CLÍNICA LAS CONDES

FACULTAD DE MEDICINA
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Asma

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Definición

- Enfermedad inflamatoria crónica de la vía aérea
- Diversas células: mastocitos, eosinòfilos, linfocitos T
- Hiperreactividad bronquial
- Sibilancias, tos y disnea
- Obstrucción al flujo aéreo variable y reversible
- Remodelación

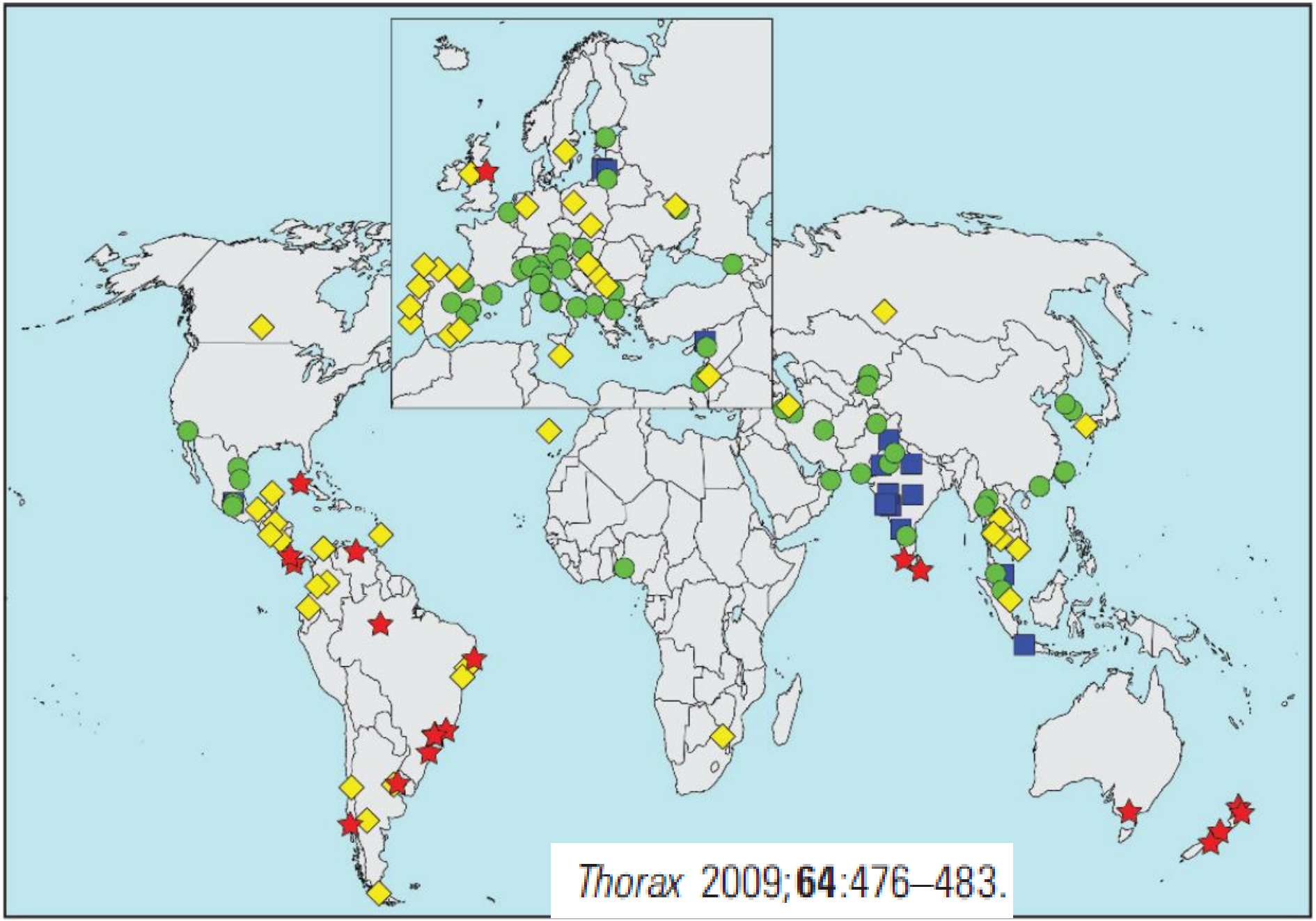


Figure 3 Prevalence of current wheeze in the 6–7 year age group. See text for definition of current wheeze. The symbols indicate prevalence values of <5% (blue square), 5 to <10% (green circle), 10 to <20% (yellow diamond) and >20% (red star).

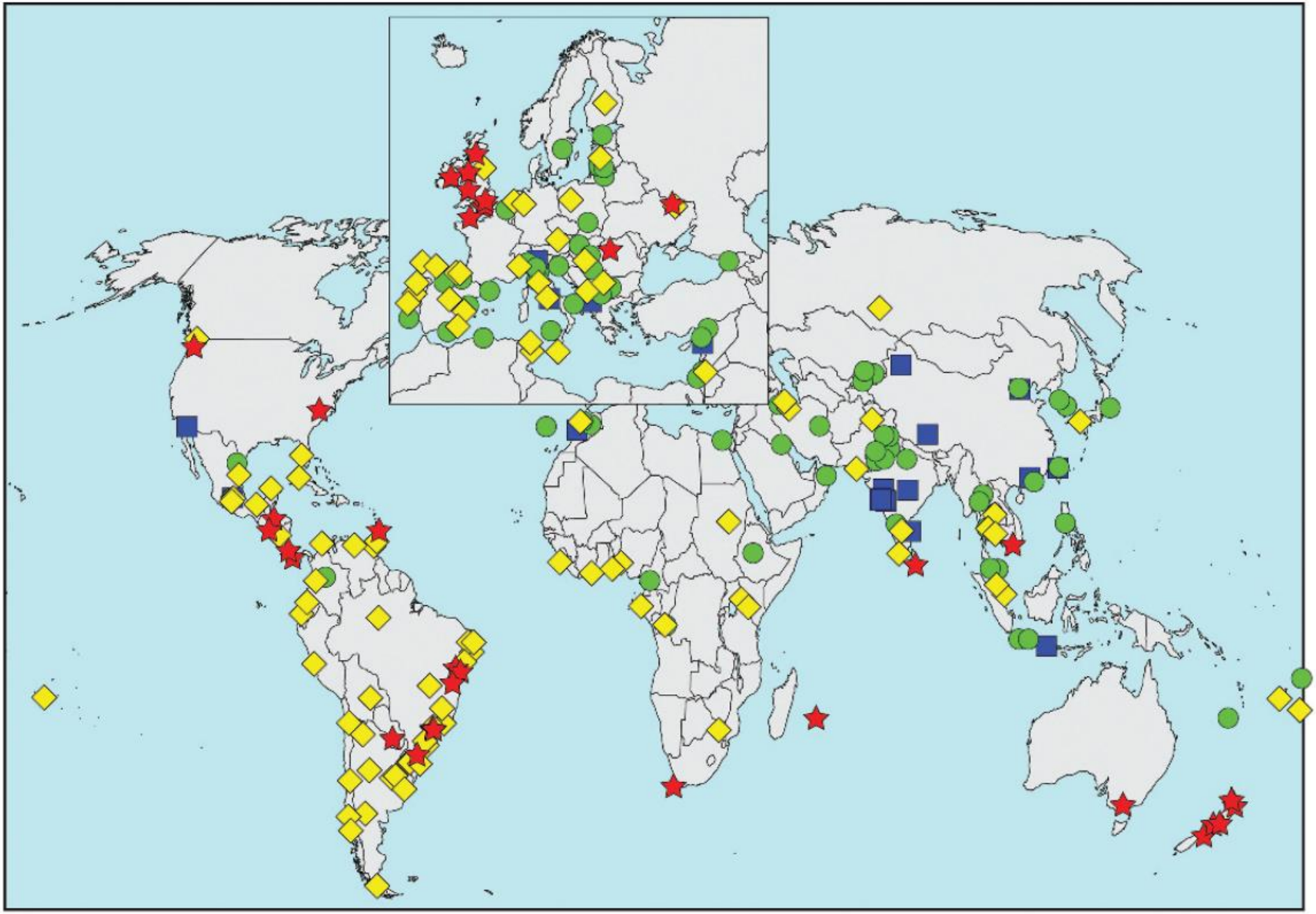


Figure 1 Prevalence of current wheeze according to the written questionnaire in the 13–14 year age group. See text for definition of current wheeze. The symbols indicate prevalence values of <5% (blue square), 5 to <10% (green circle), 10 to <20% (yellow diamond) and >20% (red star).

Worldwide trends in the burden of asthma symptoms in school-aged children: Global Asthma Network Phase I cross-sectional study

- Usa metodología ISAAC y compara con estudios ISAAC fase I (1993-1995) y fase III (2001-2003)
- 6-7 años y 13-14 años
- 119.795 participantes, 27 centros, 14 países
- 74.361 adolescentes (13-14ª)
- 45.434 niños (6-7ª)
- Adolescentes tienen mas prevalencia de asma pero menos asma severo

Lancet 2021; 398: 1569–80

	Number of individuals*	Wheeze in past 12 months			Asthma ever			Severe asthma symptoms in past 12 months			Exercise wheeze in past 12 months			Night cough in past 12 months		
		Prevalence, %*	Absolute change per decade, %†	SE change†	Prevalence, %*	Absolute change per decade, %†	SE change†	Prevalence, %*	Absolute change per decade, %†	SE change†	Prevalence, %*	Absolute change per decade, %†	SE change†	Prevalence, %*	Absolute change per decade, %†	SE change†
Africa and Eastern Mediterranean																
Nigeria (Ibadan)	2897	10·6%	−1·4%	−1·0	3·7%	−4·8%	−5·3	6·2%	−1·3%	−1·2	32·0%	−1·3%	−0·7	23·6%	−2·5%	−1·8
South Africa (Cape Town)	3979	21·3%	0·6%	0·5	16·6%	1·4%	1·5	12·0%	1·7%	2·7	36·0%	2·2%	1·3	41·4%	3·1%	2·4
Sudan (Khartoum)	1785	5·7%	−4·8%	−3·9	18·2%	1·9%	1·2	3·5%	−2·7%	−3·2	28·1%	9·6%	3·4	40·4%	14·4%	7·2
Syria (Lattakia)	1215	19·8%	7·7%	4·4	10·9%	2·8%	4·9	10·6%	4·7%	4·3	35·8%	13·6%	4·6	54·4%	19·4%	8·6
Region total	9876	15·1%	0·7%	NA	12·4%	0·1%	NA	8·6%	0·8%	NA	33·4%	5·4%	NA	37·6%	6·2%	NA
Americas																
Chile (South Santiago)	2750	13·4%	−2·7%	−3·2	13·7%	−1·7%	−2·4	3·9%	−1·4%	−3·2	16·7%	−3·0%	−3·5	32·9%	−5·7%	−5·6
Costa Rica (Costa Rica)	1338	20·8%	−4·1%	−3·9	22·0%	−0·7%	−0·6	9·4%	−2·7%	−3·7	14·4%	−3·3%	−4·4	31·2%	3·0%	2·7
Ecuador (Quito)	3000	6·3%	−7·2%	−6·5	4·5%	−1·5%	−2·5	3·0%	−1·4%	−2·5	18·2%	4·8%	3·3	28·0%	12·7%	9·4

