Should ICS be maintained for Whole Life in Mild Asthma?

이세원

울산의대 서울아산병원
호흡기내과

Stepping down to find the minimum effective dose

- Consider step down once good asthma control has been achieved and maintained for about 3 months, to find patient's lowest treatment that controls both symptoms and exacerbations

- Provide the patient with a written asthma action plan, monitor closely, and schedule a follow-up visit

- ***Do no completely withdraw ICS unless this is needed temporarily to confirm the diagnosis of asthma.***

GINA since 2014

Controller treatment may be stopped

- if the patient's asthma remains controlled on the lowest dose of controller and

- no recurrence of symptoms occurs for one year

GINA 2011

차례

1. 천식 질환의 특성

2. ICS 유지의 근거: 끊으면 어떻게 되는가?

3. ICS: 평생 안전한가?

4. ICS withdrawal: 그 이후의 대안에 대해

차례

Definition of Asthma in GINA

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation.

It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity,

together with variable expiratory airflow limitation.

GINA 2019

Definition of Asthma in GINA

다양

만성기도염증질환

(1) Heterogene**ous** ds. characterized by **c**hronic AW inflamm

(2) Hx of **res**piratory sx (e.g., wh, chest tightness, cough)

기침, 호흡곤란, 가슴 답답, 천명음

(3) Vary over time & in intensity AND

변동성

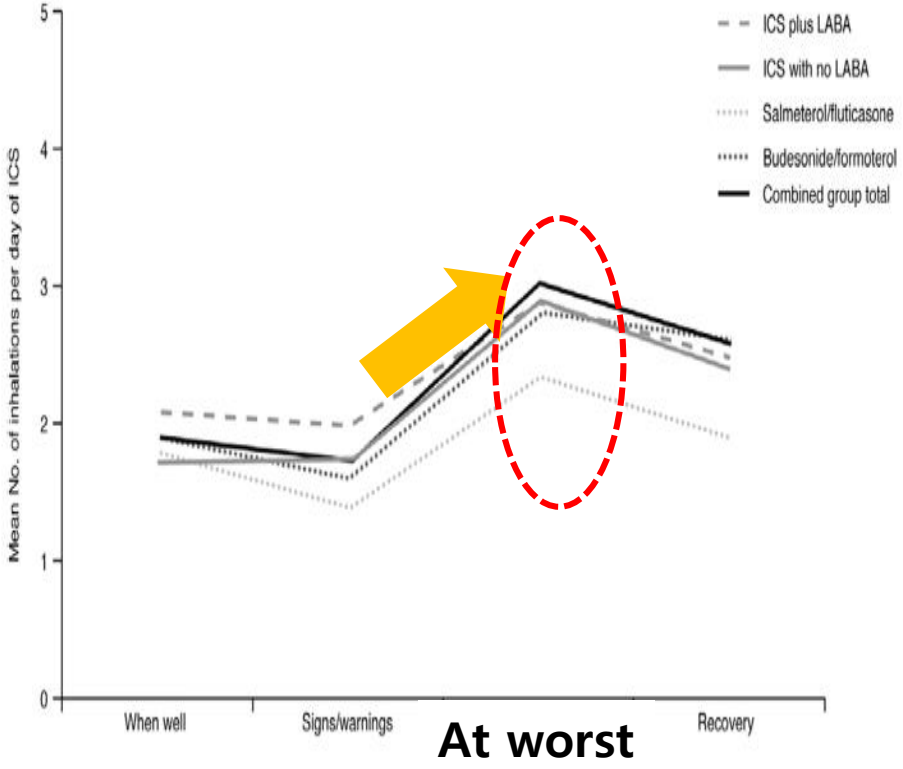
variable expiratory airflow limitation

2019 GINA

환자는 아플 때 약을 더 찾는다

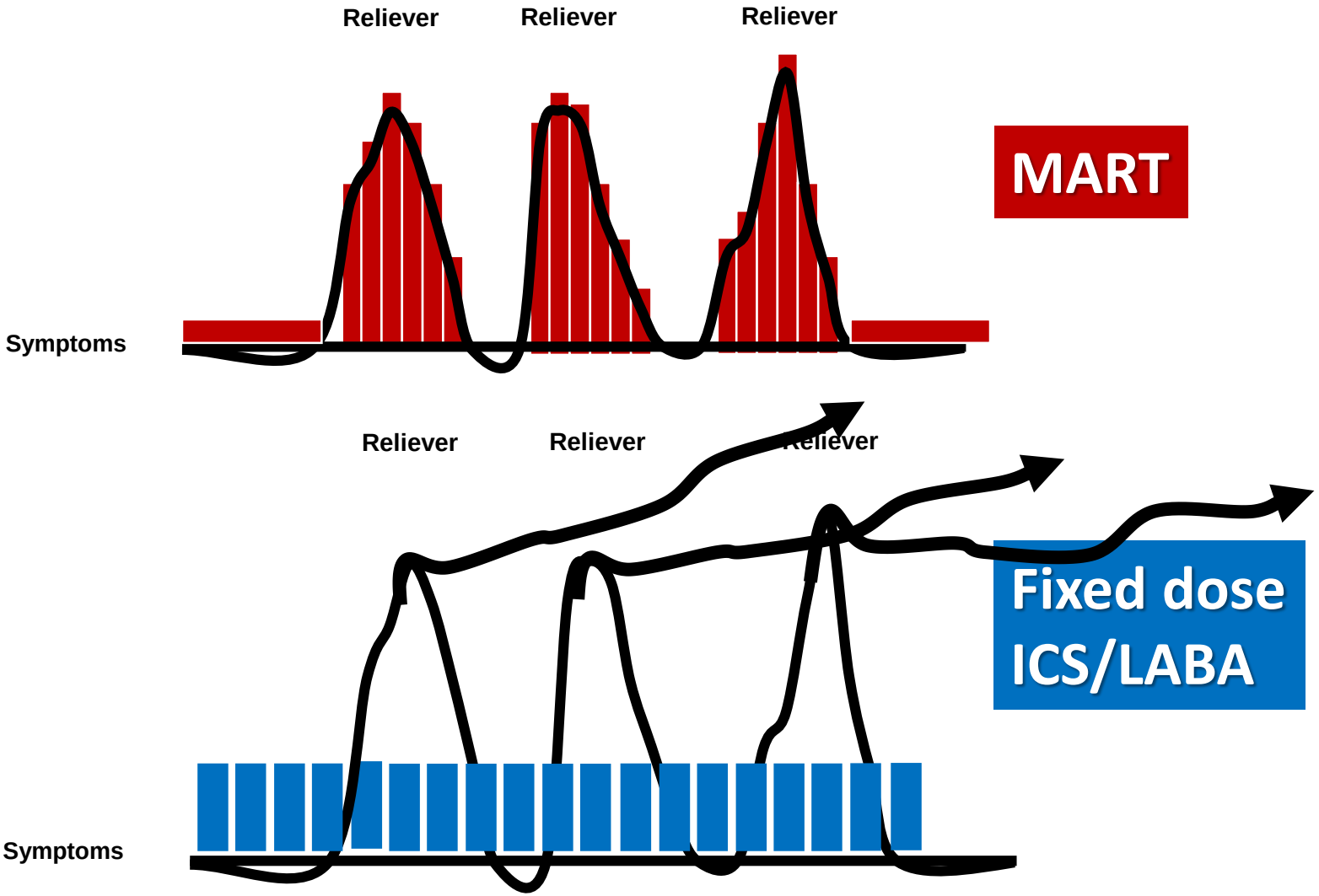
SABA 하루 사용 횟수

ICS 하루 사용 횟수

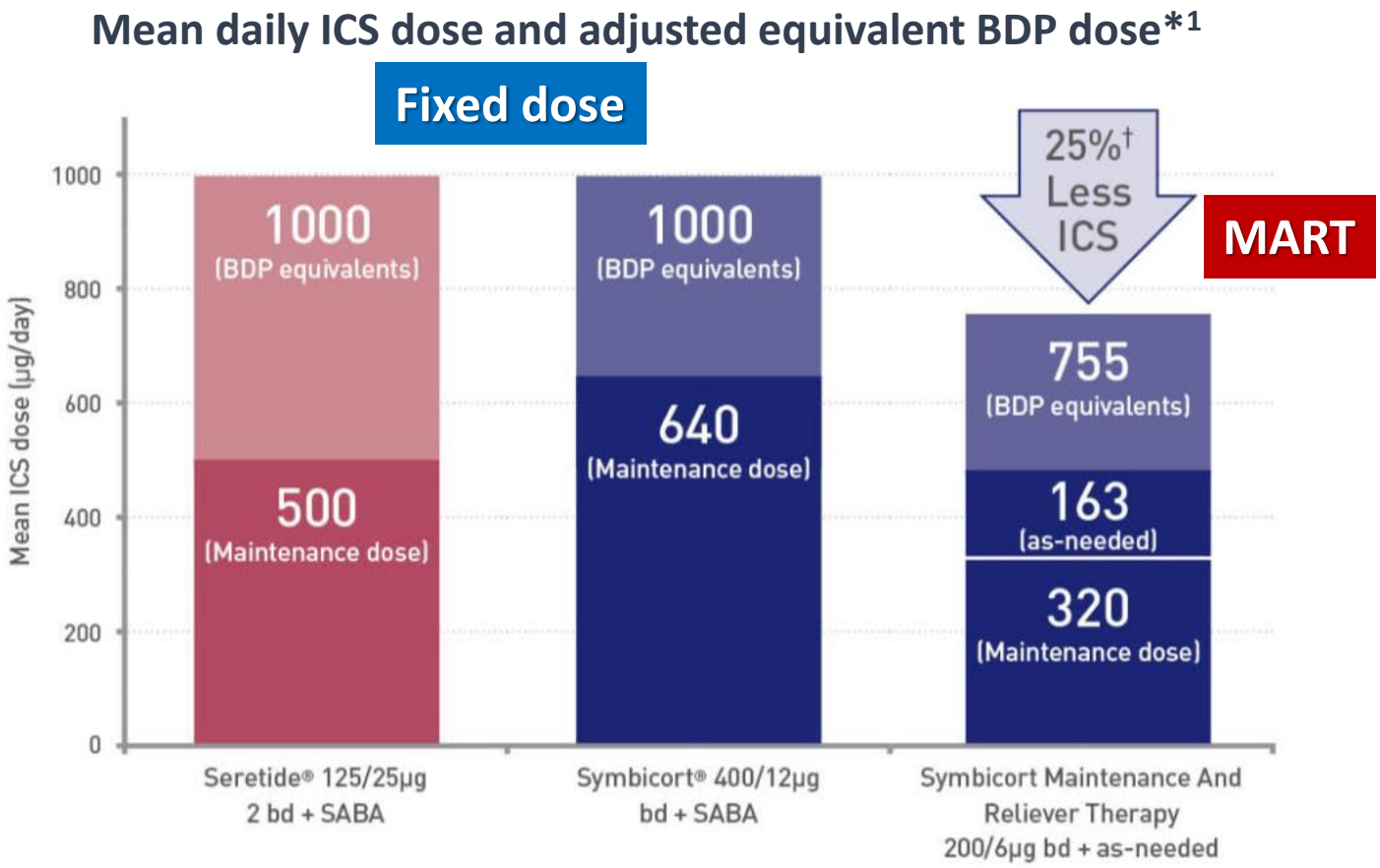


Martyn R Partridge, et al. BMC Pulmonary Medicine 2006, 6:13

MART: 천식의 변동성을 감안한 치료



천식의 변동성을 감안한 치료: ICS의 사용량 감소



Kuna P, *et al. Int J Clin Pract*. 2007; 61(5): 725–36.

천식의 변동성을 감안한 치료: FeNO values

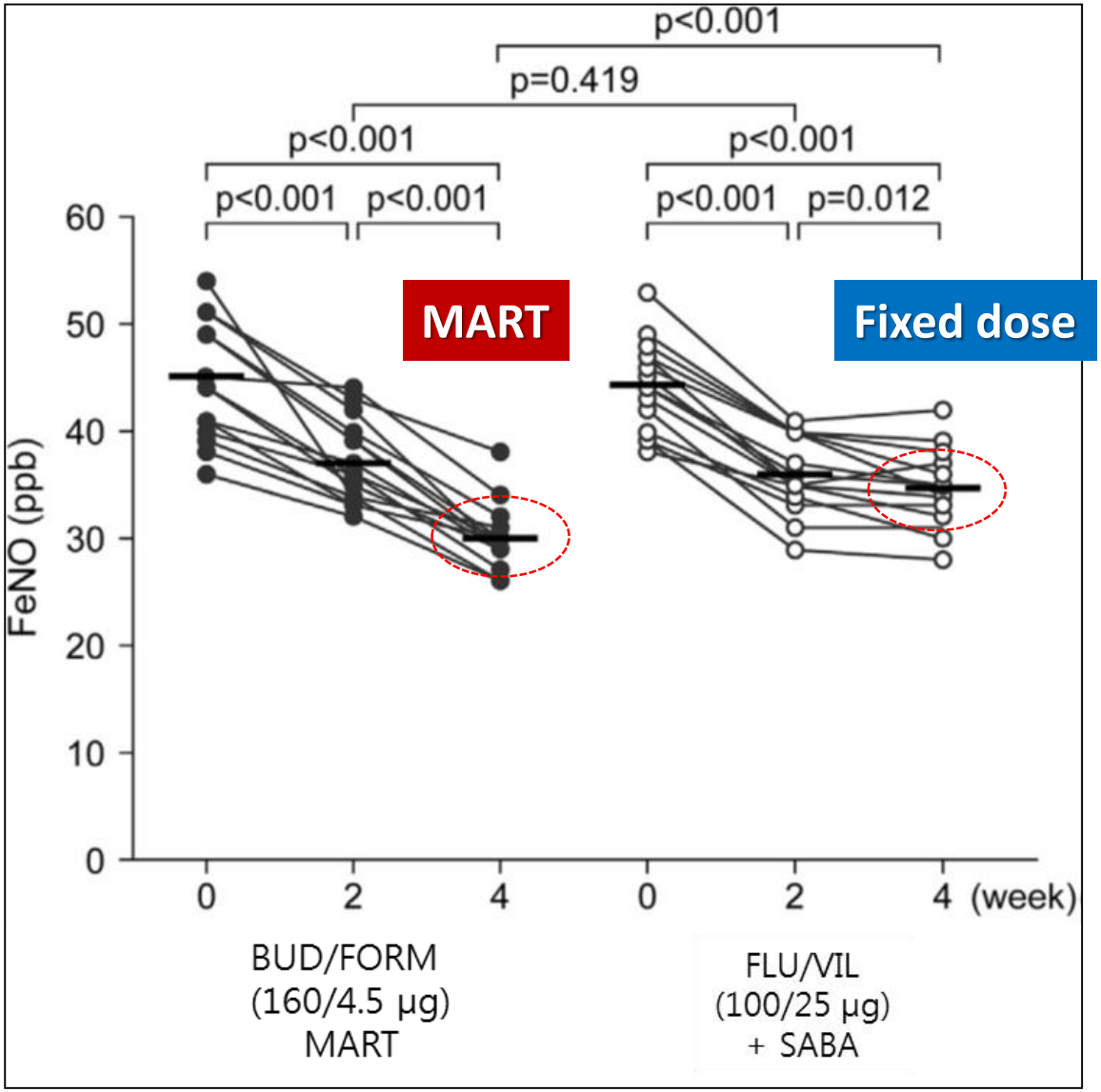


Figure modified from ref.

- As compared with FLU/VIL plus SABA treatment, **BUD/FORM MART** achieved **greater improvement in FeNO values.**

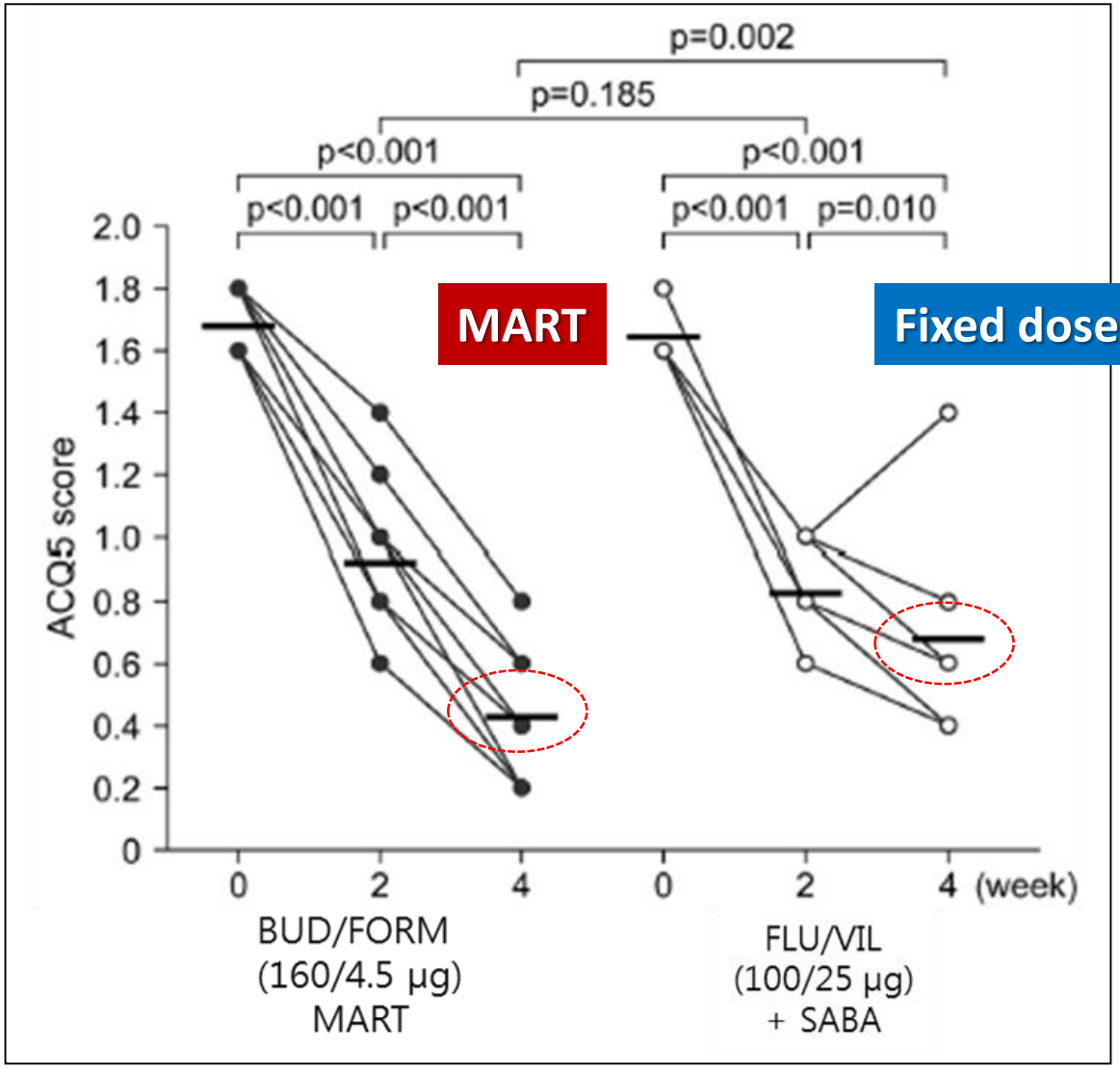
Study design: This was a 4-week, single-center, randomized, open-label study designed to compare the early effects of BUD/FORM maintenance and reliever therapy (n=15) with FLU/VIL fixed-dose (n=15) controller plus as-needed procaterol.

Safety: No adverse events were reported in either group.

FeNO, fractional exhaled nitric oxide; BUD, budesonide; FORM, formoterol; MART, maintenance and reliever therapy; FLU, fluticasone; VIL, vilanterol; SABA, short-acting β2-agonist.

Reference Hozawa S et al., Pulm Pharmacol Ther. 2016 Apr;37:15-23.

천식의 변동성을 감안한 치료: 천식 삶의 질



- As compared with FLU/VIL plus SABA treatment, **BUD/FORM MART** achieved **greater improvements in ACQ scores.**

ACQ5 score, Asthma Control Questionnaire 5-item version; BUD, budesonide; FORM, formoterol; MART, maintenance and reliever therapy; FLU, fluticasone; VIL, vilanterol; SABA, short-acting β2-agonist.

Figure modified from ref.

Reference Hozawa S et al., Pulm Pharmacol Ther. 2016 Apr;37:15-23.

천식의 변동성을 감안한 치료: Reliever의 사용 줄임

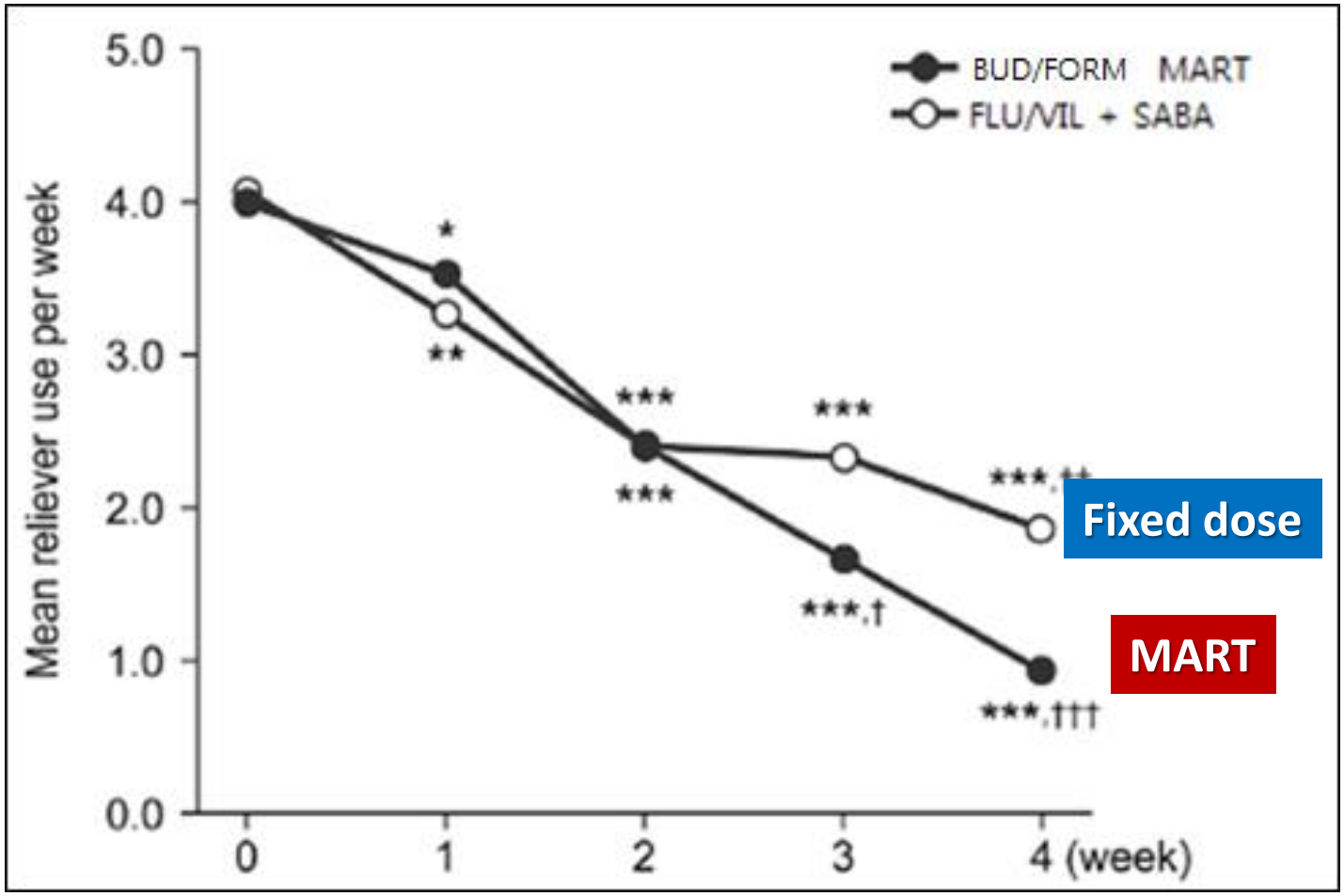


Figure modified from ref.

- **Reliever use** per week in the **BUD/FORM MART** group was significantly **lower** than that in the FLU/VIL plus SABA group at 3 and 4weeks.

