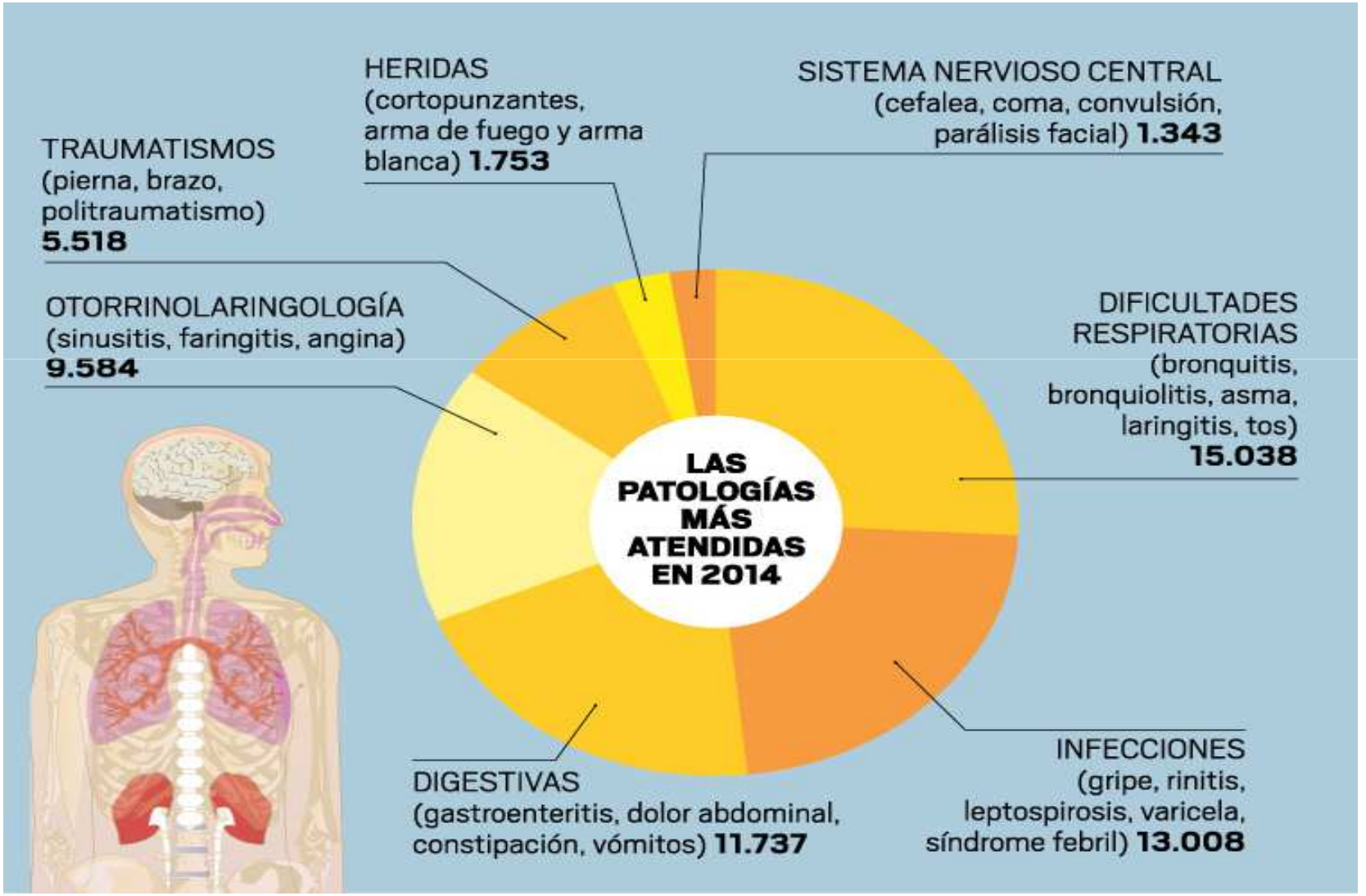

3° Jornadas Nacionales Conjuntas de Alergia e Inmunología en Pediatría
Tratamiento del asma:
¿Nuevas guías, nuevas realidades?
Córdoba, 23 de abril de 2016

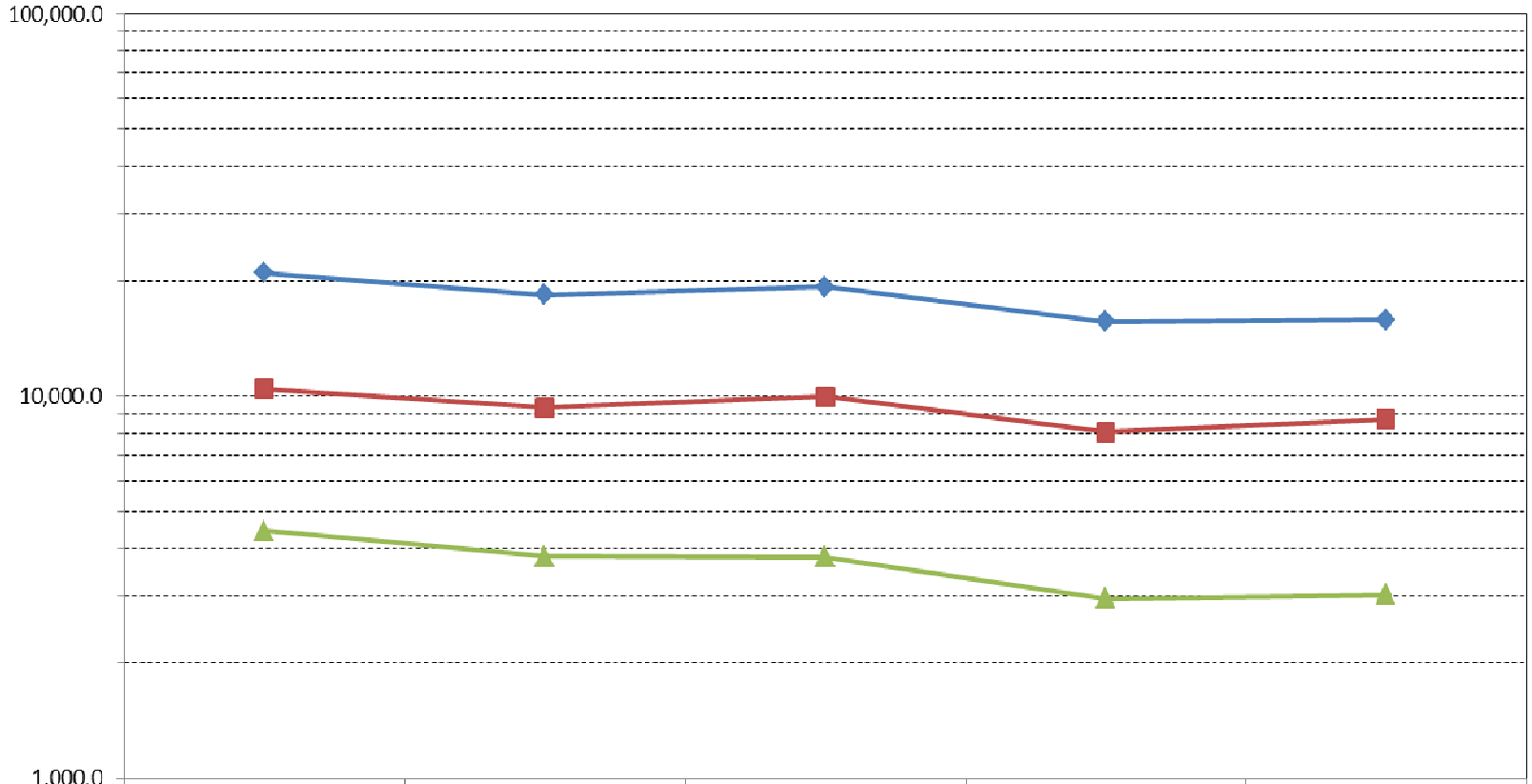
- Nuevas realidades
- Manejo del asma en menores de 5 años
- Manejo en escolares y adolescentes
- Conclusiones

- **Nuevas realidades**
- **Manejo del asma en menores de 5 años**
- **Manejo en escolares y adolescentes**
- **Conclusiones**

Hospital de Niños Orlando Alassia
2014 – Total de consultas: 92.069



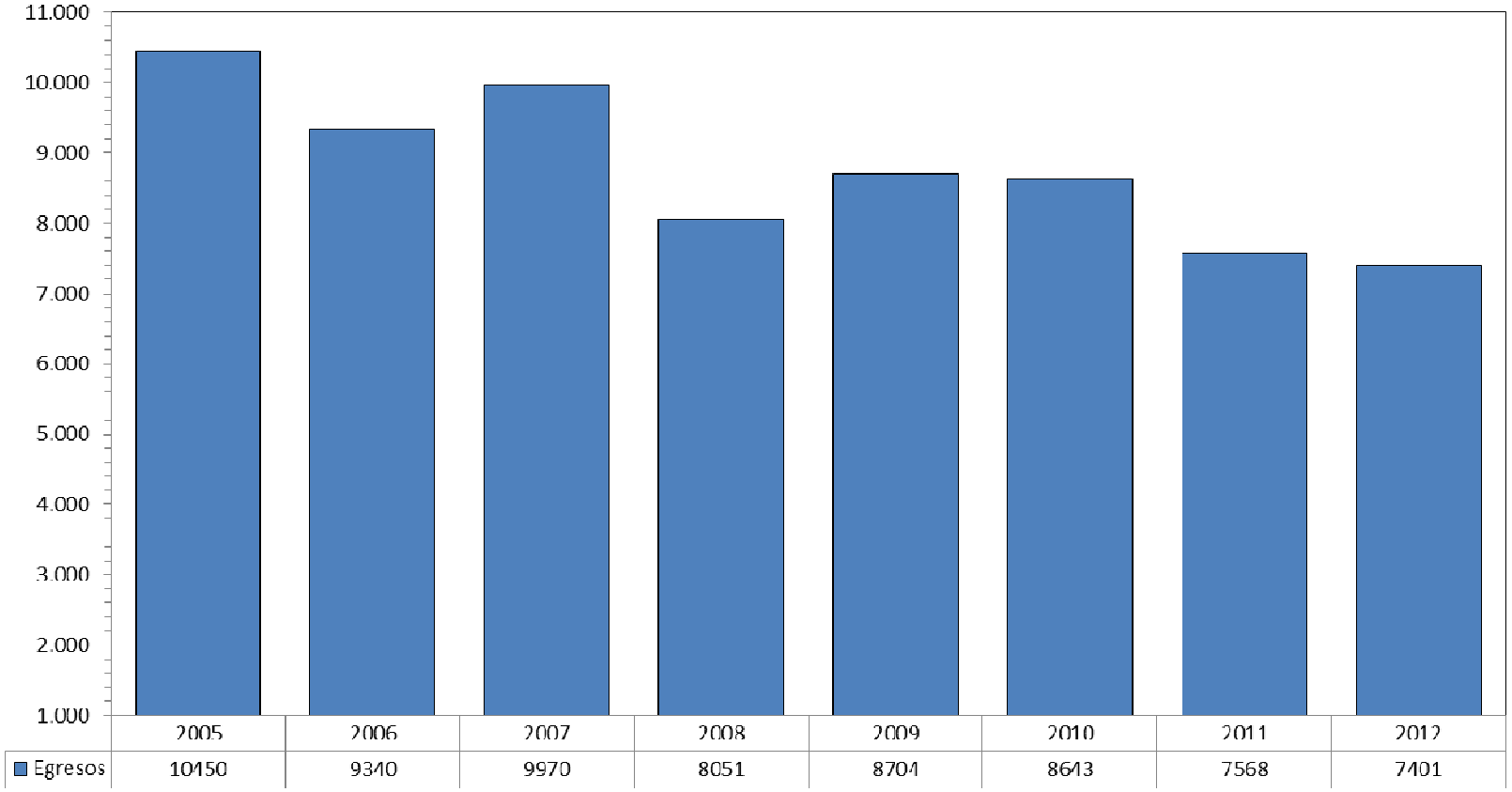
Tendencia de los Egresos Hospitalarios por Asma (J45-J46) para Todas las Edades, 5 a 39 y 40 a 64 años. República Argentina, 2005 - 2009



	2005	2006	2007	2008	2009
TODAS LAS EDADES	20984	18395	19342	15686	15862
5 A 39 AÑOS	10450	9340	9970	8051	8704
40 A 64	4447	3812	3797	2956	3021

Fuente: Instituto Nacional de Enfermedades Respiratorias (INER) "Emilio Coni", Administración Nacional de Laboratorios e Institutos de Salud (ANLIS), con base en datos de la Dirección de Estadísticas e Información de Salud (DEIS). Ministerio de Salud de la Nación, Argentina, 2012.

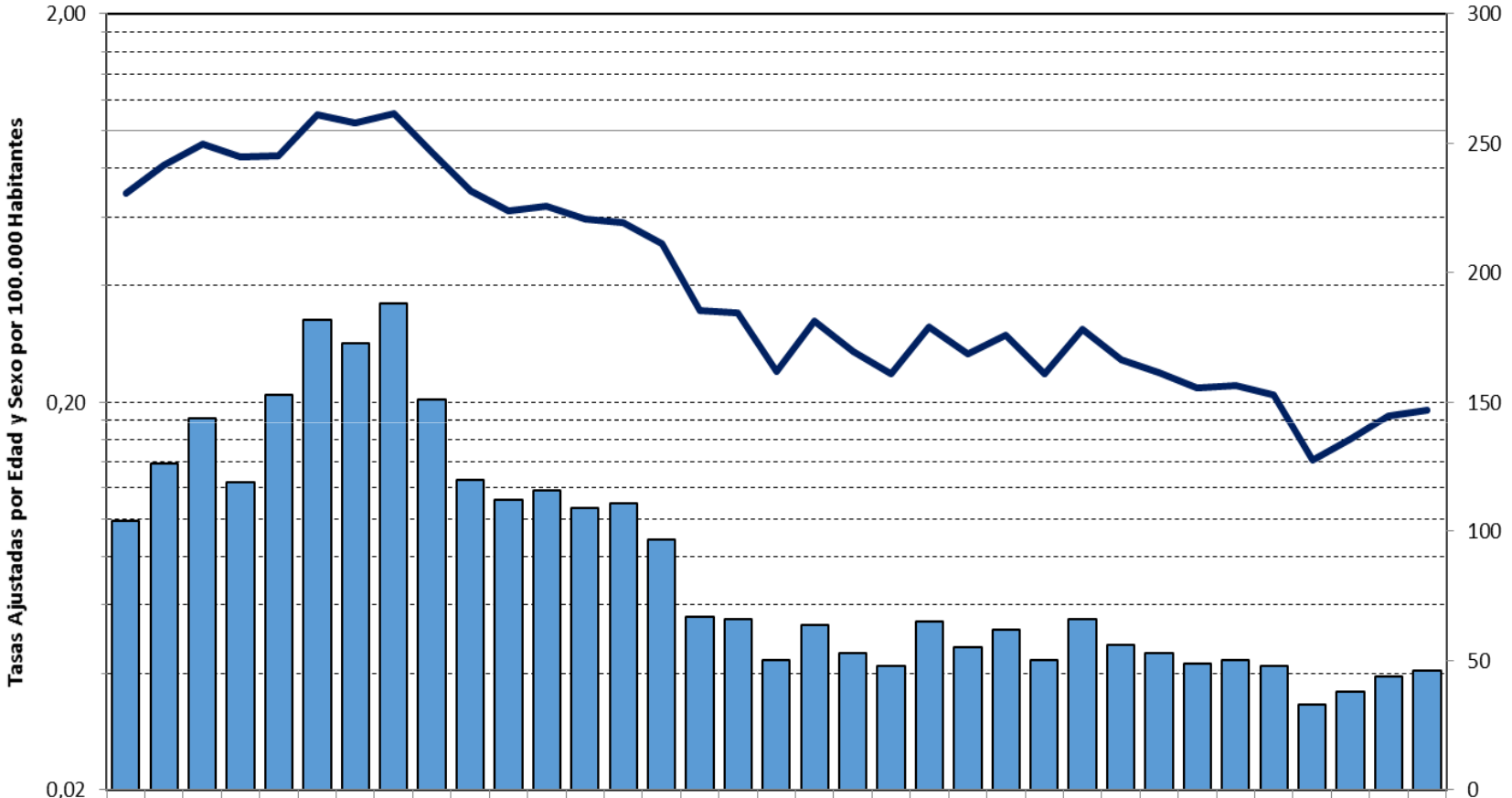
Tendencia de los Egresos Hospitalarios por Asma (J45-J46) de 5 a 39 años. República Argentina, 2005 - 2012



	2005	2006	2007	2008	2009	2010	2011	2012
Egresos	10150	9340	9970	8051	8704	8643	7568	7401

Fuente: Instituto Nacional de Enfermedades Respiratorias (INER) "Emilio Coni", Administración Nacional de Laboratorios e Institutos de Salud (ANLIS), con base en datos de la Dirección de Estadísticas e Información de Salud (DEIS). Ministerio de Salud de la Nación, Argentina, Agosto 2015.

