As needed ICS/LABA in mild asthma, pro and con

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Management of asthma in resource-limited settings: role of low-cost corticosteroid/β-agonist combination inhaler

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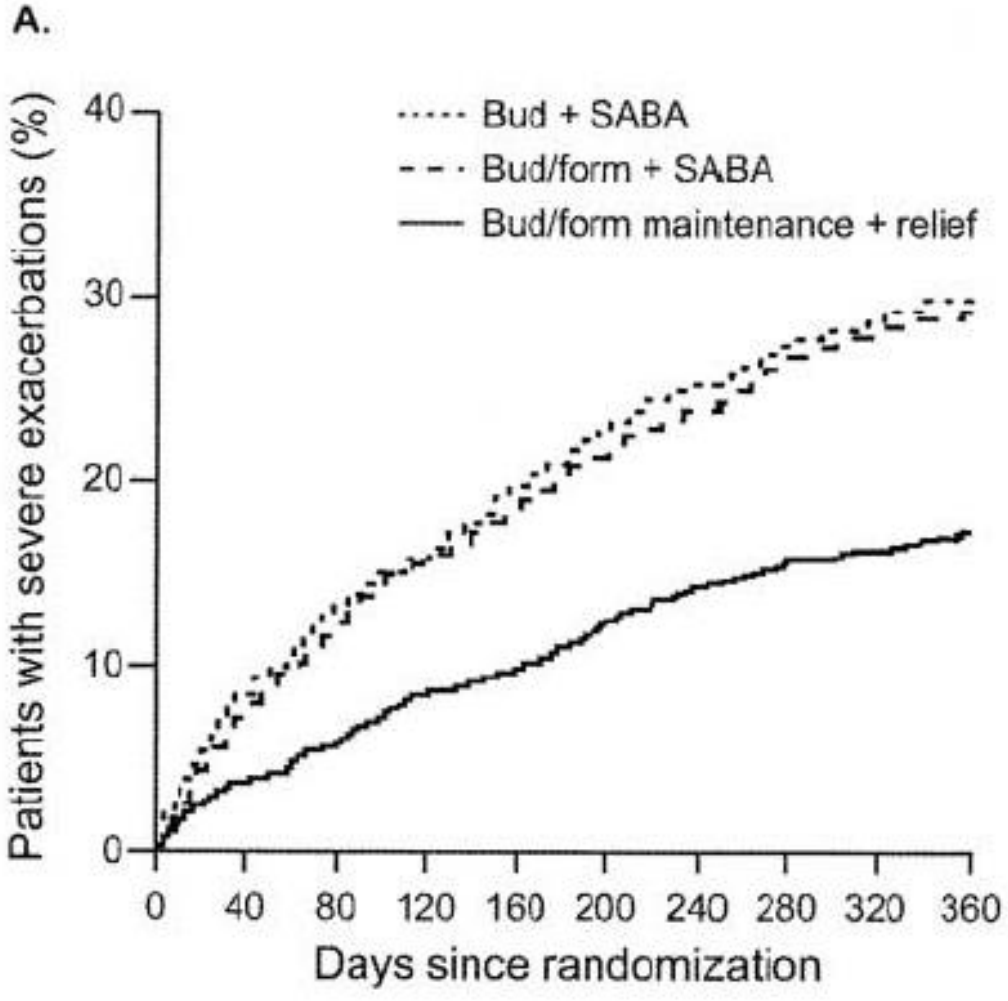
- International guidelines recommend the use of rapid acting β-agonists as needed as rescue treatment when symptoms occur.
- Studies have shown that the use of both inhaled corticosteroid and rapid-acting β-agonist as needed for symptom relief might be a better option.

Budesonide/Formoterol Combination Therapy as Both Maintenance and Reliever Medication in Asthma

	Maintenance	As needed
Bud SABA	budesonide bid	terbutaline
Bud/form SABA	budesonide–formoterol bid	terbutaline
Bud/form Maintenance Relief	budesonide–formoterol bid	budesonide–formoterol

O'Byrne PM, et al. Am J Respir Crit Care Med 2005

Budesonide/Formoterol Combination Therapy as Both Maintenance and Reliever Medication in Asthma



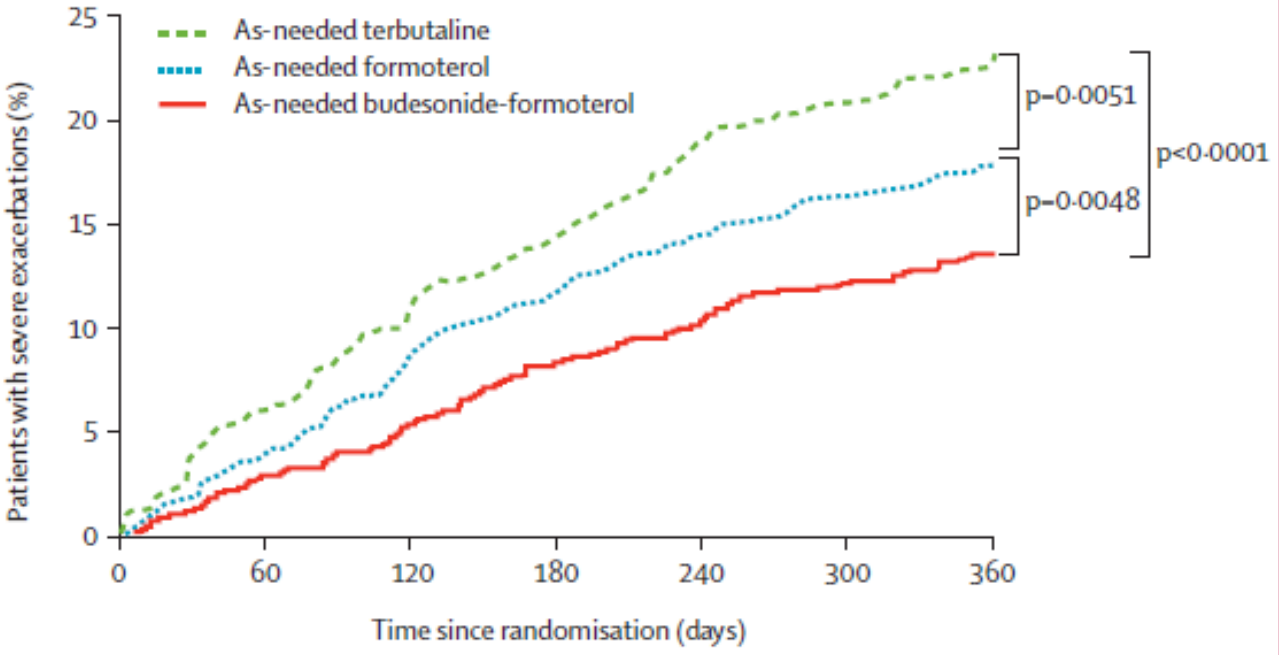
O'Byrne PM, et al. Am J Respir Crit Care Med 2005

Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations

	Maintenance	As needed
SABA	budesonide–formoterol bid	terbutaline
LABA	budesonide–formoterol bid	formoterol
Bud/form	budesonide–formoterol bid	budesonide–formoterol

Rabe KF, ret al. Lancet 2006; 368: 744–53

Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations



Numbers at risk

Terbutaline	1138	1028	958	901	846	814	729
Formoterol	1137	1050	995	944	904	872	767
Budesonide-formoterol	1107	1036	994	941	912	886	795

Figure 2: **Kaplan–Meier plot of time to first severe asthma exacerbation**
Time to first severe asthma exacerbation defined as a deterioration in asthma resulting in hospitalisation, emergency room treatment, or the need for oral steroids for 3 days or more because of asthma (as judged by investigator). Patients received maintenance budesonide-formoterol 160/4·5 µg, one inhalation twice daily, plus one of the following for as-needed relief: additional inhalations of budesonide-formoterol 160/4·5 µg; formoterol 4·5 µg; or terbutaline 0·4 mg. Significant between-group differences were derived from a log-rank test.

Lancet 2006; 368: 744–53

As needed ICS/LABA in mild asthma

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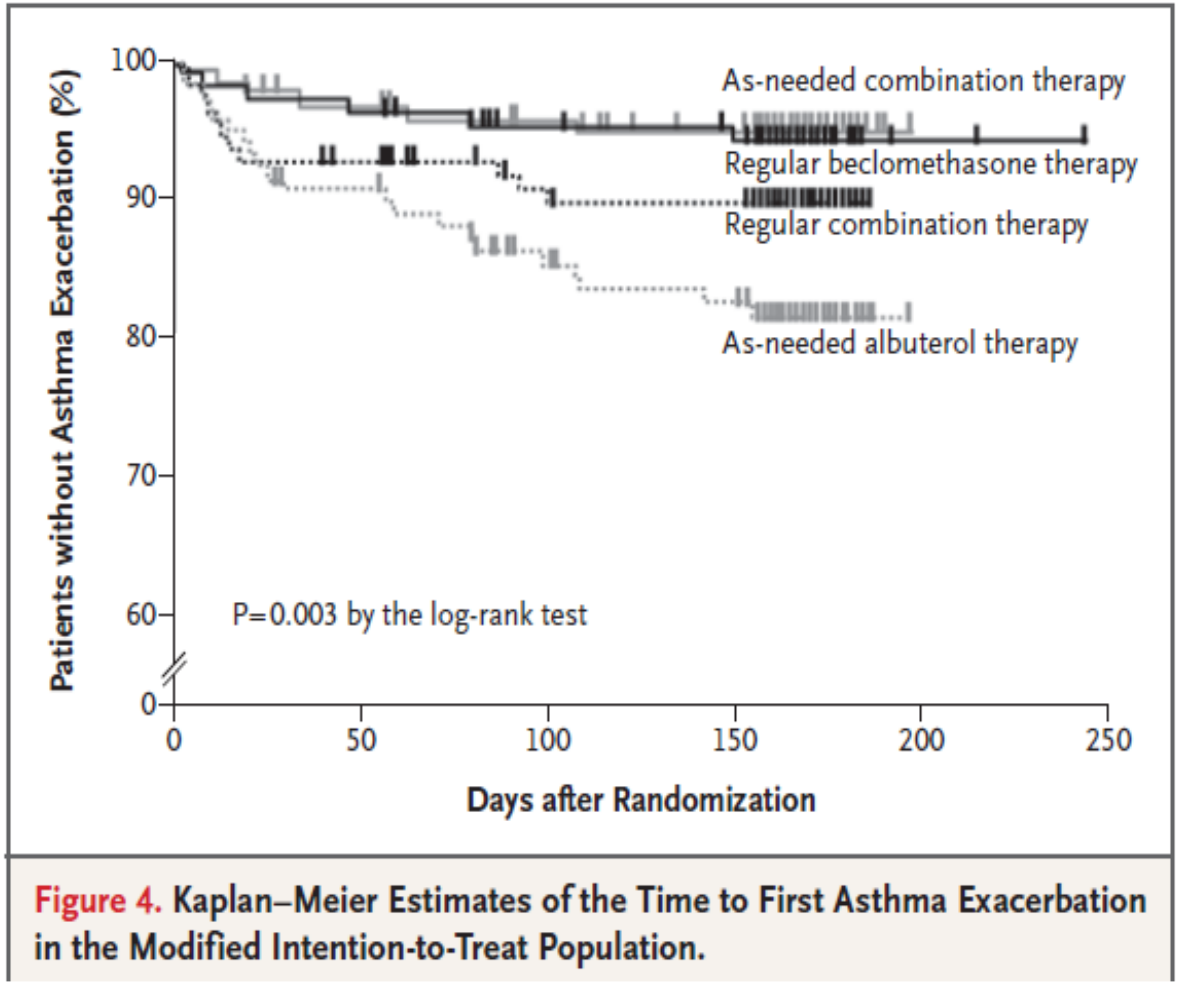
What about ICS/SABA?

Rescue Use of Beclomethasone and Albuterol in a Single Inhaler for Mild Asthma

	Maintenance	As needed
as needed combination	Placebo	Beclomethasone-albuterol
as needed albuterol	Placebo	albuterol
Regular ICS	Beclomethasone	albuterol
Regular combination	Beclomethasone-albuterol	albuterol

Papi A, et al. N Engl J Med 2007;356:2040-52.