BUD, budesonide; FORM, formoterol; MART, maintenance and reliever therapy; FLU, fluticasone; VIL, vilanterol; SABA, short-acting β2-agonist.

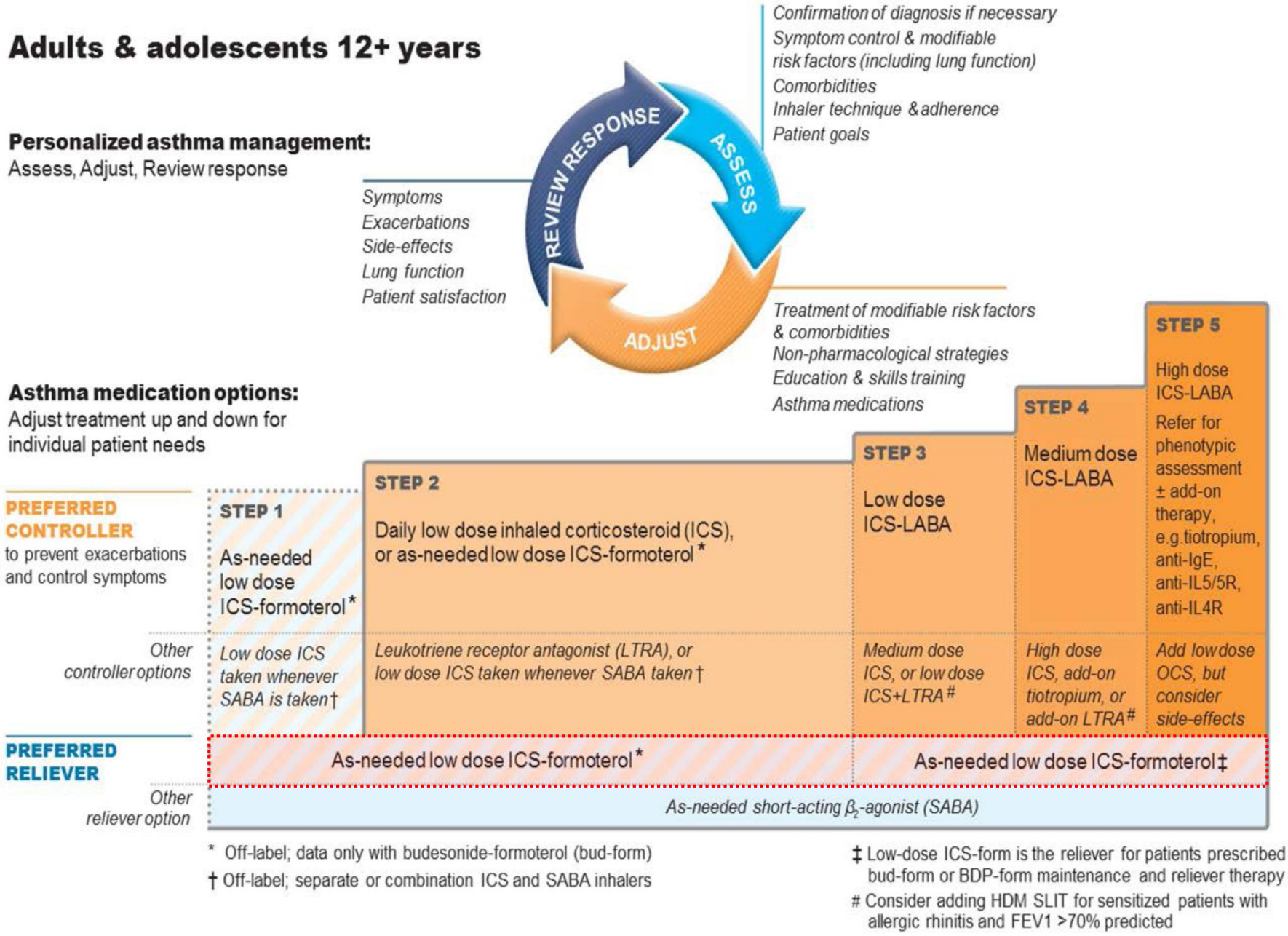
p-Values were determined using the paired t-test comparing baseline values to those obtained each week (*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$) and at 2-3 and 2-4weeks (†, $p < 0.05$; ††, $p < 0.01$; †††, $p < 0.001$) in each group.

Reference Hozawa S et al., Pulm Pharmacol Ther. 2016 Apr;37:15-23.

천식의 변동성을 감안한 치료 : 급성악화의 감소

Outcomes Follow-up calculated as weighted means, with range	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Overall heterogeneity and subgroup differences (ICS/LABA combination in control group)
	Assumed risk	Corresponding risk				
	Higher-dose ICS/LABA+ SABA	SiT for maintenance/relief				
People with exacerbations requiring hospitalisation	No data	No data	-	-	-	AstraZeneca could not provide data for hospitalisations separate to ER visits
중등 악화	10 per 100	Eight per 100 (seven to nine)	**OR 0.75 (0.65 to 0.87)**	9096 (four studies)	⊕⊕⊕⊕ **high**	I^2 = 0%; P value 0.82 Subgroup differences (P value 0.45)
부작용 (six to 12)	Four per 100	Four per 100 (three to five)	**OR 0.92 (0.74 to 1.13)**	9130 (four studies)	⊕⊕⊕◯ **moderate**[1]	I^2 = 0%; P value 0.98 Subgroup differences (P value 0.88)
응급실 입원	Five per 100	Four per 100 (three to five)	**OR 0.72 (0.57 to 0.90)**	7768 (three studies)	⊕⊕⊕⊕ **high**	I^2 = 0%; P value 0.66 Subgroup differences (P value 0.21)

Box 7. The GINA asthma treatment strategy



* Off-label; data only with budesonide-formoterol (bud-form)

† Off-label; separate or combination ICS and SABA inhalers

‡ Low-dose ICS-form is the reliever for patients prescribed bud-form or BDP-form maintenance and reliever therapy

\# Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV1 >70% predicted

Remission of Asthma: RHINE study

21,802 subjects born between 1945–1973

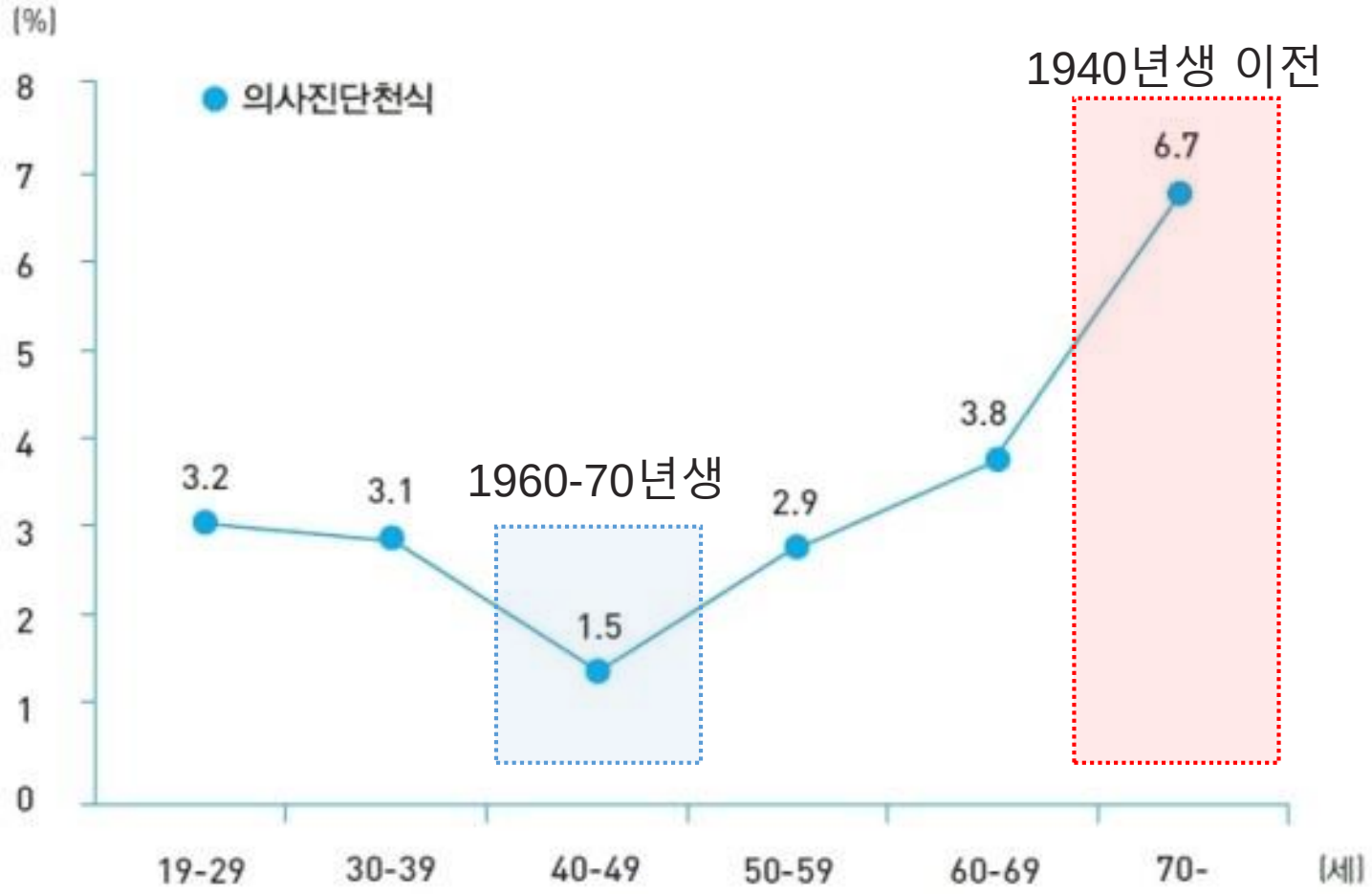
Observational

Remission: No asthma symptom without medication for 2 consecutive years

Predictor	n	Remission rate
Females	38	21.7
Males	76	17.8
Subjects born 1960–1973	119	22.5
Subjects born 1945–1959	95	17.9
Smokers	56	19.0
Quitters[#]	24	36.9*
Never-smokers	101	21.7
Any asthma symptom in the last 12 months at baseline		
Yes	903	18.4
No	250	26.5[¶]

Eur Respir J 2007; 30: 62–65

그림1-1 국내 성인 천식의 유병률 (2010년 국민건강영양조사 결과)



Outcomes of childhood asthma to the age of 50 years

Andrew Tai, MBBS, FRACP, PhD,[a] Haily Tran, BBioSc,[b] Mary Roberts, BSc,[c] Nadeene Clarke, BSc,[b] Anne-Marie Gibson, BSc,[b] Suzanna Vidmar, BSc (Hon),[d,e] John Wilson, MBBS, FRACP, PhD,[f] and Colin F. Robertson, MBBS, FRACP, MD[b,c] *North Adelaide, Parkville, Melbourne, and Prahran, Australia*

A group of children with a history of wheezing

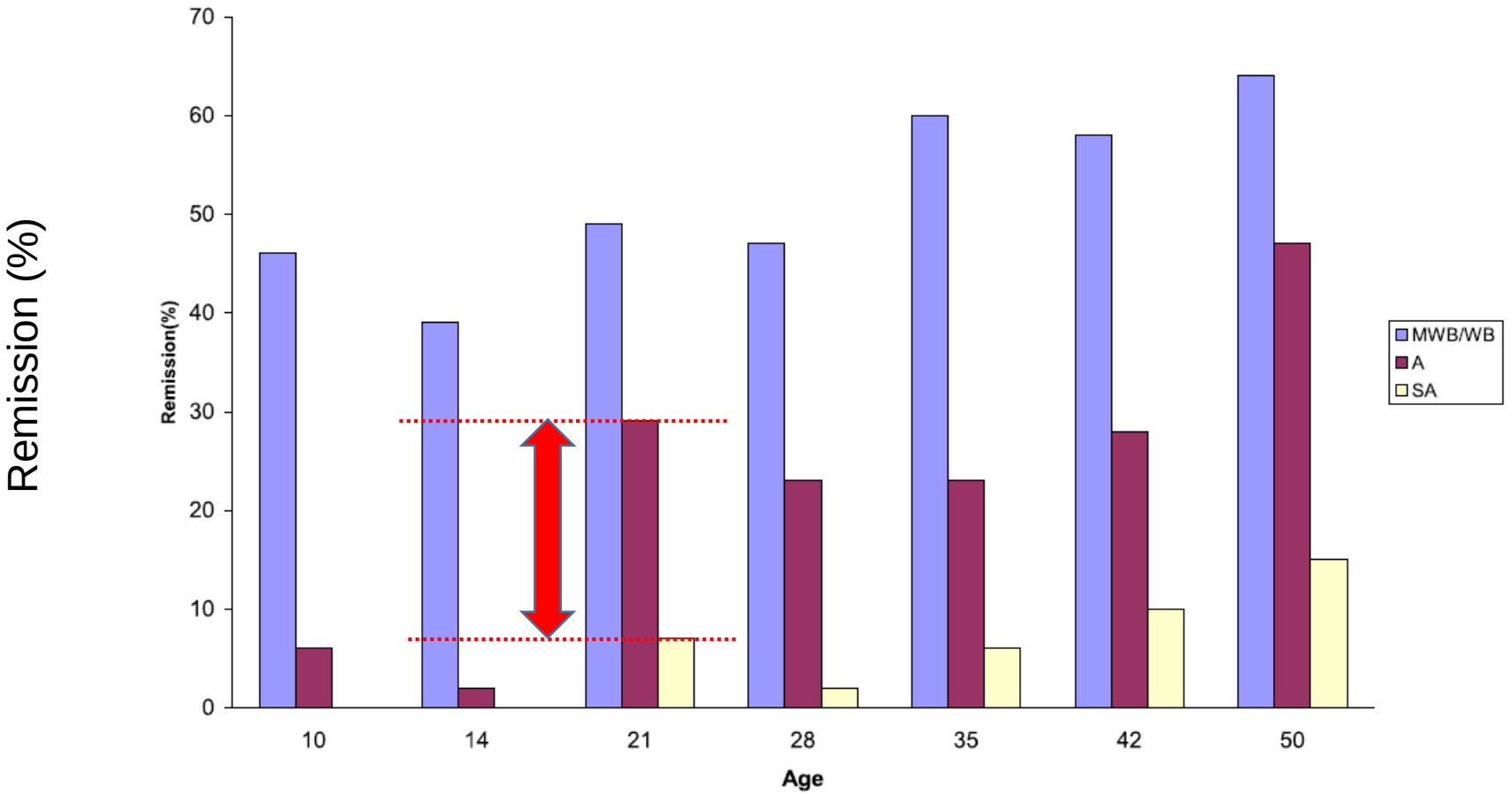
Randomly selected after a survey of 30,000 grade 2 Melbourne primary school children in 1963 to 1964 at the age of 7 years

These subjects have been followed prospectively at 7-year intervals, with the last review in 1999, when their average age was 42 years

One additional follow-up in 2006, 49 years old

J Allergy Clin Immunol 2014;133:1572-8

Asthma Remission



Asthma remission was defined as a subject who had no wheeze symptoms in the past 3 years and had not used bronchodilators, oral corticosteroids, or inhaled corticosteroids in the same time period.

J Allergy Clin Immunol 2014;133:1572-8

차례

The risk of asthma exacerbation after reducing inhaled corticosteroids: a systematic review and meta-analysis of randomized controlled trials

J. B. Hagan[1], S. A. Samant[1], G. W. Volcheck[1], J. T. Li[1], C. R. Hagan[2], P. J. Erwin[3] & M. A. Rank[4]

[1]Division of Allergic Diseases, Mayo Clinic, Rochester, MN; [2]Baylor University, Waco, TX; [3]Mayo Clinic Libraries, Rochester, MN; [4]Division of Allergy, Asthma, and Clinical Immunology, Mayo Clinic, Scottsdale, AZ, USA

Table 1 Characteristics of included studies

	N Control (continue ICS)	*N* Intervention (reduce ICS)	Setting	Trial location	Ages (years)	Inhaled cortico-st and daily dose us run-in and treatm	% ICS was Reduced	Run-in period (weeks)	Follow-up period (weeks)
Juniper 1991	8	6	Academic	Canada	>18	Budesonide 400–	50%	52	12
ZuWallack 1997	101	92	Academic/ Community	US	6–70	Flunisolide 1000	50%	4	12
Visser 2001	28	27	Academic	Netherlands	6–10	Fluticasone propi 200 µg	50%	8	26
Hawkins 2003	129	130	Academic/ Community	UK	18–86	Beclomethasone 1500, or 2000 µ Fluticasone prop 500, 1000, 1500 or 2000 µg	50%	4	12
Papi 2007	106	122	Academic	Italy, Austria, Spain, Poland	18–65	Beclomethasone	76%	4	24
Martinez 2011	72	71	Clinical/Academic	US	6–18	Beclomethasone	85%	4	44

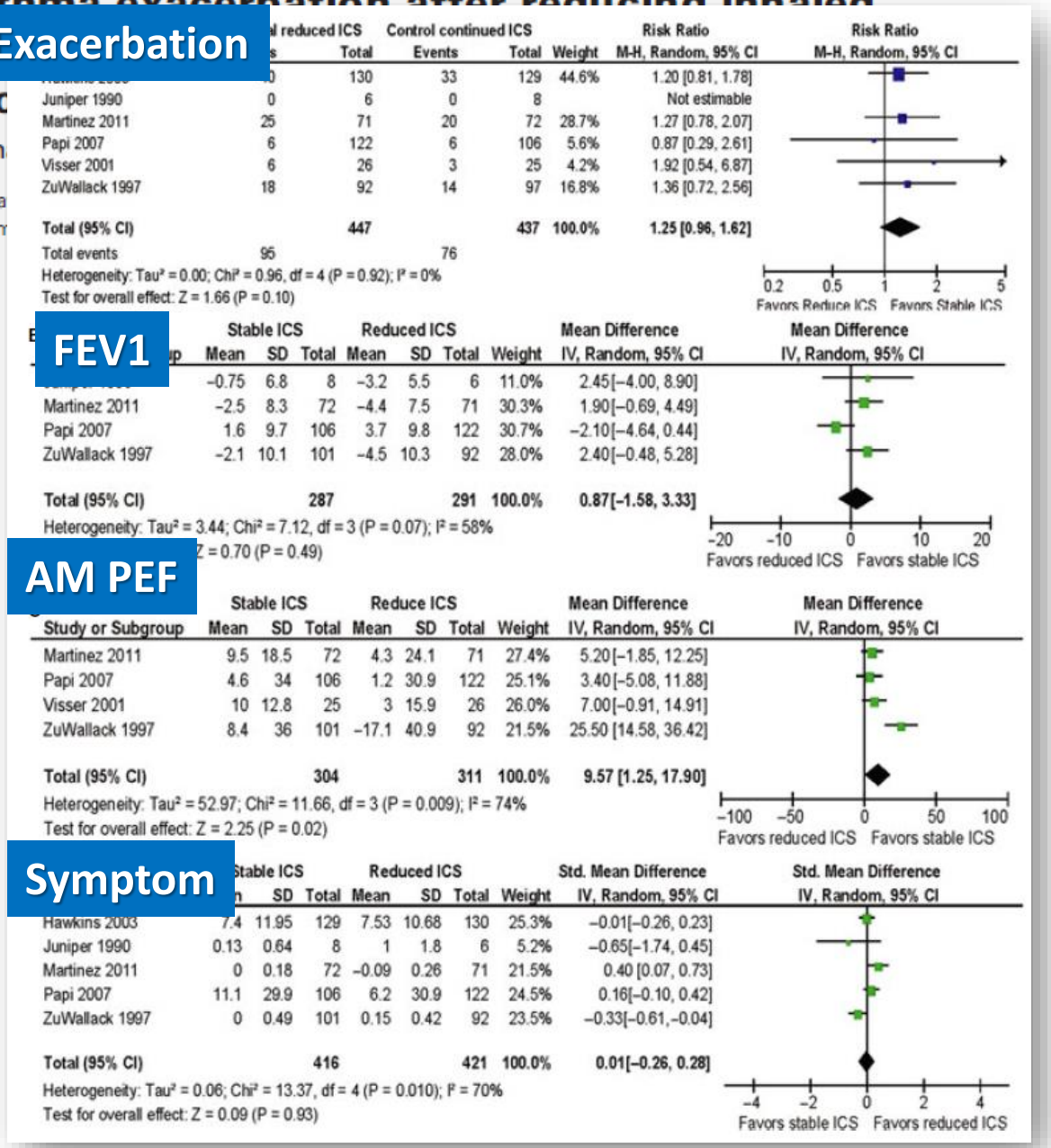
Allergy 69 (2014) 510–516

The risk of asthma exacerbation after reducing inhaled corticosteroi… randomized co…

J. B. Hagan[1], S. A. Sam…

[1]Division of Allergic Diseases, Ma… of Allergy, Asthma, and Clinical Im…

Exacerbation



FEV1

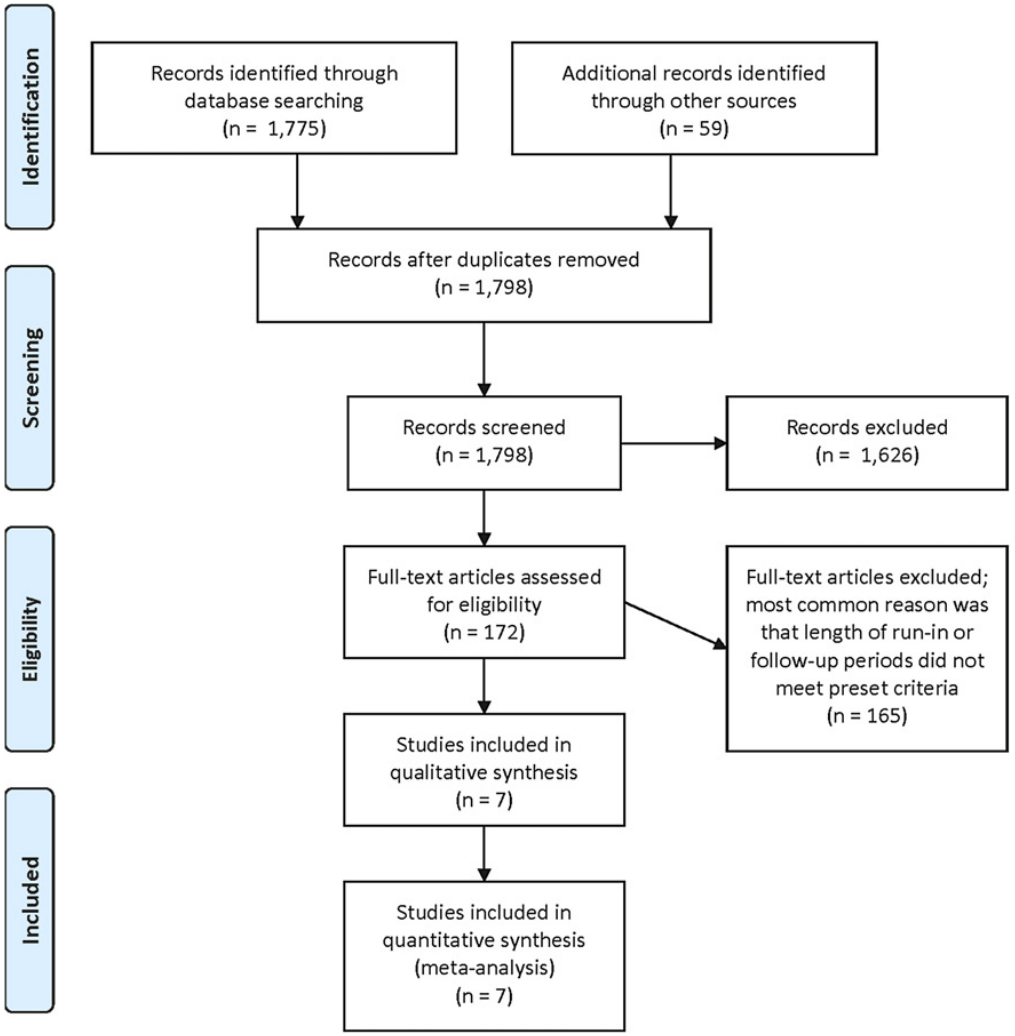
AM PEF

Symptom

Allergy 69 (2014) 510–516

The risk of asthma exacerbation after stopping low-dose inhaled corticosteroids: A systematic review and meta-analysis of randomized controlled trials

