

# Corticoides inhalados como medicación de rescate en asma

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# CONFLICTO DE INTERESES



- Ayudas para asistencia a cursos y congresos, así como actividades formativas:  
GSK, Astra-Zeneca, Novartis, Chiesi, Abvy,  
Aldo-Union, ALK-Abelló, MSD.

# Indice

- Razones para creer (o no)



- Datos, datos, datos



- Trending topics en la práctica de la medicina



- Aplicabilidad en nuestra consulta



- Back to basic



# Miquelet

## Opciones de tratamiento

- Continuar igual tratamiento y observar
- Pasar al siguiente escalón de tratamiento según las guías
- ¿Aumentar la dosis de corticoides inhalados en las exacerbaciones?



- Asma se caracteriza por exacerbaciones
- No fácilmente predecibles
- Tratamiento broncodilatadores y corticoides orales
- ¿A disposición en casa?



## **Physician and parent barriers to the use of oral corticosteroids for the prevention of paediatric URTI-induced acute asthma exacerbations at home**

**Neale Smith MA MEDes<sup>1</sup>, Anne Smith MSc<sup>2,3,4</sup>, Alice Wang BScPharm ACPR<sup>5</sup>, Kaitlyn Shaw MSc<sup>2,3,4</sup>,**

**Results:** Incidence of URTI events among participants was high (85%). Uptake of study medication was low; 44% used the medication as directed at their first URTI event. Eleven per cent of the patients who used the study medication also visited the emergency department for an exacerbation. Focus groups identified four main barriers to the effective use of parent-initiated oral corticosteroids: physician resistance and conflicting messages from providers; parent uncertainty about oral corticosteroids; multiple caregivers and relative ease of access to an emergency department.

Rev Assoc Med Bras (1992). 2017 Oct;63(10):899-903. doi: 10.1590/1806-9282.63.10.899.

## **Oral corticosteroids for asthma exacerbations might be associated with adrenal suppression: Are physicians aware of that?**

Barra CB<sup>1</sup>, Fontes MJF<sup>2</sup>, Cintra MTG<sup>3</sup>, Cruz RC<sup>3</sup>, Rocha JAG<sup>3</sup>, Guimarães MCC<sup>3</sup>, Silva IN<sup>1</sup>.



Arch Dis Child. 2016 Apr;101(4):365-70. doi: 10.1136/archdischild-2015-309522. Epub 2016 Jan 14.

## **Systematic review of the toxicity of short-course oral corticosteroids in children.**

Aljebab F<sup>1</sup>, Choonara I<sup>1</sup>, Conroy S<sup>1</sup>.

was one of the most serious ADRs; one child died after contracting varicella zoster. When measured, 144 of 369 patients showed increased blood pressure; 21 of 75 patients showed weight gain; and biochemical hypothalamic-pituitary-adrenal axis suppression was detected in 43 of 53 patients.

## Treatment of acute asthmatic exacerbations with an increased dose of inhaled steroid

J Garrett, S Williams, C Wong, D Holdaway

The 1993 British Thoracic Society asthma management guidelines<sup>1</sup> stated that although patients might be advised to increase their dose of inhaled steroids at the first sign of a cold or of asthma deterioration, there was no corroborative evidence from trials for the effectiveness of such an approach. A 1995 review of these

Despite the lack of published evidence, a step involving an increased dose of inhaled steroids is a common component of asthma self management plans. It has been shown that 95% of general practitioners and 57% of paediatricians and paediatric registrars use such a treatment approach.<sup>7</sup>

## Children aged ≤5 years – key changes



2018

- Step 2 (initial controller treatment) for children with frequent viral-induced wheezing and with interval asthma symptoms
  - A trial of regular low-dose ICS should be undertaken first
  - As-needed (pm) or episodic ICS may be considered
  - The reduction in exacerbations seems similar for regular and high dose episodic ICS (*Kaiser Pediatr 2015*)
  - LTRA is another controller option
- Step 3 (additional controller treatment)
  - First check diagnosis, exposures, inhaler technique, adherence
  - Preferred option is medium dose ICS
  - Low-dose ICS + LTRA is another controller option
    - Blood eosinophils and atopy predict greater short-term response to moderate dose ICS than to LTRA (*Fitzpatrick JACI 2016*)
    - Relative cost of different treatment options in some countries may be relevant to controller choices

# > 5 años



2018

## Modificaciones de la medicación en los planes de acción por escrito contra el asma

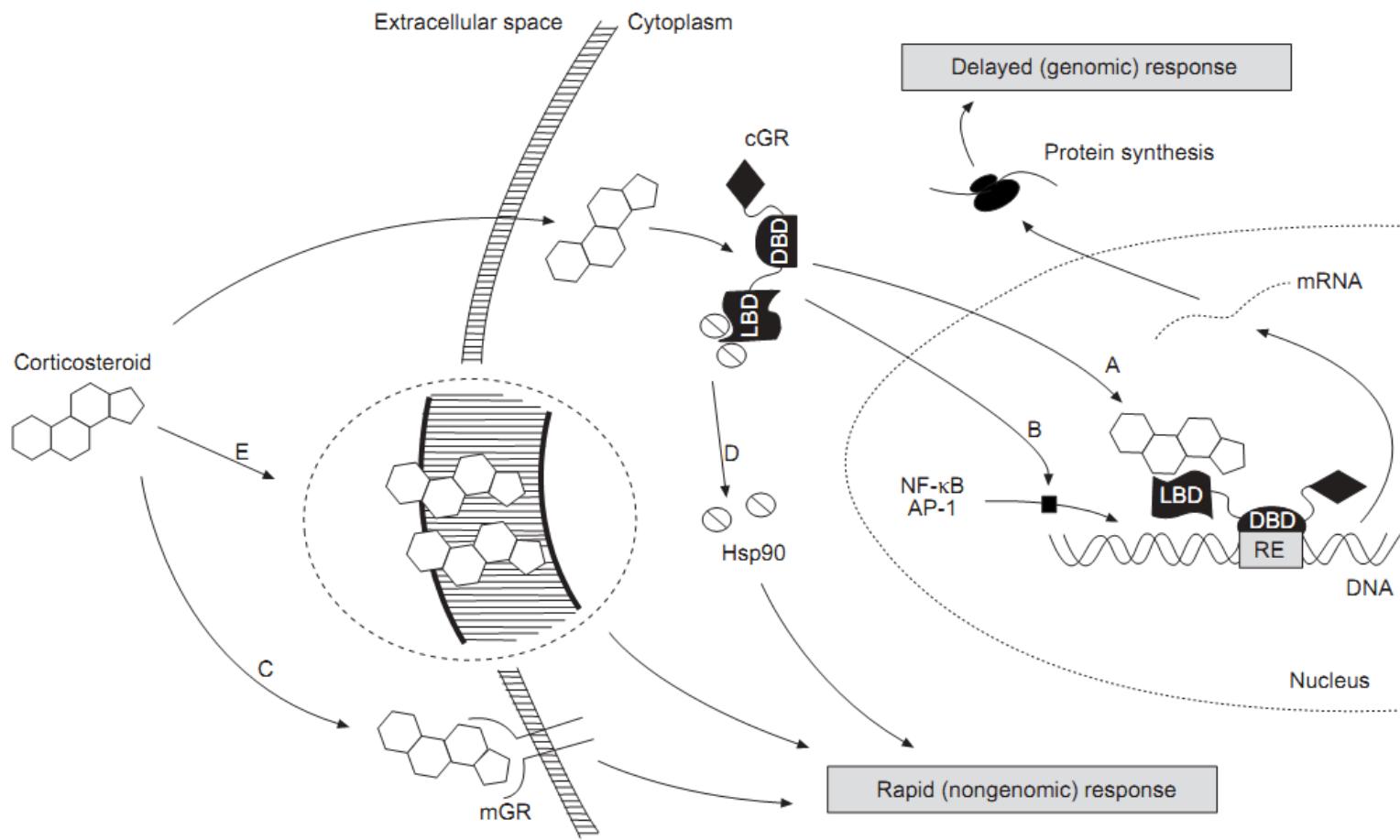
**Aumento de la frecuencia de medicación sintomática inhalada (SABA, o ICS en dosis bajas/formoterol en caso de utilizarse como régimen de mantenimiento y rescate); adición de cámara de inhalación para el pMDI.**

**Aumento de la medicación de control:** aumento rápido del componente de ICS hasta un máximo de 2000 µg o equivalente de BDP. Las opciones dependen de la medicación de control habitual, de la manera siguiente:

- *ICS:* como mínimo, dosis doble; contemplar un aumento a dosis altas.
- *ICS/formoterol de mantenimiento:* cuadruplicación de la dosis de ICS/formoterol de mantenimiento (hasta la dosis máxima de formoterol de 72 µg/día).