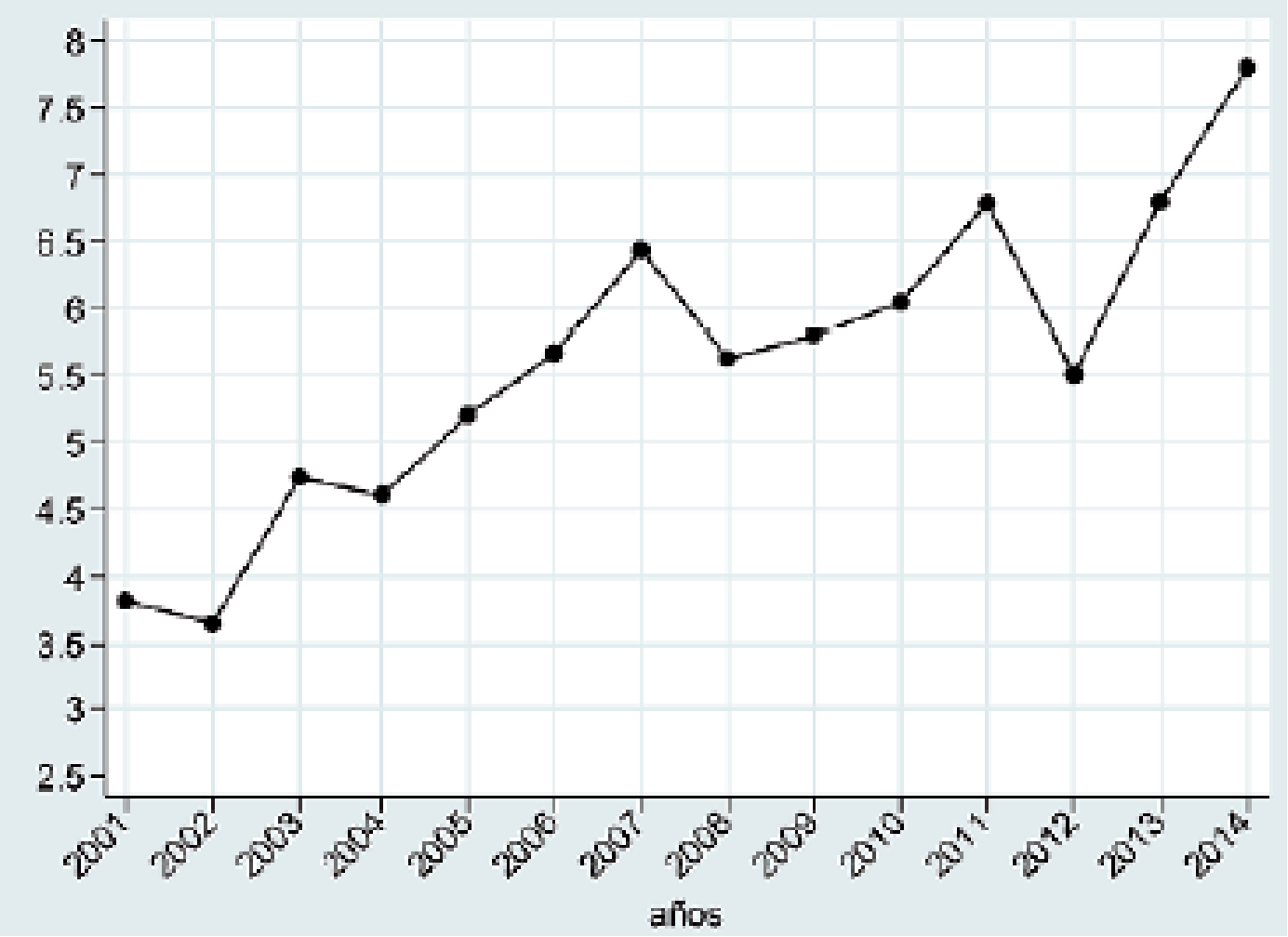
(Table 2 continues on next page)

Epidemiología

- 300 millones de asmáticos en el mundo
- Enfermedad crónica mas frecuente de la infancia
- 1° causa de ausentismo escolar
- Aumento de hospitalizaciones por Asma
- 2001. 3.8/10.000
- 2014. 7.8/10.000
- 5 fallecidos => 0.02%

Rev Chil Pediatr. 2017;88(XX):

Hospitalizaciones por asma infantil en Chile: 2001-2014



Rev Chil Pediatr. 2017;88(XX):

Diagnóstico de Asma

¿Como se realiza el diagnóstico?

Es **clínico** y se basa en los siguientes principios fundamentales:

- Presencia de historia clínica y/o examen físico sugerentes de asma: síntomas episódicos de obstrucción al flujo aéreo.
- Demostración de obstrucción al flujo aéreo con reversibilidad total o parcial a los broncodilatadores.
- Exclusión de otros diagnósticos (diagnóstico diferencial) (Ver tabla 1)

Ministerio de Salud. Guía Clínica Asma bronquial moderada y grave en menores de 15 años. Minsal, 2011.

Clínica

- Tos crónica o recurrente de predominio nocturno
- Sibilancias, tos y disnea con ejercicio, llanto, risa o resfríos
- Síntomas de Atopia
- Antecedentes familiares
- Respuesta a medicamentos

1. ¿Ha tenido algún episodio de silbido al pecho en el último año?
2. ¿Ha presentado tos persistente, silbido al pecho o dificultad respiratoria en la noche?
3. ¿Ha tenido tos o silbido al pecho relacionados con ejercicio, llanto o risa?
4. ¿Ha presentado tos o silbido al pecho cuando se ha expuesto a alergenos o contaminantes?
5. ¿Ha tenido episodios de bronquitis en forma recurrente? ¿Duran éstos más de diez días?
6. ¿Existen antecedentes de alergia, rinitis alérgica o asma en familiares directos como padres y/o hermanos?

Ministerio de Salud. Guía Clínica Asma bronquial moderada y grave en menores de 15 años. Minsal, 2011.

¿Qué esperamos en la espirometría de un asmático?

- Alteración ventilatoria obstructiva
- Cambio significativo y reversibilidad post-b2:
- VEF1: 12% y/o >200cc
- FEF 25-75: 30%

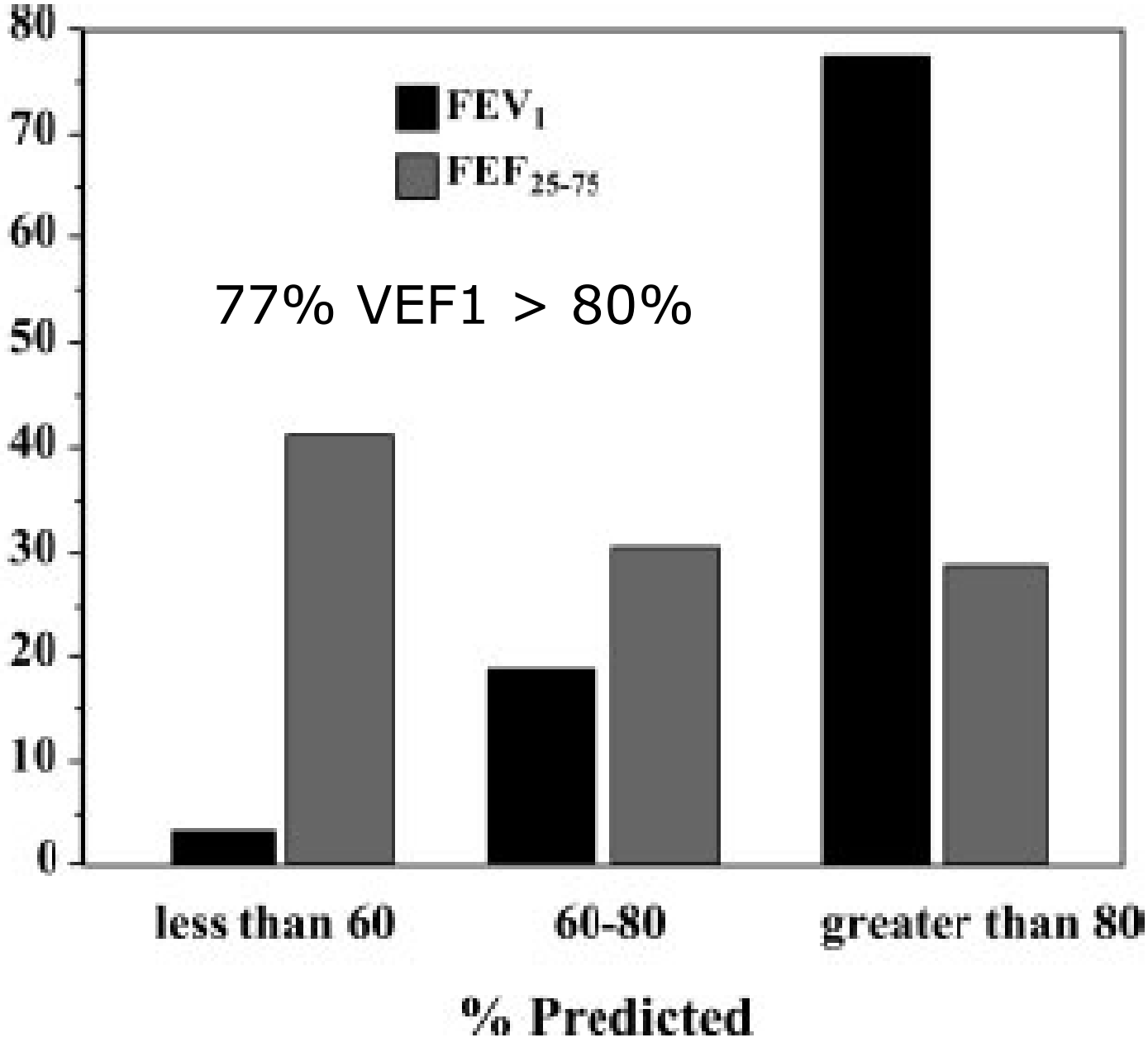
Rev Chil Enf Respir 2007; 23: 31-42

¿Y que encontramos?

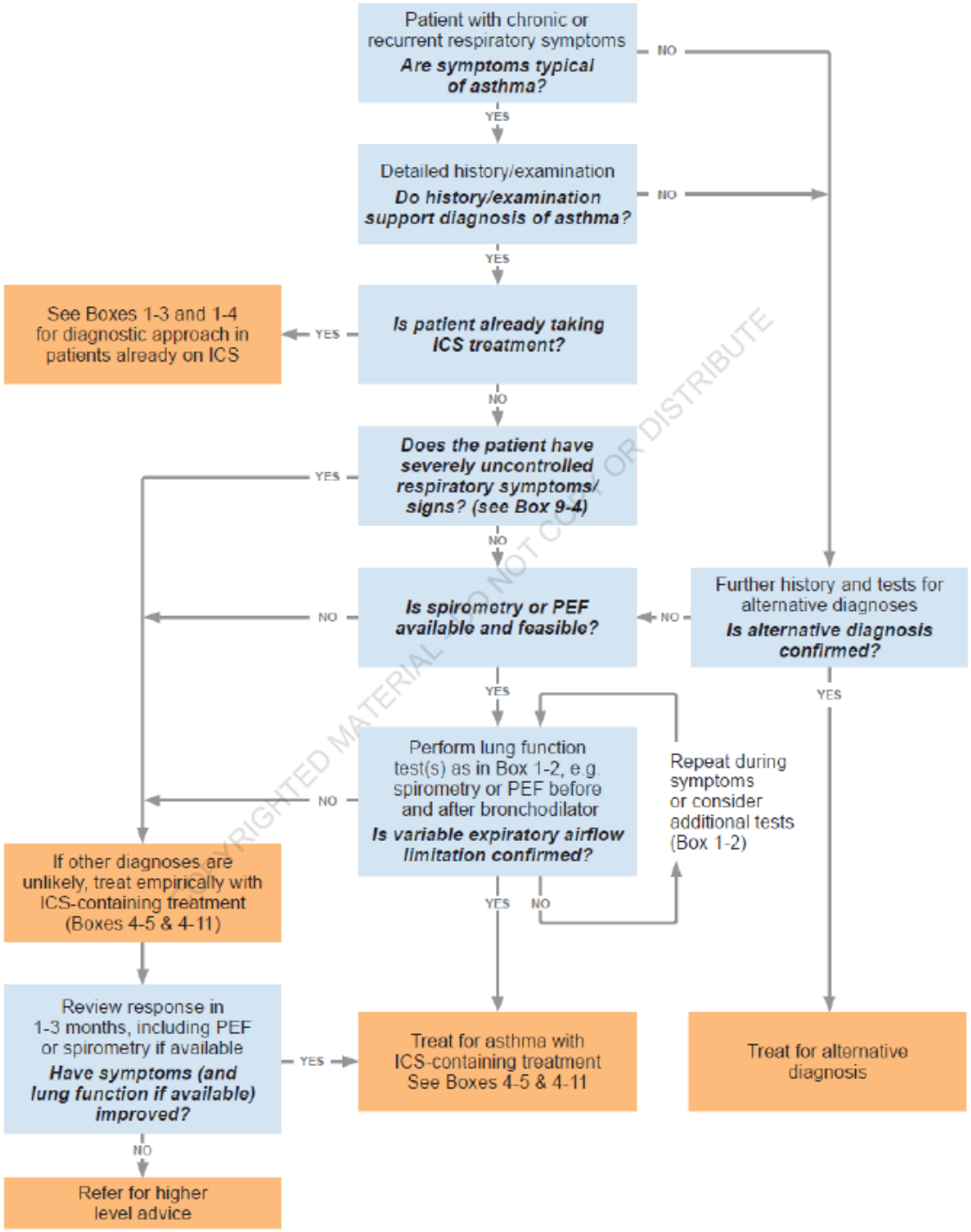
- 24.000 espirometrias en 2700 niños asmáticos de 4-18 años

