

# Análisis de la Inmunoterapia específica en asma infantil

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# Contenido

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- \* Generalidades de inmunoterapia
- \* SCIT para asma
  - \* Para tratamiento
  - \* Para prevención
- \* SLIT en asma
  - \* Para tratamiento
  - \* Para prevención

# ¿Qué es inmunoterapia con Alergenos?

Paciente **alérgico**:

Identificar alergeno

-HC

-EF

-Pruebas específicas



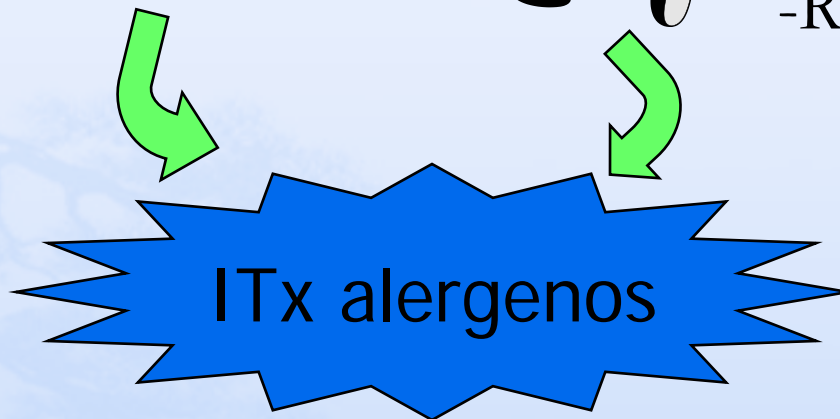
Conocimiento específico

del **Alergólogo**:

-Características alergen

-Dosis

-Reacciones X



- \* Aplicaciones seriadas: subcutáneas, sublinguales
- \* FIN: reducir síntomas y uso medicamentos, prevenir nuevas alergias y reducir alteración inmunológica.



# **Esquema de aplicación**

Inmunoterapia subcutánea y sublingual



# Esquema de aplicación SCIT

## \* Fase de aumento de dosis

- \* 1-2 inyecciones/semana
- \* Duración: 3-6 meses
- \* Mayor riesgo de reacciones sistémicas
- \* Especial: 'cluster' o 'rush' esquemas: vigilancia estrecha

## \* Fase de mantenimiento

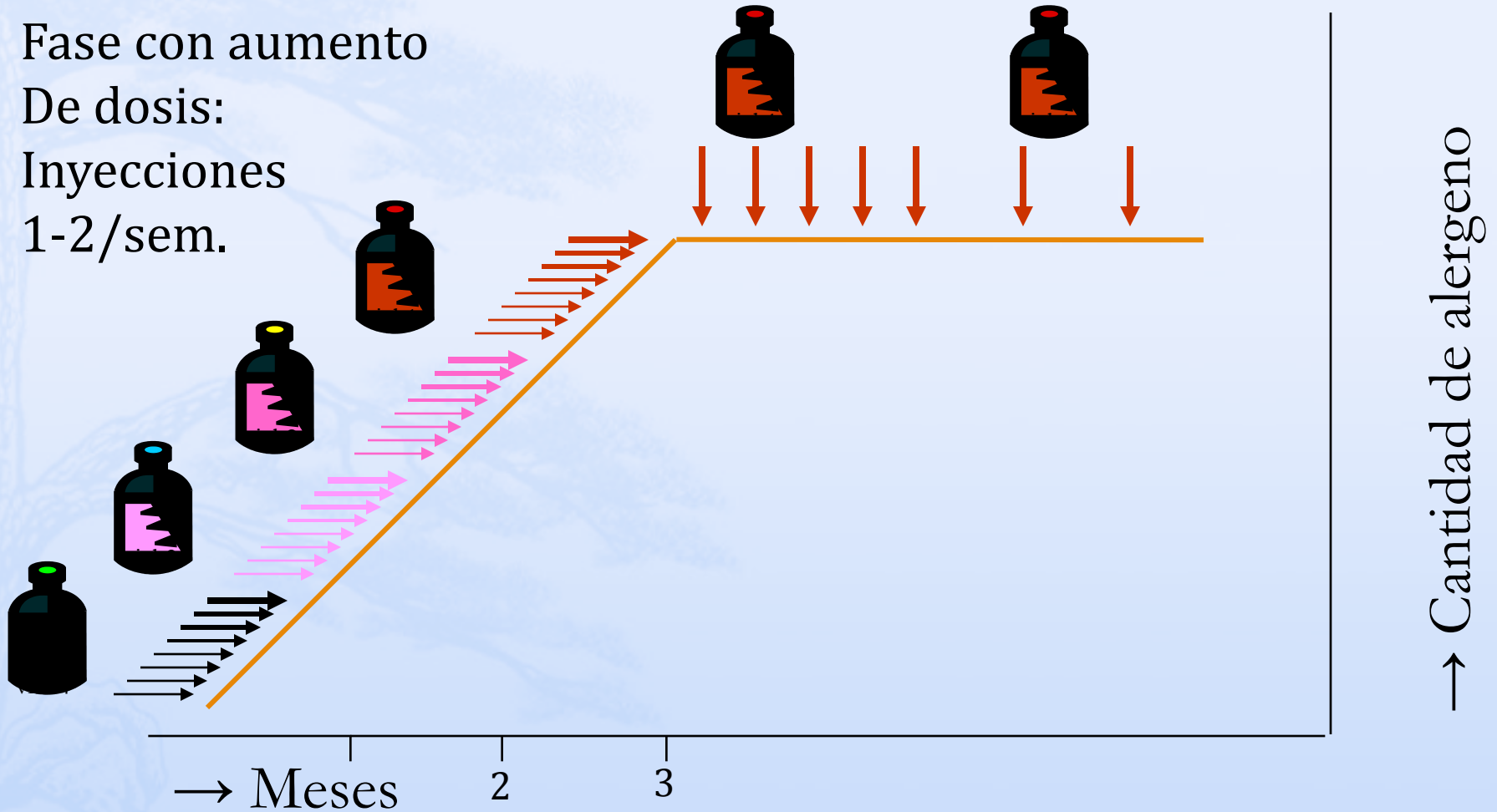
- \* Aplicación de dosis de mantenimiento: misma dosis siempre/adaptada x estación
- \* 1-2 inyecciones / mes
- \* Duración: 3-5 años
- \* Algunos presentarán recaída después de ITx exitosa (Alergia a aeroalergenos 0 a 33% en publ. recientes)



# Esquema de inmunoterapia

Fase con aumento  
De dosis:  
Inyecciones  
1-2/sem.

Fase de mant: 1-2 / mes



# Esquema de aplicación SLIT

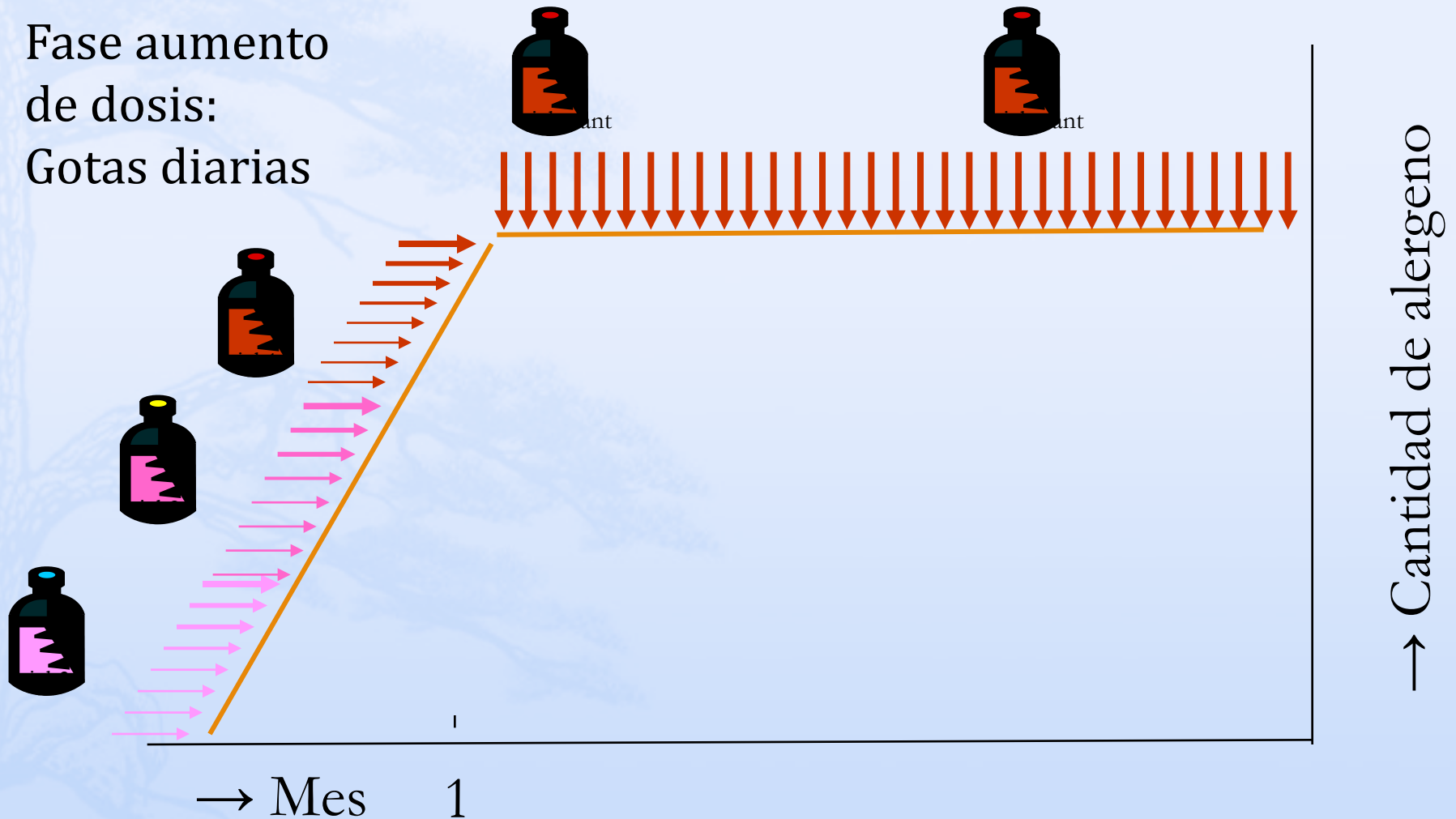
- \* Fase de aumento de dosis
  - \* 1-5 gotas diarias
  - \* Duración: 15-30 días.
- \* Fase de mantenimiento
  - \* Aplicación de dosis de mantenimiento
  - \* Diario
  - \* Duración: 3-5 años