# Justificación

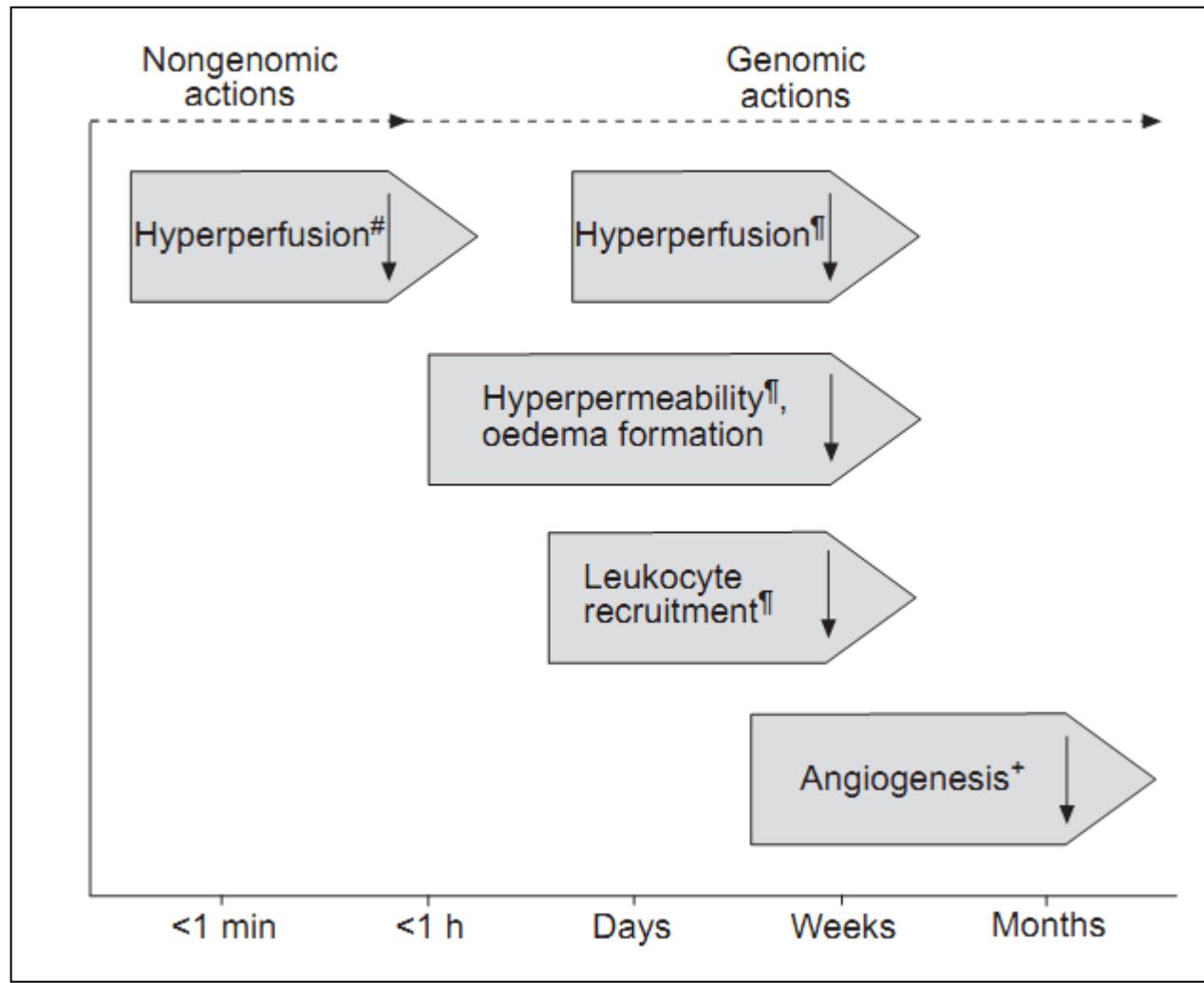




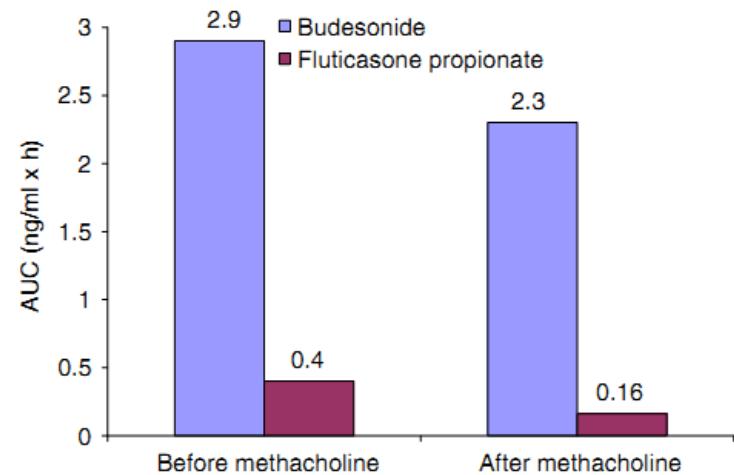
**FIGURE 1.** Schematic diagram of the complex cellular actions of corticosteroids. Genomic actions are mediated by cytoplasmic receptors, which ultimately alter transcription through A) direct DNA binding or B) transcription factor inactivation. In contrast, nongenomic actions are mediated by C) membrane-bound or D) cytoplasmic receptors, or E) nonspecific interactions with the cell membrane. cGR: cytosolic glucocorticoid receptor; mGR: membrane glucocorticoid receptor; LBD: ligand-binding domain; DBD: DNA-binding domain; Hsp90: heat-shock protein 90; RE: response element; NF-κB: nuclear factor-κB; AP-1: activating protein-1.

**TABLE 1** Genomic and nongenomic actions of corticosteroids

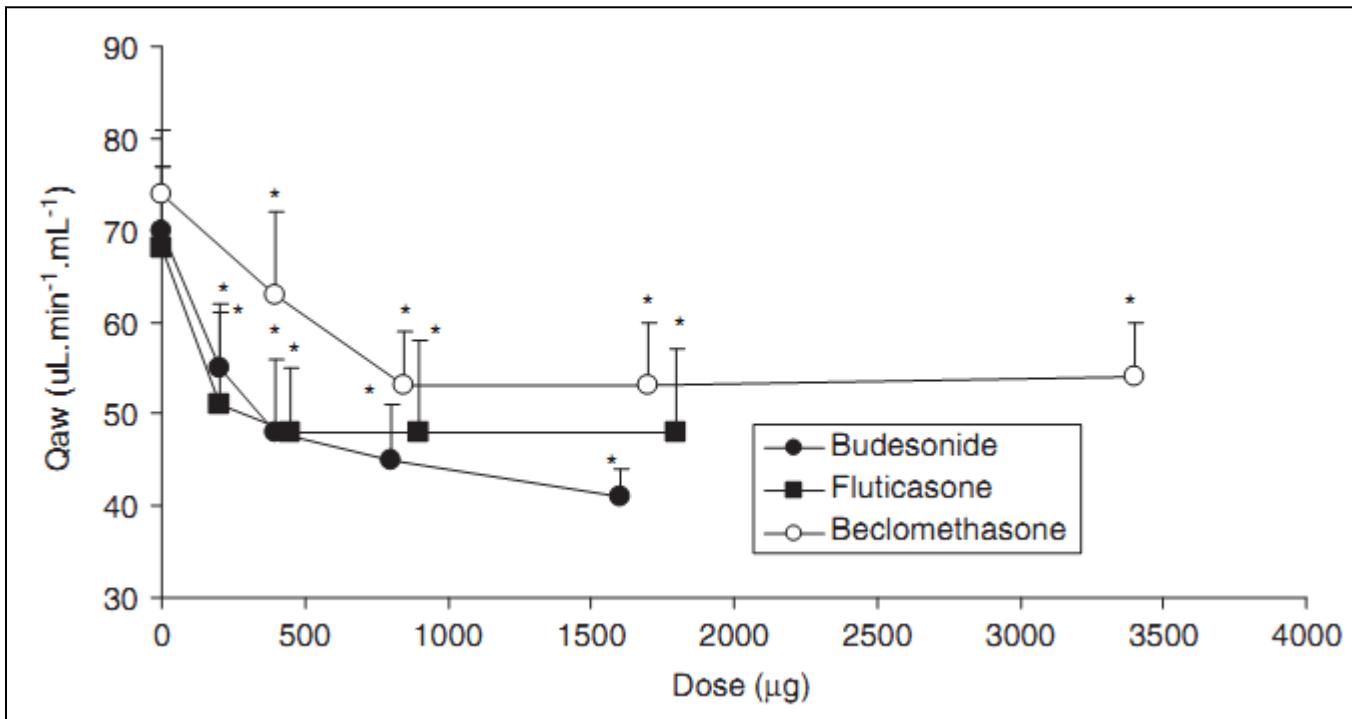
	Genomic actions	Nongenomic actions		
<b>Receptor location</b>	Cytoplasm	Cytoplasm	Membrane	Nonspecific
<b>Action's onset and reversibility</b>	Hours–days		Seconds–minutes	
<b>Sensitivity to inhibitors of transcription (actinomycin D) and protein synthesis (cycloheximide)</b>	Inhibition		No effect	
<b>Activity of membrane impermeant carrier (bovine serum albumin)-coupled drug</b>	Inactive	Inactive	Active	Active