Rescue Use of Beclomethasone and Albuterol in a Single Inhaler for Mild Asthma



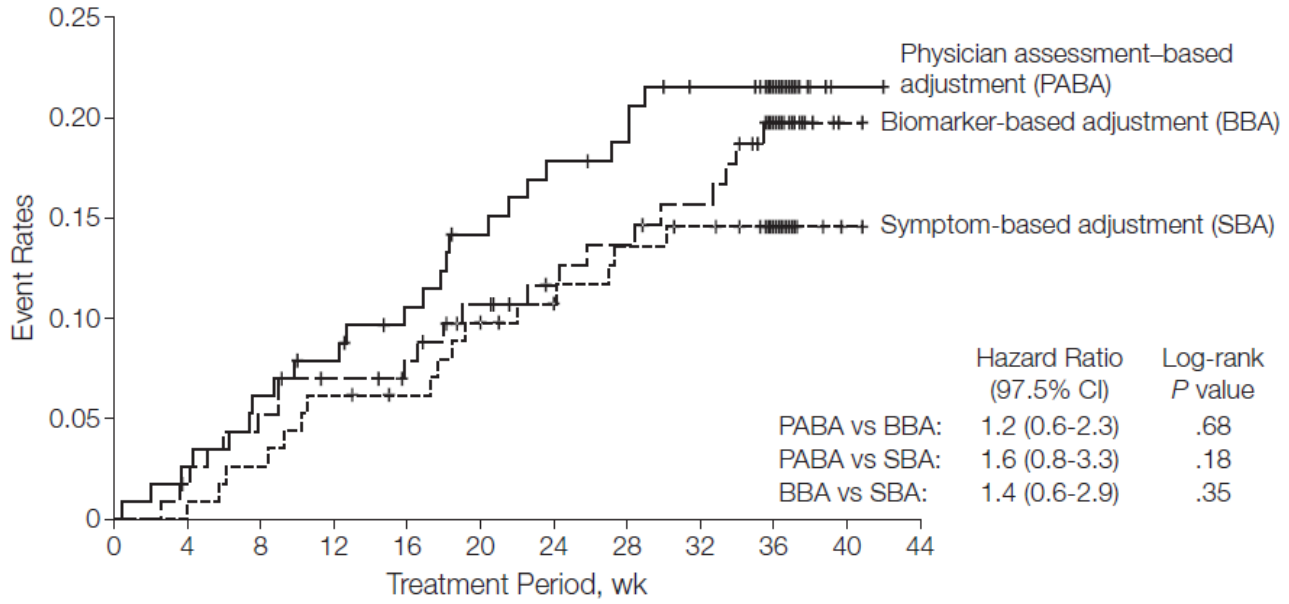
Tick marks represent a first asthma exacerbation. As-needed combination therapy consisted of placebo twice daily plus 250 μg of beclomethasone and 100 μg of albuterol in a single inhaler as needed; as-needed albuterol therapy, placebo twice daily plus 100 μg of albuterol as needed; regular beclomethasone therapy, 250 μg of beclomethasone twice daily and 100 μg of albuterol as needed; and regular combination therapy, 250 μg of beclomethasone and 100 μg of albuterol in a single inhaler twice daily plus 100 μg of albuterol as needed.

Figure 4. Kaplan–Meier Estimates of the Time to First Asthma Exacerbation in the Modified Intention-to-Treat Population.

Papi A, et al. N Engl J Med 2007;356:2040-52.

Comparison of Physician-, Biomarker-, and Symptom-Based Strategies for Adjustment of Inhaled Corticosteroid Therapy in Adults With Asthma

Figure 2. Time to First Treatment Failure



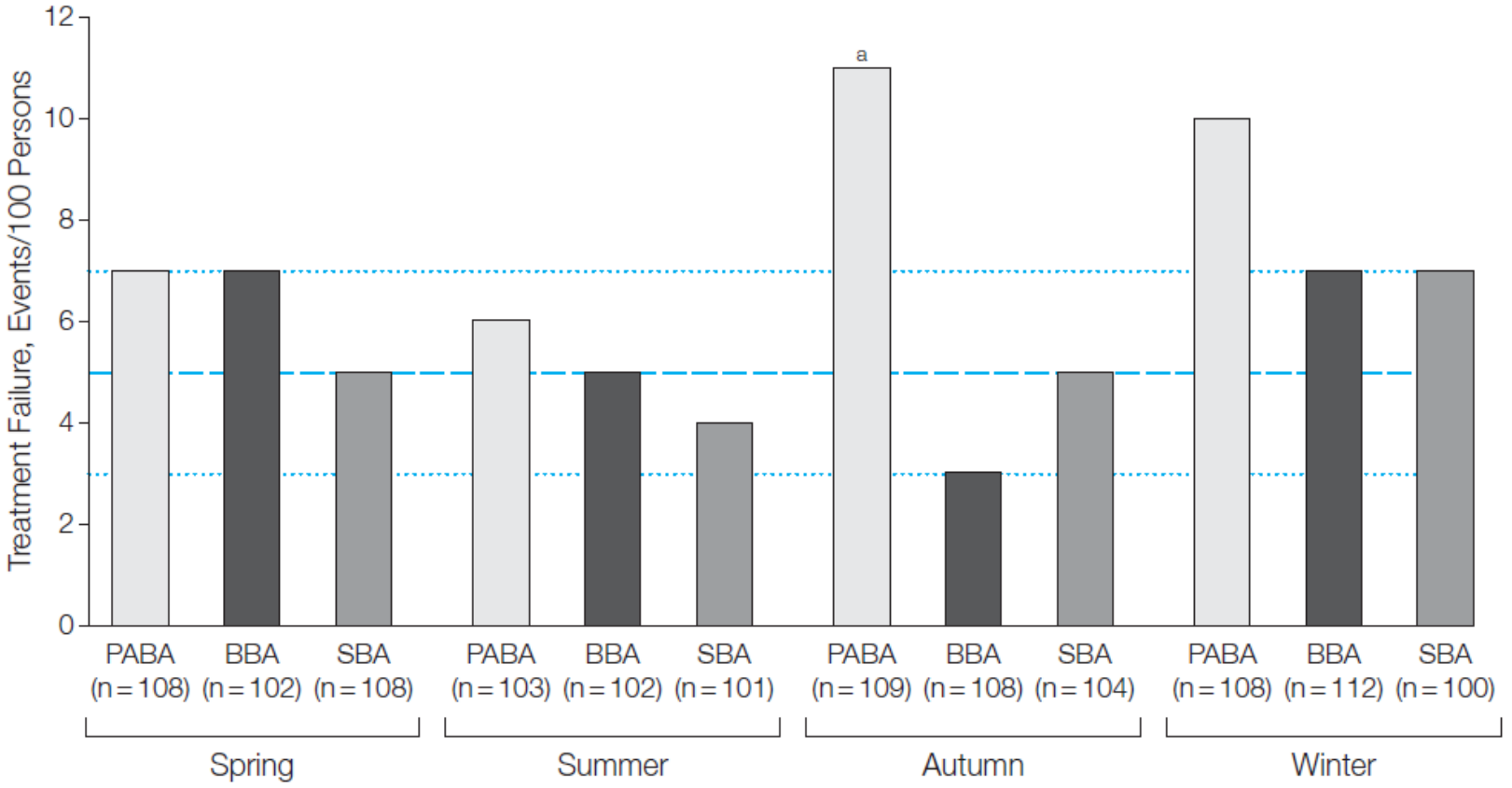
No significant differences among the 3 treatment groups were seen. A confirmatory truncated analysis was performed with truncation at day 258 (week 37), beyond which less than 10% of the study population was still in follow-up. These results confirm the primary analysis with a pairwise *P* value for PABA vs BBA of .64; PABA vs SBA, *P*=.15; and BBA vs SBA, *P*=.33. The hazard ratios and 97.5% confidence intervals were identical to 1 decimal place. Short vertical bars on the curves indicate censored data.

Symptom-Based: matching inhaled steroid use on a puff-per-puff basis with as-needed albuterol use.

JAMA 2012;308(10):987-997

Comparison of Physician-, Biomarker-, and Symptom-Based Strategies for Adjustment of Inhaled Corticosteroid Therapy in Adults With Asthma

Figure 5. Treatment Failure by Season



Asthma exacerbation: unscheduled medical contact for increased asthma symptoms that results in use of oral corticosteroids, increased inhaled corticosteroids, or additional medications for asthma.

