The methodology behind GINA and EPR-3 medication recommendations: Stepwise treatment in asthma

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Faculty Disclosures

Maureen George

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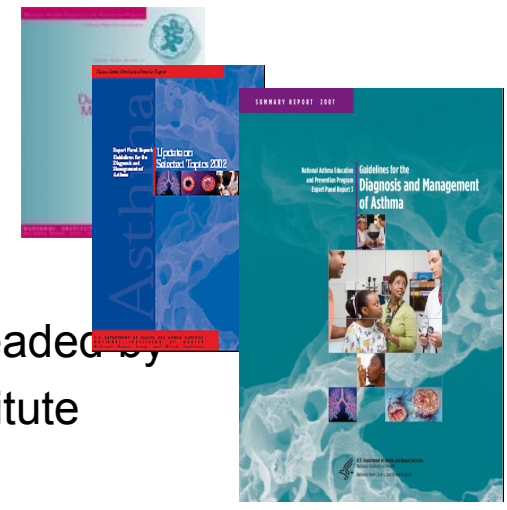
Factors Contributing to Uncontrolled Asthma

- Failure to recognize or respond to signs and symptoms of asthma
- Inadequate treatment for level of severity
- Non-adherence to recommended treatment
- Insufficient monitoring of asthma
- Failure to avoid or reduce exposure to asthma triggers
- Suboptimal patient-provider communication/ partnership

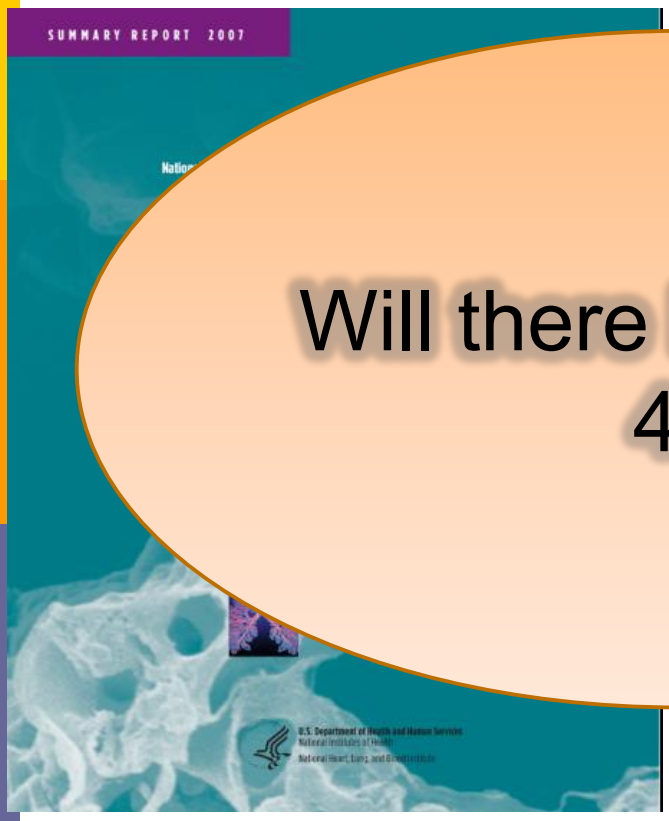
National Heart, Lung, and Blood Institute. *NAEPP Expert Panel Report 3.* Bethesda, MD: National Institutes of Health; 2007.

Evidence-based asthma guidelines

- NAEPP EPR-3
  http://www.nhlbi.nih.gov/guidelines/asthma/
  - National Asthma Education and Prevention Program's Expert Panel Report 3
  - First published in 1991
  - Full update in1997
  - Update on selected topics 2002
  - Last updated 2007
  - Source NIH expert panel spearheaded by National Heart Lung and Blood Institute



2007 Asthma Guidelines: 3 age groups (0-4, 5-11, 12+; six treatment steps for each age group)



Will there be a EPR-4?

