Pediatric vs. Adult Asthma: What is the Difference?

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Objectives

- Discuss the differences between adult and pediatric asthma
- Describe the mechanisms of action of the different asthma medications
- List the limitations of the SMART study

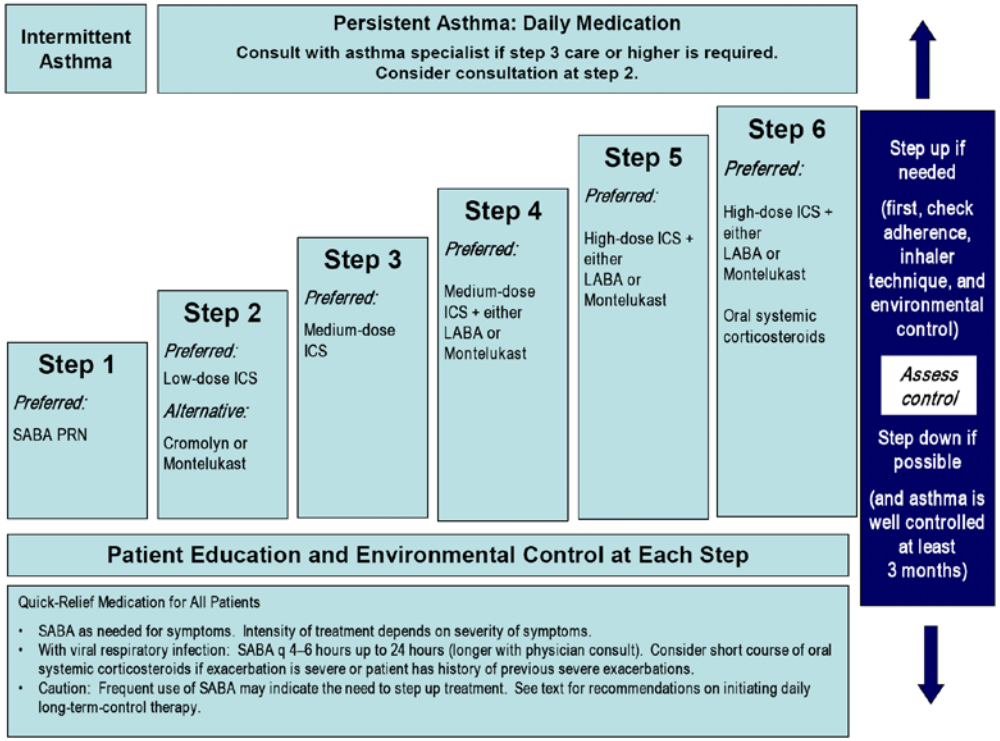
Asthma Guidelines

- Asthma treatment guidelines were revised in 2007—called the Expert Panel Report 2007
- http://www.nhlbi.nih.gov/guidelines/asthma
- Main area of difference = goal of asthma therapy = ASTHMA CONTROL

Asthma Guidelines

- Four keys areas of asthma care to help achieve and maintain control
  - Assessment & Monitoring
  - Patient Education
  - Control of factors contributing to asthma severity
  - Pharmacologic Treatment

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 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.
- 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.

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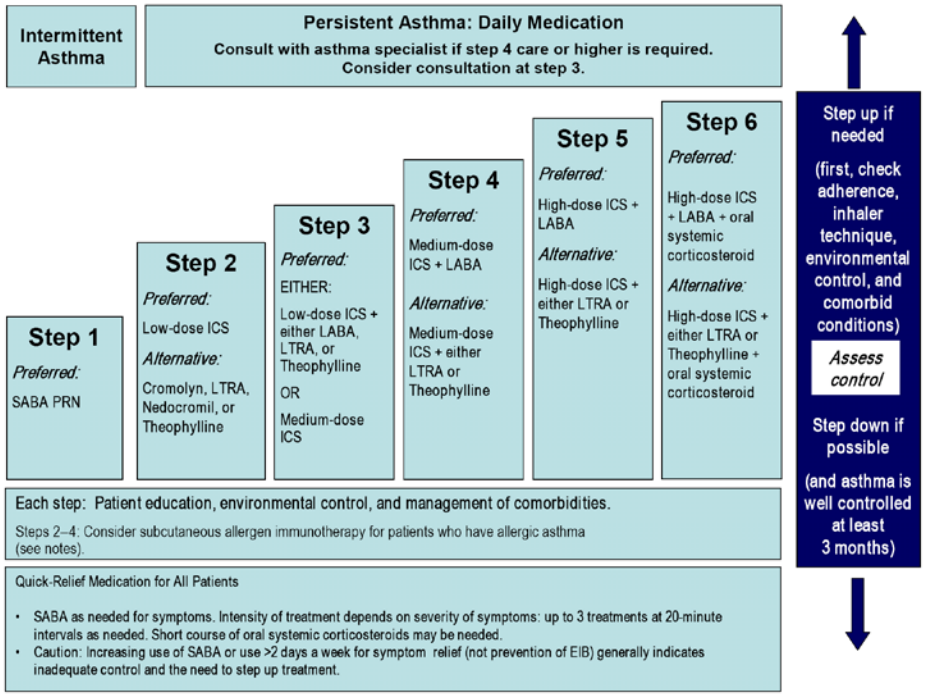
FIGURE 4–1b. STEPWISE APPROACH FOR MANAGING ASTHMA IN CHILDREN 5–11 YEARS OF AGE



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.

