

# Step Up Therapy in Children

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# Disclosure Slide

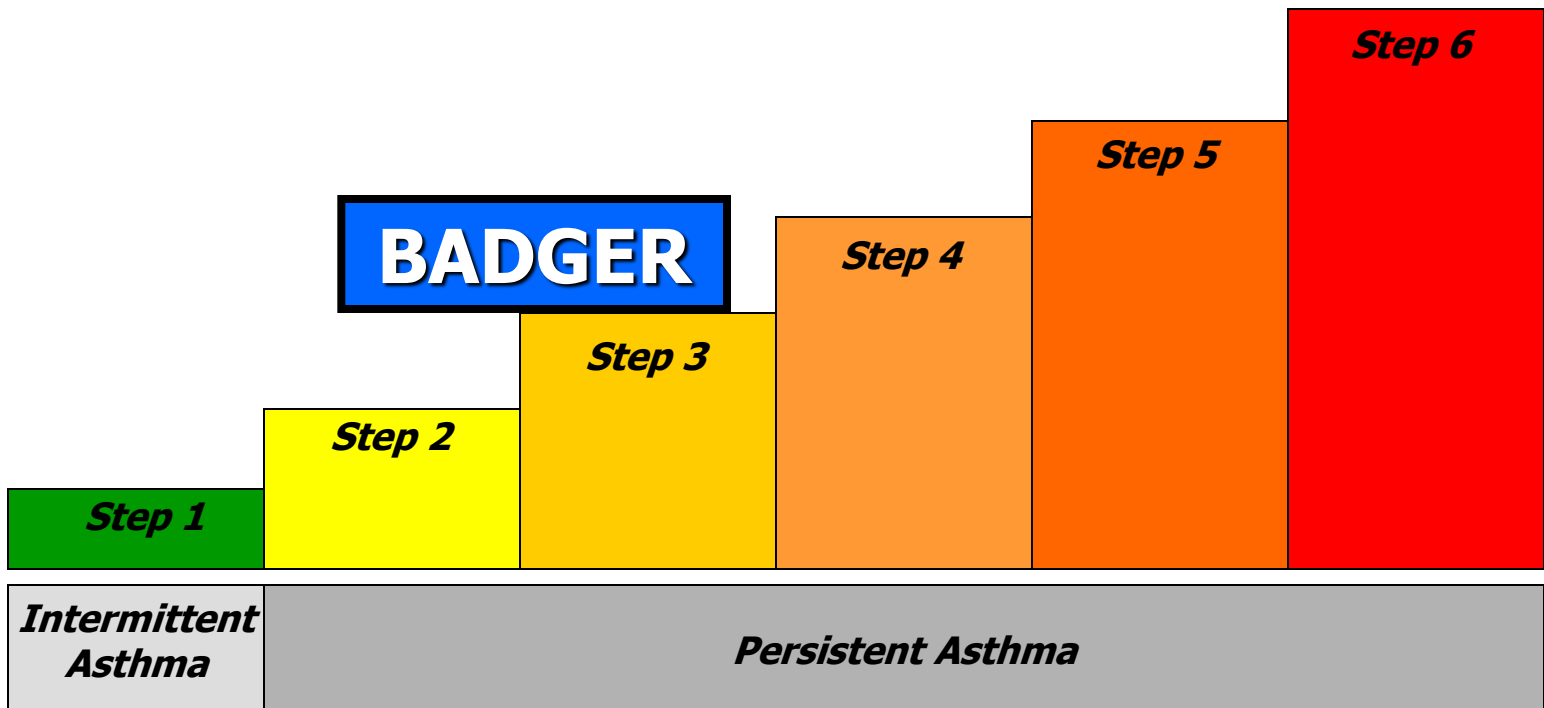
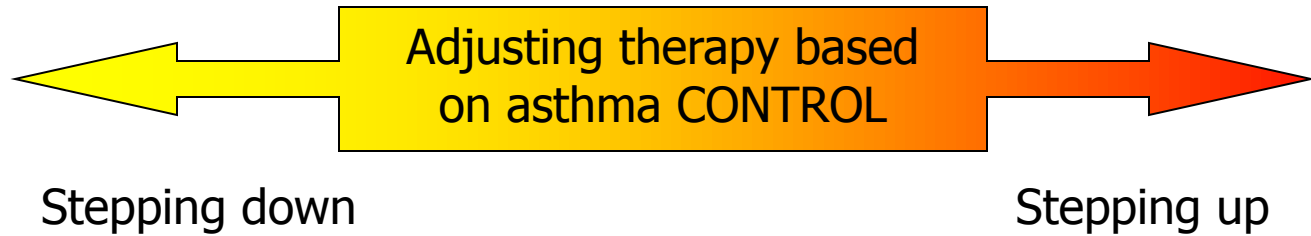
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- *Employment*  
*University of Wisconsin*
- *Financial Interests*  
*Nothing to Disclose*
- *Research Interests*  
*NIH*  
*AAAAI/GSK Career Development Award*
- *Organizational Interests*  
*Nothing to Disclose*
- *Gifts*  
*Nothing to Disclose*
- *Other Interests*  
*Nothing to Disclose*