# Esquema de SLIT

Fase aumento  
de dosis:  
Gotas diarias

Fase de mant: **diario** gotas sublinguales







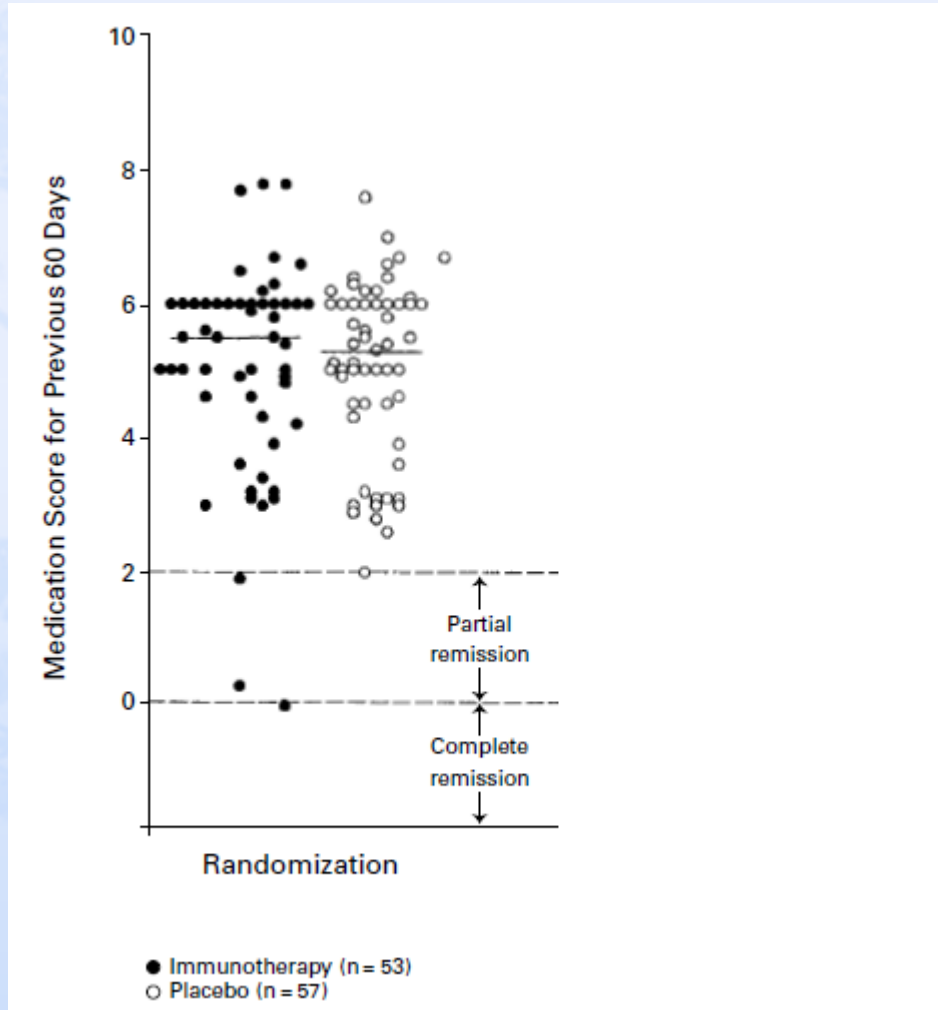
# Inmunoterapia para asma en niños

## EVIDENCIA CIENTÍFICA

# SCIT para asma

- \* Ensayo doble-ciego, placebo controlado
- \* Inmunoterapia de múltiples alérgenos durante mínimo 18 meses
- \* 121 niños alérgicos con asma moderada-a-severa, perenne (todo el año)

# SCIT para asma



# Adkinson 1997

**TABLE 2.** ALLERGEN EXTRACTS USED FOR TREATMENT AND SENSITIVITY TO ALLERGENS IN THE TWO TREATMENT GROUPS.

ALLERGEN	MAINTENANCE DOSE		SENSITIVITY		
	weight/volume	units/ml†	µg	% of children	
Dermatophagoides (dust mites)‡			6 (p I)	77	83
<i>Ambrosia elatior</i>			6 (a I)	77	77
Grass mix§			6 (p I allergen)	62	75
<i>Alternaria alternata</i>	1:2		6 (Alt a I)	64	60
<i>Cynodon dactylon</i> (Bermuda grass)	1:10			54	58
<i>Plantago lanceolata</i> (English plantain)	1:10			51	50
<i>Quercus alba</i> (white oak)	1:10			41	30
<i>Cladosporium herbarum</i>	1:2			25	27
<i>Aspergillus fumigatus</i>	1:10			8	7

The median number of extracts assigned for treatment was six (range, two to seven). Compliance with

PLACEBO (N=60)

**MIX DE 6 ALERGENOS ES DEMASIADO**

**BAJA CANTIDAD GRUPO 2**

\*Extracts were prepared and standardized as lyophilized extracts under a physician-sponsored investigational-new-drug protocol.  
 †The units were standardized units (SQ units) as defined by the manufacturer.  
 ‡The extract was a mixture of *Dermatophagoides* species obtained from whole-mite cultures.  
 §The extract was a mixture of *Phleum pratense* (timothy), *Dactylis glomerata* (orchard grass), and *Lolium perenne* (perennial ryegrass) in equal parts.

**Adkinson 1997**

**CONCLUYE:  
'INMUNOTERAPIA NO ES  
EFECTIVA PARA EL ASMA'**

# Cochrane metanálisis: SCIT para asma

- \* Ensayos randomizados, controlados: 1954-2009
- \* Sólo ensayos que enfocan en asma como patología primaria (Ensayos de RA incluidos si reportan Sx de asma separadamente)

Alergeno	Nº de ensayos
Ácaro polvo casero	42
Polen	27
Caspa de animal	10
Cladosporio	2
Látex	2
Múltiples alergenos	6
TOTAL	88

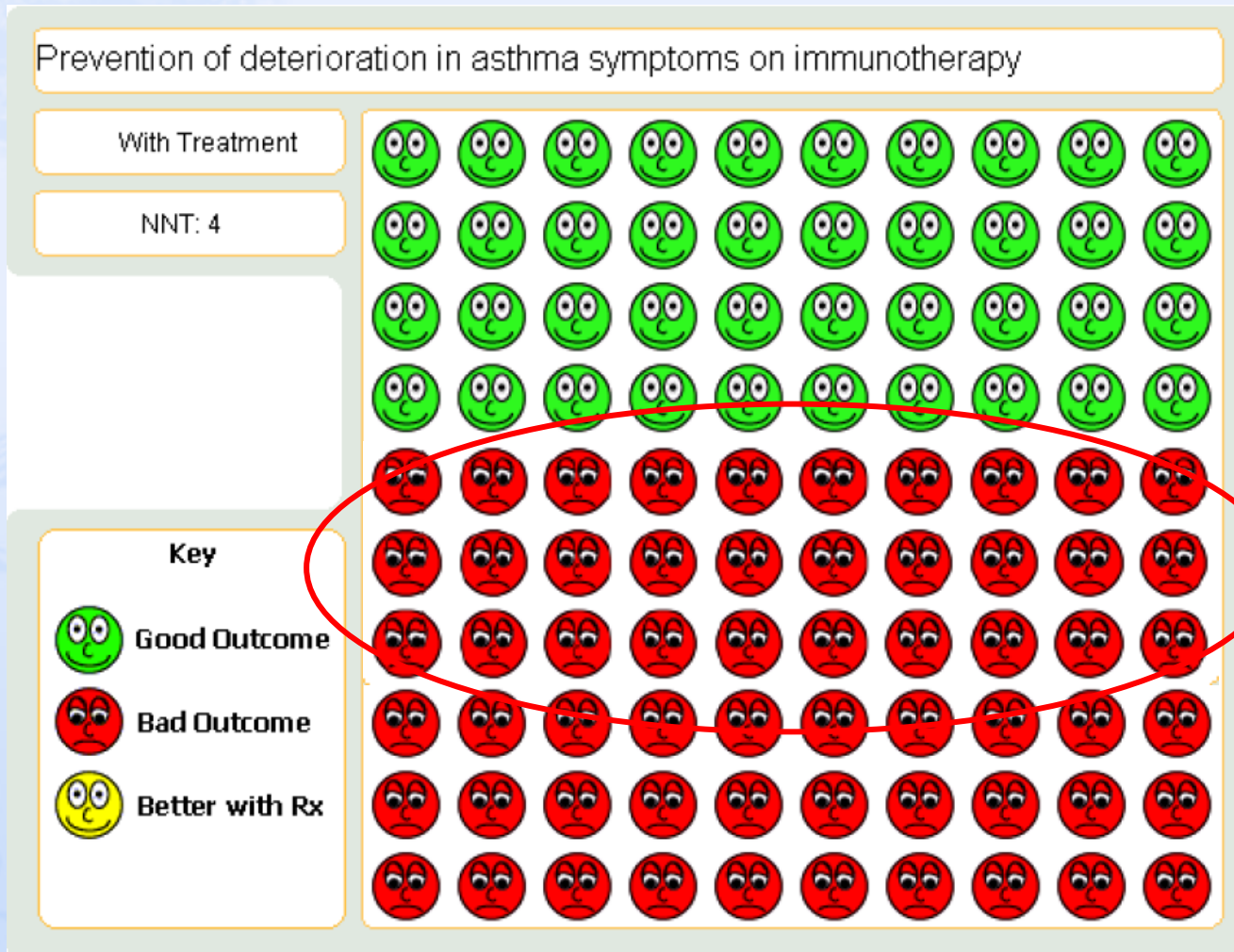
- \* Heterogenidad bastante elevada
- \* Sólo 16 ensayos describieron proceso adecuado de cegamiento

# SCIT para asma: Cochrane

- ✿ Reducción significativa de puntaje de síntomas  
(NNT = 3; 95% CI 3 a 5)
- ✿ Reducción significativa de puntaje medicación  
(NNT = 4; 95% CI 3 a 6)
- ✿ Mejora significativa de hiperreactividad específica bronquial
- ✿ No efecto consistente sobre función pulmonar
- ✿ Reacción adversa local: 1 en 16 pacientes
- ✿ Reacción adversa sistémica: 1 en 9 pacientes