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Step 1

Preferred:

SABA PRN

For Children 0-11 years old

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Short Acting Beta$_2$-Agonists

- Albuterol
- Levalbuterol
- Pirbuterol

Mechanisms

- **Bronchodilation.** Binds to the beta$_2$-adrenergic receptor, producing smooth muscle relaxation following adenylate cyclase activation and increase in cyclic AMP producing functional antagonism of bronchoconstriction.

Quick-relief Beta$_2$ Agonists

www.allergy.peds.arizona.edu
accessed 2/2/07

Spacers

www.google.com
accessed 1/30/07

Step 2

Preferred:

Low-dose ICS

Alternative:

Cromolyn or Montelukast

For Children 0-4 years old

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Step 2

Preferred:

Low-dose ICS

Alternative:

Cromolyn, LTRA, Nedocromil, or Theophylline

For Children 5-11 years old

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Inhaled Corticosteroids

- Many different inhaled corticosteroids exist on the U.S. market
- All share the same mechanism of action
- Vary based on dosing (based on potency)

Mechanisms

- **Anti-inflammatory.** Block late reaction to allergen and reduce airway hyperresponsiveness. Inhibit cytokine production, adhesion protein activation, and inflammatory cell migration and activation.
- Reverse beta$_2$-receptor downregulation. Inhibit microvascular leakage.

ERP-2007

www.allergy.peds.arizona.edu
accessed 2/02/07

Leukotriene Modifier

- Two medications exist in U.S. market that match this description
  - Zafirlukast (Accolate®)
  - Montelukast (Singular®)

Leukotriene Receptor Antagonists (LTRAs)	*Mechanisms* ■ **Leukotriene receptor antagonist;** selective competitive inhibitor of $CysLT_1$ receptor.

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www.google.com accessed 01/30/07

Methylxanthines

- Theophylline
- Aminophylline

Mechanisms

- **Bronchodilation.** Smooth muscle relaxation from phosphodiesterase inhibition and possibly adenosine antagonism.
- May affect eosinophilic infiltration into bronchial mucosa as well as decreases T-lymphocyte numbers in epithelium.
- Increases diaphragm contractility and mucociliary clearance.

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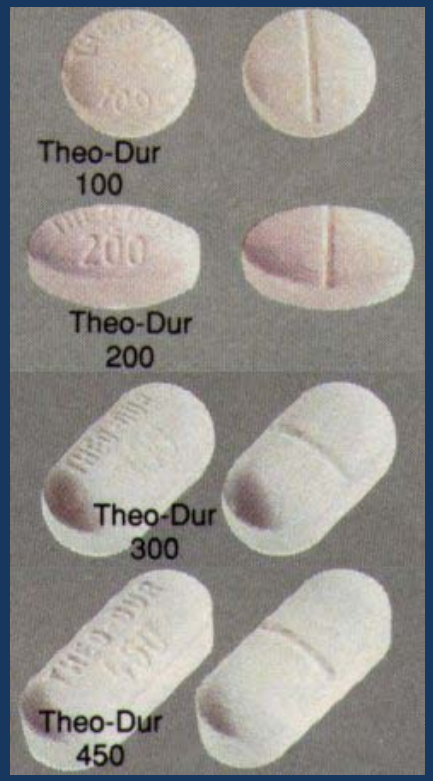

www.google.com accessed 01/30/07

Step 3

Preferred:

Medium-dose ICS

For Children 0-4 years

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Step 3

Preferred:

EITHER:

Low-dose ICS + either LABA, LTRA, or Theophylline

OR

Medium-dose ICS

For Children
5-11 years

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Long-Acting Beta$_2$-Agonists

- Salmeterol
- Formoterol
- Combinations with ICS

Mechanisms

- **Bronchodilation.** Smooth muscle relaxation following adenylate cyclase activation and increase in cyclic AMP, producing functional antagonism of bronchoconstriction.
- Compared to SABA, salmeterol (but not formoterol) has slower onset of action (15–30 minutes). Both salmeterol and formoterol have longer duration (>12 hours) compared to SABA.

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Long Acting Beta$_2$ Agonists

www.google.com accessed 01/30/07

Formoterol

Salmeterol

Fluticasone/Salmeterol

Budesonide/formoterol

www.allergy.peds.arizona.edu accessed 2/28/08

Step 5

Preferred:

High-dose ICS + either
LABA or
Montelukast

Step 6

Preferred:

High-dose ICS + either
LABA or
Montelukast

Oral systemic corticosteroids

For Children 0-4 years

ERP-2007

Step 5

Preferred:

High-dose ICS + LABA

Alternative:

High-dose ICS + either LTRA or Theophylline

Step 6

Preferred:

High-dose ICS + LABA + oral systemic corticosteroid

Alternative:

High-dose ICS + either LTRA or Theophylline + oral systemic corticosteroid

For Children 5-11 years

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Oral Corticosteroids

- Methylprednisolone
- Prednisone
- Prednisolone

Mechanisms

- **Anti-inflammatory.** Block late reaction to allergen and reduce airway hyperresponsiveness. Inhibit cytokine production, adhesion protein activation, and inflammatory cell migration and activation.
- Reverse beta$_2$-receptor downregulation. Inhibit microvascular leakage.

