การประชุมใหญ่ประจำปี ครั้งที่ 10

Easy Asthma & COPD Clinic Network

10-11 มีนาคม 2557

How to Achieve Pediatric Asthma Admission Rate Near 'Zero' ?

Jamaree Teeratakulpisarn
Department of Pediatrics
Khon Kaen University
10 March 2014

Quality Improvement Process

Input	Process	Output/ Outcome
Leader Personnel Data - Prevalence, exacerbation rate, etc - Cost	Management guideline - Adapt guideline to fit your own situation - Pitfall - Team work - Skill	- Asthma control (Zero exacerbation) - Improve quality of life - Reduce the whole cost

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Problems in pediatric asthma

Doctor & health care team

- Misdiagnosis & Under diagnosis
- Under & inappropriate treatment
- Appropriate inhalation technique
- Associated disease: AR, sinusitis
- Fear of steroid side effect

Care givers & children

- Compliance & inhalation technique
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Misdiagnosis & Under Dx

Presentation: fever, cough, dyspnea
PE: crepitation, rhonchi, wheezing

- Acute lower respiratory tr infection
  - pneumonia
  - bronchitis
  - bronchiolitis
  - viral-induced wheezing (wheezing associated respiratory infection, WARI)
- Asthma – may have no abnormal signs

Pneumonia

Criteria for diagnosis

- Clinical – fever, cough, dyspnea (including fast breathing)
- CXR – infiltration on CXR

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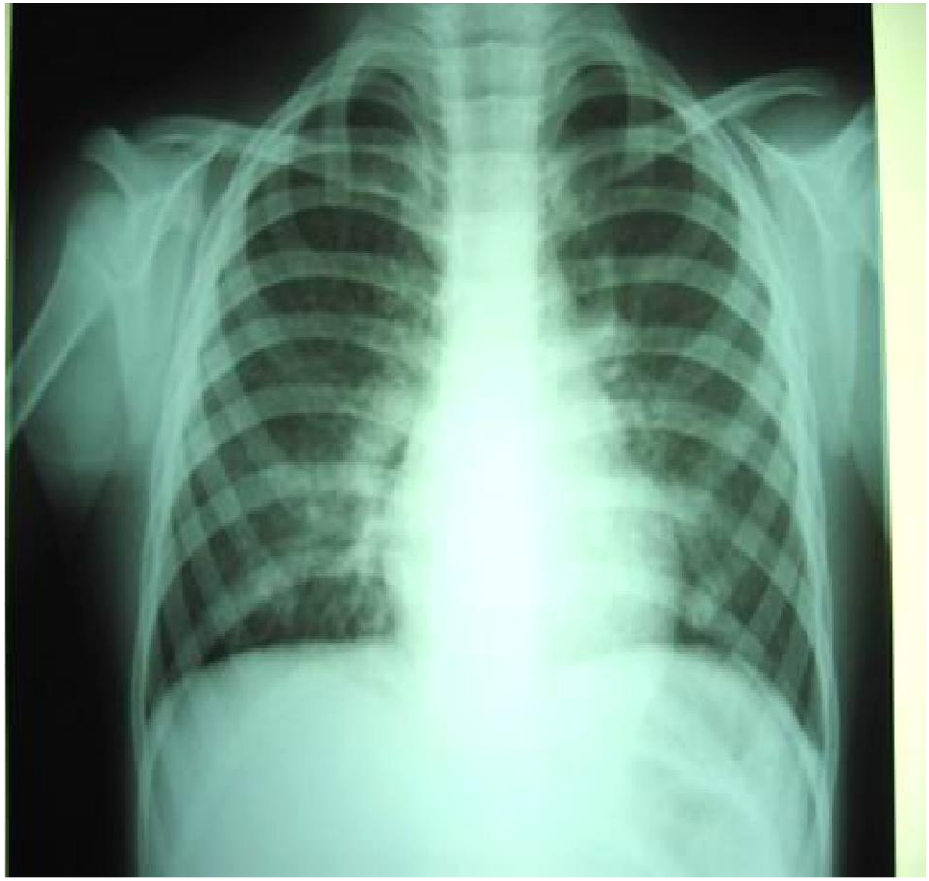
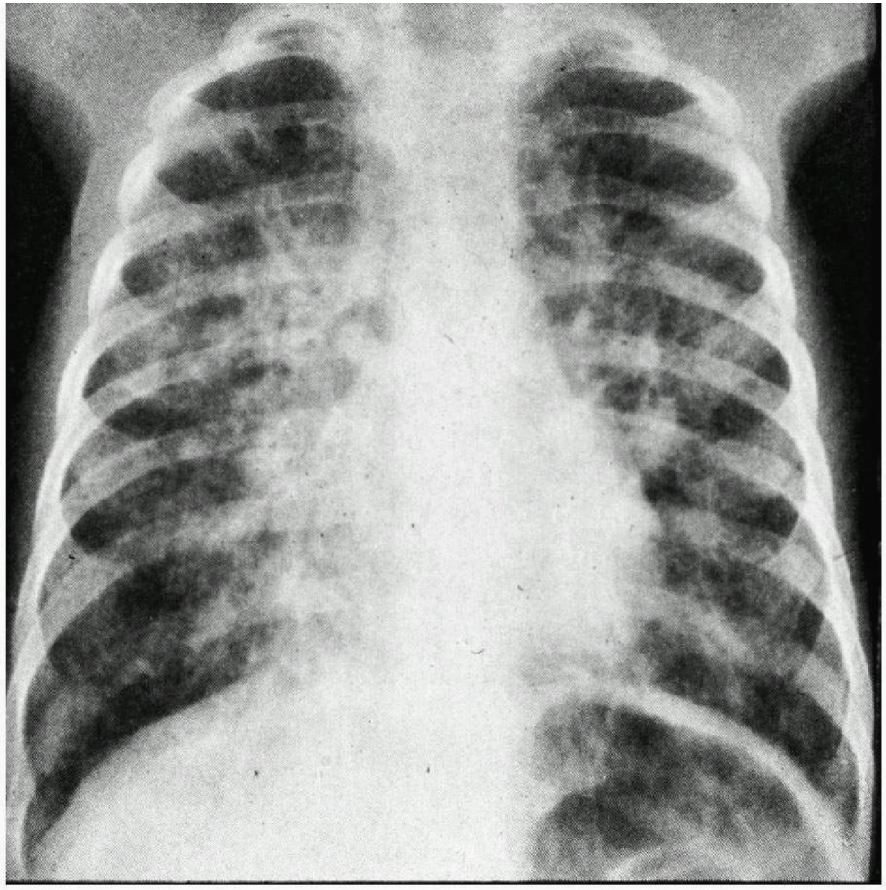
Pneumonia





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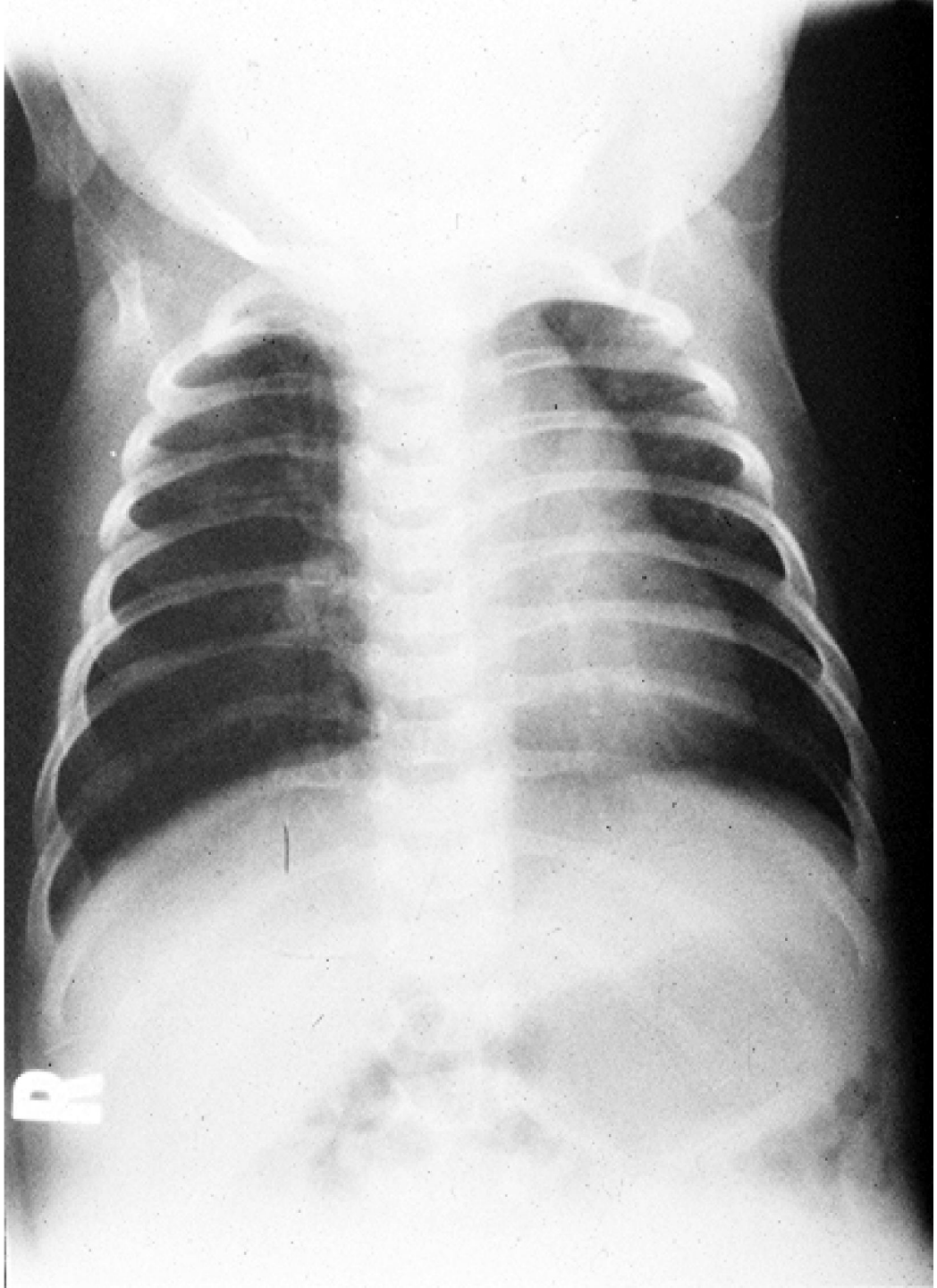
CXR