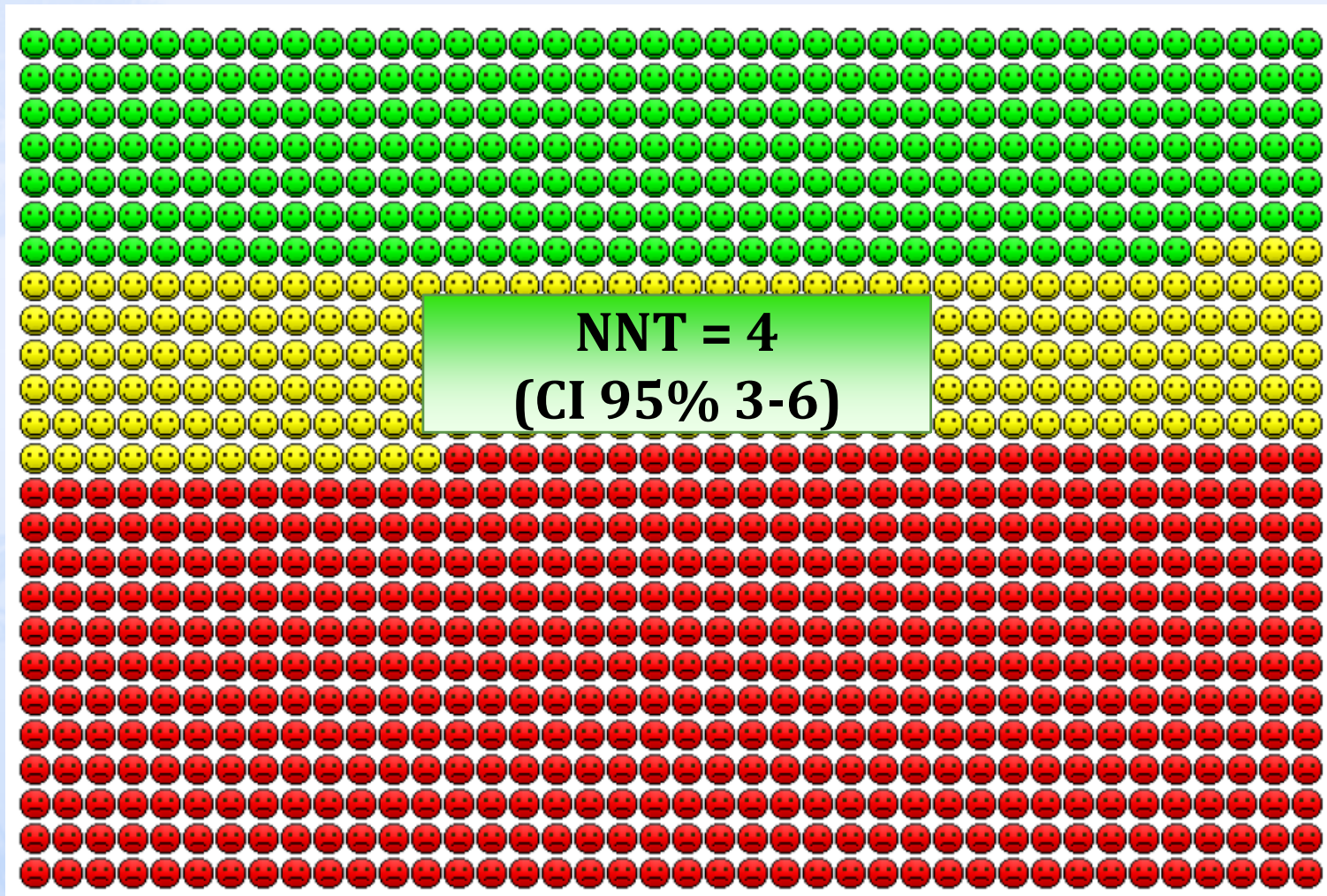
# Crisis asmática

- NNT 4 = se tienen que tratar 4 pacientes para prevenir que exacerben los síntomas en uno



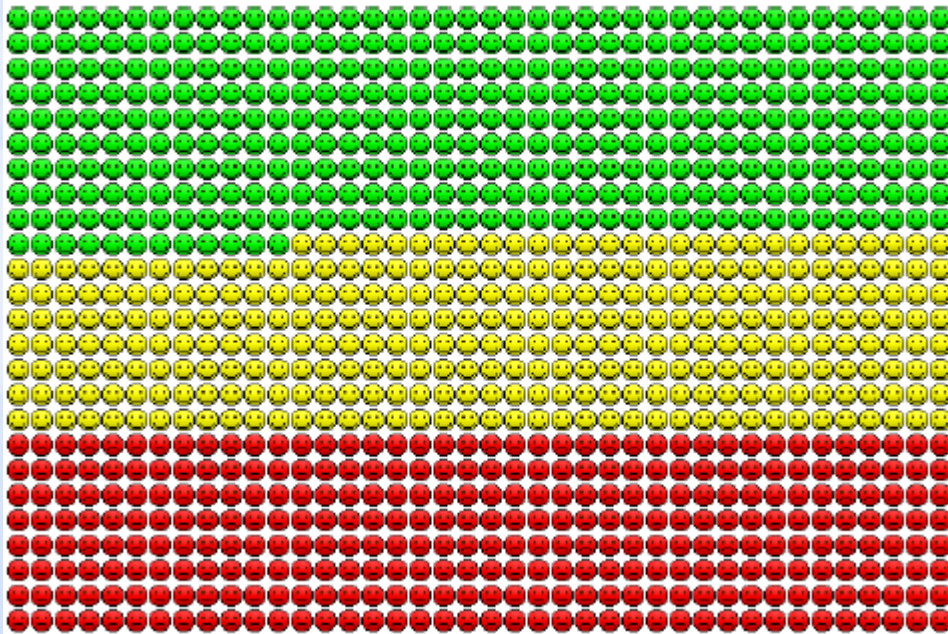


# Medicación de asma



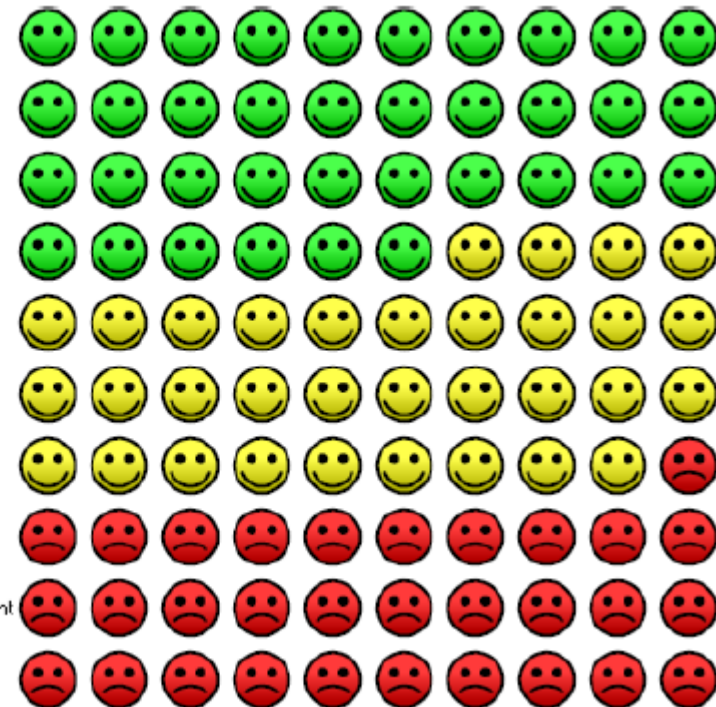
Aumento en la medicación del asma **SON** inmunoterapia

# Incremento en la hiperreactividad bronquial



Allergen specific BHR

Non specific BHR  
64% vs 31%



- Key
- Good outcome
  - Bad outcome
  - Better with treatment
  - Better with control



SCIT en niños

**EVALUACIÓN DE EVIDENCIA  
SEGÚN MÉTODO GRADE**

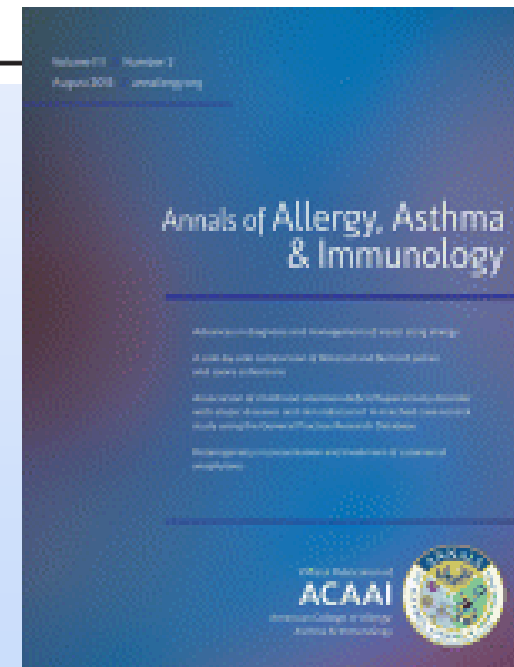
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## Review

# Evidence of effect of subcutaneous immunotherapy in children: complete and updated review from 2006 onward


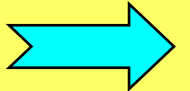
Désirée E. S. Larenas-Linnemann, MD\*\*; Dino R. Pietropaolo-Cienfuegos, MD†; and Moisés A. Calderón, MD, PhD†‡

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# GRADE

## abordaje de evaluar calidad de evidencia

Diseño estudio	Agregar/quitar puntos según características	Aumenta la calidad en caso de...	Reduce calidad en caso de...	Cálculo final de la calidad de evidencia	Calidad de evidencia
Randomizado (4)		<b>Efecto amplio***</b> 1. Large 2. Very large	<b>Limitaciones del estudio*</b> 1. Serias 2. Muy serias		Alta(4) ●●●●
Observacional (2)		<b>Dosis-respuesta</b> 1. Evidencia de un gradiente	<b>Inconsistencia</b> 1. Seria 2. Muy seria		Moderada (3) ●●●○
		<b>Confusores ...</b> 1. Reducirán un efecto demostrado, o 2. Sugirirán un efecto espurio, cuando resultados no muestran efecto	<b>Los datos son indirectos</b> 1. Seriamente 2. Muy seriamente		Baja (2) ●●○○
			<b>Imprecisión**</b> 1. Seria 2. Muy seria		Muy baja (1) ●○○○
			<b>Bias de publicación</b> 1. Probable 2. Muy probable		