1997 Asthma Guidelines

1991 Asthma Guidelines

EPR-3 Summary
http://www.nhlbi.nih.gov/guidelines/asthma/index.htm
Full report >400 pages
Summary >60 pages
Physicians Asthma Care Education (PACE) tool kit

National Heart, Lung, and Blood Advisory Council Asthma Expert Working Group

Draft Needs Assessment Report for Potential Update of the Expert Panel Report-3 (2007): Guidelines for the Diagnosis and Management of Asthma

April 2014

Priority Areas for Updating

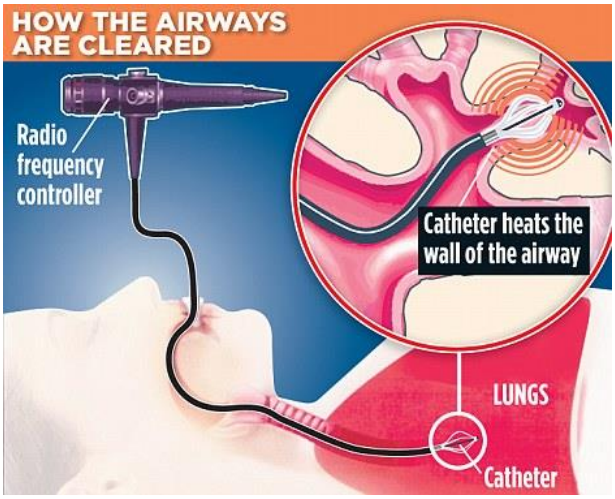
- Adjustable Medication Dosing in Recurrent Wheezing and Asthma? AKA *intermittent therapy*
  - Prn ICS?
    - Cost savings
    - Sparing potential side effects of ICS especially in children
    - Possible reducing the need for oral steroids
  - Studies have shown that patients who reduce or stop taking their asthma medications during the summer months are at greater risk of serious asthma symptoms in the fall
  - This so-called “drug holiday” leads to a spike in hospitalizations and emergency department visits due to asthma, especially among children and young adults

Priority Areas for Updating

- Long Acting Anti-Muscarinic Agents (LAMAs) in Asthma Management as Add-on to ICSs?
  - LABAs have a black box warning

Priority Areas for Updating

- Bronchial Thermoplasty in Adult Severe Asthma?
  - 3 treatments
  - Reduces number of asthma attacks



Priority Areas for Updating

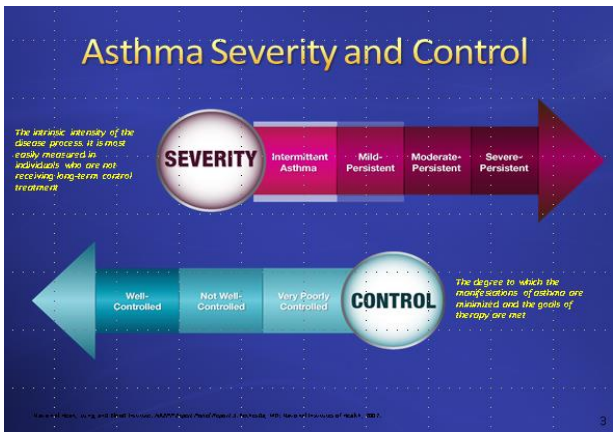
- Fractional exhaled Nitric Oxide (FeNO) in Diagnosis, Medication Selection, and Monitoring Treatment?
  - Biomarker of inflammation
  - Can FeNO help with personalizing treatment?

Priority Areas for Updating

- Remediation of Indoor Allergens (House Dust Mites/Pets)?
  - Multicomponent interventions
    - Removal of carpet
    - Mattress/pillow encasings

Topics for Acknowledgment in an Update

- Asthma heterogeneity
  - Personalized medicine
- Biomarkers
  - Other than FeNO
- Biologics
  - Interleukins
- Sublingual



Topics for Acknowledgment in an Update

- Role of community health workers in asthma management
  - Effectiveness of home visits
  - Effectiveness compared to health care professionals
- Step down from combination therapy
  - Decrease dose of ICS first?
  - Large-scale studies of LABA safety will be completed in 2016-2017
- Prevention of asthma onset
- Adherence
  - How to identify non-adherence and how to improve adherence
- Update medication charts
  - Remove nedocromil and cromolyn
  - Add dexamethasone to list of oral steroids
  - Clarify that mediciations withun a step should be tried prior to increasing

Stepwise Approach for Managing Asthma in Youths ≥ 12 Years of Age and Adults

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, 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 or Theophylline or Zileuton	**Step 5** ***Preferred:*** High-dose ICS + LABA ***AND*** Consider Omallzumab 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) Step down if possible (and asthma is well controlled at least 3
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

