2020.11.28

Asthma School

Year in Review:

Mild Asthma

문 지 용

한양대학교구리병원

Contents

GINA 2020 & SABA Overuse

ICS-formoterol as-needed

Patient Preferences

Definition of Mild Asthma

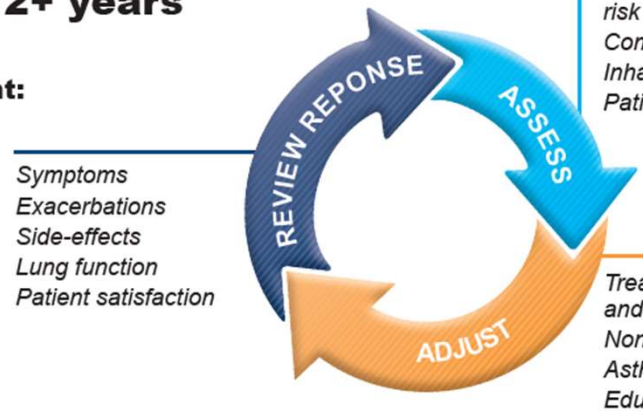
- Definition in the **GINA** document
  - "**Asthma** that is well controlled with **Step 1 or Step 2** treatment (Box 3-5, p.54), i.e. with as-needed reliever medication alone, or with **low-intensity maintenance controller** treatment such as low dose ICS, leukotriene receptor antagonists or chromones"
  - For patients prescribed **as-needed ICS-formoterol**, the **frequency** of use that should be considered to **represent well-controlled** asthma has **not yet been determined**
- Expert Panel Report 3 (**EPR-3**)
  - **Mild Intermittent**
    - Symptom 0-2/week, nighttime awakenings ≤ 2x/month (if no treatment) or **Step 1** treatment (**SABA PRN**)
  - **Mild Persistent**
    - Symptom >2/week (not daily), nighttime awakenings 3-4x/month (if no treatment) or **Step 2** treatment (**low-dose ICS, LTRA, or Theophylline**)

GINA 2020 39 page
National Asthma Education Prevention Program, J Allergy Clin Immunol 2007;120:S94-138.

Box 3-5A

Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (including lung function)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction

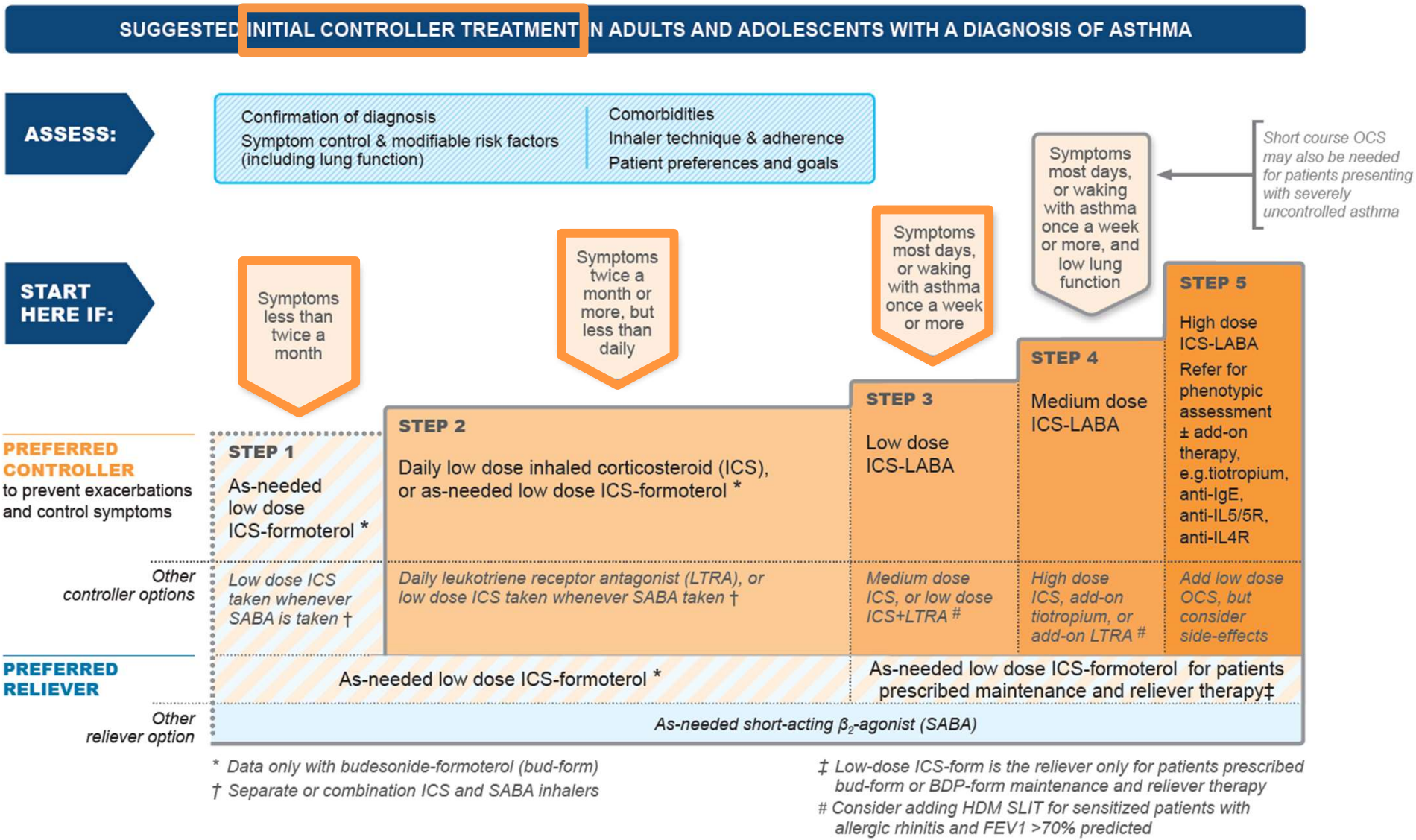
Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down or up)
Education & skills training

Asthma medication options:
Adjust treatment up and down for individual patient needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	As-needed low dose ICS-formoterol *	Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *	Low dose ICS-LABA	Medium dose ICS-LABA	High dose ICS-LABA Refer for phenotypic assessment ± add-on therapy, e.g.tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R
Other controller options	*Low dose ICS taken whenever SABA is taken †*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †*	*Medium dose ICS, or low dose ICS+LTRA #*	*High dose ICS, add-on tiotropium, or add-on LTRA #*	*Add low dose OCS, but consider side-effects*
PREFERRED RELIEVER	As-needed low dose ICS-formoterol *		As-needed low dose ICS-formoterol for patients prescribed maintenance and reliever therapy‡		
Other reliever option	*As-needed short-acting β_2-agonist (SABA)*				

* *Data only with budesonide-formoterol (bud-form)*
† *Separate or combination ICS and SABA inhalers*
‡ *Low-dose ICS-form is the reliever only 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*

GINA 2020


SUGGESTED INITIAL CONTROLLER TREATMENT IN ADULTS AND ADOLESCENTS WITH A DIAGNOSIS OF ASTHMA
ASSESS:
Confirmation of diagnosis
Symptom control & modifiable risk factors (including lung function)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals
START HERE IF:
Symptoms less than twice a month
Symptoms twice a month or more, but less than daily
Symptoms most days, or waking with asthma once a week or more
Symptoms most days, or waking with asthma once a week or more, and low lung function
Short course OCS may also be needed for patients presenting with severely uncontrolled asthma
PREFERRED CONTROLLER
to prevent exacerbations and control symptoms
STEP 1
As-needed low dose ICS-formoterol *
STEP 2
Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *
STEP 3
Low dose ICS-LABA
STEP 4
Medium dose ICS-LABA
STEP 5
High dose ICS-LABA
Refer for phenotypic assessment ± add-on therapy, e.g.tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R
Other controller options
Low dose ICS taken whenever SABA is taken †
Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †
Medium dose ICS, or low dose ICS+LTRA #
High dose ICS, add-on tiotropium, or add-on LTRA #
Add low dose OCS, but consider side-effects
PREFERRED RELIEVER
As-needed low dose ICS-formoterol *
As-needed low dose ICS-formoterol for patients prescribed maintenance and reliever therapy‡
Other reliever option
As-needed short-acting β2-agonist (SABA)
* Data only with budesonide-formoterol (bud-form)
† Separate or combination ICS and SABA inhalers
‡ Low-dose ICS-form is the reliever only 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

GINA 2020

Assessment of Symptom Control in GINA 2020

- Frequency of **SABA use** is included in symptom control assessment
  - Higher SABA use is associated with worse outcomes, even in patients taking ICS

Box 2-2. GINA assessment of asthma control in adults, adolescents and children 6–11 years

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 (SABA) for symptoms more than twice/week?*	Yes☐ No☐			
• Any activity limitation due to asthma?	Yes☐ No☐			

- Our current view is that frequency of **ICS-formoterol use should not be included** in symptom control assessment, particularly **in patients not taking maintenance ICS**
  - The as-needed ICS-formoterol is providing the patient's **controller therapy**
  - Further data awaited: this issue will be reviewed again next year

GINA 2020

ORIGINAL RESEARCH

SABINA: An Overview of Short-Acting β_2-Agonist Use in Asthma in European Countries

Christer Janson · Andrew Menzies-Gow · Cassandra Nan · Javier Nuevo · Alberto Papi · Jennifer K. Quint · Santiago Quirce · Claus F. Vogelmeier

- **SABINA**: SABA use IN Asthma
- Prescription and/or dispensing data during 2006–2017 from **electronic medical records** and/or national patient registries in the United Kingdom (**UK**), **Germany**, **Italy**, **Spain**, and **Sweden** were analyzed.
- 12 years old with a current asthma diagnosis and no other chronic respiratory conditions were included.