# SCIT para asma pediátrico: 2006-2011

## Ácaros de polvo casero

Statistically significant difference for active-placebo/control groups	No effect for active-placebo/control groups	Evidence <sup>a</sup>
<u>Prevention asthma</u> Inal et al, 2007 (G0)	No studies without effect	No evidence
<u>Asthma symptoms</u> Wang et al, 2006 (G4) Tsai et al, 2010 (G4) Cevit et al, 2007 (G0) Zang et al, 2010 (retrospective, G?) Rosewich et al, 2010 (G0) Ibero et al, 2006 (G3): improved pre-post only in active Kim et al, 2009 (G0): improved pre-post only in active Adjuk et al, 2008 (G1): improved pre-post in active Majak et al, 2010 (G3): improved pre-post in both active and placebo as all on allergen specific IT]	Ibero et al, 2006 (G3): improved symptoms, but NS active-control Reha and Ebru, 2007 (G0): 5 years after specific IT both groups improved	Yes: ●●●●
<u>Asthma medication</u> Wang et al, 2006 (G4) Tsai et al, 2010 (G4) Zielen et al, 2010 (G4) Zang et al, 2010 (retrospective, G?) Rosewich et al, 2010 (G0) Majak et al, 2009 (G4): improved pre-post in both active and placebo as all on allergen specific IT] Majak et al, 2010 (G3): improved pre-post in both active and placebo as all on allergen specific IT]	Cevit et al, 2007 (G0): NS active-control Ibero et al, 2006 (G3): much improved medication, but NS active-control	Yes: ●●●●
<u>Reduction frequency of emergency department visits</u> Tsai et al, 2010 (G4) Chen et al, 2009 (G1)	No studies without effect	Yes: ●●●●

# SCIT para asma pediátrico 2006-11: Prueba de función pulmonar

## Ácaros de polvo casero (cont)

Statistically significant difference for active-placebo/control groups

No effect for active-placebo/control groups

Evidence<sup>a</sup>

### Pulmonary function tests

Zielen et al, 2010 (G4): PEF

Chen et al, 2009 (1): FEV<sub>1</sub>, PEF

Reha and Ebru, 2007 (G0): 5 years after specific IT: FVC, FEV<sub>1</sub>, FEF<sub>25%-72%</sub>

Zang et al, 2010 (retrospective, G?): PEF pre-post

Adjuk et al, 2008 (G1): improved pre-post in active: FEV<sub>1</sub>, PEF

### Metacholine/specific bronchial challenge

Ibero et al, 2006 (G4): specific

Chen et al, 2009 (G1): FVC

Wang et al, 2006 (G4): PEF: improved pre-post in both active and placebo as all taking stable-dose ICS

Majak et al, 2010 (G3): VEF1: improved pre-post in both active and placebo, but specific IT dose reduction ICS

Zielen et al, 2010 (G4): methacholine improved in both groups, but active more ICS reduction.

Wang et al, 2006 (G4): as all taking stable-dose ICS

Cevit et al, 2007 (G0): specific, active and controls improve

Yes: when specific IT and control on ICS: for PEF

●●●○

for VEF1 ●○○○

After 5 years FEV<sub>1</sub>: ○○○○

No improvement FVC:

●○○○

Yes:

Specific ●●●●

No,<sup>b</sup> when both on ICS specific/methacholine:

●●●●

# SCIT para asma pediátrico 2006-11: hongos

## Hongos

Statistically significant difference for active-placebo/control groups	No effect for active-placebo/control groups	Evidence <sup>a</sup>
<u>Prevention asthma</u> Not studied	Not studied	No evidence
<u>Asthma symptoms</u> Tabar et al, 2008 (G2) PEF: active pre-post: Tabar et al, 2008 (G2) Active pre-post: Zapatero et al, 2011 (G1)	No studies without effect	Yes: ●●○○
<u>Asthma medication</u> Active pre-post: Zapatero et al, 2011 (G1)	No studies without effect	Yes: ●○○○ (only intragroup)
<u>Methacholine/specific</u> Not studied	Not studied	No evidence



# SCIT para asma pediátrico 2006-11: alergia a pólenes

## Pólenes

Statistically significant difference for  
active-placebo/control groups

No effect for  
active-placebo/control groups

Evidence<sup>a</sup>

Prevention asthma

Jacobsen et al, 2007 (G3-4): long term +2 years, +7 years<sup>b</sup>

Asthma symptoms

Keskin et al, 2006 (G1)

Eng et al, 2006 (G0): long term: +6 years, +12 years ( $P = .08$ )

Metacholine/specific bronchial provocation

Roberts et al, 2006 (G4): specific

No studies without effect

No studies without effect

Keskin et al, 2006 (G1): methacholine  
Jacobsen et al, 2007 (G3-4): meta-  
choline, long term +7 years<sup>a</sup>

Yes:  
7 years after ●●●○

Yes: ●○○○  
12 years after ○○○○

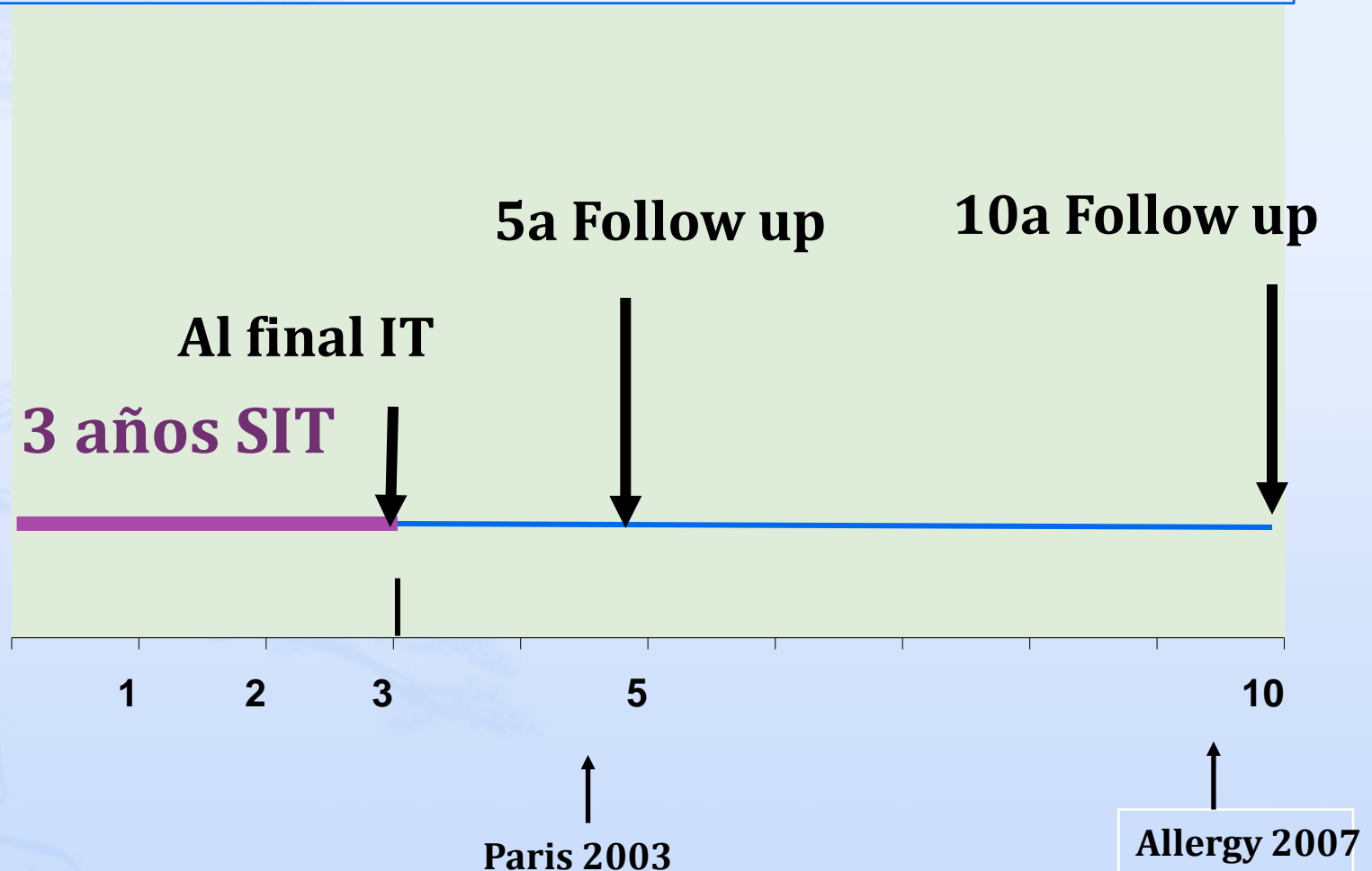
Yes, specific: ●●●●  
No, methacholine: ●○○○  
No, methacholine 7 years  
after: ●●●○

# SCIT para rinitis alérgica, previene el asma?

- \* Johnston 1968
- \* Cools 2000
  - \* 5 años
- \* Jacobson: Preventive Asthma Treatment (PAT)
  - \* 10 años después de una inmunoterapia durante 3 años
- \* Eng
  - \* 12 años después de tratamiento con SCIT