Matthew A. Rank, MD,[a] John B. Hagan, MD,[a] Miguel A. Park, MD,[a] Jenna C. Podjasek, MD,[a] Shefali A. Samant, MD,[a] Gerald W. Volcheck, MD,[a] Patricia J. Erwin, MLS,[b] and Colin P. West, MD, PhD[c,d] *Rochester, Minn*



J Allergy Clin Immunol 2013;131:724-9

The risk of asthma exacerbation after stopping low-dose inhaled corticosteroids: A systematic review and meta-analysis

Matthew A. Rank, MD,[a] John B. Hag
Gerald W. Volcheck, MD,[a] Patricia J

Asthma Exacerbation

	ed ICS			Risk Ratio	Risk Ratio
	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
	144	21.0%	2.93 [1.81, 4.74]	
	101	36.9%	2.24 [1.56, 3.22]	
Hahhtela 1994	19	4.1%	1.58 [0.53, 4.70]	
Lazaurs 2001	54	6.0%	4.05 [1.65, 9.97]	
Martinez 2011	72	25.0%	1.75 [1.13, 2.72]	
Papi 2007	110	6.4%	3.24 [1.36, 7.72]	
Waalkens 1993	8	0.6%	5.57 [0.35, 88.77]	
Total (95% CI)	**508**	**100.0%**	**2.35 [1.88, 2.92]**	

Total events 202 80
Heterogeneity: Tau² = 0.00; Chi² = 5.59, df = 6 (P = 0.47); I² = 0%
Test for overall effect: Z = 7.59 (P < 0.00001)

0.01 0.1 1 10 100
Favors no ICS Favors ICS

Favor ICS

FEV1

	no ICS			ICS				Mean Difference	Mean Difference
	Mean [L]	SD [L]	Total	Mean [L]	SD [L]	Total	Weight	IV, Random, 95% CI [L]	IV, Random, 95% CI [L]
	-0.18	0.6	95	0.07	0.49	101	17.8%	-0.25 [-0.40, -0.10]	
Hahhtela 1994	-0.25	0.38	18	0.01	0.17	19	13.5%	-0.26 [-0.45, -0.07]	
Lazaurs 2001	-0.3	0.97	56	-0.1	1.2	54	3.9%	-0.20 [-0.61, 0.21]	
Martinez 2011	0.04	0.19	74	0.1	0.19	72	35.4%	-0.06 [-0.12, 0.00]	
Papi 2007	-0.03	0.23	119	0.04	0.42	110	29.4%	-0.07 [-0.16, 0.02]	
Total (95% CI)			**362**			**356**	**100.0%**	**-0.13 [-0.21, -0.04]**	

Heterogeneity: Tau² = 0.00; Chi² = 8.54, df = 4 (P = 0.07); I² = 53%
Test for overall effect: Z = 3.00 (P = 0.003)

-1 -0.5 0 0.5 1
Favors ICS Favors No ICS

Favor ICS

AM PEF

	no ICS			ICS				Mean Difference	Mean Difference
	[L/min]	SD [L/min]	Total	Mean [L/min]	SD [L/min]	Total	Weight	IV, Random, 95% CI [L/min]	IV, Random, 95% CI [L/min]
Condemi 1997	-28	40	101	-6	39	95	20.1%	-22.00 [-33.06, -10.94]	
Hahhtela 1994	-22	25	19	-5	31	18	15.4%	-17.00 [-35.21, 1.21]	
Lazaurs 2001	-18	16	56	14	16	54	22.9%	-32.00 [-37.98, -26.02]	
Martinez 2011	-17	42	74	-16	26	72	19.9%	-1.00 [-12.30, 10.30]	
Papi 2007	-8	39	119	5	35	110	21.0%	-13.00 [-22.59, -3.41]	
Waalkens 1993	-11	124	20	20	188	8	0.7%	-31.00 [-172.16, 110.16]	
Total (95% CI)			**389**			**357**	**100.0%**	**-17.51 [-29.28, -5.75]**	

Heterogeneity: Tau² = 147.74; Chi² = 27.70, df = 5 (P < 0.0001); I² = 82%
Test for overall effect: Z = 2.92 (P = 0.004)

-100 -50 0 50 100
Favors ICS Favors no ICS

Favor ICS

Symptom

	o ICS			ICS				Std. Mean Difference	Std. Mean Difference
		SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
		1.9	95	-0.1	1	101	27.0%	0.53 [0.24, 0.81]	
Hahhtela 1994	0.5	0.8	18	0.2	0.9	19	5.2%	0.34 [-0.31, 0.99]	
Lazaurs 2001	0.35	0.72	56	0.06	0.3	54	15.2%	0.52 [0.14, 0.90]	
Martinez 2011	0.05	0.17	74	0.006	0.09	72	20.6%	0.32 [-0.01, 0.65]	
Papi 2007	0.05	0.1	119	-0.33	1.4	110	32.0%	0.39 [0.13, 0.65]	
Total (95% CI)			**362**			**356**	**100.0%**	**0.43 [0.28, 0.58]**	

Heterogeneity: Tau² = 0.00; Chi² = 1.27, df = 4 (P = 0.87); I² = 0%
Test for overall effect: Z = 5.69 (P < 0.00001)

-2 -1 0 1 2
Favors no ICS Favors ICS

Favor ICS

J Allergy Clin Immunol 2013;131:724-9

GINA 2011

Controller treatment may be stopped

- if the patient's asthma remains controlled on the lowest dose of controller and

- no recurrence of symptoms occurs for one year

GINA since 2014

Do no completely withdraw ICS

unless this is needed temporarily to confirm the diagnosis of asthma.

	No. control (continue ICSs)	No. intervention (stop ICSs)	Setting	Country or countries of origin	Age (y)	ICS and daily dose used in run-in and treatment periods	Run-in period (wk)	Follow-up period (wk)	Funding
Berger et al,[6] 2010	144	150	Community	United States	>16	Budesonide, 320 μg	4	12	Pharmaceutical company
Condemi et al,[7] 1997	101	95	Community	United States	>12	Triamcinolone, 800 μg	4	24	Pharmaceutical company
Haahtela et al,[8] 1994	19	18	Academic	Finland	>15	Budesonide, 400 μg	4	52	Not stated
Lazarus et al,[9] 2001	54	56	Academic	United States	12-65	Triamcinolone, 800 μg	6	16	US government (equipment and medicine donated by private companies)
Martinez et al,[10] 2011	72	74	Academic	United States	6-18	Beclomethasone, 80 μg	4	44	US government (pharmaceutical company donated medications)
Papi et al,[11] 2007	110	119	Academic	Italy, Austria, Spain, Poland	18-65	Beclomethasone, 500 μg	4	24	Pharmaceutical company
Waalkens et al,[12] 1993	8	20	Academic	The Netherlands	7-16	Budesonide, 150 μg	112-144	16	The Netherlands' government (pharmaceutical company donated medications)

EFFECTS OF REDUCING OR DISCONTINUING INHALED BUDESONIDE IN PATIENTS WITH MILD ASTHMA

TARI HAAHTELA, M.D., MARKKU JÄRVINEN, M.D., TUOMO KAVA, M.D., KIRSTI KIVIRANTA, M.D., SIRKKA KOSKINEN, M.D., KAARINA LEHTONEN, M.D., KURT NIKANDER, B.A., TORE PERSSON, PH.D., OLOF SELROOS, M.D., ANSSI SOVIJÄRVI, M.D., BRITA STENIUS-AARNIALA, M.D., THORE SVAHN, M.SC., RITVA TAMMIVAARA, M.D., AND LAURI A. LAITINEN, M.D.

CHARACTERISTIC	DOUBLE-BLIND BUDESONIDE, 400 μg/DAY (N = 19)	DOUBLE-BLIND PLACEBO (N = 18)	OPEN-LABEL BUDESONIDE, 1200 μg/DAY (N = 37)
Sex (M/F)	4/15	7/11	8/29
Age (yr)	35.9±2.4	41.0±2.8	38.2±2.1
Height (cm)	167.8±2.1	166.6±1.9	165.2±1.2
Weight (kg)	70.6±3.9	73.6±3.2	68.9±2.8
Duration of asthma (mo)	8.1±0.7	6.4±0.7	6.9±0.5
Atopy (yes/no)	13/6	12/6	32/5
Blood eosinophils (10^9/liter)†	0.40±0.06	0.42±0.05	0.36±0.05
FEV_1			
In liters	3.17±0.14	2.98±0.14	3.03±0.10
As % of predicted‡	88.0±2.5	84.2±2.4	88.8±2.1
FVC			
In liters	4.01±0.20	3.92±0.19	3.84±0.14
As % of predicted‡	93.9±3.0	92.2±2.7	94.9±2.0
Morning PEF			
In liters per min§	449±17	425±18	428±11
As % of predicted¶	88.8±2.4	81.4±2.8	85.6±1.5
PC_{15}			
In mg/ml‖	9.3	4.2	6.8
As dose steps	3.2±0.5	2.1±0.5	2.8±0.4

*Plus–minus values are means ±SE

4 weeks run-in period
600mcg budesonide twice daily

2 year treatment period
terbutaline vs. budesonide

1 year open arm period
Budesonide vs. placebo

NEJM 1994;331:700-5

EFFECTS OF REDUCING OR DISCONTINUING INHALED BUDESONIDE IN PATIENTS WITH MILD ASTHMA

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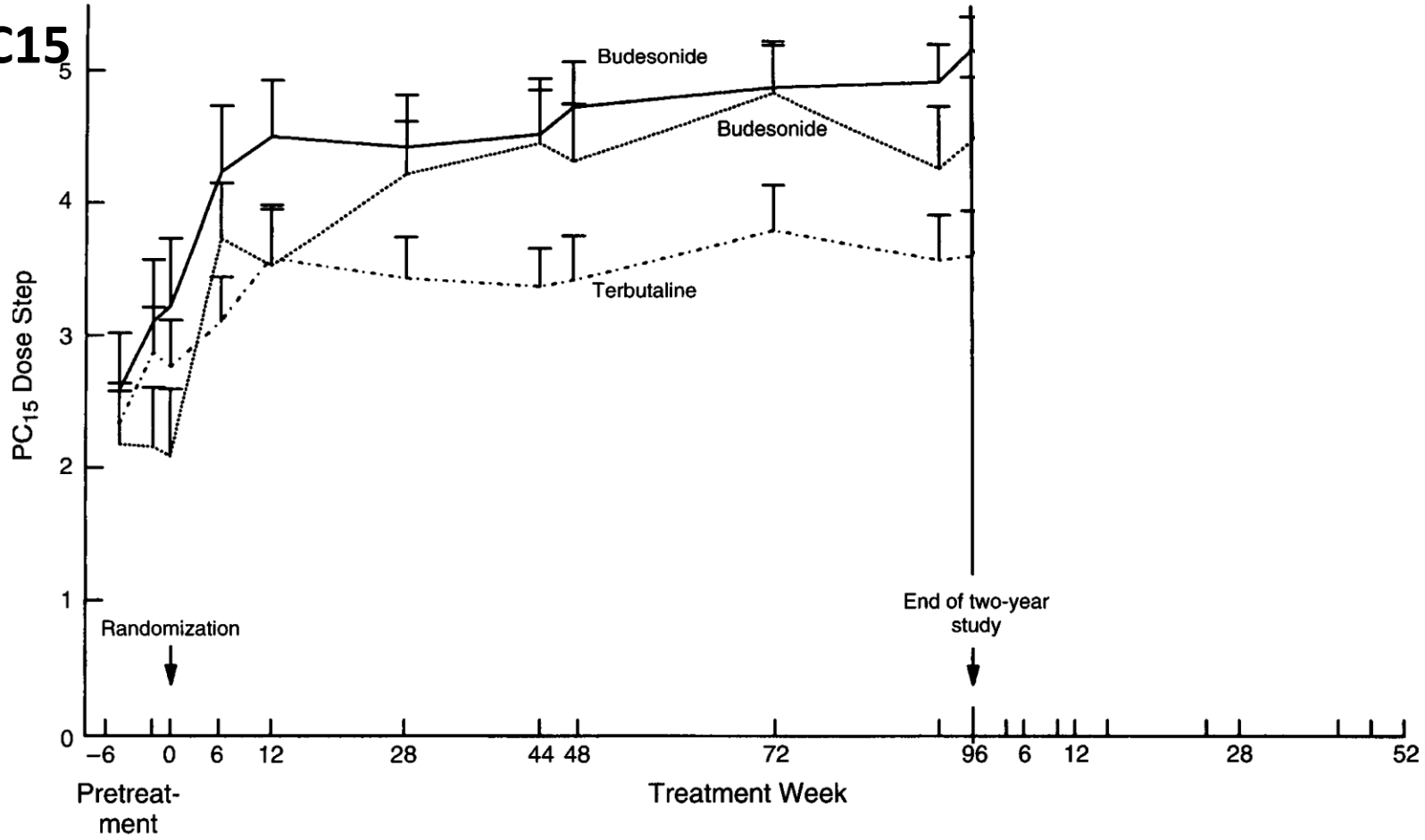
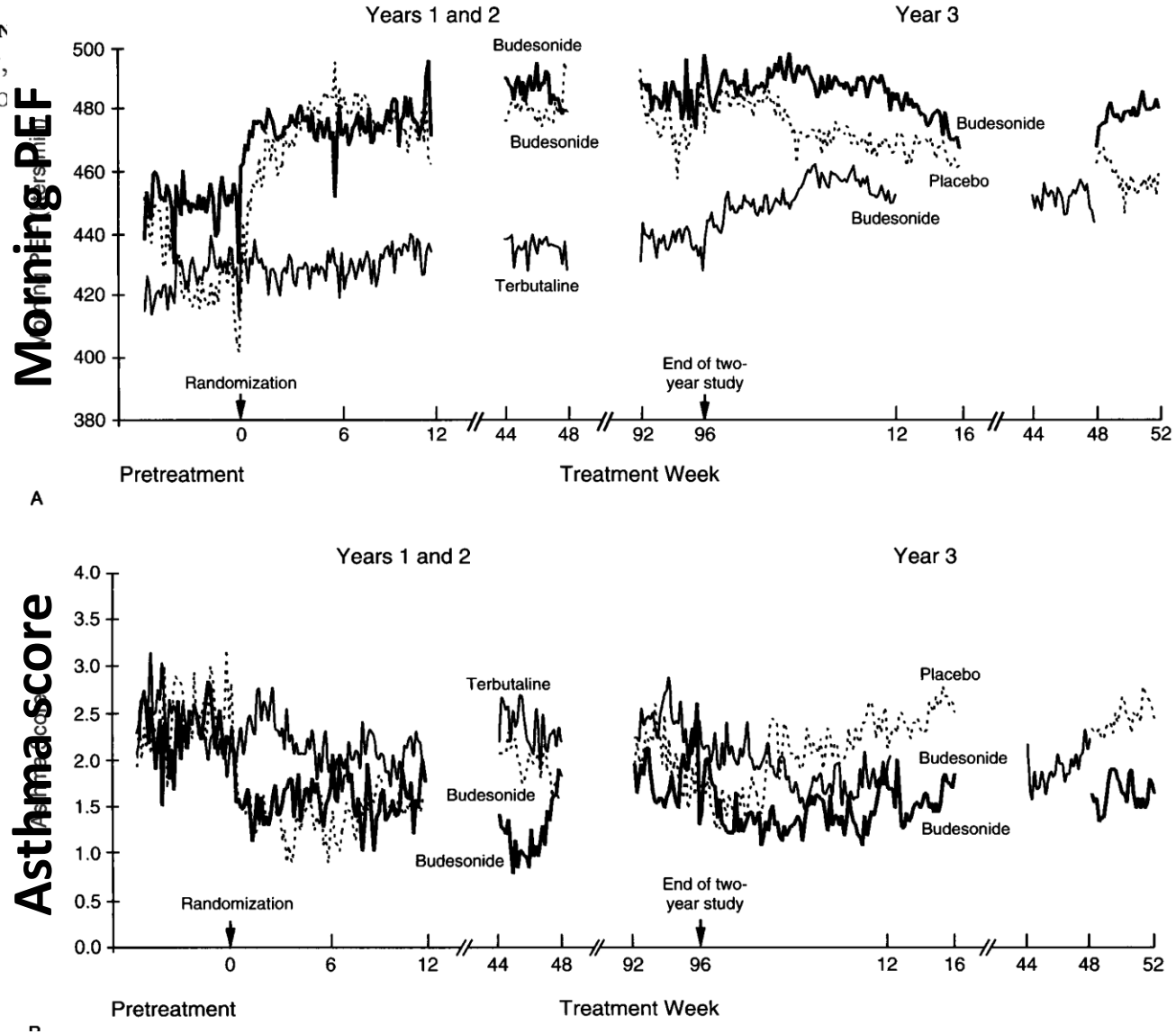
PC15



NEJM 1994;331:700-5

EFFECTS OF REDUCING OR DISCONTINUING INHALED BUDESONIDE IN PATIENTS WITH MILD ASTHMA

KIRSTI KIVIRAN
TORE PERSSON,
THO



ORIGINAL CONTRIBUTION

Long-Acting β_2-Agonist Monotherapy vs Continued Therapy With Inhaled Corticosteroids in Patients With Persistent Asthma

A Randomized Controlled Trial

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Context Long-acting β_2-agonists are prescribed for patients with persistent asthma and are sometimes used without inhaled corticosteroids (ICSs). No evidence exists, however, to support their use as monotherapy in adults with persistent asthma.

Objective To examine the effectiveness of salmeterol xinafoate, a long-acting β_2-agonist, as replacement therapy in patients whose asthma is well controlled by low-dose triamcinolone acetonide, an ICS.

Design and Setting A 28-week, randomized, blinded, placebo-controlled, parallel group trial conducted at 6 National Institutes of Health–sponsored, university-based ambulatory care centers from February 1997 to January 1999.

Participants One hundred sixty-four patients aged 12 through 65 years with persistent asthma that was well controlled during a 6-week run-in period of treatment with inhaled triamcinolone (400 µg twice per day).

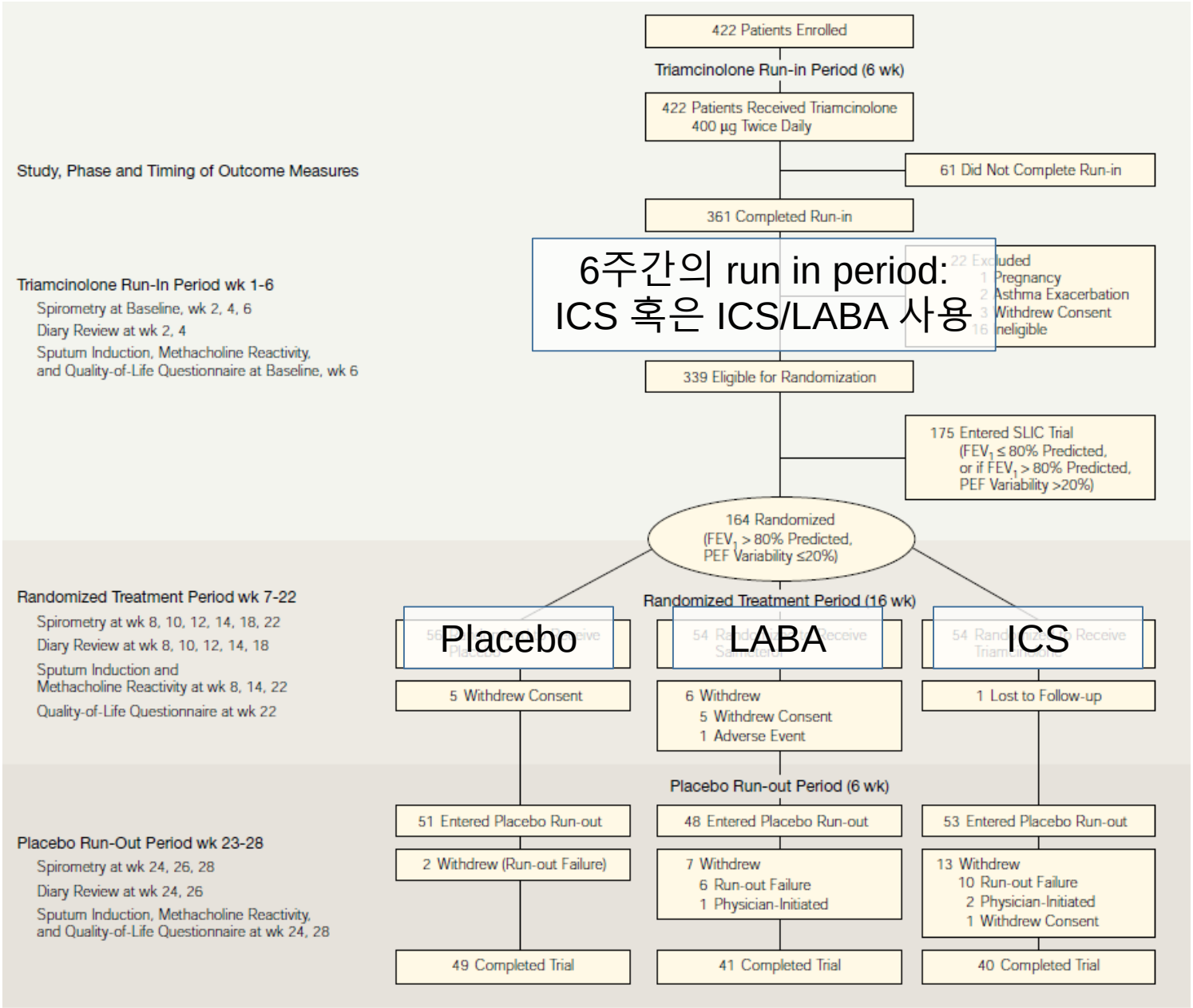
Interventions Patients were randomly assigned to continue triamcinolone therapy (400 µg twice per day; n=54) or switch to salmeterol (42 µg twice per day; n=54) or to placebo (n=56) for 16 weeks, after which all patients received placebo for an additional 6-week run-out period.

Main Outcome Measures Change in morning and evening peak expiratory flow (PEF), forced expiratory volume in 1 second (FEV_1), self-assessed asthma symptom scores, rescue albuterol use, asthma-specific quality-of-life scores, treatment failure, asthma exacerbation, bronchial reactivity, and markers of airway inflammation, compared among the 3 treatment groups.