Recurrent Pneumonia

Definition

defined as more than 1 episode per year or more than 3 episodes in a lifetime

These children require

- more extensive workup to find out underlying condition or

- find out another diagnosis

Nicholas John Bennett, et al. eMedicine

Acute bronchitis

- Recurrent episodes of acute or chronic infectious bronchitis are unusual in children and should alert the clinician to the likelihood of asthma

Patrick L Carolan. Et al. eMedicine

Acute bronchiolitis

- Present with cough and dyspnea (wheezing or rhonchi, may have crepitation)

  after common cold (viral URI)
- First episode in children under 2 years old

Viral-induced wheezing

Wheezing associated respiratory infection

- Wheezing follow common cold or viral URI (like acute bronchiolitis)
- Usually used in recurrent episodes in children <5 years old
- Have to differentiate with ASTHMA

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How to differentiate between viral-induced wheezing vs asthma?

Viral-induced wheezing & asthma

- Asthma predictive index (API)
- Therapeutic diagnosis

Viral-induced wheezing & asthma

- Asthma predictive index (API)
- Therapeutic diagnosis

Asthma Predictive Index (API)

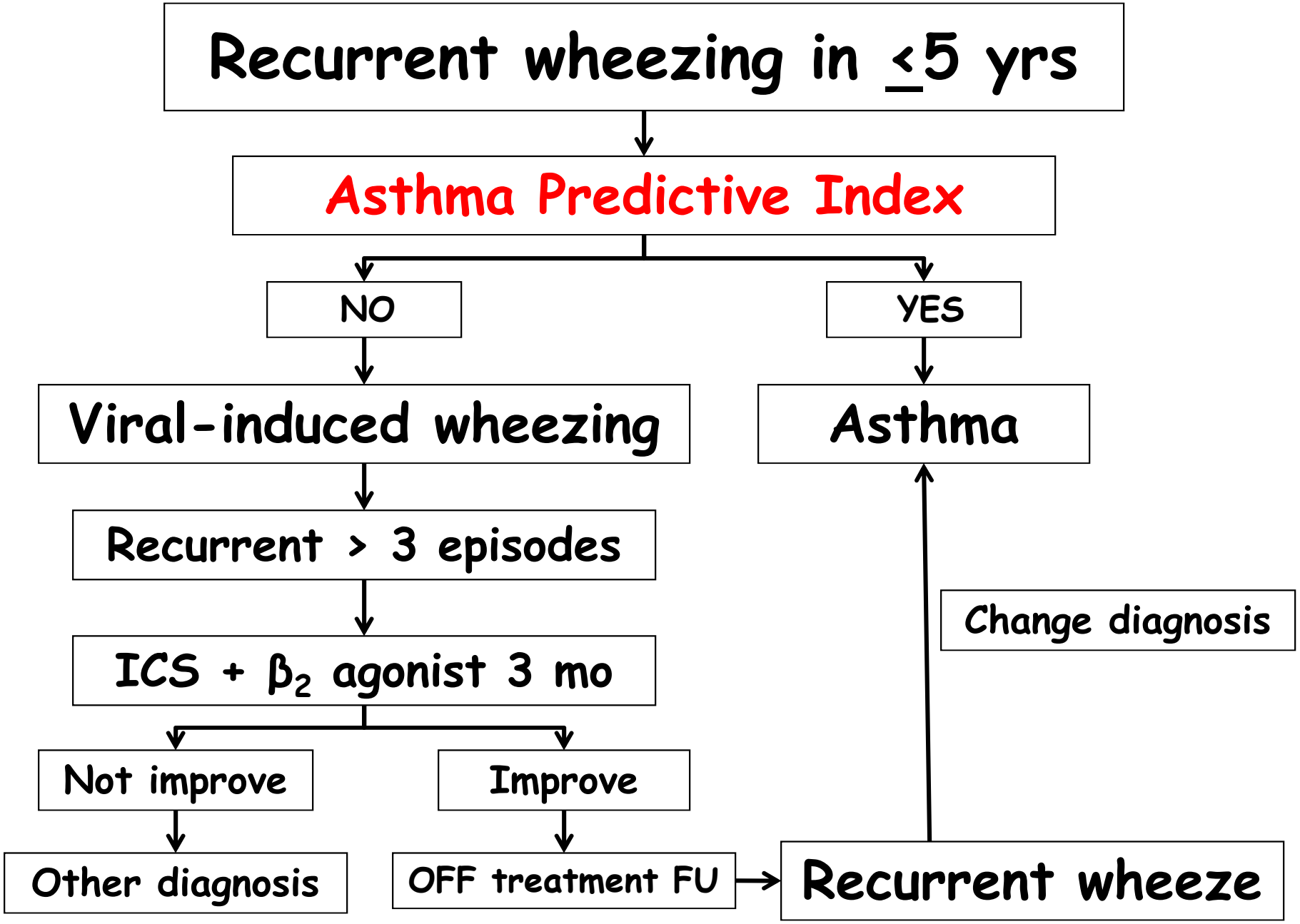
Major criteria

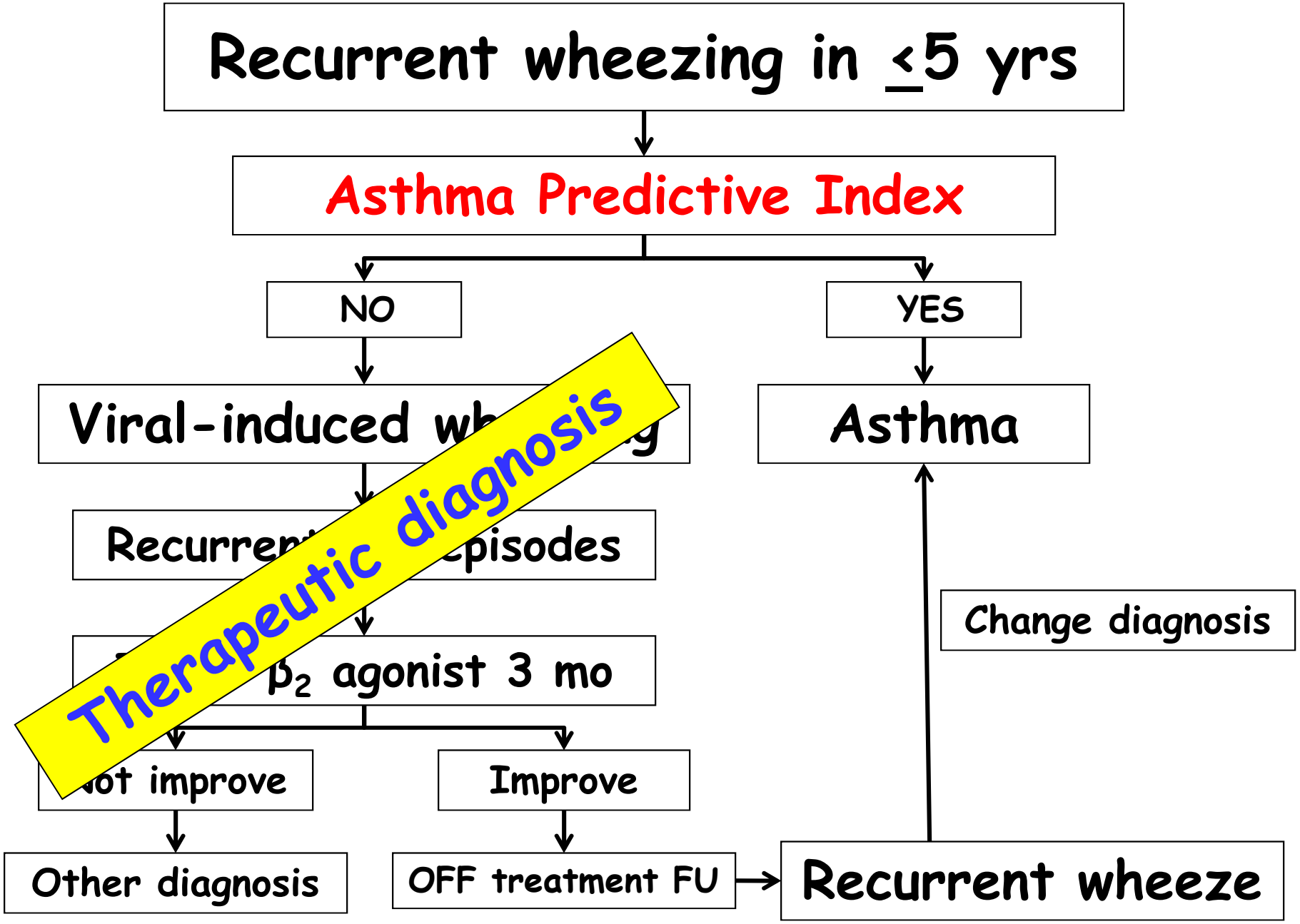
1. Parental asthma (MD diagnosis)
2. MD diagnosed atopic eczema (child)