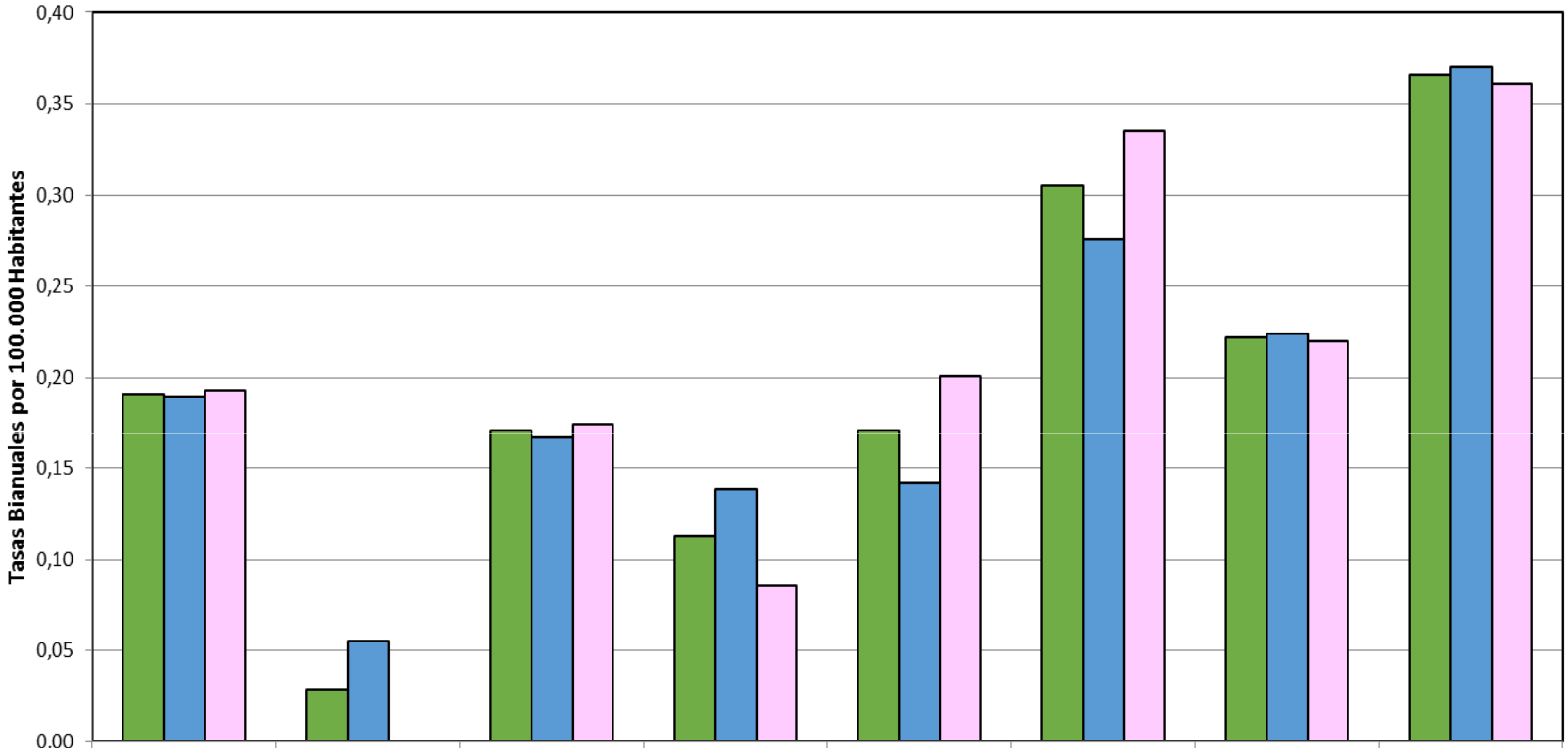
Tendencia de la Mortalidad por Asma (CIE 9: 493; CIE 10: J45-J46) en Población de 5 a 39 Años, Ambos Sexos. Número de Defunciones, Tasas Crudas y Tasas Ajustadas por Edad y Sexo, por 100.000 Habitantes. Argentina, 1980-2014



	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Muertes	104	126	144	119	153	182	173	188	151	120	112	116	109	111	97	67	66	50	64	53	48	65	55	62	50	66	56	53	49	50	48	33	38	44	46
Tasa Cruda	0,66	0,79	0,88	0,72	0,91	1,06	0,99	1,06	0,84	0,66	0,60	0,62	0,57	0,58	0,50	0,34	0,33	0,25	0,31	0,26	0,23	0,31	0,26	0,29	0,23	0,30	0,25	0,24	0,22	0,22	0,21	0,14	0,16	0,19	0,19
Tasa Ajustada	0,69	0,82	0,92	0,86	0,86	1,10	1,05	1,11	0,88	0,70	0,62	0,64	0,59	0,58	0,51	0,35	0,34	0,24	0,32	0,27	0,24	0,31	0,27	0,30	0,24	0,31	0,26	0,24	0,22	0,22	0,21	0,14	0,16	0,19	0,19
Total	1,19	1,13	1,00	1,01	1,02	0,93	0,95	0,93	0,92	0,90	0,88	0,89	0,92	0,89	0,94	0,92	0,95	0,94	0,92	0,91	0,88	0,89	0,88	0,83	0,77	0,78	0,80	0,82	0,84	0,86	0,82	0,83	0,85	0,85	0,84

Fuente: Información Procesada en el Instituto Nacional de Enfermedades Respiratorias (INER) "Emilio Coni", Administración Nacional de Laboratorios e Institutos de Salud (ANLIS), con base en datos de la Dirección de Estadísticas e Información de Salud, Ministerio de Salud de la Nación, República Argentina, Marzo de 2016.

Mortalidad por Asma (CIE 9: 493; CIE 10: J45-J46) en Población de Ambos Sexos de 5 a 39 Años, por Grupos de Edad. Tasas Bianuales por 100.000 Habitantes. Argentina, 2013-2014

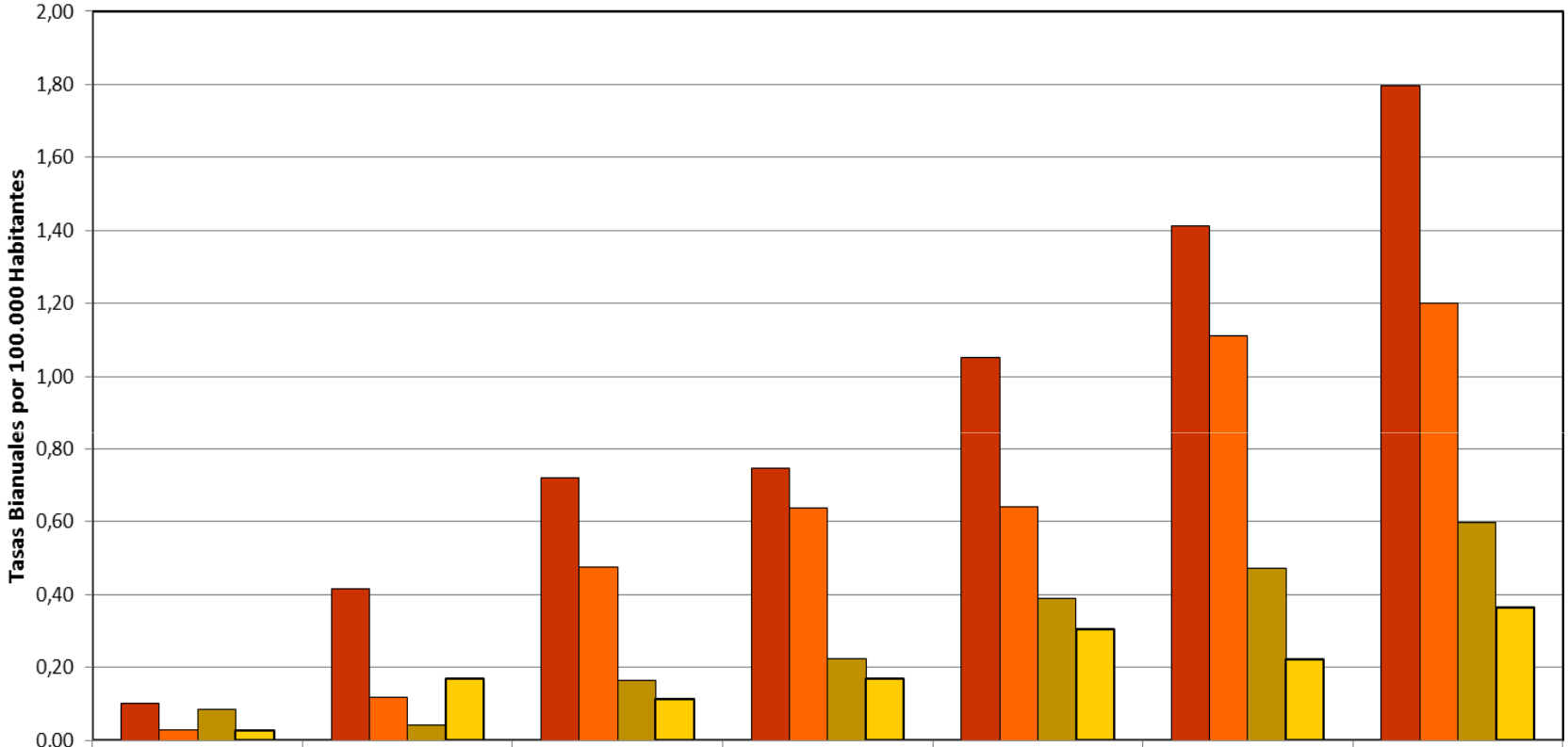


	Total	5 a 9	10 a 14	15 a 19	20 a 24	25 a 29	30 a 34	35 a 39
Ambos Sexos	0,19	0,03	0,17	0,11	0,17	0,31	0,22	0,37
Varones	0,19	0,06	0,17	0,14	0,14	0,28	0,22	0,37
Mujeres	0,19	0,00	0,17	0,09	0,20	0,34	0,22	0,36

Grupos de Edad

Fuente: Información Procesada en el Instituto Nacional de Enfermedades Respiratorias (INER) "Emilio Coni", Administración Nacional de Laboratorios e Institutos de Salud (ANLIS), con base en datos de la Dirección de Estadísticas e Información de Salud, Ministerio de Salud de la Nación, República Argentina, Marzo de 2016.

Mortalidad por Asma (CIE 9: 493; CIE 10: J45-J46) en Población de Ambos Sexos de 5 a 39 Años, por Grupos de Edad. Tasas Bianuales por 100.000 Habitantes. Argentina, 1983-2014



	5 a 9	10 a 14	15 a 19	20 a 24	25 a 29	30 a 34	35 a 39
1983-1984	0,10	0,42	0,72	0,75	1,05	1,41	1,80
1993-1994	0,03	0,12	0,47	0,64	0,64	1,11	1,20
2003-2004	0,09	0,04	0,16	0,23	0,39	0,47	0,60
2013-2014	0,03	0,17	0,11	0,17	0,31	0,22	0,37

Grupos de Edad

Fuente: Información Procesada en el Instituto Nacional de Enfermedades Respiratorias (INER) "Emilio Coni", Administración Nacional de Laboratorios e Institutos de Salud (ANLIS), con base en datos de la Dirección de Estadísticas e Información de Salud, Ministerio de Salud de la Nación, República Argentina, Marzo de 2016.

FÁRMACOS ASMA Y EPOC - ARGENTINA 2012 (IMS)

Fármacos	Unidades	Porcentaje
LABA + CI	2 514 858	(35.58%)
SABA + CI	392 881	(5.56%)
CI MDI PS	867 542	(12.27%)
CI NEB.	329 890	(4.67%)
SABA + AC	869 237	(12.3%)
MONTELUKAST	768 568	(10.8%)
ANTICOLINÉRGICOS	731541	(10.3%)
TEOFILINAS	220 203	(3.12%)
SABA ORAL	98 947	(1.40%)
LABA	98 302	(1.33%)

FÁRMACOS ASMA Y EPOC PEDIATRÍA 2015/16 (8,54 / 8,63%)

Fármacos	03/2015 %	03/2016 %
AGO. B-2 + CORT.	11,65	11,81
SABA	39,6	37,83
CORT. INH.	29,65	30,02
ANTILEUCOTRIENOS	15,85	17,13
ANTICOLINÉRGICOS	1,34	1,51
SABA + AC	0,76	0,76
ANTIINFLAM. ORALES	0.84	0,69
XANTINAS	0,26	0,17

- Nuevas realidades
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Diagnosis and management of asthma in children 5 years and younger

GINA Global Strategy for Asthma Management and Prevention 2015

Probability of asthma diagnosis or response to asthma treatment in children ≤5 years

GINA assessment of asthma control in children ≤5 years

A. Symptom control

In the past 4 weeks, has the child had:

- Daytime asthma symptoms for more than few minutes, more than once/week? Yes❑ No❑
- Any activity limitation due to asthma? (runs/plays less than other children, tires easily during walks/playing) Yes❑ No❑
- Reliever needed* more than once a week? Yes❑ No❑
- Any night waking or night coughing due to asthma? Yes❑ No❑