Results During the 16-week randomized treatment period, no significant differences between the salmeterol and triamcinolone groups were observed for conventional outcomes of clinical studies of asthma therapy—morning PEF, evening PEF, asthma symptom scores, rescue albuterol sulfate use, or quality of life. Both active treatments were superior to placebo. However, the salmeterol group had more treatment failures than the triamcinolone group (13/54 [24%] vs 3/54 [6%]; $P=.004$), as well as more asthma exacerbations (11/54 [20%] vs 4/54 [7%]; $P=.04$), greater increases in median (interquartile range) sputum eosinophils (2.4% [0.0% to 10.6%] vs –0.1% [–0.7% to 0.3%]; $P<.001$), eosinophil cationic protein (71 [–2 to 430] U/L vs –4 [–31 to 56] U/L; $P=.005$), and tryptase (3.1

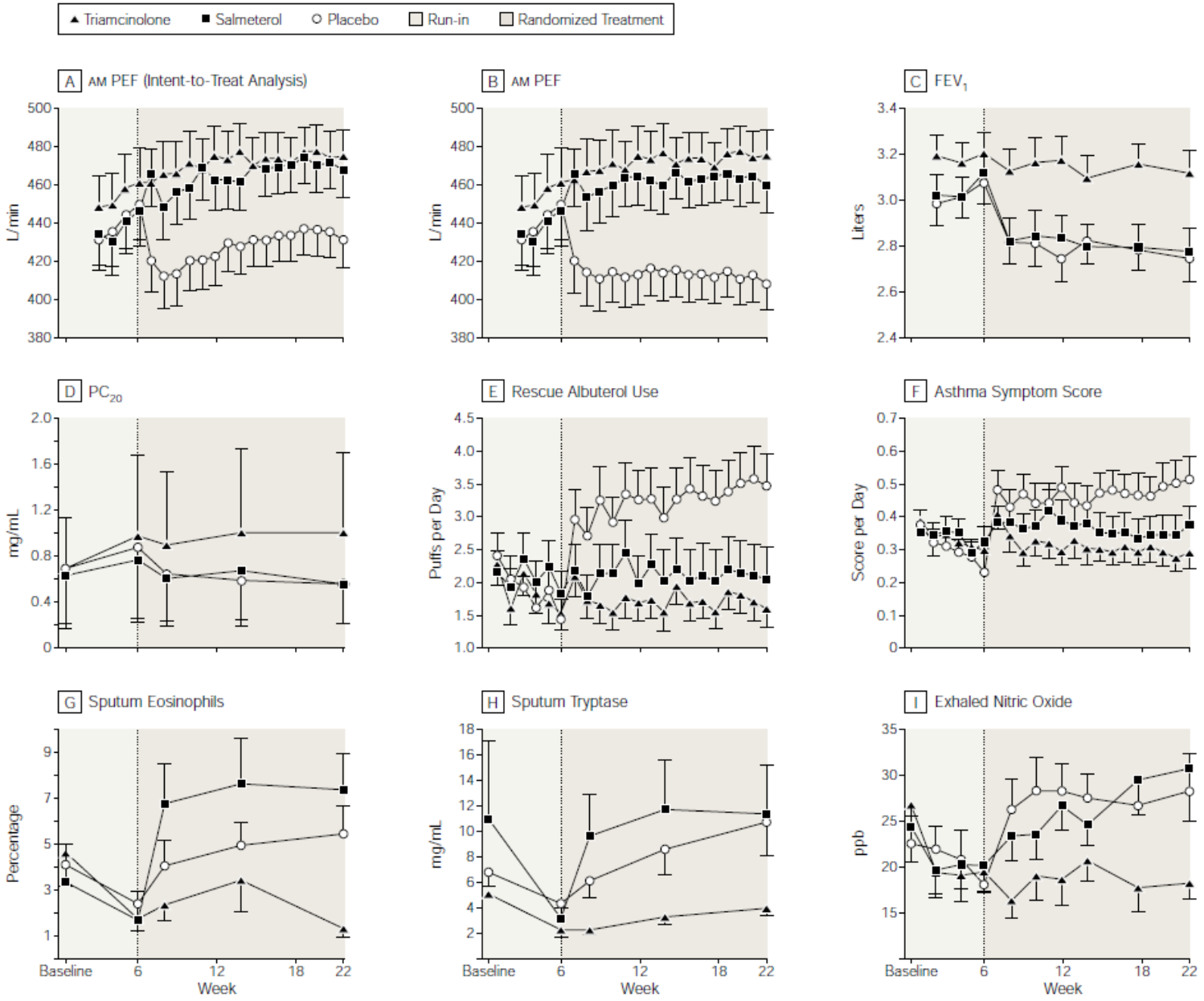
REGULAR USE OF LONG-ACTING β_2-agonists has been shown to

JAMA. 2001 May 23-30;285(20):2583-93

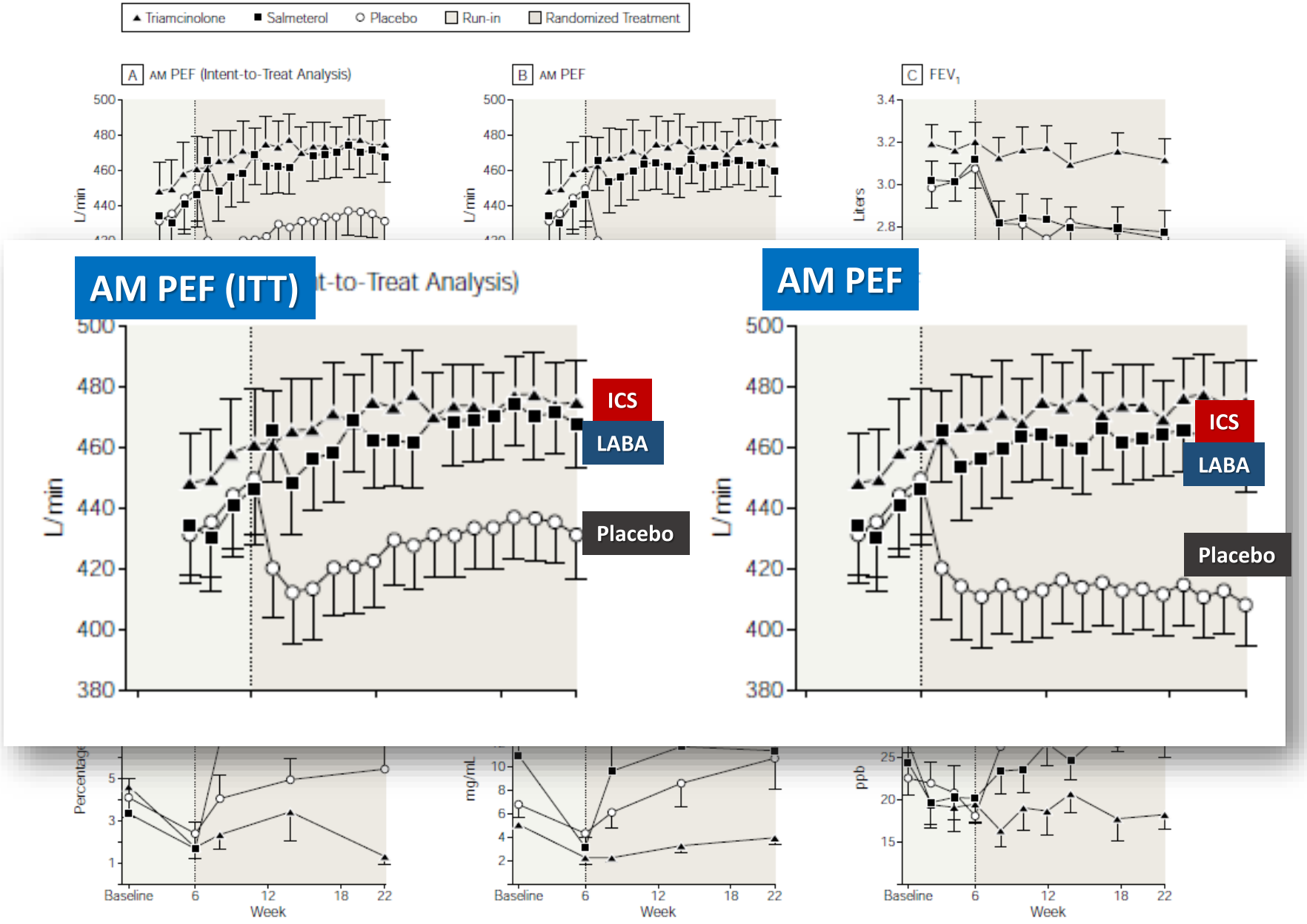


6주간의 run in period:
ICS 혹은 ICS/LABA 사용

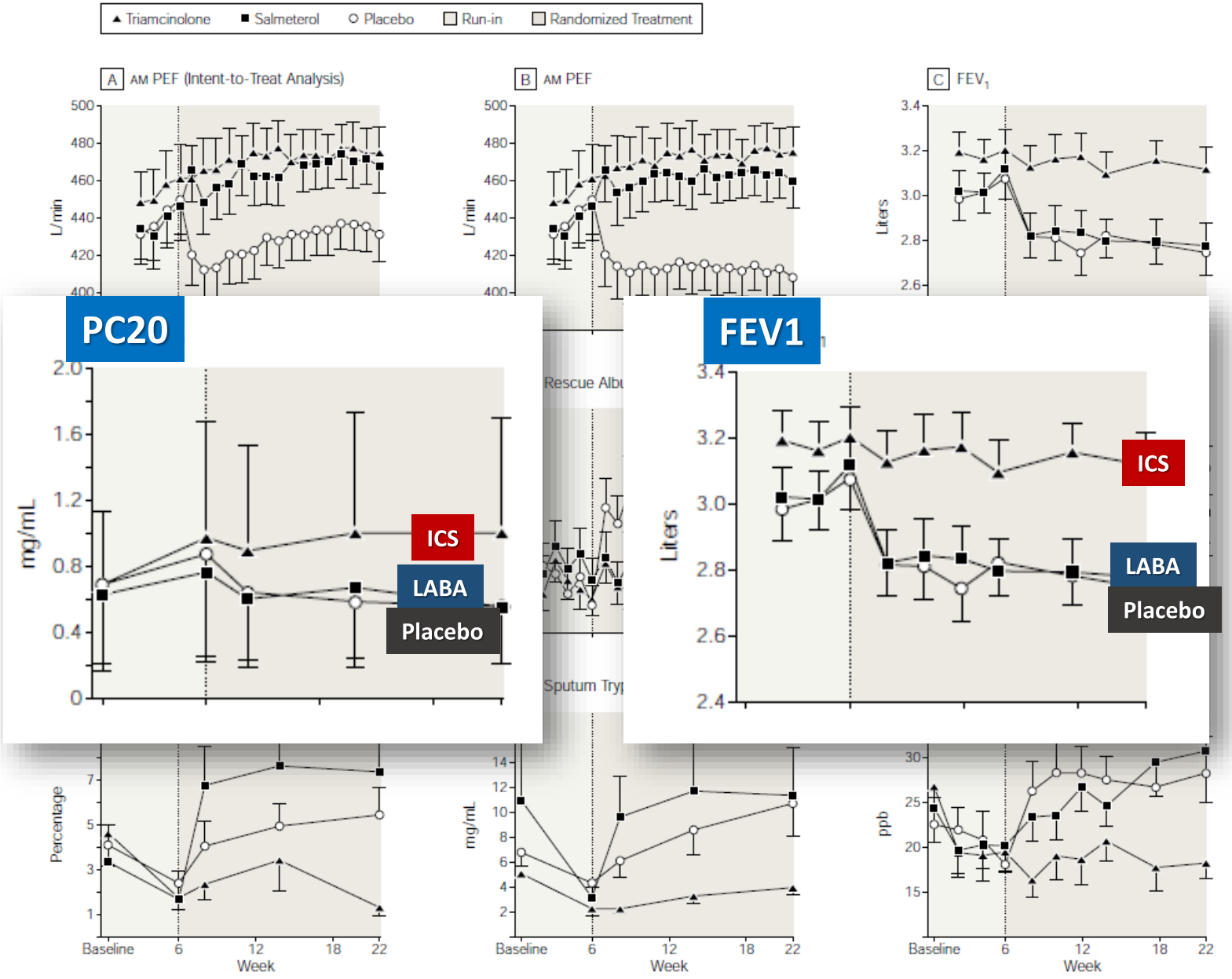
JAMA. 2001 May 23-30;285(20):2583-93



JAMA. 2001 May 23-30;285(20):2583-93



JAMA. 2001 May 23-30;285(20):2583-93



JAMA. 2001 May 23-30;285(20):2583-93

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

Fernando D Martinez, Vernon M Chinchilli, Wayne J Morgan, Susan J Boehmer, Robert F Lemanske Jr, David T Mauger, Robert C Strunk, Stanley J Szefler, Robert S Zeiger, Leonard B Bacharier, Elizabeth Bade, Ronina A Covar, Noah J Friedman, Theresa W Guilbert, Hengameh Heidarian-Raissy, H William Kelly, Jonathan Malka-Rais, Michael H Mellon, Christine A Sorkness, Lynn Taussig

Lancet 2011; 377: 650–57
Published Online February 15, 2011
DOI:10.1016/S0140-6736(10)62145-9

See Comment page 614

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Summary

Background Daily inhaled corticosteroids are an effective treatment for mild persistent asthma, but some children have exacerbations even with good day-to-day control, and many discontinue treatment after becoming asymptomatic. We assessed the effectiveness of an inhaled corticosteroid (beclomethasone dipropionate) used as rescue treatment.

Methods In this 44-week, randomised, double-blind, placebo-controlled trial we enrolled children and adolescents with mild persistent asthma aged 5–18 years from five clinical centres in the USA. A computer-generated randomisation sequence, stratified by clinical centre and age group, was used to randomly assign participants to one of four treatment groups: twice daily beclomethasone with beclomethasone plus albuterol as rescue (combined group); twice daily beclomethasone with placebo plus albuterol as rescue (daily beclomethasone group); twice daily placebo with beclomethasone plus albuterol as rescue (rescue beclomethasone group); and twice daily placebo with placebo plus albuterol as rescue (placebo group). Twice daily beclomethasone treatment was one puff of beclomethasone (40 µg per puff) or placebo given in the morning and evening. Rescue beclomethasone treatment was two puffs of beclomethasone or placebo for each two puffs of albuterol (180 µg) needed for symptom relief. The primary outcome was time to first exacerbation that required oral corticosteroids. A secondary outcome measured linear growth. Analysis was by intention to treat. This study is registered with clinicaltrials.gov, number NCT00394329.

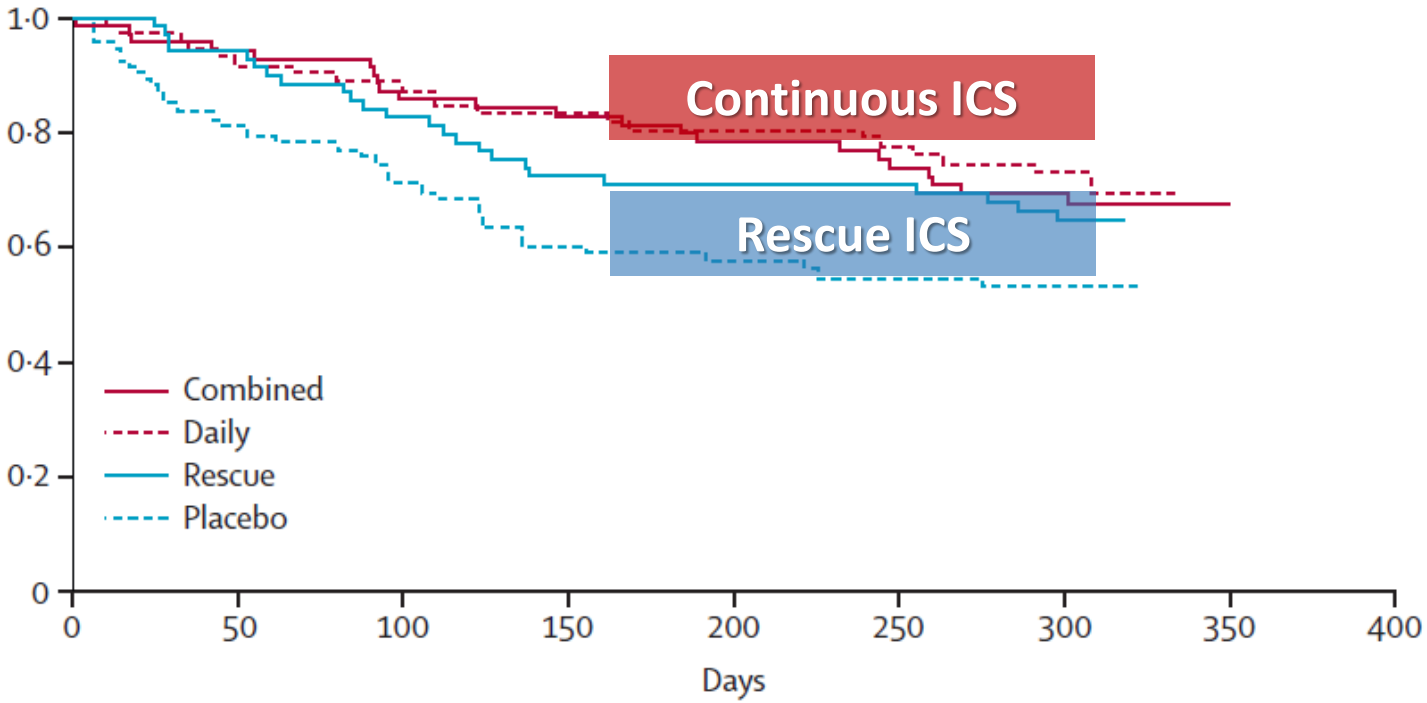
Results 843 children and adolescents were enrolled into this trial, of whom 288 were assigned to one of four treatment groups; combined (n=71), daily beclomethasone (n=72), rescue beclomethasone (n=71), and placebo (n=74)—555 individuals were excluded during the run-in, according to predefined criteria. Compared with the placebo group (49%, 95% CI 37–61), the frequency of exacerbations was lower in the daily (28%, 18–40, p=0·03), combined (31%, 21–43, p=0·07), and rescue (35%, 24–47, p=0·07) groups. Frequency of treatment failure was 23% (95% CI 14–43) in the placebo group, compared with 5·6% (1·6–14) in the combined (p=0·012), 2·8% (0–10) in the daily (p=0·009), and 8·5% (2–15) in the rescue (p=0·024) groups. Compared with the placebo group, linear growth was 1·1 cm (SD 0·3) less in the combined and daily arms (p<0·0001), but not the rescue group (p=0·26). Only two individuals had severe adverse events; one in the daily beclomethasone group had viral meningitis and one in the combined group had bronchitis.

Interpretation Children with mild persistent asthma should not be treated with rescue albuterol alone and the most effective treatment to prevent exacerbations is daily inhaled corticosteroids. Inhaled corticosteroids as rescue medication with albuterol might be an effective step-down strategy for children with well controlled, mild asthma because it is more effective at reducing exacerbations than is use of rescue albuterol alone. Use of daily inhaled corticosteroid treatment and related side-effects such as growth impairment can therefore be avoided.

Funding National Heart, Lung and Blood Institute.

Lancet 2011; 377: 650–57

Time to first exacerbation



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

Lancet 2011; 377: 650–57

Asthma

Persistent asthma

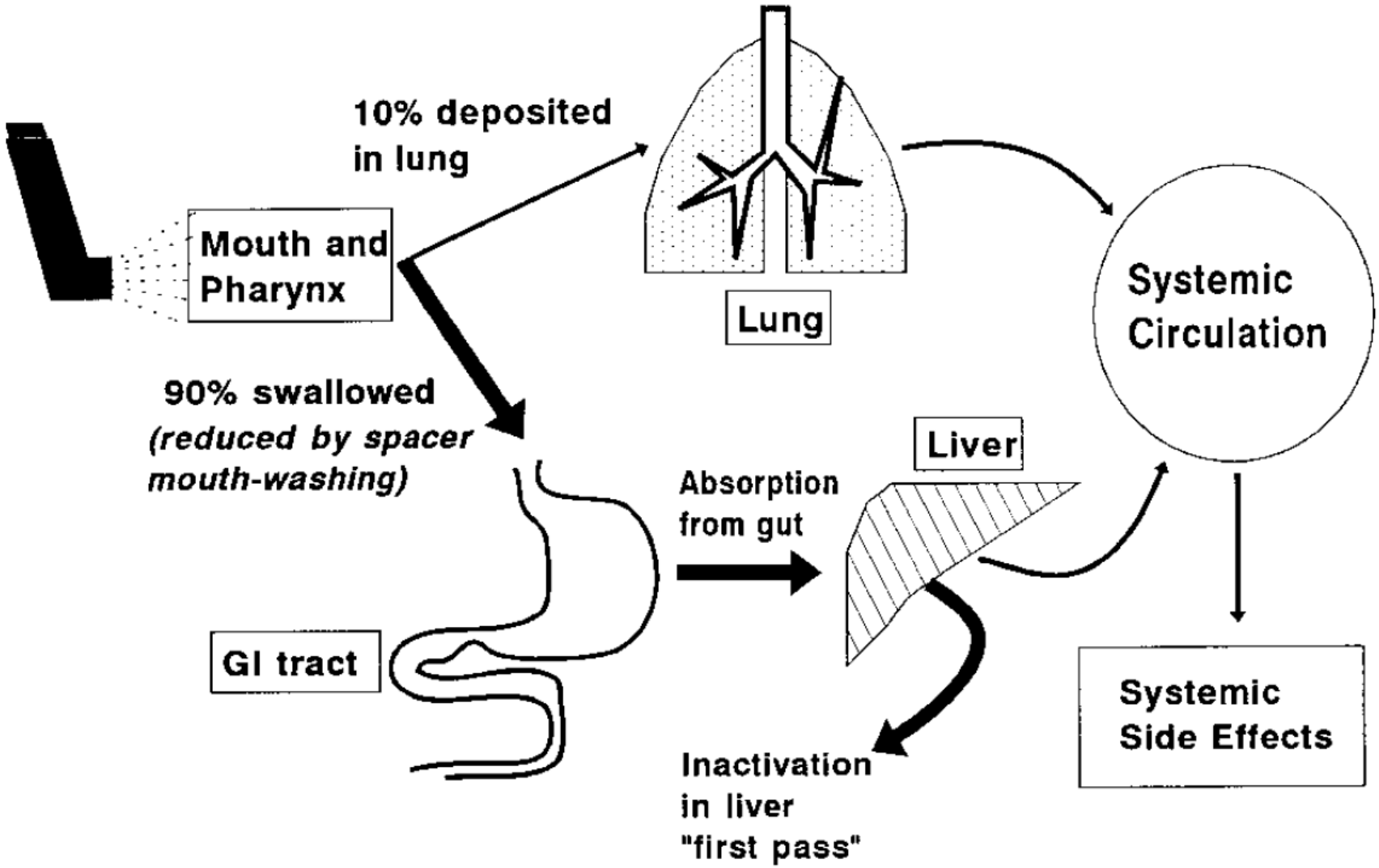
Mild persistent asthma

	No. control (continue ICSs)	No. intervention (stop ICSs)	Setting	Country or countries of origin	Age (y)	ICS an dose u run-i treat per	Run-in period (wk)	Follow-up period (wk)	ding
Berger et al,[6] 2010	144	150	Community	United States	>16	Budesor 320 µ	4	12	eutical ny
Condemi et al,[7] 1997	101	95	Community	United States	>12	Triamci 800 µ	4	24	eutical ny
[illegible] 1994	19	18	Academic	Finland	>15	Budesor 400 µ	4	52	d
[illegible]	[illegible]	56	Academic	United States	12-65	Triamci 800 µ	6	16	rnment ment edicine d by nies)
[illegible]	[illegible]	74	Academic	United States	6-18	Beclom 80 µg			rnment naceutical ny d ations)
Papi et al,[11] 2007	110	119	Academic	Italy, Austria, Spain, Poland	18-65	Beclom 500 µ	4	44	eutical ny
Waalkens et al,[12] 1993	8	20	Academic	The Netherlands	7-16	Budesor 150 µ			herlands' ment naceutical ny d ations)
							4	24	

J Allergy Clin Immunol 2013;131:724-9

차례

Fate of ICS



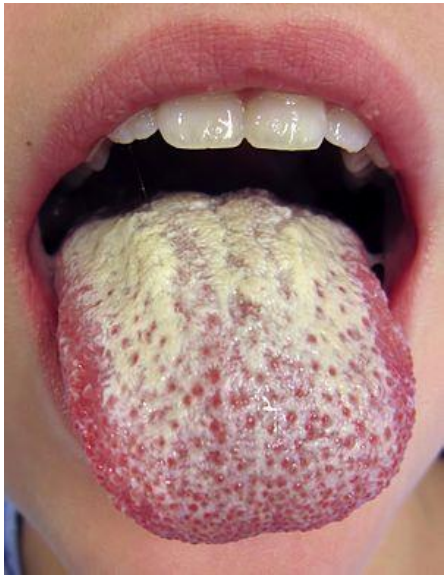
Am J Respir Crit Care Med Vol 157. pp S1–S53, 1998

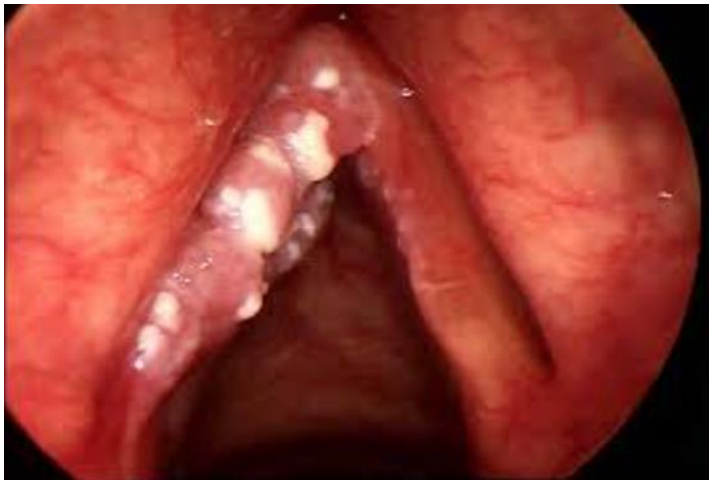
Side Effects of ICS

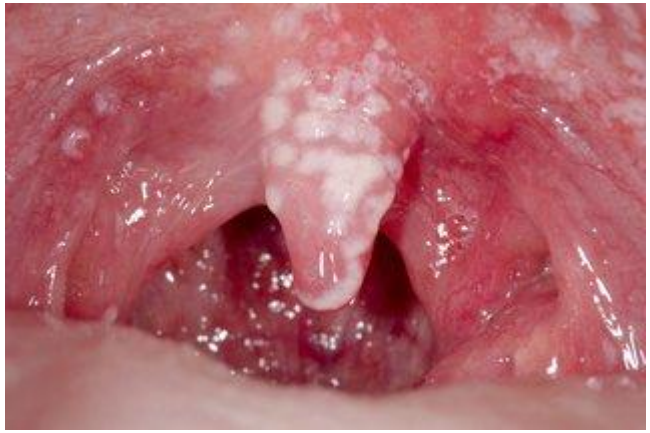
Short-term effects
Cough
Dysphonia
Thrush
Suppression of basal cortisol secretion
Suppression of ACTH and CRH secretion
Suppression of lower leg growth
Suppression of bone formation
Sex hormone suppression