Minor criteria

1. MD diagnosed allergic rhinitis (child)
2. Wheezing apart from cold
3. Eosinophilia (≥ 4%)

Castro-Rodriguez JA. J Allergy Clin Immunol. 2010 Aug;126(2):212-6.


Recurrent wheezing in ≤5 yrs
Asthma Predictive Index
NO
YES
Viral-induced wheezing
Asthma
Recurrent > 3 episodes
ICS + β2 agonist 3 mo
Change diagnosis
Not improve
Improve
Other diagnosis
OFF treatment FU
Recurrent wheeze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Misdiagnosis & Under Dx

Presentation: fever, cough, dyspnea
PE: crepitation, rhonchi, wheezing

- Acute lower respiratory tr infection
  - pneumonia: recurrent - unusual
  - bronchitis: recurrent - unusual
  - bronchiolitis: 1st episode in <2 years
  - viral-induced wheezing (wheezing associated respiratory infection, WARI): recurrent episodes, no API
- Asthma: recurrent episodes with Asthma Predictive Index (API)

Problems in pediatric asthma

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- Associated disease: AR, sinusitis
- Fear of steroid side effect

Care givers & children

- Compliance & inhalation technique
- Fear of steroid side effect

Under & inappropriate treatment

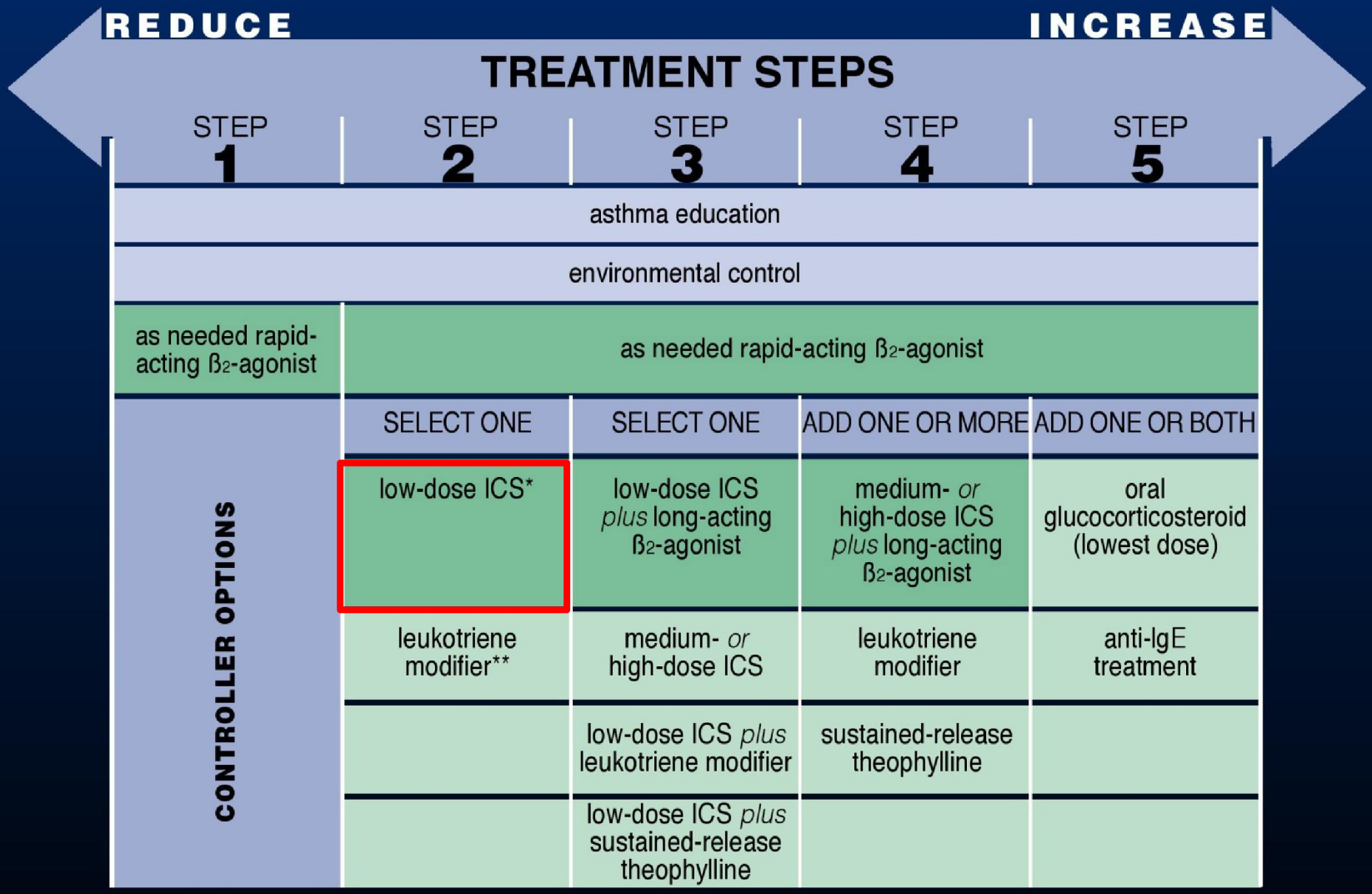
- Delay start controller
- Inappropriate step up
- Inadequate treatment of acute exacerbation at ER – lead to admission

Global Strategy for Asthma Management and Prevention in Children 5 Years and Younger