- **SABA overuse** was defined as at least **three** SABA canisters **per year**

Janson C, Adv Ther 2020;37:1124-35 [PMID 31981105]

	SABINA I (UK)	SABINA II			
		Germany	Italy	Sweden	Spain
Data source	Primary care records (CPRD GOLD), linked with secondary care (HES) and mortality (ONS) data	IMS® Disease Analyzer: electronic medical records from general practitioner and pulmonologist panels	IQVIA® databases: electronic medical records from primary care (Longitudinal Patient Database) and secondary care (Patient Analyzer) physicians	Nationwide longitudinal cohort study (HERA): linked data from national patient, pharmacy dispensing, and mortality registries	BIG-PAC® database: electronic medical records from primary and specialized healthcare
Study period	2007–2017	2013–2018	2015–2018	2006–2016	2017–2018
Age	≥ 12 years	≥ 12 years	≥ 12 years	12–45 years	≥ 12 years
Asthma definition	Asthma diagnosis code within 3 years of index date	Asthma diagnosis code during study period	Asthma diagnosis code 1 year prior to index date	≥ 2 collections for a chronic obstructive pulmonary disease medication within 12 months	Asthma diagnosis code and ≥ 2 healthcare uses within study period
Asthma treatment steps	2016 BTS guidelines	2018 GINA recommendations	2018 GINA recommendations	2018 GINA recommendations	2018 GINA recommendations

BTS British Thoracic Society, *CPRD* Clinical Practice Research Datalink, *GINA* Global Initiative for Asthma, *HERA* High Efficiency Reliable Access (to data stores), *HES* Hospital Episode Statistics, *ONS* Office for National Statistics, *SABINA* SABA use IN Asthma

Table 2 Baseline characteristics of individuals with asthma

	Italy	Germany	Spain	Sweden	UK
Total number of included individuals with asthma	22,102	53,866	39,555	365,324	574,913
Mean age in years at study entry (SD)	50.8 (19.1)	51.0 (18.0)	49.8 (20.7)	27.6 (11.0)	50.0 (20.6)
Male gender (%)	42	40	36	45	54
Individuals with mild asthma (treatment step[a] 1–2) (%)	37	60	27	48[b]	65
Individuals with moderate-to-severe asthma (treatment step[a] 3–5) (%)	63	40	73	50	35

BTS British Thoracic Society, *GINA* Global Initiative for Asthma, *SD* standard deviation

[a] Treatment steps were based on GINA 2018 for all countries, except the UK (BTS 2016)

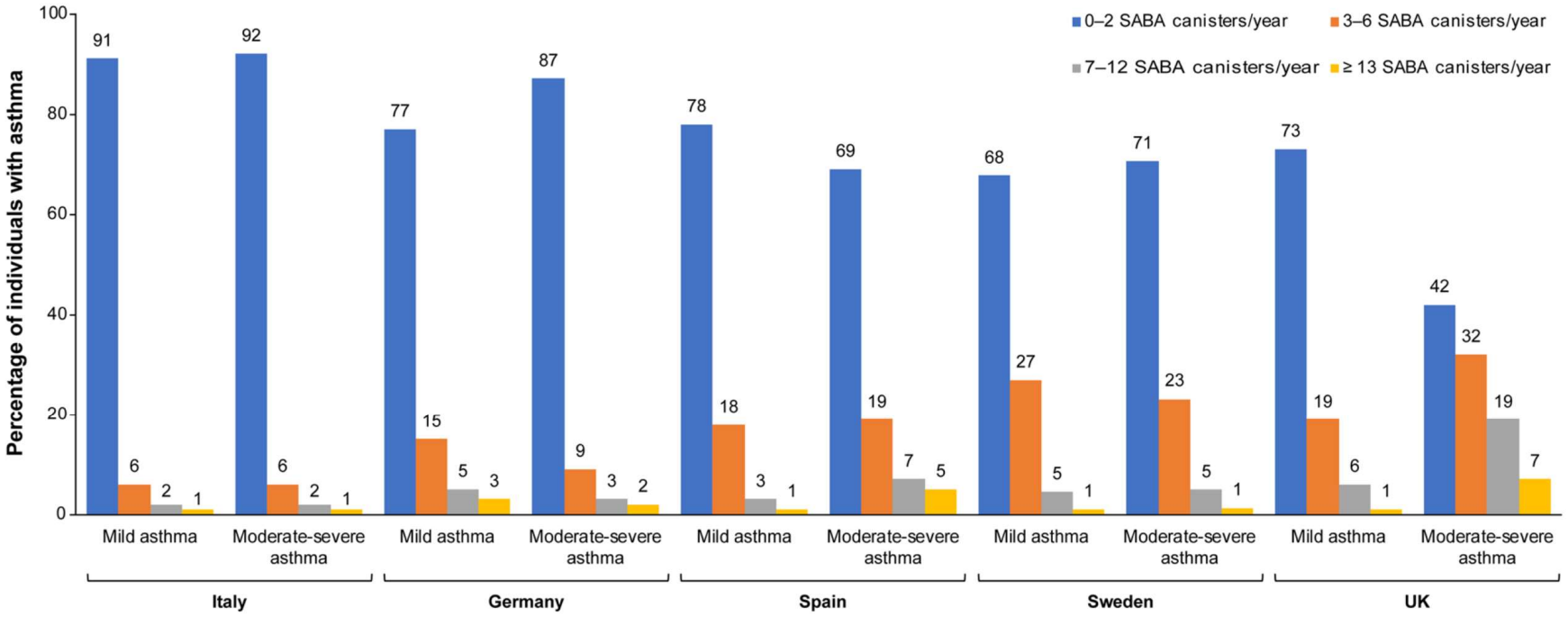
[b] Approximately 2% of individuals could not be classified into a GINA therapy step in Sweden

Table 3 Treatment characteristics: overall SABA use

	Italy	Germany[a]	Spain	Sweden	UK
Mean (SD) number of annual SABA canisters	3.1 (4.0)	1.6 (3.9)	3.3 (3.6)	1.9 (2.9)	4.2 (5.1)
Individuals with 0–2 SABA canisters/year (%)	91	84	71	70	62
Individuals with ≥ 3 SABA canisters/year (%)	9	16	29	30	38
Individuals with 3–6 SABA canisters/year (%)	6	10	19	25	24
Individuals with 7–12 SABA canisters/year (%)	2	3	6	5	11
Individuals with ≥ 13 SABA canisters/year (%)	1	2	4	1	4

GP general practitioner, *SABA* short acting β_2-agonist, *SD* standard deviation

[a] This analysis was based on GP-treated individuals only (n = 29,636)



- In the **UK**, **SABA overuse** was **greater** in individuals with **moderate-to-severe** asthma versus individuals with **mild** asthma (58% versus **27%**, respectively),
- while SABA overuse was similar in individuals with both **mild** (**9–32%**) and moderate-to-severe (8–31%) asthma in the other European countries.

Janson C, Adv Ther 2020;37:1124-35 [PMID 31981105]