FVC (% predicted)	92.2 ± 18.0
FEV_1 (% predicted)	92.7 ± 16.2
FEV_1/FVC ratio (%)	85.3 ± 9.3
FEF_{25-75} (% predicted)	78.0 ± 36.5
Peak expiratory flow (% predicted)	87.8 ± 31.3

Pediatric Pulmonology 39:311–317 (2005)


80
70
60
50
40
30
20
10
0
FEV1
FEF25-75
77% VEF1 > 80%
less than 60
60-80
greater than 80
% Predicted

GINA 2024


Patient with chronic or recurrent respiratory symptoms
Are symptoms typical of asthma?
NO
YES
Detailed history/examination
Do history/examination support diagnosis of asthma?
NO
YES
See Boxes 1-3 and 1-4 for diagnostic approach in patients already on ICS
YES
Is patient already taking ICS treatment?
NO
Does the patient have severely uncontrolled respiratory symptoms/ signs? (see Box 9-4)
YES
NO
Is spirometry or PEF available and feasible?
NO
Further history and tests for alternative diagnoses
Is alternative diagnosis confirmed?
YES
YES
Perform lung function test(s) as in Box 1-2, e.g. spirometry or PEF before and after bronchodilator
Is variable expiratory airflow limitation confirmed?
NO
Repeat during symptoms or consider additional tests (Box 1-2)
YES
NO
If other diagnoses are unlikely, treat empirically with ICS-containing treatment (Boxes 4-5 & 4-11)
Review response in 1-3 months, including PEF or spirometry if available
Have symptoms (and lung function if available) improved?
YES
Treat for asthma with ICS-containing treatment See Boxes 4-5 & 4-11
Treat for alternative diagnosis
NO
Refer for higher level advice

Clasificación

Tabla 3. Clasificación de asma según severidad

	Episódica *Infrecuente*	Episódica *Frecuente*	*Persistente*
Número de exacerbaciones	5 o menos al año	6 o más al año	Semanales
Síntomas nocturnos	No.	Ocasionales	Frecuentes
Períodos intercríticos	Asintomáticos	Tos y sibilancias ocasionales	Tos y sibilancias persistentes
Tos inducida por ejercicio en intercrisis	No	Si	Persistente
Ausentismo escolar	No	Frecuente. sumado 1 mes al año)	Frecuente.(Sumado > 1 mes al año)
Consultas de Urgencia (oxígeno y corticoides)	No	Ocasionales Máximo 2	Frecuentes
Hospitalizaciones (cuadro respiratorio).	No	Infrecuentes 1 al año sin UTI	Frecuentes, o UTI
PEF o VEF1	Normal	Normal *	Alterada

Nota: cualquier paciente que tenga 2 o más criterios de la columna de mayor severidad debe ser catalogado como tal.

MINISTERIO DE SALUD. ***Guía Clínica Infección Respiratoria Aguda Baja de Manejo Ambulatorio en menores de 5 años***. 1st Ed. Santiago: Minsal, 2005.

Clasificación

Clasificación de asma según severidad (GINA 2005)

	Síntomas diurnos	**Síntomas nocturnos**	**PEF o VEF1 Variabilidad PEF**
Nivel 1 Leve Intermitente	< 1 vez semana Exacerbaciones breves Asintomático y PEF normal entre crisis	≤ 2 veces al mes	≥ 80% < 20%
Nivel 2 Leve Persistente	> 1 vez por semana, pero < 1 vez al día Exacerbaciones que pueden afectar la actividad física y el sueño Tos por ejercicio	> 2 veces mes	≥ 80% 20-30%
Nivel 3 Moderada Persistente	Síntomas diarios Exacerbaciones que comprometen la actividad física y el sueño Uso diario de ß2 agonista de acción corta	> 1 vez a la semana	60-80% > 30%
Nivel 4 Severa Persistente	Síntomas continuos Exacerbaciones frecuentes Limitación de la actividad física	Frecuente	≤ 60% > 30%

A. Asthma symptom control		Level of asthma symptom control		
In the past 4 weeks, has the patient had:		**Well controlled**	**Partly controlled**	**Uncontrolled**
• Daytime asthma symptoms more than twice/week?	Yes☐ No☐	None of these	1–2 of these	3–4 of these
• Any night waking due to asthma?	Yes☐ No☐			
• Reliever needed for symptoms* more than twice/week?	Yes☐ No☐			
• Any activity limitation due to asthma?	Yes☐ No☐			

B. Risk factors for poor asthma outcomes

Assess risk factors at diagnosis and periodically, particularly for patients experiencing exacerbations.

Measure FEV_1 at start of treatment, after 3–6 months of controller treatment to record the patient's personal best lung function, then periodically for ongoing risk assessment.

Having uncontrolled asthma symptoms is an important risk factor for exacerbations.[81]

Additional potentially modifiable risk factors for flare-ups (exacerbations), even in patients with few symptoms,† include:

- Medications: High SABA use[82] (with increased mortality if >1 x 200-dose canister/month[83]); inadequate ICS: not prescribed ICS; poor adherence;[84] incorrect inhaler technique[85]
- Comorbidities: obesity;[86,87] chronic rhinosinusitis;[87,88] GERD;[87] confirmed food allergy;[89] pregnancy[90]
- Exposures: smoking;[91] allergen exposure if sensitized;[91] air pollution.[92-94]
- Context: Major psychological or socioeconomic problems[95]
- Lung function: low FEV1, especially <60% predicted[91,96]; high bronchodilator reversibility[87,97,98]
- Other tests in patients with Type 2 inflammation: blood eosinophils;[87,97,99]; elevated FENO (in adults with allergic asthma taking ICS)[100]

Other major independent risk factors for flare-ups (exacerbations)

- Ever intubated or in intensive care unit for asthma[101]
- ≥1 severe exacerbation in last 12 months[102]

Having any of these risk factors increases the patient's risk of exacerbations *even if they have few asthma symptoms*

Risk factors for developing persistent airflow limitation

- History: preterm birth, low birth weight and greater infant weight gain;[103] chronic mucus hypersecretion[104,105]
- Medications: lack of ICS treatment[106]
- Exposures: tobacco smoke;[104] noxious chemicals; occupational exposures[36]
- Investigations: low initial FEV_1;[105] sputum or blood eosinophilia[105]

Risk factors for medication side-effects

- Systemic: frequent OCS; long-term, high dose and/or potent ICS; also taking P450 inhibitors[107]
- Local: high-dose or potent ICS;[107,108] poor inhaler technique[109]

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Tratamiento

Tratamiento. Pilares.

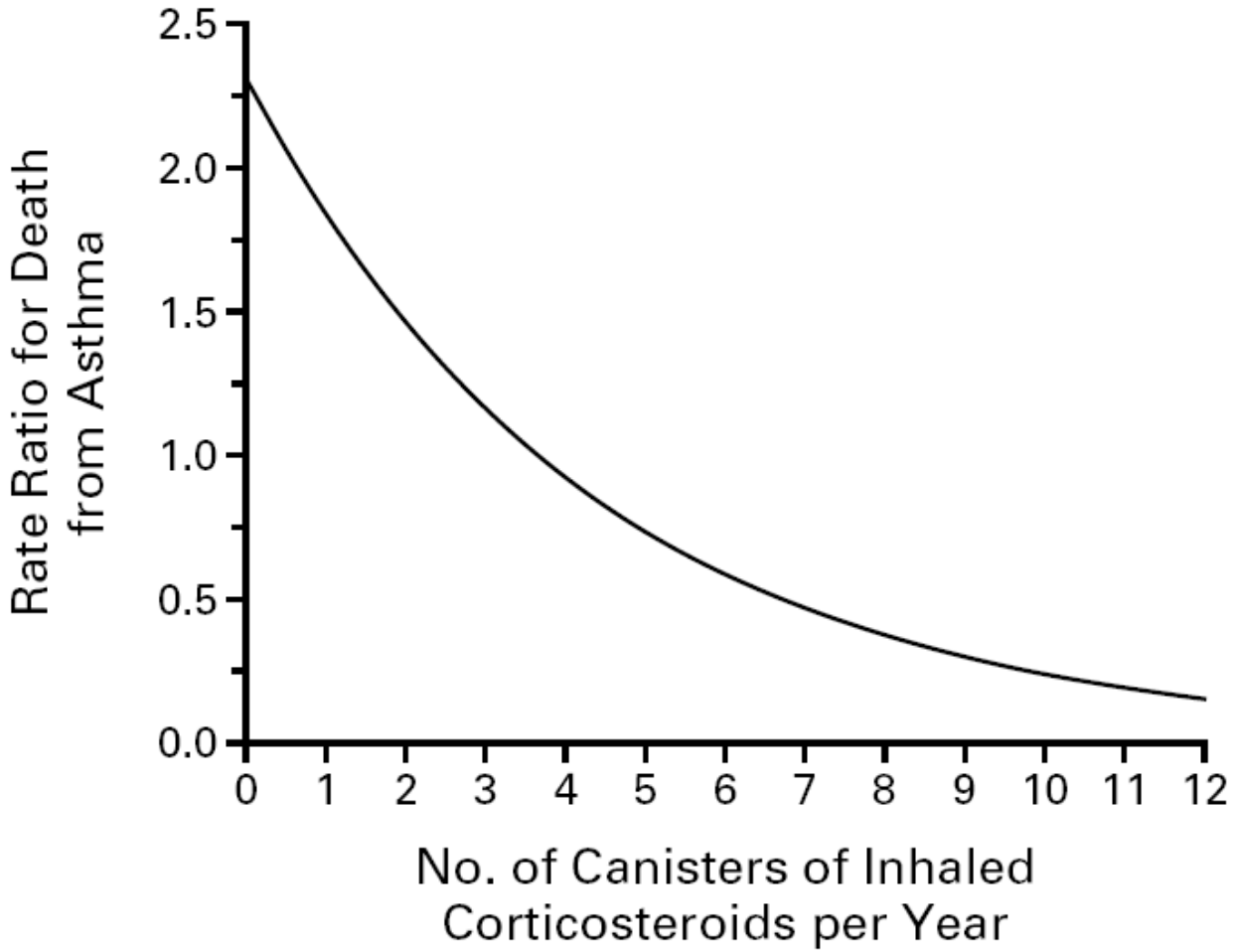
- Educación
- Medicamentos

Educación

- Información clínica
- Técnica inhalatoria
- Reconocimiento y manejo inicial de exacerbaciones
- Manejo ambiental
- Cumplimiento de tratamiento
- Autocuidado. PEF

LOW-DOSE INHALED CORTICOSTEROIDS AND THE PREVENTION OF DEATH FROM ASTHMA

SAMY SUISSA, PH.D., PIERRE ERNST, M.D., SERGE BENAYOUN, M.SC., MARC BALTZAN, M.D., AND BING CAI, M.SC.