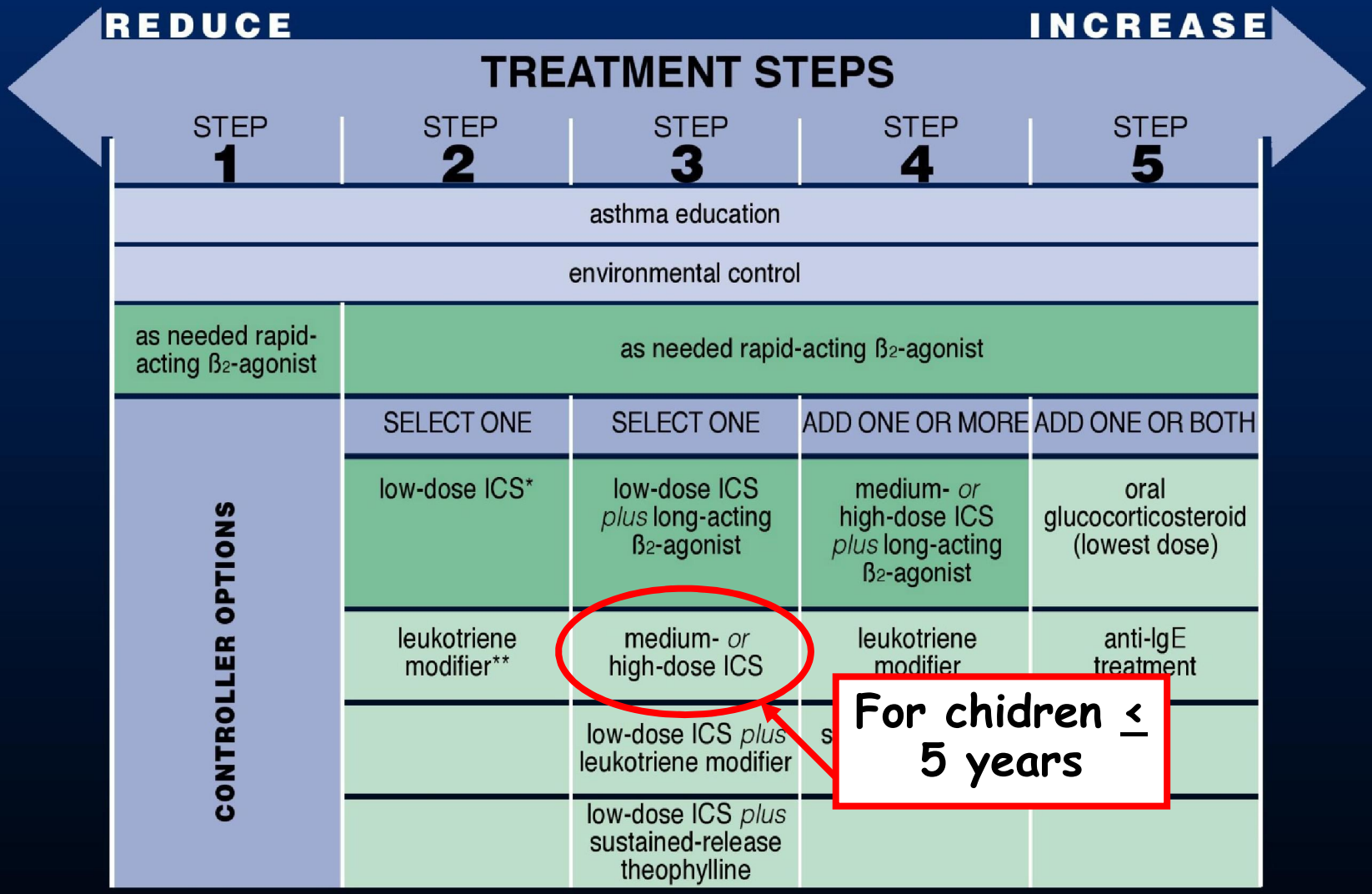
Levels of Asthma Control

Characteristic	Controlled	Partly controlled (any measure present in any week)	Uncontrolled (≥3 features of partly controlled present in any week)
Daytime symptoms: wheezing, cough, difficult breathing	None (less than twice/week, typically for short periods of the order of minutes and rapidly relieved by use of a rapid-acting bronchodilator)	>Twice a week (typically for short periods of the order of minutes and rapidly relieved by use of a rapid-acting bronchodilator	>Twice a week (typically last minutes or hours or recur, but partially or fully relieved by a rapid-acting bronchodilator
Limitations of activities	None (child is fully active, plays and runs without limitation or symptoms)	Any (cough, wheeze or difficulty breathing,during exercise, play or laughing)	Any (cough, wheeze or difficulty breathing,during exercise, play or laughing)
Nocturnal symptoms or awakening	None (including no nocturnal coughing during sleep)	Any (coughs during sleep or wakes with cough, wheezing, and/or difficult breathing)	Any (coughs during sleep or wakes with cough, wheezing, and/or difficult breathing)
Need for reliever/rescue	≤ 2 days/week	> 2 days/week	> 2 days/week

Any *exacerbation* should prompt review of maintenance treatment



*inhaled glucocorticosteroids
** receptor antagonist or synthesis inhibitors



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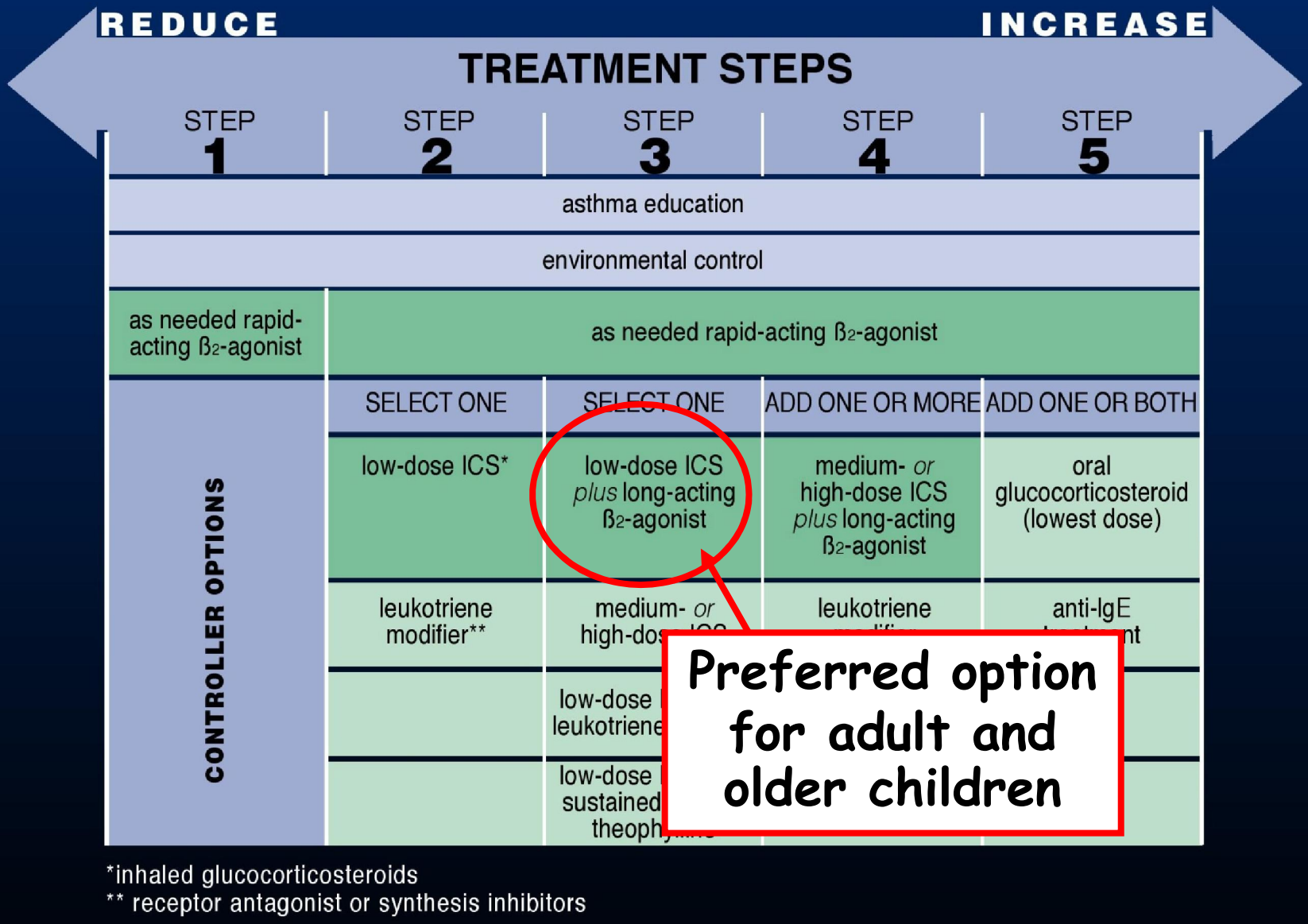

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How to start & step up

- Initial
  - ICS: Budesonide 100-200 ug bid
    Fluticasone 125-250 ug bid

  Via spacer

  For 2 – 3 months

How to start & step up

- Initial
  - ICS: Budesonide 100-200 ug bid
    Fluticasone 125-250 ug bid

  Via spacer

  For 2 – 3 months: if not improve
- Ask for compliance
- Assess proper inhalation technique
- Assess associated disease – allergic rhinitis, sinusitis

How to start & step up

- Initial
  - ICS: Budesonide 100-200
    Fluticasone 125 bid

  Via spacer

  For 2 – 3 mo not improve
- Ask for ice: good
- Ass per inhalation technique: OK
- Asse associated disease – allergic rhinitis, sinusitis: OK

