_1, forced expiratory volume in 1 second; ICS, inhaled corticosteroid; MDI, metered dose inhaler; PCO_2, partial pressure carbon dioxide; PEF, peak expiratory flow; SABA, short-acting $beta_2$-agonist; SaO_2, oxygen saturation

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FIGURE 5-5. DOSAGES OF DRUGS FOR ASTHMA EXACERBATIONS

Medication	Dosages: Child Dose	Dosages: Adult Dose*	Comments
Inhaled Short-Acting Beta$_2$-Agonists (SABA)			
Albuterol			
Nebulizer solution A. (0.63 mg/3 mL, 1.25 mg/3 mL, 2.5 mg/3 mL, 5.0 mg/mL)	0.15 mg/kg (minimum dose 2.5 mg) every 20 minutes for 3 doses then 0.15-0.3 mg/kg up to 10 mg every 1-4 hours as needed, or 0.5 mg/kg/hour by continuous nebulization.	2.5-5 mg every 20 minutes for 3 doses, then 2.5-10 mg every 1-4 hours as needed, or 10-15 mg/hour continuously.	Only selective beta$_2$-agonists are recommended. For optimal delivery, dilute aerosols to minimum of 3 mL at gas flow of 6-8 L/min. Use large volume nebulizers for continuous administration. May mix with ipratropium nebulizer solution.
MDI B. (90 mcg/puff)	4-8 puffs every 20 minutes for 3 doses, then every 1-4 hours inhalation maneuver as needed. Use VHC; add mask in children <4 years.	4-8 puffs every 20 minutes up to 4 hours, then every 1-4 hours as needed.	In mild-to-moderate exacerbations, MDI plus VHC is as effective as nebulized therapy with appropriate administration technique and coaching by trained personnel.
Bitolterol			
Nebulizer solution C. (2 mg/mL)	See albuterol dose; thought to be half as potent as albuterol on mg basis.	See albuterol dose.	Has not been studied in severe asthma exacerbations. Do not mix with other drugs.
MDI D. (370 mcg/puff)	See albuterol MDI dose.	See albuterol MDI dose.	Has not been studied in severe asthma exacerbations.
Levalbuterol (R-albuterol)			
Nebulizer solution E. (0.63 mg/3 mL, 1.25 mg/0.5 mL 1.25 mg/3 mL)	0.075 mg/kg (minimum dose 1.25 mg) every 20 minutes for 3 doses, then 0.075-0.15 mg/kg up to 5 mg every 1-4 hours as needed.	1.25-2.5 mg every 20 minutes for 3 doses, then 1.25-5 mg every 1-4 hours as needed.	Levalbuterol administered in one-half the mg dose of albuterol provides comparable efficacy and safety. Has not been evaluated by continuous nebulization.
MDI F. (45 mcg/puff)	See albuterol MDI dose.	See albuterol MDI dose.	
Pirbuterol			
MDI G. (200 mcg/puff)	See albuterol MDI dose; thought to be half as potent as albuterol on a mg basis.	See albuterol MDI dose.	Has not been studied in severe asthma exacerbations.
Systemic (Injected) Beta$_2$-Agonists			
Epinephrine H. 1:1,000 (1 mg/mL)	0.01 mg/kg up to 0.3-0.5 mg every 20 minutes for 3 doses sq.	0.3-0.5 mg every 20 minutes for 3 doses sq.	No proven advantage of systemic therapy over aerosol.
Terbutaline I. (1 mg/mL)	0.01 mg/kg every 20 minutes for 3 doses then every 2-6 hours as needed sq.	0.25 mg every 20 minutes for 3 doses sq.	No proven advantage of systemic therapy over aerosol.

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FIGURE 5-5. DOSAGES OF DRUGS FOR ASTHMA EXACERBATIONS (CONTINUED)

Medication	Dosages		
	Child Dose*	Adult Dose	Comments
Anticholinergics			
Ipratropium bromide			
Nebulizer solution J. (0.25 mg/mL)	0.25-5 mg every 20 minutes for 3 doses, then as needed	0.5 mg every 20 minutes for 3 doses then as needed	May mix in same nebulizer with albuterol. Should not be used as first-line therapy; should be added to SABA therapy for severe exacerbations. The addition of ipratropium has not been shown to provide further benefit once the patient is hospitalized.
MDI K. (18 mcg/puff)	4-8 puffs every 20 minutes as needed up to 3 hours	8 puffs every 20 minutes as needed up to 3 hours	Should use with VHC and face mask for children <4 years. Studies have examined ipratropium bromide MDI for up to 3 hours.
Ipratropium with albuterol			
Nebulizer solution (Each 3 mL vial contains 0.5 mg ipratropium bromide and 2.5 mg albuterol.)	1.5 mL every 20 minutes for 3 doses, then as needed	3 mL every 20 minutes for 3 doses, then as needed	May be used for up to 3 hours in the initial management of severe exacerbations. The addition of ipratropium to albuterol has not been shown to provide further benefit once the patient is hospitalized.
MDI (Each puff contains 18 mcg ipratropium bromide and 90 mcg of albuterol.)	4-8 puffs every 20 minutes as needed up to 3 hours	8 puffs every 20 minutes as needed up to 3 hours	Should use with VHC and face mask for children <4 years.
Systemic Corticosteroids			
	(Applies to all three corticosteroids)		
Prednisone Methylprednisolone Prednisolone	1 mg/kg in 2 divided doses (maximum = 60 mg/day) until PEF is 70% of predicted or personal best	40-80 mg/day in 1 or 2 divided doses until PEF reaches 70% of predicted or personal best	For outpatient "burst," use 40-60 mg in single or 2 divided doses for total of 5-10 days in adults (children: 1-2 mg/kg/day maximum 60 mg/day for 3-10 days).

*Children ≤ 12 years of age

Key: ED, emergency department; MDI, metered-dose inhaler; PEF, peak expiratory flow; VHC, valved holding chamber

Notes:

There is no known advantage for higher doses of corticosteroids in severe asthma exacerbations, nor is there any advantage for intravenous administration over oral therapy provided gastrointestinal transit time or absorption is not impaired.

The total course of systemic corticosteroids for an asthma exacerbation requiring an ED visit of hospitalization may last from 3 to 10 days. For corticosteroid courses of less than 1 week, there is no need to taper the dose. For slightly longer courses (e.g., up to 10 days), there probably is no need to taper, especially if patients are concurrently taking ICSs.

ICSs can be started at any point in the treatment of an asthma exacerbation.

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