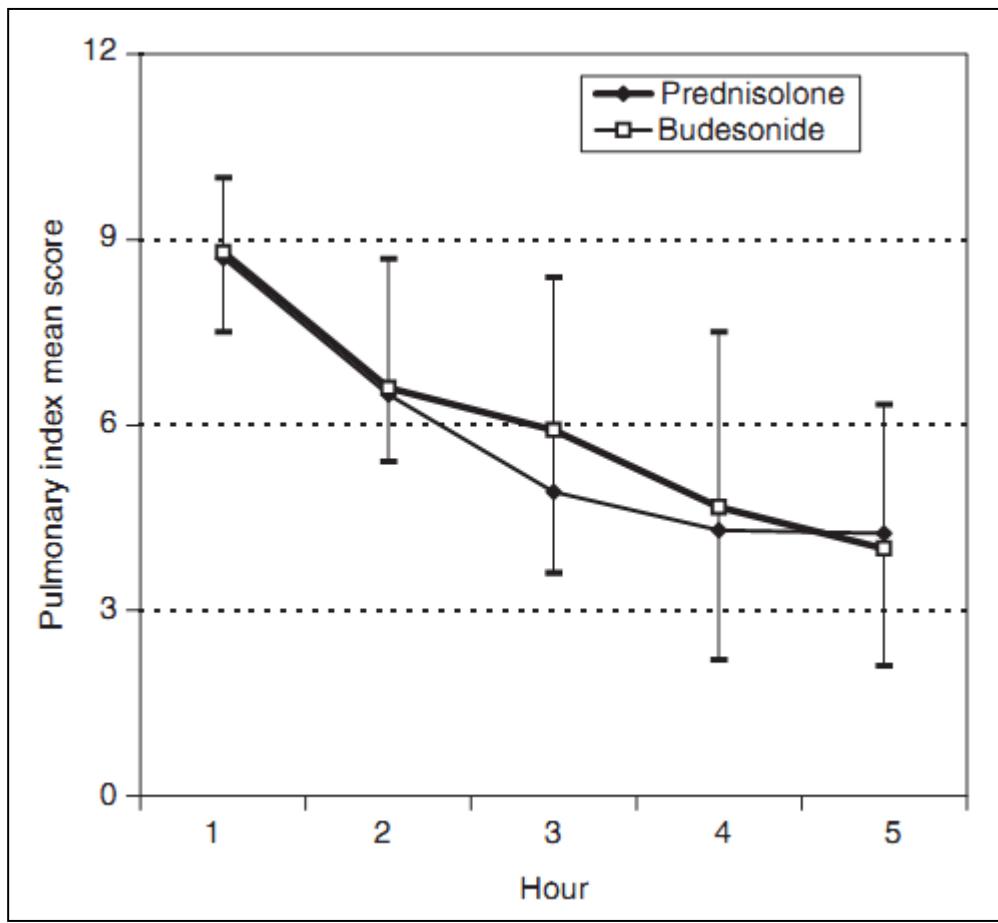
- Altas dosis
- Alta frecuencia
- Diferencias entre compuestos (lipofilicidad)



**Figure 2** Mean areas under curves of plasma drug concentration vs. time (AUC) for single inhaled doses of budesonide (800 µg) and fluticasone (1000 µg) before and challenge with methacholine.<sup>52</sup> The relative reduction in AUC caused by methacholine challenge was significantly greater for fluticasone than for budesonide ( $P = 0.003$ ).

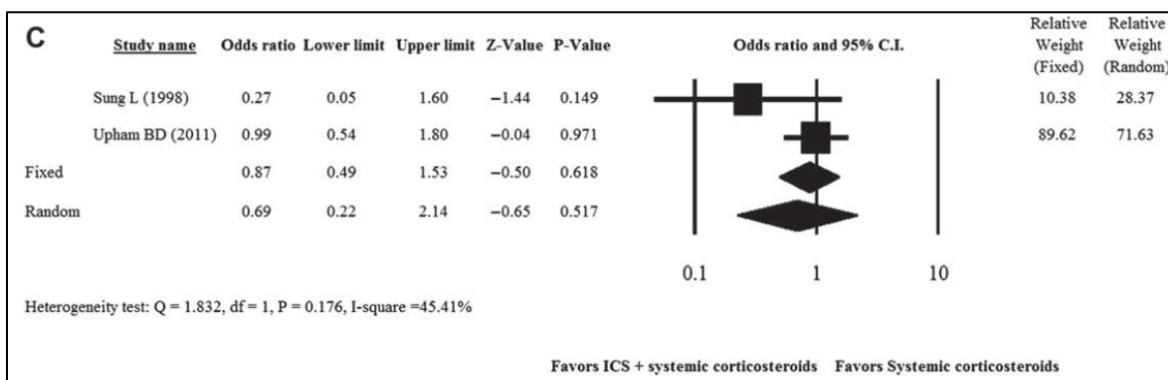
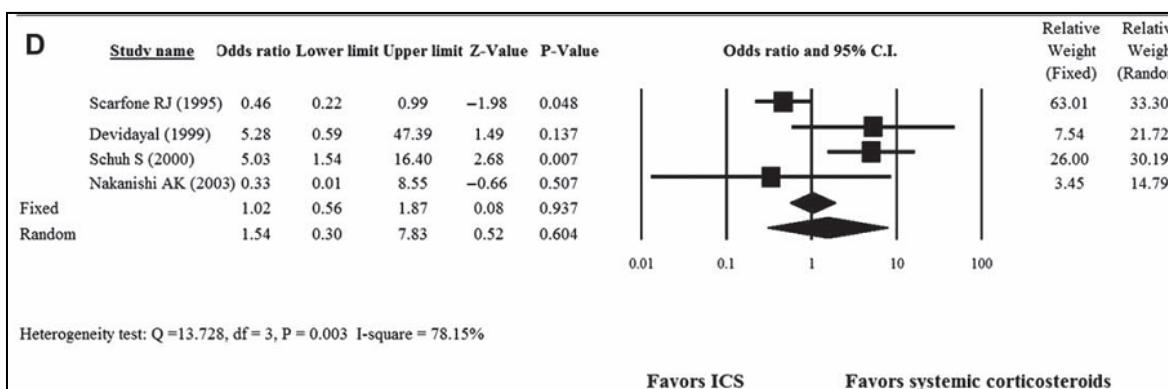
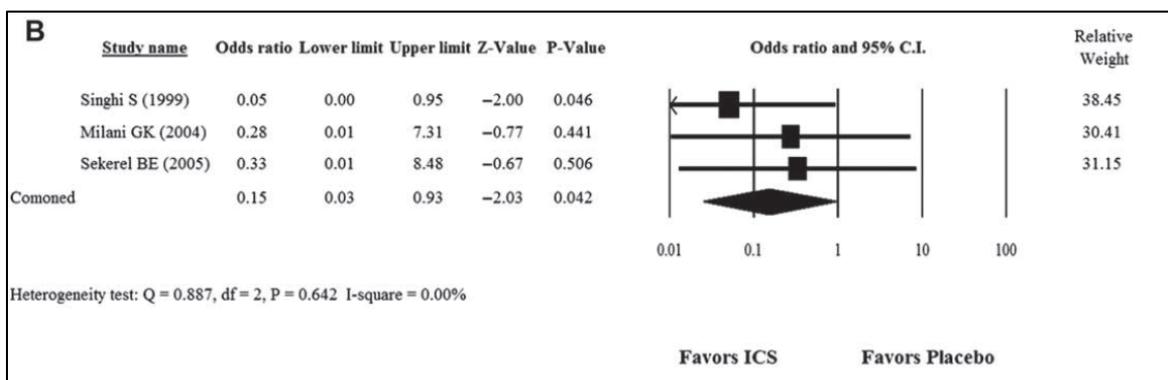


Comparative vasoconstrictor efficacy of three inhaled corticosteroids in 10 corticosteroid naïve patients with asthma



**Figure 4** Time course of effect of inhaled budesonide (1600 µg via dry powder inhaler) and oral prednisolone (2 mg/kg) in children treated for acute asthma in the emergency department setting.<sup>14</sup>

# Effectiveness of inhaled corticosteroids in the treatment of acute asthma in children in the emergency department: A meta-analysis



Pediatrics. 2016 Jun;137(6). pii: e20154496. doi: 10.1542/peds.2015-4496.