# El estudio PAT: ¿SCIT previene asma?

Randomizado, controlado, investigadores blindados, asma bien definida

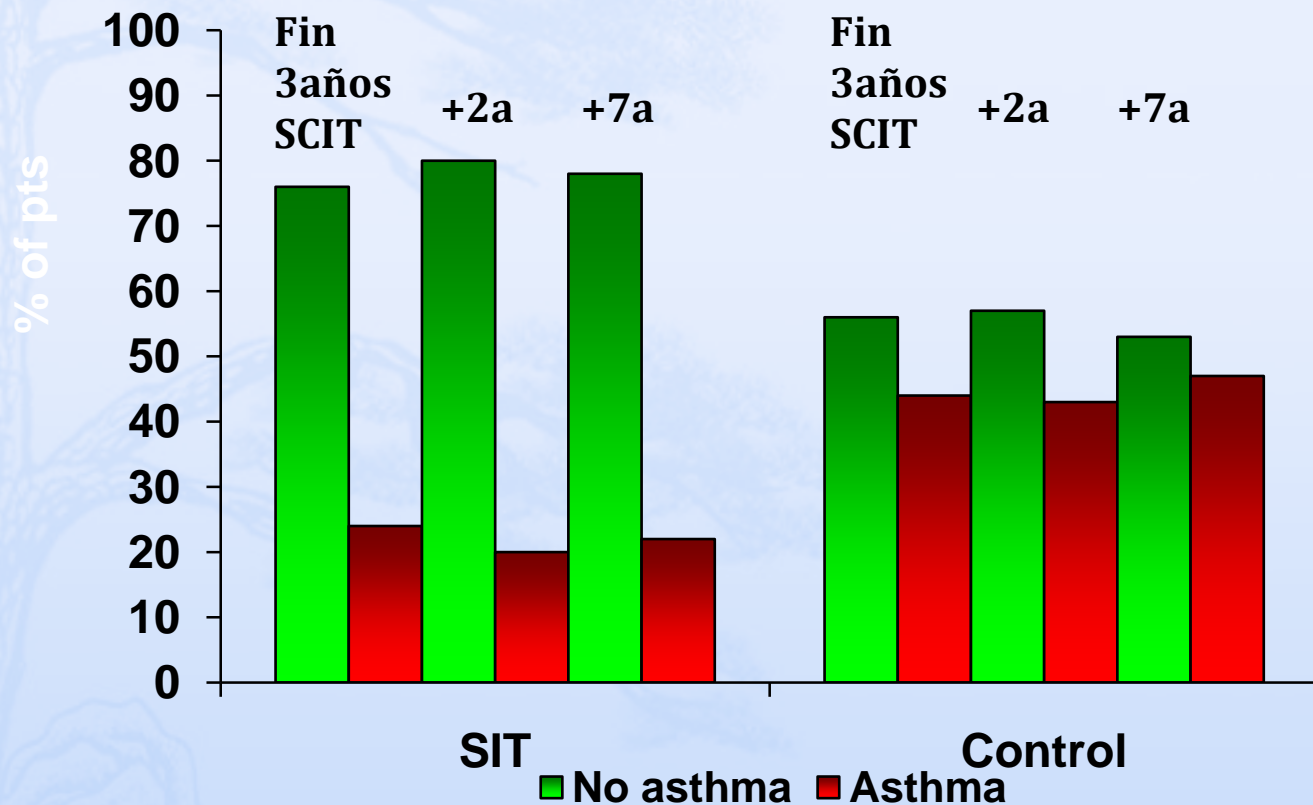


# Estudio PAT 3 años SCIT, seguimiento

## Prevención de asma en niños con Rinitis

Dosis mensual:  
 100,000 SQ-U  
 20mcg Phl p 5 o  
 12mcg Bet v 1

N=151/142/109 (Pacientes sin asma al inicio del estudio)



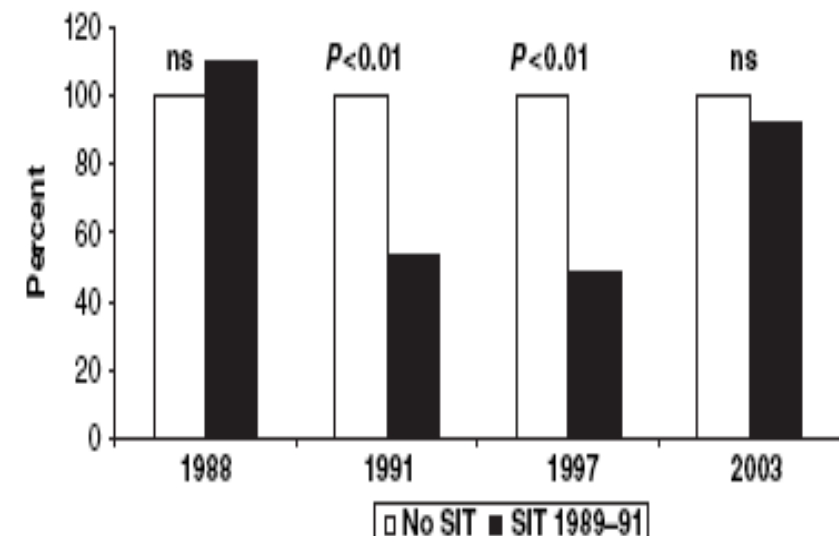
Odds-ratio:  
 3 años = 2.52  
 (1.3 - 5.1)

5 años = 2.68  
 (1.3 - 5.7)

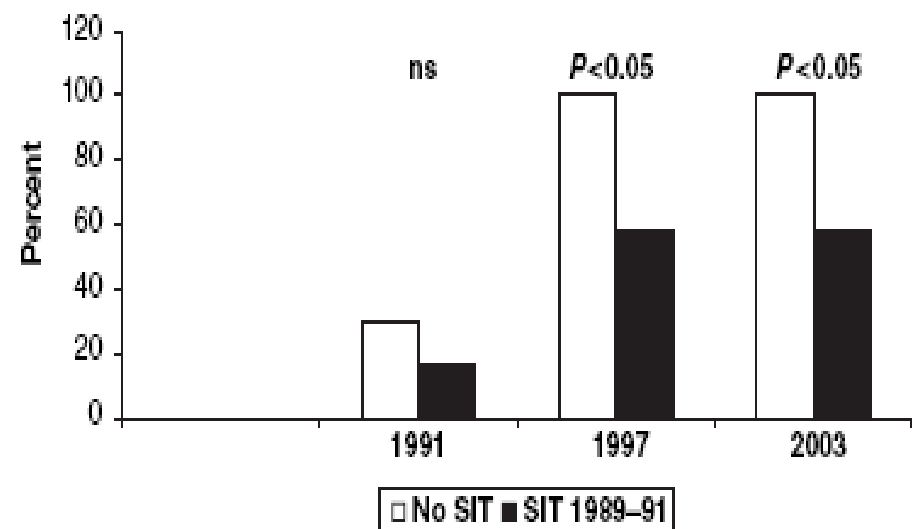
10 años = 3.19  
 (1.3 - 8.1)