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GINA 2020 & SABA Overuse

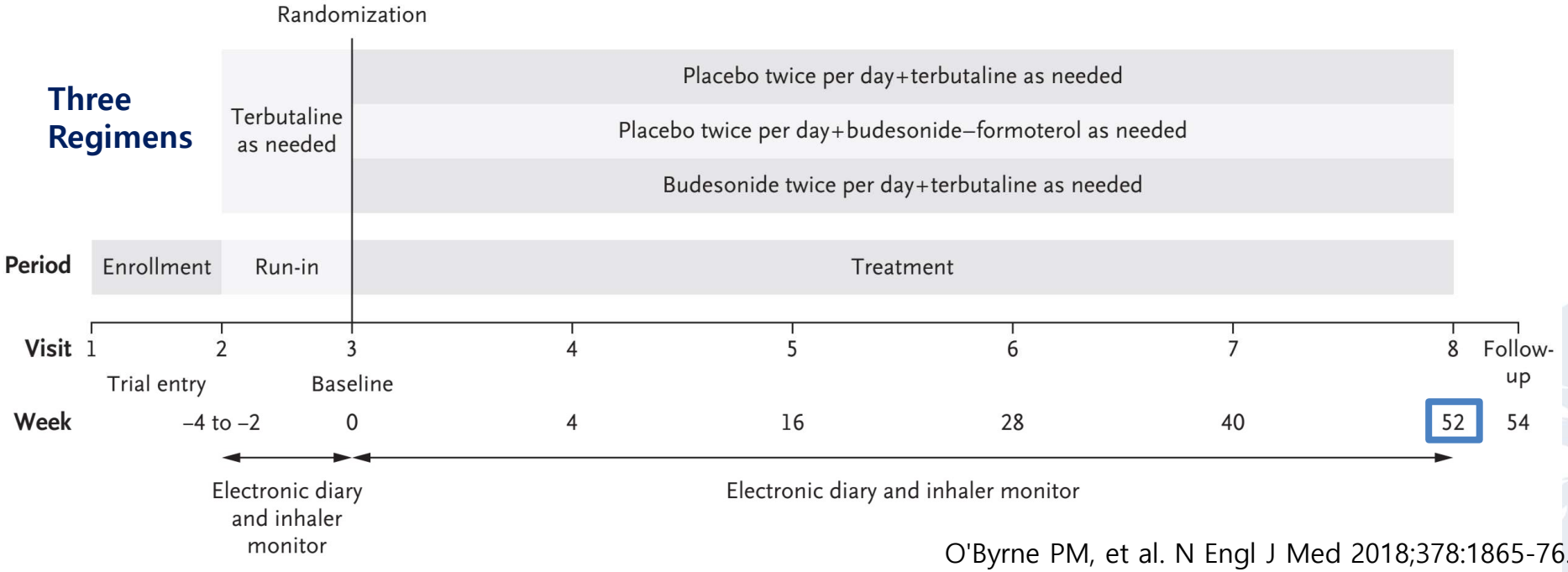
ICS-formoterol as-needed

Patient Preferences

- SYGMA 1 -

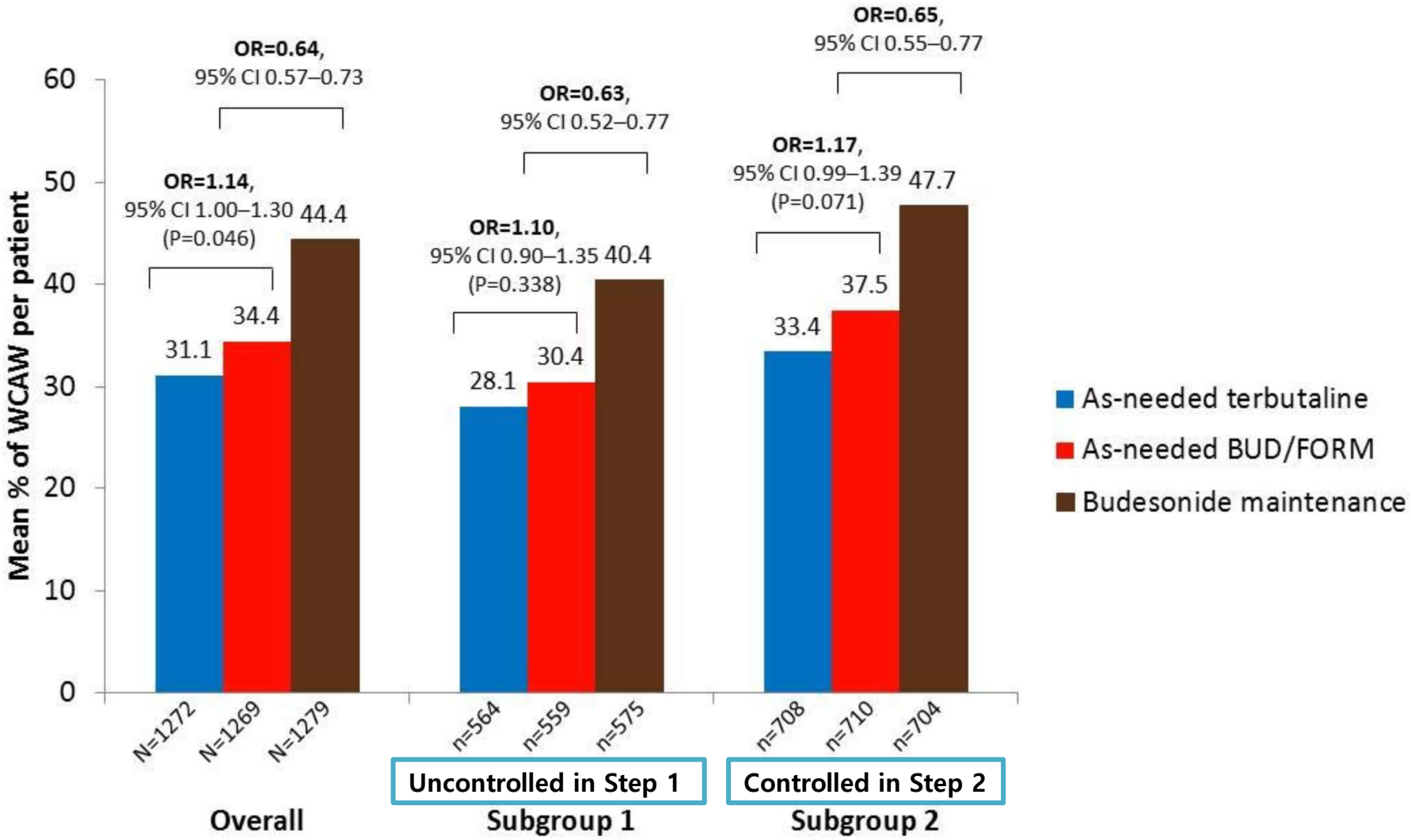
Symbicort Given as Needed in Mild Asthma 1

- **52 weeks, double-blind trial**
- **12 years of age or older (GINA step 2, n=3836), 52 weeks, double-blind trial**
  - 200 μg of budesonide and 6 μg of formoterol (**Symbicort** Turbuhaler) as needed
  - 200 μg of budesonide (**Pulmicort** Turbuhaler) as twice-daily maintenance therapy plus terbutaline at a dose of 0.5 mg (Turbuhaler) used as needed
  - Terbutaline at a dose of 0.5 mg (Turbuhaler) used as needed.



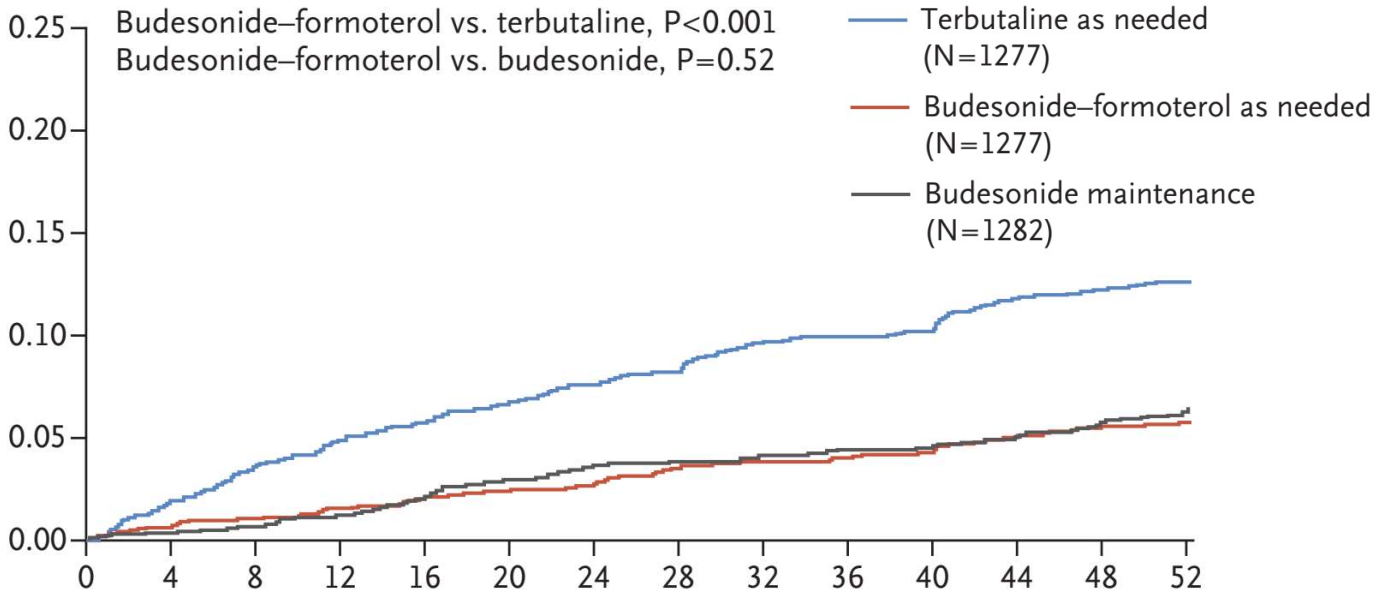
O'Byrne PM, et al. N Engl J Med 2018;378:1865-76.

Primary Outcome: eWCAW
eDiary-Derived Well-Controlled Asthma Weeks

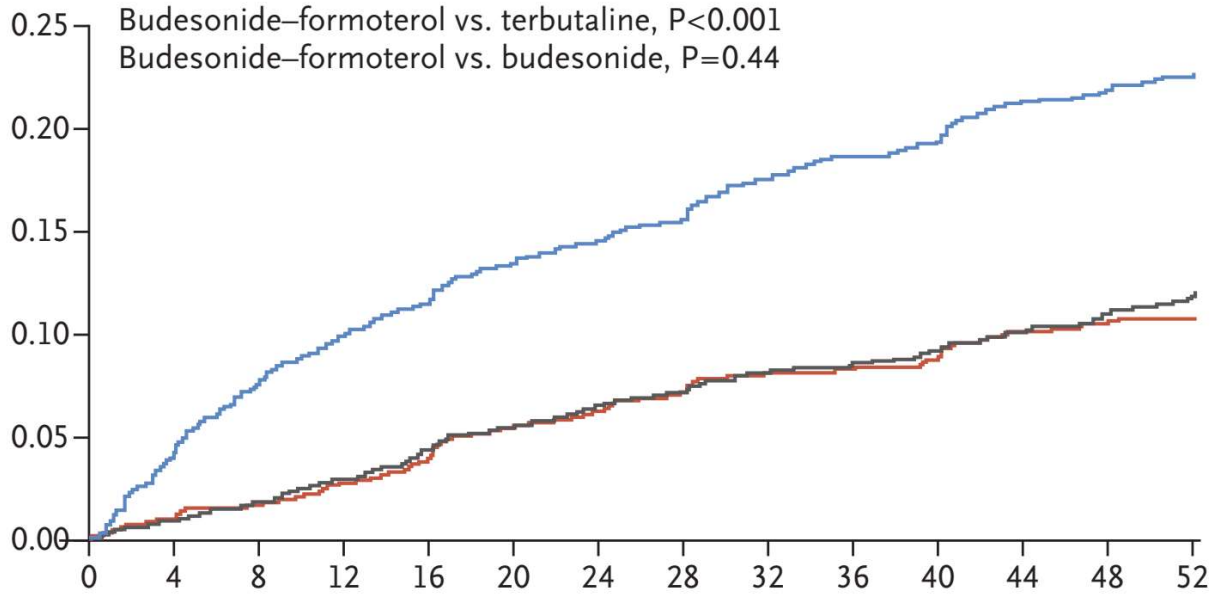


O'Byrne PM, et al. N Engl J Med 2018;378:1865-76.