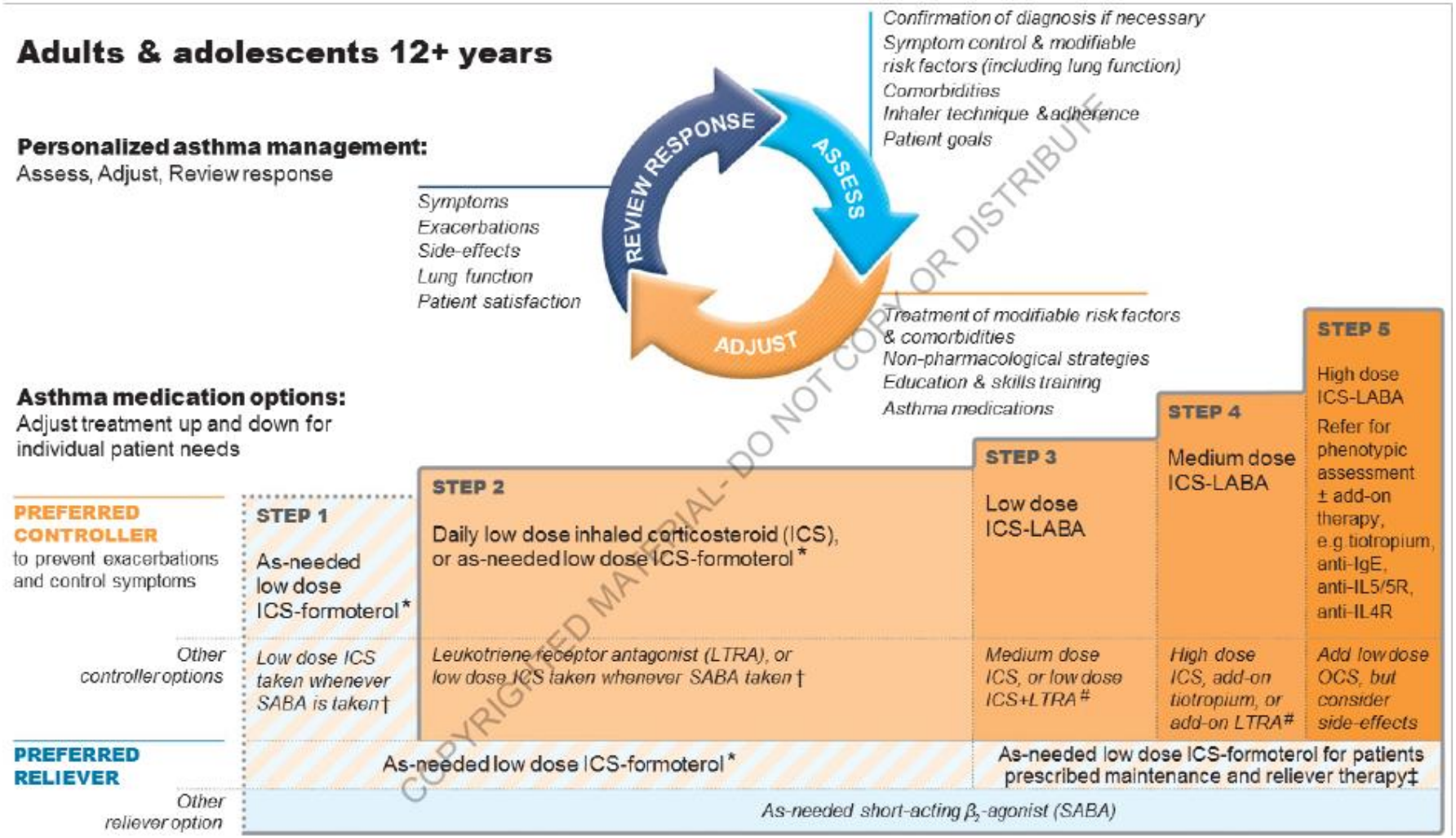
N Engl J Med 2000;343:1980

GINA 2019: a fundamental change in asthma management

Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents

Helen K. Reddel[1], J. Mark FitzGerald[2], Eric D. Bateman[3], Leonard B. Bacharier[4], Allan Becker[5], Guy Brusselle[6], Roland Buhl[7], Alvaro A. Cruz[8], Louise Fleming[9], Hiromasa Inoue[10], Fanny Wai-san Ko[11], Jerry A. Krishnan[12], Mark L. Levy[13], Jiangtao Lin[14], Søren E. Pedersen[15], Aziz Sheikh[16], Arzu Yorgancioglu[17] and Louis-Philippe Boulet[18]

Box 3-5A. Personalized management for adults and adolescents to control symptoms and minimize future risk



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“El tratamiento solo con salbutamol mata”

Higher use of SABA is associated with adverse clinical outcomes

- Dispensing of ≥3 canisters per year (i.e. daily use) is associated with higher risk of severe exacerbations *(Stanford, AAAI 2012; Nwaru, ERJ 2021)*
- Dispensing of ≥12 canisters per year is associated with much higher risk of death *(Suissa, AJRCCM 1994; Nwaru, ERJ 2021)*

LA TERCERA

QUÉ PASA

Inhalador azul: piden terminar su uso en Chile por estudios que muestran poca eficacia para tratar asma

Cristina Pérez

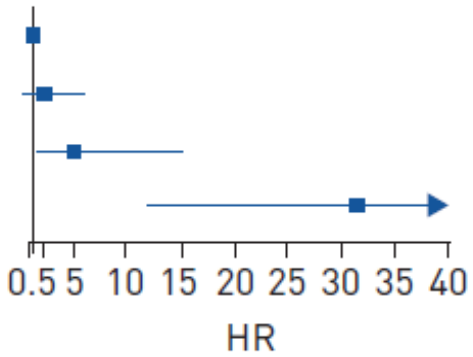
3 MAY 2023 05:04 PM

Overuse of short-acting β_2-agonists in asthma is associated with increased risk of exacerbation and mortality: a nationwide cohort study of the global SABINA programme

- Registro sueco de despacho de medicamentos y muertes.
- 365.324 asmáticos mayores de 12 años

b)

Base-period SABA use	Patients/deaths n/n	HR (95% CI)
≤2 canisters	254 500/7	1.00
3–5 canisters	76 619/4	1.70 (0.49–5.88)
6–10 canisters	27 065/5	4.70 (1.47–15.04)
≥11 canisters	7140/12	31.72 (11.88–84.70)



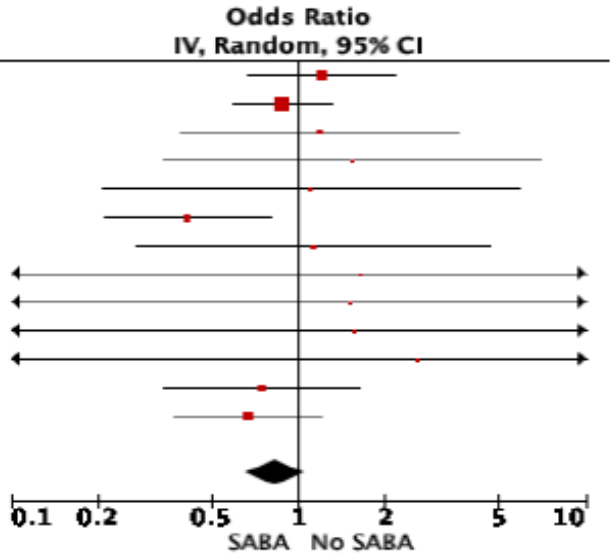
Eur Respir J 2020; 55: 1901872

Short Acting Beta Agonist Use Associated with Increased Mortality and Morbidity in Asthma Patients: A Systematic Review and Meta-Analysis

- 14 estudios, 28 179 pacientes
- Sin diferencias en muerte, ingreso UCI, hospitalización ni exacerbaciones

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Anderson HR, 2004	0.19	0.3	15.7%	1.21 [0.67, 2.18]
Castle W, 1993	−0.13	0.2	35.3%	0.88 [0.59, 1.30]
Crane J, 1989	0.17	0.57	4.4%	1.19 [0.39, 3.62]
Crane J*, 1989	0.43	0.77	2.4%	1.54 [0.34, 6.95]
Grainger J, 1991	0.1	0.85	2.0%	1.11 [0.21, 5.85]
Miller BD, 1989	−0.89	0.34	12.2%	0.41 [0.21, 0.80]
Pearce N, 1990	0.12	0.72	2.7%	1.13 [0.27, 4.62]
Pearce N, 2009	0.5	4.64	0.1%	1.65 [0.00, 14679.88]
Spitzer WO, 1992 (albuterol nebulizer)	0.42	3.2	0.1%	1.52 [0.00, 805.84]
Spitzer Wo, 1992 (albutrol)	0.45	1.68	0.5%	1.57 [0.06, 42.21]
Spitzer WO, 1992 (Fenoterol)	0.95	6.4	0.0%	2.59 [0.00, 724885.87]
Strunk RC, 1985	−0.29	0.4	8.8%	0.75 [0.34, 1.64]
Woodman K, 1991	−0.4	0.3	15.7%	0.67 [0.37, 1.21]
Total (95% CI)			100.0%	0.83 [0.66, 1.05]

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 8.07$, df = 12 (P = 0.78); $I^2 = 0\%$
Test for overall effect: Z = 1.57 (P = 0.12)



*nebulizer

Figure 2. Forest plot for SABA use and mortality.

J Pharm Pharm Sci (www.cspsCanada.org) 25, 193 - 200, 2022

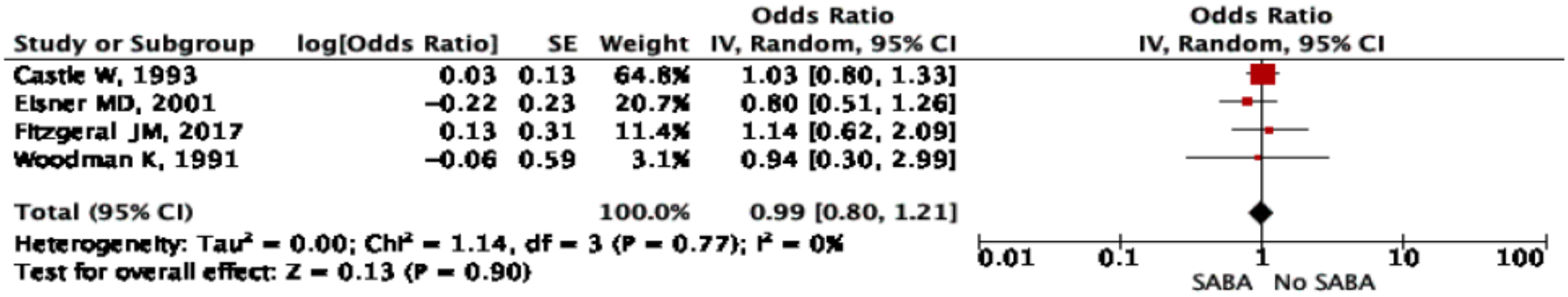


Figure 3. Forest plot for SABA use and ICU admission.

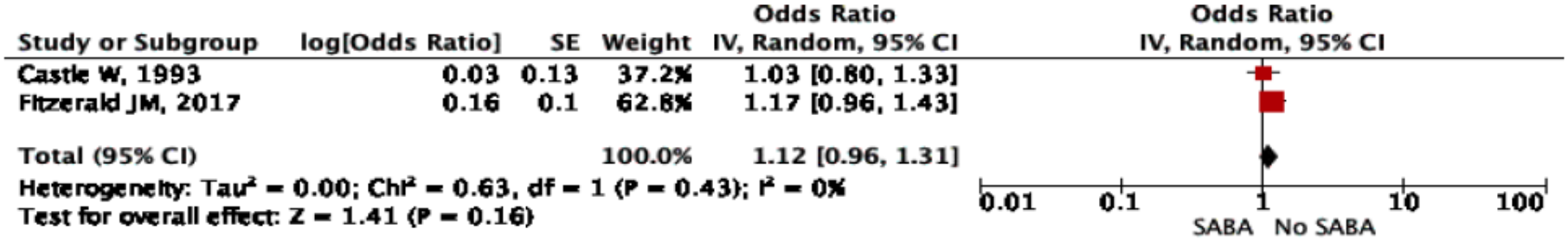


Figure 4. Forest plot for SABA use and hospitalization

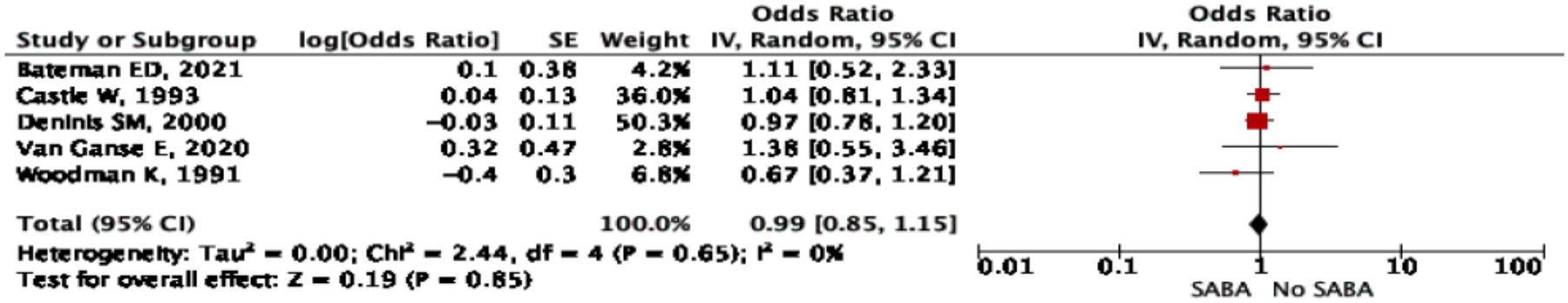


Figure 5. Forest plot for SABA use and exacerbation.