Level of asthma symptom control

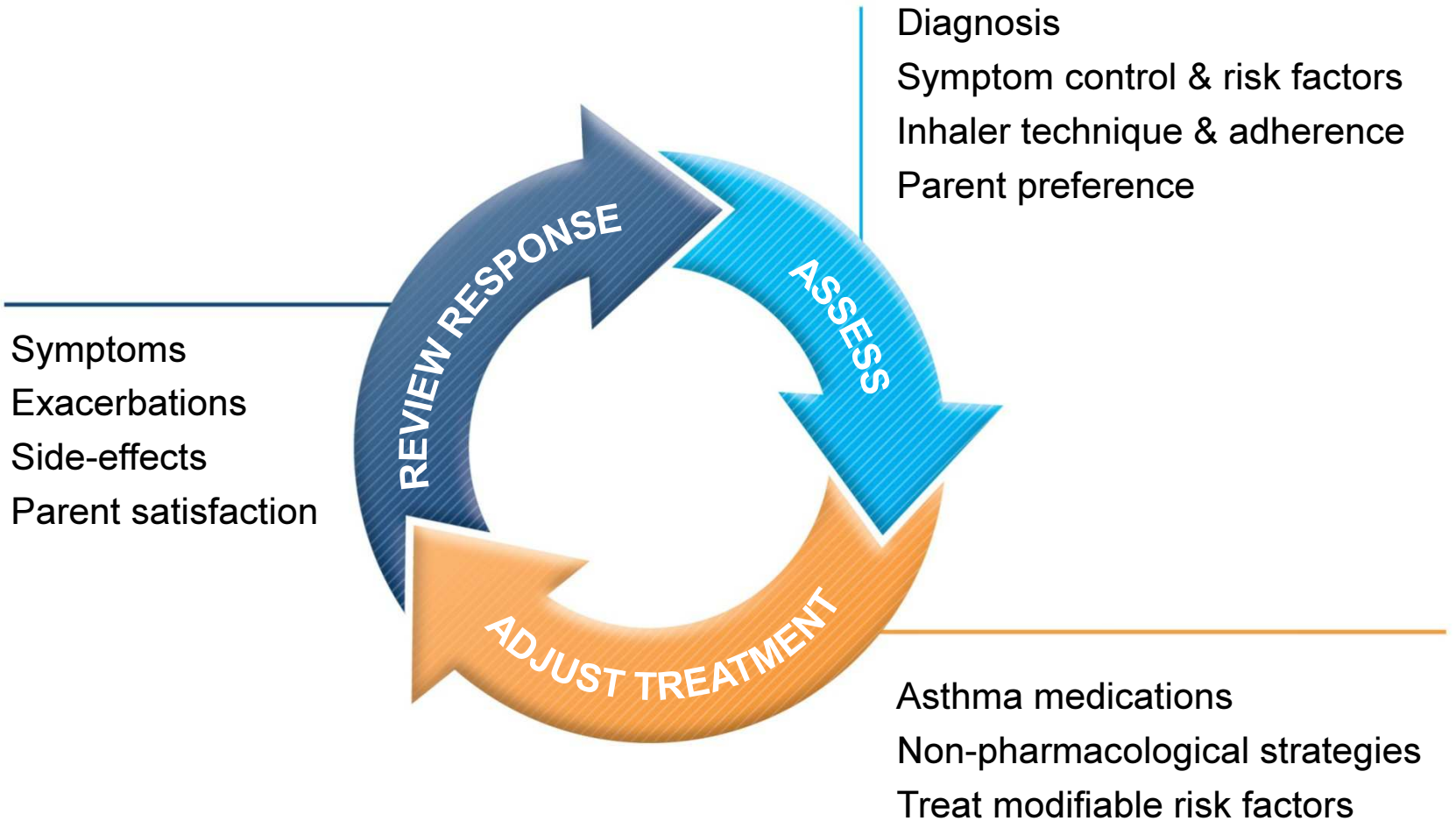
Well-controlled	Partly controlled	Uncontrolled
None of these	1-2 of these	3-4 of these

B. Risk factors for poor asthma outcomes

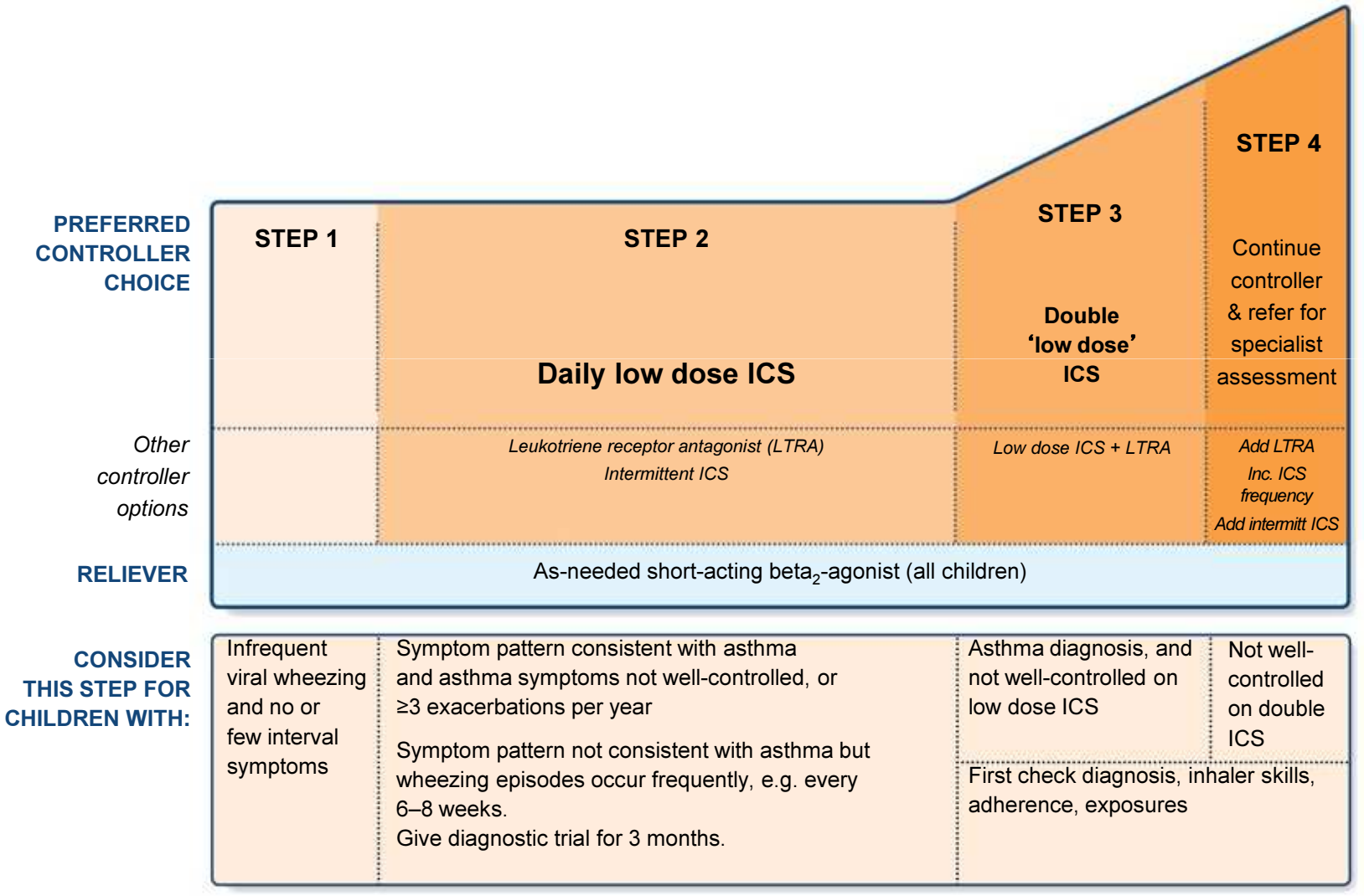
ASSESS CHILD'S RISK FOR:

- Exacerbations within the next few months
- Fixed airflow limitation
- Medication side-effects

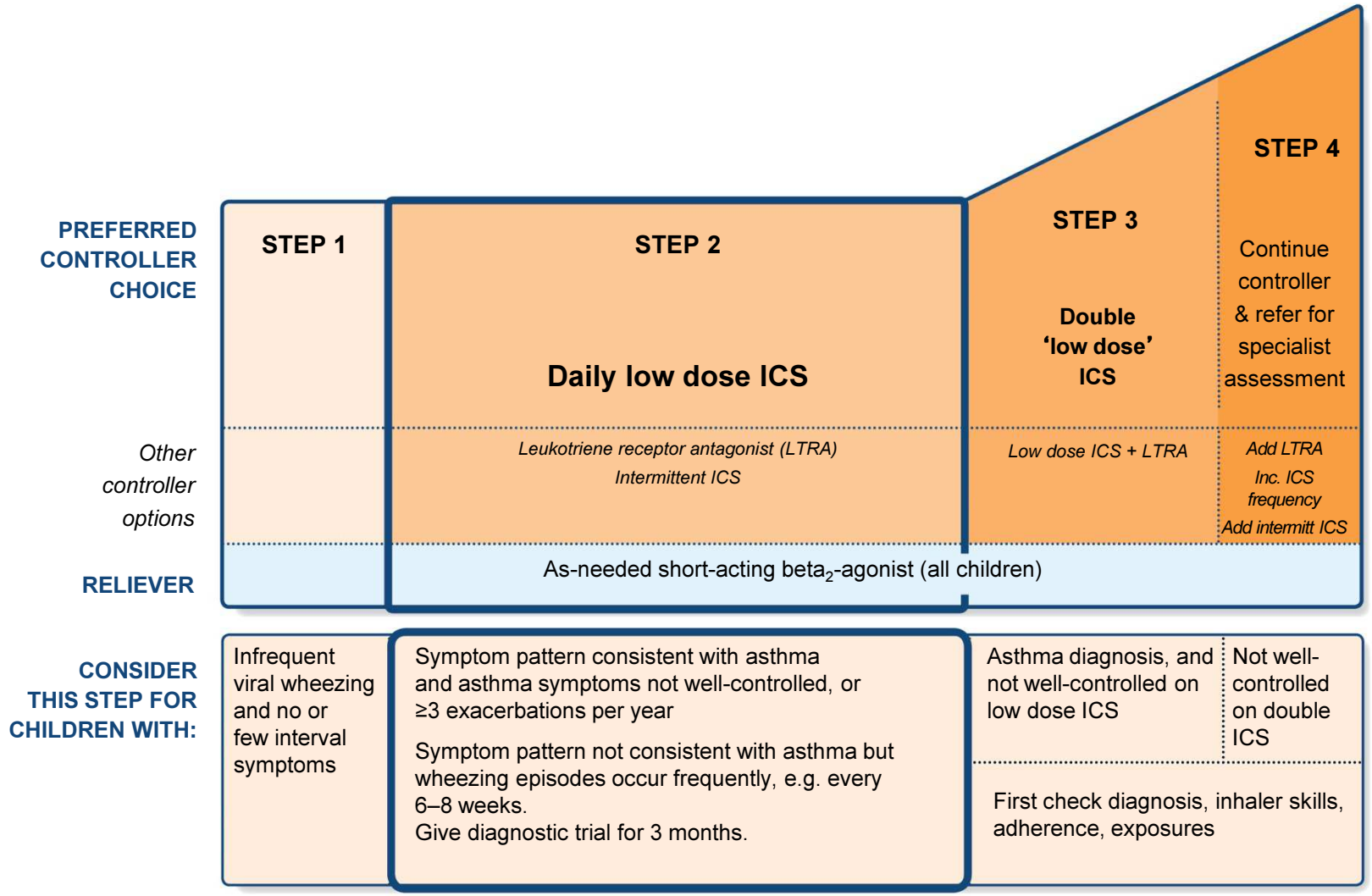
Control-based asthma management cycle in children ≤5 years



Stepwise approach – pharmacotherapy (children ≤5 years)



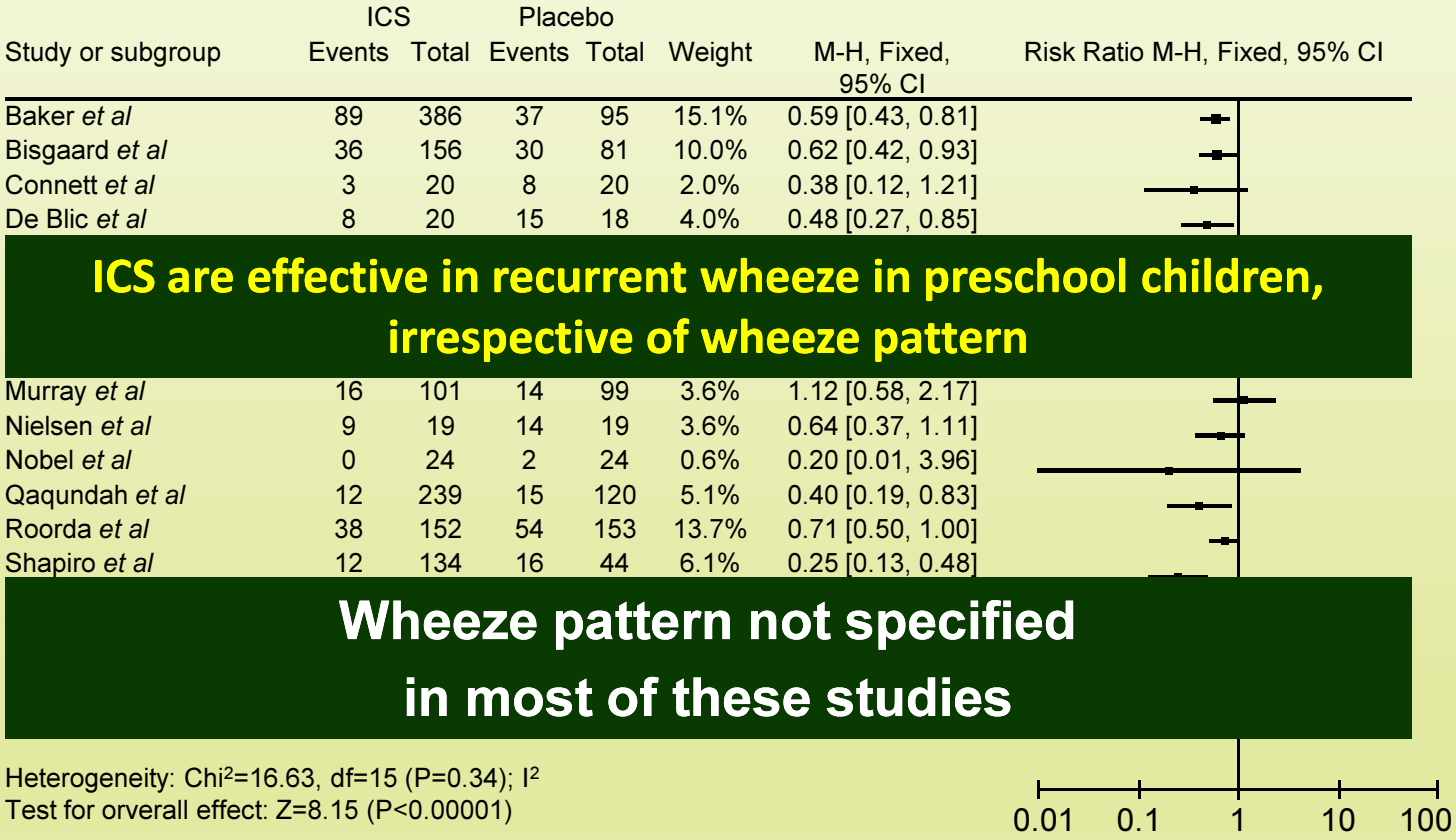
Step 2 (children ≤5 years) – initial controller + as-needed SABA



Step 2 (children ≤5 years) – initial controller + as-needed SABA

- Indication
  - Child with symptom pattern consistent with asthma, and symptoms not well-controlled, or ≥3 exacerbations per year
  - May also be used as a diagnostic trial for children with frequent wheezing episodes
- Preferred option: regular daily low dose ICS + as-needed inhaled SABA
  - Give for ≥3 months to establish effectiveness, and review response
- Other options depend on symptom pattern
  - (Persistent asthma) – regular leukotriene receptor antagonist (LTRA) leads to modest reduction in symptoms and need for OCS compared with placebo
  - (Intermittent viral-induced wheeze) – regular LTRA improves some outcomes but does not reduce risk of exacerbations
  - (Frequent viral-induced wheeze with interval symptoms) – consider episodic or as-needed ICS**, but give a trial of regular ICS first**