Severe AE



Moderate or Severe AE



O'Byrne PM, et al. N Engl J Med 2018;378:1865-76.

Effect of a single day of increased as-needed budesonide–formoterol use on short-term risk of severe exacerbations in patients with mild asthma: a post-hoc analysis of the SYGMA 1 study

Paul M O'Byrne, J Mark FitzGerald, Eric D Bateman, Peter J Barnes, Jinping Zheng, Per Gustafson, Rosa Lamarca, Margareta Puu, Christina Keen, Vijay K T Alagappan, Helen K Reddel

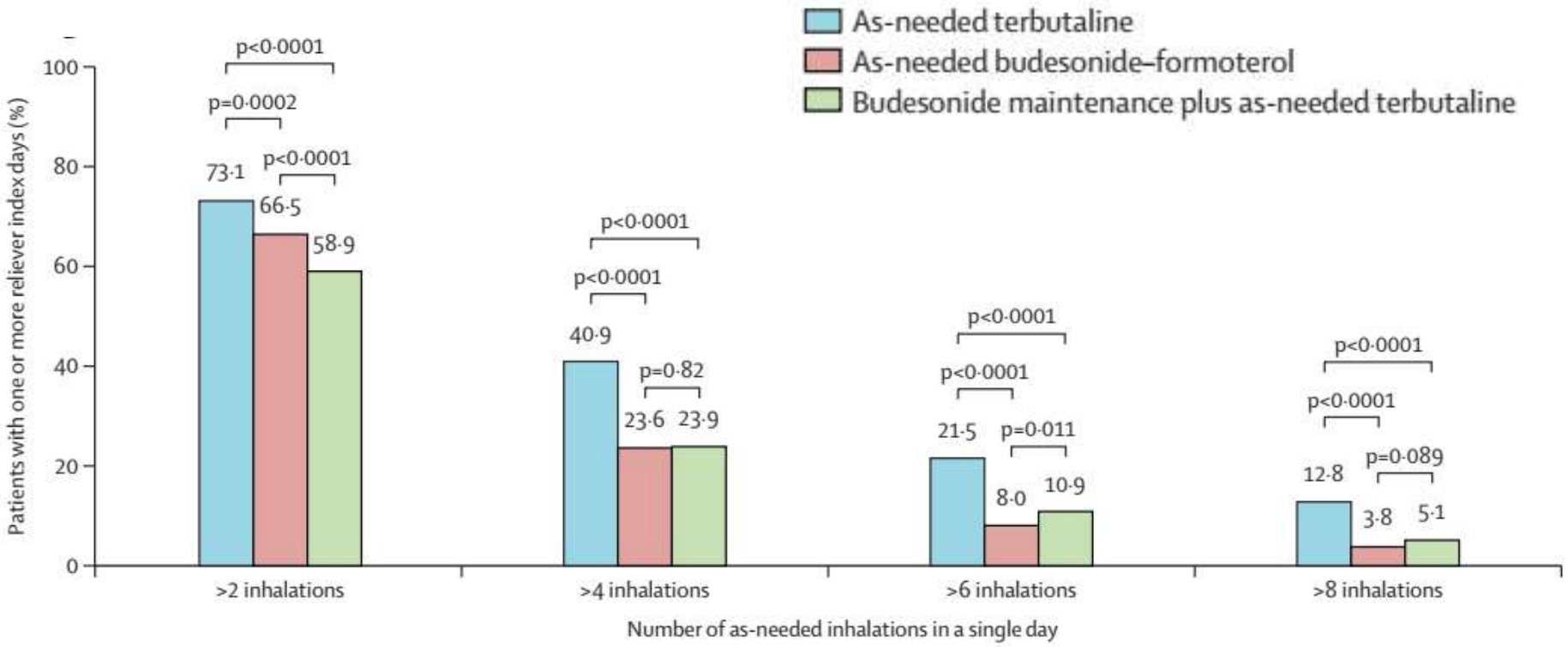
- In this post-hoc analysis, we assessed the **frequency of reliever use** and **the risk of a severe exacerbation** in the 21 days after first use of more than **two**, **four**, **six**, or **eight reliever** inhalations **in 24 h**

	All patients (n=3836)	No days with more than two inhalations (n=1292)	At least 1 day with more than two inhalations (n=2544)	At least 1 day with more than four inhalations (n=1140)	At least 1 day with more than six inhalations (n=525)	At least 1 day with more than eight inhalations (n=286)
Age, years	39·6 (16·6)	39·7 (17·1)	39·6 (16·4)	38·2 (16·3)	36·6 (16·4)	35·4 (16·1)
Sex						
Female	2345 (61%)	817 (63%)	1528 (60%)	651 (57%)	293 (56%)	169 (59%)
Male	1491 (39%)	475 (37%)	1016 (40%)	489 (43%)	232 (44%)	117 (41%)
Region						
Europe	1193 (31%)	525 (41%)	668 (26%)	225 (20%)	90 (17%)	50 (17%)
East Asia	966 (25%)	364 (28%)	602 (24%)	283 (25%)	131 (25%)	80 (28%)
Latin America	773 (20%)	160 (12%)	613 (24%)	319 (28%)	166 (32%)	89 (31%)
Rest of the world	904 (24%)	243 (19%)	661 (26%)	313 (27%)	138 (26%)	67 (23%)
Time since asthma diagnosis, years	6·4 (2·4–13·9)	5·3 (2·0–12·0)	7·0 (2·6–15·0)	7·3 (2·8–15·9)	6·5 (2·8–15·0)	6·6 (2·5–14·3)
Baseline pre-bronchodilator FEV_1, % predicted	84·2 (14·1)	85·1 (12·8)	83·7 (14·6)	82·9 (14·9)	82·3 (15·1)	82·7 (15·5)
Baseline post-bronchodilator FEV_1, % predicted	95·6 (13·7)	96·2 (12·5)	95·3 (14·2)	94·7 (14·3)	94·3 (14·6)	95·2 (15·8)
Baseline reversibility, %	14·6 (11·5)	13·9 (11·7)	15·0 (11·4)	15·5 (11·9)	16·0 (12·7)	16·4 (12·4)
Baseline ACQ-5 score	1·57 (0·96)	1·39 (0·94)	1·65 (0·96)	1·72 (0·98)	1·76 (0·97)	1·81 (1·01)
Pre-study treatment						
Uncontrolled* on short-acting bronchodilator alone	1706 (44%)	526 (41%)	1180 (46%)	575 (50%)	264 (50%)	144 (50%)
Controlled* on inhaled corticosteroid or LTRA	2130 (56%)	766 (59%)	1364 (54%)	565 (50%)	261 (50%)	142 (50%)
Severe exacerbation in past 12 months	754 (20%)	215 (17%)	539 (21%)	264 (23%)	131 (25%)	68 (24%)