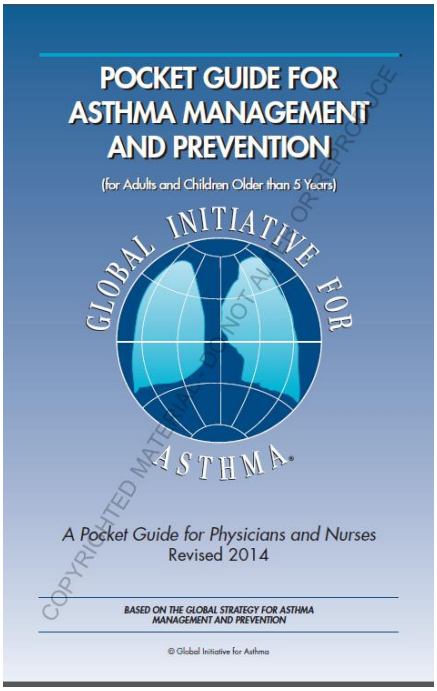
- **SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20- minute intervals as needed. Short course of oral systemic corticosteroids may be needed.**
- **Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate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

Global INitiative for Asthma

Full reports, pocket guides in multiple languages, teaching slide sets, patient resources, World Asthma Day world headquarters since its inception by GINA in 2001

Evidence-based asthma guidelines

- GINA http://www.ginasthma.org/
  - Global Initiative for Asthma
  - First published A Global Strategy for Asthma Management and Prevention in 1995
  - Updated in 2002 and 2006
  - Yearly updates released in December beginning in 2007 (search ends July 1 of each year
  - Launched in 1993 in collaboration with the National Heart, Lung, and Blood Institute, NIH and the World Health Organization



From expert opinion to graded evidence

- In the late 1990s and 2000s, guidelines underwent a major paradigm shift from opinion to
  - Evidence-based classification where conflict of interest is "managed"
  - Implementation oriented
    - Diagnosis
    - Management
    - Prevention
  - Outcomes can be evaluated

Methodology of EPR-3 guidelines

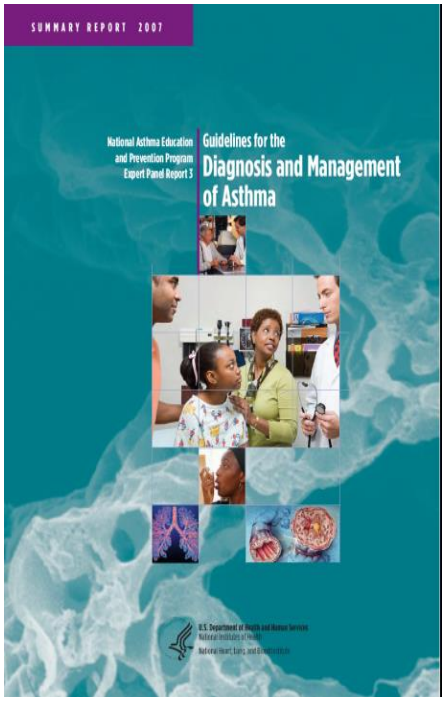
- Committees reviewed published science from Jan 2001 - March 2006 using standard search criteria in MEDLINE
- Discussed by conference calls
  - 15,444 titles were retrieved:
    - 4,747 abstracts reviewed
    - 2,122 full-text reviewed
    - 1,654 articles serving as a bibliography of references

Ranking the evidence –EPR-3

Methodology of GINA guidelines

- Committees review published science yearly (July 1- June 30) using standard search criteria in electronic databases
  - Hand searches of citations
  - Referred in peer-reviewed papers
- Abstracts are reviewed by at least two committee members to determine if they warrant retrieval of the full text