## **Preventing Exacerbations in Preschoolers With Recurrent Wheeze: A Meta-analysis.**

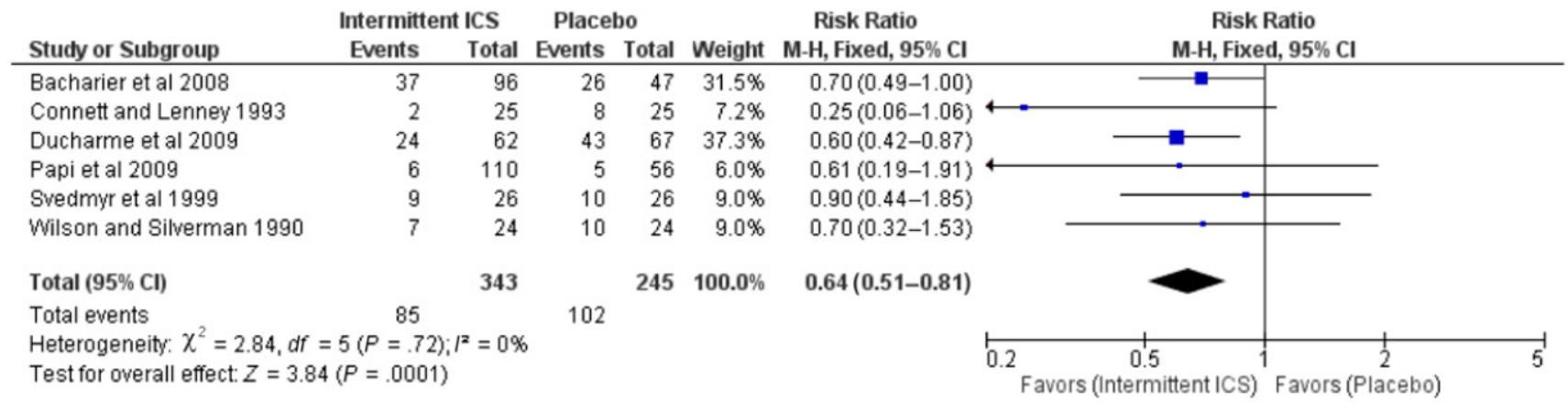
Kaiser SV<sup>1</sup>, Huynh T<sup>2</sup>, Bacharier LB<sup>3</sup>, Rosenthal JL<sup>4</sup>, Bakel LA<sup>5</sup>, Parkin PC<sup>6</sup>, Cabana MD<sup>7</sup>.

compared with montelukast (1 study,  $N = 202$ ; RR 0.59; 95% CI, 0.38–0.92). Subgroup analysis of children with intermittent asthma or viral-triggered wheezing showed reduced exacerbations with preemptive high-dose intermittent ICS compared with placebo (5 studies,  $N = 422$ ; RR 0.65; 95% CI, 0.51–0.81; NNT = 6).

**CONCLUSIONS:** There is strong evidence to support daily ICS for preventing exacerbations in preschool children with recurrent wheeze, specifically in children with persistent asthma. For preschool children with intermittent asthma or viral-triggered wheezing, there is strong evidence to support intermittent ICS for preventing exacerbations.

# PEDIATRICS®

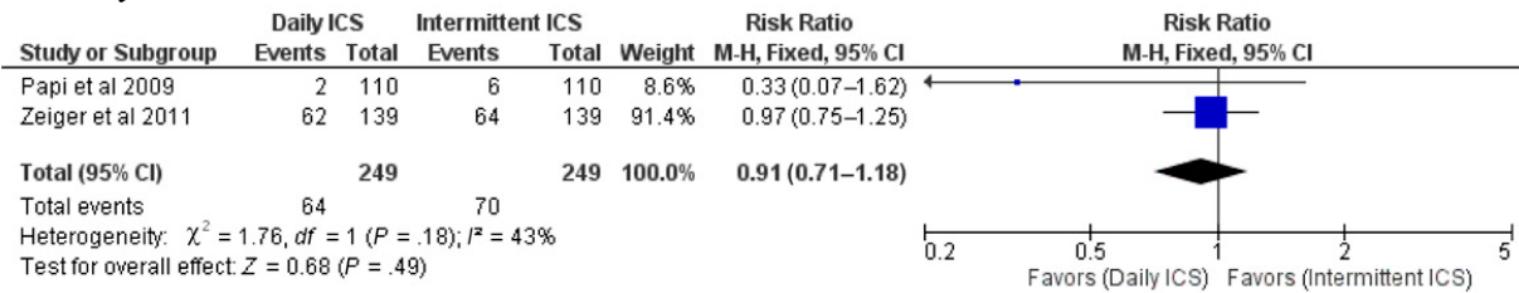
## **II. Intermittent ICS versus Placebo**



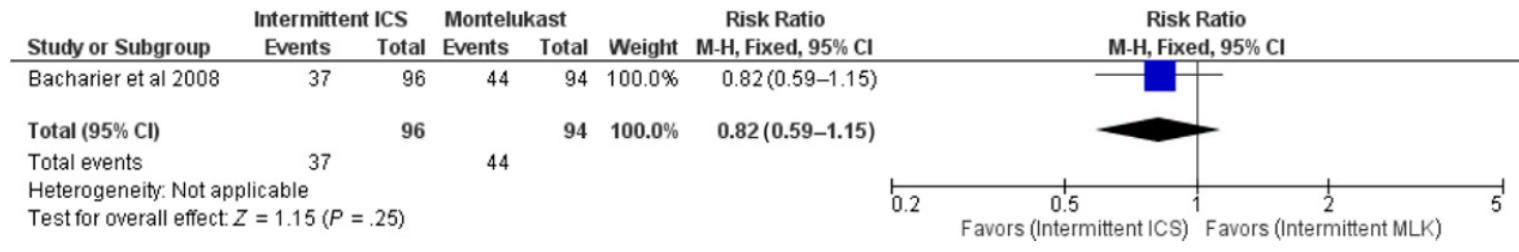
Preventing Exacerbations in Preschoolers With Recurrent Wheeze: A Meta-analysis. Pediatrics. 2016;137(6):e20154496

# Tratamiento de mantenimiento vs a PEDIATRICS

## III. Daily ICS versus Intermittent ICS



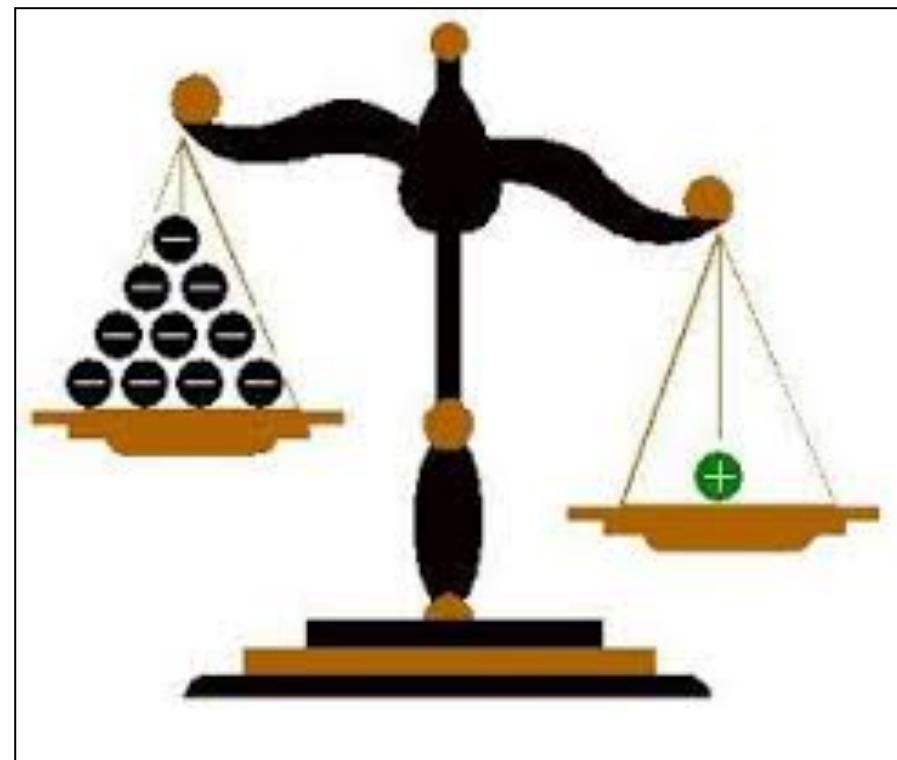
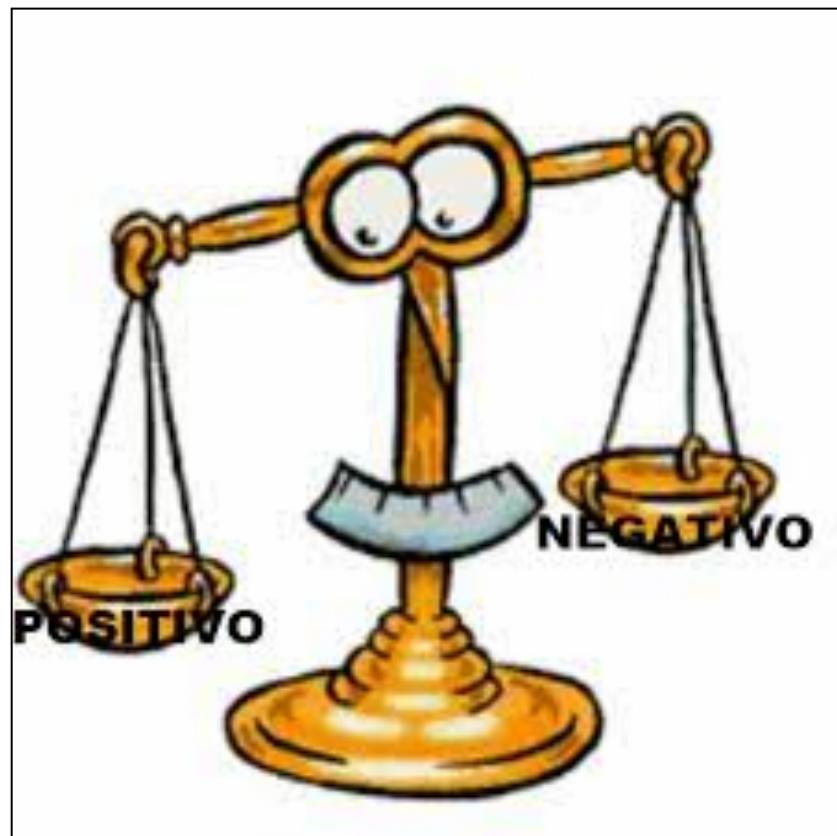
## IV. Intermittent ICS versus Intermittent Montelukast



Preventing Exacerbations in Preschoolers With Recurrent Wheeze: A Meta-analysis.  
 Pediatrics. 2016;137(6):e20154496

Cuanto más, ¿mejor?