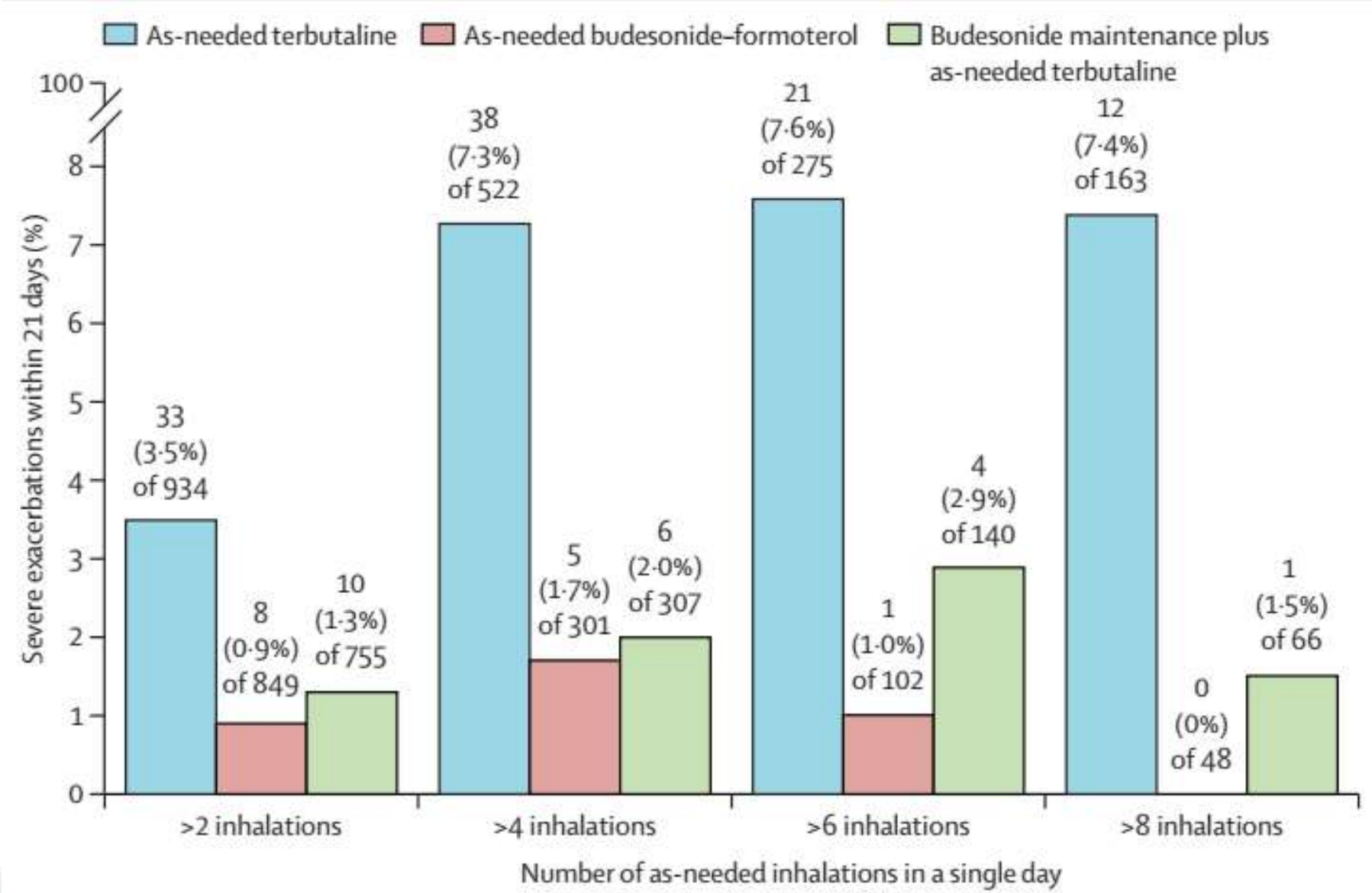
Data are n (%), mean (SD), or median (IQR). Baseline is defined as the assessment at visit 3 (ie, the timepoint at which random assignment to treatment took place). ACQ-5=Asthma Control Questionnaire 5. LTRA=leukotriene receptor antagonist. *Level of asthma control on pre-study treatment was physician assessed.

Table: **Baseline demographics and clinical characteristics**

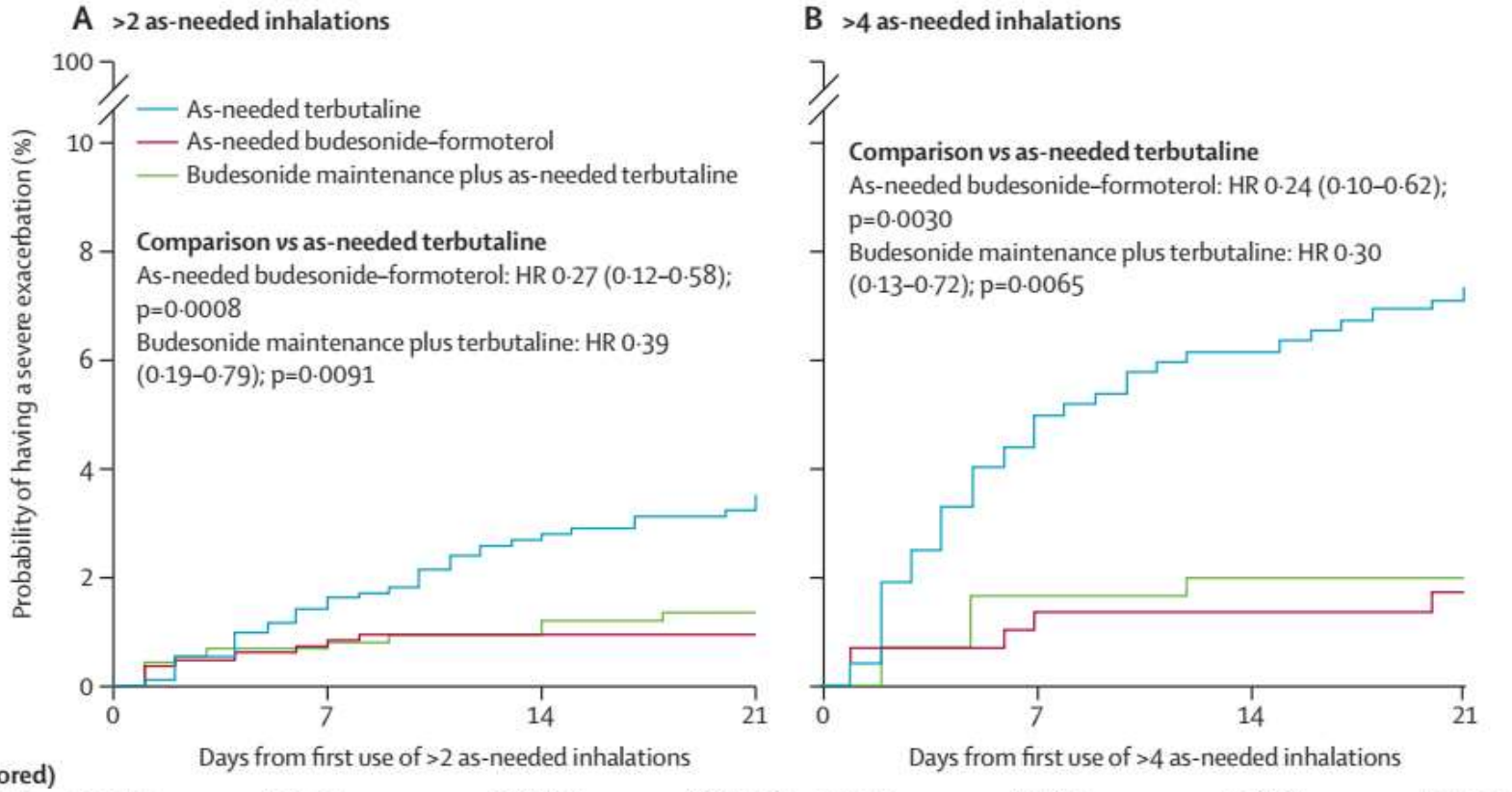
O'Byrne PM, Lancet Respir Med 2020.



O'Byrne PM, Lancet Respir Med 2020.

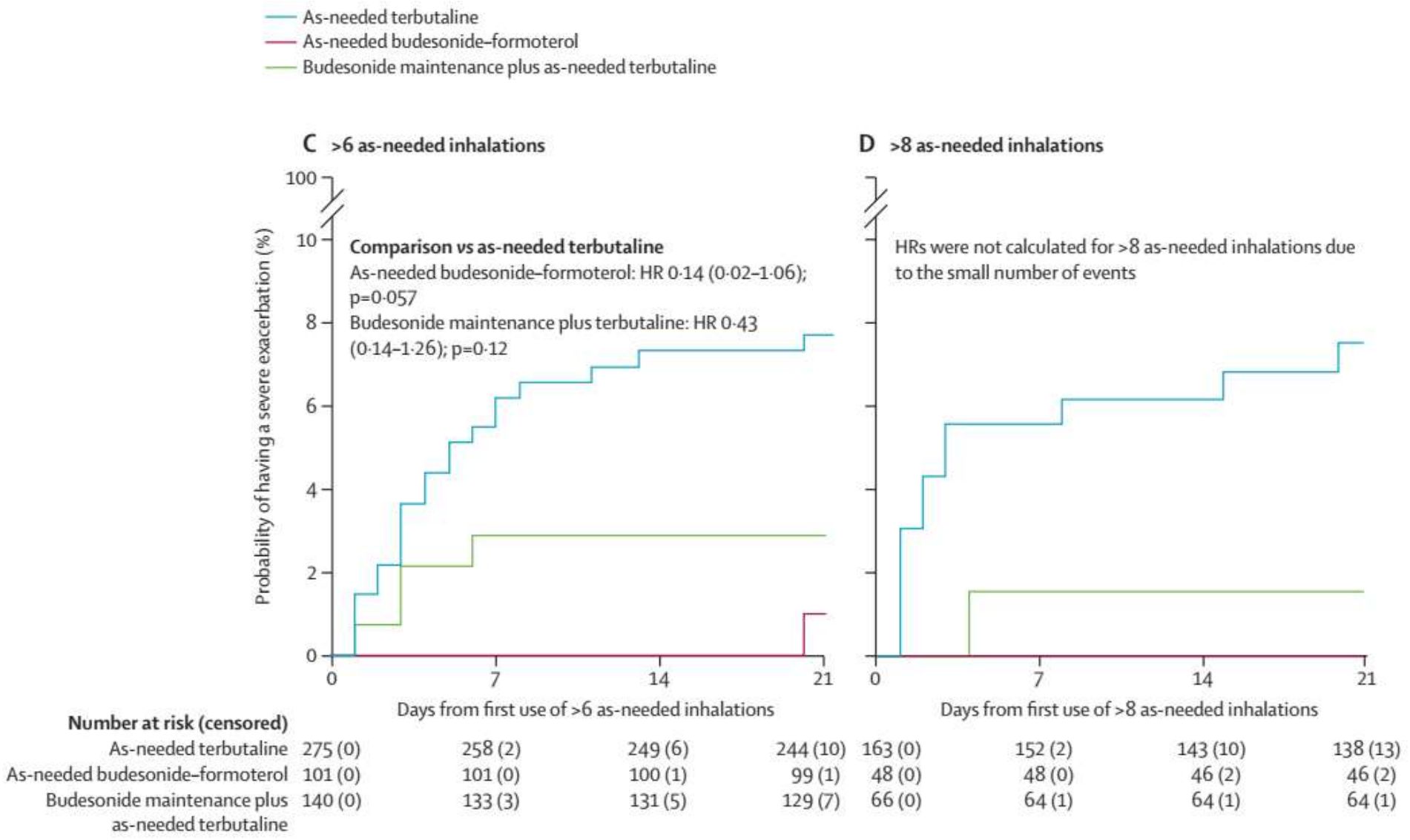


O'Byrne PM, Lancet Respir Med 2020.