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www.google.com accessed 01/30/07

Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

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Immunotherapy

- Omalizumab (anti-IgE)

Mechanisms

- Binds to circulating IgE, preventing it from binding to the high-affinity (FcεRI) receptors on basophils and mast cells.
- Decreases mast cell mediator release from allergen exposure.
- Decreases the number of FcεRIs in basophils and submucosal cells.

www.google.com accessed 02/28/08

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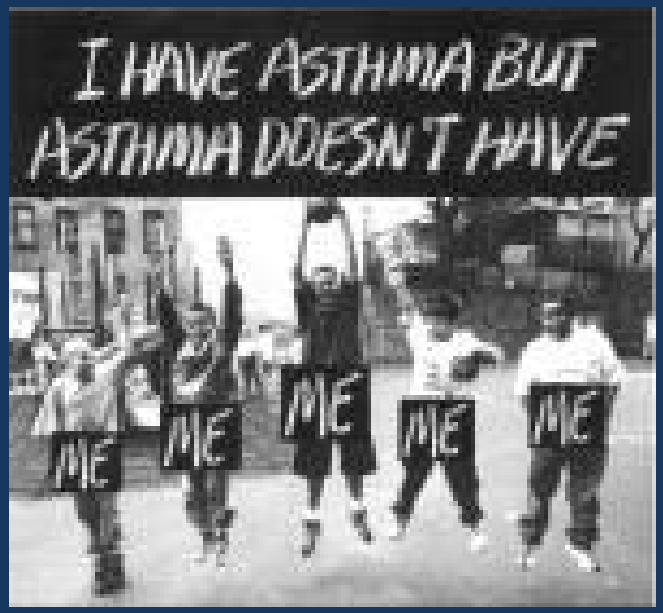
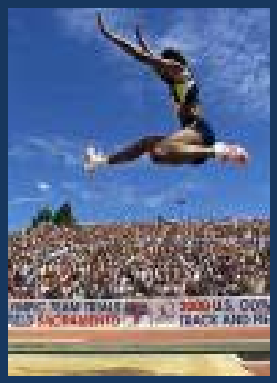
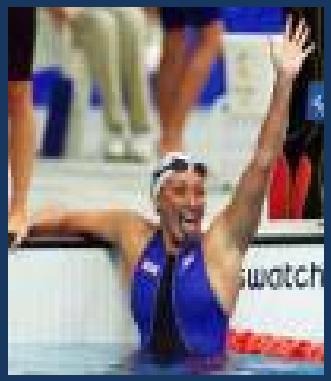

I HAVE ASTHMA BUT
ASTHMA DOESN'T HAVE
ME
ME
ME
ME
ME





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 (See figure 4–5 for treatment steps.)		Step 1	Step 2	Step 3	Step 4 or 5
				and consider short course of oral systemic corticosteroids	
		In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			

EPR 3, 2007

Intermittent Asthma

Persistent Asthma: Daily Medication

Consult with asthma specialist if step 4 care or higher is required.
Consider consultation at step 3.

Step 1

Preferred:

SABA PRN

Step 2

Preferred:

Low-dose ICS

Alternative:

Cromolyn, LTRA, Nedocromil, or Theophylline

Step 3

Preferred:

Low-dose ICS + LABA
OR
Medium-dose ICS

Alternative:

Low-dose ICS + either LTRA, Theophylline, or Zileuton

Step 4

Preferred:

Medium-dose ICS + LABA

Alternative:

Medium-dose ICS + either LTRA, Theophylline, or Zileuton

Step 5

Preferred:

High-dose ICS + LABA

AND

Consider Omalizumab for patients who have allergies

Step 6

Preferred:

High-dose ICS + LABA + oral corticosteroid

AND

Consider Omalizumab for patients who have allergies

Step up if needed

(first, check adherence, environmental control, and comorbid conditions)

Assess control

Step down if possible

(and asthma is well controlled at least 3 months)

Each step: Patient education, environmental control, and management of comorbidities.

Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

Quick-Relief Medication for All Patients

- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

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	0	1–2	3–4
	ACQ	≤0.75*	≥1.5	N/A
	ACT	≥20	16–19	≤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.

AsthmaControl.com

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and share your results with your doctor.

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Take Control!

Are you committed to taking control of your asthma?

Take the Asthma Control Test and join the Take Control Program!

Ages 12 and over | Ages 4-11 | En Español

1. In the past **4 weeks**, how much of the time did your **asthma** keep you from getting as much done at work, school or at home?

All of the time	Most of the time	Some of the time	A little of the time	None of the time

2. During the past **4 weeks**, how often have you had shortness of breath?

More than once a day	Once a day	3 to 6 times a week	Once or twice a week	Not at all

3. During the past **4 weeks**, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?

4 or more nights a weeky	2 or 3 nights a week	Once a week	Once or twice	Not at all

4. During the past **4 weeks**, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?

3 or more times per day	1 or 2 times per day	2 or 3 times per week	Once a week or less	Not at all

5. How would you rate your **asthma** control during the **past 4 weeks**?

Not controlled at all	Poorly controlled	Somewhat controlled	Well controlled	Completely controlled

Please enter your ZIP code: Why my ZIP Code?