# 12 años seguimiento después de discontinuar SCIT pre-estacional con polen de gramíneas en niños

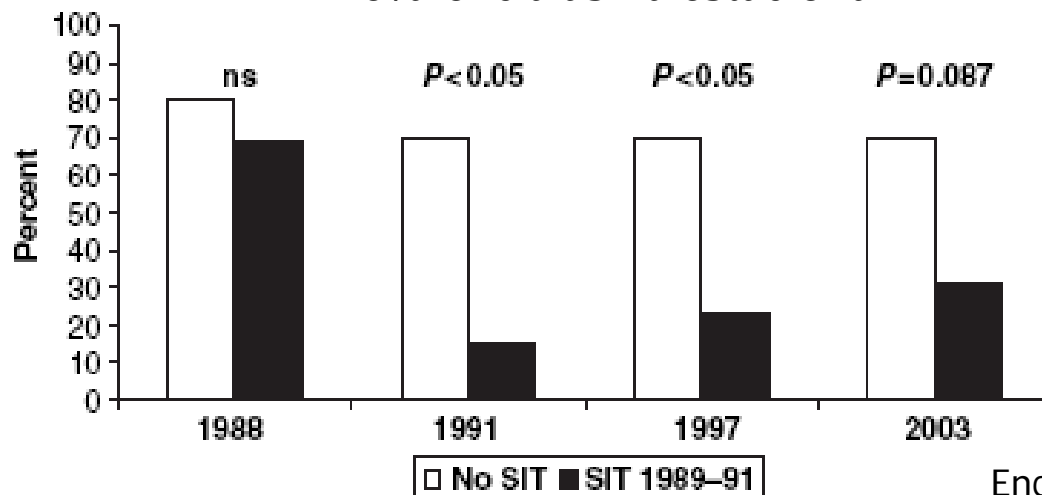
A Reactividad en SPT a polen césped



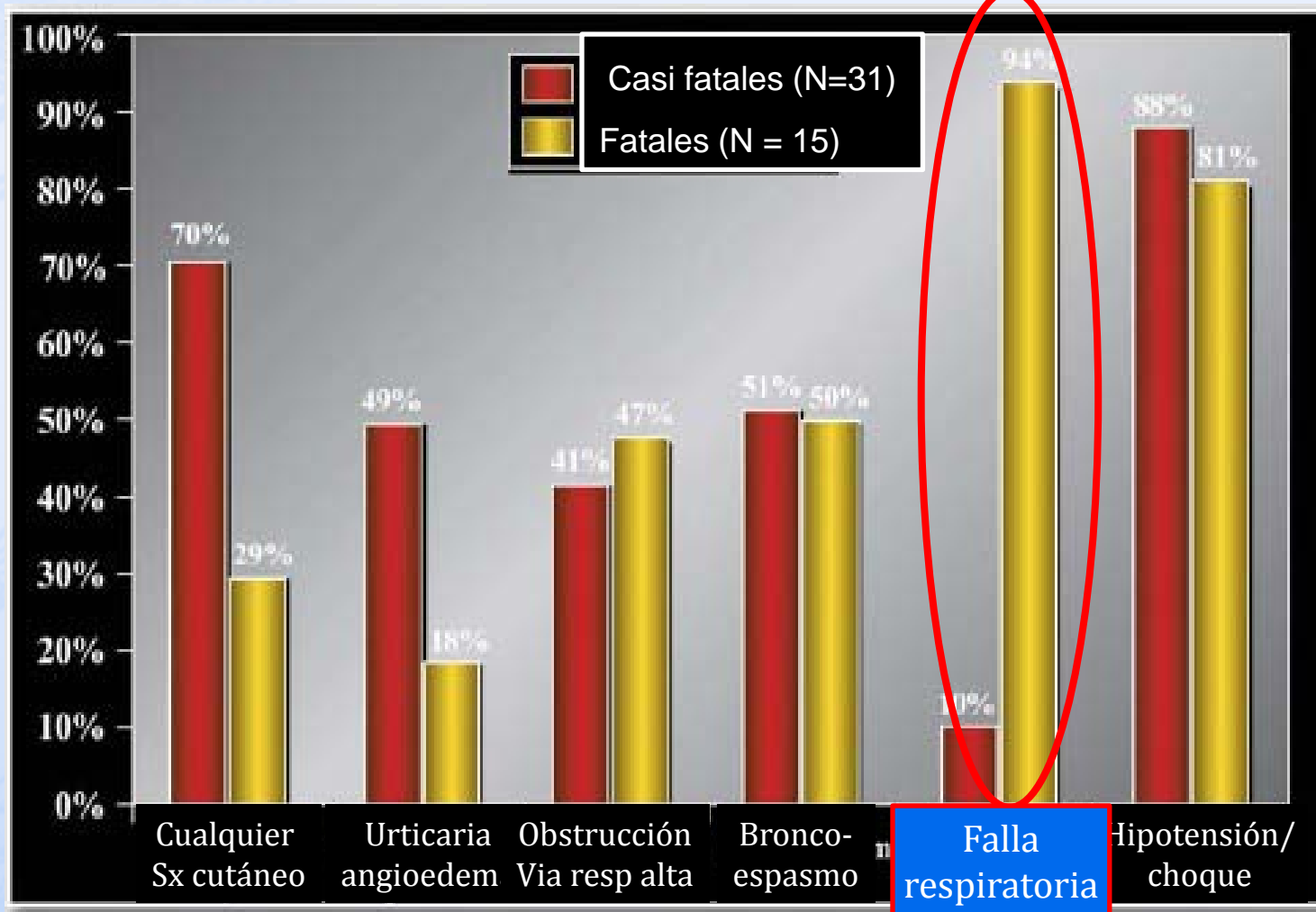
B Desarrollo nuevas sensibilizaciones



C Prevalencia asma estacional

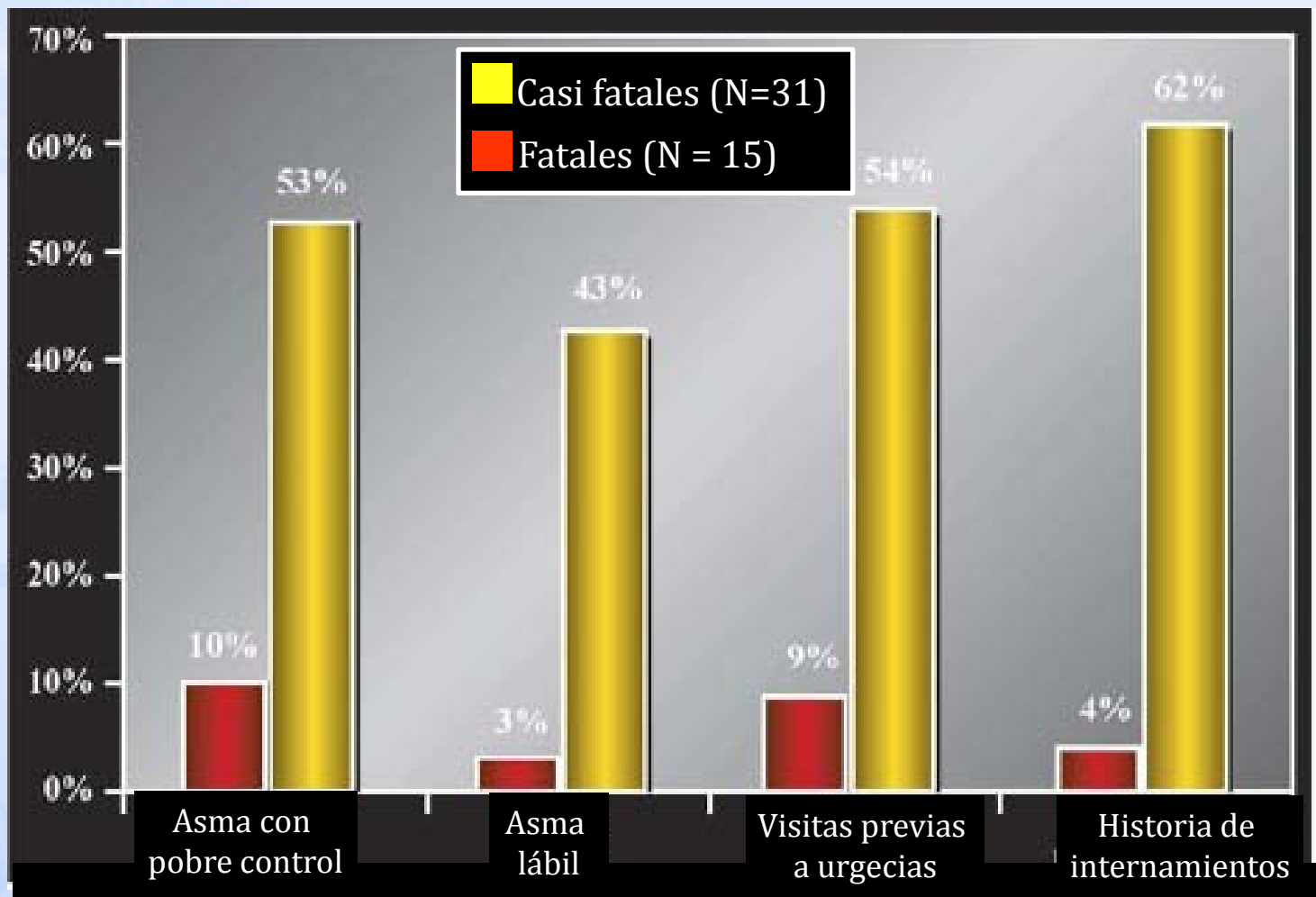


# Comparación de síntomas: Reacciones fatales y casi-fatales



Amin HS, Liss GM, Bernstein DI. Evaluation of near-fatal reactions to allergen immunotherapy injections. J Allergy Clin Immunol 2006; 117:169-75

# Comparación de síntomas: Reacciones fatales y casi-fatales



Amin HS, Liss GM, Bernstein DI. Evaluation of near-fatal reactions to allergen immunotherapy injections. *J Allergy Clin Immunol* 2006; 117:169-75



# SLIT PARA ASMA





ELSEVIER

Contents lists available at [SciVerse ScienceDirect](http://SciVerse.ScienceDirect.com)



Review Article

## Pediatric sublingual immunotherapy efficacy: evidence analysis, 2009-2012

Désirée Larenas-Linnemann, MD<sup>\*</sup>; Michael Blaiss, MD<sup>†</sup>; Hugo P. Van Bever, MD, PhD<sup>‡</sup>;  
Enrico Compalati, MD, PhD<sup>§</sup>; and Carlos E. Baena-Cagnani, MD<sup>¶,||</sup>

<sup>\*</sup>Hospital Médica Sur, Mexico City, Mexico

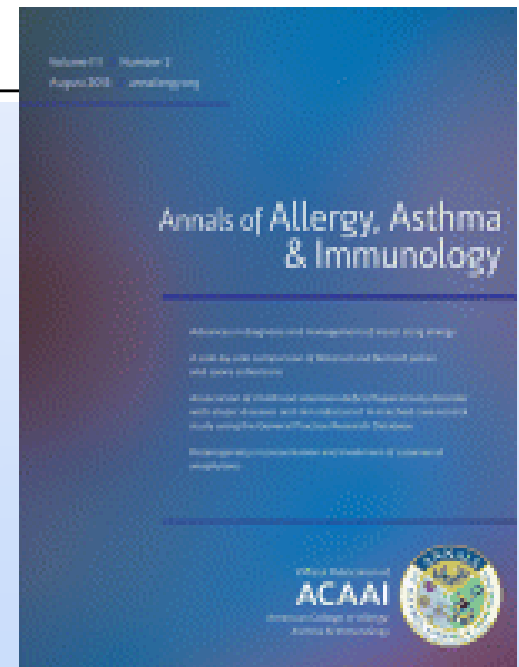
<sup>†</sup>Departments of Pediatrics and Medicine, University of Tennessee Health Science, Memphis, Tennessee

<sup>‡</sup>National University Singapore, Singapore

<sup>§</sup>Allergy & Respiratory Diseases Clinic, Department of Internal Medicine, University of Genoa, Genoa, Italy

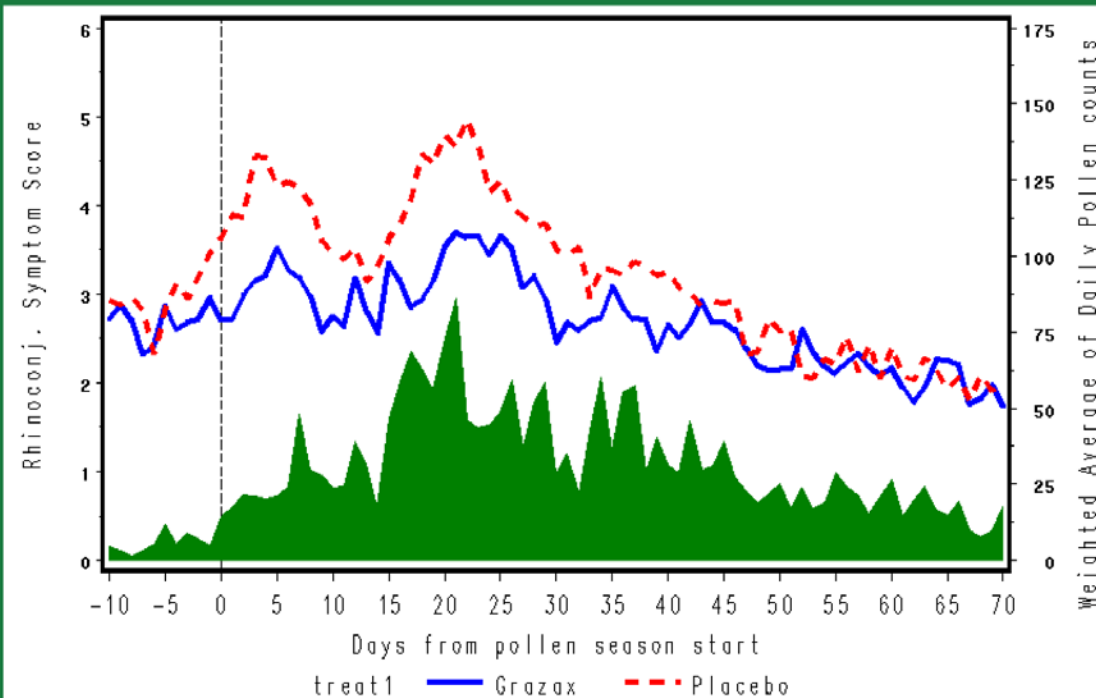
<sup>¶</sup>Research Centre in Respiratory Medicine, Faculty of Medicine, Catholic University, Cordoba, Argentina

<sup>||</sup>School of Specialization, Respiratory Medicine, University of Genoa, Genoa, Italy