“El asma leve puede matar”

Patients with apparently mild asthma are still at risk of serious adverse events

- 30–37% of adults with acute asthma
- 16% of patients with near-fatal asthma
- 15–20% of adults dying of asthma

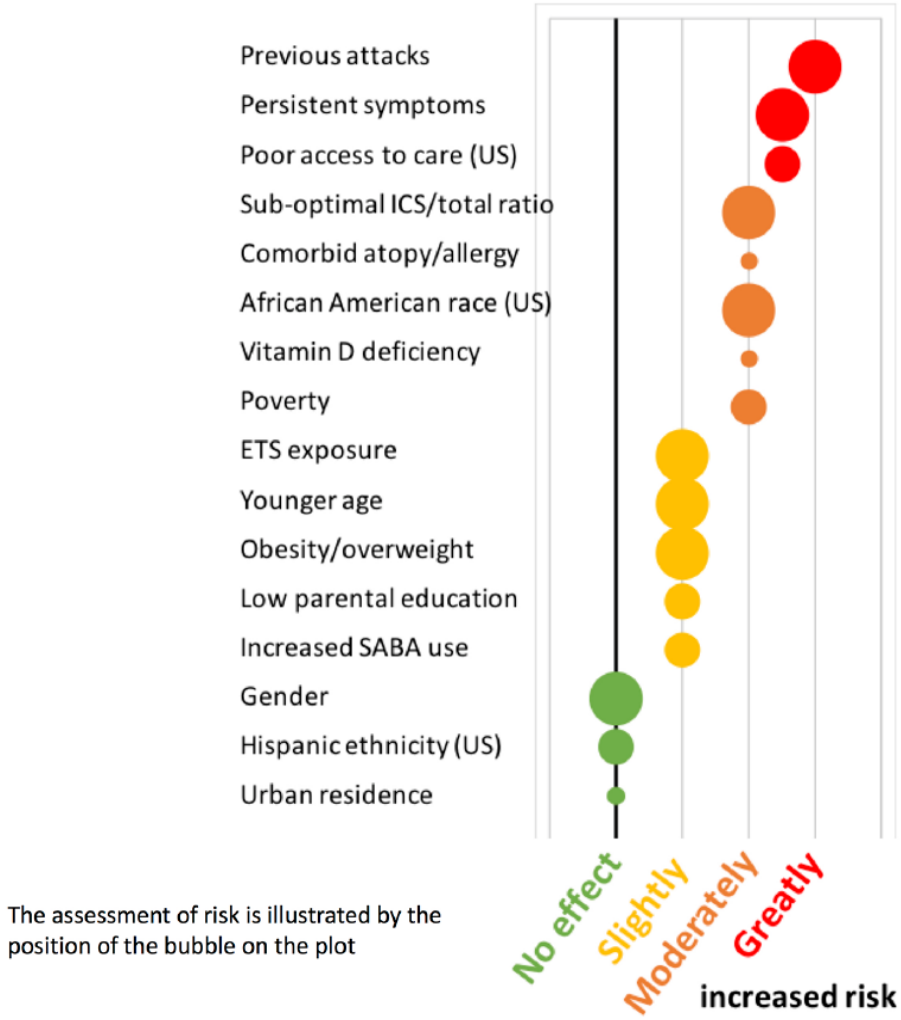
} had symptoms less than weekly in previous 3 months *(Dusser, Allergy 2007)*

A systematic review of risk factors associated with near-fatal and fatal asthma

RESULTS: Four hundred and three articles were identified, of which 27 met the inclusion criteria. Increased use of medications such as beta-agonists via metered dose inhalers (OR=1.67, 95% CI 0.99 to 2.84, P=0.057) and nebulizers (OR=2.45, 95% CI 1.52 to 3.93, P=0.0002), oral steroids (OR=2.71, 95% CI 1.34 to 5.51, P=0.006) and oral theophylline (OR=2.02, 95% CI 1.03 to 3.98, P=0.04) and a history of hospital (OR=2.62, 95% CI 1.04 to 6.58, P=0.04) and/or intensive care unit (OR=5.14, 95% CI 1.91 to 13.86, P=0.001) admissions and mechanical ventilation (OR=6.69, 95% CI 2.80 to 15.97, P=0.0001) due to asthma were predictors of NFA and FA. Prior emergency

Can Respir J Vol 12 No 5 July/August 2005

At-risk children with asthma (ARC): a systematic review



The assessment of risk is illustrated by the position of the bubble on the plot

Buelo A, *et al*. *Thorax* 2018;**73**:813–824.

Inhaled Combined Budesonide–Formoterol as Needed in Mild Asthma

- Mayores de 12 años con asma “leve”
- 1 año de duración
- 3849 pacientes. 3 grupos. 1280 pctes c/u aprox
- Salbutamol sos
- Budesonida + formoterol sos
- Budesonida permanente + sbt sos

N Engl J Med 2018;378:1865-76.

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline, According to Treatment Group.*

Characteristic	Terbutaline as Needed (N=1277)	Budesonide–Formoterol as Needed (N=1277)	Budesonide Maintenance Therapy (N=1282)	Total (N=3836)
Age — yr	40.0±16.3	39.8±16.9	39.0±16.7	39.6±16.6
Female sex — no. (%)	771 (60.4)	777 (60.8)	797 (62.2)	2345 (61.1)
Time since asthma diagnosis — yr				
Median	6.3	6.5	6.3	6.4
Range	0.5–62.4	0.4–65.7	0.5–57.1	0.4–65.7
ACQ-5 score†				
Mean score				
At trial entry	1.52±0.96	1.57±0.97	1.53±0.97	1.54±0.97
At baseline	1.54±0.95	1.61±0.97	1.55±0.96	1.57±0.96
Score ≥1.5 — no./total no. (%)				
At trial entry‡	549/1160 (47.3)	601/1174 (51.2)	568/1177 (48.3)	1718/3511 (48.9)
At baseline	602/1256 (47.9)	649/1257 (51.6)	596/1257 (47.4)	1847/3770 (49.0)
AQLQ score§	5.25±0.99	5.20±1.01	5.27±1.01	5.24±1.00
FEV_1 — % of predicted value				
Before bronchodilator use	84.13±14.08	84.18±14.24	84.23±13.91	84.18±14.07
After bronchodilator use	95.27±13.53	95.86±14.02	95.67±13.43	95.60±13.66
Peak expiratory flow ≥80% of the predicted value every morning — no./total no. (%)¶	362/1276 (28.4)	340/1277 (26.6)	376/1282 (29.3)	1078/3835 (28.1)
Bronchodilator reversibility — %	14.4±11.5	14.9±11.3	14.6±11.6	14.6±11.5
Asthma control according to pretrial treatment — no. (%)‖				
Uncontrolled with short-acting bronchodilator alone	565 (44.2)	565 (44.2)	576 (44.9)	1706 (44.5)
Controlled with inhaled glucocorticoid or leukotriene-receptor antagonist	712 (55.8)	712 (55.8)	706 (55.1)	2130 (55.5)
Severe exacerbation in previous 12 mo — no. (%)	256 (20.0)	257 (20.1)	241 (18.8)	754 (19.7)

* Plus–minus values are means ±SD. There were no significant between-group differences in the demographic or clinical characteristics at baseline. Baseline was defined as the assessment at visit 3 (i.e., the point at which randomization took place). FEV_1 denotes forced expiratory volume in 1 second.

† The Asthma Control Questionnaire (ACQ-5) consists of five questions about asthma symptoms during the previous week, each of which is scored on a range from 0 (no impairment) to 6 (maximum impairment); the minimal clinically important difference is 0.5 units. Trial entry was defined as the assessment at the visit before the run-in period (i.e., visit 1 or 2). Data at trial entry were missing for 117 patients in the terbutaline group, for 103 in the budesonide–formoterol group, and for 105 in the budesonide maintenance group; and data at baseline were missing for 21, 20, and 25 patients, respectively.

‡ These calculations for data at trial entry were performed post hoc.

§ The standardized version of the Asthma Quality of Life Questionnaire (AQLQ) contains 32 questions about asthma-related symptoms and limitations during the preceding 2 weeks. Each item is scored on a scale of 1 (severely impaired) to 7 (no impairment at all); the minimal clinically important difference is 0.5 units.

¶ Peak expiratory flow at this level was defined as a morning peak expiratory flow of at least 80% of the predicted value on every day of the previous 10 days in the run-in period.

‖ Control of asthma by the pretrial treatment was assessed by the physician.

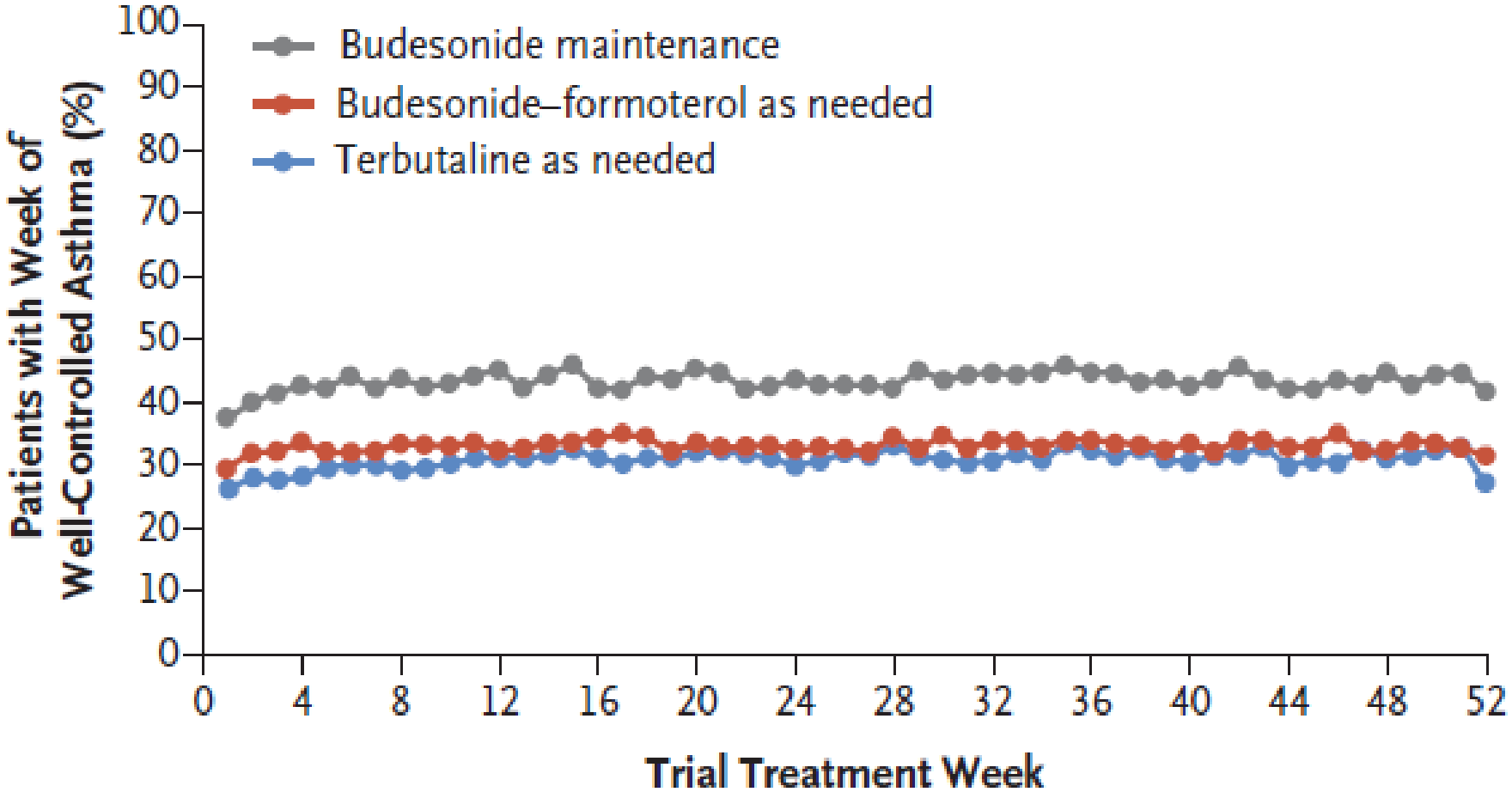


Figure 2. Overall Weeks of Well-Controlled Asthma, According to Data in the Electronic Diary.

Asthma-Control Questionnaire and Lung Function

There were differences in the change from baseline in the ACQ-5 score in favor of the budesonide–formoterol group versus the terbutaline group (mean difference, −0.15; 95% CI, −0.20 to −0.11) and in favor of the budesonide maintenance group versus the budesonide–formoterol group (mean difference, 0.15; 95% CI, 0.10 to 0.20) (Table S7 in the Supplementary Appendix).