Reset Form

1 2 3 SEE YOUR SCORE ▶

Take the Asthma Control Test and click the button to see your score.

www.asthmacontrol.com accessed 4/07

Stepping UP (EPR 3, 2007)

- Asthma NOT WELL CONTROLLED
  - Review adherence, inhaler technique, environmental control, co morbid conditions
  - Step up 1 step and reevaluate in 2-6 weeks
- Asthma VERY POORLY CONTROLLED
  - Review adherence, inhaler technique, environmental control, co morbid conditions
  - Consider short course of oral steroid
  - Step up 1 or 2 steps and reevaluate in 2 weeks

Intermittent Asthma

Persistent Asthma: Daily Medication

Consult with asthma specialist if step 4 care or higher is required.
Consider consultation at step 3.

Step 1

Preferred:

SABA PRN

Step 2

Preferred:

Low-dose ICS

Alternative:

Cromolyn, LTRA, Nedocromil, or Theophylline

Step 3

Preferred:

Low-dose ICS + LABA
OR
Medium-dose ICS

Alternative:

Low-dose ICS + either LTRA, Theophylline, or Zileuton

Step 4

Preferred:

Medium-dose ICS + LABA

Alternative:

Medium-dose ICS + either LTRA, Theophylline, or Zileuton

Step 5

Preferred:

High-dose ICS + LABA

AND

Consider Omalizumab for patients who have allergies

Step 6

Preferred:

High-dose ICS + LABA + oral corticosteroid

AND

Consider Omalizumab for patients who have allergies

Step up if needed

(first, check adherence, environmental control, and comorbid conditions)

Assess control

Step down if possible

(and asthma is well controlled at least 3 months)

Each step: Patient education, environmental control, and management of comorbidities.

Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

Quick-Relief Medication for All Patients

- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

ICS + LABA in asthma

	FEV-1	PEF AM/PM	Asthma symptoms	SABA use	Exacerbation Rate
VanNoord 1999 FP/SLM vs FP	⬆	⬆	⬇ Daytime & nightime	⬇	~
Baraniuk 1999 FP/SLM vs FP vs TAA	⬆	⬆	⬇	⬇	n/a
Wenzel 1998 SLM vs ALB	n/a	⬆	⬇	n/a	n/a
Woolcock 1996 BDP/SALM vs BDP	⬆	⬆	⬇	n/a	~
Greening 1994 BDP/SALM vs BDP	n/a	⬆	⬇	⬇	~

ICS + LABA in asthma

	FEV-1	PEF AM/PM	Asthma symptoms	Reliever medicine use	Exacerbation Rate
Rabe2006 BUD/FORM vs BUD (2x)	⬆	⬆	⬇	⬇	⬇
O'Byrne 2005 BUD/FORM vs BUD	⬆	⬆	⬇	⬇	⬇
Lallo 2003 BUD/FORM vs BUD	~	⬆	⬇	⬇	⬇
O'Byrne 2001 BUD/FORM vs BUD	⬆	n/a	⬇	n/a	⬇
Pauwels 1999 BUD/FORM vs BUD	⬆	⬆	⬇	⬇	⬇

Stepping DOWN (GINA, 2009) (asthma is controlled ≥3months)

- If pt on Medium-High dose
  - Reduce dose 50% at 3 month intervals (Evidence B)
- If control achieved on low dose
  - Switch to once daily (Evidence A)
- If pt taking ICS + LABA
  - Reduce ICS dose 50% + LABA (Evidence B)
  - Once control achieved on low dose + LABA (Evidence D)
    - Attempt to d/c LABA
- If pt taking ICS + other controller
  - Reduce ICS dose 50% + other controller (Evidence D)
  - Once control achieved on low dose + other controller (Evidence D)
    - Attempt to d/c other controller
- If pt on lowest dose of controller and no symptoms for *1 year*
  - Attempt to d/c controller

Intermittent Asthma

Persistent Asthma: Daily Medication

Consult with asthma specialist if step 4 care or higher is required.
Consider consultation at step 3.

Step 1

Preferred:

SABA PRN

Step 2

Preferred:

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Alternative:

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Step 3

Preferred:

Low-dose ICS + LABA
OR
Medium-dose ICS

Alternative:

Low-dose ICS + either LTRA, Theophylline, or Zileuton

Step 4

Preferred:

Medium-dose ICS + LABA

Alternative:

Medium-dose ICS + either LTRA, Theophylline, or Zileuton

Step 5

Preferred:

High-dose ICS + LABA

AND

Consider Omalizumab for patients who have allergies

Step 6

Preferred:

High-dose ICS + LABA + oral corticosteroid

AND

Consider Omalizumab for patients who have allergies

Step up if needed

(first, check adherence, environmental control, and comorbid conditions)

Assess control

Step down if possible

(and asthma is well controlled at least 3 months)

Each step: Patient education, environmental control, and management of comorbidities.

Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

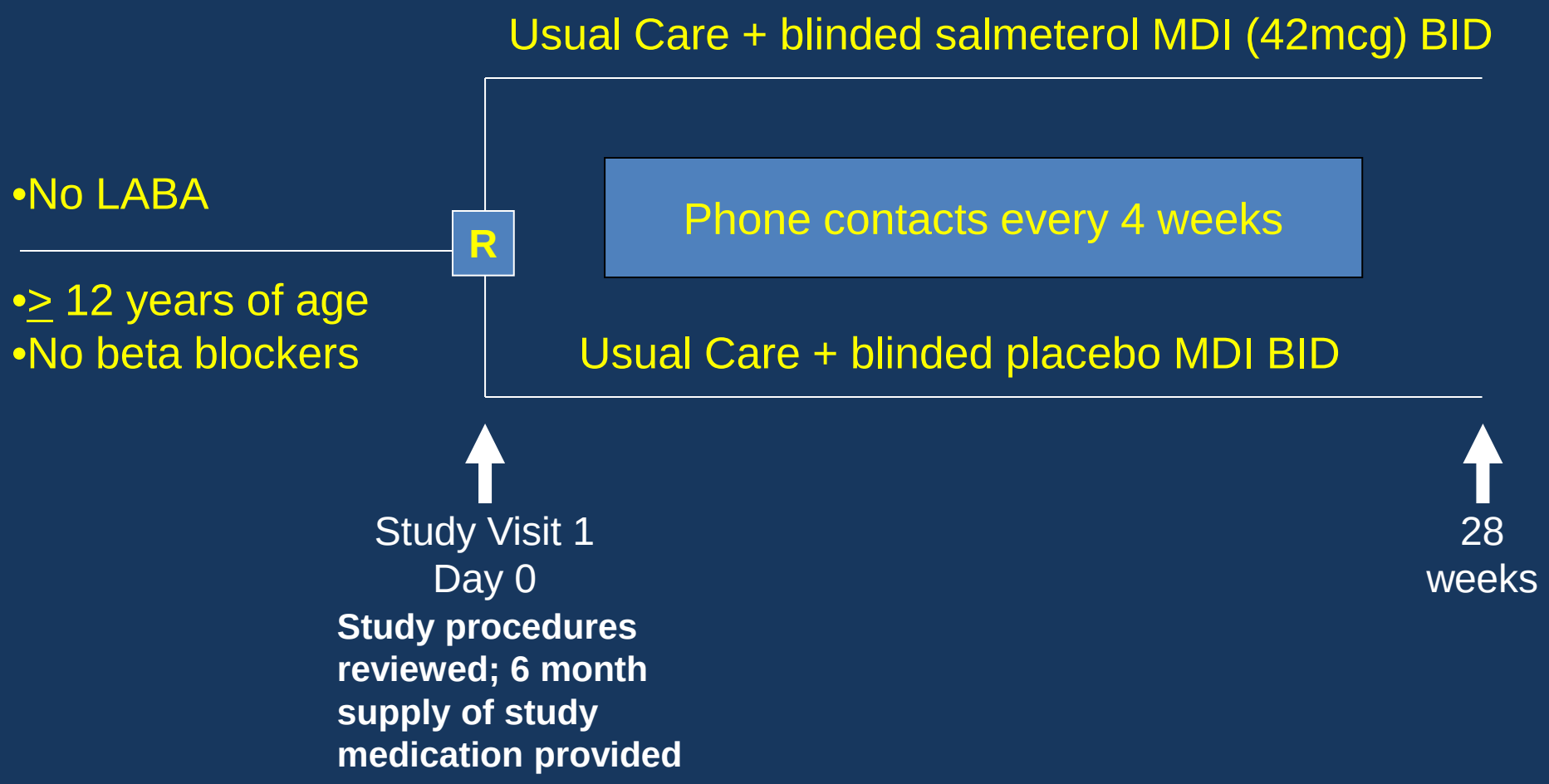
Quick-Relief Medication for All Patients

- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

SMART Study Design (Nelson HS et al. Chest 2006)

- Salmeterol Multicenter Asthma Research Trial (SMART)
- 28-week, multi-center, randomized, double-blind, placebo-controlled, observational surveillance trial initiated in July 1996
- 6163 US sites; 1316 investigators
- Target enrollment: ~60,000 patients
- ≥12 yrs with asthma currently using prescription asthma medications
  - no history of previous salmeterol/formoterol use
- All therapy taken on outpatient basis

SMART Study Design



Study Endpoints

- Primary Endpoint
  - Combined number of respiratory-related deaths or respiratory-related life-threatening experiences (intubation and ventilation)
- Secondary Endpoints
  - Combined asthma-related deaths or life-threatening experiences
  - Asthma-related deaths