Intermediate effects
HPA axis suppression
Linear growth velocity reduction
BMD reduction
Weight gain
Cushing syndrome
Mood swings, psychosis
Hypokalemia
Hyperglycemia
Dermal thinning and skin bruising
Glaucoma

Long-term effects
Adrenal insufficiency and crisis
Growth suppression
Failure to attain expected adult height
Osteoporosis and fractures
Cataracts

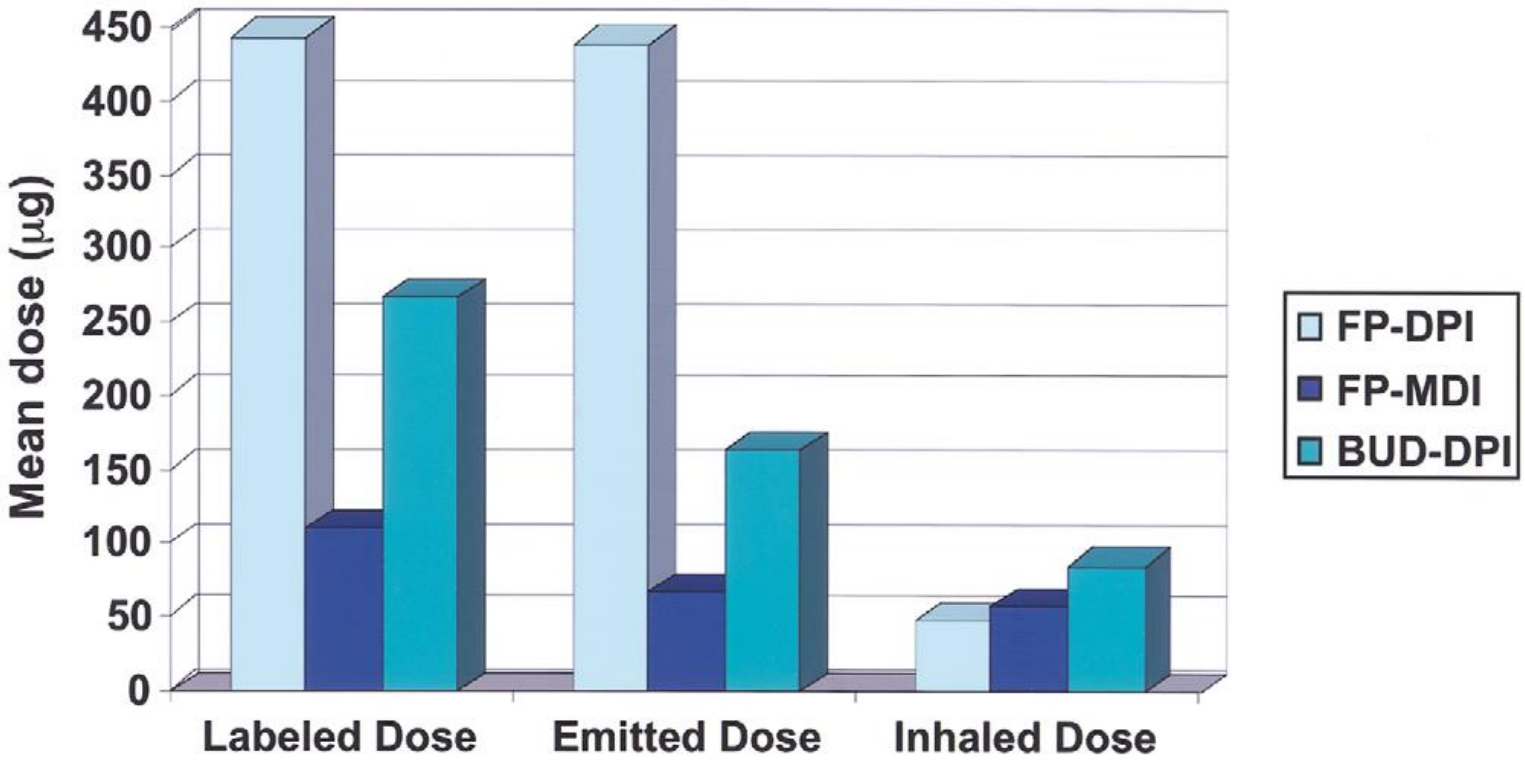






HPA axis suppression

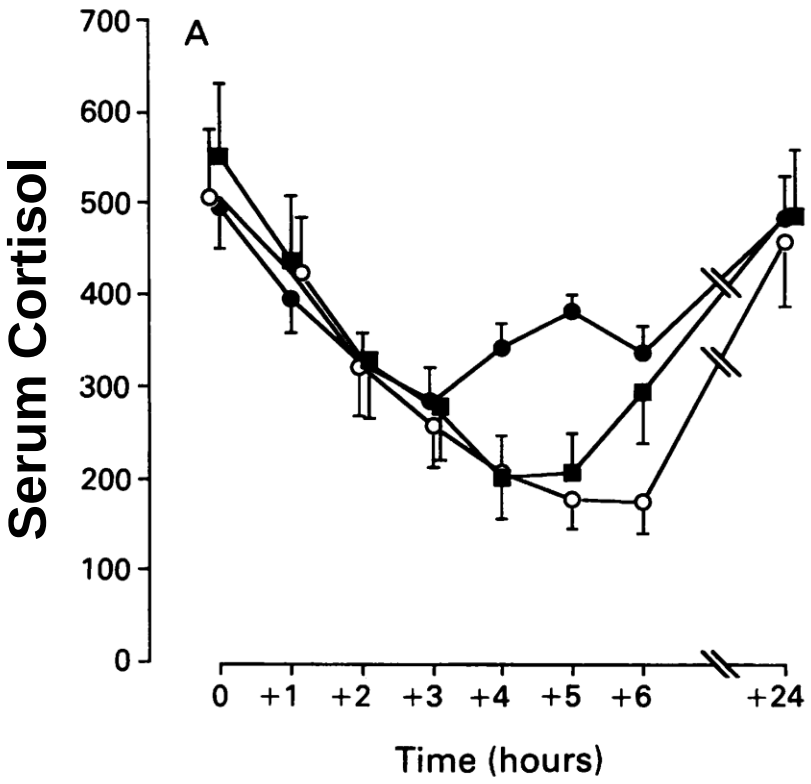
Doses of ICSs required to produce 10% suppression of basal cortisol secretion



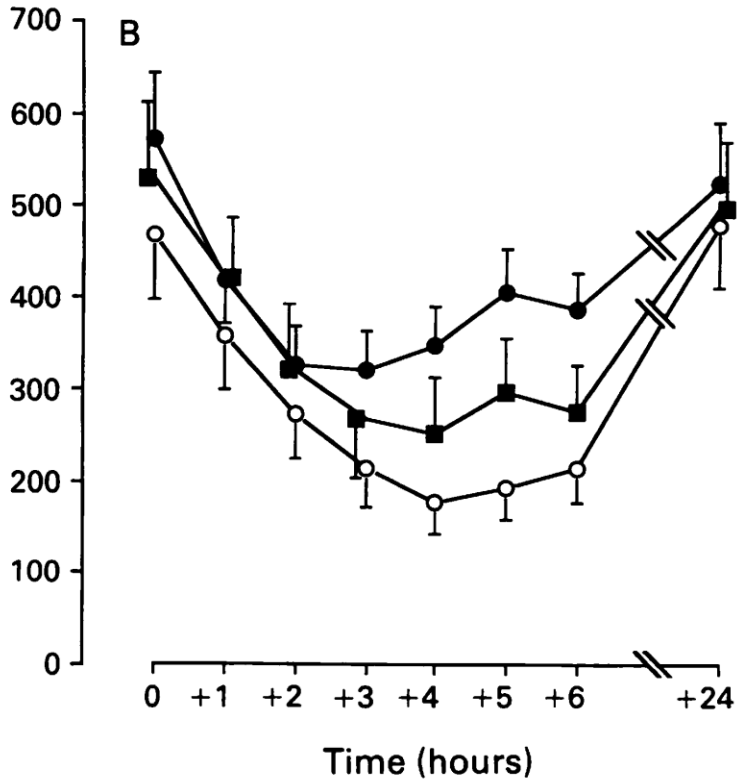
J Allergy Clin Immunol. 2003 Sep;112(3):469-78

HPA axis suppression

Beclomethasone

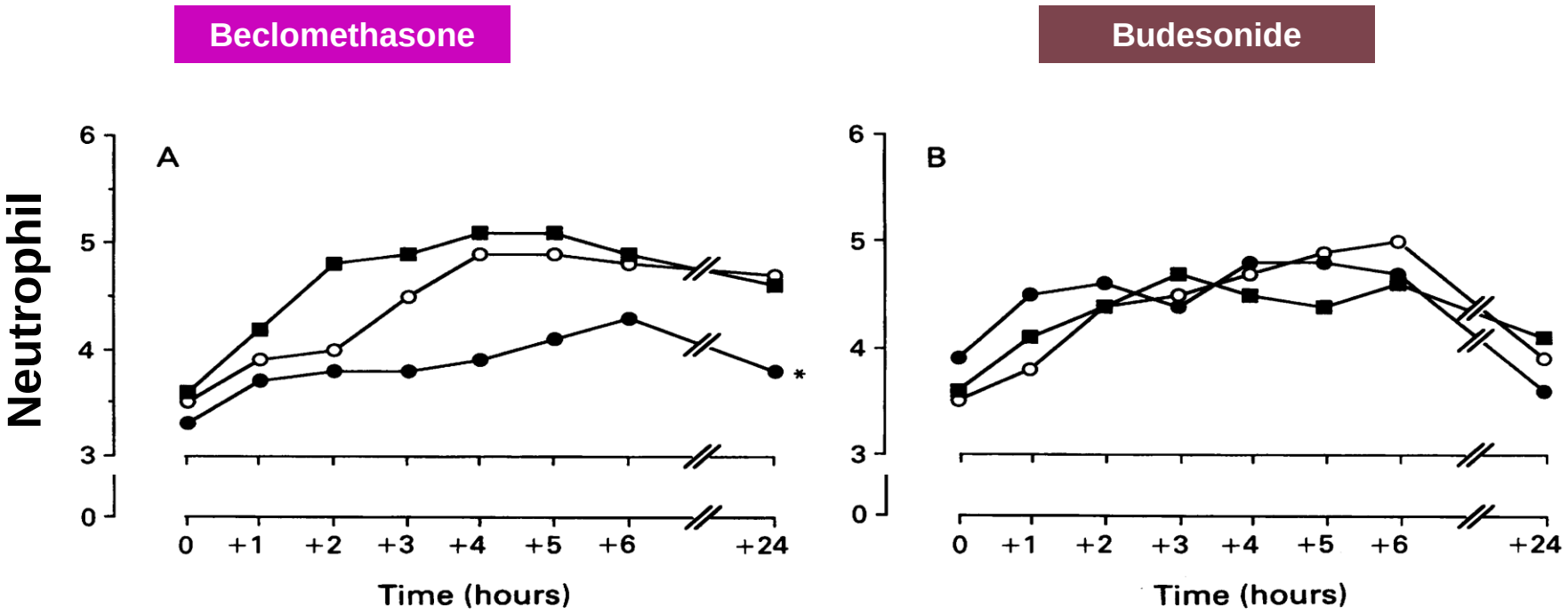


Budesonide



Thorax 1993;48:967-973

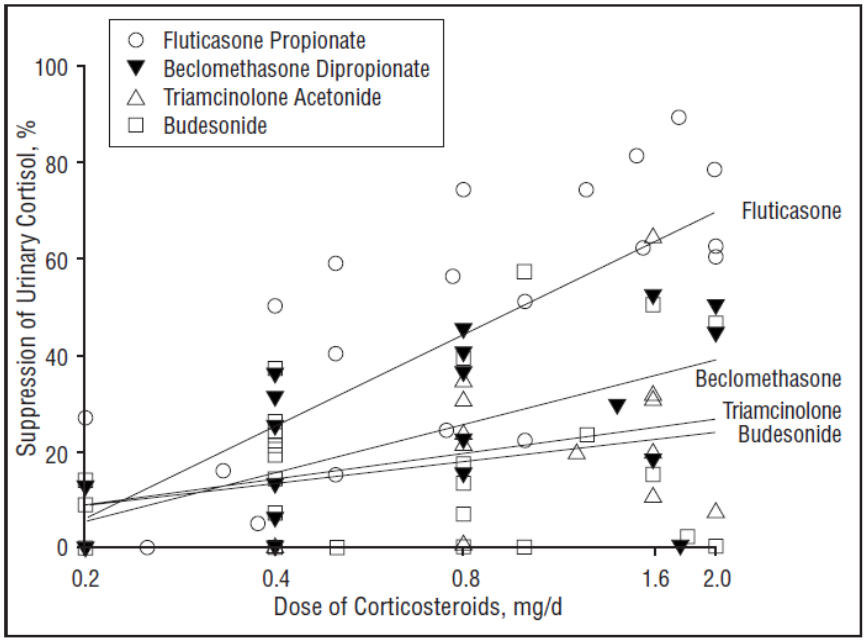
HPA axis suppression



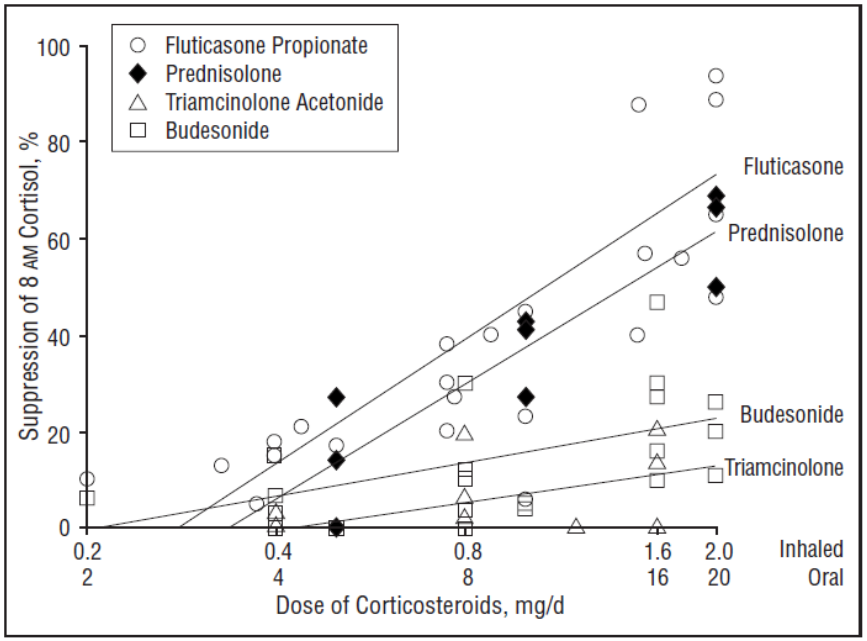
Thorax 1993;48:967-973

HPA axis suppression by drug

Suppression of Urinary Cortisol (%)



Suppression of 8AM Cortisol (%)



Arch Intern Med 1999;159: 941-955

Bone Mineral Density 감소

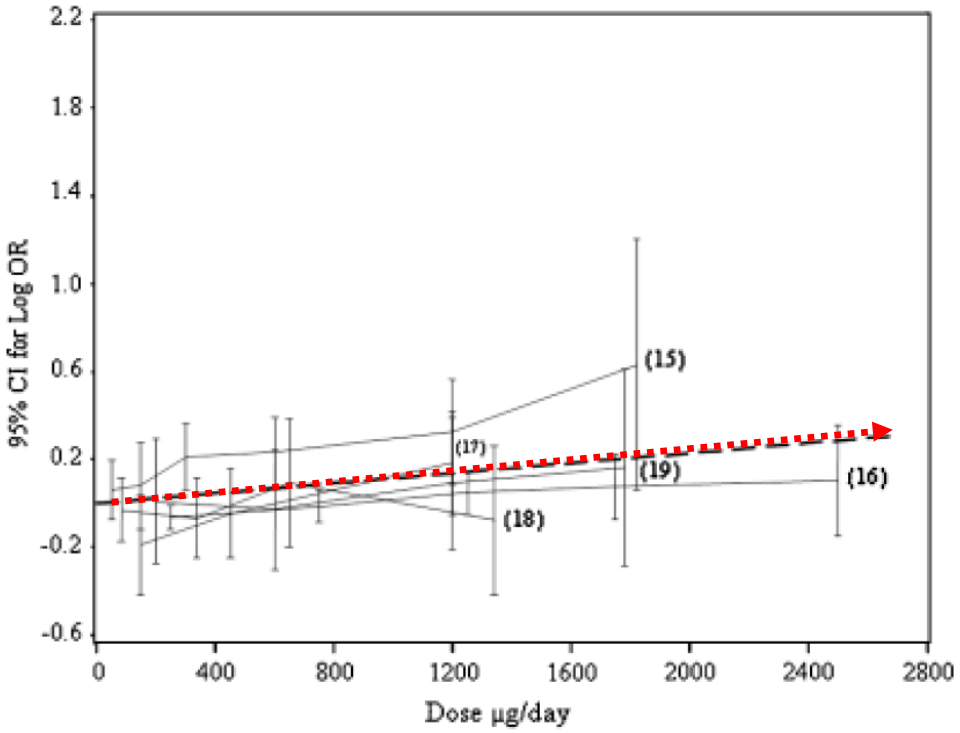
TABLE 3. BONE MINERAL DENSITY OF PARTICIPANTS FOR WHOM ALL THREE MEASUREMENTS WERE AVAILABLE.*

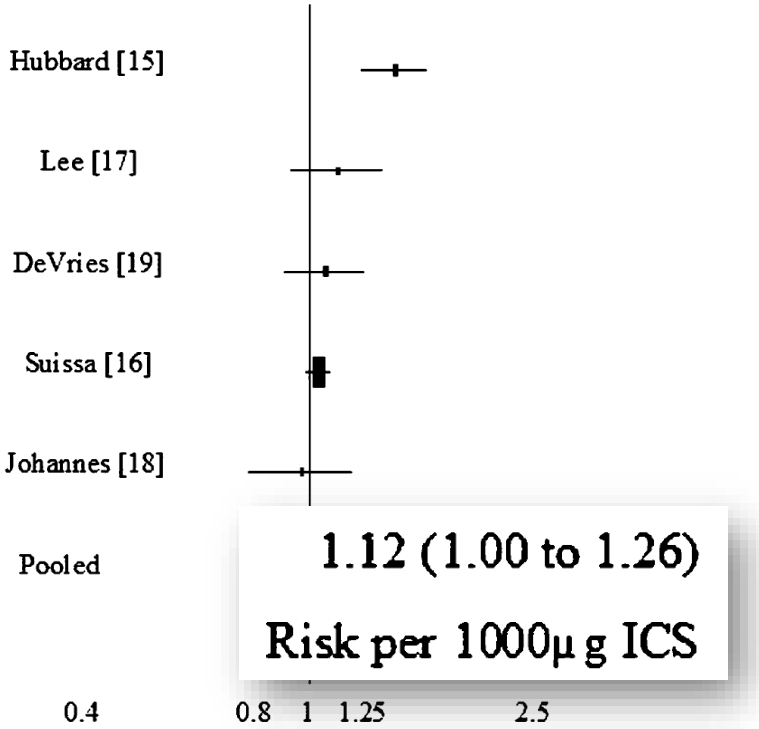
MEASUREMENT	TRIAMCINOLONE	PLACEBO	P VALUE
Lumbar spine			
No. of participants	158	170	
Base line (g/cm²)	0.988±0.013	0.979±0.013	0.60
12 mo (g/cm²)	0.988±0.013	0.973±0.013	0.43
36 mo (g/cm²)	0.985±0.013	0.988±0.014	0.89
% Change from base line to 36 mo	−0.35±0.33	0.98±0.36	0.007
Femoral neck			
No. of participants	176	183	
Base line (g/cm²)	0.762±0.010	0.754±0.010	0.54
12 mo (g/cm²)	0.760±0.010	0.751±0.010	0.53
36 mo (g/cm²)	0.747±0.010	0.752±0.010	0.73
% Change from base line to 36 mo	−2.00±0.35	−0.22±0.32	<0.001

*P values were calculated by the t-test, with only the patients with technically satisfactory measurements at all three visits included. Results are expressed as means ±SE.