# Step-up Approaches in Asthma

STEP-UP LONG-TERM (SLT)	STEP-UP SHORT-TERM (SST)	STEP-UP INTERMITTENT (SUI)
increase in therapy for uncontrolled asthma (weeks)	increase in therapy for brief loss of control (days)	increase in therapy for variable symptoms (day-to-day)
persistent loss of control	brief loss of control (upper respiratory tract infections, pet exposure)	mild symptoms
step-down therapy when control achieved after 3-6 months	step-down therapy when control achieved after 3-10 days	intermittent use

# Step-up Long Term





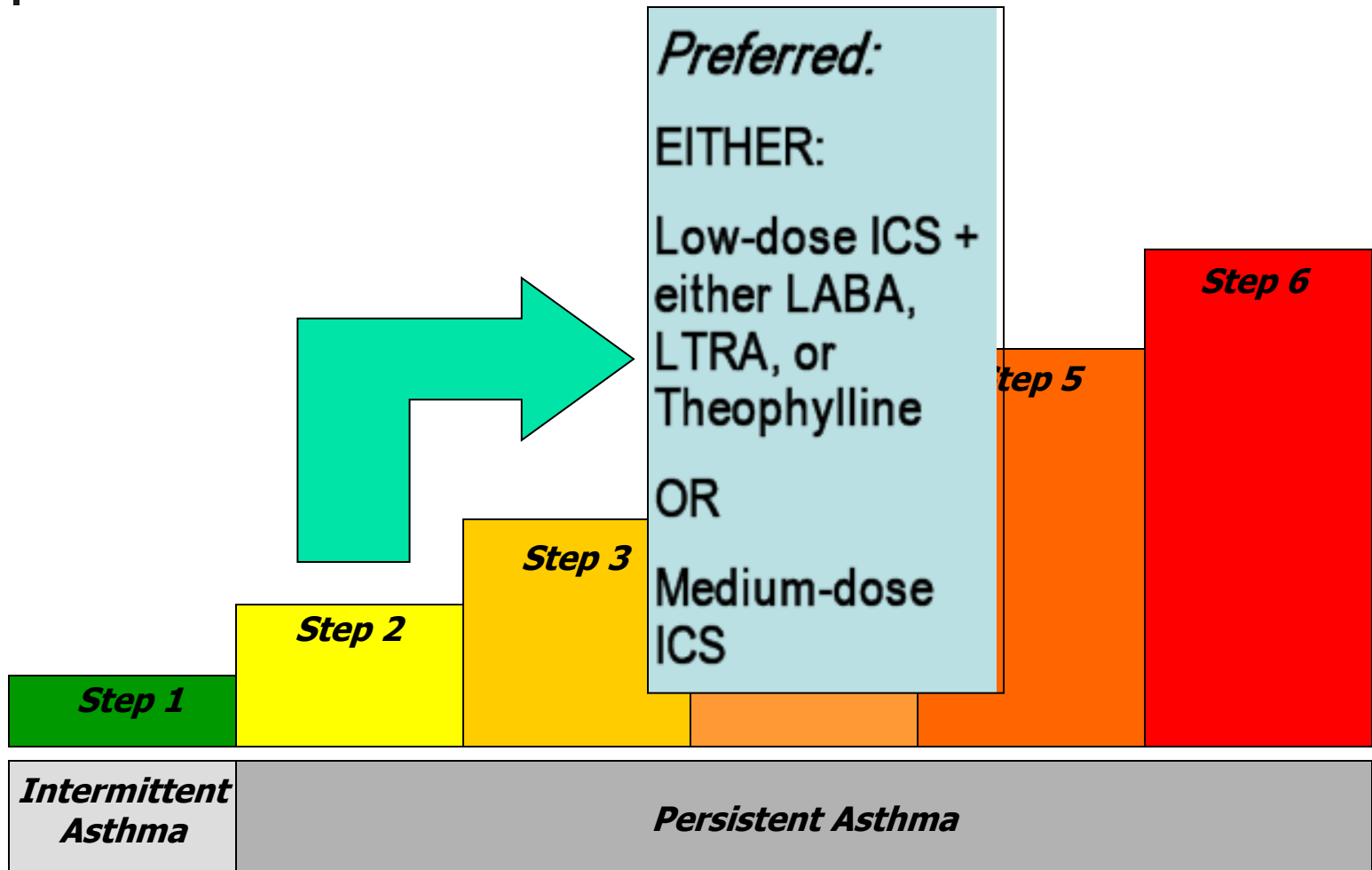
# Research Question: Children

***BADGER***

***Best Add-on Therapy Giving  
Effective Responses***

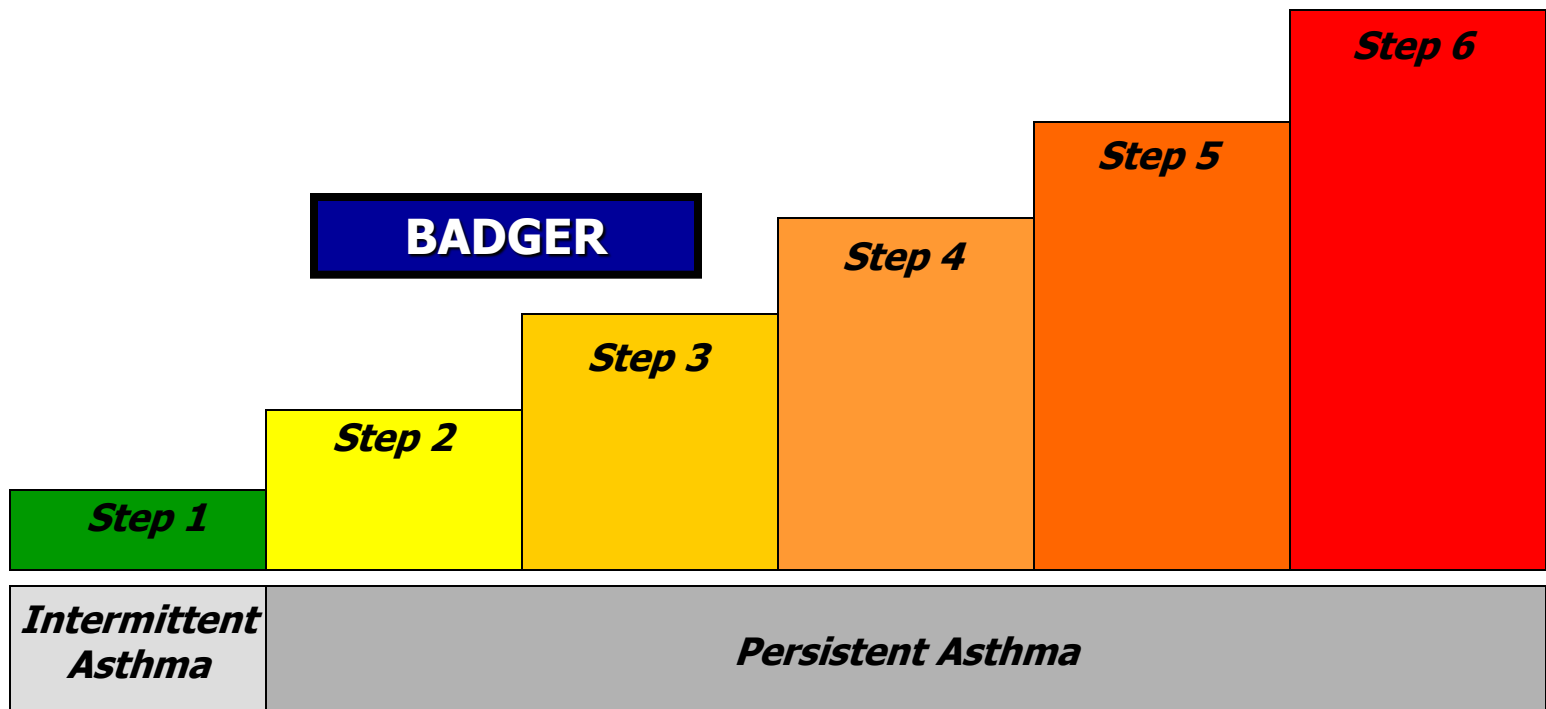
- In patients receiving daily low dose ICS treatment who are not well controlled, what are the next best treatment options?