Table 2. Summary of Asthma Exacerbations, According to Treatment Group.

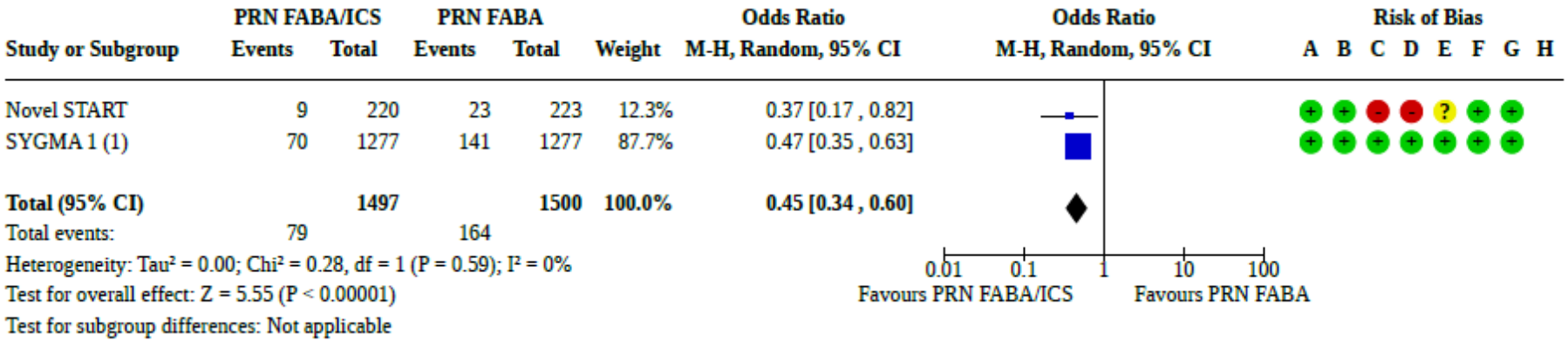
Variable	Terbutaline as Needed (N=1277)	Budesonide–Formoterol as Needed (N=1277)	Budesonide Maintenance Therapy (N=1282)
All severe exacerbations			
Patients with ≥1 exacerbation — no. (%)	152 (11.9)	71 (5.6)	78 (6.1)
Total no. of exacerbations	188	77	89
Annualized exacerbation rate	0.20	0.07	0.09
Comparison between as-needed budesonide–formoterol and other regimen			
Rate ratio	0.36	—	0.83
95% CI	0.27–0.49	—	0.59–1.16
P value	<0.001	—	0.28
Severe exacerbation leading to hospitalization			
Patients with ≥1 exacerbation — no. (%)	15 (1.2)	6 (0.5)	8 (0.6)
Total no. of exacerbations	21	6	8
Severe exacerbation leading to emergency department visit and systemic glucocorticoid use			
Patients with ≥1 exacerbation — no. (%)	29 (2.3)	7 (0.5)	10 (0.8)
Total no. of exacerbations	29	8	10
Severe exacerbation leading to systemic glucocorticoid use for ≥3 days			
Patients with ≥1 exacerbation — no. (%)	141 (11.0)	70 (5.5)	74 (5.8)
Total no. of exacerbations	173	76	84
All moderate or severe exacerbations			
Patients with ≥1 exacerbation — no. (%)	274 (21.5)	131 (10.3)	143 (11.2)
Total no. of exacerbations	372	164	170
Annualized exacerbation rate	0.36	0.14	0.15

CONCLUSIONS

In patients with mild asthma, as-needed budesonide–formoterol provided superior asthma-symptom control to as-needed terbutaline, assessed according to electronically recorded weeks with well-controlled asthma, but was inferior to budesonide maintenance therapy. Exacerbation rates with the two budesonide-containing regimens were similar and were lower than the rate with terbutaline. Budesonide–formoterol used as needed resulted in substantially lower glucocorticoid exposure than budesonide maintenance therapy. (Funded by AstraZeneca; SYGMA 1 ClinicalTrials.gov number, NCT02149199.)

Combination fixed-dose beta agonist and steroid inhaler as required for adults or children with mild asthma (Review)

- 5 estudios, 9657 pctes. > 12 años, edad media 36 a 42 años
- Falta evidencia en menores de 12 años

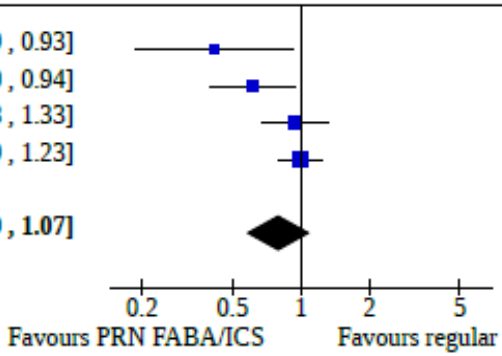


Study or Subgroup	PRN FABA/ICS Events	PRN FABA/ICS Total	Regular ICS Events	Regular ICS Total	Weight	Odds Ratio M-H, Random, 95% CI
Novel START	9	220	21	225	10.8%	0.41 [0.19 , 0.93]
PRACTICAL	37	437	59	448	23.5%	0.61 [0.40 , 0.94]
SYGMA 1	70	1277	74	1282	29.1%	0.95 [0.68 , 1.33]
SYGMA 2	171	2089	173	2087	36.7%	0.99 [0.79 , 1.23]
Total (95% CI)		**4023**		**4042**	**100.0%**	**0.79 [0.59 , 1.07]**
Total events:	287		327			

Heterogeneity: Tau² = 0.05; Chi² = 7.32, df = 3 (P = 0.06); I² = 59%

Test for overall effect: Z = 1.51 (P = 0.13)

Test for subgroup differences: Not applicable



ACQ

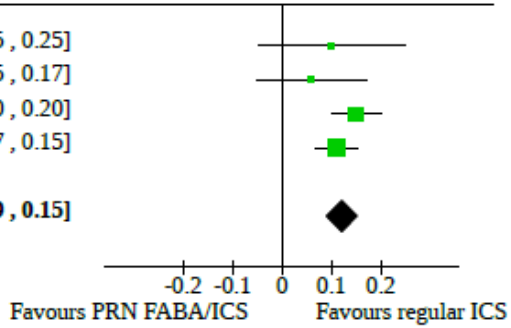
Analysis 2.4. Comparison 2: Fixed dose combination inhaler as required versus regular inhaled steroid plus as required short acting beta agonist, Outcome 4: ACQ-5

Study or Subgroup	PRN FABA/ICS Mean	SD	Total	Regular ICS Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Novel START	0.8	0.7	196	0.7	0.8	197	4.2%	0.10 [-0.05 , 0.25]
PRACTICAL	0.86	0.75	403	0.8	0.86	406	7.5%	0.06 [-0.05 , 0.17]
SYGMA 1	-0.33	0.629	1241	-0.48	0.628	1237	38.1%	0.15 [0.10 , 0.20]
SYGMA 2	-0.35	0.671	1862	-0.46	0.668	1840	50.1%	0.11 [0.07 , 0.15]
Total (95% CI)			**3702**			**3680**	**100.0%**	**0.12 [0.09 , 0.15]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.80$, df = 3 (P = 0.42); $I^2 = 0\%$

Test for overall effect: Z = 7.77 (P < 0.00001)

Test for subgroup differences: Not applicable



VEF1

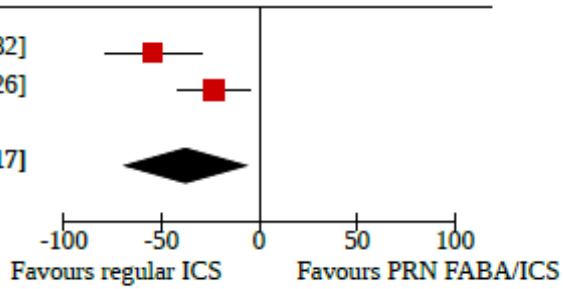
Analysis 2.6. Comparison 2: Fixed dose combination inhaler as required versus regular inhaled steroid plus as required short acting beta agonist, Outcome 6: FEV1 change from baseline

Study or Subgroup	MD	SE	PRN FABA/ICS Total	Regular ICS Total	Weight	Mean Difference IV, Random, 95% CI
SYGMA 1	-54.3	12.492225	1261	1261	46.7%	-54.30 [-78.78 , -29.82]
SYGMA 2	-23.1	9.61443	1902	1863	53.3%	-23.10 [-41.94 , -4.26]
Total (95% CI)			**3163**	**3124**	**100.0%**	**-37.68 [-68.19 , -7.17]**

Heterogeneity: $Tau^2 = 362.47$; $Chi^2 = 3.92$, df = 1 (P = 0.05); $I^2 = 74\%$

Test for overall effect: Z = 2.42 (P = 0.02)

Test for subgroup differences: Not applicable



FENO

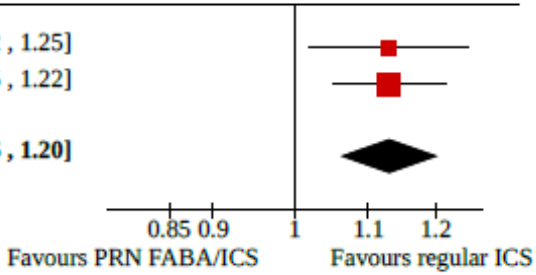
Analysis 2.7. Comparison 2: Fixed dose combination inhaler as required versus regular inhaled steroid plus as required short acting beta agonist, Outcome 7: FeNO [ppb]

Study or Subgroup	log[Geometric mean]	SE	PRN FABA/ICS Total	Regular ICS Total	Weight	Geometric mean IV, Random, 95% CI
Novel START	0.1222	0.0523	194	196	34.0%	1.13 [1.02 , 1.25]
PRACTICAL	0.1222	0.0375	401	406	66.0%	1.13 [1.05 , 1.22]
Total (95% CI)			**595**	**602**	**100.0%**	**1.13 [1.06 , 1.20]**

Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0%

Test for overall effect: Z = 4.01 (P < 0.0001)

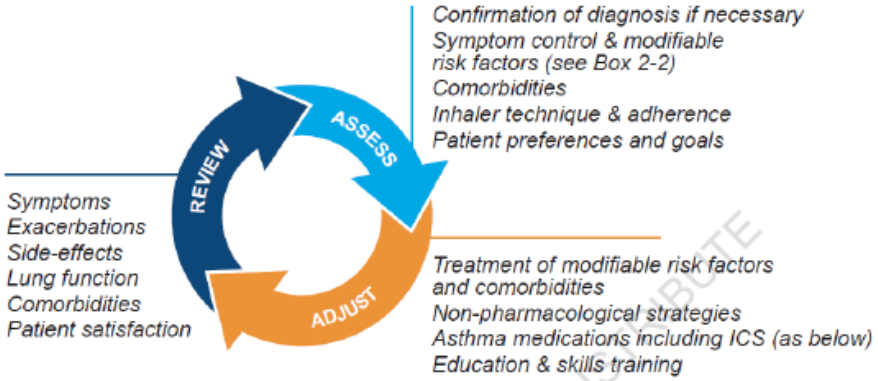
Test for subgroup differences: Not applicable



GINA 2024

GINA 2024 – Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs



TRACK 1: PREFERRED CONTROLLER and RELIEVER
Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed-only low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

TRACK 2: Alternative CONTROLLER and RELIEVER
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken*	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed ICS-SABA*, or as-needed SABA

Other controller options (limited indications, or less evidence for efficacy or safety – see text)				
Low dose ICS whenever SABA taken, or daily LTRA†, or add HDM SLIT*	*Medium dose ICS, or add LTRA†, or add HDM SLIT*	*Add LAMA or add LTRA† or add HDM SLIT, or switch to high dose ICS-only*	*Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects*	