**Cochrane**  
**Library**

**Cochrane** Database of Systematic Reviews

## **Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma in adults and children (Review)**

Kew KM, Quinn M, Quon BS, Ducharme FM

# *The* NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

MARCH 8, 2018

VOL. 378 NO. 10

## Quintupling Inhaled Glucocorticoids to Prevent Childhood Asthma Exacerbations

D.J. Jackson, L.B. Bacharier, D.T. Mauger, S. Boehmer, A. Beigelman, J.F. Chmiel, A.M. Fitzpatrick, J.M. Gaffin,

### **CONCLUSIONS**

In children with mild-to-moderate persistent asthma treated with daily inhaled glucocorticoids, quintupling the dose at the early signs of loss of asthma control did not reduce the rate of severe asthma exacerbations or improve other asthma outcomes and may be associated with diminished linear growth. (Funded by the National

ORIGINAL ARTICLE

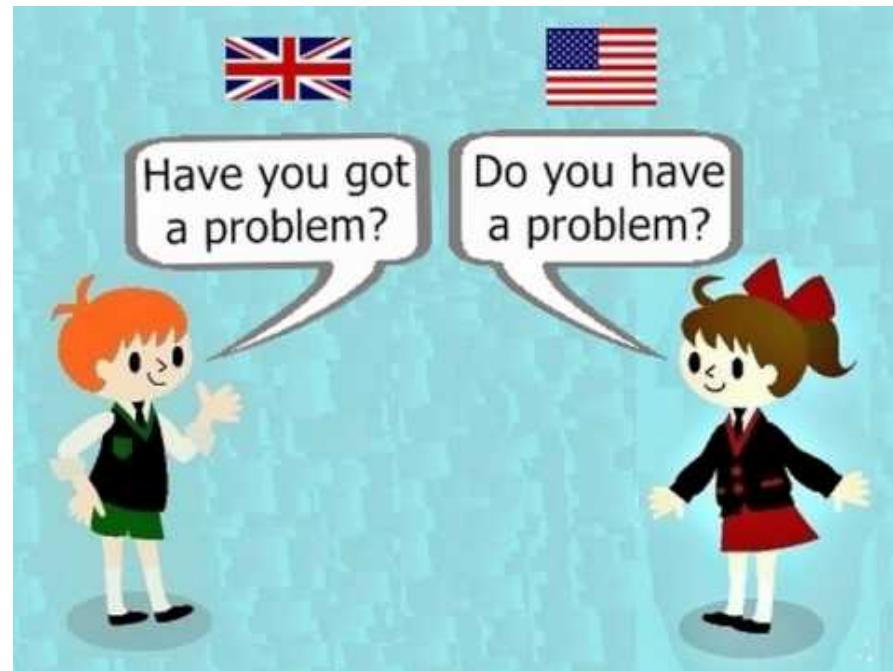
# Quadrupling Inhaled Glucocorticoid Dose to Abort Asthma Exacerbations

Tricia McKeever, Ph.D., Kevin Mortimer, Ph.D., Andrew Wilson, M.D.,

## CONCLUSIONS

In this trial involving adults and adolescents with asthma, a personalized self-management plan that included a temporary quadrupling of the dose of inhaled glucocorticoids when asthma control started to deteriorate resulted in fewer severe asthma exacerbations than a plan in which the dose was not increased. (Funded

Asi que 2 estudios similares mostrando resultados diferentes...uhmmm

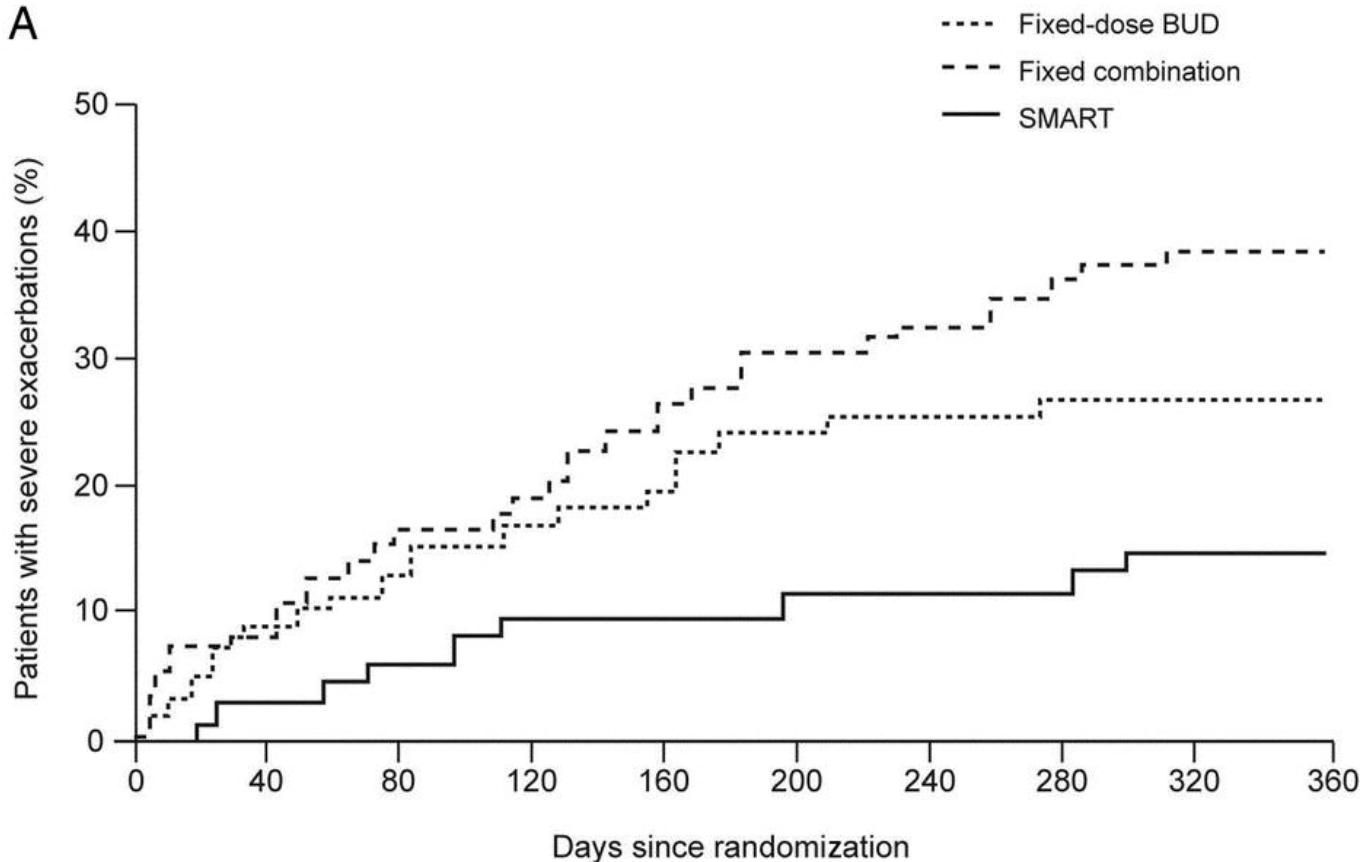


# Encuentra las 7 diferencias...

- Estudio pragmático vs ensayo clínico
- Atención primaria vs superespecializada
- 5-11 años en tratamiento con corticoides inhalados
- Adherencia !!! (95%)
- Incremento fluticasona después de varias horas de síntomas (o días)
- Dosis cada 12 horas
- Baja tasa de exacerbaciones ( mala potencia estadística)

Original Research: Asthma

## Budesonide/Formoterol Maintenance Plus Reliever Therapy: A New Strategy in Pediatric Asthma

Bisgaard, Hans MD, DMSci <sup>a</sup>   Le Roux, Pascal MD <sup>b</sup>, Bjåmer, Ditlef MD <sup>c</sup>,**A**SMART vs fixed combination  $p<0.001$ SMART vs fixed-dose BUD  $p=0.02$ Fixed combination vs fixed-dose BUD  $p=0.12$

JAMA. 2018 Apr 10;319(14):1485-1496. doi: 10.1001/jama.2018.2769.