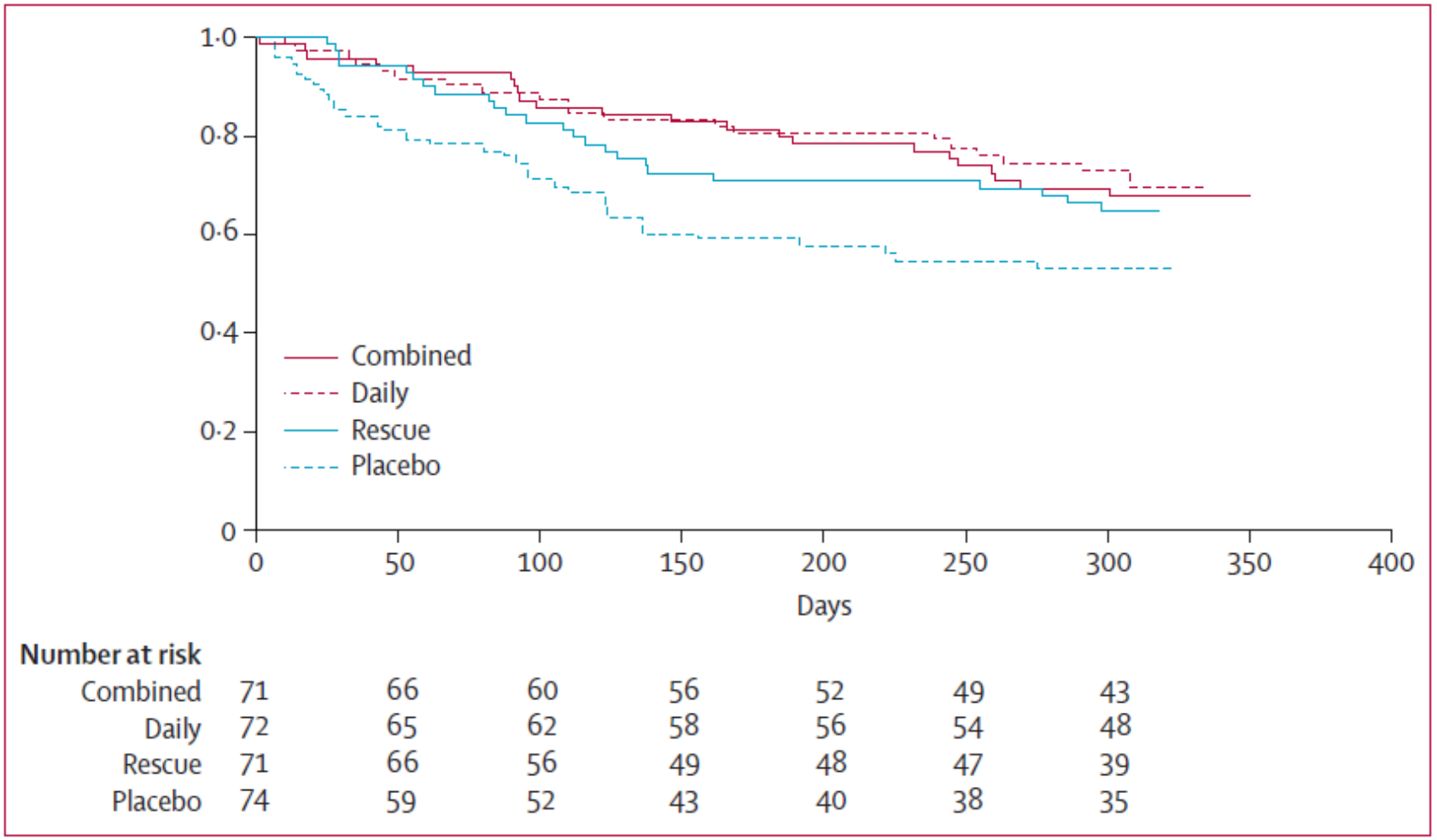
JAMA 2012;308(10):987-997

Use of beclomethasone dipropionate as rescue treatment for children with mild persistent asthma (TREXA): a randomised, double-blind, placebo-controlled trial

	Maintenance	As needed
Combined group	Beclomethasone bid	Beclomethasone-albuterol
Daily group	Beclomethasone bid	albuterol
Rescue group	Placebo	Beclomethasone-albuterol
Placebo	Placebo	albuterol

Fernando D Martinez, et al. Lancet 2011; 377: 650–57

Use of beclomethasone dipropionate as rescue treatment for children with mild persistent asthma (TREXA): a randomised, double-blind, placebo-controlled trial