# EPR-3 Recommendations



# EPR-3 Recommendations

In children, is there a best choice for Step 2 to Step 3 care?



# BADGER: Research Question

- In children not satisfactorily controlled on low dose ICS (fluticasone 100 µg BID) therapy, what is the best next treatment approach?
  - Increased doses of ICS (fluticasone 250 µg BID)?
  - Add a LABA (salmeterol/fluticasone combination)?
  - Add a LTRA (montelukast)?



# Differential Response

- At the end of the study, each child was identified as either a **differential** or **non-differential** treatment responder.
- A **differential responder** was someone who exhibited significantly better outcomes on one treatment than on another.
- Effective treatment response was based on (in order of importance):
  1. Asthma exacerbations
  2. Asthma control days (ACD)
  3. Change in FEV<sub>1</sub>.

# Definitions for Differential Response: Asthma Exacerbations

- Differential response with respect to asthma exacerbations occurred when the total amount of prednisone prescribed to control asthma symptoms was at least 180 milligrams\* greater on one treatment than on either of the other two treatments.

*\*Based on “prednisone burst” of 2 mg/kg/day for 2 days, 1 mg/kg/day for 2 days to a maximum of 60-60-30-30 mg*

# ***Definitions for Differential Response: Asthma Control Days***

- Differential response with respect to ACD occurred when the number of annualized ACD (AACD) achieved on one treatment was at least 31 days more than on either of the other two treatments.



# Asthma Control Day (ACD)

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- An ACD was defined as a day without:
  - Albuterol rescue use (pre-exercise treatment permitted)
  - Use of non-study asthma medications
  - Nighttime awakenings
  - Daytime asthma symptom score more than mild
  - Unscheduled health care provider visits for asthma
  - Yellow-zone PEF or Red-zone PEF

# *Definitions for Differential Response:*

## *FEV<sub>1</sub>*

- Differential response with respect to FEV<sub>1</sub> occurred when the FEV<sub>1</sub> change on one treatment was at least 5% higher than on either of the other two treatments.
- The FEV<sub>1</sub> change for each treatment was defined as the percent difference between the FEV<sub>1</sub> from the end of the run-in to the end of the treatment period

$$\frac{\text{FEV}_{\text{treatment}} - \text{FEV}_{\text{run-in}}}{\text{FEV}_{\text{run-in}}}$$