EPR-3: Four Components; 3 age groups and 6 treatment steps



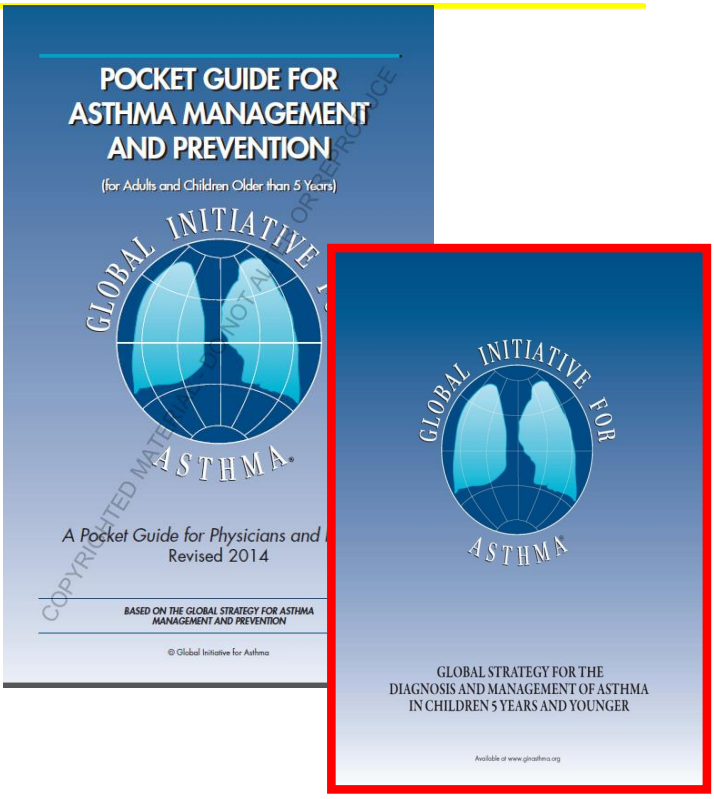
- <u>Reduce Impairment</u>
  - Prevent chronic & troublesome symptoms
  - Require infrequent use (<u>≤</u> 2days a week) of inhaled short acting beta$_2$-agonist (SABA)
  - Maintain normal pulmonary function
  - Maintain normal activity levels
  - Meet patient's & families expectations of & satisfaction with asthma care
- <u>Reduce Risk</u>
  - Prevent recurrent exacerbations of asthma & minimize the need for ED visits or hospitalizations
  - Prevent loss of lung function; for children, prevent reduced lung growth
  - Provide optimal pharmacotherapy with minimal or no adverse effects of therapy

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.

GINA: Five Components; 2+ age groups and 5 treatment steps

- 1Achieve and maintain control of symptoms and maintain normal activity levels
- To minimize future risk of exacerbation, fixed airflow limitation's and side effects



GINA assessment of asthma control

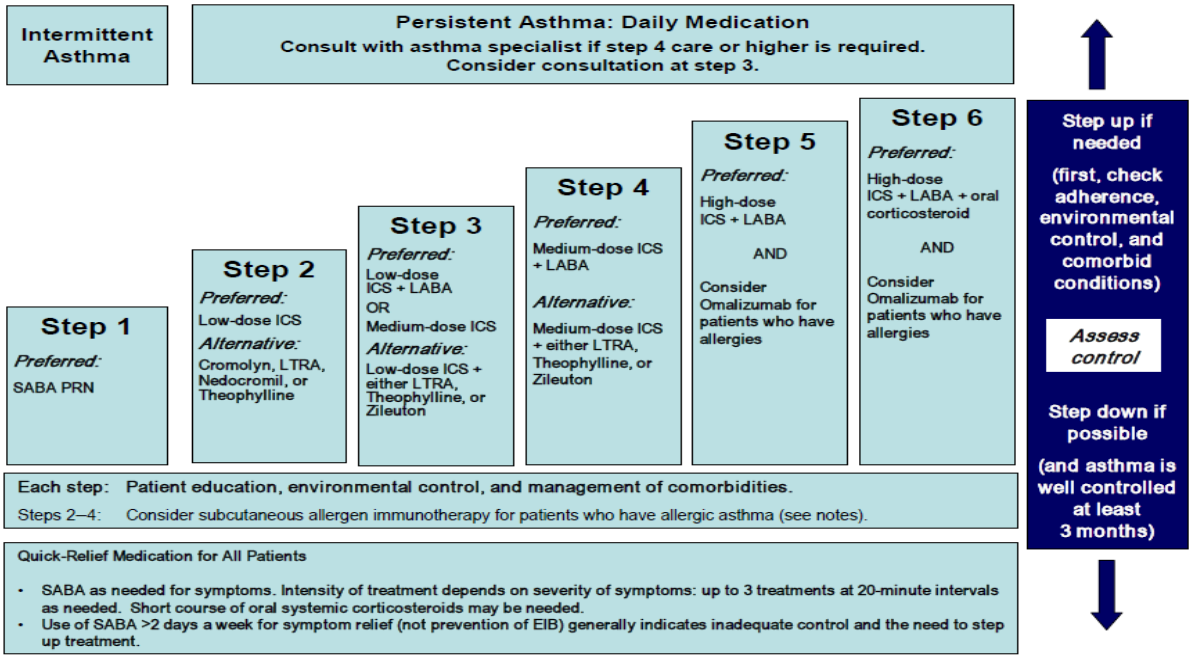
A. Symptom control		Level of asthma symptom control		
In the past 4 weeks, has the patient had:		**Well-controlled**	**Partly controlled**	**Uncontrolled**
• Daytime asthma symptoms more than twice a week?	Yes❑ No❑	None of these	1-2 of these	3-4 of these
• Any night waking due to asthma?	Yes❑ No❑			
• Reliever needed for symptoms* more than twice a week?	Yes❑ No❑			
• Any activity limitation due to asthma?	Yes❑ No❑			