# Grazax en niños

Mean Rhinoconjunctivitis Symptom Score and Weighted Mean Grass Pollen Counts



126 SLIT /127 placebo  
5-16 años.

Pre-coseason

Grazax 1 tabl. SL diario

Mejora RA:  $p= 0.0195$

Medicación:  $p= 0.0156$

Asma mejoría:  $p= 0.034$

# GRADE ensayos SLIT en niños

Author, year Some study details	Design (Starting score)	Large effect	Confound Annulated*	Dose-response gradient	TOTAL (+)	Limitations in design / execution	Inconsistent results	Indirectness of evidence	Imprecision of results	Publ bias	TOTAL (-)	Quality of evidence
<b>Wahn 2009 (1)</b> SAR (21% mild asthma) 131 SLIT, 135 Plac 4-17y; pre-coseason 25mcg grp 5 grass tabl/d	DBPC (4)	X	X	X	0	X	X	X	X	X	0	Rhinitis reduction: High
<b>Bufe 2009 (2)</b> SAR (42% mild asthma) 114 SLIT, 120 Placebo, 5-16yrs, Pre-coseason 15mcg Phl p 5 tablet/day	DBPC (4) Rhinitis DBPC (4) Asthma	X	X	X	0	X	X	X	X	X	0	Rhinitis reduction: High
<b>Rdriguez-Santos '08 (3)</b> Asthma and/or rhinitis HDM 69, placebo 69; 2-5 years; for 2 years Intermediate dose daily	RCT (4)	RR emergency visit 0.39; Corticoster. use 0.37	X	X	+1	No concealment of allocation, no blinding	X	x	No symptoms analyzed	No report other med	-3	Asthma reduction: Low Rhinitis reduction: Low
<b>Stelmach 2009 (4)</b> Asthma mild-moderate persistent 20 SLIT, 15 Placebo 6-17y; pre-coseason x 2y 10mcg grp 5 grass drops daily	DBPC (4)	+1	X	X	+1	40% drop-out placebo group. Sympt/med adjusted for pollen count	X	X	No pollen count reported	X	-3	Asthma reduction: Low
<b>Agostinis 2008 (5)</b> Safety, mono- vs multiple pollen SLIT 179 single pollen SLIT, 254 multiple 3-18 yrs; during 6-24 mo Various manufacturers, dosing varied	Post-market (2)	X	X	X	0	No blinding of outcome	X	X	X	X	-1	Safety data: Very low

1. Wahn U, et al. J Allergy Clin Immunol. 2009 Jan;123(1):160-6
2. Bufo A, et al. J Allergy Clin Immunol. 2009 Jan;123(1):167-73
3. Rodriguez-Santos O. Revista Alergia México. 2008;55(2):71-5
4. Stelmach I, et al. Clin Exp Allergy. 2009 Mar;39(3):401-8.
5. Agostinis F, et al. Allergy. 2008 Dec;63(12):1637-9.

# GRADE classification

## pediatric SLIT trials: Asthma

Asthma trials												Total
Stelmach 2009(15) Asthma mild-moderate persistent SLIT 20, Placebo 15; 6-17y pre-coseasonal for 2 years 10mcg grp 5 grass drops daily	DBPC (4)	+1	X	X	+1	40% drop-out in placebo group. Symptoms/med adjusted for pollen count	x	x	No pollen count reported	x	-3	Low
Rodriguez-Santos 2008(16) Asthma and/or rinitis SLIT HDM 69, placebo 69; 2-5 years Intermediate dose daily for 2 years	RCT (4)	Relative Risk emergency visit 0.39; CS use 0.37	x	X	+1	No concealment of allocation, no blinding	x	x	No symptoms analyzed	No report other med	-3	Low

Author, year Some study details	Design (Starting score)	Large effect	Confound annulated *	Dose- response gradient	TOTAL (+)	Limitations in design / execution	Inconsistenc y of results	Indirectness of evidence	Impre- cision of results	Publ bias	TOTAL (--)	Quality of evidence
<b>ASTHMA</b>												
Yukselen 2012 <sup>44</sup> (see also above) Asthma and rhinitis, mean 10 yrs SCIT 10pts, SLIT 10, Placebo 10pts SLIT: 1000TU HDM 28 drops, 3/week for 1 year SCIT: 3365 TU each 4wk, no mcg dose stated (allergopharma)	DBdouble dummy PC (4) SCIT vs SLIT	x	Small groups, even so stat.sign. improved SCIT sympt vs SLIT	x	+1	No combined Sx'Med score, no mcg dose stated; small groups: underpowered to compare SLIT vs SCIT	x	x	x	x	-1.5	SLIT vs SCIT: 2.5 = low-med (Sympt 3.5)
	SCIT vs placebo  SLIT vs placebo	x	Small groups, even so stat.sign. improved	x	+1		x	x	x	x	-1.5	SCIT and SLIT vs placebo: 3.5 = Med- high.
Pajno 2011 <sup>44</sup> Seasonal asthma and AR to grass 72 children, 8-16yrs 8mcg grp 5 grass, 5 x week; for 3 yrs Continuous versus co-seasonal	Randomize d (4)	x	x	x	0	No control group (IRB: not allowed)	x	x	x	x	-1	3, moderate
Keles 2011 <sup>44</sup> Asthma and AR, 5-12 years, 1. SCIT, 2. SLIT, 3. Build-up SCIT, then SLIT 4. pharmacotherapy Respectively: 15-15-15-15 pts SCIT: 13mcg Der p+f 1/m SLIT: 0.75mcg Der p+f 1 3 times/week For 18 months.	Randomize d Asthma outcome (4) Rhinitis outcome (4)	x	x	x	0	Drop-out just below 15% (13.8)	x	x	x	x	0	4 (very low dose SLIT)
Marogna 2011 <sup>44</sup> Allergic rhinitis + intermittent asthma (positive MCh challenge at inclusion) 68 children , 5-17years, HDM allergy 34pts: passive smokers, 34 not. Each group 17-17: SLIT 1000AU 1/w or Cetirizine for 3 years.	Randomize d (4)	MCh challenge SLIT-no versus SLIT-yes Passive smoke	x	x	0 (+1 MCh challenge)	Patient selection based on RAST class II+. Poor statistical evaluation.	x	x	Statistica l calculatio ns only vs.baseli ne, not between groups	x	-2	2 (3 for MCh challenge, SLIT-no versus SLIT-yes Passive smoke)
Eifan 2010 <sup>44</sup> Asthma (+AR), 5-10yrs HDM drops (dose stated is confusing), for 12m	Randomize d controlled	x	SLIT and SCIT vs PHARMA: small groups but even so stat sign difference	x	+1 (compared against PHARMA)	SCIT vs SLIT: underpowered to show stat sign difference.	x	x	x	x	-1	SLIT vs SCIT: 3, SLIT and SCIT vs PHARMA: 4

# SLIT en asma pediátrica 2009-12

Author, year Some study details	Design (Starting score)	Quality of evidence
<b>ASTHMA</b>		
<p><b>Yukselen 2012<sup>11</sup></b> (see also above)  <b>Asthma and rhinitis, mean 10 yrs</b>  <b>SCIT 10pts, SLIT 10, Placebo 10pts</b>  <b>SLIT: 1000TU HDM 28 drops, 3/week for 1 year<sup>4</sup></b>  <b>SCIT: 3365 TU each 4wk, no mcg dose stated (allergopharma)</b></p>	<p>DBdouble dummy PC            (4)            SCIT vs SLIT</p>	<p>SLIT vs SCIT: 2.5 = low-med            (Sympt 3.5)</p>
<p><b>Pajno 2011<sup>12</sup></b>  <b>Seasonal asthma and AR to grass</b>  <b>72 children, 8-16yrs</b>  <b>8mcg grp 5 grass, 5 x week; for 3 yrs Continuous versus co-seasonal</b></p>	<p>Randomized (4)</p>	<p>3, moderate</p>
<p><b>Keles 2011<sup>13</sup></b>  <b>Asthma and AR, 5-12 years,</b>  <b>1. SCIT, 2. SLIT, 3. Build-up SCIT, then SLIT 4. pharmacotherapy</b>  <b>Respectively: 15-15-15-15 pts</b>  <b>SCIT: 13mcg Der p+f 1/m</b>  <b>SLIT: 0.75mcg Der p+f 1 3 times/week</b>  <b>For 18 months.</b></p>	<p>Randomized            Asthma outcome (4)            Rhinitis outcome (4)</p>	<p>4 (very low dose SLIT)</p>
<p><b>Marogna 2011<sup>14</sup></b>  <b>Allergic rhinitis + intermittent asthma (positive MCh challenge at inclusion)</b>  <b>68 children , 5-17years, HDM allergy</b>  <b>34pts: passive smokers, 34 not.</b>  <b>Each group 17-17: SLIT 1000AU 1/w or Cetirizine for 3 years.</b></p>	<p>Randomized (4)</p>	<p>2 (3 for MCh challenge,            SLIT-no versus SLIT-yes            Passive smoke)</p>
<p><b>Eifan 2010<sup>15</sup></b>  <b>Asthma (+AR), 5-10yrs</b>  <b>HDM drops (dose stated is confusing), for 12m</b></p>	<p>Randomized controlled</p>	<p>SLIT vs SCIT: 3, SLIT and            SCIT vs PHARMA: 4</p>

# Seguridad SLIT en asma pediátrica 2009-12

Author, year Some study details	Design (Starting score)	Large effect	Confound annulate d*	Dose- response gradient	TOTAL (+)	Limitations in design / execution	Inconsiste ncy of results	Indirectne ss of evidence	Impre- cision of results	Publ bias	TOTAL (--)	Quality of evidence
<b>ASTHMA</b>												
<b>SAFETY</b>												
Mosges 2010 <sup>14</sup> Mild-moderate asthma, 6-14y, 27SLIT, 27Placebo Tree pollen SLIT ultra-rush build-up (in 90min to 30-90- 150-300IR) No serious adverse events, PFR increase more than in placebo.	Randomiz ed (4)	x	x	x	0	x	PFR is supposed to drop when SLIT is started: it rose=proba bly learning effect.	One of the primary outcome measures: PFR: reflected learning effect instead of lung function	x	x	-2	4 for SAE, 2 for PFR
Seidenberg 2009 <sup>14</sup> Rhinitis (58% mild-moderate asthma) High dose daily co-seasonal SLIT Build-up in 90min, 4months; 5-17yrs Varying allergens	Observati onal (2)	x	x	X	0	28% did not finish study	x	x	x	x	-1	Very low