Step up treatment

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REDUCE INCREASE

TREATMENT STEPS

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
	asthma education				
	environmental control				
	as needed rapid-acting ß2-agonist	as needed rapid-acting ß2-agonist			
CONTROLLER OPTIONS		SELECT ONE	SELECT ONE	ADD ONE OR MORE	ADD ONE OR BOTH
		low-dose ICS*	low-dose ICS *plus* long-acting ß2-agonist	medium- *or* high-dose ICS *plus* long-acting ß2-agonist	oral glucocorticosteroid (lowest dose)
		leukotriene modifier**	medium- *or* high-dose ICS	leukotriene modifier	anti-IgE treatment
			low-dose ICS *plus* leukotriene modifier	sustained-release theophylline	
			low-dose ICS *plus* sustained-release theophylline		

*inhaled glucocorticosteroids
** receptor antagonist or synthesis inhibitors

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BADGER Study

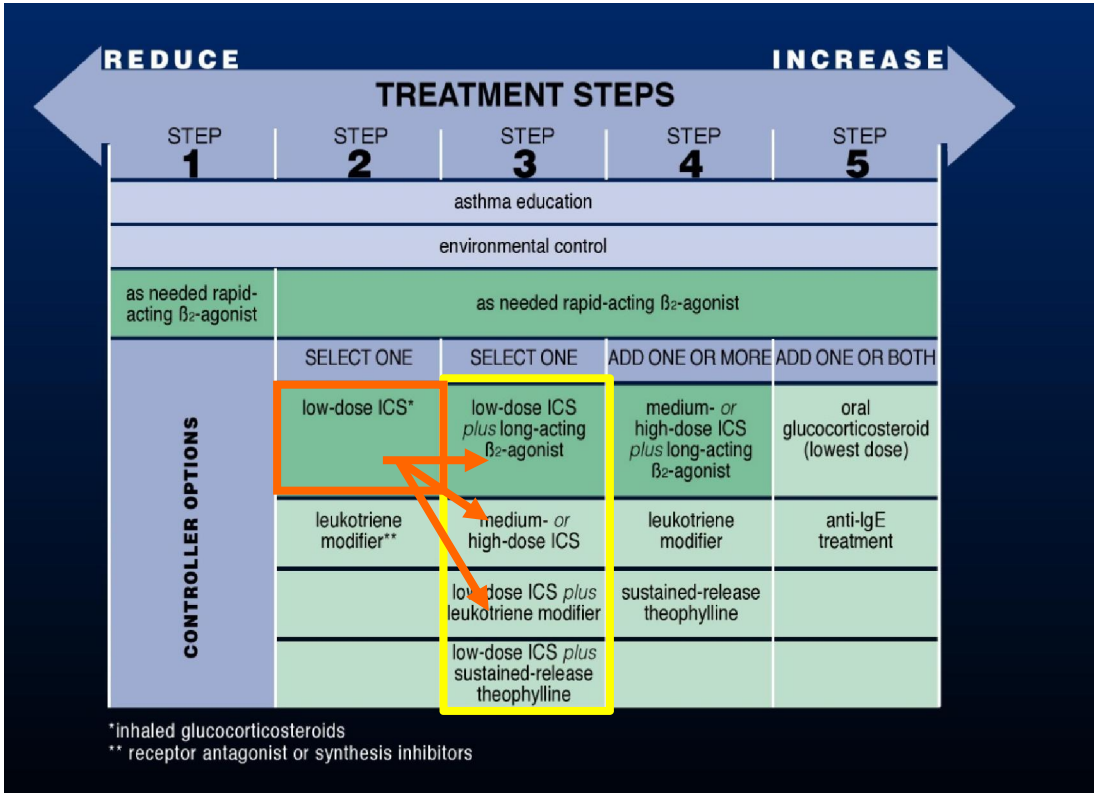
(Best ADd-on therapy Giving Effective Response)

Robert F. Lemanske et al, N Engl J Med. 2010 Mar 18;362(11):975-85

The NEW ENGLAND JOURNAL of MEDICINE

Background

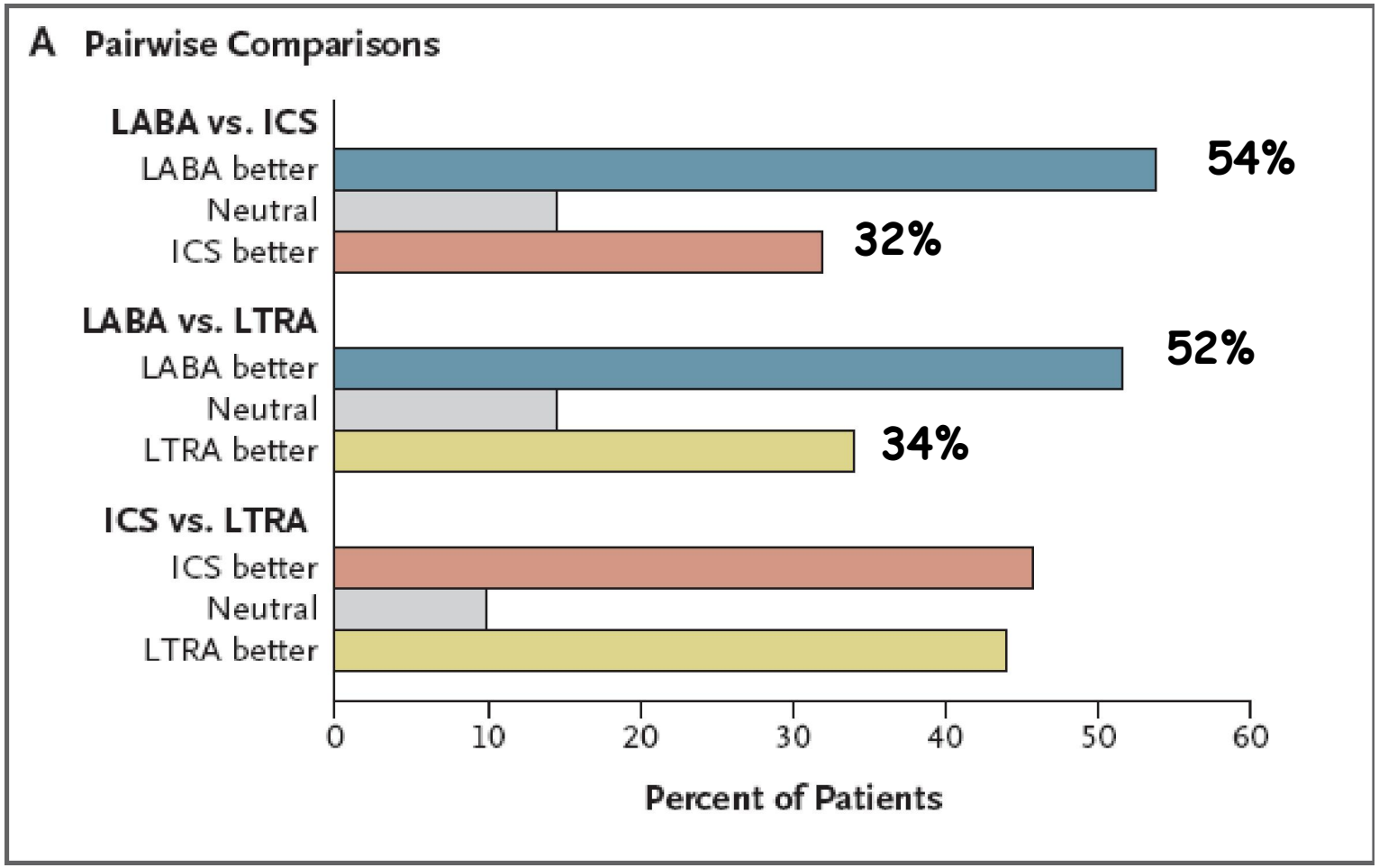
- For children who have uncontrolled asthma despite the use of low-dose inhaled corticosteroids (ICS), evidence to guide step-up therapy is lacking.