## **Association of Inhaled Corticosteroids and Long-Acting $\beta$ -Agonists as Controller and Quick Relief Therapy With Exacerbations and Symptom Control in Persistent Asthma: A Systematic Review and Meta-analysis.**

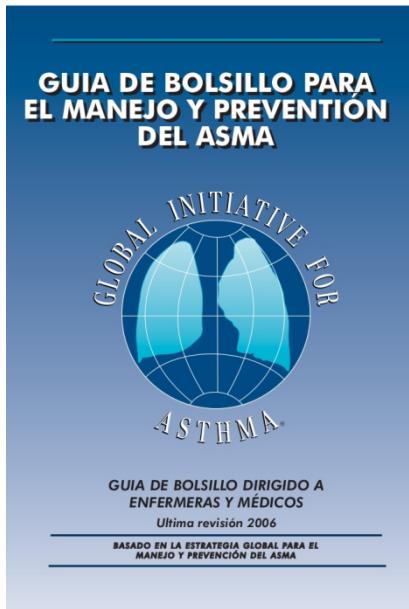
Sobieraj DM<sup>1</sup>, Weeda ER<sup>1</sup>, Nguyen E<sup>1</sup>, Coleman CI<sup>1</sup>, White CM<sup>1</sup>, Lazarus SC<sup>2</sup>, Blake KV<sup>3</sup>, Lang JE<sup>4</sup>, Baker WL<sup>1</sup>.



Respir Res. 2017 Dec 6;18(1):203. doi: 10.1186/s12931-017-0687-6.

## **Corticosteroid plus $\beta_2$ -agonist in a single inhaler as reliever therapy in intermittent and mild asthma: a proof-of-concept systematic review and meta-analysis.**

Wang G<sup>1,2,3</sup>, Zhang X<sup>1,2</sup>, Zhang HP<sup>1,2</sup>, Wang L<sup>1,2</sup>, Kang Y<sup>4</sup>, Barnes PJ<sup>5</sup>, Wang G<sup>6,7</sup>.



GUÍA ESPAÑOLA PARA EL MANEJO DEL ASMA



One size  
does **NOT**  
fit all.



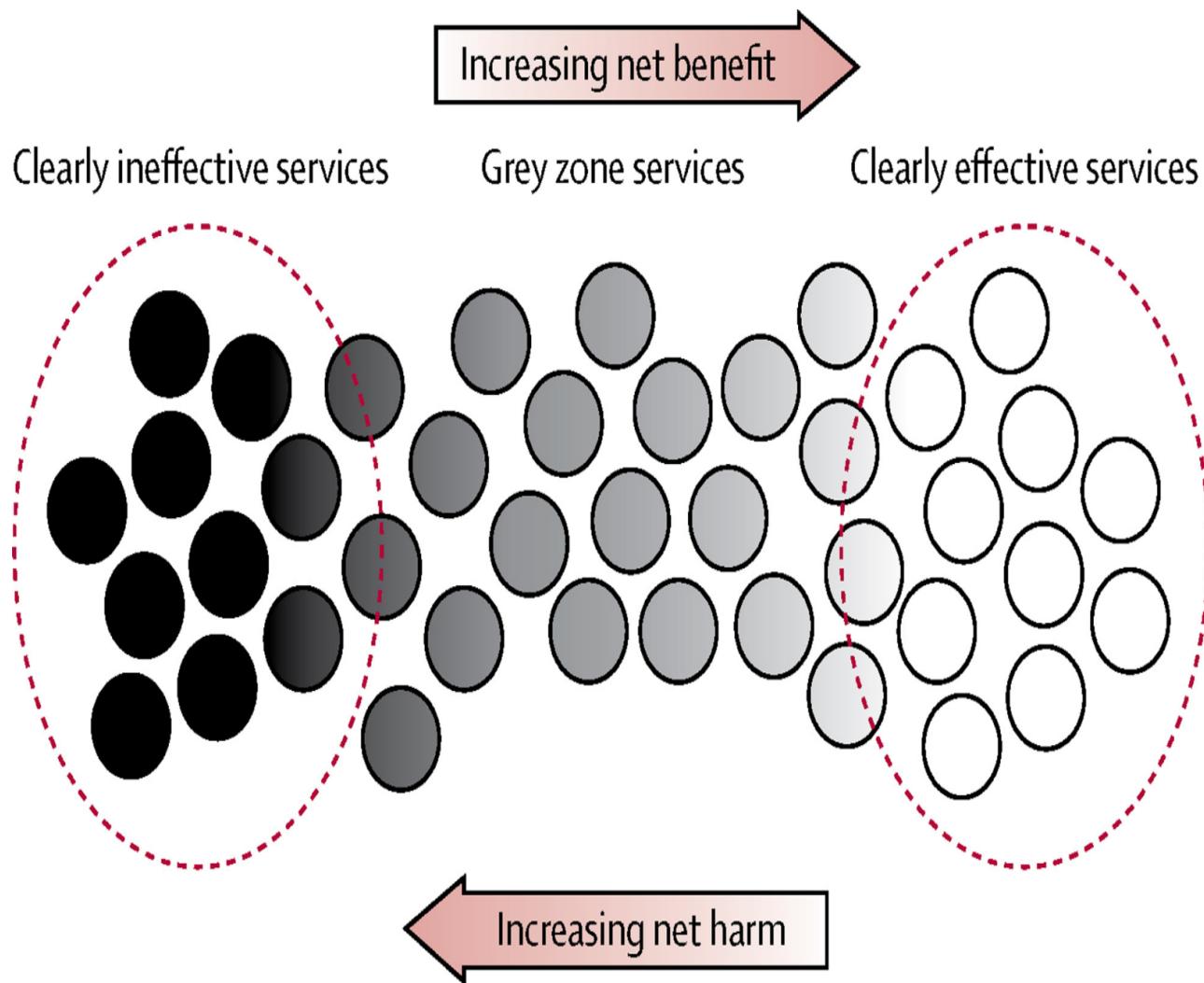


The NEW ENGLAND  
JOURNAL of MEDICINE

# Tolerating Uncertainty—The Next Medical Revolution?

Arabella L. Simpkin, B.M., B.Ch., M.M.Sc, and Richard M. Schwartzstein, M.D.

N Engl J Med 2016; 375:1713-1715







personalized  
medicine



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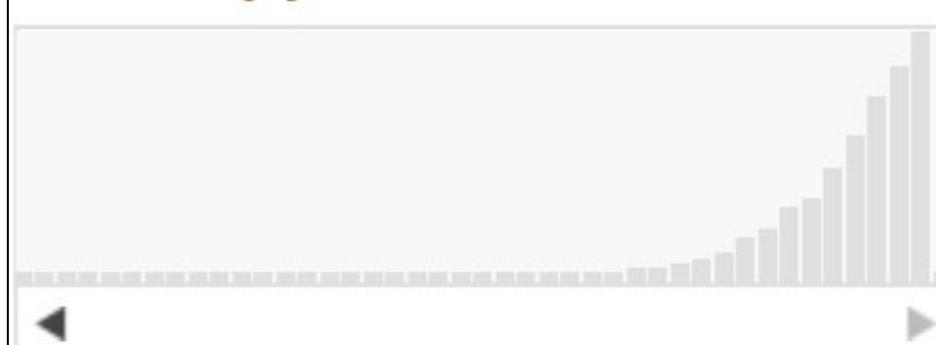
## Search results

Items: 1 to 20 of 52212

<< First < Prev Page  of 2611 [Next >](#) [Last >>](#)

- [Ginsenoside 20\(S\)-Rg3 Prevents PKM2-Targeting miR-324-5p from H19 Sponging to](#)