ICS for recurrent preschool wheeze



Study or subgroup	ICS Events	ICS Total	Placebo Events	Placebo Total	Weight	M-H, Fixed, 95% CI
Baker *et al*	89	386	37	95	15.1%	0.59 [0.43, 0.81]
Bisgaard *et al*	36	156	30	81	10.0%	0.62 [0.42, 0.93]
Connett *et al*	3	20	8	20	2.0%	0.38 [0.12, 1.21]
De Blic *et al*	8	20	15	18	4.0%	0.48 [0.27, 0.85]
Murray *et al*	16	101	14	99	3.6%	1.12 [0.58, 2.17]
Nielsen *et al*	9	19	14	19	3.6%	0.64 [0.37, 1.11]
Nobel *et al*	0	24	2	24	0.6%	0.20 [0.01, 3.96]
Qaqundah *et al*	12	239	15	120	5.1%	0.40 [0.19, 0.83]
Roorda *et al*	38	152	54	153	13.7%	0.71 [0.50, 1.00]
Shapiro *et al*	12	134	16	44	6.1%	0.25 [0.13, 0.48]

Castro-Rodriguez JA & Rodrigo GJ. *Pediatrics* 2009;123:e519-25

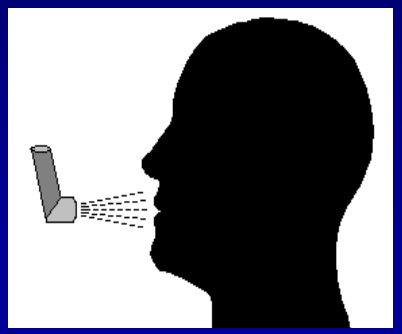
SEGURIDAD

FARMACO

EFICIACIA CLINICA

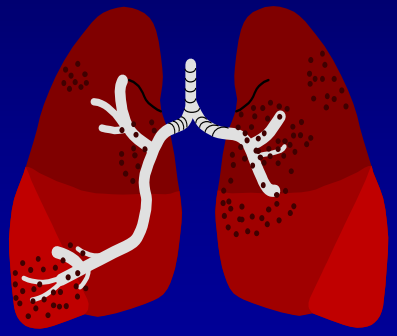
ORGANISMO

The Fate of Inhaled Corticosteroids



Mouth and pharynx

10% - 40%
Deposited in lung

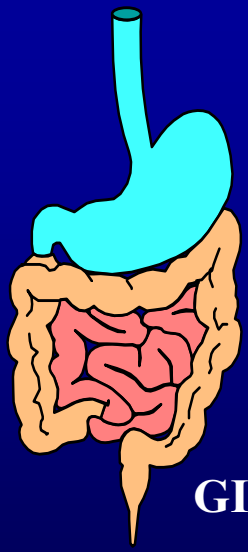


Lung

Complete absorption
from the lung

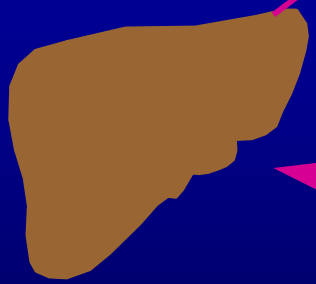
Systemic
circulation

60% - 90% Swallowed
(reduced by spacer
or mouth rinsing)



GI tract

Absorption
from gut



Liver

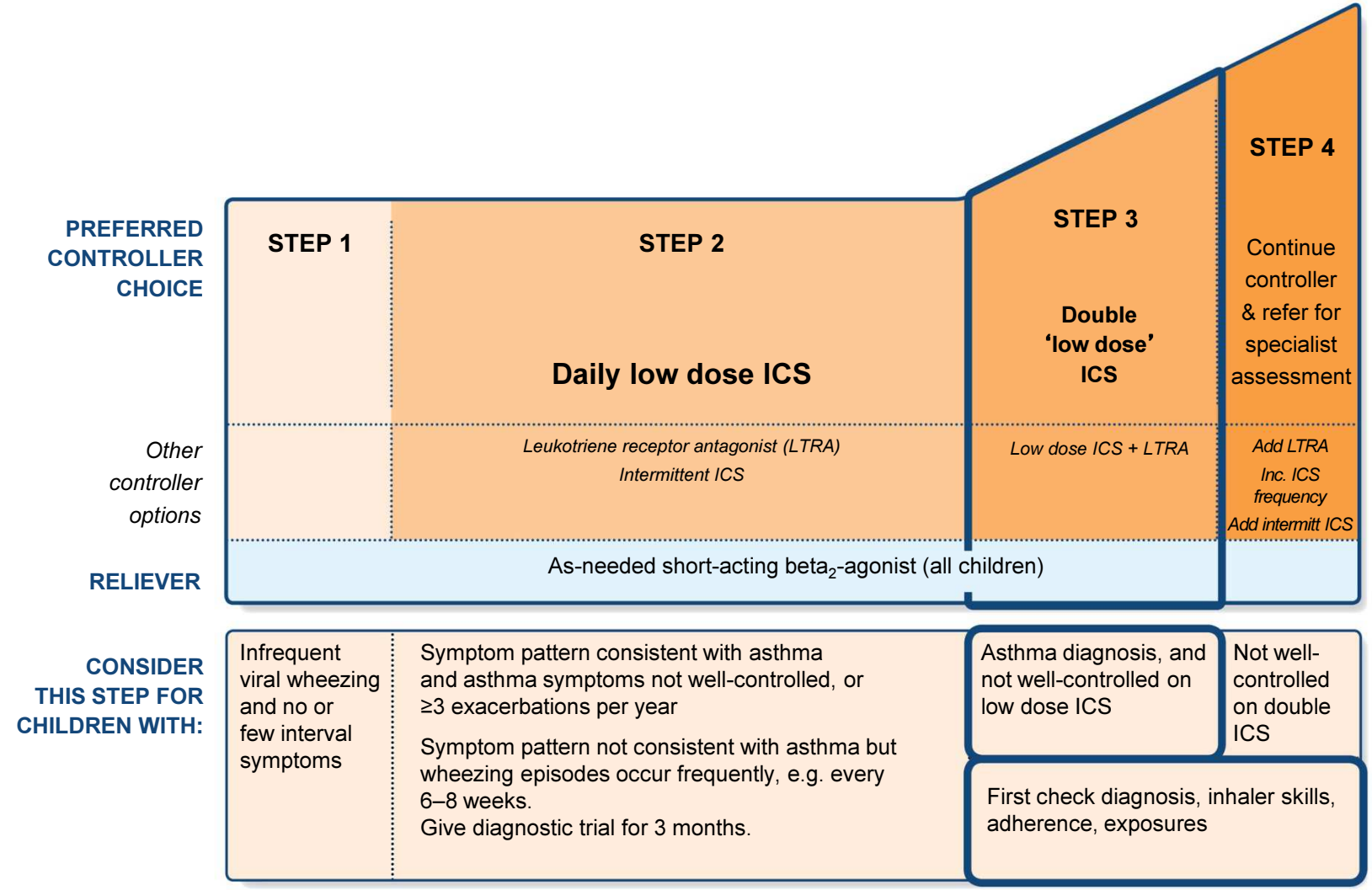
Orally bioavailable
fraction

First-pass
inactivation

Systemic
side effects

Adapted from Derendorf H. *Respir Med.* 1997;91(suppl A):22-28.

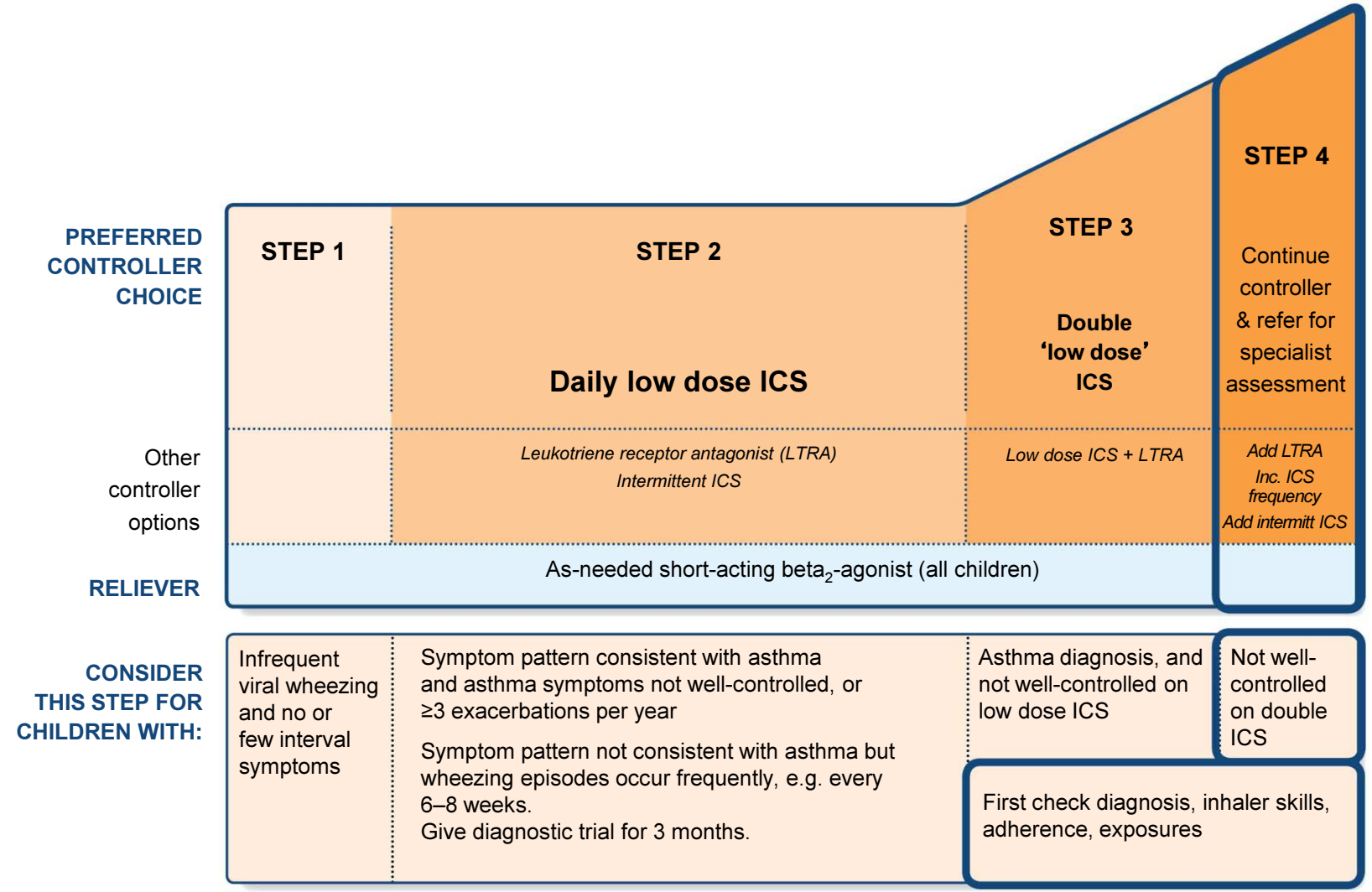
Step 3 (children ≤5 years) – medium dose ICS + as-needed inhaled SABA



Step 3 (children ≤5 years) – medium dose ICS + as-needed inhaled SABA

- Indication
  - Asthma diagnosis, and symptoms not well-controlled on low dose ICS
  - First check symptoms are due to asthma, and check adherence, inhaler technique and environmental exposures
- Preferred option: medium dose ICS with as-needed inhaled SABA
  - Review response after 3 months
- Other options
  - Consider adding LTRA to low dose ICS (based on data from older children)

Step 4 (children ≤5 years) – refer for expert assessment



Step 4 (children ≤5 years) – refer for expert assessment

- Indication
  - Asthma diagnosis, and symptoms not well-controlled on medium dose ICS
  - First check symptoms are due to asthma, and check adherence, inhaler technique and environmental exposures
- Preferred option: continue controller treatment and refer for expert assessment
- Other options (preferably with specialist advice)
  - Higher dose ICS and/or more frequent dosing (for a few weeks)
  - Add LTRA, theophylline or low dose OCS (for a few weeks only)
  - Add intermittent ICS to regular daily ICS if exacerbations are the main problem
  - **ICS/LABA not recommended in this age group**

‘Low dose’ inhaled corticosteroids (mcg/day) for children ≤5 years

Inhaled corticosteroid	Low daily dose (mcg)
Beclometasone dipropionate (HFA)	100
Budesonide (pMDI + spacer)	200
Budesonide (nebulizer)	500
Fluticasone propionate (HFA)	100
Ciclesonide	160
Mometasone furoate	Not studied below age 4 years
Triamcinolone acetonide	Not studied in this age group

- This is not a table of equivalence
- A low daily dose is defined as the dose that has not been associated with clinically adverse effects in trials that included measures of safety

Choosing an inhaler device for children ≤5 years

Age	Preferred device	Alternate device
0–3 years	Pressurized metered dose inhaler plus dedicated spacer with face mask	Nebulizer with face mask
4–5 years	Pressurized metered dose inhaler plus dedicated spacer with mouthpiece	Pressurized metered dose inhaler plus dedicated spacer with face mask, or nebulizer with mouthpiece or face mask

- Nuevas realidades
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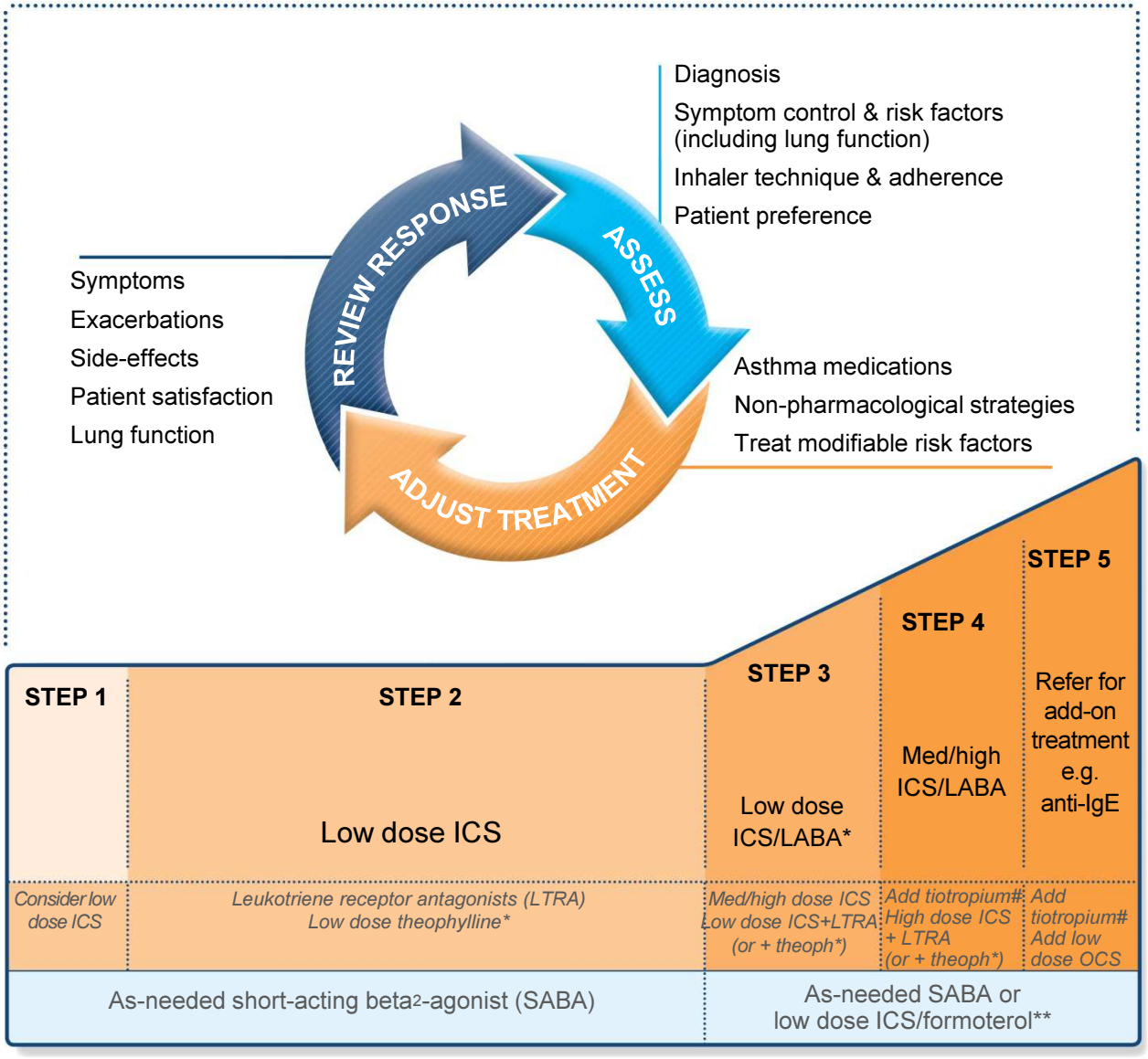
Initial controller treatment for adults, adolescents and children 6–11 years