Results

- **165 patients completed the study period**
- ***A* differential response occurred in 161/165 (98%)**

Pairwise Comparison of Three Step-up Therapies and the Overall Probability of Best Response



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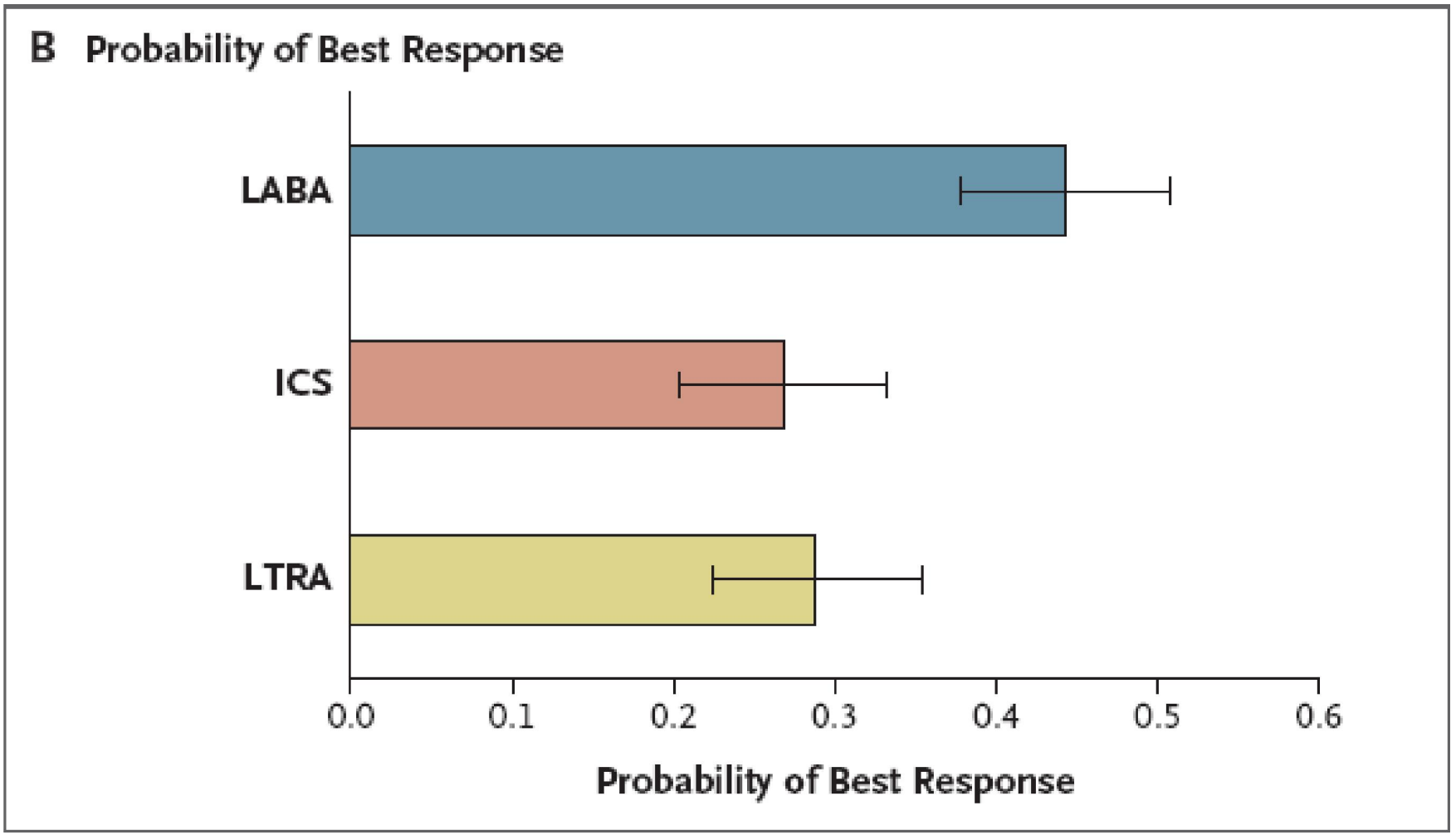


BADGER Conclusion

- Nearly all the children had a differential response to each step-up therapy
- LABA step-up was significantly more likely to provide the best response than either ICS or LTRA step-up
- However, many children had a best response to ICS or LTRA step-up therapy, highlighting the need to regularly monitor and appropriately adjust each child's asthma therapy

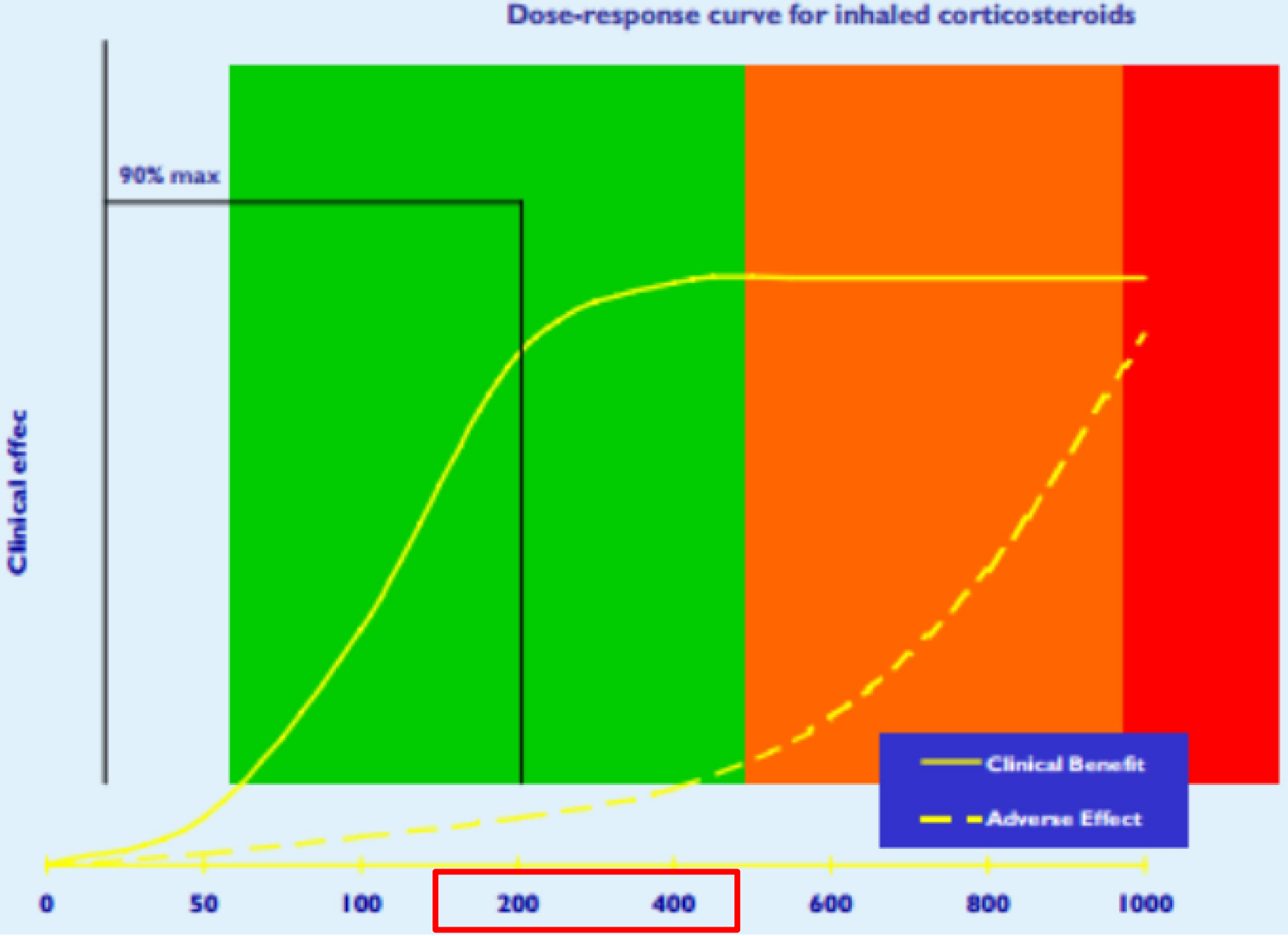
Common pitfall

- Inadequate dose of ICS
- Inappropriate use of combination Px
  - Too low ICS
  - Too high ICS
- Inadequate assessment before step up

Long term prophylaxis

Consideration

- Increase in dose of ICS is not accompanied by proportional increase in effects but increases systemic bioavailability