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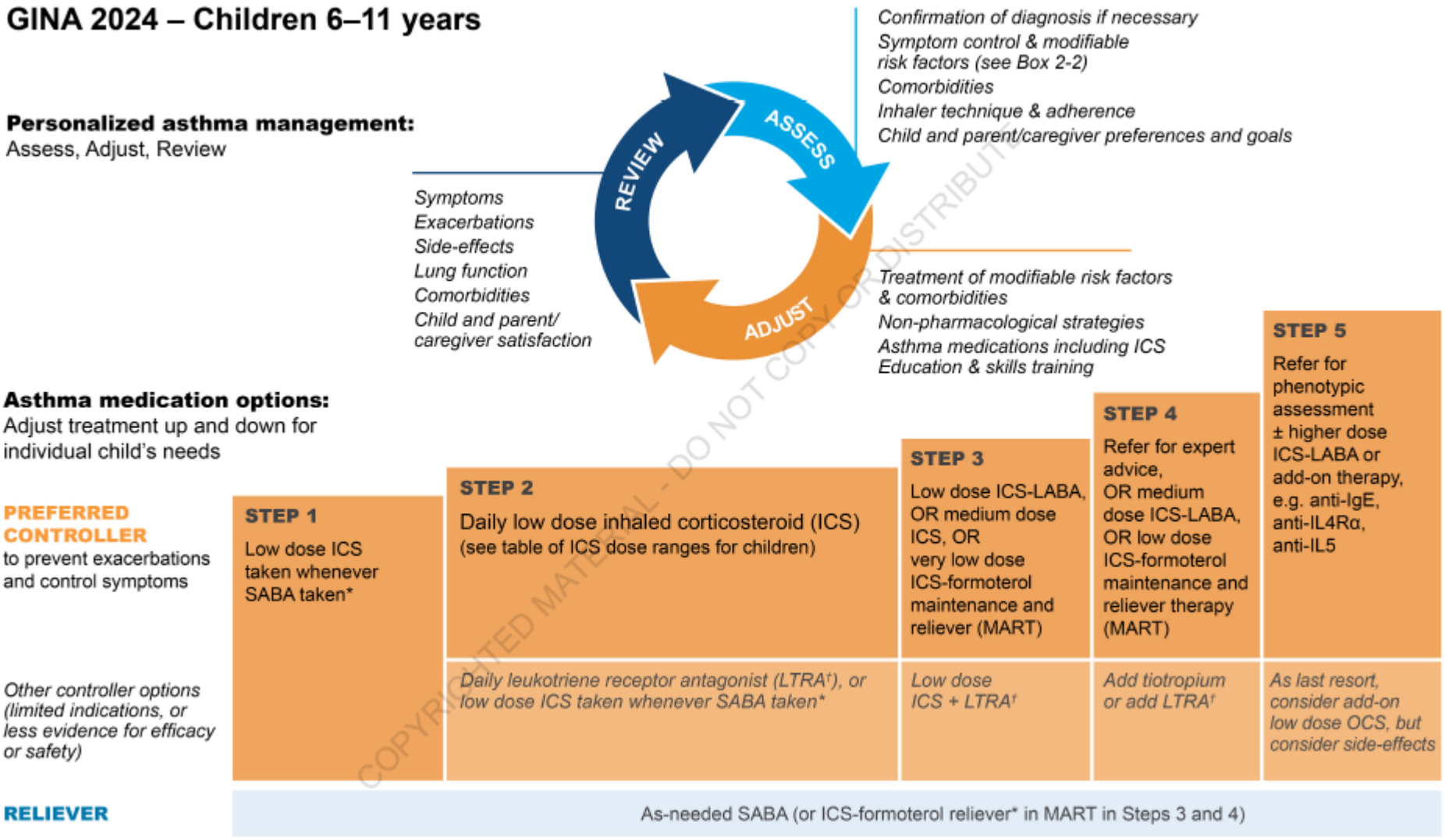
GINA 2024



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- Pero…..
- ¿es GINA la única guía de asma?
- ¿Qué dicen las otras guías de asma?

2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group

Check for updates

Expert Panel Working Group of the National Heart, Lung, and Blood Institute (NHLBI) administered and coordinated National Asthma Education and Prevention Program Coordinating Committee (NAEPPCC)* *Bethesda, Md*

AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

Treatment	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years				
	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6■
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA▲	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily medium-high dose ICS-LABA + LAMA and PRN SABA▲	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA,▲ or daily low-dose ICS + LTRA,* and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton,* and PRN SABA	Daily medium-dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA▲ or Daily medium-dose ICS + LTRA,* or daily medium-dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA	
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

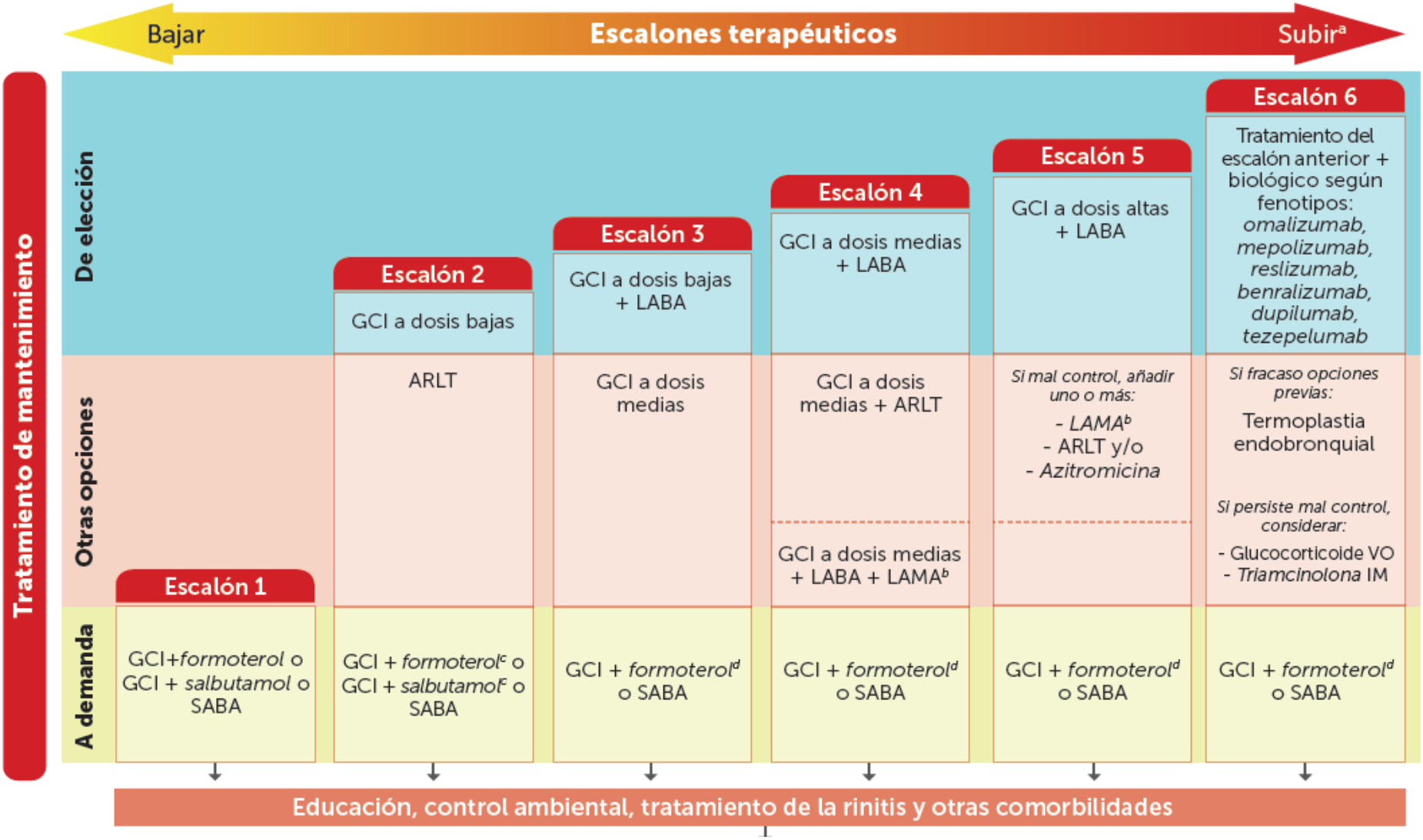
AGES 5–11 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

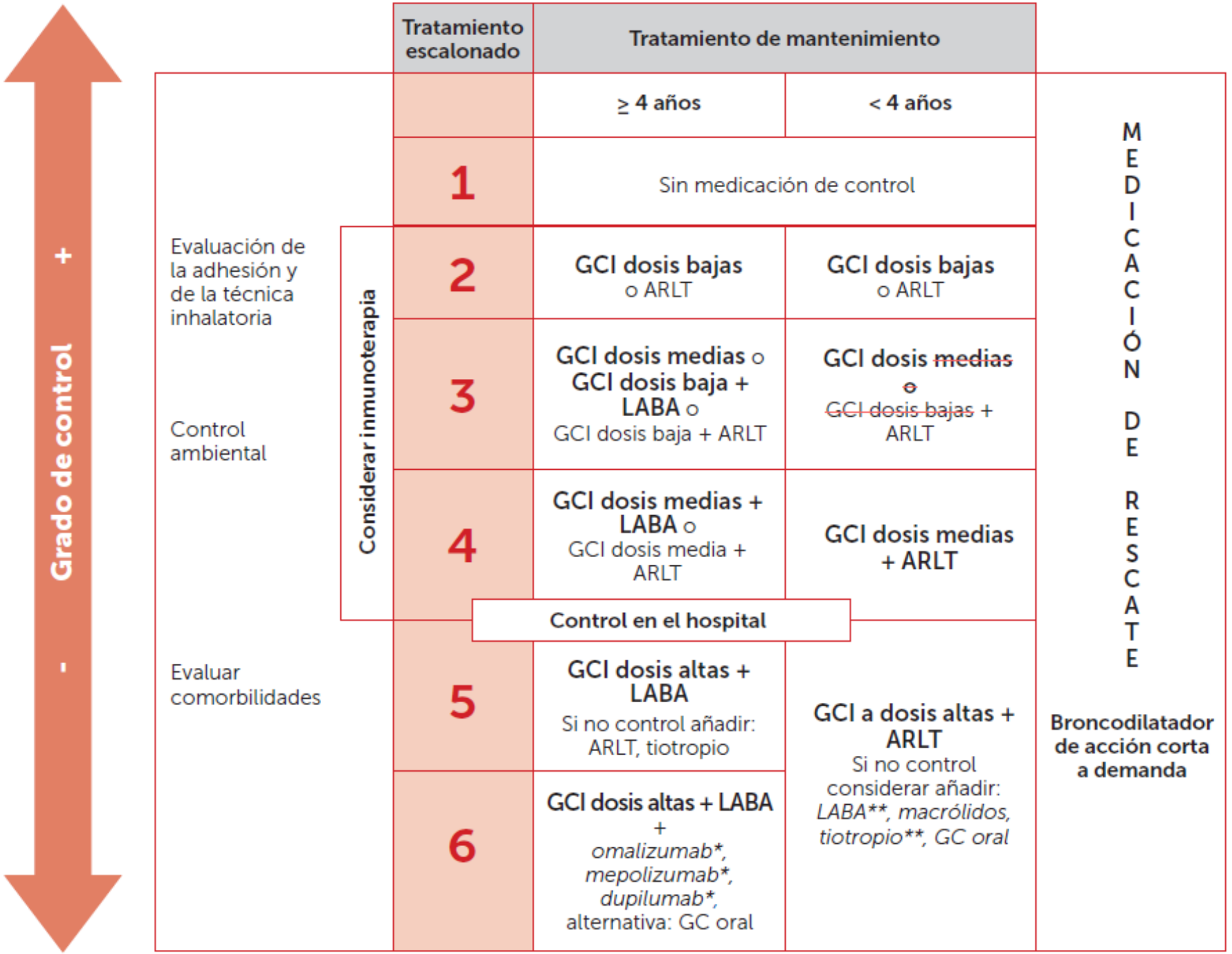
	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 5–11 Years				
Treatment	**STEP 1**	**STEP 2**	**STEP 3**	**STEP 4**	**STEP 5**	**STEP 6**
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily LTRA,* or Cromolyn,* or Nedocromil,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LTRA,* or daily low-dose ICS +Theophylline,* and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA or Daily medium-dose ICS + LTRA* or daily medium-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* or daily high-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* + oral systemic corticosteroid or daily high-dose ICS + Theophylline* + oral systemic corticosteroid, and PRN SABA
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider Omalizumab**▲	

Updated guidelines (2021) for management and follow-up of asthmatic patients of the French Society of Pneumology (SPLF) and the French Society of Pediatric Pneumology and Allergology (SP2A). Short version

	Therapeutic education, environmental control, treatment of comorbidities				
	Step 1	Step 2	Step 3	Step 4	Step 5
Background treatment		**Low-dose ICS**	**Low-dose ICS + LABA**	**Medium-dose ICS + LABA**	**High-dose ICS + LABA** If poorly controlled Add tiotropium Add anti-IgE or anti-IL-5/IL-5R or thermoplasty
Rescue treatments	SABA on demand				
			CSI-formotérol à la demande*		
Other background treatments	Low-dose ICS	Leukotriene receptor antagonists (LTRA) or ICS/Formoterol on demand	Medium-dose ICS Low-dose ICS + LTRA** Low-dose ICS + theophylline***	High-dose ICS High-dose ICS + LTRA** High-dose ICS + theophylline***	Low-dose oral CS
Rescue treatment	SABA on demand				
			Add AIT if allergy to dust mites		