### Results by year





## Personalised medicine in asthma: time for action

Kian Fan Chung<sup>1,2</sup>

 @ERSpublications

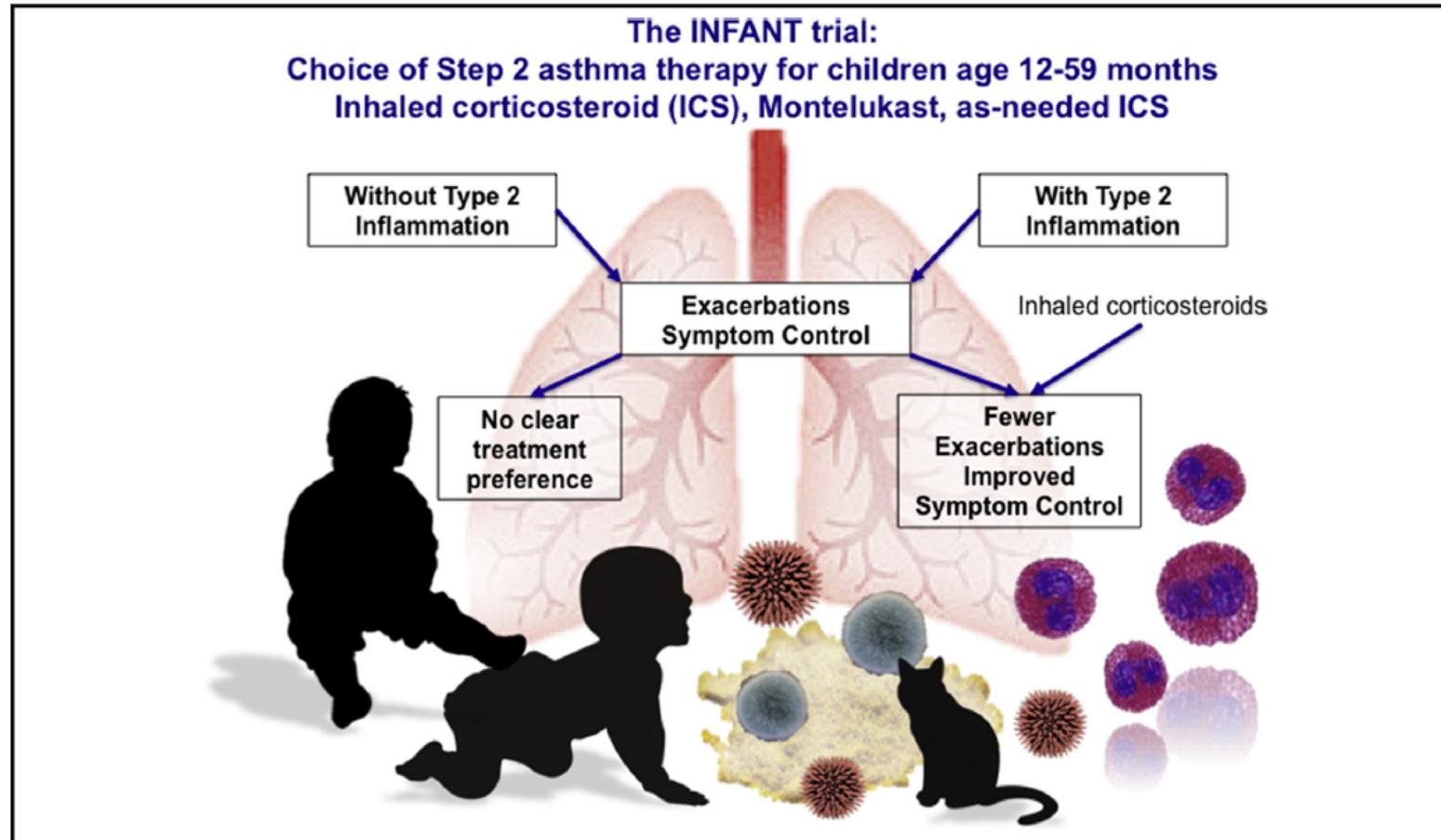
We need to start applying personalised medicine at all levels of severity of asthma  
<http://ow.ly/EoXQ30e8p24>

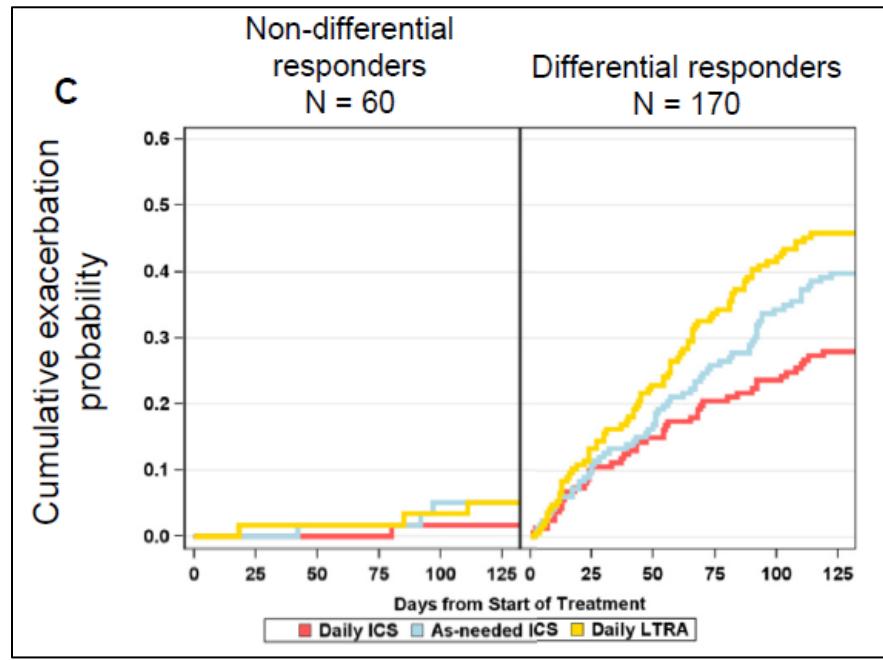
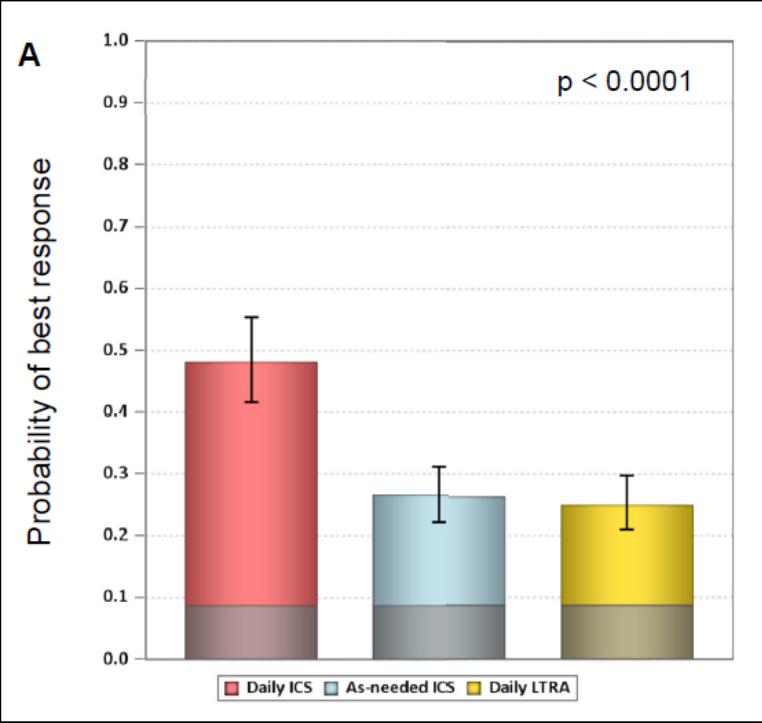


# Individualized therapy for persistent asthma in young children



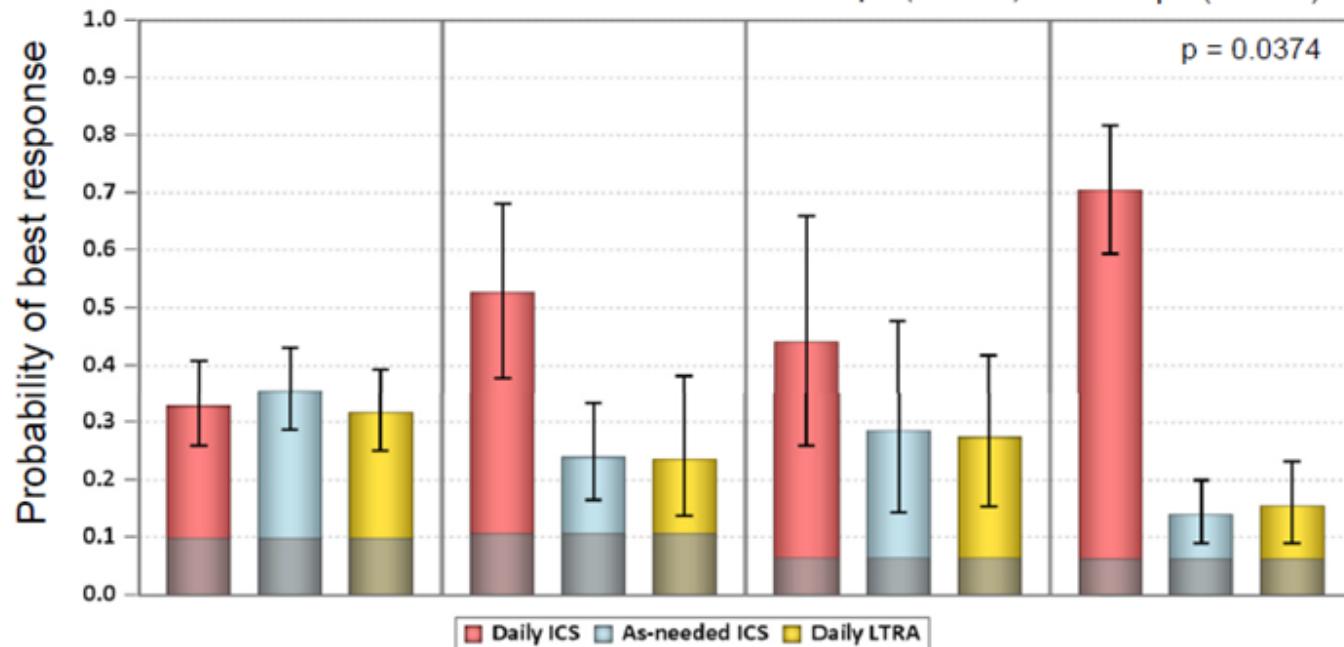
## GRAPHICAL ABSTRACT





E

Not sensitized and eosinophils <300/ $\mu$ L (N = 87)      Not sensitized and eosinophils  $\geq$ 300/ $\mu$ L (N = 28)      Sensitized and eosinophils <300/ $\mu$ L (N = 26)      Sensitized and eosinophils  $\geq$ 300/ $\mu$ L (N = 64)