National Asthma Council Australia

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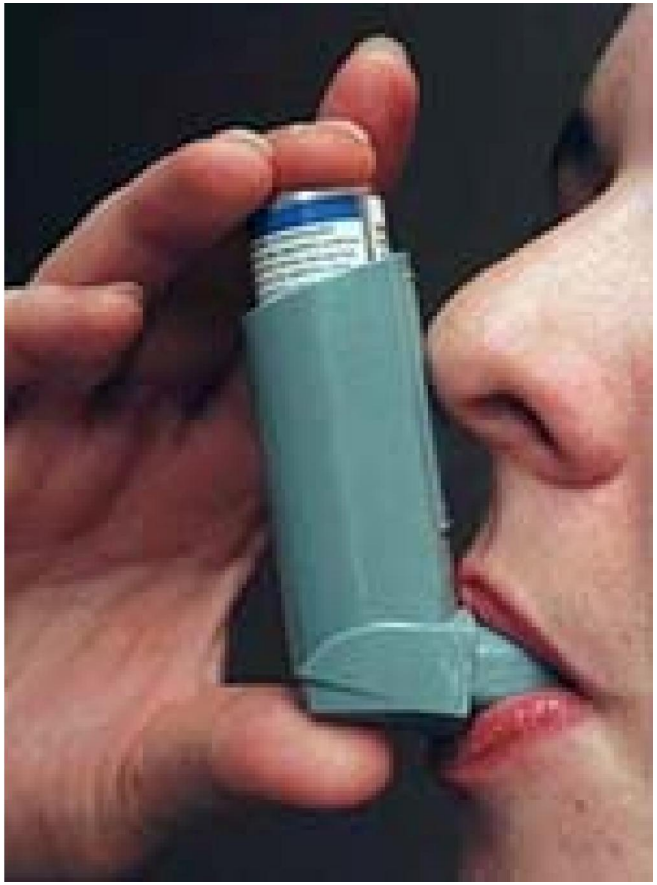
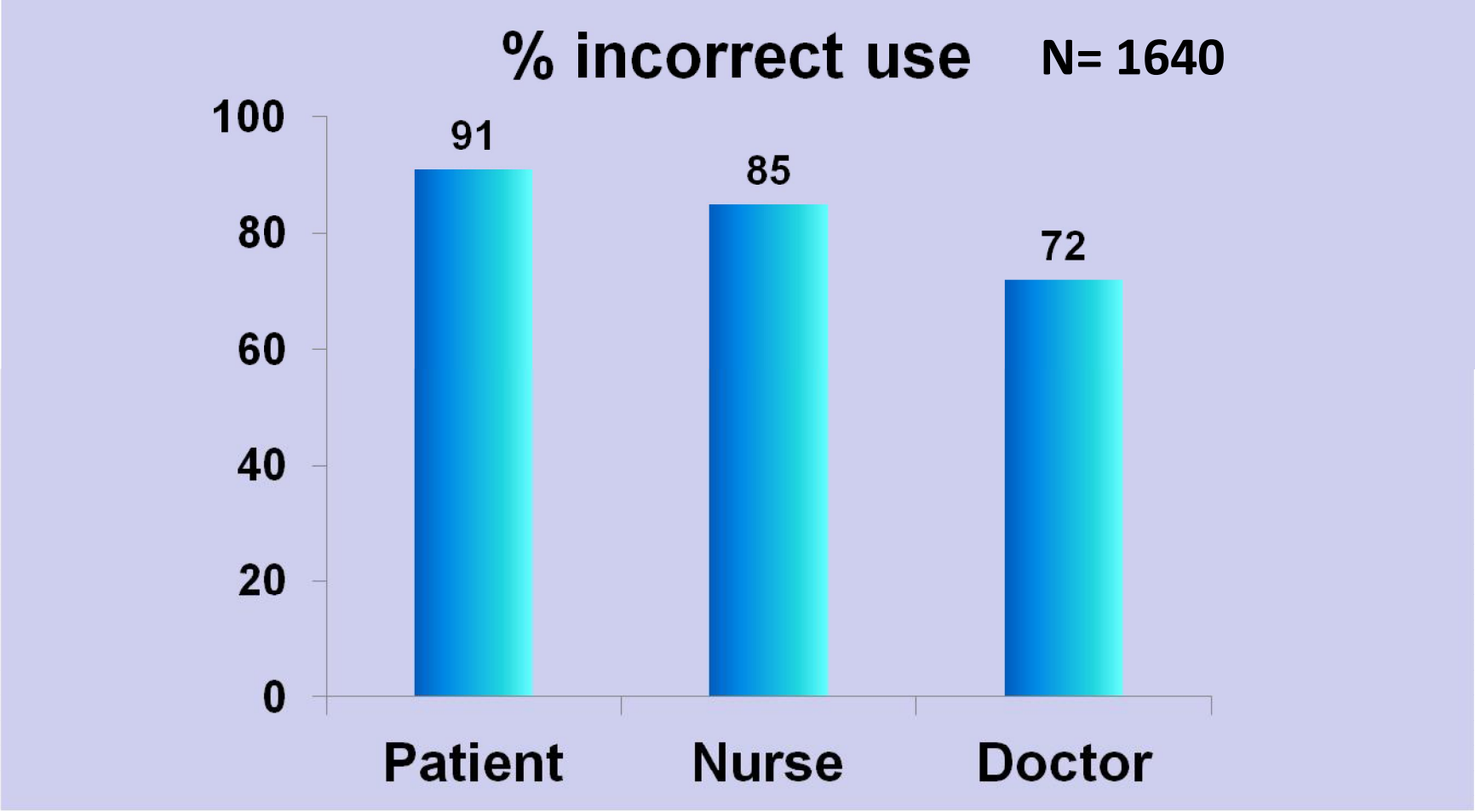
Using an MDI

Need a proper hand-lung synchronism

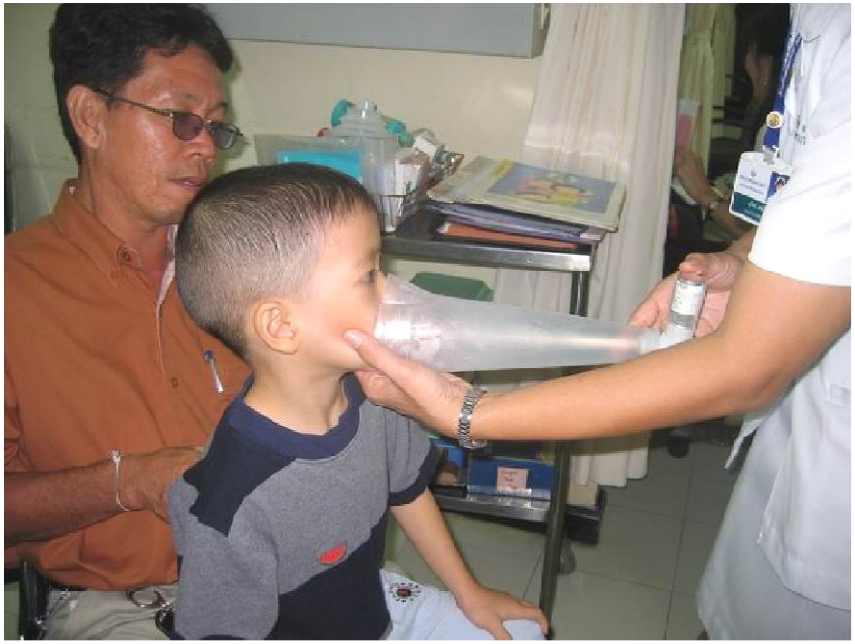


Incorrect Use of pMDI



Plaza V, et al. CESEA group. Respiration 1998;65:195–8.