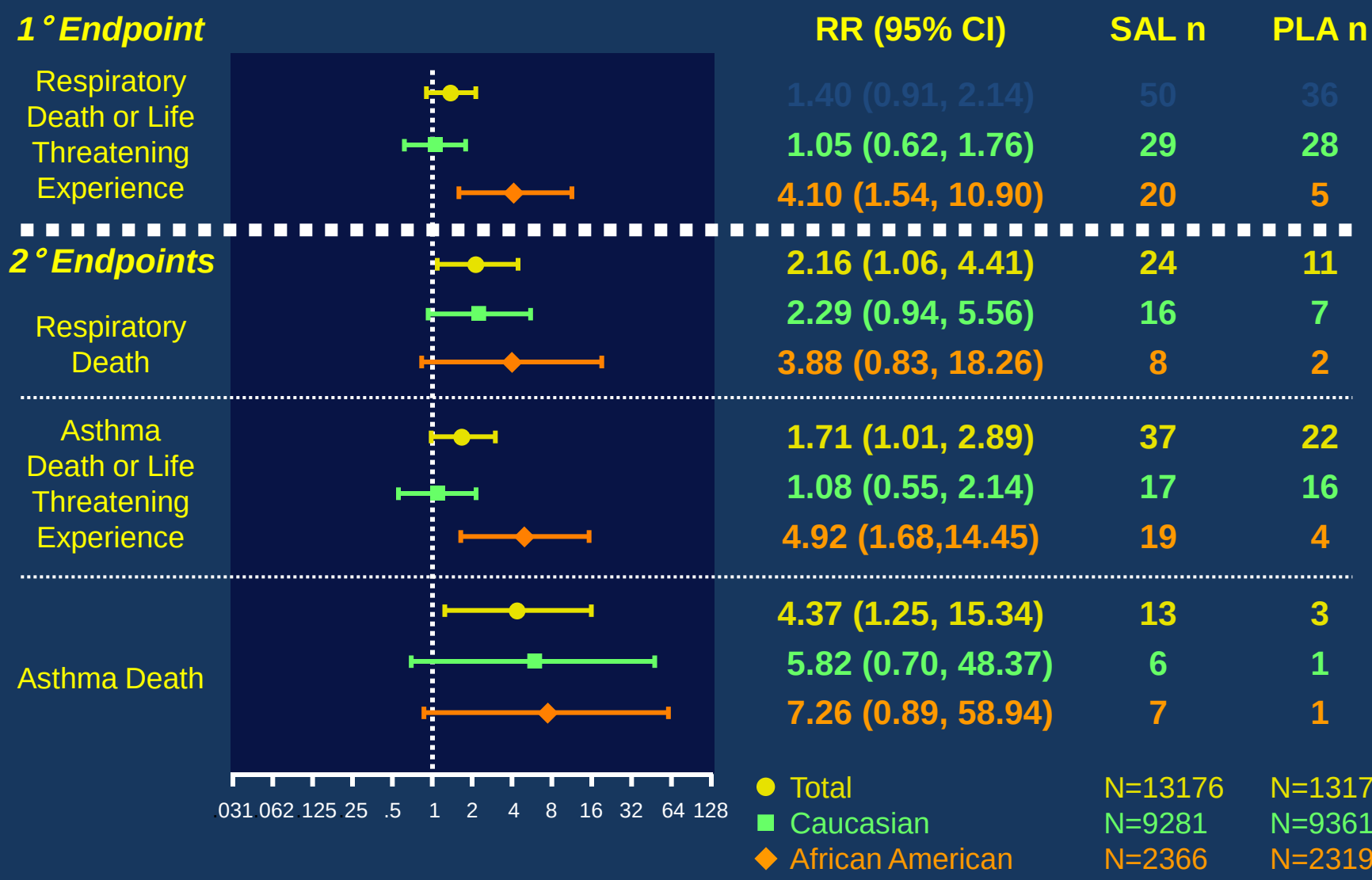
Demographics

	Salmeterol (n=13,176)	Placebo (n=13,179)
Age, mean	**39.2**	**39.1**
Sex, n (%)		
Female	8334 (64)	8337 (64)
Male	4703 (36)	4686 (36)
Ethnic Origin, n (%)		
Caucasian	9281 (71)	9361 (72)
African American	2366 (18)	2319 (18)
Hispanic	996 (8)	999 (8)
Asian	173 (1)	149 (1)
Other	230 (2)	224 (2)

Baseline Asthma Characteristics in Caucasians and African Americans

	Caucasian (n=18,642)	African American (n=4683)
Age (yrs), mean	40.3	36.5
Sex, n (%) Female Male	 11,718 (64) 6733 (36)	 3086 (67) 1545 (33)
PEF % Predicted	85.3	78.1
Baseline ICS Use	49%	38%
≥1 ER visit in last 12 mths	22%	41%
≥1 ER visit in lifetime	59%	72%
≥1 hospitalization in last 12 mths	6%	15%
≥1 hospitalization in lifetime	30%	45%
≥1 intubation for asthma in lifetime	4%	8%
Nocturnal symptoms present	59%	67%