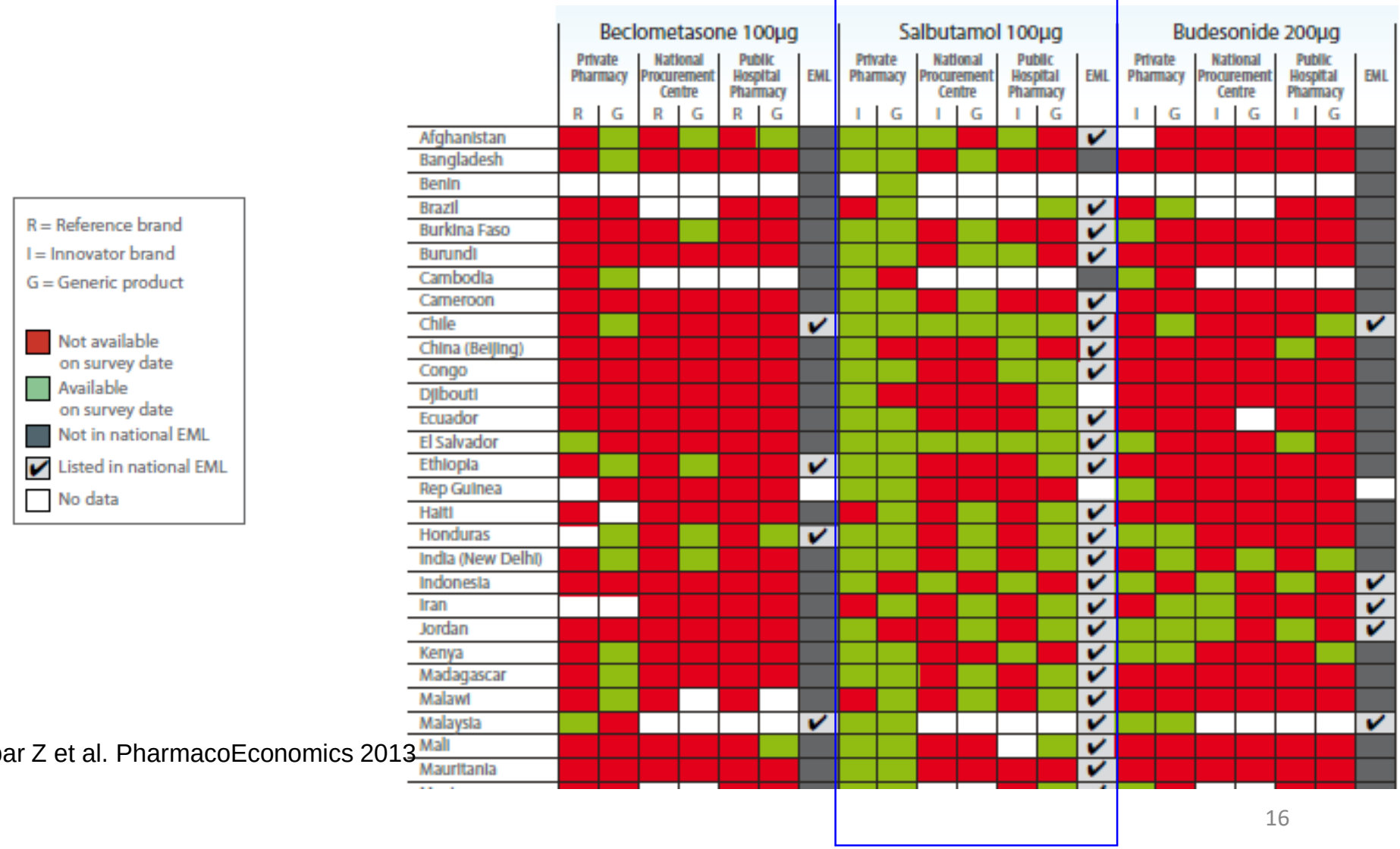
Number at risk

Combined	71	66	60	56	52	49	43
Daily	72	65	62	58	56	54	48
Rescue	71	66	56	49	48	47	39
Placebo	74	59	52	43	40	38	35

Figure 2: Kaplan-Meier curves showing the time to first exacerbation

Fernando D Martinez, et al. Lancet 2011; 377: 650–57

Availability of surveyed inhalers by country, type of health facility and national Essential Medicines List



Babar Z et al. PharmacoEconomics 2013

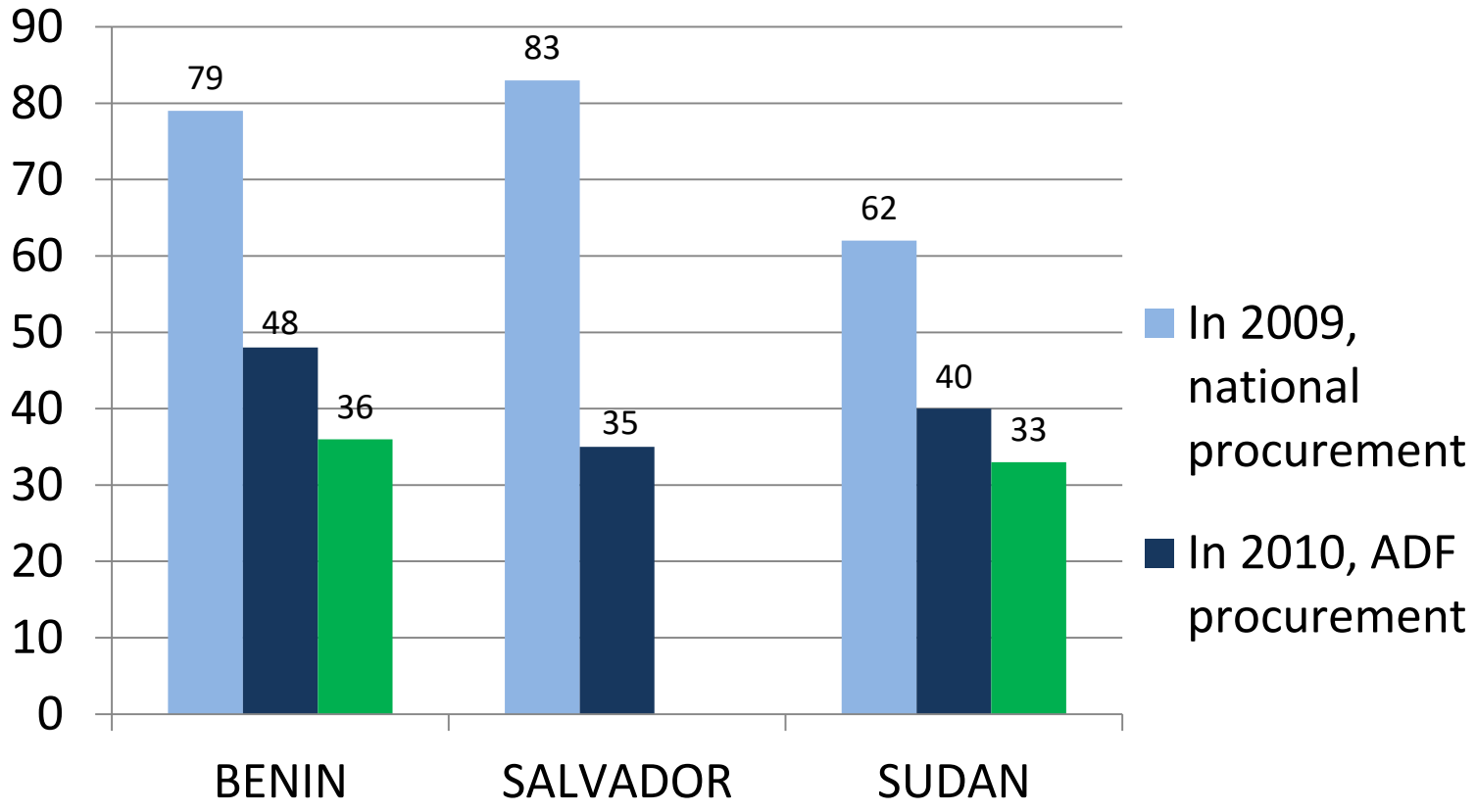
The Asthma Drug Facility (ADF)

- Provides affordable access to quality-assured, essential asthma medicines for low- and middle-income countries
- Promotes a quality improvement package for the diagnosis, treatment and management of asthma

  - Benin
  - Burundi
  - El Salvador
  - Honduras
  - Kenya
  - Sudan
  - Vanuatu
  - Vietnam

ADF ASTHMA DRUG FACILITY
Affordable Access

Around 50% reductions in annual costs for a patient with severe asthma when medicines purchased through ADF (in Euros, based on 2009/2012 ADF prices)