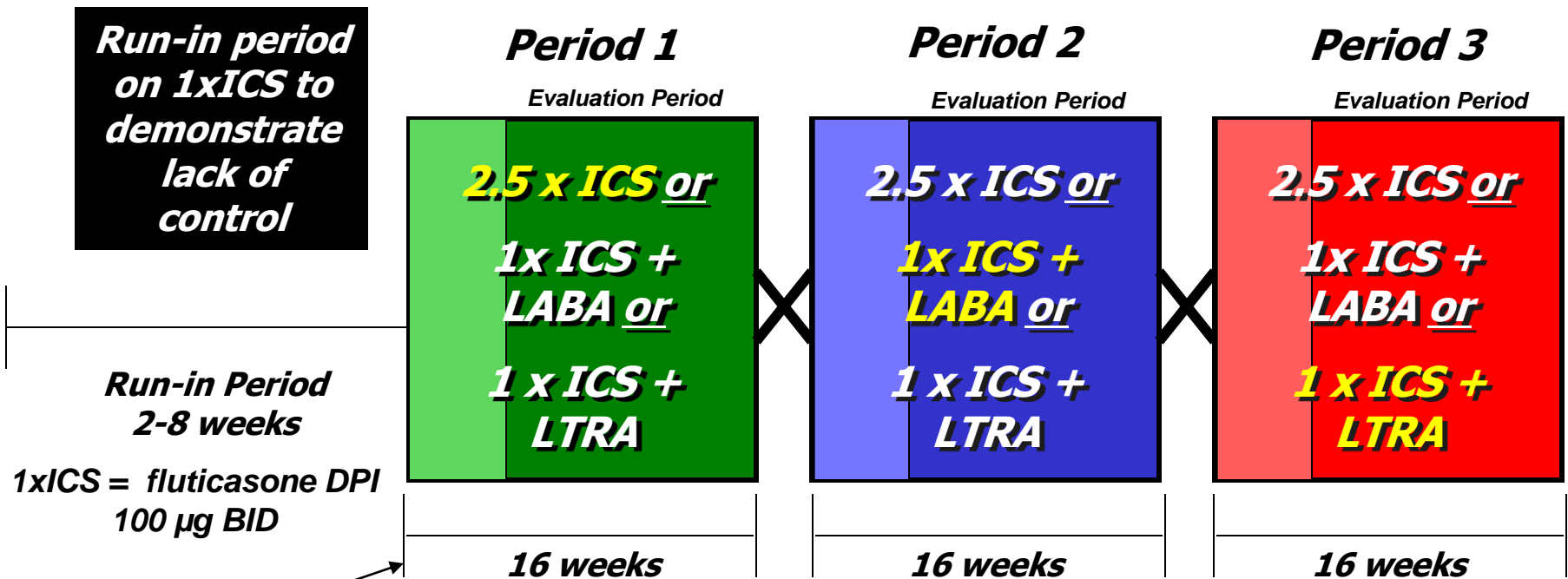
# Inclusion Criteria

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- Age 6-18 years
- Able to perform reproducible spirometry based on ATS criteria
- $FEV_1$  reversibility  $\geq 12\%$  OR
- Methacholine  $PC_{20} \leq 12.5$  mg/ml

# BADGER Protocol: Overview

*Three Treatment Period, Double blind, 3 way cross-over*



**Randomization**

**2.5 x ICS = fluticasone DPI 250 µg BID**

**1xICS+LABA = fluticasone/salmeterol DPI 100/50 BID**

**1xICS+LTRA = fluticasone DPI 100 µg BID + montelukast**



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# Primary Outcome Stage 1

Was a differential response  
observed in  $\geq 25\%$  of the  
participants?





# Results: Differential Response

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Differential response occurred in  
161/165 participants (98%)  
( $p < 0.0001$ )



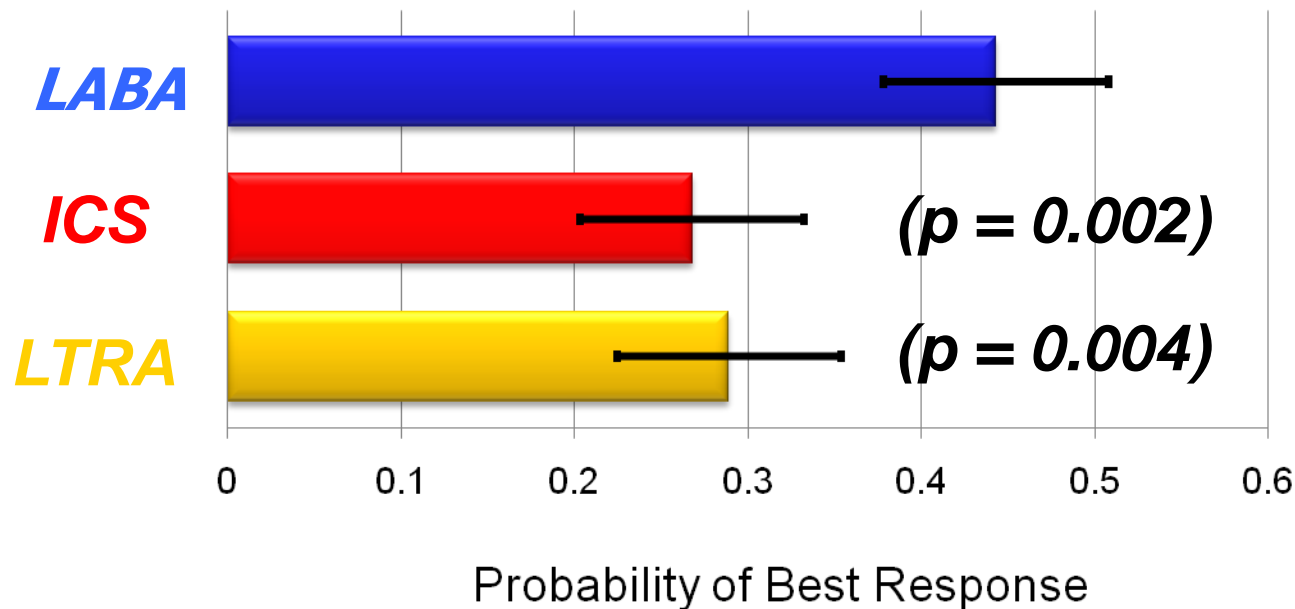
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# Primary Outcome Stage 2