N Engl J Med. 2000 Dec 28;343(26):1902-9

Non-vertebral Fracture





Clinical and Experimental Allergy, 38, 1451–1458

Cataract 증가

	Cases	Controls	Crude RR	Adjusted[#] RR (95% CI)
Subjects n	27708	110832		
ICS		299.0±448.5	1.24	
Ra				
0		45662	1.0	1.0 (reference)
>		39600	1.17	1.11 (1.07–1.14)
>		15855	1.26	1.18 (1.13–1.35)
>		6668	1.38	1.27 (1.20–1.40)
>		2370	1.55	1.44 (1.31–1.57)
>		677	1.50	1.36 (1.16–1.59)
NC		14.1±51.2	1.11	1.08 (1.05–1.10)[¶]
Ra				
0		90265	1.0	
>		15714	1.24	
>100–200 (141) μg·day^{-1}	893	2861	1.31	1.21 (1.12–1.31)
>200 (316) μg·day^{-1}	610	1992	1.28	1.18 (1.07–1.30)

Range (mean) of ICS dose[+] n

- 0 (0) μg·day^{-1}
- >0–500 (196) μg·day^{-1}
- >500–1000 (734) μg·day^{-1}
- >1000–1500 (1205) μg·day^{-1}
- >1500–2000 (1701) μg·day^{-1}
- >2000 (2458) μg·day^{-1}

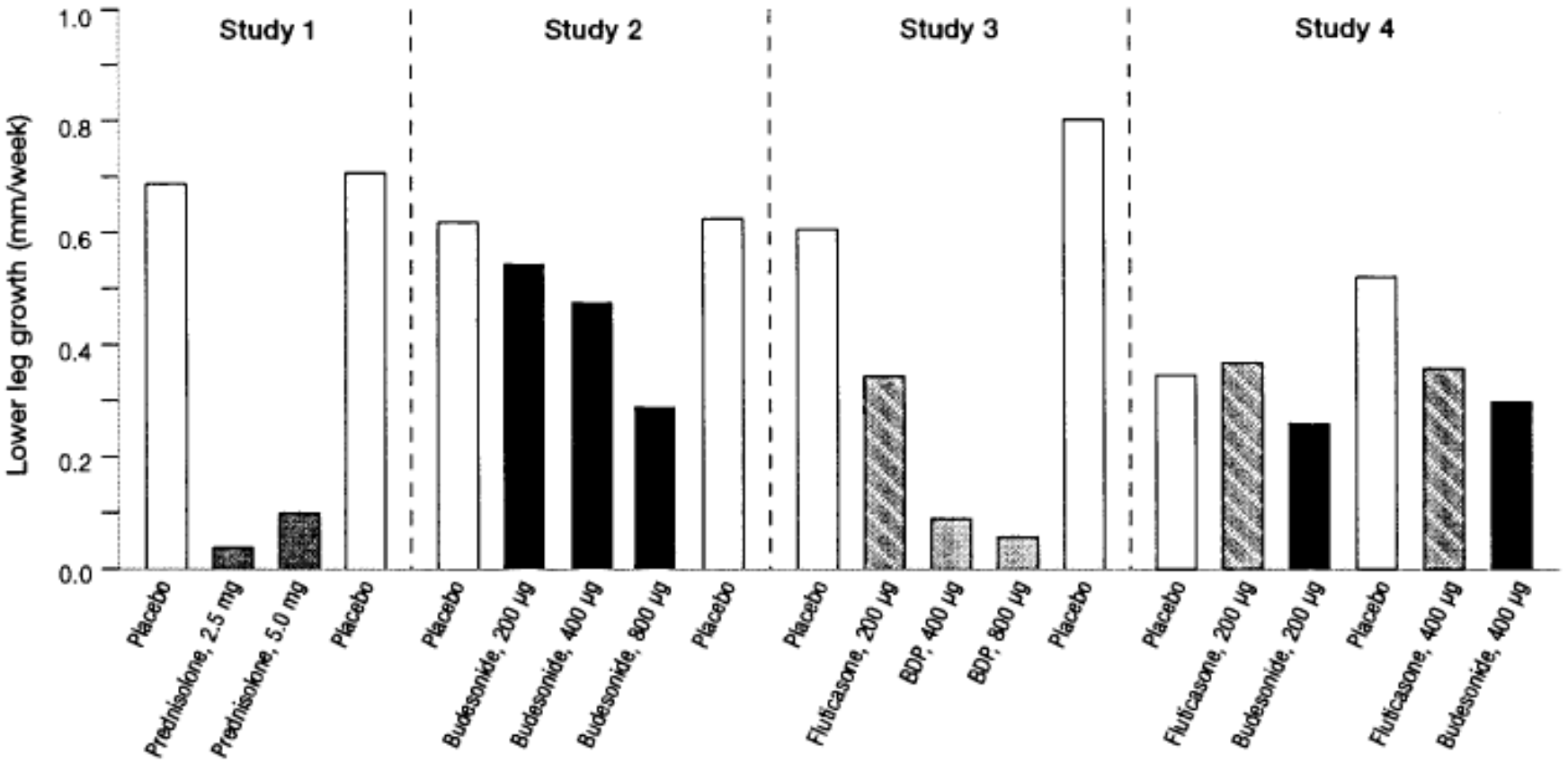
Eur Respir J 2006; 27: 1168–1174

Cataract 증가

Variable	No. of Subjects	Type of Cataract		
		Cortical	Nuclear	Posterior Subcapsular
		prevalence ratio (95 percent confidence interval)		
Inhaled corticosteroids				
Never used	3011	1.0	1.0	1.0
Used at some time	370	1.1 (0.9–1.3)	1.5 (1.2–1.9	1.9 (1.3–2.8)
Formerly	206	0.9 (0.7–1.2)	1.6 (1.1–2.3	1.1 (0.6–2.0)
Currently	164	1.4 (1.1–1.7)	1.5 (1.1–2.0	2.6 (1.7–4.0)
Weekly dose among all users				
≤14 puffs	96	0.9 (0.6–1.4)	1.4 (0.9–2.4)	1.3 (0.6–2.8)
15–28 puffs	87	1.3 (0.9–1.8)	0.9 (0.5–1.7)	2.1 (1.1–3.9)
>28 puffs	59	1.4 (0.9–2.1)	1.9 (1.1–3.2)	3.1 (1.7–5.7)
P for trend		0.06	0.05	
Lifetime inhaled dose among current users†				
<1000 mg	40	0.9 (0.5–1.6)	0.5 (0.2–1.4	2.5 (1.1–5.8)
1000–1999 mg	15	1.0 (0.3–3.5)	1.3 (0.2–8.0	5.4 (2.0–14.7)
≥2000 mg	15	1.7 (0.8–3.6)	4.0 (1.8–9.3	5.5 (2.3–13.0)
P for trend		0.39	0.08	<0.001
Oral corticosteroids				
Never used	3114	1.0	1.0	1.0
Used at some time	303	1.1 (0.9–1.3)	1.2 (0.9–1.6)	1.5 (1.0–2.3)
Formerly	244	1.1 (0.8–1.3)	1.1 (0.8–1.6)	1.5 (0.9–2.4)
Currently	59	1.2 (0.8–1.7)	1.3 (0.8–2.2)	1.7 (0.8–3.6)
Duration of use among all users				
<1 yr	175	1.2 (0.9–1.5)	1.2 (0.8–1.8)	1.1 (0.6–2.1)
1–4.9 yr	44	0.6 (0.3–1.1)	0.9 (0.4–2.4)	1.8 (0.7–4.7)
≥5 yr	33	1.6 (1.0–2.4)	1.6 (0.9–2.8)	2.7 (1.3–5.6)
P for trend		0.22	0.14	0.009

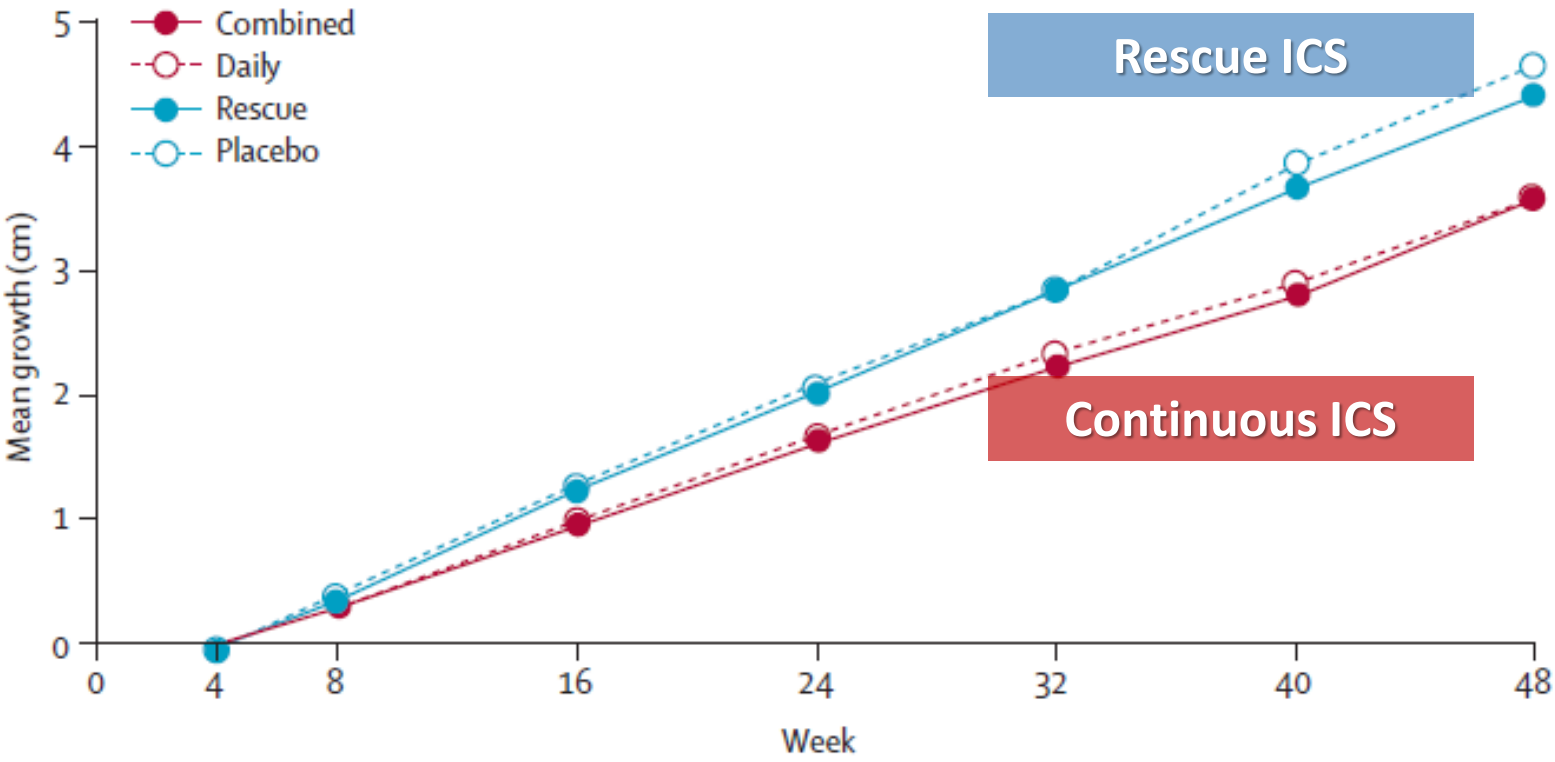
N Engl J Med 1997;337:8-14

Leg Growth Retardation



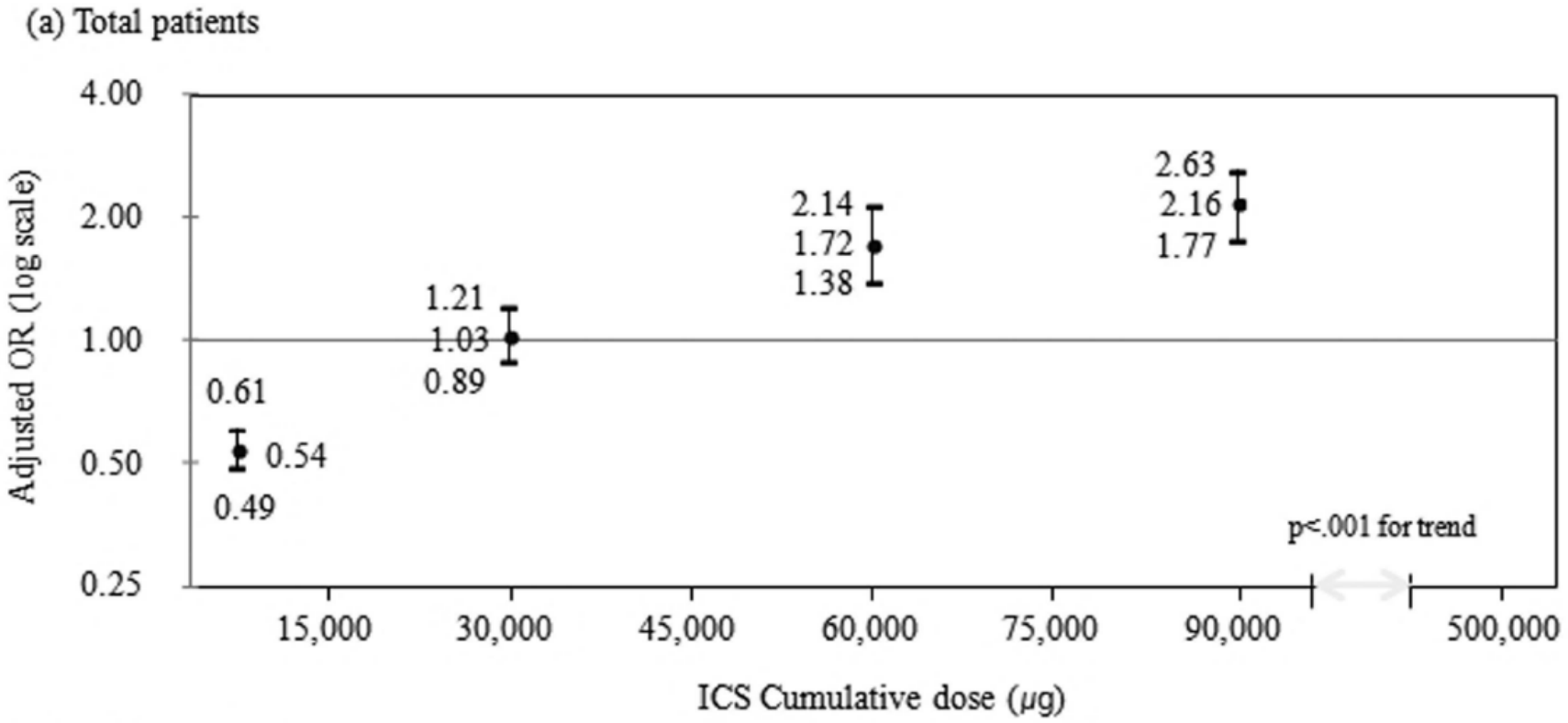
J Pediatr 2015;166(

Growth curve of ICS



J Pediatr 2015

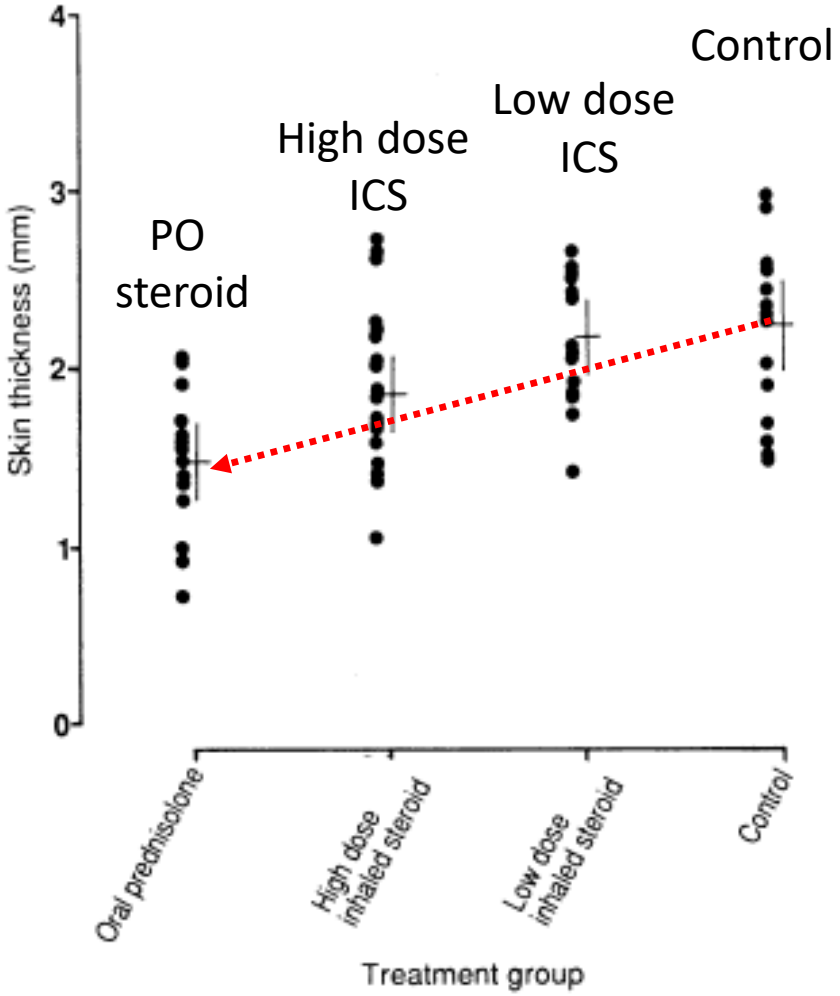
ICS increased TB

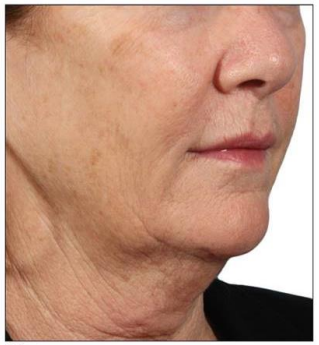


Thorax 2013;68:1105–1113

Skin Thinning with ICS

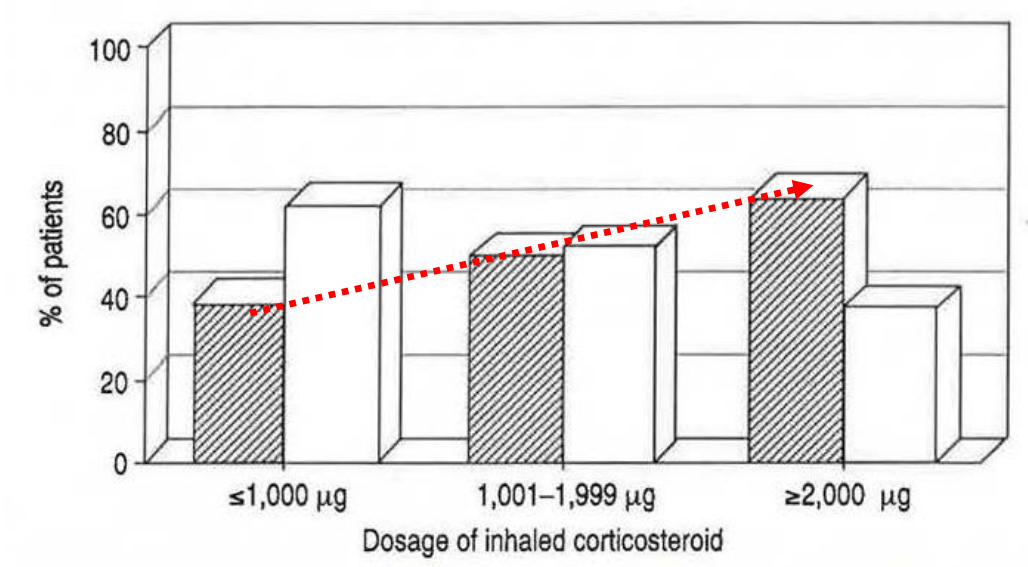
Skin thickness

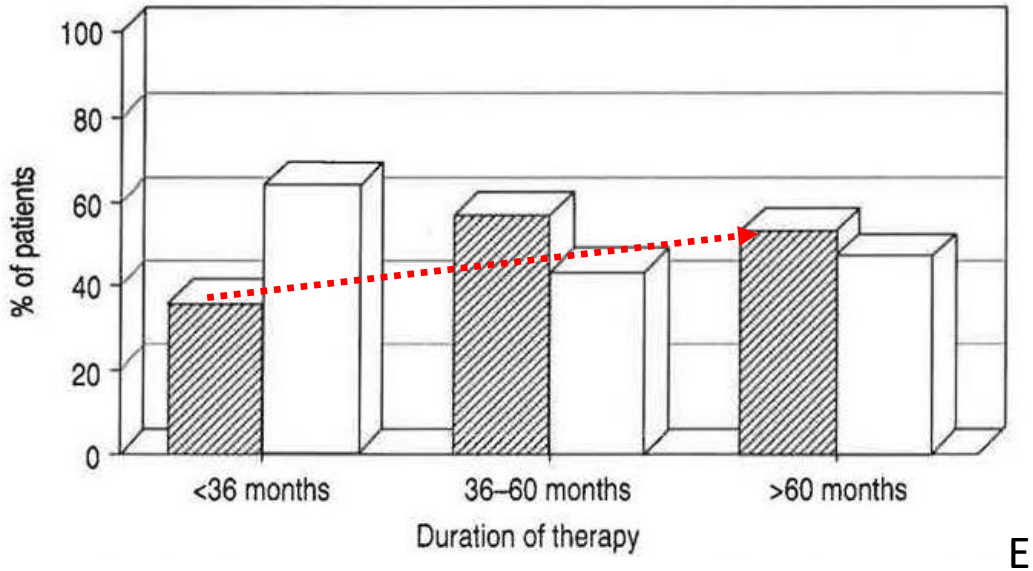




BMJ 1990;300:1548-51

Bruising





ERJ 1992, 5, 1068-1074

차례

ORIGINAL ARTICLE

As-Needed Budesonide–Formoterol versus Maintenance Budesonide in Mild Asthma

Eric D. Bateman, M.D., Helen K. Reddel, M.B., B.S., Ph.D., Paul M. O'Byrne, M.B., Peter J. Barnes, M.D., Nanshan Zhong, Ph.D., Christina Keen, M.D., Carin Jorup, M.D., Rosa Lamarca, Ph.D., Agnieszka Siwek-Posluszna, M.D., and J. Mark FitzGerald, M.D.

ABSTRACT

BACKGROUND

Patients with mild asthma often rely on inhaled short-acting β_2-agonists for symptom relief and have poor adherence to maintenance therapy. Another approach might be for patients to receive a fast-acting reliever plus an inhaled glucocorticoid component on an as-needed basis to address symptoms and exacerbation risk.

METHODS

We conducted a 52-week, double-blind, multicenter trial involving patients 12 years of age or older who had mild asthma and were eligible for treatment with regular inhaled glucocorticoids. Patients were randomly assigned to receive twice-daily placebo plus budesonide–formoterol (200 μg of budesonide and 6 μg of formoterol) used as needed or budesonide maintenance therapy with twice-daily budesonide (200 μg) plus terbutaline (0.5 mg) used as needed. The primary analysis compared budesonide–formoterol used as needed with budesonide maintenance therapy with regard to the annualized rate of severe exacerbations, with a prespecified noninferiority limit of 1.2. Symptoms were assessed according to scores on the Asthma Control Questionnaire–5 (ACQ-5) on a scale from 0 (no impairment) to 6 (maximum impairment).

RESULTS

A total of 4215 patients underwent randomization, and 4176 (2089 in the budesonide–formoterol group and 2087 in the budesonide maintenance group) were included in the full analysis set. Budesonide–formoterol used as needed was noninferior to budesonide maintenance therapy for severe exacerbations; the annualized rate of severe exacerbations was 0.11 (95% confidence interval [CI], 0.10 to 0.13) and 0.12 (95% CI, 0.10 to 0.14), respectively (rate ratio, 0.97; upper one-sided 95% confidence limit, 1.16). The median daily metered dose of inhaled glucocorticoid was lower in the budesonide–formoterol group (66 μg) than in the budesonide maintenance group (267 μg). The time to the first exacerbation was similar in the two groups (hazard ratio, 0.96; 95% CI, 0.78 to 1.17). The change in ACQ-5 score showed a difference of 0.11 units (95% CI, 0.07 to 0.15) in favor of budesonide maintenance therapy.

CONCLUSIONS

In patients with mild asthma, budesonide–formoterol used as needed was noninferior to twice-daily budesonide with respect to the rate of severe asthma exacerbations during 52 weeks of treatment but was inferior in controlling symptoms. Patients in the budesonide–formoterol group had approximately one quarter of the inhaled glucocorticoid exposure of those in the budesonide maintenance group. (Funded by AstraZeneca; SYGMA 2 ClinicalTrials.gov number, NCT02224157.)

From the Division of Pulmonology, Department of Medicine, University of Cape Town, Cape Town, South Africa (E.D.B.); Woolcock Institute of Medical Research, University of Sydney, Sydney (H.K.R.); Firestone Institute for Respiratory Health, St. Joseph's Healthcare and Department of Medicine, Michael G. DeGroote School of Medicine, McMaster University, Hamilton, ON (P.M.O.), and the Institute for Heart and Lung Health, University of British Columbia, Vancouver (J.M.F.) — both in Canada; Airway Disease Section, National Heart and Lung Institute, Imperial College, London (P.J.B.); State Key Laboratory of Respiratory Diseases, First Affiliated Hospital, Guangzhou Medical University, Guangzhou, China (N.Z.); AstraZeneca Research and Development, Gothenburg, Sweden (C.K., C.J.); AstraZeneca Research and Development, Barcelona (R.L.); and AstraZeneca Research and Development, Warsaw, Poland (A.S.-P.). Address reprint requests to Dr. Bateman at the University of Cape Town Lung Institute, George St., Cape Town 7700, South Africa, or at eric.bateman@uct.ac.za.

N Engl J Med 2018;378:1877-87.
DOI: 10.1056/NEJMoa1715275

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 17, 2018 VOL. 378 NO. 20

Inhaled Combined Budesonide–Formoterol as Needed in Mild Asthma

Paul M. O'Byrne, M.B., J. Mark FitzGerald, M.D., Eric D. Bateman, M.D., Peter J. Barnes, M.D., Nanshan Zhong, Ph.D., Christina Keen, M.D., Carin Jorup, M.D., Rosa Lamarca, Ph.D., Stefan Ivanov, M.D., Ph.D., and Helen K. Reddel, M.B., B.S., Ph.D.

ABSTRACT

BACKGROUND

In patients with mild asthma, as-needed use of an inhaled glucocorticoid plus a fast-acting β_2-agonist may be an alternative to conventional treatment strategies.

METHODS

We conducted a 52-week, double-blind trial involving patients 12 years of age or older with mild asthma. Patients were randomly assigned to one of three regimens: twice-daily placebo plus terbutaline (0.5 mg) used as needed (terbutaline group), twice-daily placebo plus budesonide–formoterol (200 μg of budesonide and 6 μg of formoterol) used as needed (budesonide–formoterol group), or twice-daily budesonide (200 μg) plus terbutaline used as needed (budesonide maintenance group). The primary objective was to investigate the superiority of as-needed budesonide–formoterol to as-needed terbutaline with regard to electronically recorded weeks with well-controlled asthma.