Public Health Action
International Union Against Tuberculosis and Lung Disease
Health solutions for the poor
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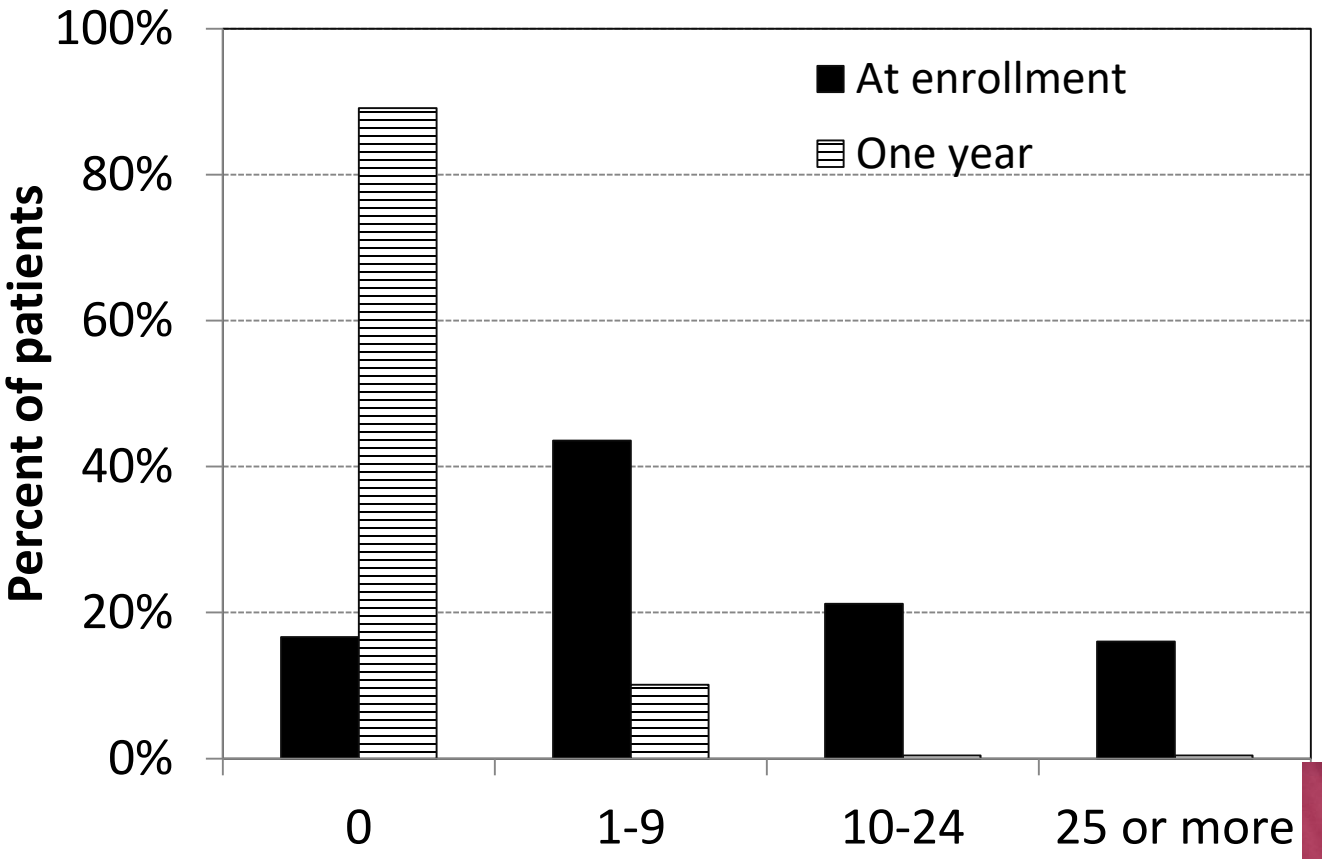
Standard case management of asthma in Sudan: a pilot project

A. I. El Sony,[1] C-Y. Chiang,[2,3,4] E. Malik,[5] S. A. Hassanain,[1] H. Hussien,[1] A. H. Khamis,[1,6]
A. F. Bassilli,[7] D. A. Enarson[2]

- Inhaled beclometasone was not available in the public sector;
- it was available in the private sector and local pharmacies, but was expensive

Standard case management of asthma in Sudan

Frequency of emergency visits in past year



PHA 2013; 3(3): 247–252

The use of both inhaled orticosteroid and rapid-acting β-agonist as needed

	Maintenance therapy	Rescue therapy	Exacerbation %
Papi[29]*			
A	None	ICS/SABA	4.9
B	None	SABA	17.8
C	ICS	SABA	5.7
D	ICS/SABA	SABA	10.1
Martinez[30]*			
A	ICS	ICS/SABA	28
B	ICS	SABA	31
C	None	ICS/SABA	35
D	None	SABA	49
Rabe[31†]			
A	ICS/LABA	ICS/LABA	19/100
B	ICS/LABA	LABA	29/100
C	ICS/LABA	SABA	37/100

* ICS = beclometasone, SABA = albuterol (salbutamol).
† ICS = budesonide, LABA = formoterol, SABA = terbutaline.
ICS = inhaled corticosteroid; SABA = short-acting β_2 agonist; LABA = long-acting β_2 agonist.

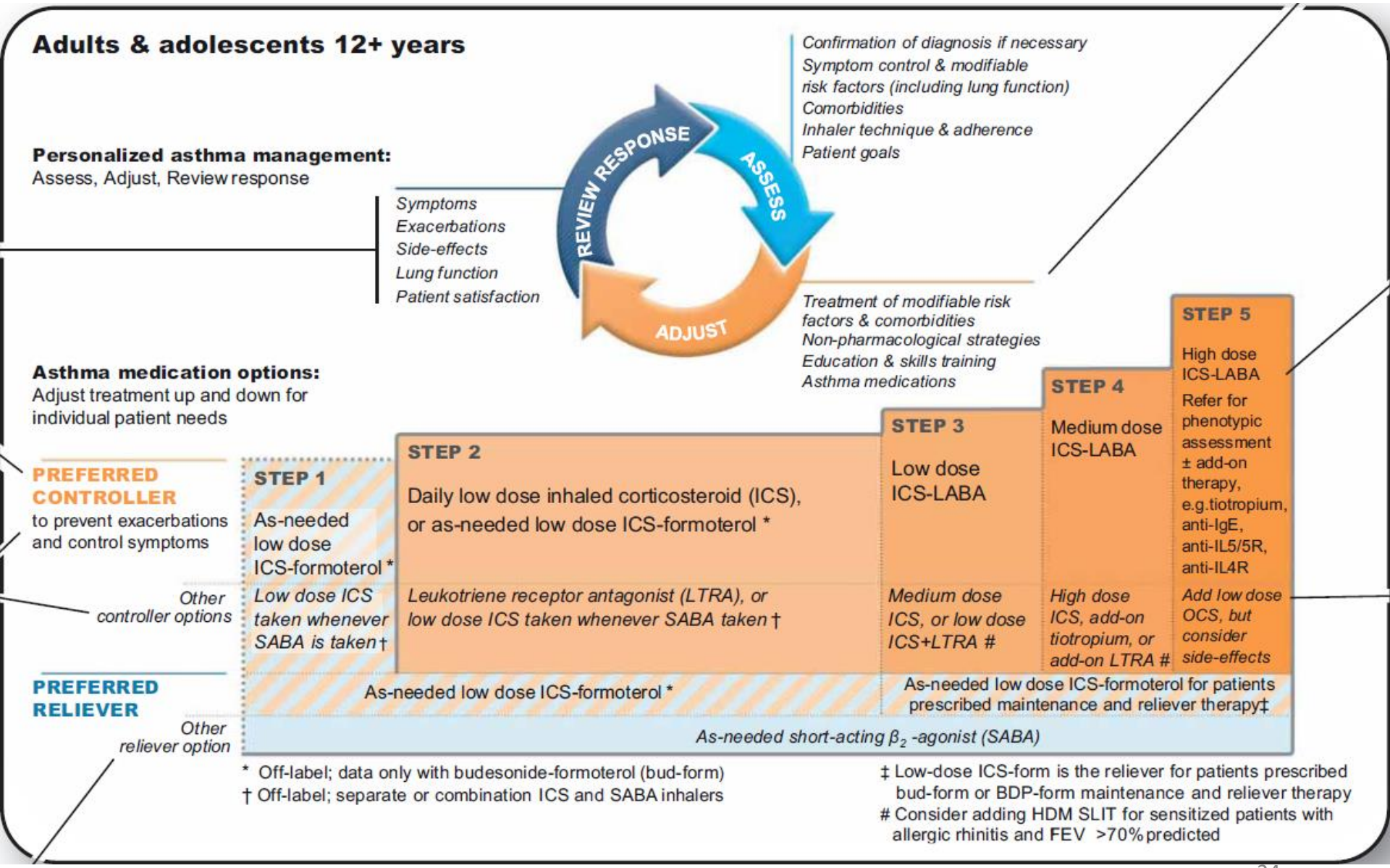
Chiang C-Y, et al. Int J Tuberc Lung Dis 2015