- Start controller treatment early
  - For best outcomes, initiate controller treatment as early as possible after making the diagnosis of asthma
- Indications for regular low-dose ICS - any of:
  - Asthma symptoms more than twice a month
  - Waking due to asthma more than once a month
  - Any asthma symptoms plus any risk factors for exacerbations
- Consider starting at a higher step if:
  - Troublesome asthma symptoms on most days
  - Waking from asthma once or more a week, especially if any risk factors for exacerbations
- If initial asthma presentation is with an exacerbation:
  - Give a short course of oral steroids and start regular controller treatment (e.g. high dose ICS or medium dose ICS/LABA, then step down)

Stepwise management - pharmacotherapy

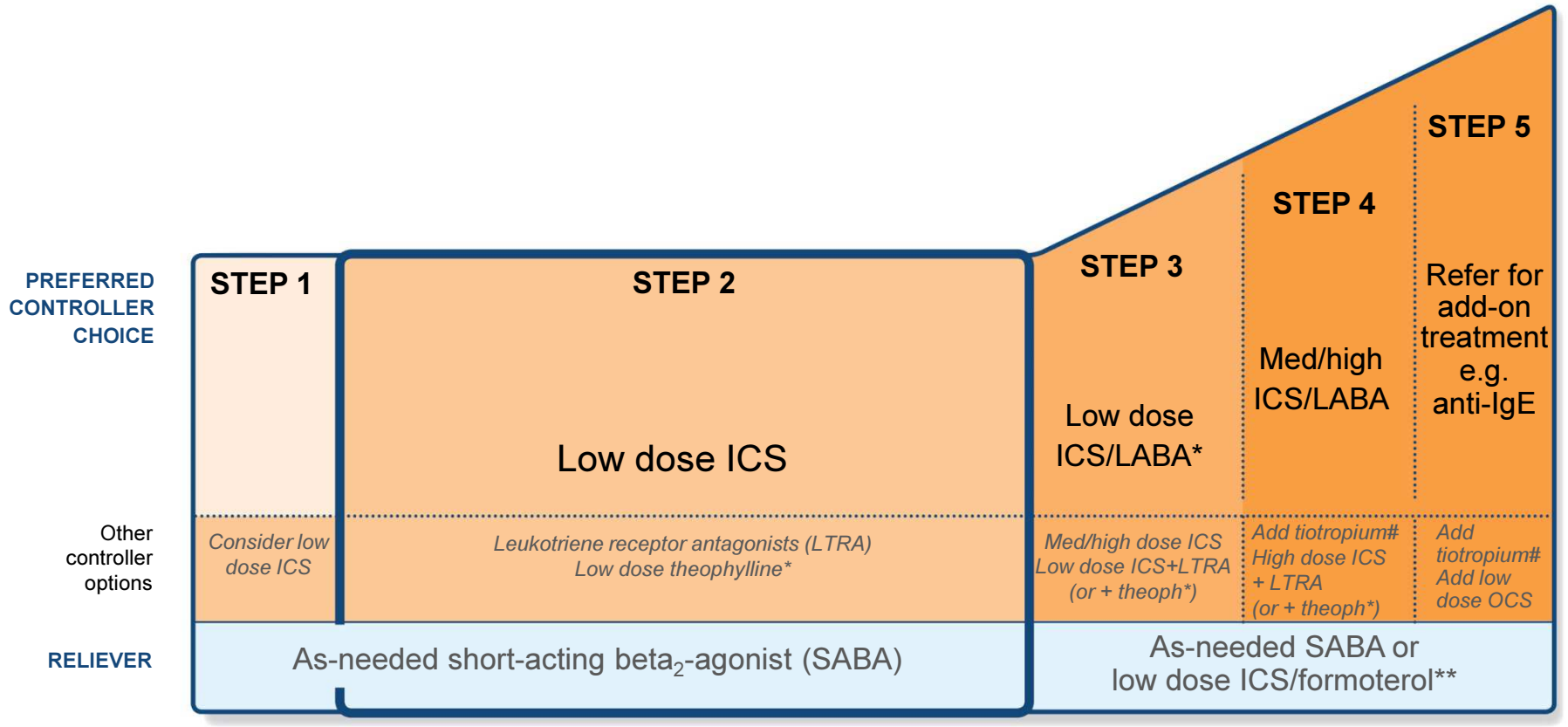


*For children 6-11 years, theophylline is not recommended, and preferred Step 3 is medium dose ICS

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

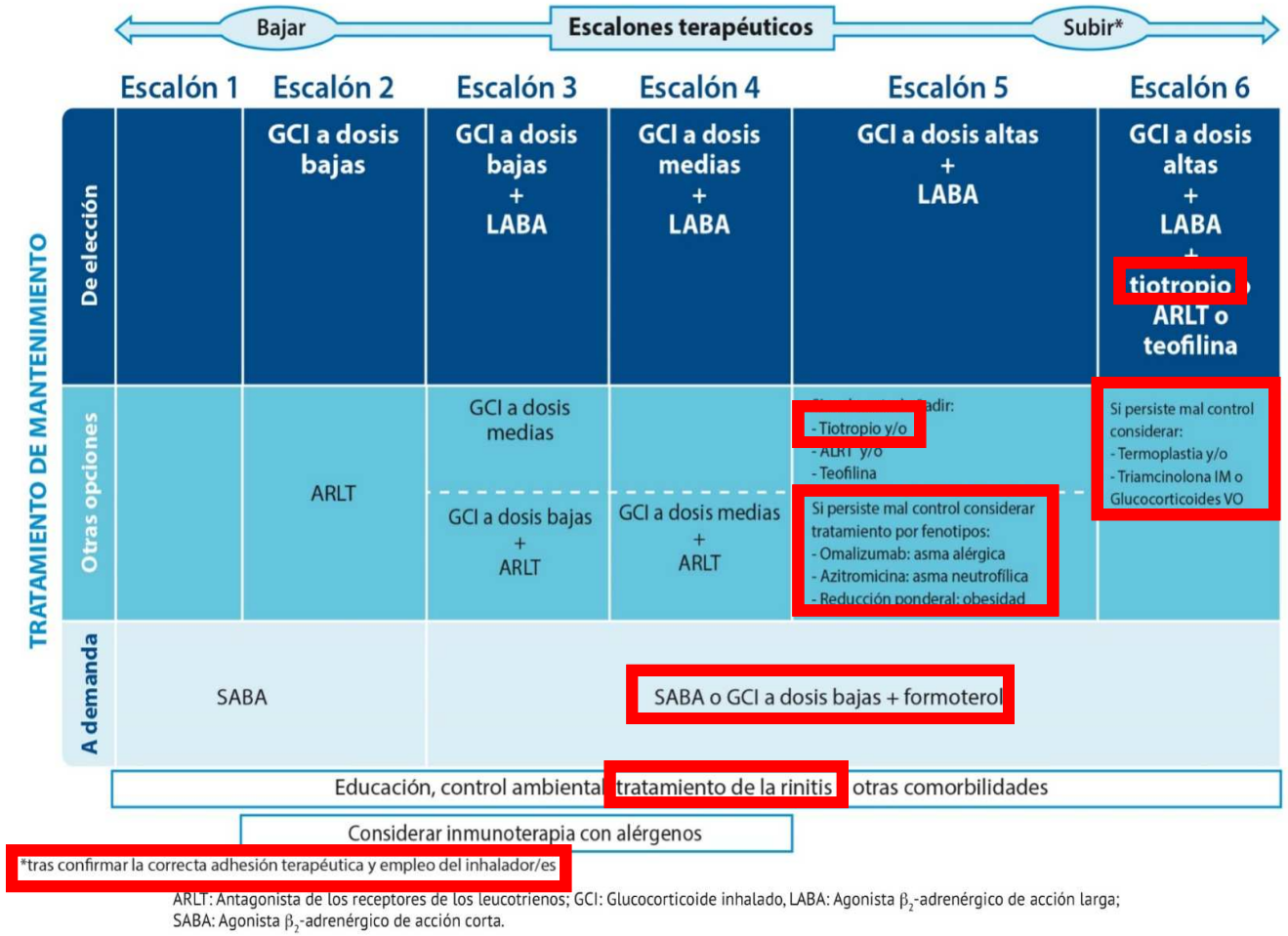
Tiotropium by soft-mist inhaler is indicated as add-on treatment for adults (≥18 yrs) with a history of exacerbations

Step 2 – low-dose controller + as-needed inhaled SABA



*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
Tiotropium by soft-mist inhaler is indicated as add-on treatment for patients with a history of exacerbations; it is not indicated in children <18 years.

Tratamiento de mantenimiento adultos – GEMA 2015



ARLT: Antagonista de los receptores de los leucotrienos; GCI: Glucocorticoide inhalado, LABA: Agonista β_2-adrenérgico de acción larga; SABA: Agonista β_2-adrenérgico de acción corta.

(DMMA) de los aerosoles generados por los diferentes dispositivos – GEMA 2015

	Depósito pulmonar (%)		Depósito orofaríngeo (%)		DMMA (µm)
	in vivo	*in vitro*	*in vivo*	*in vitro*	
pMDI					
pMDI convencional	7,8-34	-	53,9-82,2	-	1,4-8
pMDI convencional + cámara inhalación	11,2-68,3	-	31,2	40	2-3,2
pMDI autodisparo	50-60	-	30	-	-
Modulite®	31-34	-	33-58	-	1-2
Alvesco®	50-52	-	32,9	-	-
Respimat®	40-53	-	19,3-39	-	-
DPI (por orden alfabético)					
Accuhaler®	7,6-18	15-30	-	-	3,5
Aerolizer®	13-20	21,7-28	73	-	1,9-7,9
Breezhaler®	36	39	-	45	2,8
Easyhaler®	18,5-31	29	-	-	-
Genuair®	30,1	-	54,7	-	-
Handihaler®	17,8	17,3-22	-	71	3,9
Inhalador Ingelheim®	16	-	59	-	-
Nexthaler®	56	-	43	-	1,4-1,5
Spinhaler®	11,5	-	30,9	-	-
Turbuhaler®	14,2-38	28	53-71,6	57,3-69,3	1,7-5,4
Twisthaler®	36-37	-	-	-	2-2,2

Tomado de la Normativa SEPAR-ALAT terapia inhalada. Arch Bronconeumol 2013

Systematic review on the use of omalizumab for the treatment of asthmatic children and adolescents

Gustavo J. Rodrigo & Hugo Neffen

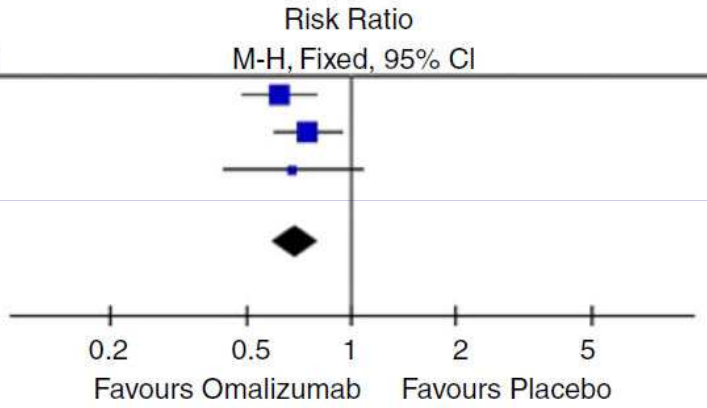
Pediatric Allergy and Immunology, 2015: 26: 551–556

Number of patients with at least one significant asthma exacerbations

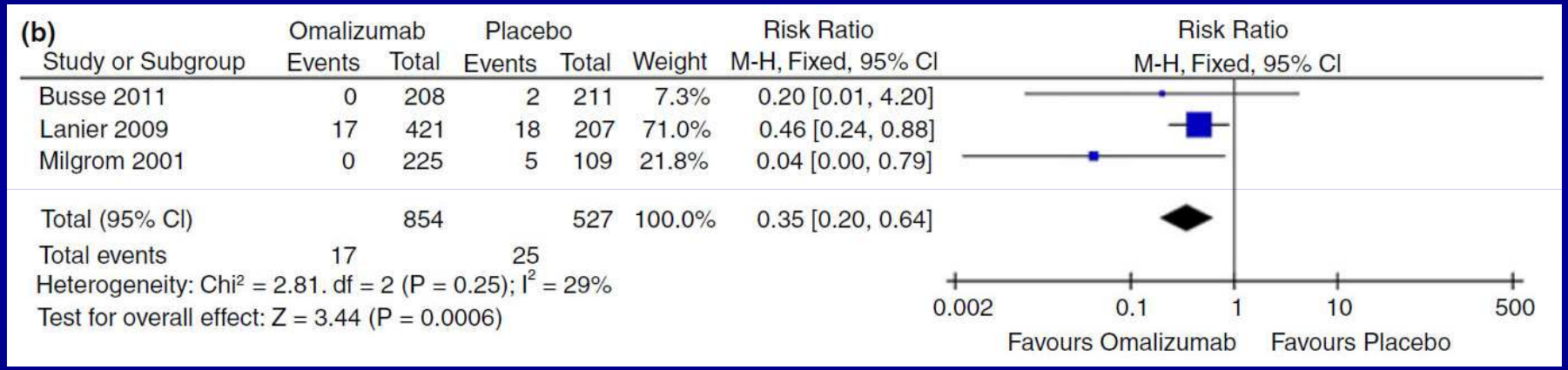
(a) Study or Subgroup	Omalizumab Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Busse 2011	63	208	103	211	42.2%	0.62 [0.48, 0.80]
Lanier 2009	120	384	80	192	44.0%	0.75 [0.60, 0.94]
Milgrom 2001	35	225	25	109	13.9%	0.68 [0.43, 1.07]
Total (95% CI)		817		512	100.0%	0.69 [0.59, 0.80]
Total events	218		208			

Heterogeneity: $Chi^2 = 1.24$, $df = 2$ ($P = 0.54$): $I^2 = 0\%$

Test for overall effect: $Z = 4.73$ ($P < 0.00001$)



Number of patients with a serious exacerbation requiring hospitalization

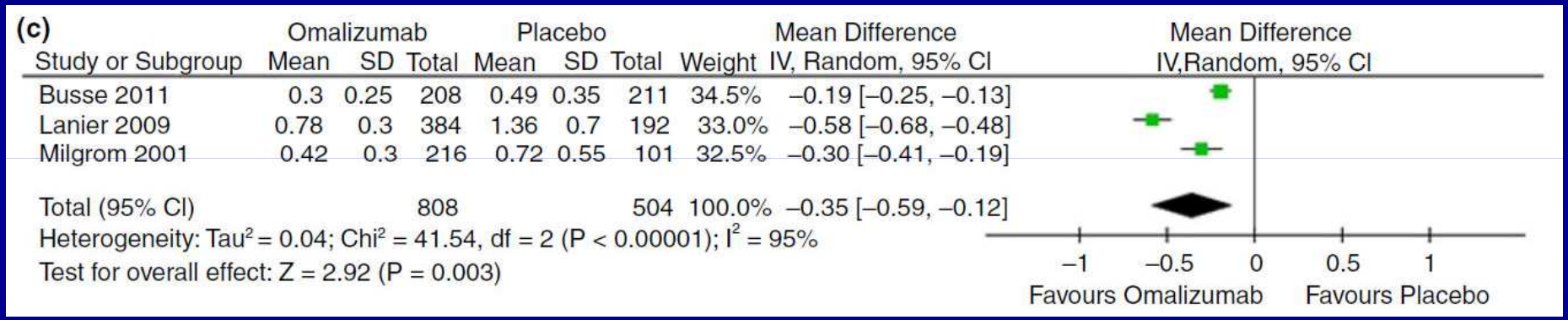


(b) Study or Subgroup	Omalizumab Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Busse 2011	0	208	2	211	7.3%	0.20 [0.01, 4.20]
Lanier 2009	17	421	18	207	71.0%	0.46 [0.24, 0.88]
Milgrom 2001	0	225	5	109	21.8%	0.04 [0.00, 0.79]
Total (95% CI)		854		527	100.0%	0.35 [0.20, 0.64]
Total events	17		25			

Heterogeneity: $Chi^2 = 2.81$. $df = 2$ ($P = 0.25$); $I^2 = 29\%$

Test for overall effect: $Z = 3.44$ ($P = 0.0006$)

Mean asthma exacerbations per patient (with 95% confidence interval) of eligible studies comparing omalizumab with placebo at the end of the stable-steroid phase.