Number at risk (censored)								
As-needed terbutaline	934 (0)	916 (5)	898 (11)	888 (16)	522 (0)	494 (5)	478 (12)	470 (15)
As-needed budesonide–formoterol	849 (0)	841 (2)	835 (6)	834 (7)	301 (0)	293 (5)	291 (6)	289 (7)
Budesonide maintenance plus as-needed terbutaline	755 (0)	745 (5)	740 (8)	732 (13)	307 (0)	299 (3)	295 (6)	289 (12)

O'Byrne PM, Lancet Respir Med 2020.



◆ **the greater the risk of severe exacerbation** (as suggested by increased reliever use), **the greater the benefit of as-needed budesonide–formoterol**.

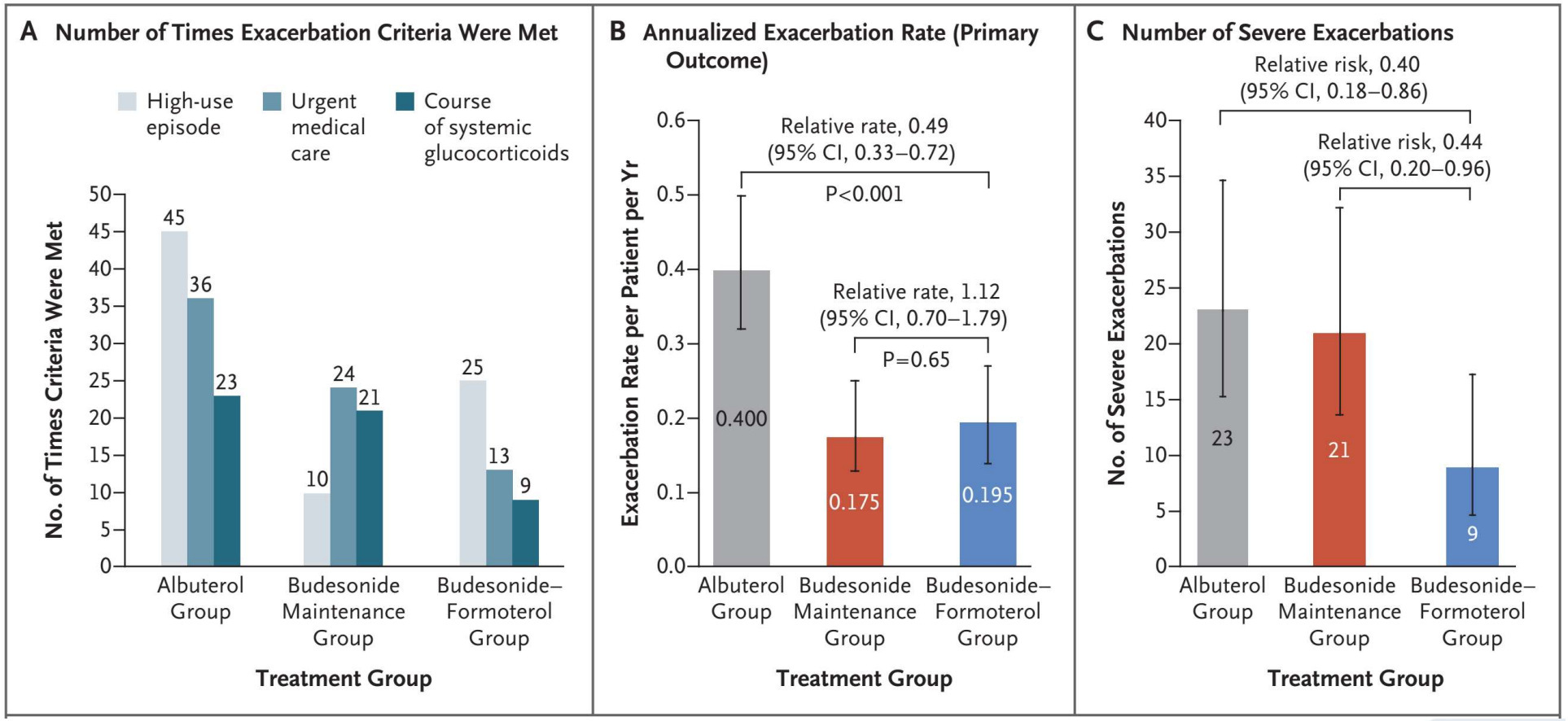
O'Byrne PM, Lancet Respir Med 2020.

- Novel START -

- patients with **mild intermittent** asthma as well as patients with **mild persistent** asthma.
- 12-month, pragmatic, randomized, open-label, parallel-group, multicenter study(N=675)
- adults were randomly assigned to one of three treatments.
  - **albuterol** as needed for relief of asthma symptoms
  - **budesonide**, 200 μg twice daily, as maintenance therapy plus as needed albuterol
  - **budesonide–formoterol** as needed for relief of symptoms

- **Primary outcome** : **Annualized rate of asthma exacerbations**
- Secondary outcome : Score on the Asthma Control Questionnaire–5, the on treatment FEV1, the fraction of exhaled nitric oxide, the number of severe exacerbations
- **Exacerbation** defined as worsening asthma that resulted in an episode of **high β2-agonist inhaler use**, in an **urgent medical care** consultation, or in a course of **systemic glucocorticoids**

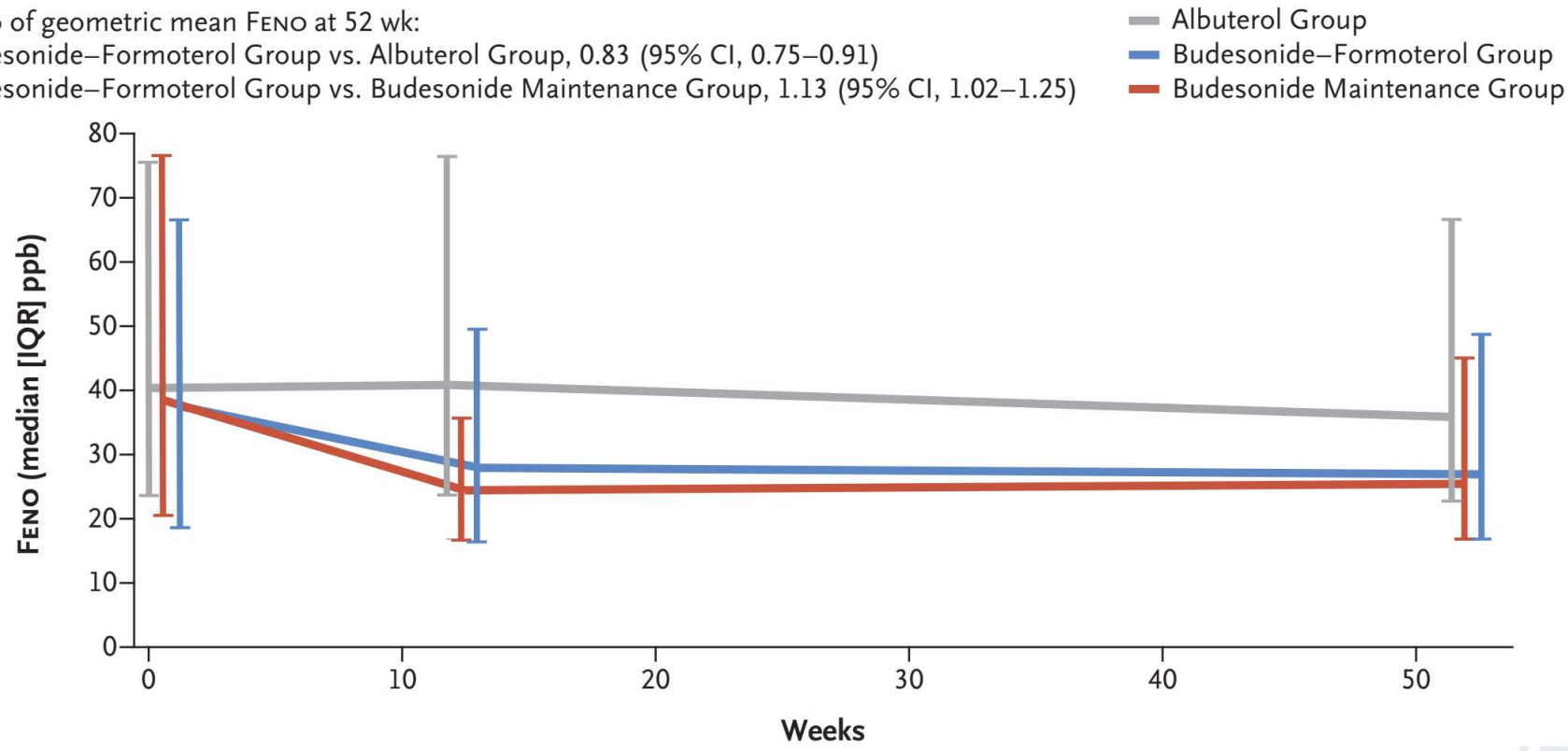
Beasley R, N Engl J Med 2019;380:2020-30.