As needed ICS/LABA in mild asthma

As needed ICS/LABA in mild asthma

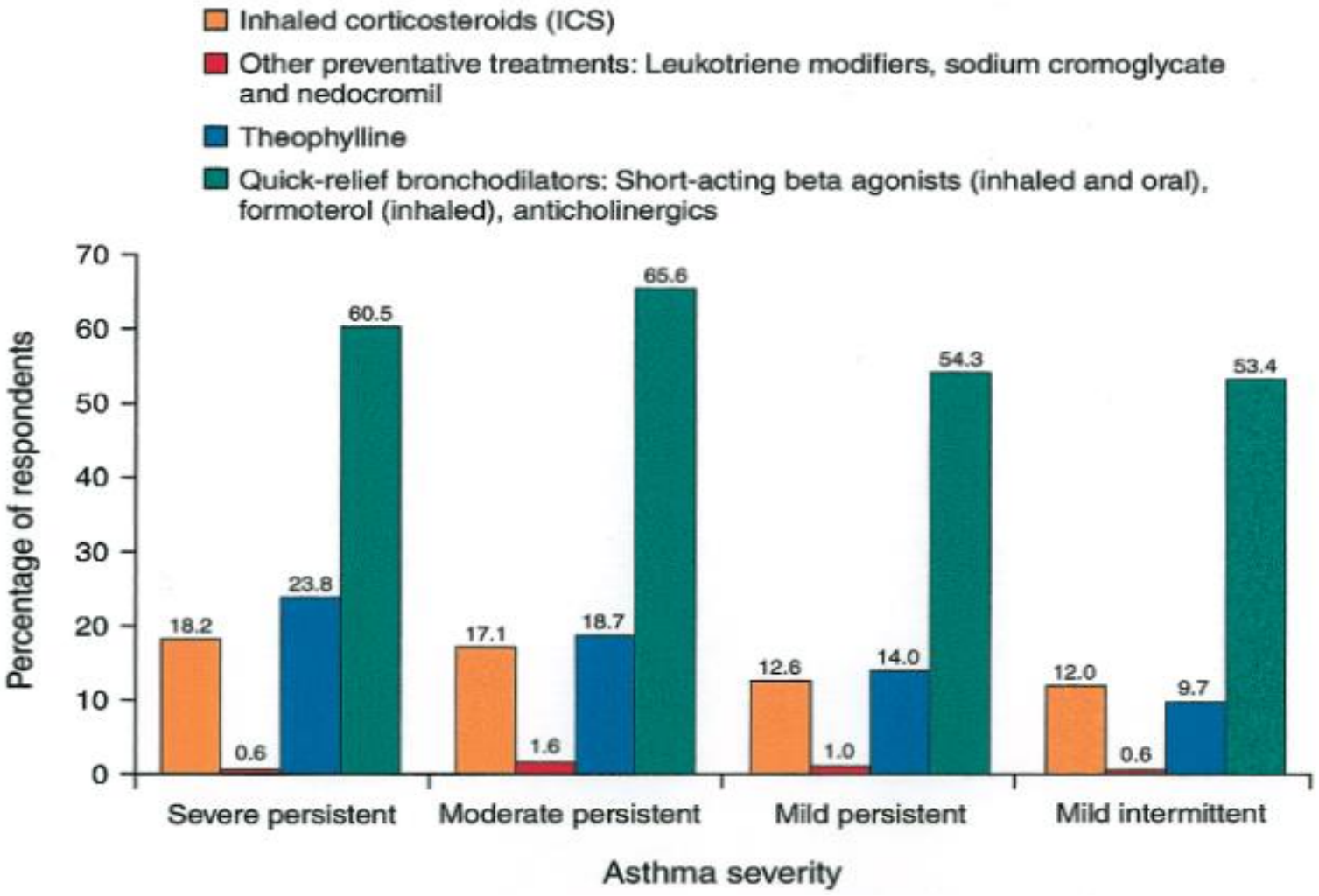
What about moderate and severe asthma?