(c)

Study or Subgroup	Omalizumab Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Busse 2011	0.3	0.25	208	0.49	0.35	211	34.5%	–0.19 [–0.25, –0.13]
Lanier 2009	0.78	0.3	384	1.36	0.7	192	33.0%	–0.58 [–0.68, –0.48]
Milgrom 2001	0.42	0.3	216	0.72	0.55	101	32.5%	–0.30 [–0.41, –0.19]
Total (95% CI)			808			504	100.0%	–0.35 [–0.59, –0.12]

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 41.54$, df = 2 ($P < 0.00001$); $I^2 = 95\%$

Test for overall effect: Z = 2.92 (P = 0.003)

- Nuevas realidades
- Manejo del asma en menores de 5 años
- Manejo en escolares y adolescentes
- Conclusiones


NOT EVERYTHING THAT
LOOKS LIKE ASTHMA IS ASTHMA

Principal findings of systematic reviews for chronic treatment in childhood asthma

José A. Castro Rodríguez MD, Gustavo J. Rodrigo MD & Carlos E. Rodríguez-Martínez MD.

Journal of Asthma, 52:4, 407-416 - 2015

Table 2. Principal findings of the 39 SRCTs included according to the international asthma guideline's steps [2,3].

Outcomes	Step 1	Step 2	Step 3	Steps 4 and 5
Reduction of severe exacerbations	SABA = IB SABA = SABA + IB	ICS > LTRA ICS > cromones ICS > xanthines FP = HFA-DBP or ciclosenide Daily = intermittent ICS Moderate = low ICS doses	ICS + LTRA = ICS ICS + LABA = ICS ICS + LABA = 2ICS	ICS + OMA > ICS
Improvement of clinical outcomes	SABA = IB SABA = SABA + IB	ICS > LTRA ICS > cromones ICS > xanthines FP = HFA-DBP or ciclosenide Daily > intermittent ICS Moderate = low ICS doses	ICS + LTRA = ICS ICS + LABA = ICS ICS + LABA = 2ICS	
Improvement of lung function parameters	SABA = IB SABA = SABA + IB	ICS > LTRA ICS > cromones Daily > intermittent ICS Moderate > low ICS doses FP > BDP or BUD FP = HFA-BDP or ciclosenide	ICS + LTRA > ICS ICS + LABA > ICS ICS + LABA > 2ICS	

ıan); = (equal to); + (plus), 2 (double doses). BDP, beclomethasone dipropionate; BUD, budesonide; FP, fluticasone propionate; ICS, ɔrticosteroids; HFA, hydrofluoroalkane; IB, ipratropium bromuro; LABA, long acting beta2-agonits; OMA, omalizumab; SABA, short-a2-agonists; SRCTs, systematic reviews of randomized clinical trials.

> (better t
inhaled c
acting be

Muchas Gracias

Antonio Berni (1905-1981).

Algoritmo Predictor Asma (Asthma Predict Index)

*Premio Mundial Investigación

Montreal 2002

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute
2007

International Union Against Tuberculosis and Lung Disease

Sibilancias frecuentes

(> 3 episodios/año en primeros 3 años vida)

+

GLOBAL INITIATIVE FOR ASTHMA 2006

1 criterio mayor ó 2 criterios menores

- Criterios mayores:
  - *Diagnóstico médico de eczema* (<3 a)
  - *Antecedente asma padres*
- Criterios menores:
  - *Diagnóstico médico de rinitis alérgica* (<3a)
  - *Sibilancias no asociada de resfríos*(<3a)
  - *Eosinofilia ≥4%*

Castro-Rodríguez JA, et al AJRCCM 2000

Table 1. The Modified Asthma Predictive Index[2]

Major criteria	Minor criteria
Parental history of asthma	Allergic sensitization to egg, milk, or peanut
Physician-diagnosed atopic dermatitis	Wheezing apart from colds
Allergic sensitization to ≥1 aeroallergens	Blood eosinophilia (eosinophil count, ≥4%)

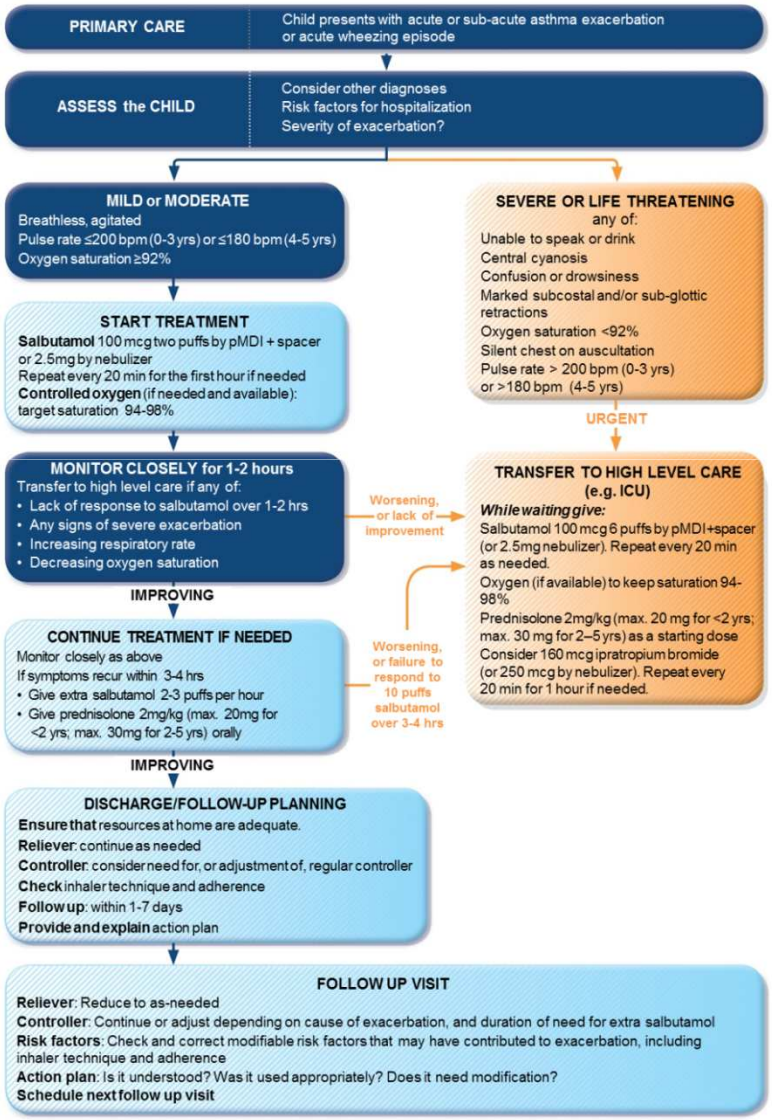
Chipps B. Ann Allergy Asthma Immunol 2010;104

A very interesting precedent
The ERS 2008 Guideline

	Episodic Viral Wheeze	Multi Trigger Wheeze
Wheeze episodes	Only with URTIs	With URTIs, but also with other triggers
Interval symptoms	No	Yes, with other triggers
Response to ICS	-	++
Response to montelukast	+	+
Many people think:		
Allergy	Thought to play no role	Important driver/trigger
Long-term outcome	Transient wheeze	Persistent wheeze

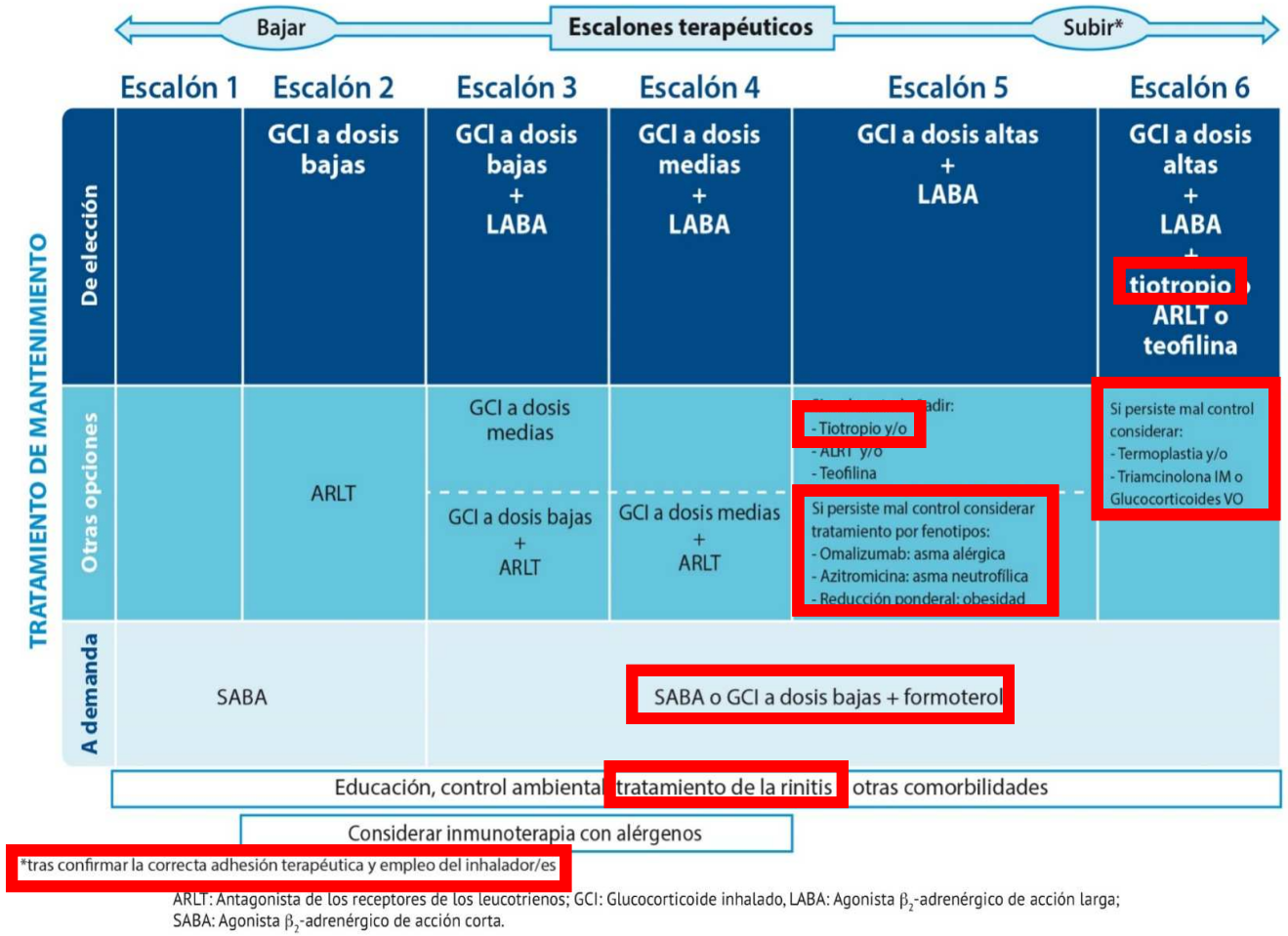
Brand PLP, *et al. Eur Respir J* 2008;32:1096-1110

Primary care management of acute asthma or wheezing in pre-schoolers



NEW!