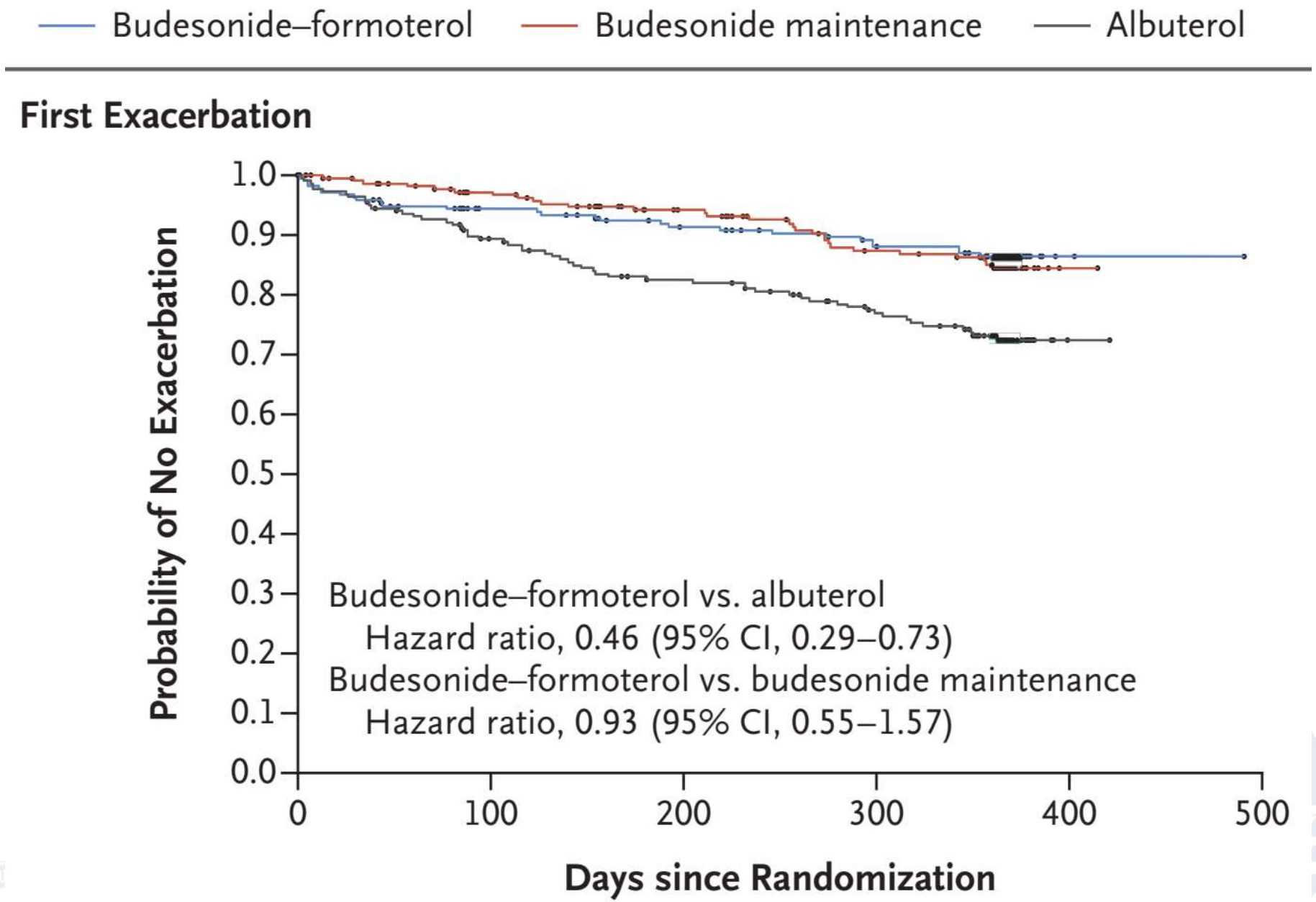
Beasley R, N Engl J Med 2019;380:2020-30.

Fraction of Exhaled Nitric Oxide

Ratio of geometric mean FENO at 52 wk:
Budesonide–Formoterol Group vs. Albuterol Group, 0.83 (95% CI, 0.75–0.91)
Budesonide–Formoterol Group vs. Budesonide Maintenance Group, 1.13 (95% CI, 1.02–1.25)

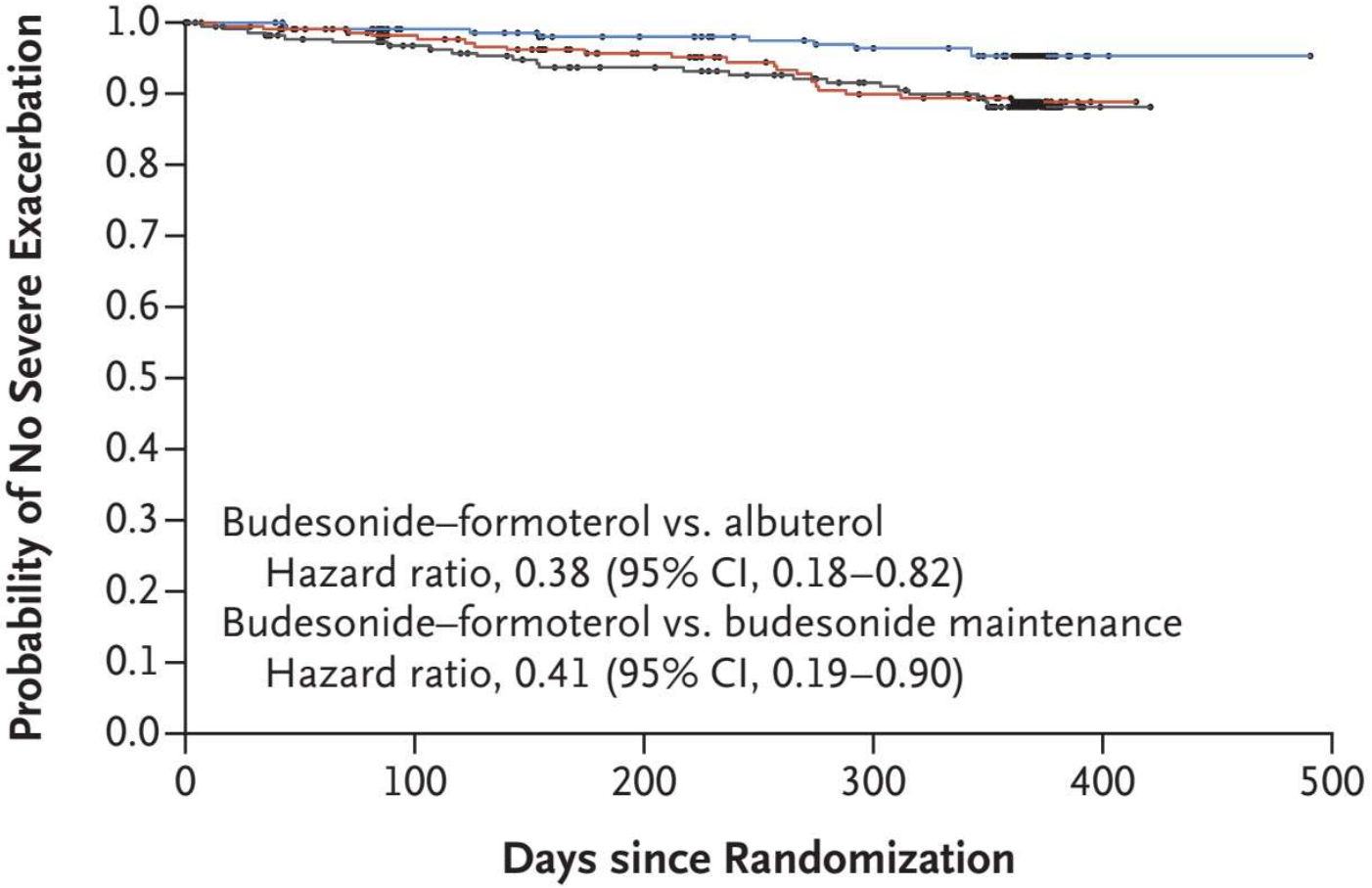


Beasley R, N Engl J Med 2019;380:2020-30.



Beasley R, N Engl J Med 2019;380:2020-30.

First Severe Exacerbation



No. at Risk

Budesonide–formoterol	220	197	184	172	2
Budesonide maintenance	225	199	176	157	1
Albuterol	223	197	180	164	1

Beasley R, N Engl J Med 2019;380:2020-30.

Predictive value of blood eosinophils and exhaled nitric oxide in adults with mild asthma: a prespecified subgroup analysis of an open-label, parallel-group, randomised controlled trial

Ian D Pavord, Mark Holliday, Helen K Reddel, Irene Braithwaite, Stefan Ebmeier, Robert J Hancox, Tim Harrison, Claire Houghton, Karen Oldfield, Alberto Papi, Mathew Williams, Mark Weatherall, Richard Beasley, on behalf of the Novel START Study Team

- in this prespecified subgroup analysis, we assessed whether **annual exacerbation rates** in each treatment group were significantly different depending on levels of **blood eosinophil count**, **FeNO**, or a **composite score** of both

Blood eosinophil count (×10⁹/L)		
<0·15 (n=184)	0·15 to <0·30 (n=256)	≥0·30 (n=216)

FeNO (ppb)		
<20 (n=159)	20 to 50 (n=249)	>50 (n=260)

Composite score		
1: blood eosinophils <0·15×10⁹/L and FeNO <20 ppb (n=78)	2: any pattern other than scores 1 or 3 (n=432)	3: blood eosinophils ≥0·3×10⁹/L and FeNO >50 ppb (n=146)

Pavord ID, Lancet Respir Med 2020;8:671-80.