What was the direction  
of the best response?

# Primary Outcome: Probability of BEST Response Based on Composite Outcome\*

*LABA step-up was more than 1.5 times as likely to produce the best response*

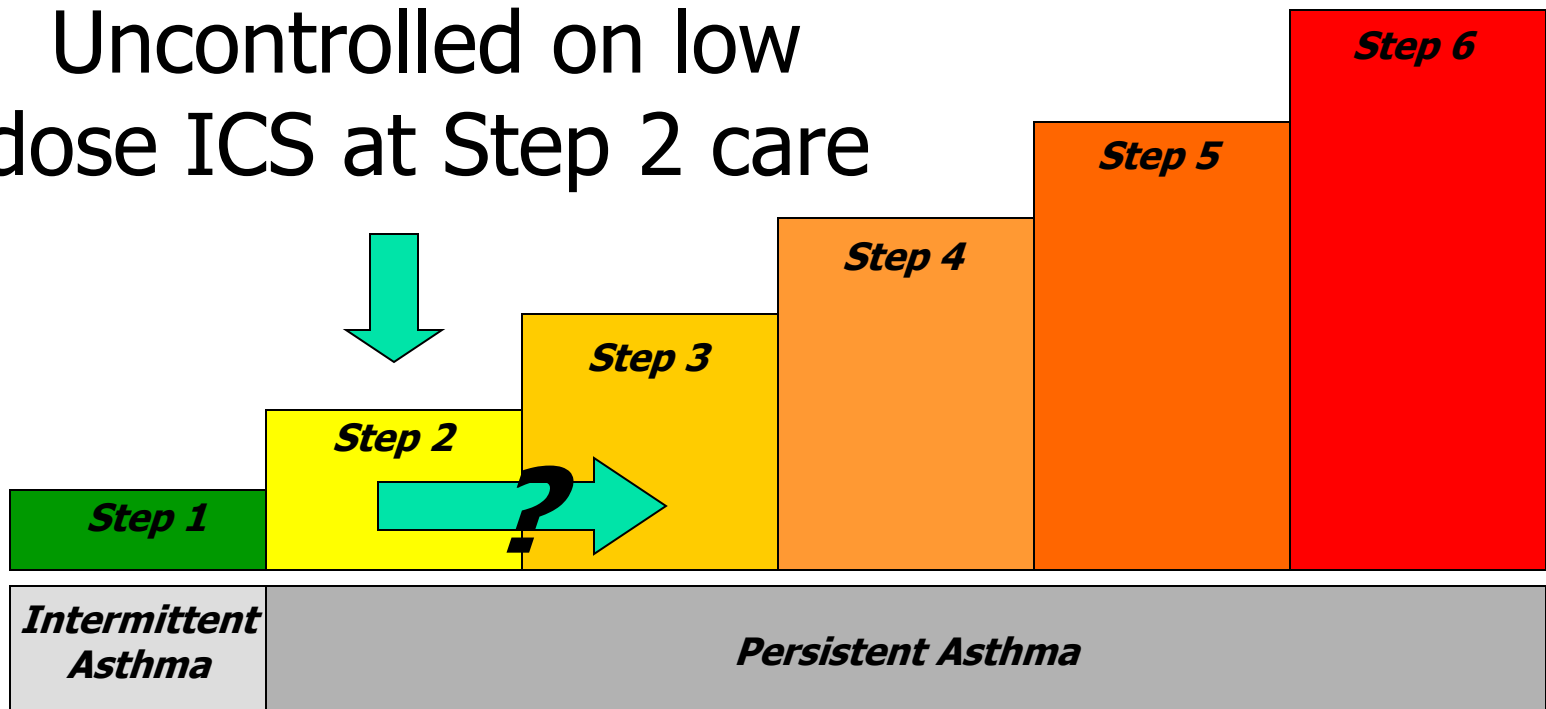


\*Covariate adjusted model

Lemanske RF et al. NEJM 362:975, 2010

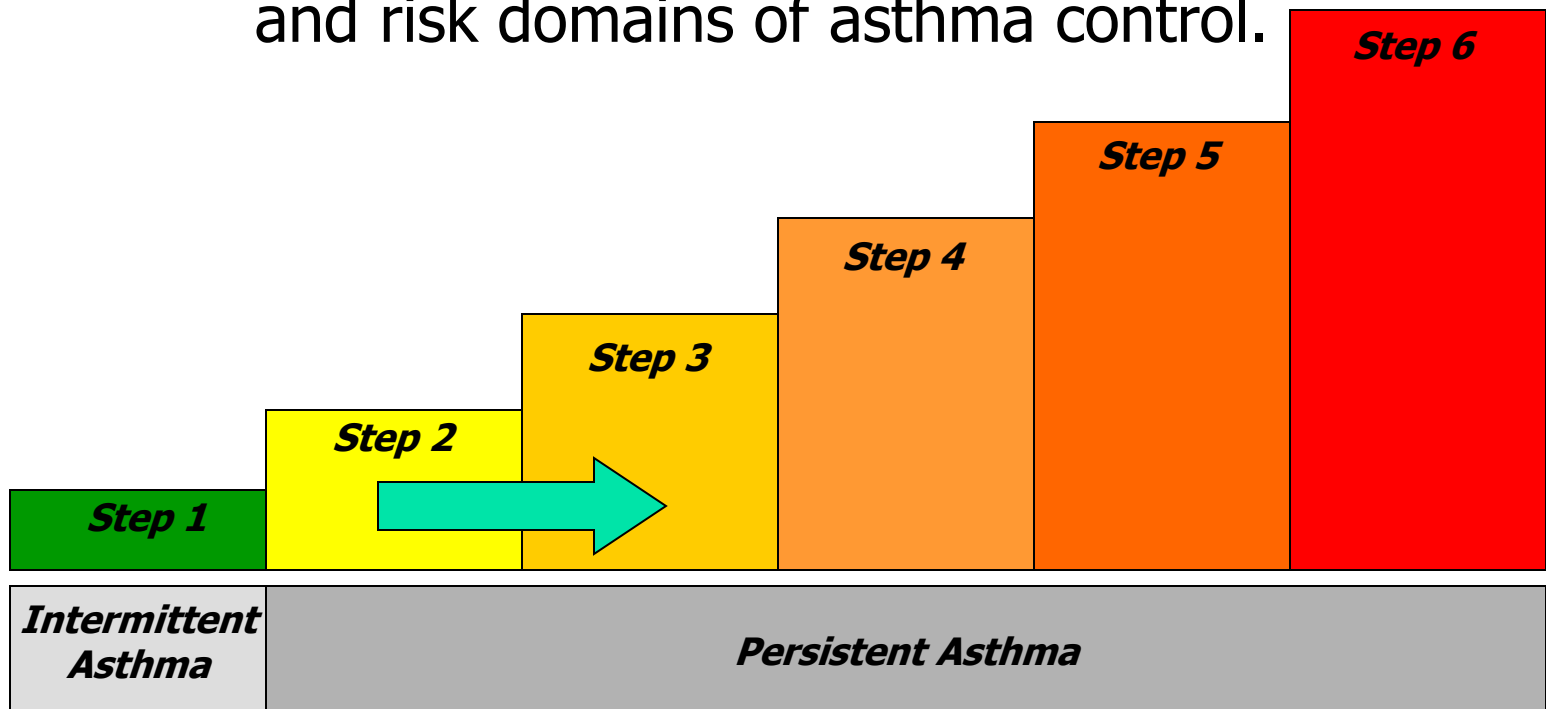