2019 Global Initiative for Asthma (GINA) treatment strategy



Helen K. Reddel, et al. Eur Respir J 2019

The Asthma Insights and Reality in Asia-Pacific Study

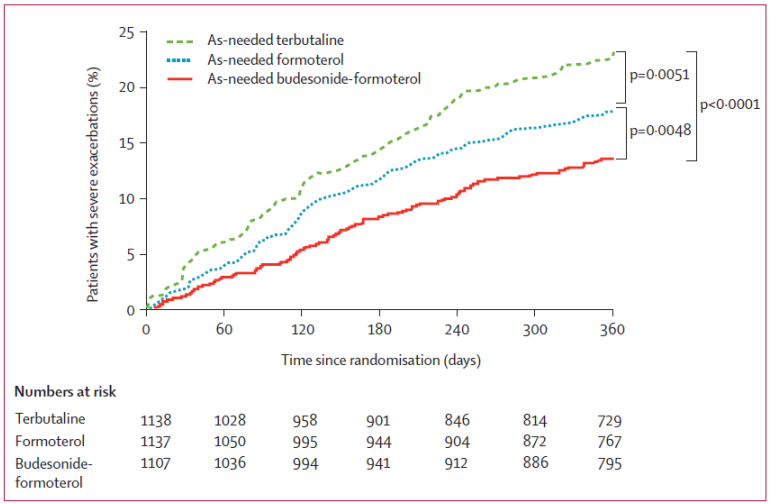


Asthma medication use according to asthma severity

Lai CKW, et al. J Allergy Clin Immunol 2003;111:263-8

Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations

	Maintenance	As needed
SABA	budesonide–formoterol bid	terbutaline
LABA	budesonide–formoterol bid	formoterol
Bud/form	budesonide–formoterol bid	budesonide–formoterol



	Terbutaline as-needed group (n=1141)	Formoterol as-needed group (n=1140)	Budesonide-formoterol as-needed group (n=1113)
Men, n (%)	450 (39%)	458 (40%)	437 (39%)
Age, years	43 (12–83)	42 (12–81)	42 (12–89)
Median (range) asthma duration, years	10 (1–69)	10 (1–77)	9 (0–64)
FEV_1 L	2·16 (0·68–4·58)	2·20 (0·74–4·58)	2·21(0·61–4·68)
FEV_1 (pre-terbutaline), % predicted	72 (39†–100)	72 (38†–115†)	72 (30†–110†)
FEV_1 reversibility, %	24 (11†–90)	24 (0†–96)	24 (6†–132)
ICS dose at entry, µg/day	751 (250†–1600)	758 (320†–1600)	757 (160†–1600)
Inhaled LABA use at entry, % of patients	59%	59%	59%
Mean daily asthma control measures ‡			
Total asthma symptom score (scale 0–6)	1·74 (0·00–6·00)	1·70 (0·00–6·00)	1·71 (0·00–5·71)
Reliever use, number of inhalations per 24 h	1·9 (0·3–9·7)	1·9 (0·0–9·1)	1·8 (0·0–8·9)
Nights with awakenings, %	30·3 (0–100)	28·0 (0–100)	31·1 (0–100)
Asthma-control days§, %	8·3 (0–50)	8·3 (0–80)	9·2 (0–90)
ACQ-5¶	1·9 (0–4·8)	1·9 (0–5·4)	1·9 (0–4·8)

Rabe KF, ret al. Lancet 2006

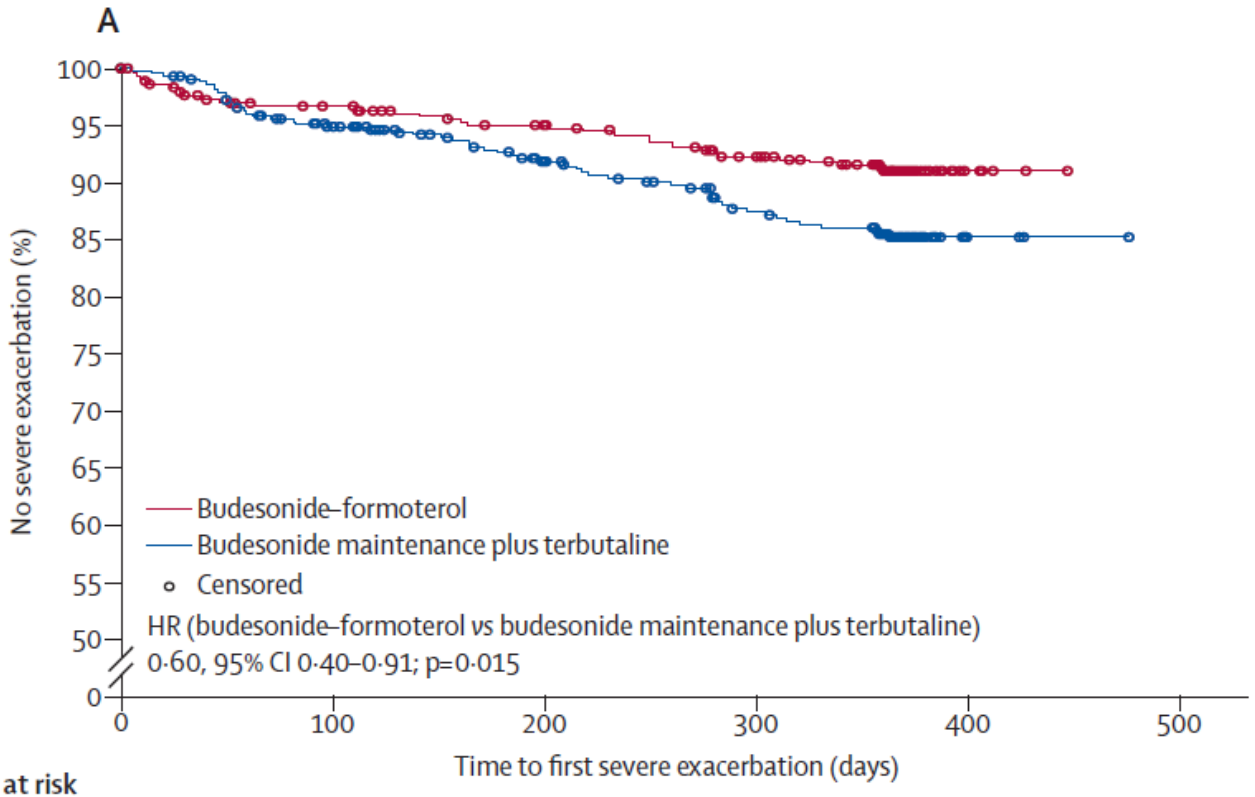
Budesonide-formoterol reliever therapy versus maintenance budesonide plus terbutaline reliever therapy in adults with mild to moderate asthma (PRACTICAL): a 52-week, open-label, multicentre, superiority, randomised controlled trial

- 52-week, open-label, parallel-group, multicentre, superiority, randomised controlled trial in New Zealand

	Maintenance	As needed
Reliever therapy	-	budesonide–formoterol
Maintenance therapy	twice-daily budesonide	terbutaline 250 µg turbuhaler (two inhalations as needed

Lancet 2019; 394: 919–28

Budesonide-formoterol reliever therapy versus maintenance budesonide plus terbutaline reliever therapy in adults with mild to moderate asthma (PRACTICAL): a 52-week, open-label, multicentre, superiority, randomised controlled trial



Number at risk						
Budesonide–formoterol	437	406	385	362	6	0
Budesonide maintenance plus terbutaline	448	399	358	326	4	0

Lancet 2019; 394: 919–28

In conclusion

- The use of both inhaled corticosteroid and rapid-acting β-agonist as needed for symptom relief in individuals with asthma, regardless of severity, might be a better option than the use of rapid acting β-agonists as needed as rescue treatment when symptoms occur.

- To improve asthma management, access to quality assured affordable essential asthma medicine needs to be ensure.