## Treatment plan for the use of budesonide and fluticasone Inhalers

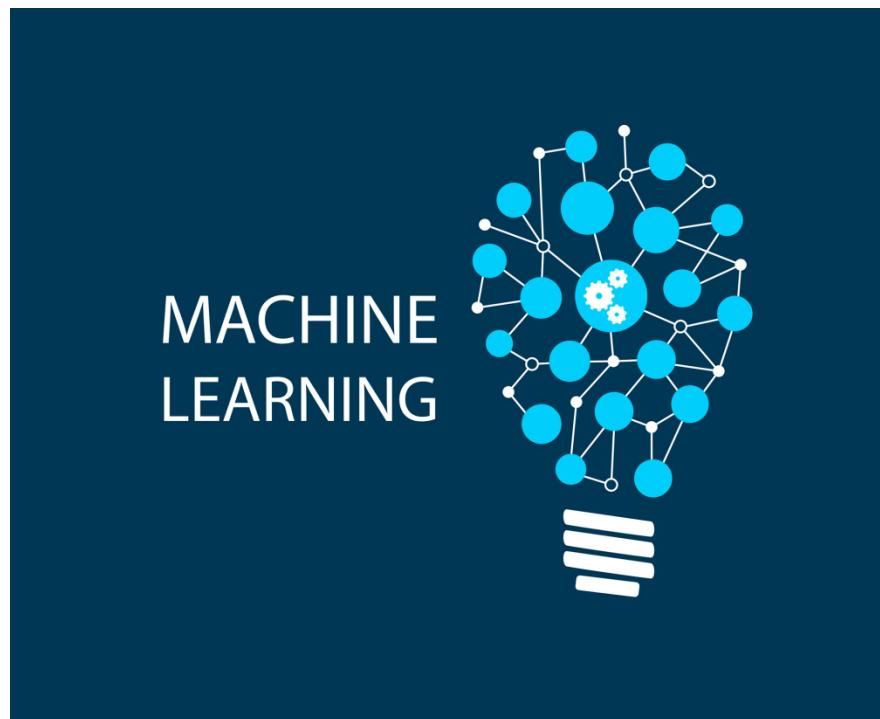
At the beginning of asthma attack or When starting preventive treatment	Administer first	Followed by			
	Terbutaline (Blue) or Ventolin (Green)	Budesonide 200 (brown) or Fluticasone 125 (orange)			
				4-day Protocol	8-day Protocol
Regular treatment (mild attack)	Enhanced treatment (severe attack)	Opens the airways	Keeps them open		
To be taken on day:	To be taken on day:	Number of puffs to be taken (One after the other)	Number of times per day	At Interval of:	
Day 1	Day 1 and 2	2	1 or 2	4	3-4 hr
Day 2	Day 3 and 4	2	1 or 2	3	3-4 hr
Day 3	Day 5 and 6	0	1 or 2	3	3-4 hr
Day 4	Day 7 and 8	0	1	2	3-4 hr
After the 4 <sup>th</sup> day (regular treatment) or 8 <sup>th</sup> day (enhanced treatment)					
O Stop treatment or continue as on day 4 or 8 for several additional days					
O Continue treatment as on day 4 or 8 for a period of ___ weeks / months					
O If no attacks occur, reduce treatment to once daily for another ___ weeks / months					
O Visit the clinic for follow-up in ___ weeks / months, or during uncontrolled attack					

# Annals of the American Thoracic Society

Home > All AnnalsATS Issues > Vol. 15, No. 1 | Jan 01, 2018

## Discovering Pediatric Asthma Phenotypes on the Basis of Response to Controller Medication Using Machine Learning

 Mindy K. Ross <sup>1</sup>,  Jinsung Yoon <sup>2</sup>, Auke van der Schaar <sup>3</sup>, and  Mihaela van der Schaar <sup>2,4</sup>



**BACK TO  
BASICS**

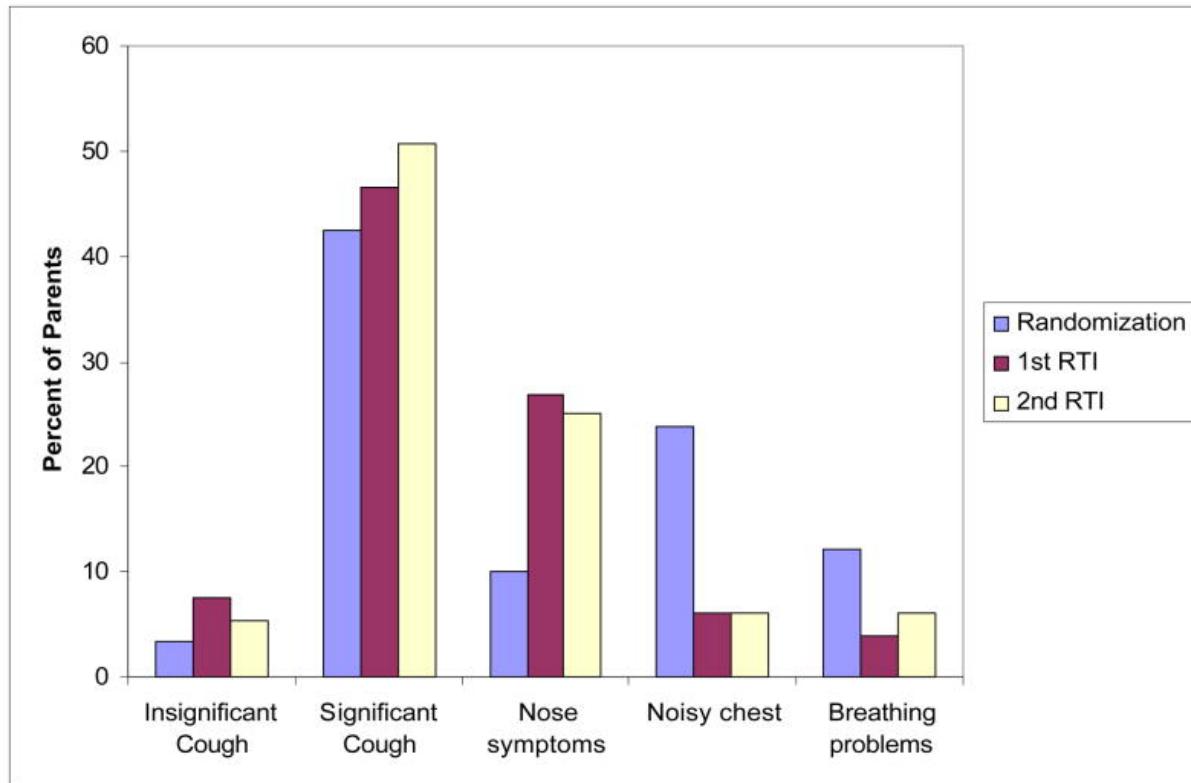
$$1+1=2$$

# Oportunidades

En las visitas de seguimiento chequear:



# El paciente comprende las causas y síntomas que preceden a la exacerbación



# Técnicas de inhalación y dispositivos

Journal of Aerosol Medicine and Pulmonary Drug Delivery, VOL. 25, NO. 1 | Original Research



## Physicians' Knowledge of Inhaler Devices and Inhalation Techniques Remains Poor in Spain

Vicente Plaza [✉](#), Joaquín Sanchis, Pere Roura, Jesús Molina, Myriam Calle, Santiago Quirce, José Luís Viejo

**Results:** A total of 1514 respondents completed the questionnaire. Dry powder inhalers (DPI) were preferred by 61.2% physicians, but only 46.1% identified "inhale deeply and forcefully" as the most significant step in the inhalation maneuver using these devices. Only 27.7% stated that they always checked the patient's inhalation technique when prescribing a new inhaler. A composite variable, *general inhaled therapy knowledge*, which pooled the correct answers related to knowledge, revealed that only 14.2% physicians had an adequate knowledge of inhaled therapy. Multivariate analysis showed that this knowledge was lowest among internal medicine and primary care physicians.



# Salbutamol solo a demanda, no regular



# Adherencia

tómatelo bien  
tómatelo en serio



## CAMPAÑA DE ADHERENCIA AL TRATAMIENTO

Entre un 20 - 50% de  
pacientes no toma su  
medicación **correctamente**



# BUDESONIDA ALDO-UNIÓN

200 mcg  
50mcg

CON INDICADOR DE DOSIS



Dosis que quedan



Cuando quedan ≈ 40 dosis, cambia de color **verde** a **rojo**  
Cuando el indicador marca “0”: Desechar el inhalador !

## Facilita

- ✓ Mayor adherencia al tratamiento
- ✓ Mejor control de la medicación disponible y del cumplimiento

## Evita

- ✓ Administración de tomas falsas (sólo de propelentes)
- ✓ Desechar el envase con parte del producto
- ✓ Repetir recetas antes de tiempo

La FDA y la IMEA lo exigen a los nuevos dispositivos para tratamiento del asma