*Excludes reliever taken before exercise, because many people take this routinely

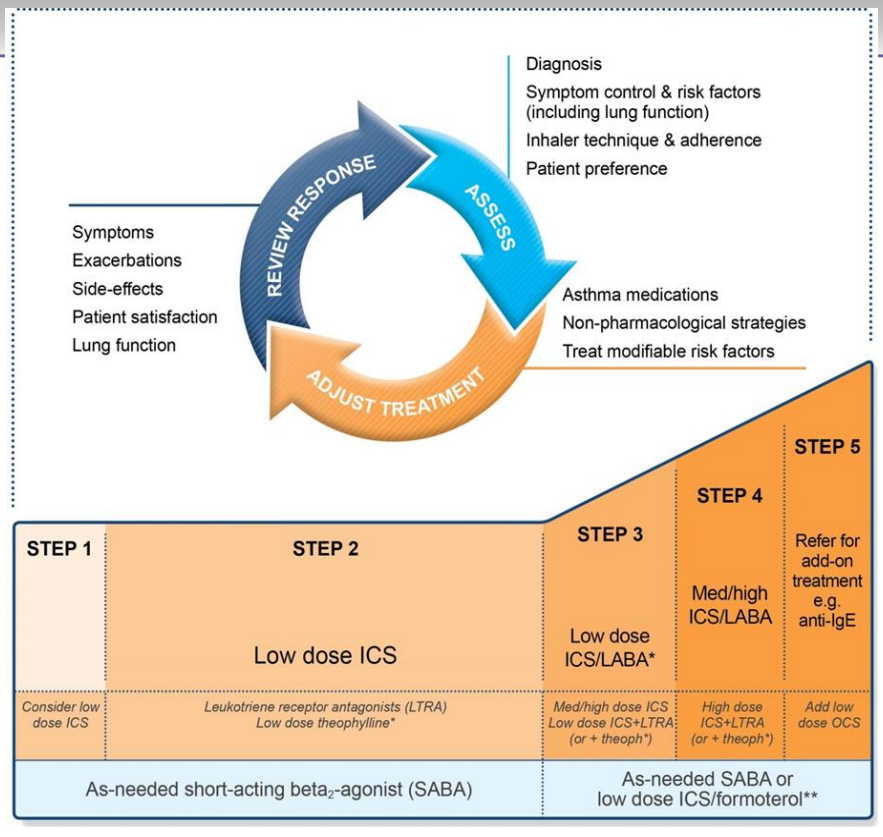
This classification is the same as the GINA 2010-12 assessment of 'current control', except that lung function now appears only in the assessment of risk factors

EPR-3 Treatment Steps

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



Stepwise management - pharmacotherapy



*For children 6-11 years, theophylline is not recommended, and preferred Step 3 is medium dose ICS

**For patients prescribed BDP/formoterol or BUD/formoterol maintenance and reliever therapy

GINA 2014, Box 3-5 (upper part)

Summary

GINA 2014

- 2 goals
- 5 treatment steps for 2+ age groups
  - 5 and under
  - 6 and older
- Archived severity classification

EPR-3 2007

- 4 goals
- 6 treatment steps for 3 age groups
  - 0-4
  - 5 -11
  - 12 and older
- 4 levels of severity