RESULTS

A total of 3849 patients underwent randomization, and 3836 (1277 in the terbutaline group, 1277 in the budesonide–formoterol group, and 1282 in the budesonide maintenance group) were included in the full analysis and safety data sets. With respect to the mean percentage of weeks with well-controlled asthma per patient, budesonide–formoterol was superior to terbutaline (34.4% vs. 31.1% of weeks; odds ratio, 1.14; 95% confidence interval [CI], 1.00 to 1.30; P=0.046) but inferior to budesonide maintenance therapy (34.4% and 44.4%, respectively; odds ratio, 0.64; 95% CI, 0.57 to 0.73). The annual rate of severe exacerbations was 0.20 with terbutaline, 0.07 with budesonide–formoterol, and 0.09 with budesonide maintenance therapy; the rate ratio was 0.36 (95% CI, 0.27 to 0.49) for budesonide–formoterol versus terbutaline and 0.83 (95% CI, 0.59 to 1.16) for budesonide–formoterol versus budesonide maintenance therapy. The rate of adherence in the budesonide maintenance group was 78.9%. The median metered daily dose of inhaled glucocorticoid in the budesonide–formoterol group (57 μg) was 17% of the dose in the budesonide maintenance group (340 μg).

CONCLUSIONS

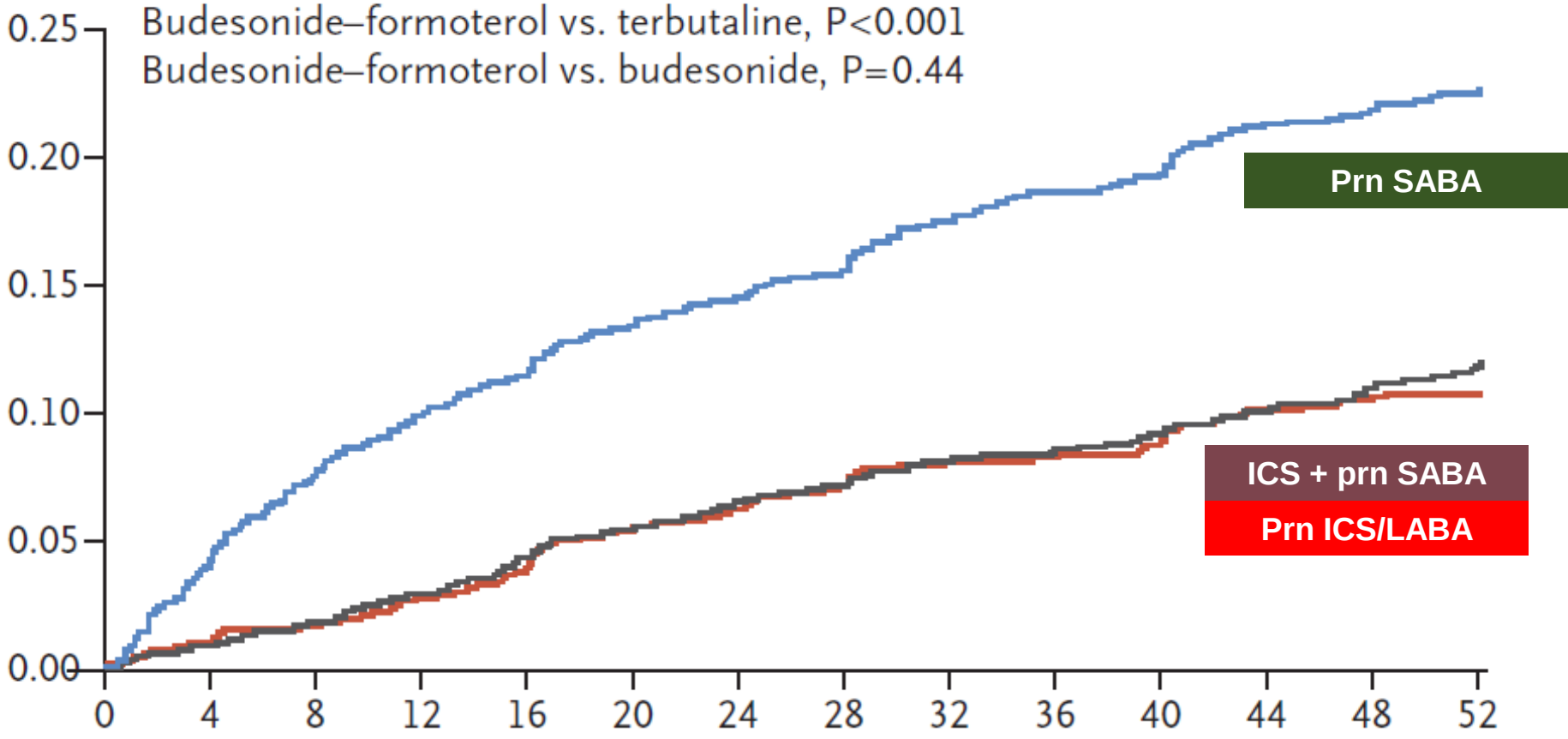
In patients with mild asthma, as-needed budesonide–formoterol provided superior asthma-symptom control to as-needed terbutaline, assessed according to electronically recorded weeks with well-controlled asthma, but was inferior to budesonide maintenance therapy. Exacerbation rates with the two budesonide-containing 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.)

From the Firestone Institute for Respiratory Health, St. Joseph's Healthcare and Department of Medicine, Michael G. DeGroote School of Medicine, McMaster University, Hamilton, ON (P.M.O.), and the Institute for Heart and Lung Health, University of British Columbia, Vancouver (J.M.F.) — both in Canada; the Division of Pulmonology, Department of Medicine, University of Cape Town, Cape Town, South Africa (E.D.B.); Airway Disease Section, National Heart and Lung Institute, Imperial College, London (P.J.B.); State Key Laboratory of Respiratory Diseases, First Affiliated Hospital, Guangzhou Medical University, Guangzhou, China (N.Z.); AstraZeneca Research and Development, Gothenburg, Sweden (C.K., C.J., S.I.); AstraZeneca Research and Development, Barcelona (R.L.); and Woolcock Institute of Medical Research, University of Sydney, Sydney (H.K.R.). Address reprint requests to Dr. O'Byrne at the Firestone Institute for Respiratory Health, St. Joseph's Healthcare and Department of Medicine, McMaster University, Rm. 2E1, 1280 Main St. West, Hamilton, ON L8S 4K1, Canada, or at obyrnep@mcmaster.ca.

N Engl J Med 2018;378:1865-76.
DOI: 10.1056/NEJMoa1715274

SYGMA1: 급성 악화 차이 없음

급성악화

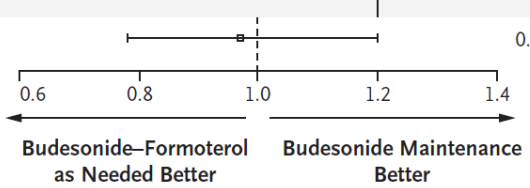


N Engl J Med 2018;378:1865-76.

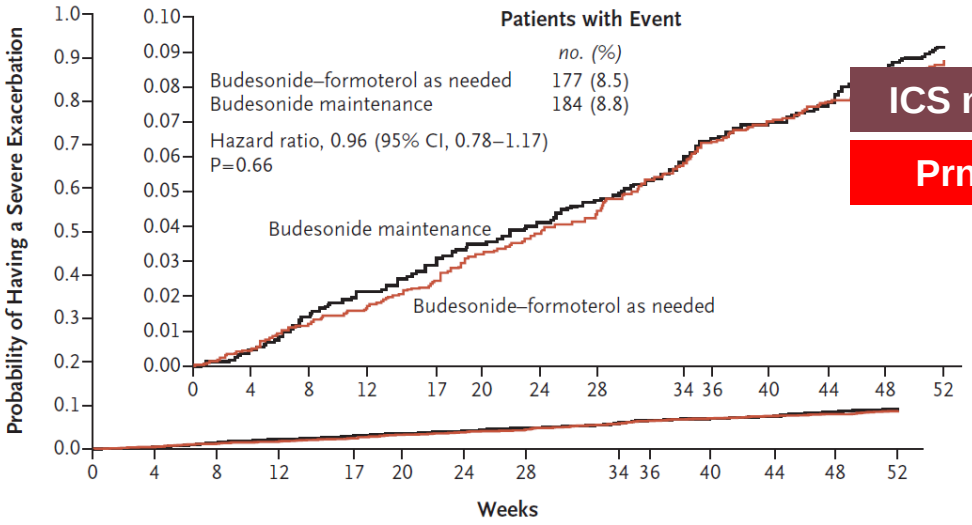
SYGMA2: 급성 악화 차이 없음

A Annualized Rate of Severe Asthma Exacerbations

Test	Budesonide–Formoterol as Needed	Budesonide Maintenance	Rate Ratio (95% CI)	P Value
Noninferiority test	2084	2083	0.97 (NA–1.16)	—
Superiority test	2089	2087	0.97 (0.78–1.20)	0.75



B Time to First Severe Exacerbation



ICS maintenance

Prn ICS/LABA

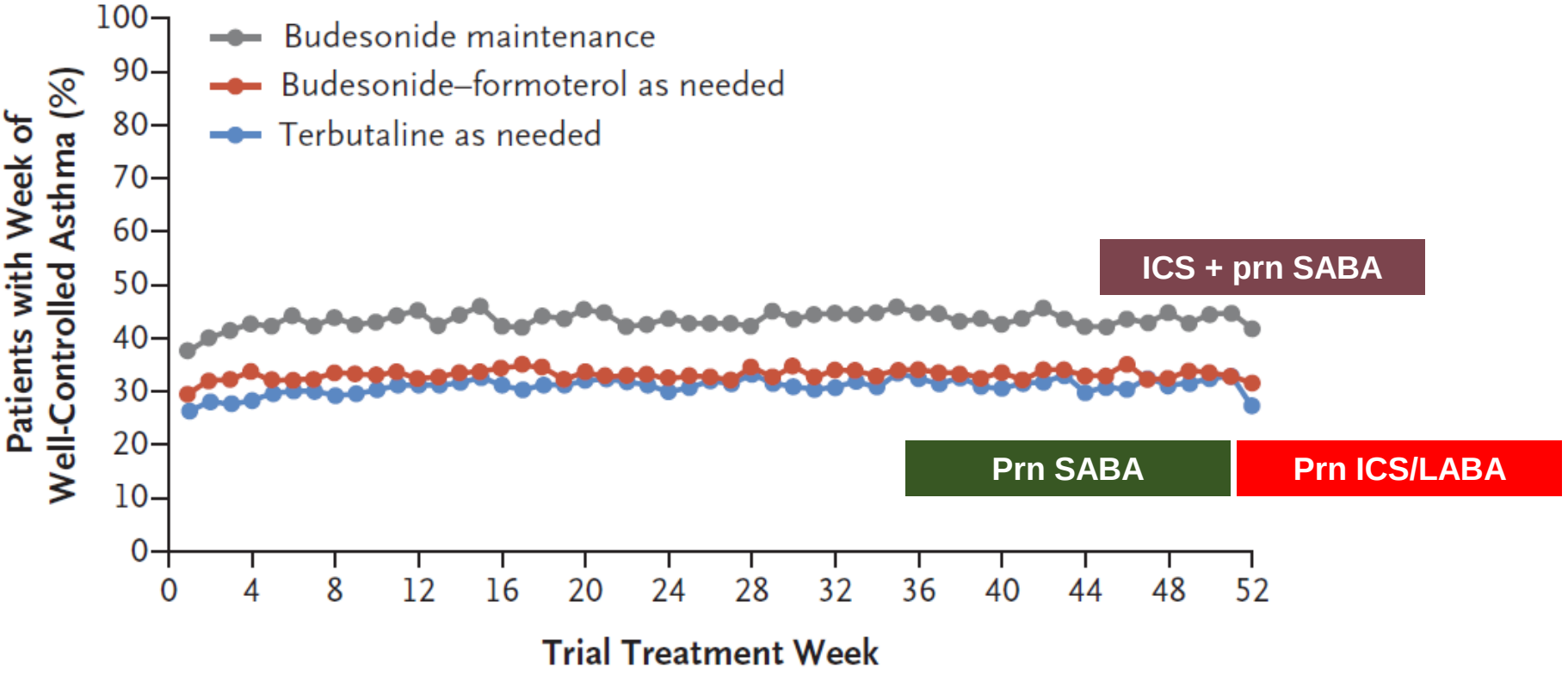
No. at Risk

Budesonide–formoterol as needed	2089	2065	2039	2012	1982	1944	1926	1904	1862	1840	1821	1799	1782	1208
Budesonide maintenance	2087	2060	2027	1987	1957	1929	1909	1883	1848	1826	1811	1786	1760	1222

N Engl J Med 2018;378:1877-87.

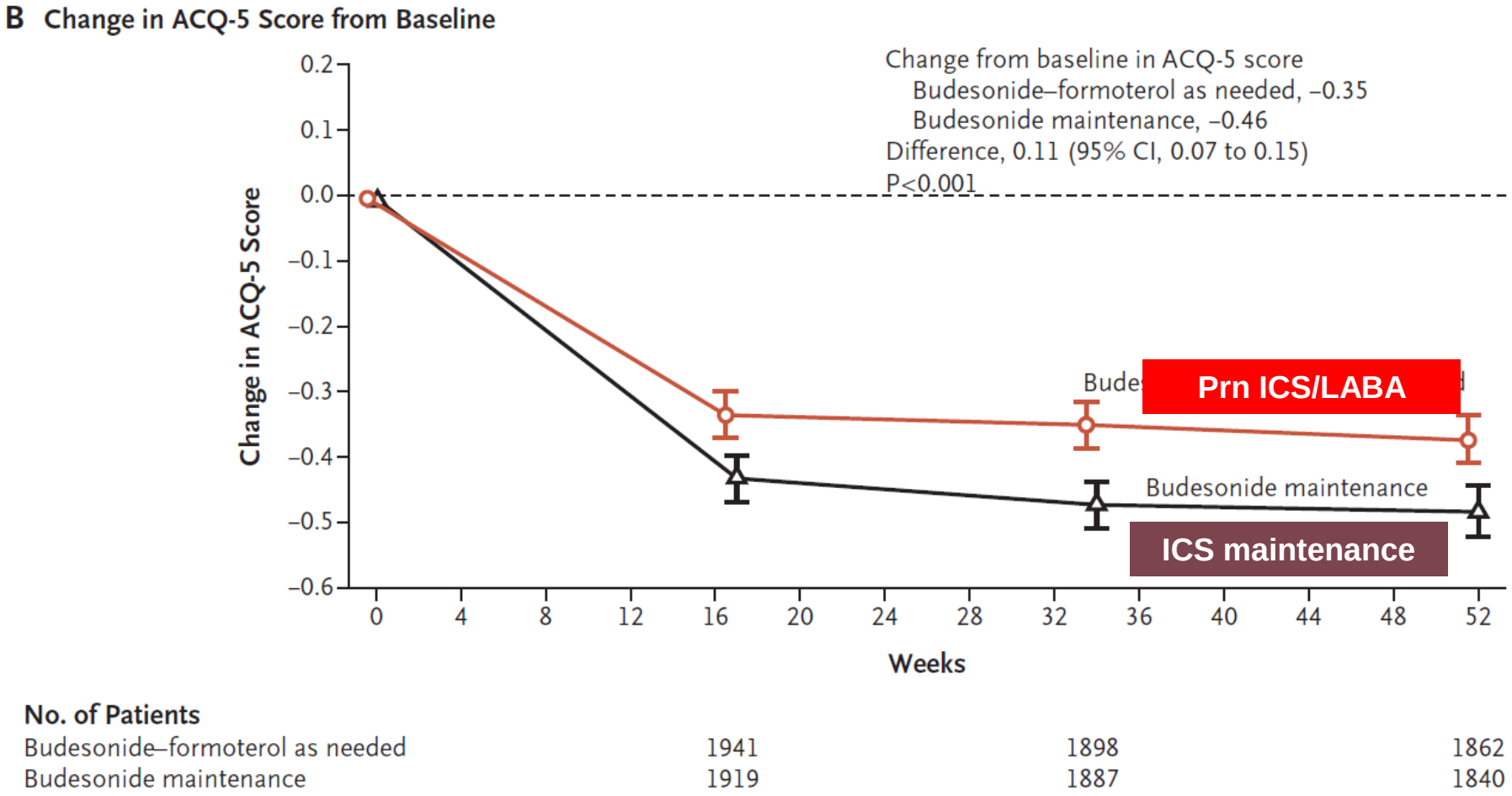
천식조절: ICS 유지가 유리

천식 조절



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

천식조절: ICS 유지가 유리



N Engl J Med 2018;378:1877-87

ORIGINAL ARTICLE

Controlled Trial of Budesonide–Formoterol as Needed for Mild Asthma

Richard Beasley, D.Sc., Mark Holliday, B.Sc., Helen K. Reddel, Ph.D., Irene Braithwaite, Ph.D., Stefan Ebmeier, B.M., B.Ch., Robert J. Hancox, M.D., Tim Harrison, M.D., Claire Houghton, B.M., B.S., Karen Oldfield, M.B., Ch.B., Alberto Papi, M.D., Ian D. Pavord, F.Med.Sci., Mathew Williams, Dip.Ex.Sci., and Mark Weatherall, F.R.A.C.P., for the Novel START Study Team*

ABSTRACT

BACKGROUND

In double-blind, placebo-controlled trials, budesonide–formoterol used on an as-needed basis resulted in a lower risk of severe exacerbation of asthma than as-needed use of a short-acting β_2-agonist (SABA); the risk was similar to that of budesonide maintenance therapy plus as-needed SABA. The availability of data from clinical trials designed to better reflect clinical practice would be beneficial.

METHODS

We conducted a 52-week, randomized, open-label, parallel-group, controlled trial involving adults with mild asthma. Patients were randomly assigned to one of three treatment groups: albuterol (100 μg, two inhalations from a pressurized metered-dose inhaler as needed for asthma symptoms) (albuterol group); budesonide (200 μg, one inhalation through a Turbuhaler twice daily) plus as-needed albuterol (budesonide maintenance group); or budesonide–formoterol (200 μg of budesonide and 6 μg of formoterol, one inhalation through a Turbuhaler as needed) (budesonide–formoterol group). Electronic monitoring of inhalers was used to measure medication use. The primary outcome was the annualized rate of asthma exacerbations.

RESULTS

The analysis included 668 of 675 patients who underwent randomization. The annualized exacerbation rate in the budesonide–formoterol group was lower than that in the albuterol group (absolute rate, 0.195 vs. 0.400; relative rate, 0.49; 95% confidence interval [CI], 0.33 to 0.72; P<0.001) and did not differ significantly from the rate in the budesonide maintenance group (absolute rate, 0.195 in the budesonide–formoterol group vs. 0.175 in the budesonide maintenance group; relative rate, 1.12; 95% CI, 0.70 to 1.79; P=0.65). The number of severe exacerbations was lower in the budesonide–formoterol group than in both the albuterol group (9 vs. 23; relative risk, 0.40; 95% CI, 0.18 to 0.86) and the budesonide maintenance group (9 vs. 21; relative risk, 0.44; 95% CI, 0.20 to 0.96). The mean (±SD) dose of inhaled budesonide was 107±109 μg per day in the budesonide–formoterol group and 222±113 μg per day in the budesonide maintenance group. The incidence and type of adverse events reported were consistent with those in previous trials and with reports in clinical use.

CONCLUSIONS

In an open-label trial involving adults with mild asthma, budesonide–formoterol used as needed was superior to albuterol used as needed for the prevention of asthma exacerbations. (Funded by AstraZeneca and the Health Research Council of New Zealand; Novel START Australian New Zealand Clinical Trials Registry number, ACTRN12615000999538.)

From the Medical Research Institute of New Zealand (R.B., M.H., I.B., S.E., C.H., K.O., M. Williams), the Capital and Coast District Health Board (R.B.), and the University of Otago Wellington (M. Weatherall), Wellington, the Department of Respiratory Medicine, Waikato Hospital, Hamilton (R.J.H.), and the Department of Preventive and Social Medicine, University of Otago, Dunedin (R.J.H.) — all in New Zealand; Woolcock Institute of Medical Research, University of Sydney, Sydney (H.K.R.); the Nottingham NIHR Biomedical Research Centre, University of Nottingham, Nottingham (T.H.), and the Oxford Respiratory NIHR BRC, Nuffield Department of Medicine, University of Oxford, Oxford (I.D.P.) — both in the United Kingdom; and the Respiratory Medicine Unit, Department of Medical Sciences, Università di Ferrara, Ferrara, Italy (A.P.). Address reprint requests to Dr. Beasley at the Medical Research Institute of New Zealand, Private Bag 7902, Newtown, Wellington 6242, New Zealand, or at richard.beasley@mrinz.ac.nz.

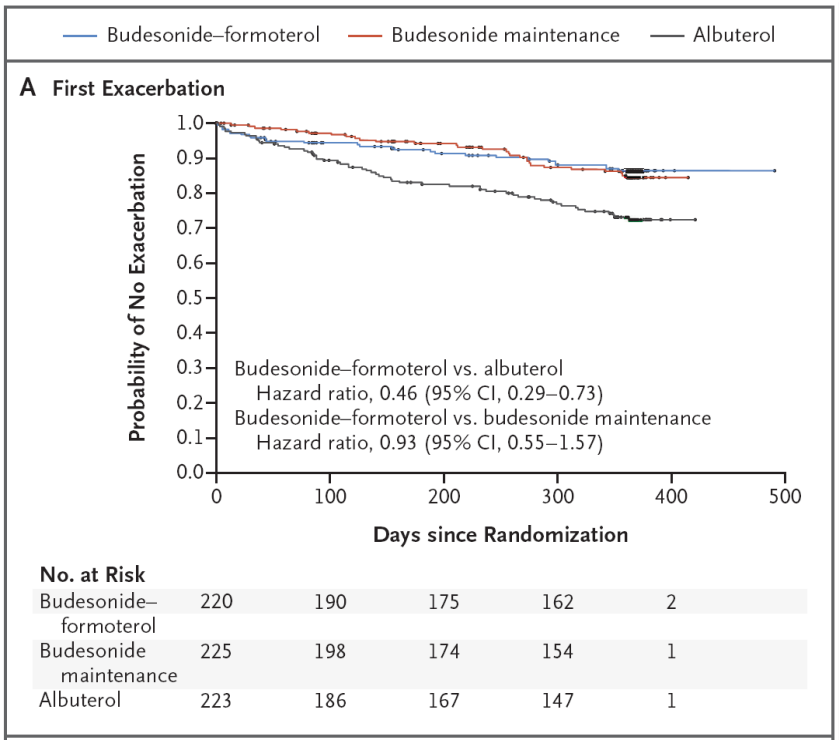
*A complete list of investigators in the Novel START trial is provided in the Supplementary Appendix, available at NEJM.org.

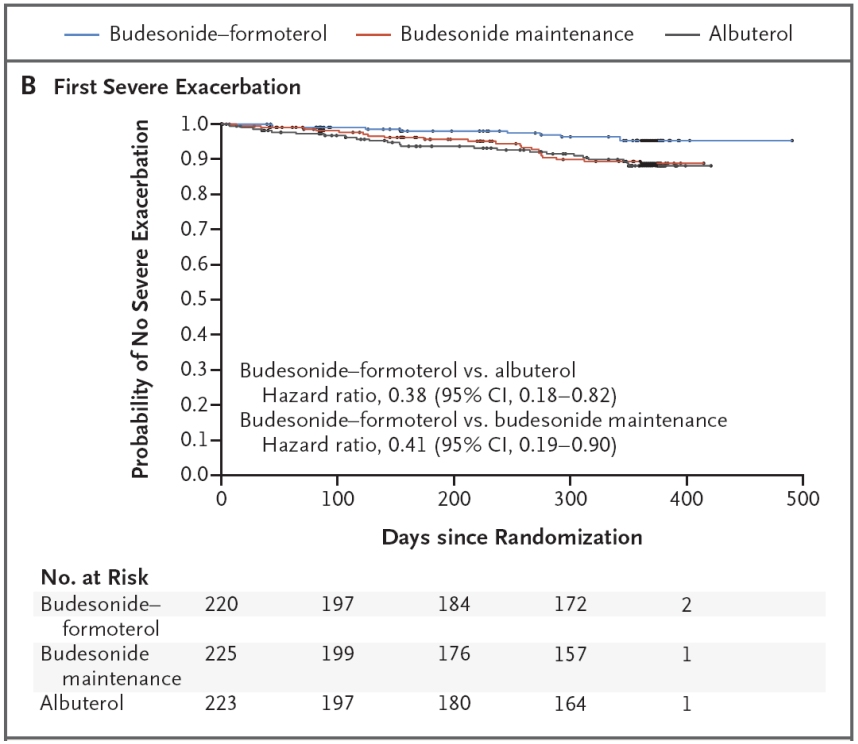
This article was published on May 19, 2019, at NEJM.org.