SMART Results
Total and Subgroups



SMART Results
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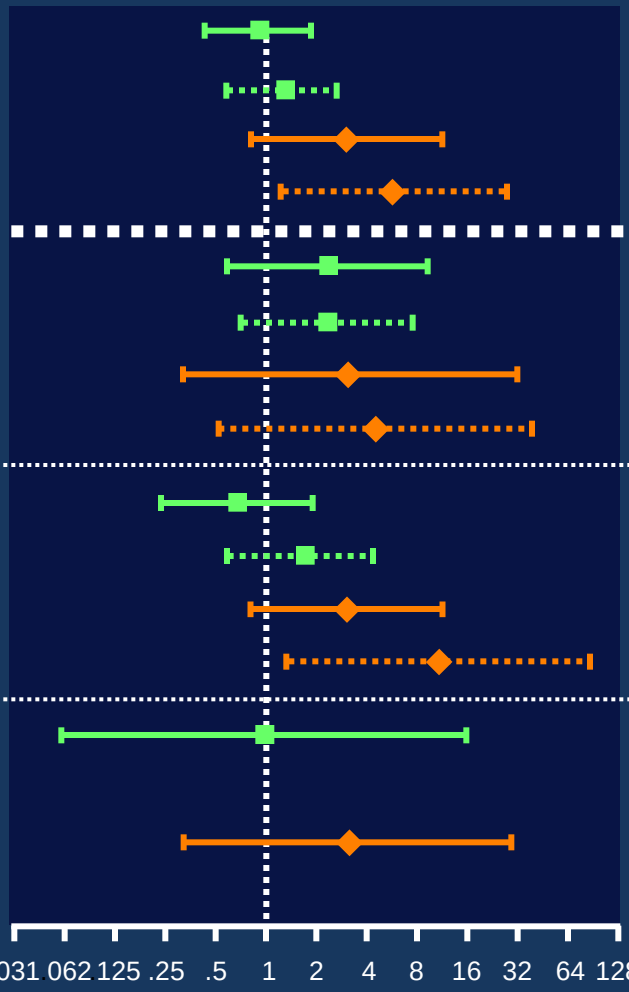


		RR (95% CI)	SAL n	PLA n
1° Endpoint				
Respiratory Death or Life Threatening Experience	Cauc. ICS	0.88 (0.42, 1.84)	13	15
	Cauc. Non-ICS	1.25 (0.60, 2.60)	16	13
	African American ICS	3.02 (0.82, 11.11)	9	3
	African American Non-ICS	5.61 (1.25, 25.26)	11	2
2° Endpoints				
Respiratory Death	Cauc. ICS	2.31 (0.60, 8.93)	7	3
	Cauc. Non-ICS	2.29 (0.70, 7.42)	9	4
	African American ICS	3.12 (0.33, 29.92)	3	1
	African American Non-ICS	4.43 (0.52, 37.89)	5	1
Asthma Death or Life Threatening Experience	Cauc. ICS	0.68 (0.24, 1.90)	6	9
	Cauc. Non-ICS	1.62 (0.63, 4.17)	11	7
	African American ICS	3.02 (0.82, 11.11)	9	3
	African American Non-ICS	10.46 (1.34, 81.58)	10	1
Asthma Death	Cauc. ICS	0.96 (0.06, 15.35)	1	1
	Cauc. Non-ICS		5	0
	African American ICS	3.12 (0.33, 29.92)	3	1
	African American Non-ICS		4	0

Cauc. ICS (SAL N=4586, PLA N=4637)
Cauc. Non-ICS (SAL N=4695, PLA N=4724)
African American ICS (SAL N=906, PLA N=785)
African American Non-ICS (SAL N=1460, PLA N=1444)

Summary of SMART Results

- Total Population
  - No significant differences in the primary endpoint
  - A significant increase (?), in secondary endpoint of asthma-related deaths was observed in patients receiving salmeterol
    - 13 vs. 3 pts
- African Americans
  - Statistically significant increase in combined respiratory and asthma-related deaths
    - Worse asthma at baseline
    - NO baseline ICS led to increased risk
  - No difference in asthma-related death alone
- Caucasians
  - No significant increase in primary or secondary endpoint s

Safety LABA (EPR 3, 2007)