GEMA 5.4


Bajar
Escalones terapéuticos
Subir[a]
Tratamiento de mantenimiento
De elección
Otras opciones
A demanda
Escalón 1
GCI+formoterol o GCI + salbutamol o SABA
Escalón 2
GCI a dosis bajas
ARLT
GCI + formoterol[c] o GCI + salbutamol[c] o SABA
Escalón 3
GCI a dosis bajas + LABA
GCI a dosis medias
GCI + formoterol[d] o SABA
Escalón 4
GCI a dosis medias + LABA
GCI a dosis medias + ARLT
GCI a dosis medias + LABA + LAMA[b]
GCI + formoterol[d] o SABA
Escalón 5
GCI a dosis altas + LABA
Si mal control, añadir uno o más:
- LAMA[b]
- ARLT y/o
- Azitromicina
GCI + formoterol[d] o SABA
Escalón 6
Tratamiento del escalón anterior + biológico según fenotipos: omalizumab, mepolizumab, reslizumab, benralizumab, dupilumab, tezepelumab
Si fracaso opciones previas:
Termoplastia endobronquial
Si persiste mal control, considerar:
- Glucocorticoide VO
- Triamcinolona IM
GCI + formoterol[d] o SABA
Educación, control ambiental, tratamiento de la rinitis y otras comorbilidades


Grado de control
+
-
Tratamiento escalonado
Tratamiento de mantenimiento
≥ 4 años
< 4 años
1
Sin medicación de control
2
GCI dosis bajas o ARLT
GCI dosis bajas o ARLT
3
GCI dosis medias o GCI dosis baja + LABA o GCI dosis baja + ARLT
GCI dosis ~~medias~~ o ~~GCI dosis bajas~~ + ARLT
4
GCI dosis medias + LABA o GCI dosis media + ARLT
GCI dosis medias + ARLT
Considerar inmunoterapia
Control en el hospital
5
GCI dosis altas + LABA
Si no control añadir: ARLT, tiotropio
GCI a dosis altas + ARLT
Si no control considerar añadir: LABA**, macrólidos, tiotropio**, GC oral
6
GCI dosis altas + LABA + omalizumab*, mepolizumab*, dupilumab*, alternativa: GC oral
Evaluación de la adhesión y de la técnica inhalatoria
Control ambiental
Evaluar comorbilidades
MEDICACIÓN DE RESCATE
Broncodilatador de acción corta a demanda

Asma no controlada. ERS/ATS 2020

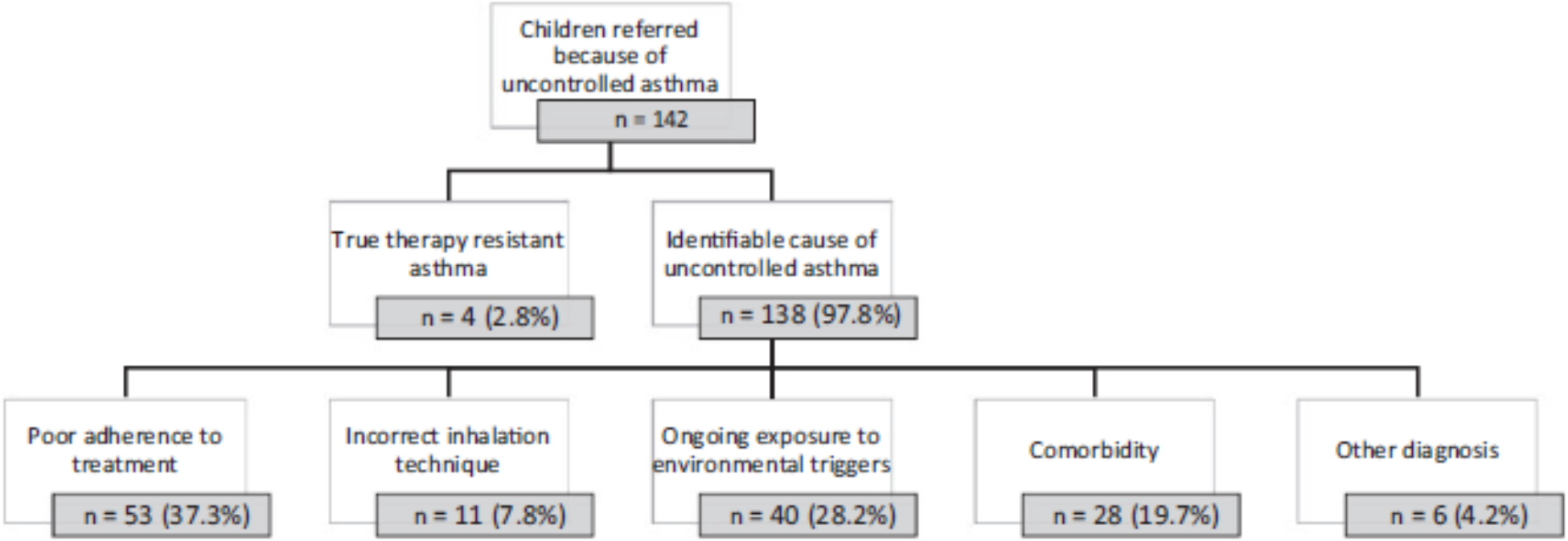
Cumple uno de los siguientes 4 criterios a pesar de tratamiento con altas dosis:

1. Pobre control de síntomas: ACQ ≥1.5 o ACT < 20
2. Exacerbaciones graves frecuentes: uso de corticoides sistémicos > 2 ocasiones, por > 3 días en el año anterior.
3. Exacerbaciones graves: al menos una hospitalización, estancia en UCI o VM en el año anterior.
4. Limitación del flujo aéreo: VEF1 < 80% o VEF1/CVF por debajo del límite inferior de la normalidad (LIN).

Eur Respir J. 2020;55:1900588

Asma de difícil control

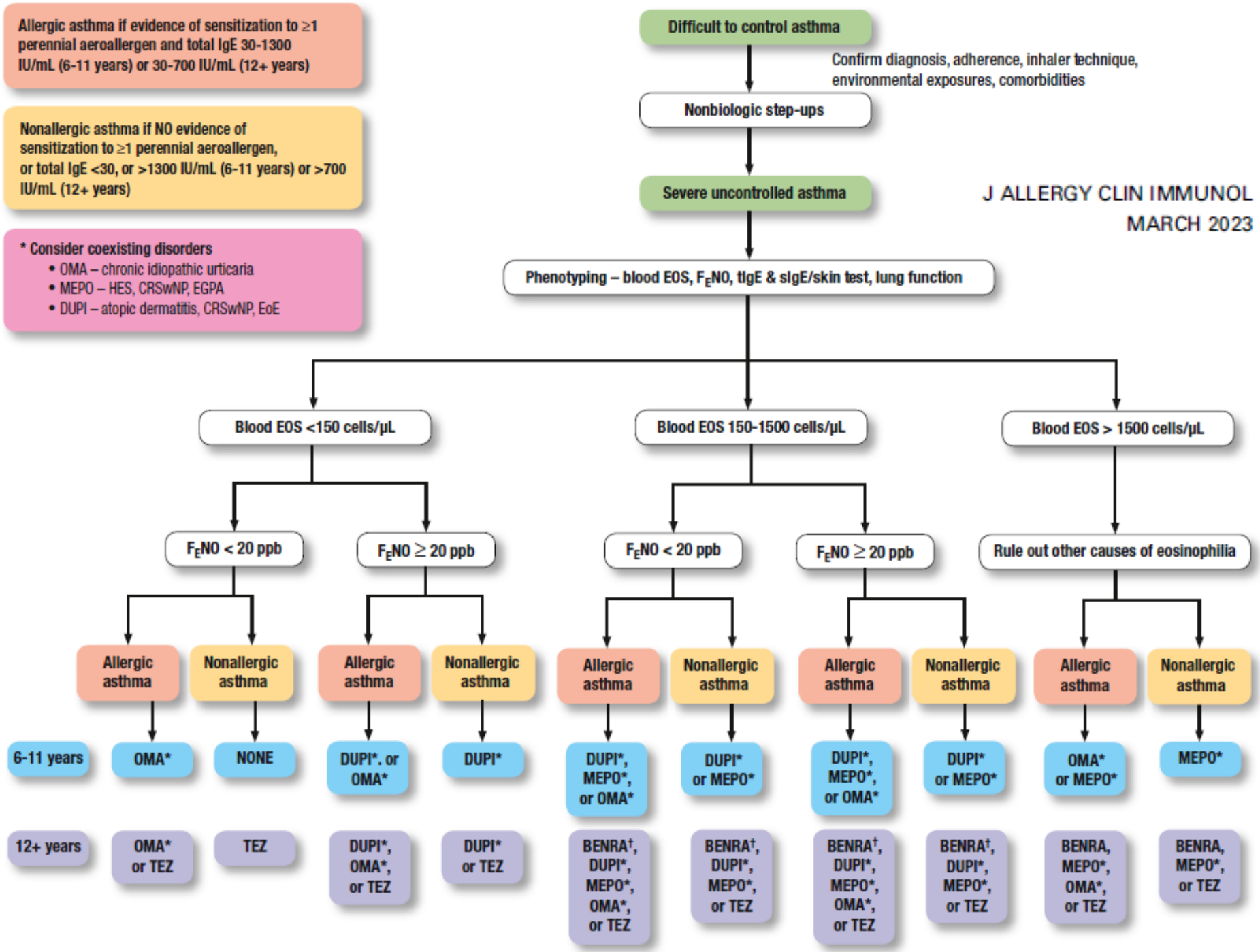
- Aquel que no se controla con CI altas dosis + LABAs (step 4)
- Diagnóstico
- Manejo ambiental
- Adherencia
- Técnica inhalatoria
- Comorbilidades => obesidad, rinitis
- Si no se controla => asma severo refractario



Acta Paediatrica. Published by John Wiley & Sons Ltd 2015 **104**, pp. 916–921

Opciones terapéuticas

- Montelukast
- Anticolinergicos => ej. Tiotropio. > 6 años
- Termoplastia Bronquial => adultos
- Macrólidos => adultos
- Terapias Biológicas


Allergic asthma if evidence of sensitization to ≥1 perennial aeroallergen and total IgE 30-1300 IU/mL (6-11 years) or 30-700 IU/mL (12+ years)
Nonallergic asthma if NO evidence of sensitization to ≥1 perennial aeroallergen, or total IgE <30, or >1300 IU/mL (6-11 years) or >700 IU/mL (12+ years)
* Consider coexisting disorders
• OMA – chronic idiopathic urticaria
• MEPO – HES, CRSwNP, EGPA
• DUPI – atopic dermatitis, CRSwNP, EoE
Difficult to control asthma
Confirm diagnosis, adherence, inhaler technique, environmental exposures, comorbidities
Nonbiologic step-ups
Severe uncontrolled asthma
J ALLERGY CLIN IMMUNOL
MARCH 2023
Phenotyping – blood EOS, FENO, tIgE & sIgE/skin test, lung function
Blood EOS <150 cells/µL
Blood EOS 150-1500 cells/µL
Blood EOS > 1500 cells/µL
FENO < 20 ppb
FENO ≥ 20 ppb
FENO < 20 ppb
FENO ≥ 20 ppb
Rule out other causes of eosinophilia
Allergic asthma
Nonallergic asthma
Allergic asthma
Nonallergic asthma
Allergic asthma
Nonallergic asthma
Allergic asthma
Nonallergic asthma
Allergic asthma
Nonallergic asthma
6-11 years
OMA*
NONE
DUPI*. or OMA*
DUPI*
DUPI*, MEPO*, or OMA*
DUPI* or MEPO*
DUPI*, MEPO*, or OMA*
DUPI* or MEPO*
OMA* or MEPO*
MEPO*
12+ years
OMA* or TEZ
TEZ
DUPI*, OMA*, or TEZ
DUPI* or TEZ
BENRA†, DUPI*, MEPO*, OMA*, or TEZ
BENRA†, DUPI*, MEPO*, or TEZ
BENRA†, DUPI*, MEPO*, OMA*, or TEZ
BENRA†, DUPI*, MEPO*, or TEZ
BENRA, MEPO*, OMA*, or TEZ
BENRA, MEPO*, or TEZ

Muchas Gracias