Tratamiento de mantenimiento adultos – GEMA 2015

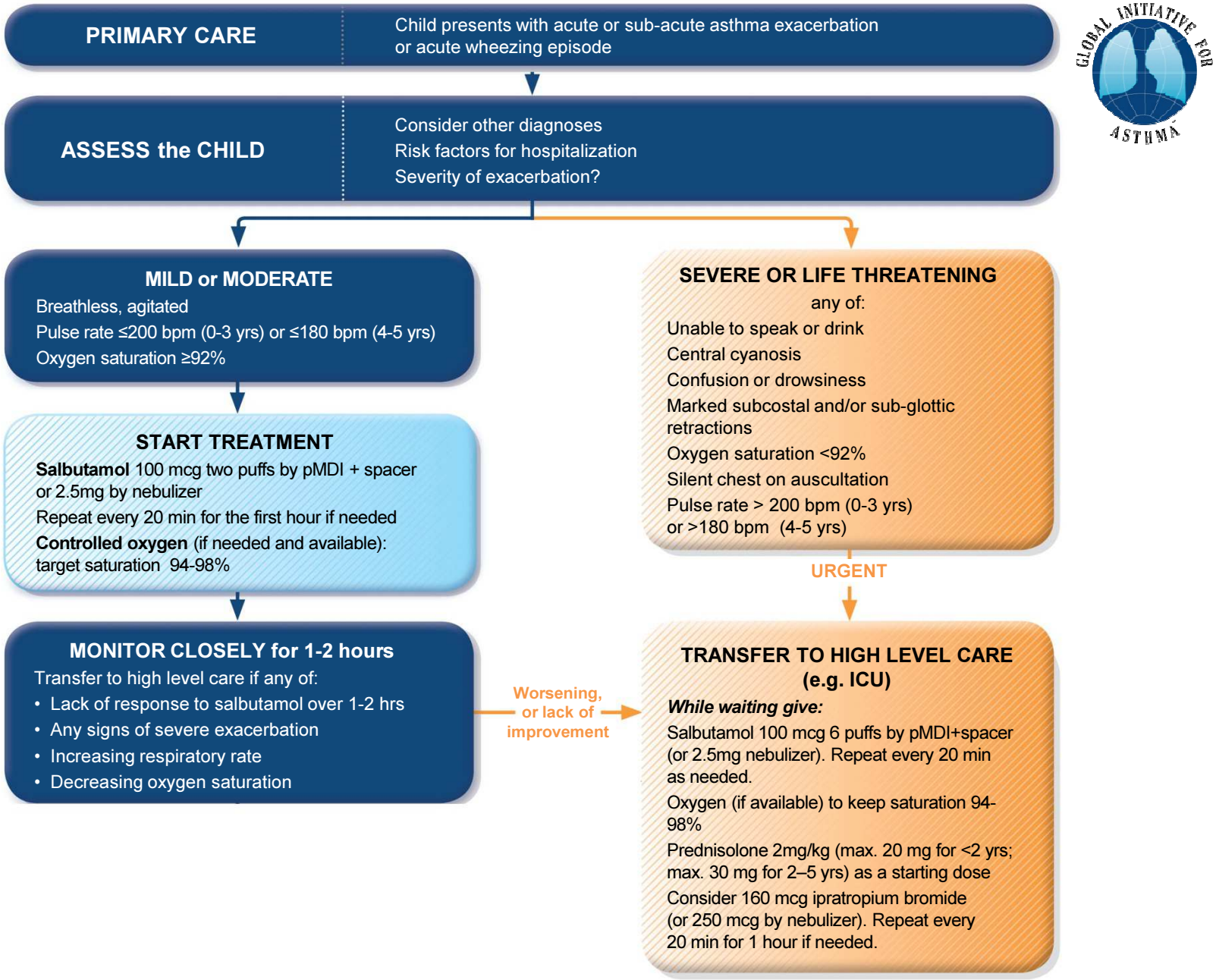


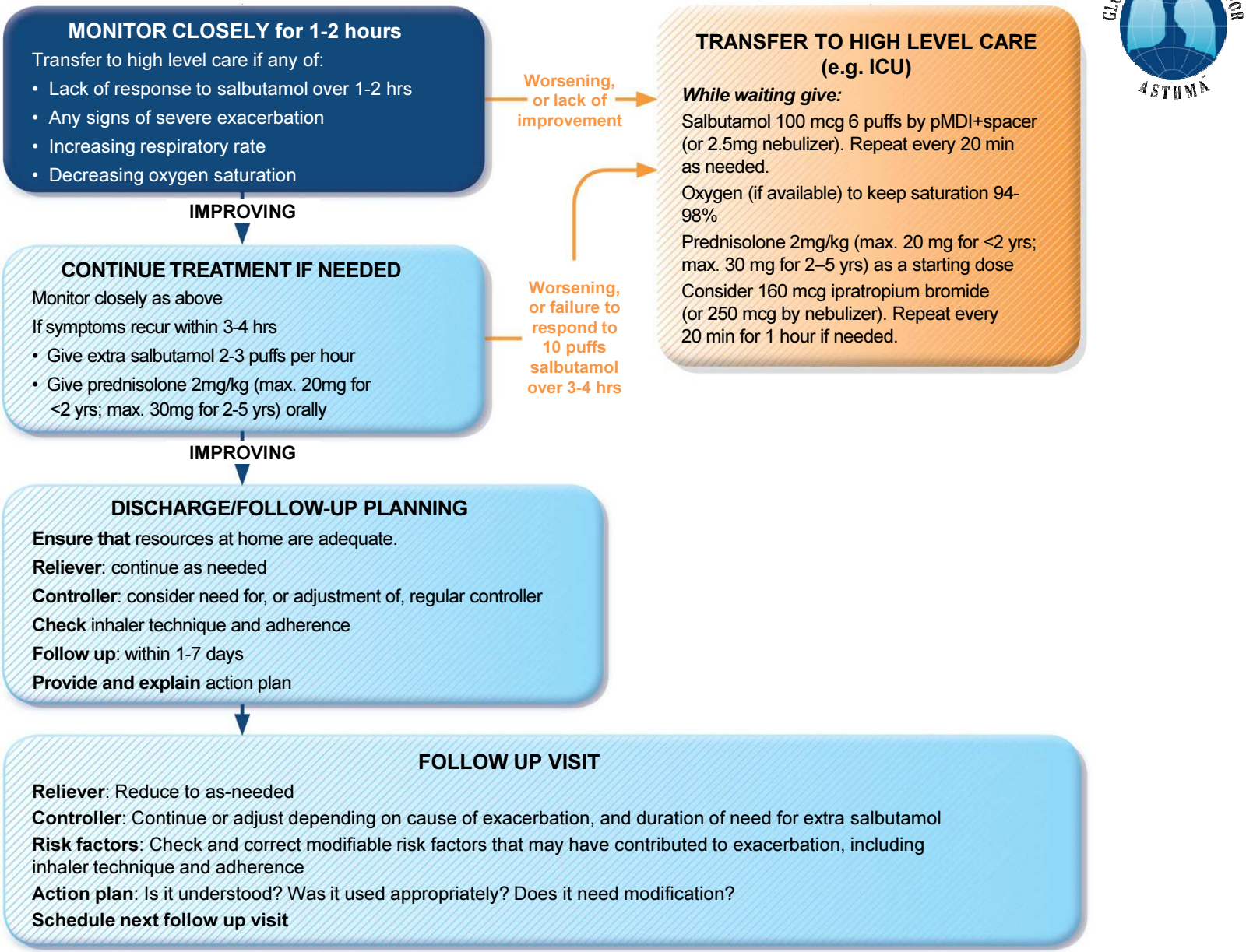
ARLT: Antagonista de los receptores de los leucotrienos; GCI: Glucocorticoide inhalado, LABA: Agonista β_2-adrenérgico de acción larga; SABA: Agonista β_2-adrenérgico de acción corta.

(DMMA) de los aerosoles generados por los diferentes dispositivos – GEMA 2015

	Depósito pulmonar (%)		Depósito orofaríngeo (%)		DMMA (µm)
	in vivo	*in vitro*	*in vivo*	*in vitro*	
pMDI					
pMDI convencional	7,8-34	-	53,9-82,2	-	1,4-8
pMDI convencional + cámara inhalación	11,2-68,3	-	31,2	40	2-3,2
pMDI autodisparo	50-60	-	30	-	-
Modulite®	31-34	-	33-58	-	1-2
Alvesco®	50-52	-	32,9	-	-
Respimat®	40-53	-	19,3-39	-	-
DPI (por orden alfabético)					
Accuhaler®	7,6-18	15-30	-	-	3,5
Aerolizer®	13-20	21,7-28	73	-	1,9-7,9
Breezhaler®	36	39	-	45	2,8
Easyhaler®	18,5-31	29	-	-	-
Genuair®	30,1	-	54,7	-	-
Handihaler®	17,8	17,3-22	-	71	3,9
Inhalador Ingelheim®	16	-	59	-	-
Nexthaler®	56	-	43	-	1,4-1,5
Spinhaler®	11,5	-	30,9	-	-
Turbuhaler®	14,2-38	28	53-71,6	57,3-69,3	1,7-5,4
Twisthaler®	36-37	-	-	-	2-2,2

Tomado de la Normativa SEPAR-ALAT terapia inhalada. Arch Bronconeumol 2013





Initial assessment of acute asthma exacerbations in children ≤5 years

Symptoms	Mild	Severe*
Altered consciousness	No	Agitated, confused or drowsy
Oximetry on presentation (SaO_2)**	>95%	<92%
Speech†	Sentences	Words
Pulse rate	<100 beats/min	>200 beats/min (0–3 years) >180 beats/min (4–5 years)
Central cyanosis	Absent	Likely to be present
Wheeze intensity	Variable	Chest may be quiet

*Any of these features indicates a severe exacerbation
**Oximetry before treatment with oxygen or bronchodilator
† Take into account the child's normal developmental capability

Indications for immediate transfer to hospital for children ≤5 years

Transfer immediately to hospital if ANY of the following are present:

Features of severe exacerbation at initial or subsequent assessment

- Child is unable to speak or drink
- Cyanosis
- Subcostal retraction
- Oxygen saturation <92% when breathing room air
- Silent chest on auscultation

Lack of response to initial bronchodilator treatment

- Lack of response to 6 puffs of inhaled SABA (2 separate puffs, repeated 3 times) over 1-2 hours
- Persisting tachypnea* despite 3 administrations of inhaled SABA, even if the child shows other clinical signs of improvement

Unable to be managed at home

- Social environment that impairs delivery of acute treatment
- Parent/carer unable to manage child at home

*Normal respiratory rates (breaths/minute): 0-2 months: <60; 2-12 months: <50; 1-5 yrs: <40

Initial management of asthma exacerbations in children ≤5 years

Therapy	Dose and administration
Supplemental oxygen	24% delivered by face mask (usually 1L/min) to maintain oxygen saturation 94-98%
Inhaled SABA	2–6 puffs of salbutamol by spacer, or 2.5mg by nebulizer, every 20 min for first hour, then reassess severity. If symptoms persist or recur, give an additional 2-3 puffs per hour. Admit to hospital if >10 puffs required in 3-4 hours.
Systemic corticosteroids	Give initial dose of oral prednisolone (1-2mg/kg up to maximum of 20mg for children <2 years; 30 mg for 2-5 years)

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Systemic corticosteroids	Give initial dose of oral prednisolone (1-2mg/kg up to maximum of 20mg for children <2 years; 30 mg for 2-5 years)
Additional options in the first hour of treatment	
Ipratropium bromide	For moderate/severe exacerbations, give 2 puffs of ipratropium bromide 80mcg (or 250mcg by nebulizer) every 20 minutes for one hour only
Magnesium sulfate	Consider nebulized isotonic $MgSO_4$ (150mg) 3 doses in first hour for children ≥2 years with severe exacerbation

Primary prevention of asthma

GINA Global Strategy for Asthma Management and Prevention 2015

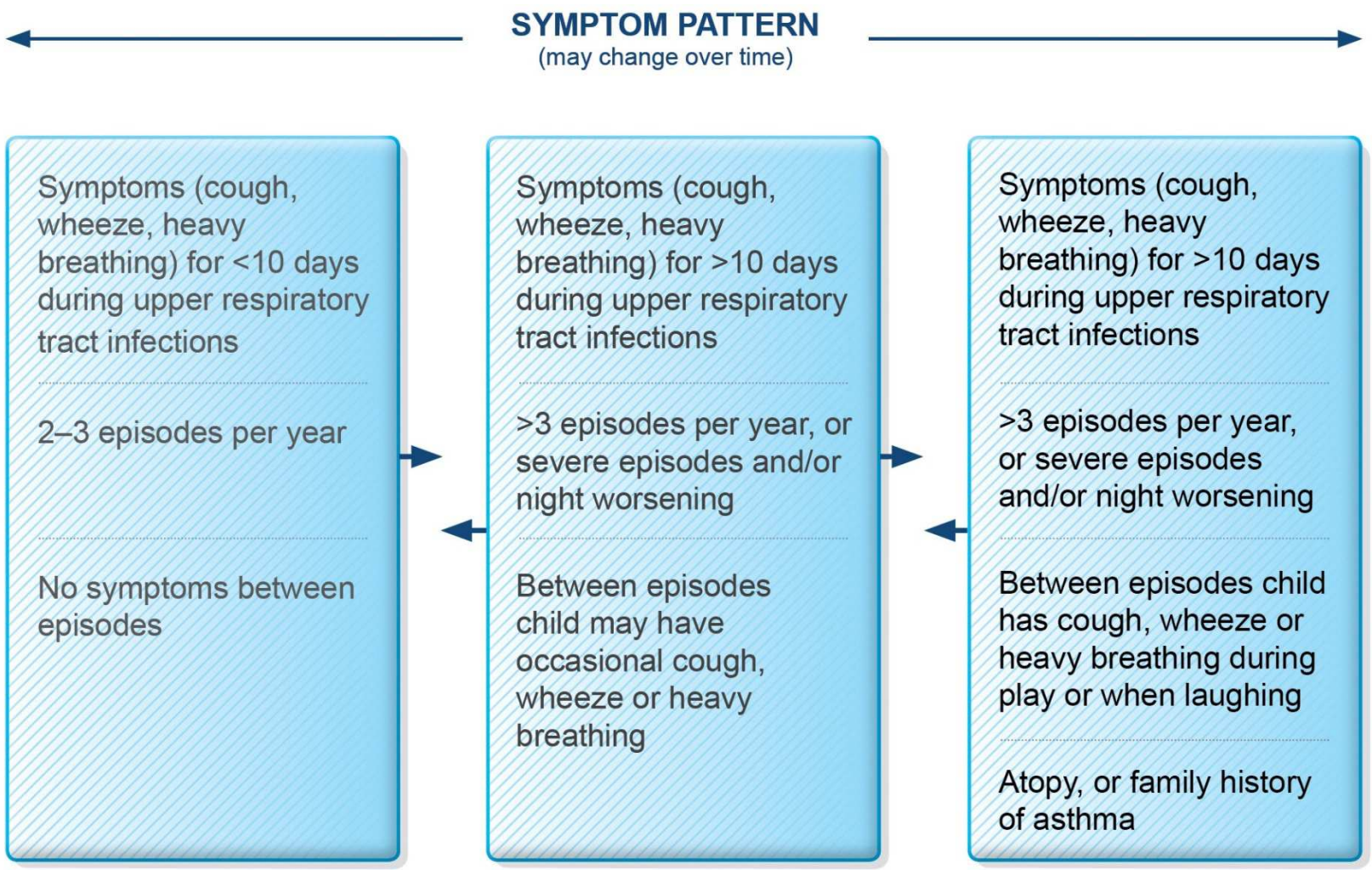
Primary prevention of asthma

- The development and persistence of asthma are driven by gene-environment interactions
- For children, a 'window of opportunity' exists *in utero* and in early life, but intervention studies are limited
- For intervention strategies including allergen avoidance
  - Strategies directed at a single allergen have not been effective
  - Multifaceted strategies may be effective, but the essential components have not been identified
- Current recommendations are
  - Avoid exposure to tobacco smoke in pregnancy and early life
  - Encourage vaginal delivery
  - Advise breast-feeding for its general health benefits
  - Where possible, avoid use of paracetamol (acetaminophen) and broad-spectrum antibiotics in the first year of life

Principales Guías Clínicas sobre Asma

GUIA CLINICA	Ultima edición	Páginas	Comentarios
GINA	GINA Diciembre 2007	96	Pocket Guide (Asma en niños y adultos) de 28 páginas Disponible en ppt http://www.ginasthma.org
U.S. Department of Health and Human Services National Institutes of Health National Heart, Lung, and Blood Institute	NAEPP-EPR 3 Agosto 2007	415	No Pocket Guide No disponible en ppt http://www.nhlbi.nih.gov/guidelines/index.htm
	British Guideline Mayo 2008	94	No Pocket Guide Disponible en ppt http://www.brit-thoracic.org.uk/guidelines.html
PRACTALL EAACI and AAAAI Consensus Report	Enero 2008	30	Consenso de Diagnóstico y Tratamiento del Asma en Niños. Allergy 2008;63(1):5-34 http://www.blackwell-synergy.com

Symptom patterns in children ≤5 years



Features suggesting asthma in children ≤5 years

Feature	Characteristics suggesting asthma
Cough	Recurrent or persistent non-productive cough that may be worse at night or accompanied by some wheezing and breathing difficulties. Cough occurring with exercise, laughing, crying or exposure to tobacco smoke in the absence of an apparent respiratory infection
Wheezing	Recurrent wheezing, including during sleep or with triggers such as activity, laughing, crying or exposure to tobacco smoke or air pollution
Difficult or heavy breathing or shortness of breath	Occurring with exercise, laughing, or crying
Reduced activity	Not running, playing or laughing at the same intensity as other children; tires earlier during walks (wants to be carried)
Past or family history	Other allergic disease (atopic dermatitis or allergic rhinitis) Asthma in first-degree relatives
Therapeutic trial with low dose ICS and as-needed SABA	Clinical improvement during 2–3 months of controller treatment and worsening when treatment is stopped

Common differential diagnoses of asthma in children ≤5 years

Condition	Typical features
Recurrent viral respiratory infections	Mainly cough, runny congested nose for <10 days; wheeze usually mild; no symptoms between infections
Gastroesophageal reflux	Cough when feeding; recurrent chest infections; vomits easily especially after large feeds; poor response to asthma medications
Foreign body aspiration	Episode of abrupt severe cough and/or stridor during eating or play; recurrent chest infections and cough; focal lung signs
Tracheomalacia or bronchomalacia	Noisy breathing when crying or eating, or during URTIs; harsh cough; inspiratory or expiratory retraction; symptoms often present since birth; poor response to asthma treatment
Tuberculosis	Persistent noisy respirations and cough; fever unresponsive to normal antibiotics; enlarged lymph nodes; poor response to BD or ICS; contact with someone with TB
Congenital heart disease	Cardiac murmur; cyanosis when eating; failure to thrive; tachycardia; tachypnea or hepatomegaly; poor response to asthma medications