# SLIT

## EFFECTOS PREVENTIVOS



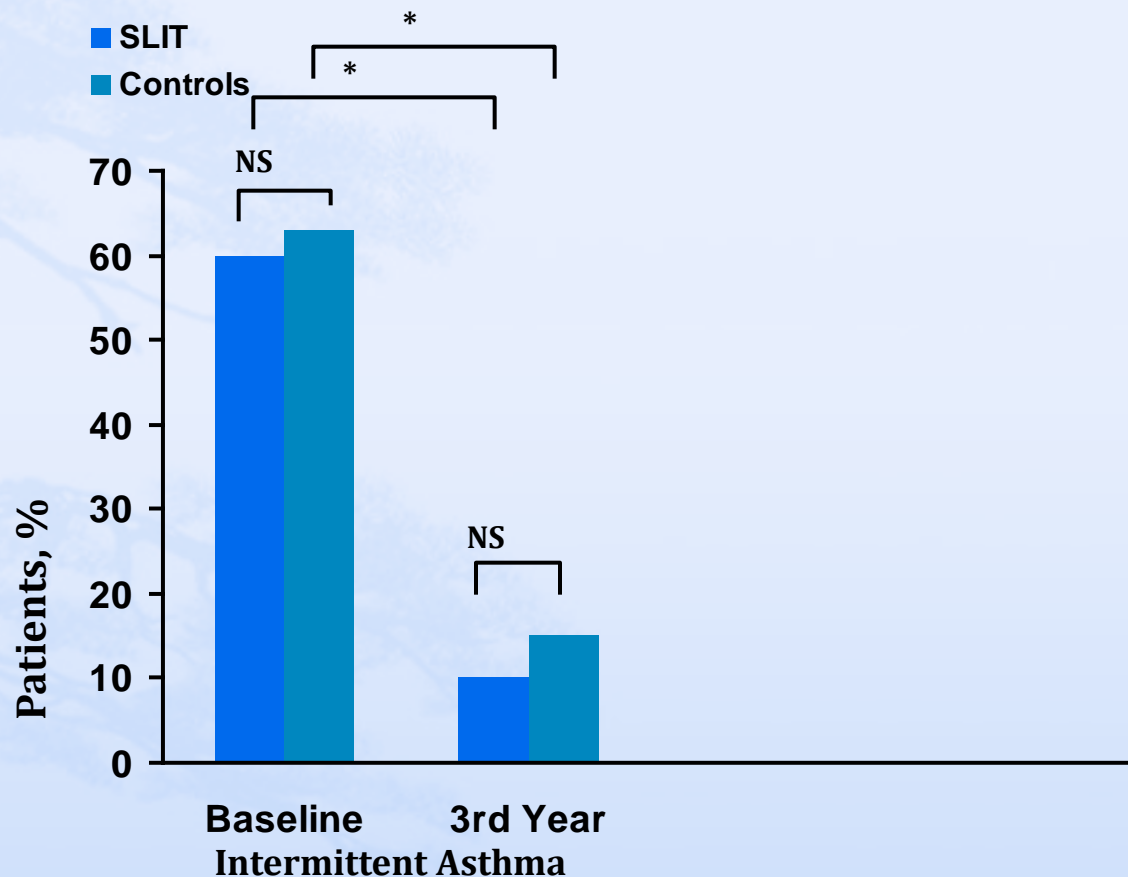
# Preventive effects of SLIT:

## Only weak evidence with older studies

- \* **Abierto** controlado, paralelo (Di Rienzo 2003)
  - \* HDM: SLIT durante 5 años. 35 SLIT, 25 controles.  
Reducción de desarrollo de asma en grupo activo, aún 5 años después
- \* **Abierto** randomizado (Novembre 2004)
  - \* 8/45 SLIT y 18/44 controles con RinitisA desarrollaron asma
- \* **Abierto** randomizado (Marogna 2004)
  - \* Reducción nuevas sensibilizaciones: 5.9% con SLIT, 38% en controles  
( $p < 0.01$ )

# Reducción de asma después de 3 años SLIT

## Randomized controlled open trial: 216 niños

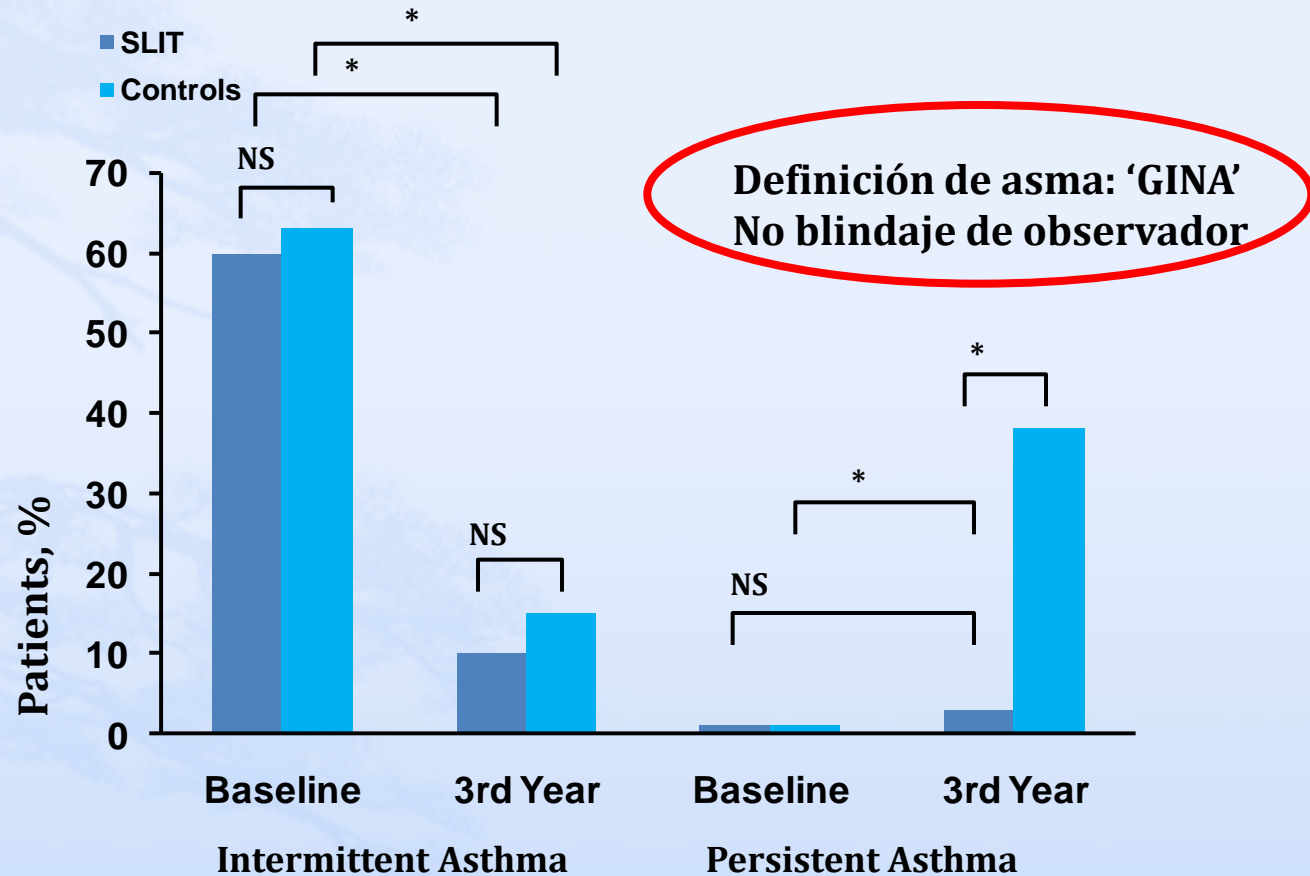


\* $P < 0.001$ .

Marogna. *Ann Allergy Asthma Immunol.* 2008;101:206.

# Reducción de asma después de 3 años SLIT

## Randomized controlled open trial: 216 niños



\* $P < 0.001$ .

SLIT: Reto con Metacolina (+): 82 (56.9%) después: 23 (17.7%)  $p < .001$

# Indicaciones para SLIT: prevención y efectos a largo plazo

Author, year Some study details	Design (Starting score)	Large effect	Confound Annulated*	Dose-response gradient	TOTAL (+)	Limitations in design / execution	Inconsistent results	Indirect evidence	Imprecision of results	Publ bias	TOTAL (-)	Quality of evidence
<b>Tahamiler 2008(13)</b> PAR, no asthma; 12-51 yrs 97 SLIT, 96 SCIT 3yrs + observation 3yrs House dust mite Low dose SLIT 3/week	Random open 2 treatments (4) Symptoms Long-term	X	X	X	0	No control group. No blinding of patients nor investigators	X	X	(no Med score, only antihistamines allowed)	X	-2	Low
<b>Marogna 2008(14)</b> SAR and PAR (59% mild asthma) SLIT 130, Placebo 66; 5-17 years Pollen/HDM SLIT , 3yrs Median-low dose, 3/week	RCT (4) Development persistent asthma RCT (4) New sensitizations	RR* mild persistent asthma 0.5; MCh positive 0.38 RR new sensitizations 0.08	X	X	+1	No blinding of investigator. No blinding patients. Symptoms baseline active group higher p< 0.001	X	X	X	X	-2	Moderate
<b>Durham 2009 (15)</b> Adults 3y grass tablet SLIT 15mcg daily	DBPC (4) A 4 años	X	X	X	0	X	X	X	X	X	0	High

13. Tahamiler R, et al. Ear Nose Throat J. 2008 Dec;87(12):E29.

14. Marogna M, et al. Ann Allergy Asthma Immunol. 2008 Aug;101(2):206-11.

# Prevencción desarrollo asma con inmunoterapia en niños con RA

SCIT en niños		
Dpt/Df	Prevencción RA → asma	○ ○ ○ ○
Pólenes	Prevencción RA → asma	● ● ● ○
Hongos	Prevencción RA → asma	○ ○ ○ ○

SLIT en niños		
Dpt/Df	Prevencción RA → asma	● ● ● ○*
Pólenes	Prevencción RA → asma	● ● ● ○
Hongos	Prevencción RA → asma	○ ○ ○ ○

\* Marogna 2008

# Concluyendo acerca de SCIT para asma...

- ✿ Adkinson estudio negativo tiene sus defectos
- ✿ Metanálisis Abramson SCIT para asma: resultados positivos para sínt+med (2011)
- ✿ GRADE análisis: con SCIT para asma
  - ✿ Mayor evidencia con ácaros
  - ✿ Reducción de síntomas /medicación
  - ✿ Mejoría en prueba de reto bronquial específica
  - ✿ Prevención de desarrollo de asma (evidencia moderada)
- ✿ **SEGURIDAD!!**

# Concluyendo acerca de SLIT para asma...

- \* No hay metanálisis Cochrane
- \* GRADE análisis: con SLIT para asma
  - \* Mayor evidencia con ácaros
  - \* Reducción de síntomas /medicación (moderada)
  - \* Mejoría en prueba de reto bronquial específica
  - \* Prevención de desarrollo de asma (evidencia moderada)