# BADGER: Conclusions

Uncontrolled on low dose ICS at Step 2 care



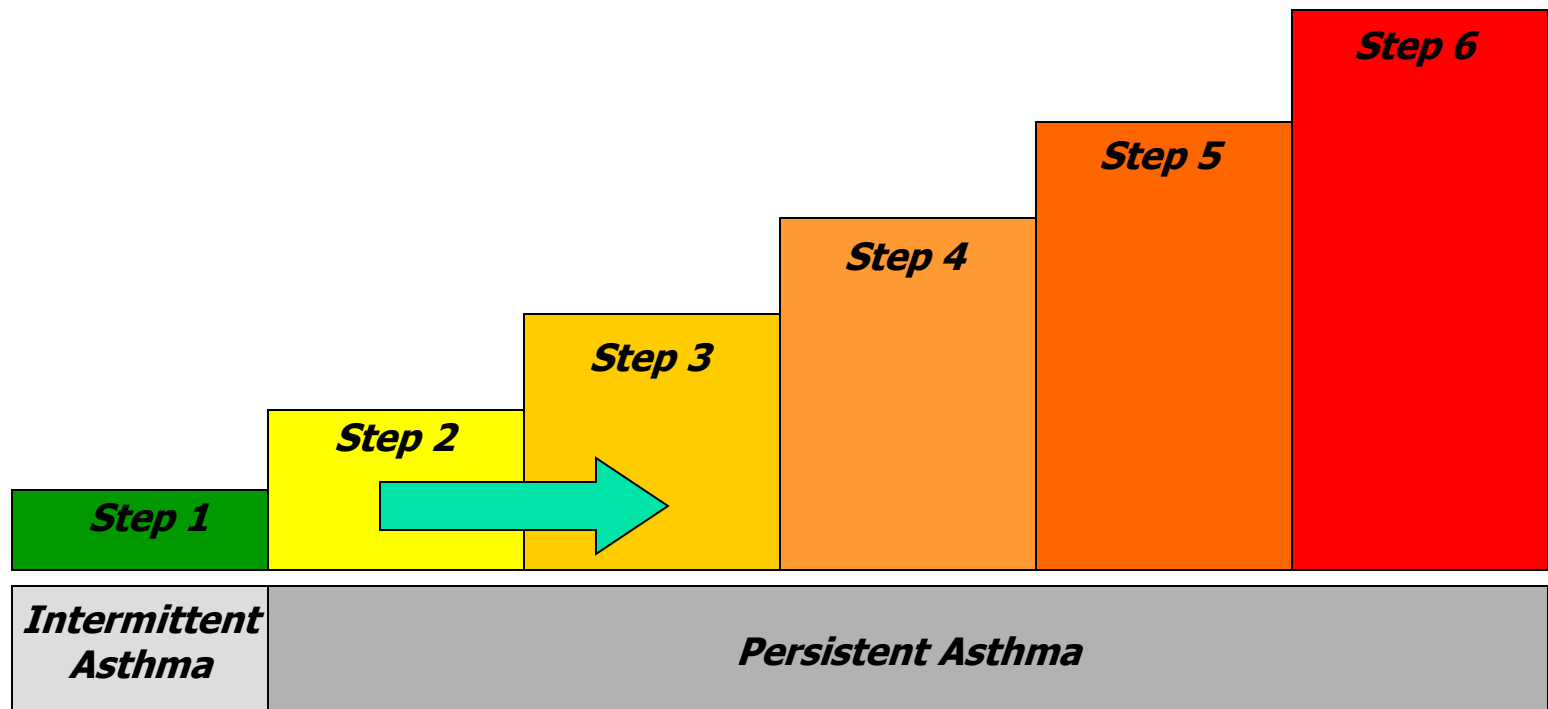
# BADGER: Conclusions

A differential response to step-up therapy was demonstrated in nearly all subjects ( $\geq 95\%$ ) using a composite evaluation of components in both impairment and risk domains of asthma control.



# BADGER: Conclusions

The probability of experiencing the best overall response was more than 1.5 times as likely with LABA step-up.



# BADGER: Conclusions

Many children demonstrated a best response to either ICS or LTRA step-up, highlighting the need to regularly monitor and appropriately adjust each child's asthma therapy.