Common differential diagnoses of asthma in children ≤5 years (continued)

Condition	Typical features
Cystic fibrosis	Cough starting shortly after birth; recurrent chest infections; failure to thrive (malabsorption); loose greasy bulky stools
Primary ciliary dyskinesia	Cough and recurrent mild chest infections; chronic ear infections and purulent nasal discharge; poor response to asthma medications; situs inversus (in ~50% children with this condition)
Vascular ring	Respirations often persistently noisy; poor response to asthma medications
Bronchopulmonary dysplasia	Infant born prematurely; very low birth weight; needed prolonged mechanical ventilation or supplemental oxygen; difficulty with breathing present from birth
Immune deficiency	Recurrent fever and infections (including non-respiratory); failure to thrive

Risk factors for poor asthma outcomes in children ≤5 years

Risk factors for exacerbations in the next few months

- Uncontrolled asthma symptoms
- One or more severe exacerbation in previous year
- The start of the child's usual 'flare-up' season (especially if autumn/fall)
- Exposures: tobacco smoke; indoor or outdoor air pollution; indoor allergens (e.g. house dust mite, cockroach, pets, mold), especially in combination with viral infection
- Major psychological or socio-economic problems for child or family
- Poor adherence with controller medication, or incorrect inhaler technique

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Risk factors for fixed airflow limitation

- Severe asthma with several hospitalizations
- History of bronchiolitis

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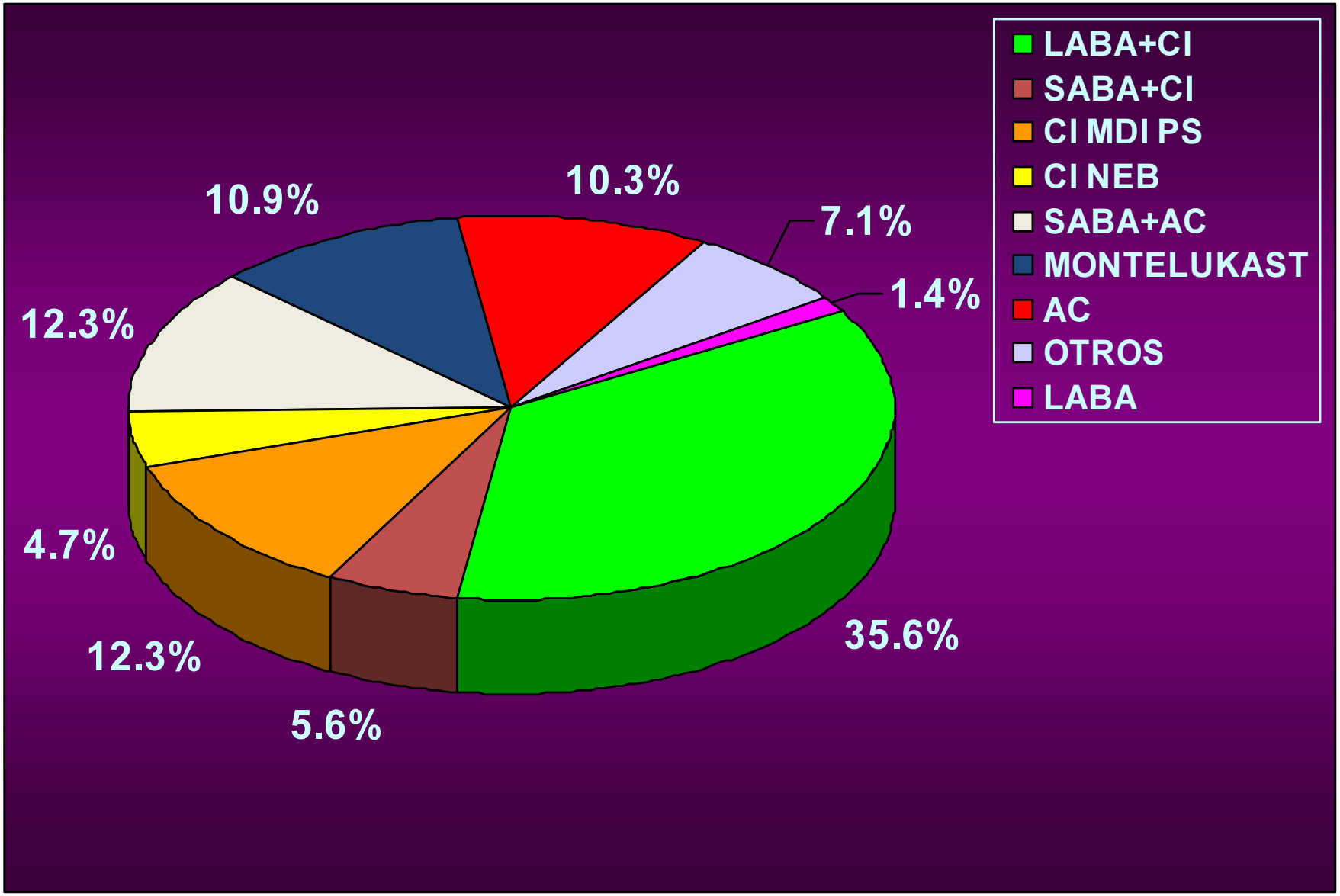
Risk factors for fixed airflow limitation

- Severe asthma with several hospitalizations
- History of bronchiolitis

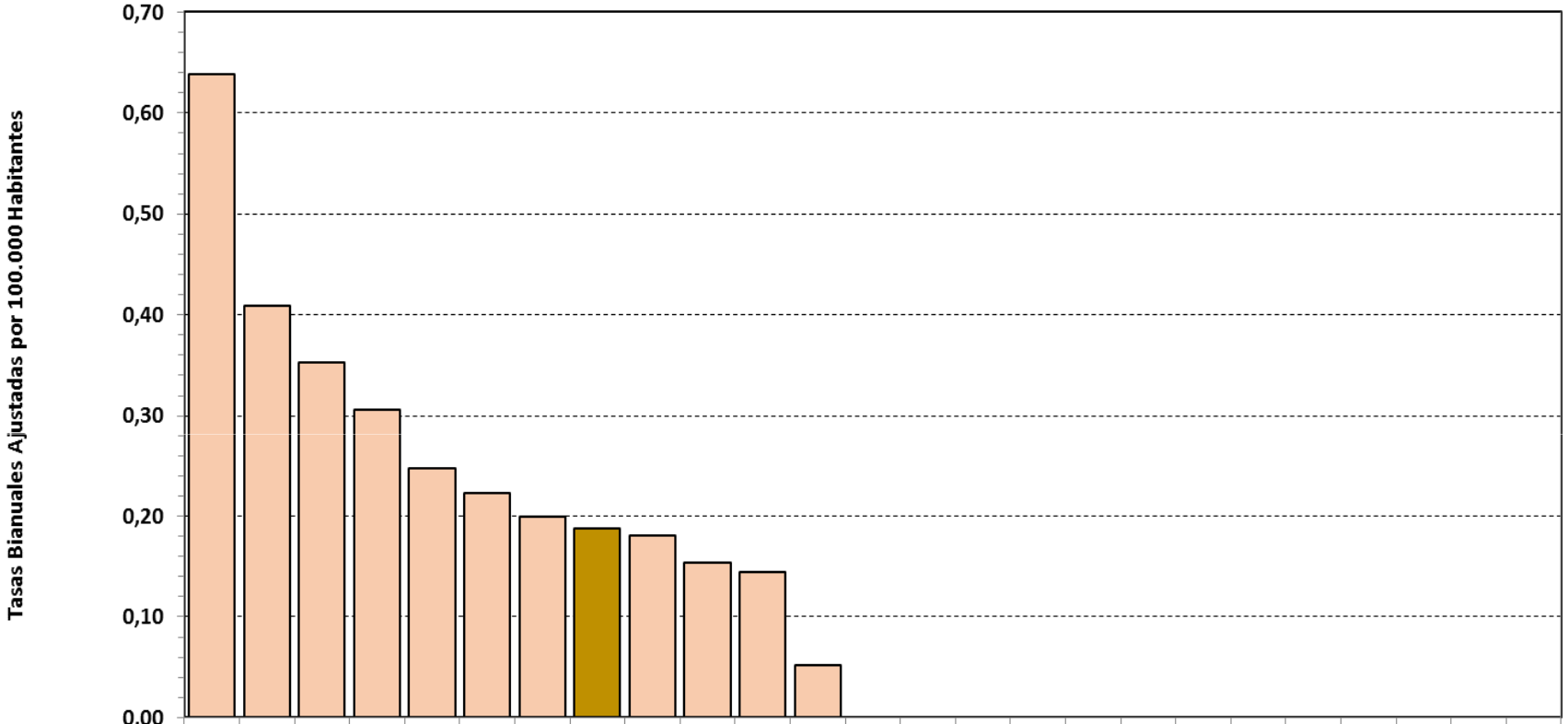
Risk factors for medication side-effects

- Systemic: Frequent courses of OCS; high-dose and/or potent ICS
- Local: moderate/high-dose or potent ICS; incorrect inhaler technique; failure to protect skin or eyes when using ICS by nebulizer or spacer with face mask

FÁRMACOS ASMA Y EPOC - ARGENTINA 2012 (IMS)



Mortalidad por Asma (J45-J46) en Población de 5 a 39 Años de Ambos Sexos, por Jurisdicción. Defunciones, Tasas Crudas y Ajustadas por Edad y Sexo por 100.000 Habitantes. Argentina, Bienio 2013-2014



	FOR	CHA	MIS	CBA	BUE	LAR	ENR	ARG	SFE	COR	CABA	TUC	CAT	CHU	JUJ	LAP	MEN	NEU	RNO	SAL	SJU	SLU	STU	SGO	TFU
Tasas Ajustadas	0,64	0,41	0,35	0,31	0,25	0,22	0,20	0,19	0,18	0,15	0,14	0,05	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
2013	1	2	4	7	23	1	0	44	4	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
2014	3	3	1	5	22	0	3	46	3	2	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tasas Crudas	0,59	0,37	0,35	0,31	0,25	0,23	0,21	0,19	0,19	0,16	0,17	0,05	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00

Jurisdicción

Fuente: Información Procesada en el Instituto Nacional de Enfermedades Respiratorias (INER) "Emilio Coni", Administración Nacional de Laboratorios e Institutos de Salud (ANLIS), con base en datos de la Dirección de Estadísticas e Información de Salud, Ministerio de Salud de la Nación, República Argentina, Marzo de 2016.

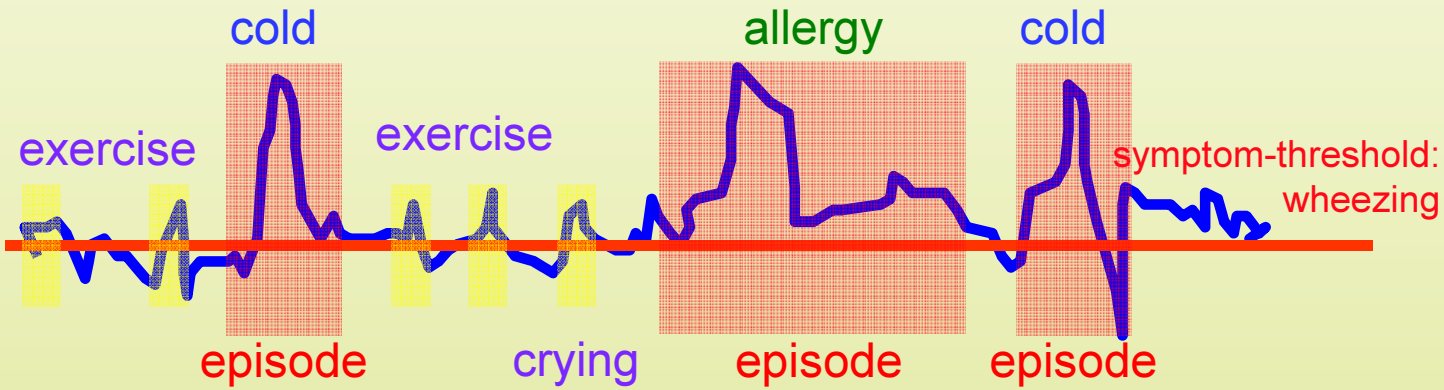
Defining clinical phenotypes

- Transient wheezing symptoms associated with viral colds
- Discrete episodes, with the child being well between episodes

➔ ***Episodic (viral) wheeze***

Brand PLP, *et al. Eur Respir J* 2008;32:1096-1110

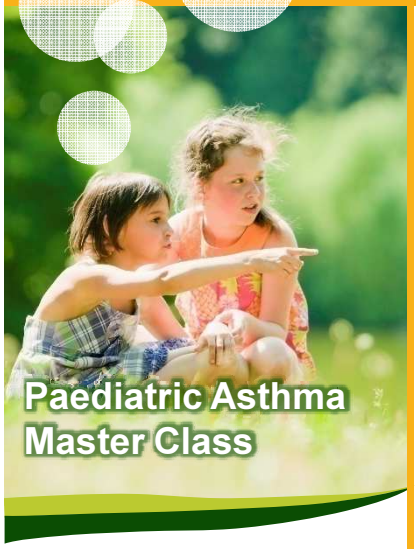
Defining clinical phenotypes



- Wheeze also between (viral) episodes
- Wheeze in response to other triggers than infection

➔ *Multiple-trigger wheeze*

Brand PLP, *et al. Eur Respir J* 2008;32:1096-1110



Supporting GSK on World Asthma Day

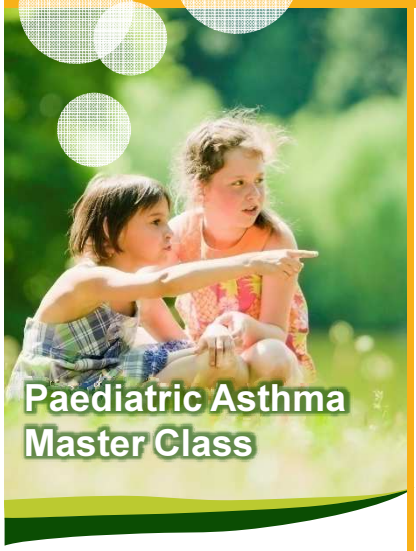
Organised and funded by

Asthma in small children: the diagnostic dilemma

Many children wheeze during infancy - only some will have asthma

- Asthma diagnosis can be challenging in young children!
  - Heterogeneity
  - Overlapping diseases
  - Objective assessment difficult to impossible

- Asthma diagnosis is important in young children
  - Severe episodes of asthma begin in early childhood
  - **Early treatment may influence disease course**
  - Frequent symptoms, exacerbations, hospitalizations



Supporting GSK on World Asthma Day

Organised and funded by

Preschool asthma is different

Table 1. Natural history and pathophysiologic changes of asthma by age

	Age (y)			
	<5	5-11	12-17	≥18
Prevalence by sex	M > F	M > F	Before puberty: M > F After puberty: F > M	F > M
Predominant effector cell	Neutrophil Eosinophil	Eosinophil	Eosinophil	Eosinophil Significance of neutrophils in some patients controversial phenotypes
RBM thickening	Begins after the first birthday	Not as thick as adults	Thickening approaches that seen in adults	Established
Lung function findings	Lung function measures difficult to obtain	Lung function changes associated with duration of asthma symptoms	Lung function deficits present in those patients who began wheezing before age 3y but might not be present in those who began wheezing in later childhood	Progressive decrease in lung function can occur, irreversible airway obstruction might also be seen
Incidence of exacerbations	++++	+++	++	++

Szefler SJ, *et al. Asthma across the ages: Knowledge gaps in childhood asthma. J Allergy Clin Immunol* 2014;133(1):3-14.
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