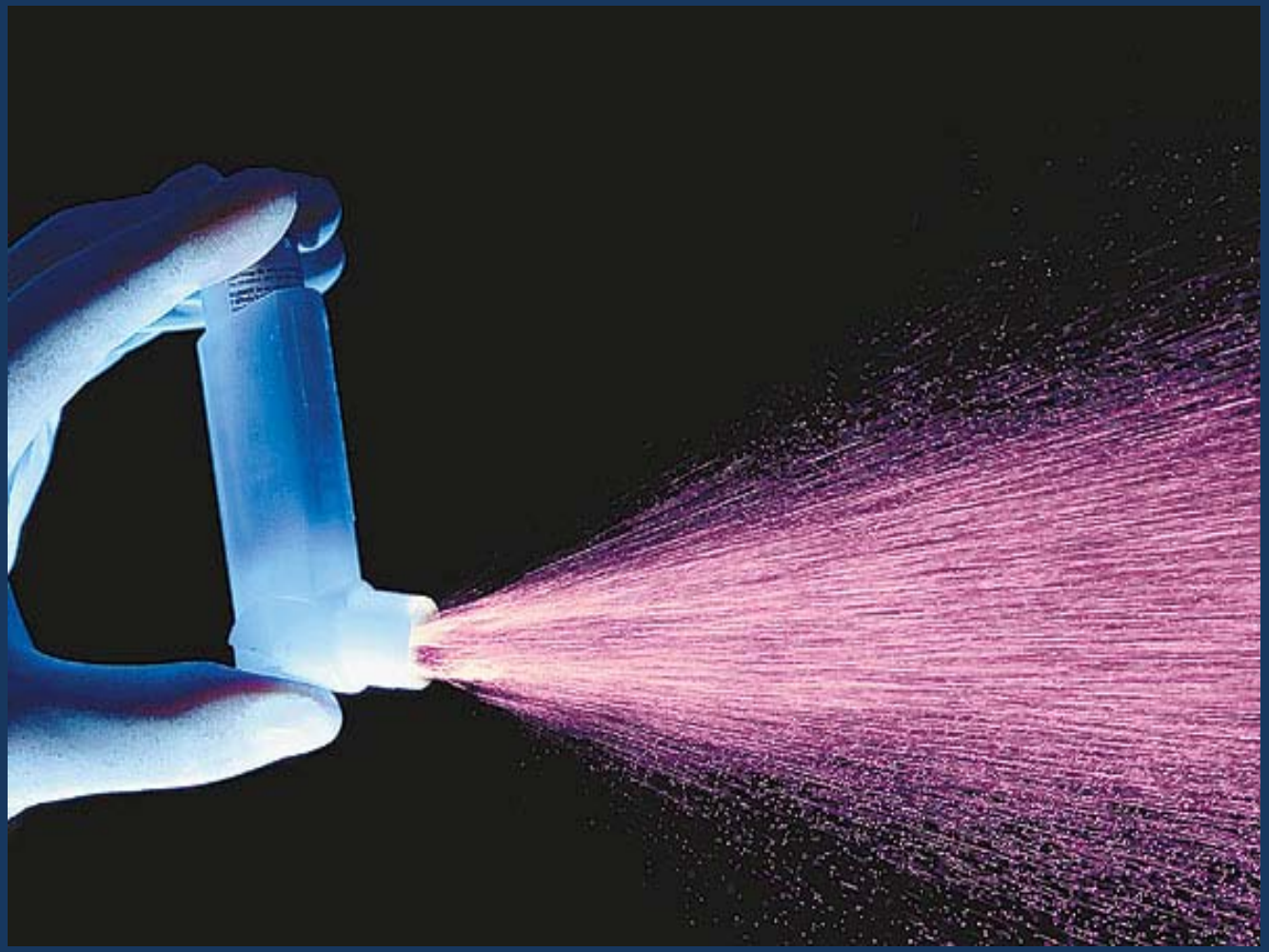
- If asthma not sufficiently controlled with ICS alone, the option of increasing the ICS dose=to addition of LABA
  - Based Salmeterol Multicenter Asthma Research Trial (SMART) conducted by Nelson et al. Chest 2006
  - High dose formoterol trial conducted by Mann et al. Chest 2007
- In general do not exceed salmeterol 100mcg or 24mcg formoterol daily

Safety LABA (FDA, 2010)

- Use of a LABA alone without use of a long-term asthma control medication, such as an inhaled corticosteroid, is contraindicated (absolutely advised against) in the treatment of asthma.
- LABAs should not be used in patients whose asthma is adequately controlled on low or medium dose inhaled corticosteroids.
- LABAs should only be used as additional therapy for patients with asthma who are currently taking but are not adequately controlled on a long-term asthma control medication, such as an inhaled corticosteroid.

Safety LABA (FDA, 2010)

- Once asthma control is achieved and maintained, patients should be assessed at regular intervals and step down therapy should begin (e.g., discontinue LABA), if possible without loss of asthma control, and the patient should continue to be treated with a long-term asthma control medication, such as an inhaled corticosteroid.
- Pediatric and adolescent patients who require the addition of a LABA to an inhaled corticosteroid should use a combination product containing both an inhaled corticosteroid and a LABA, to ensure adherence with both medications.



http://hamptonroads.com/files/images/6161.jpg. accessed 3/08

MDI-technique "Is significant"

- Lindgren et al. Eur J Resp Dis 1987;70:93-98.
  - 56% of patients made errors in MDI-technique which resulted in a 30% decrease in bronchodilation versus control ($p<0.01$)
- Giraud et al. Eur Resp J 2002;19:246-251
  - 71% of patients misused MDI's (47% due to poor coordination)
  - Asthma less stable in misusers ($p<0.001$)
  - Among misusers, asthma less stable in poor coordinators ($p<0.001$)

MDI technique

- 50% of adults and children do not perform all steps correctly **(Crompton GK. Lung 1990;Suppl 168:658-662)**
- Reasons for noncompliance
  - **Not taking off cap**
  - **Not shaking**
  - **Failure to coordinate actuation with inspiration**
  - **Inhale through nose and not mouth**
  - **Inhale too fast**
  - **Failure to breath-hold after dose**
  - **"Cold freon" effect**
  - **Holding MDI upside down**

MDI technique

- Shim et al. Am J Med 1980;69:891-894.
  - **50% of patients reverted back to incorrect technique after one to 30 days after instruction.**
- Epstein et al. Can Med Assoc J 1979;120:813-816.
  - **Only 10.8% of patients performed all steps required for proper MDI-technique.**

MDI technique

- Plaza et al. Resp 1998;65:195-198
  - **9% of patients, 15% of nurses, and 28% of physicians showed correct MDI-technique.**
- Interiano et al. Arch Intern Med 1993;153:81-85
  - **65% of patients, 39% of housestaff, 82% of nurses were categorized as having "poor" MDI-technique.**

Conclusions

- Asthma is a very serious problem
- Guidelines have been developed & recently amended to focus on control
- Medications vary by their mechanism of action & purpose
- Cooperation between patient, family, medical team is essential