N Engl J Med 2019;380:2020-30.
DOI: 10.1056/NEJMoa1901963

BUD/FOR prn may be better

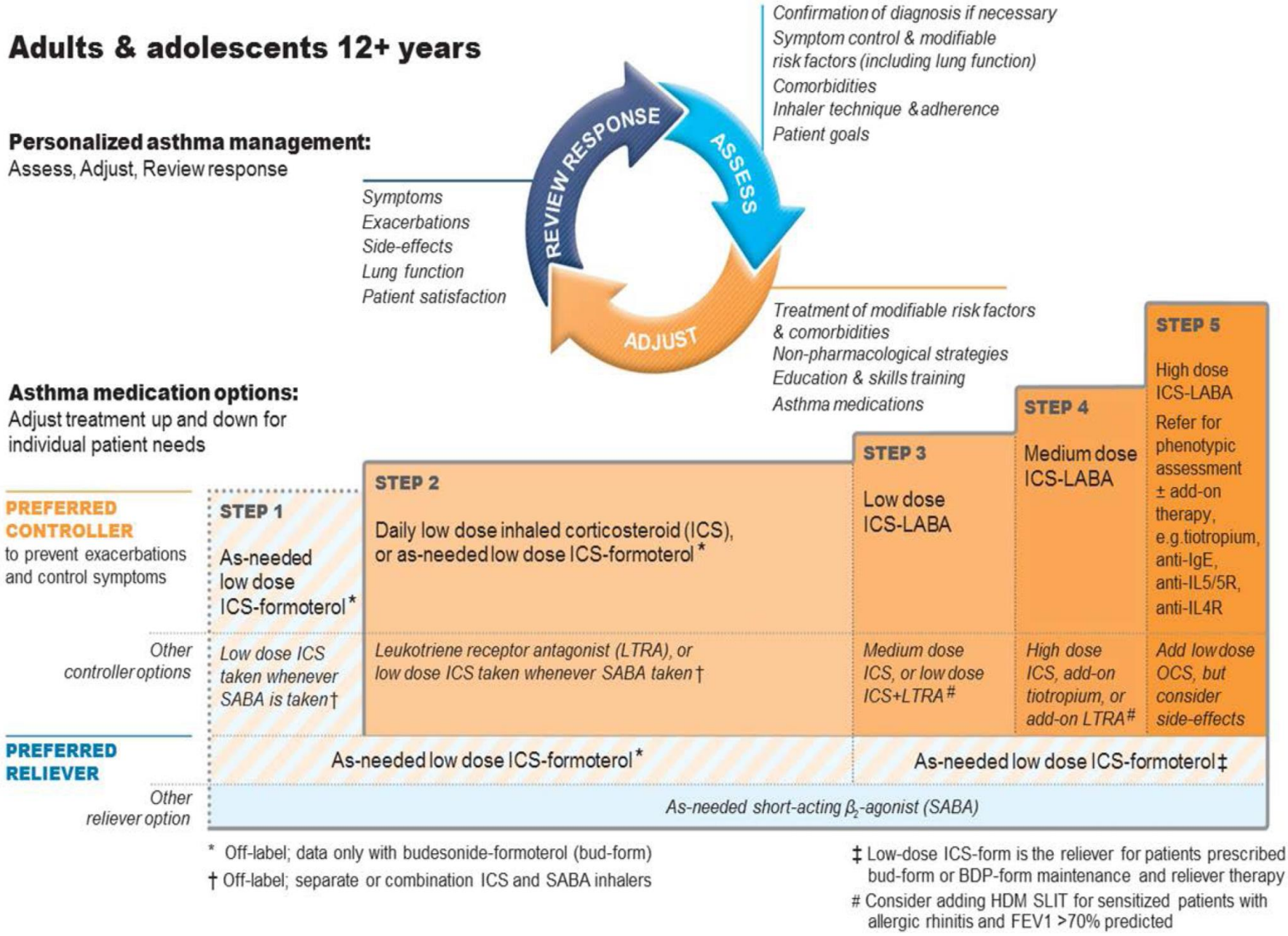
The use of a SABA as the sole asthma therapy in the previous 3 months and patient report of the use of the SABA on at least two occasions
On an average of two or fewer occasions per day in the previous 4 weeks





N Engl J Med 2019; 380:2020-30

Box 7. The GINA asthma treatment strategy



* Off-label; data only with budesonide-formoterol (bud-form)

† Off-label; separate or combination ICS and SABA inhalers

‡ Low-dose ICS-form is the reliever for patients prescribed bud-form or BDP-form maintenance and reliever therapy

\# Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV1 >70% predicted

요약

1. 천식 질환의 특성

변동성

2. ICS 유지의 근거: 끊으면 어떻게 되는가?

조절된 천식
- 추가 근거 필요

3. ICS: 평생 안전한가?

입과 폐로 전신 흡수 – 부작용 가능

4. ICS withdrawal: 그 이후의 대안에 대해

최근의 여러 근거

Stepping down to find the minimum effective dose

- Consider step down once good asthma control has been achieved and maintained for about 3 months, to find patient's lowest treatment that controls both symptoms and exacerbations

- Provide the patient with a written asthma action plan, monitor closely, and schedule a follow-up visit

- ***Do no completely withdraw ICS unless this is needed temporarily to confirm the diagnosis of asthma.***

GINA since 2014

Stepping down to find the minimum effective dose

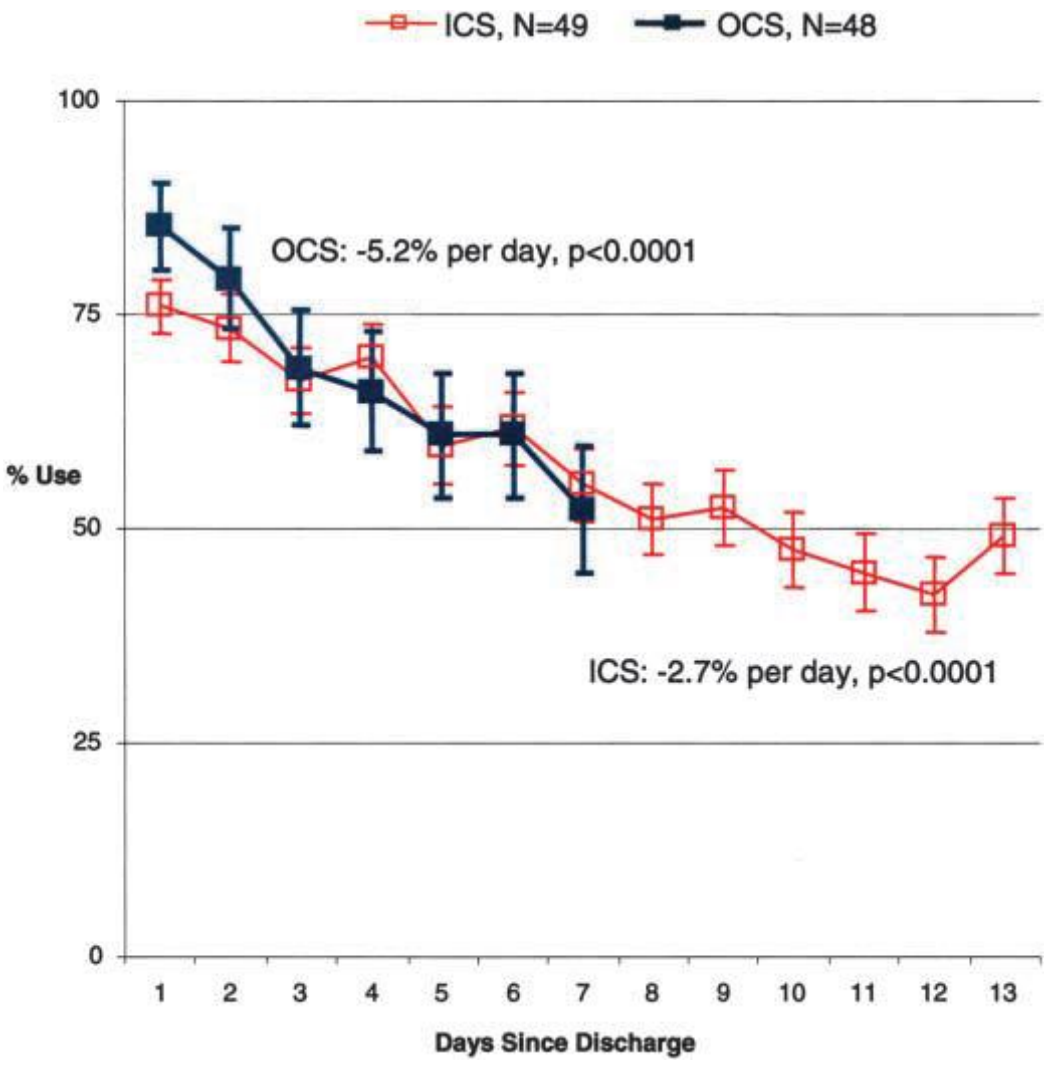
- Consider step down once good asthma control has been achieved and maintained for about 3 months, to find patient's lowest treatment that controls both symptoms and exacerbations

- Provide the patient with a written asthma action plan, monitor closely, and schedule a follow-up visit

- ***ICS may be withdrawn*** *for stable asthmatics for long time with low dose ICS* ***with appropriate education for rescue therapy and action plan.***

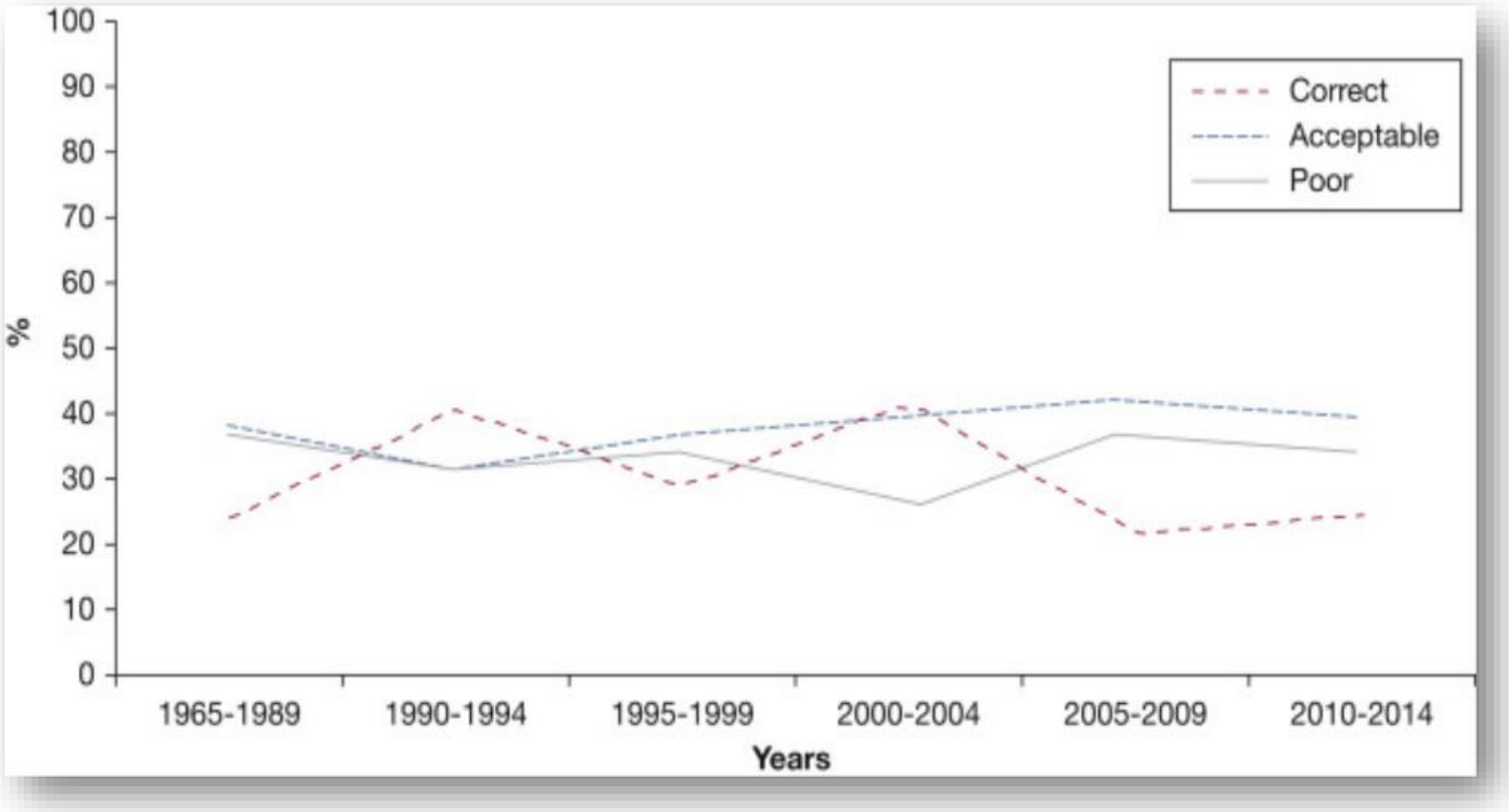
GINA since 2014

천식 악화 퇴원 후 ICS 유지



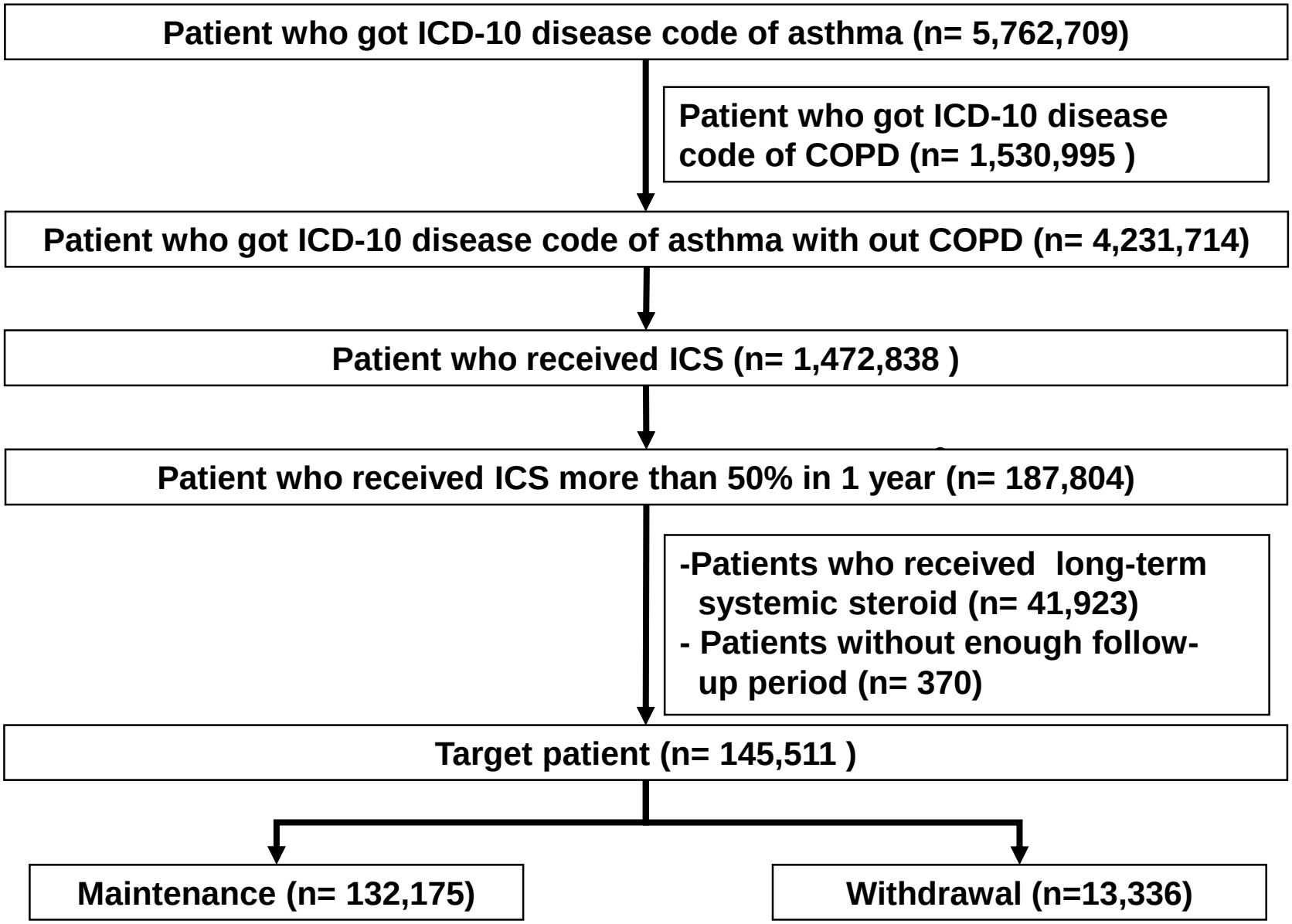
Am J Respir Crit Care Med Vol 170. pp 1281–1285, 2004

Inhaler Technique Over Time

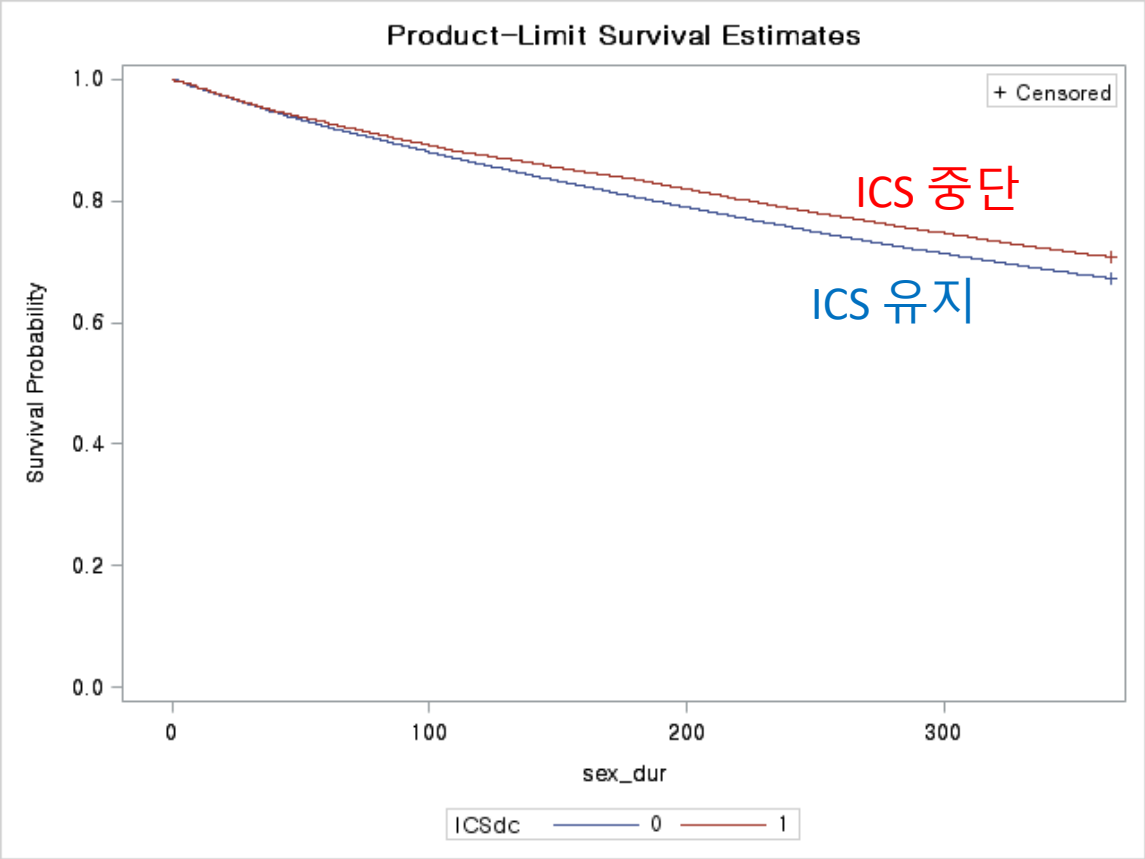


Chest. 2016;150(2):394-406.

Real-World Study in Korea



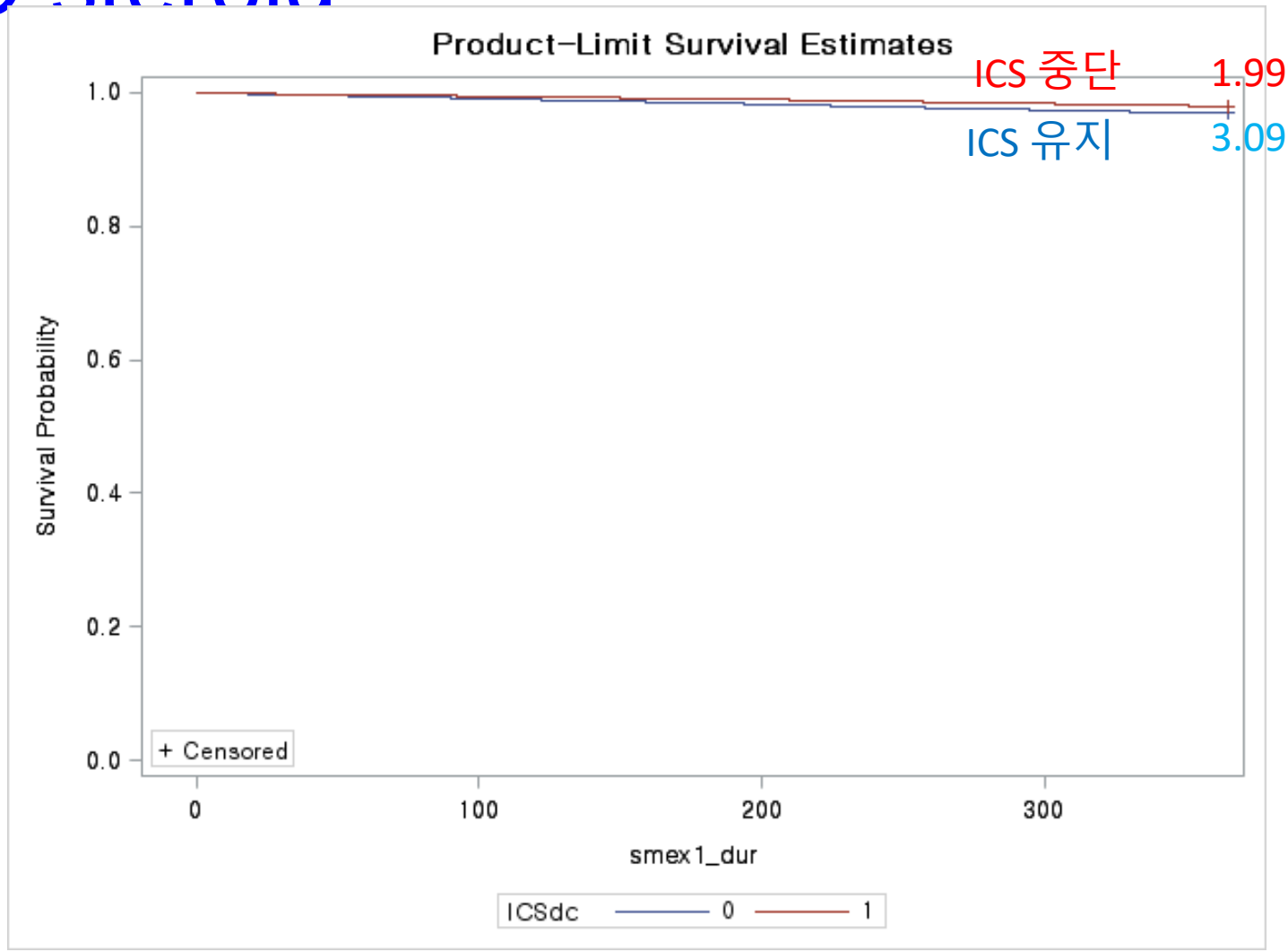
Proportion without Hospitalization



29.2%

32.7%

Patients without Hospitalization + PO steroid



ICS restart rate