MDIs must be used with spacer in children



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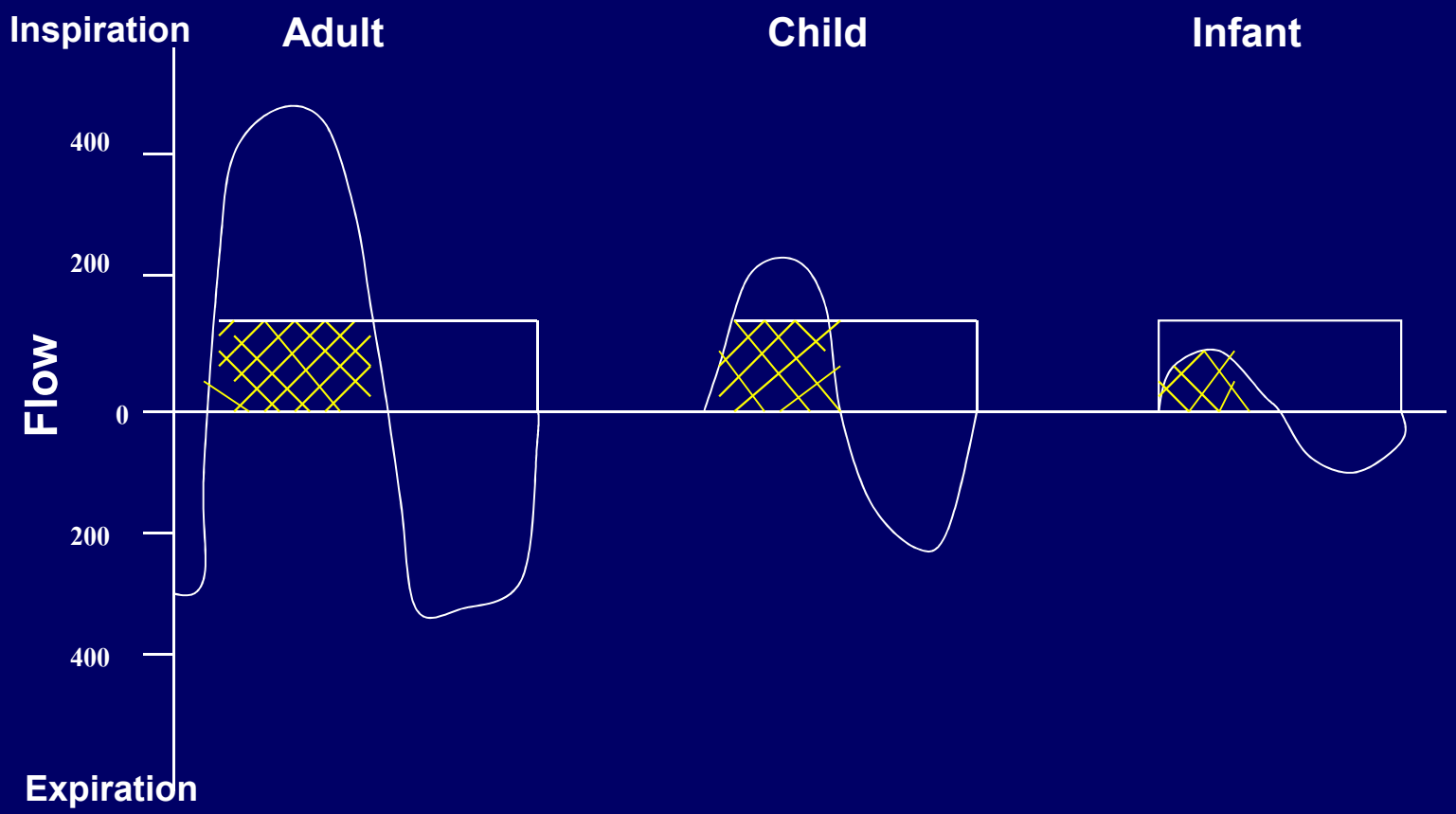
- Inappropriate step up
- Inadequate treatment of acute exacerbation at home and ER
  - lead to admission

Common pitfall

- Inadequate dose of β_2 agonist
  - MDI
  - Nebulization
- Delay systemic corticosteroid

Typical inhalation and exhalation airflow traces from an adult, a child and an infant



Both pMDI & Nebulization

- Low lung deposition
- Loss drug in device

Depend on

- **Gas flow**
- **Different device used**
- **Volume of drug solution**

Common pitfall

- Inadequate dose of β_2 agonist: initial
  - MDI initial ~ 2 – 4 puffs q 15-20 min
  - Nebulization 2.5 – 4 mL
- Delayed systemic corticosteroid
  - Start prednisolone 1-2 mg/kg/day or
  - Hydrocortisone 5 mg/kg/dose IV q 6 hr

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Steroid phobia

Safety profile of ICS

Growth

- No significant effects on growth of low dose ICS (100-200 ug/day)
- Reduction on growth rate ~ delay in skeleton maturation
- Attain normal adult height (predict from family members) but at a later age
- Uncontrolled or severe asthma adversely affects growth and final adult height

REVIEW ARTICLE

Drug Safety 2006; 29 (7): 599-612
0114-5916/06/0007-0599/$39.95/0

Clinical Safety of Inhaled Corticosteroids for Asthma in Children

An Update of Long-Term Trials

Søren Pedersen

Department of Paediatrics, University of Southern Denmark, Kolding Hospital, Kolding, Denmark

Contents

Table I. Summary of randomised, prospective studies of the effects of ≥12 months' inhaled corticosteroid therapy on childhood growth

Study	Year	Inhaler type	Drug regimen	Study duration (months)	Age (years)	Principal growth outcomes
Merkus et al.[13]	1993	pMDI	BUD 600 µg/day plus salbutamol (albuterol) 600 µg/day vs placebo plus salbutamol 600 µg/day	22	9–14	No significant between-group differences in growth
Roux et al.[14]	2003	DPI	FP 200 µg/day vs nedocromil 8–16 mg/day	24	6–14	No between-group differences in growth
Allen et al.[15]	1998	DPI	FP 100 µg/day vs 200 µg/day vs placebo	12	4–11, prepubertal	Growth not significantly impaired in children receiving FP 100 µg/day or 200 µg/day
Price et al.[16]	1997	pMDI	FP 100 µg/day vs sodium cromoglicate (cromolyn sodium) 20mg qid	12	4–10, prepubertal	No significant between-group differences in growth velocity or growth velocity standard deviation scores
Bisgaard et al.[17]	2004	pMDI	FP 200 µg/day vs sodium cromoglicate 5mg qid	12	11–47 months	No between-group differences in growth
Jonasson et al.[18]	2000	DPI	BUD 100 µg/day vs 200 µg/day vs placebo	27	7–16	Growth not significantly affected, except in 7–11 year olds at 12 months
Childhood Asthma Management Program Research Group[19]	2000	DPI	BUD 400 µg/day vs nedocromil 16 mg/day vs placebo	4–6 years	5–12	Small, transient reduction in growth velocity with BUD compared with placebo or nedocromil (22.7 vs 23.8 vs 23.7cm, respectively, over 5 years)
Verberne et al.[20]	1997	DPI	BDP 400 µg/day vs salmeterol 100 µg/day	12	6–16	Smaller height increase with BDP vs salmeterol (4.7 vs 6.1 cm)
Tinkelman et al.[21]	1993	pMDI	BDP 336 µg/day vs theophylline	12	6–17	Significantly slower growth in the BDP group (4.2 vs 5.5 cm/year)
Simons[22]	1997	DPI	BDP 400 µg/day vs salmeterol 100 µg/day vs placebo	12	6–14	Significantly slower growth in the BDP group than with either salmeterol or placebo (3.96 vs 5.40 and 5.04 cm/year, respectively)
Skoner et al.[23]a	2000	Nebuliser	BUD 500–1000 µg/day vs non-ICS	12	5 (approx.)	Small decrease in growth with BUD (6.55 vs 7.39 cm/year)
Visser et al.[24]b	2004	DPI	FP 200 µg/day (constant dose) vs 1000 µg/day step-down (100 µg/day from 6 months)	2 years	6–10	Growth velocity significantly lower in the step-down group at 2 months, significantly higher at 1 year, with no significant difference at 2 years
de Benedictis et al.[25]	2001	DPI	FP 200 µg/day vs BDP 200 µg/day	12	4–11	Growth velocity faster with FP
Rao et al.[26]	1999	pMDI	FP 200 µg/day vs BDP 400 µg/day	20	5–10	Significantly slower growth observed in the BDP group (4.94 vs 5.75 cm/year)

To assess the safety of long-term use of inhaled corticosteroids in children with asthma, a systematic review of the literature was performed focusing on randomised, controlled studies of ≥12 months' duration, to obtain data with maximum relevance to clinical practice. Specific searches were conducted to identify studies examining each of the following three areas: growth, bone mineral density and cortisol levels.

In conclusion, this literature review supports the theory that recommended doses of inhaled corticosteroids can be administered to children for the long-term management of asthma with minimal risk of clinically relevant adverse effects on growth, bone density or cortisol levels.

Safety profile of ICS

<u>Oral candidiasis, hoarseness, teeth</u>

- Relate to concomitant use of antibiotics and high daily dose
- Reduction by spacer, mouth rinsing
- Increase dental erosion due to oral pH reduction result from β_2 agonist inhalation

Safety profile of ICS

<u>Lower respiratory tract infection</u>
(pneumonia and TB)

- Long-term use of ICS is NOT associated with an increase incidence of LRI and TB

Summary

- Recurrent wheezing ≥ 3 times – ICS as therapeutic treatment
- Appropriate dose of ICS
- Before step up – look for
  - Inhalation technique
  - Compliance
  - Environmental avoidance
  - Co-morbidity esp. AR, sinusitis, OSA

Asthma control can be achieved in pediatric patients ?

- Early diagnosis and treatment
- All ICSs are essential medications and supported by Government
- Cost-effectiveness
  - Improve quality of life
  - Cheap price of ICS
  - Few side effects of ICS either growth, superimpose infection

‘Zero’ admission!

Make it real

We all can do

THANK YOU

Faculty of Medicine, KKU

การประชุมใหญ่ประจำปี ครั้งที่ 10

Easy Asthma & COPD Clinic Network

10-11 มีนาคม 2557