Predictive value of blood eosinophils and exhaled nitric oxide in adults with mild asthma: a prespecified subgroup analysis of an open-label, parallel-group, randomised controlled trial

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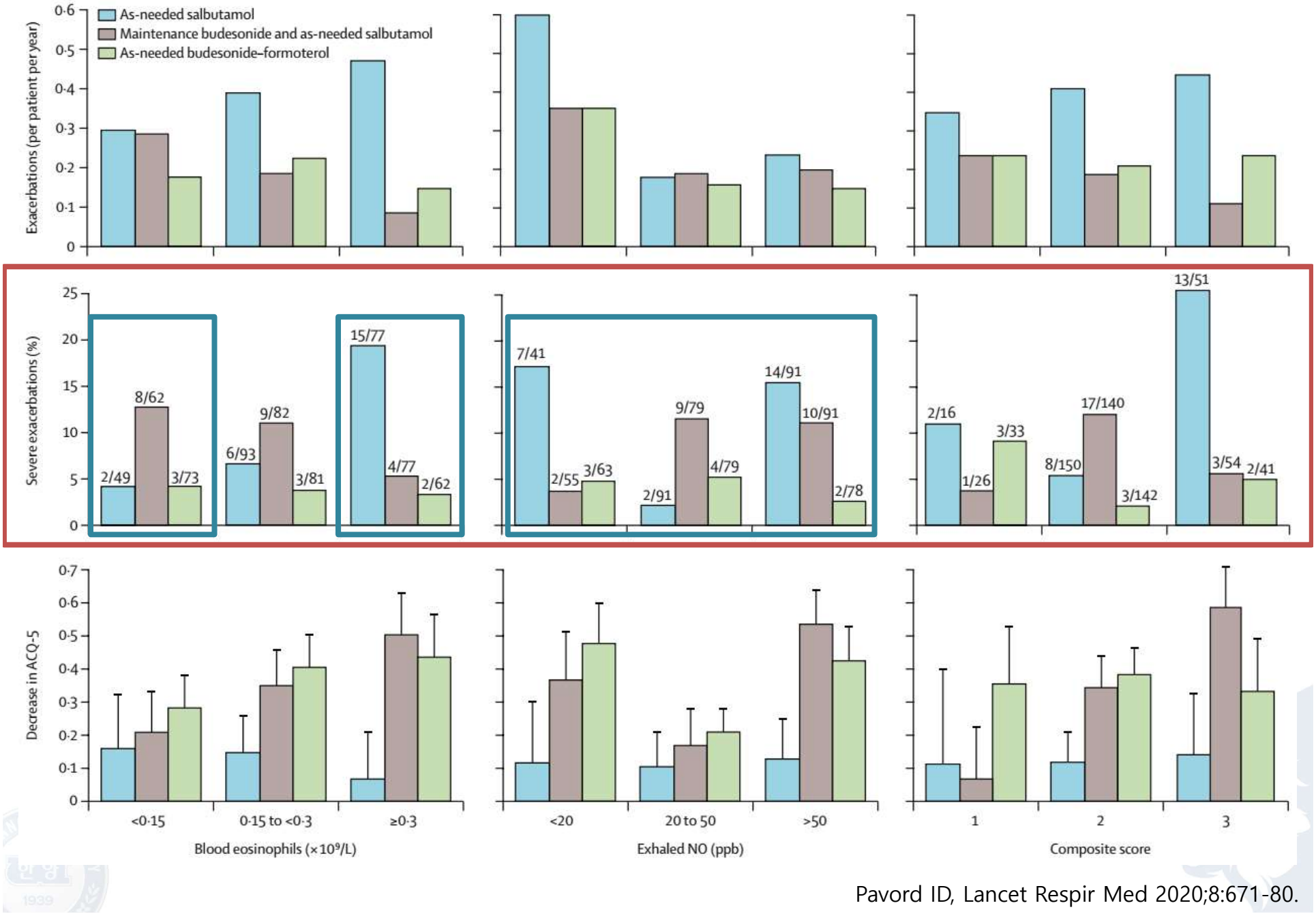
	Blood eosinophil count (×10⁹/L)			FeNO (ppb)			Composite score		
	<0·15 (n=184)	0·15 to <0·30 (n=256)	≥0·30 (n=216)	<20 (n=159)	20 to 50 (n=249)	>50 (n=260)	1: blood eosinophils <0·15×10⁹/L and FeNO <20 ppb (n=78)	2: any pattern other than scores 1 or 3 (n=432)	3: blood eosinophils ≥0·3×10⁹/L and FeNO >50 ppb (n=146)
Sex									
Female	114 (62%)	132 (52%)	111 (51%)	117 (74%)	130 (52%)	117 (45%)	61 (78%)	223 (52%)	73 (50%)
Male	70 (38%)	124 (48%)	105 (49%)	42 (26%)	119 (48%)	143 (55%)	17 (22%)	211 (48%)	73 (50%)
Current smoker	19 (10%)	24 (9%)	21 (10%)	31 (19%)	17 (7%)	16 (6%)	12 (15%)	42 (10%)	10 (7%)
≥1 exacerbation in past year	16 (9%)	14 (5%)	18 (8%)	9 (6%)	23 (9%)	17 (7%)	6 (8%)	30 (7%)	12 (8%)
Hospitalisation with asthma ever	10 (5%)	41 (16%)	44 (20%)	15 (9%)	44 (18%)	48 (18%)	5 (6%)	69 (16%)	30 (21%)
Age, years	36·0 (14·9)	38·1 (14·4)	31·9 (12·3)	36·1 (14·2)	38·0 (14·9)	33·0 (12·9)	36·2 (15·1)	36·7 (14·3)	31·2 (12·1)
Age at onset of asthma, years	16·0 (12·9)	15·0 (14·9)	12·3 (11·9)	18·3 (13·9)	14·6 (14·0)	12·0 (12·5)	19·2 (14·1)	14·4 (13·8)	11·7 (11·5)
Body-mass index	27·3 (7·0)	28·1 (6·5)	26·6 (5·8)	28·7 (7·6)	28·0 (6·5)	26·0 (5·2)	27·7 (7·8)	27·9 (6·5)	25·7 (5·2)
SABA puffs per week	3·5 (3·3)	3·4 (3·3)	3·6 (3·3)	3·8 (3·7)	3·2 (2·9)	3·6 (3·3)	3·9 (3·5)	3·4 (3·3)	3·6 (3·2)
ACQ-5	1·0 (0·7)	1·1 (0·7)	1·2 (0·7)	1·2 (0·8)	1·0 (0·7)	1·1 (0·7)	1·1 (0·7)	1·1 (0·7)	1·2 (0·7)
FEV_1, % predicted	92·6 (14·3)	89·2 (13·9)	88·0 (13·0)	92·3 (14·3)	89·1 (13·8)	88·9 (13·4)	95·3 (14·0)	89·5 (13·8)	87·5 (13·0)
FeNO (ppb)	30·4 (24·8)	45·9 (38·8)	82·9 (50·7)	12·9 (4·0)	33·2 (8·2)	97·7 (42·1)	12·9 (3·9)	42·8 (33·2)	107·3 (42·8)
Blood eosinophil count (×10⁹/L)	0·10 (0·03)	0·22 (0·04)	0·51 (0·22)	0·18 (0·15)	0·24 (0·17)	0·38 (0·24)	0·09 (0·03)	0·23 (0·15)	0·52 (0·22)

Data are n (%) or mean (SD), unless otherwise stated. FeNO=fraction of exhaled nitric oxide. ppb=parts per billion. SABA=short-acting β agonist. ACQ-5=Asthma Control Questionnaire 5-item version.

Table 1: **Baseline characteristics by baseline biomarker group**

Pavord ID, Lancet Respir Med 2020;8:671-80.



Pavord ID, Lancet Respir Med 2020;8:671-80.

	Exacerbation rate ratios (95% CI)			Severe exacerbation risk odds ratios (95% CI)		
	As-needed budesonide–formoterol *vs* as-needed salbutamol	Maintenance budesonide plus as-needed salbutamol *vs* as-needed salbutamol	$p_{interaction}$	As-needed budesonide–formoterol *vs* as-needed salbutamol	Maintenance budesonide plus as-needed salbutamol *vs* as-needed salbutamol	$p_{interaction}$
FeNO	..	..	0·28	..	..	0·009
High (>50 ppb)	0·53 (0·24–1·15)	0·72 (0·35–1·50)	..	0·32 (0·06–1·75)	1·93 (0·62–5·92)	..
Low (<20 ppb)	0·36 (0·17–0·76)	0·19 (0·08–0·47)	..	0·18 (0·04–0·84)	0·09 (0·02–0·50)	..
p value (high *vs* low)	0·51	0·028	..	0·65	0·0040	..
Blood eosinophils count	..	..	0·014	..	..	0·009
High (≥0·3 × 10^9/L)	0·28 (0·12–0·63)	0·13 (0·05–0·33)	..	0·15 (0·03–0·79)	0·11 (0·03–0·45)	..
Low (<0·15 × 10^9/L)	0·63 (0·27–1·44)	1·15 (0·51–1·28)	..	1·42 (0·19–10·50)	5·72 (0·97–33·60)	..
p value (high *vs* low)	0·18	0·0006	..	0·10	0·0007	..
Composite score	..	..	0·54	..	..	0·005
High (FeNO >50 ppb and eosinophils ≥0·3 × 10^9/L)	0·52 (0·23–1·22)	0·24 (0·90–0·65)	..	0·15 (0·03–0·71)	0·17 (0·05–0·65)	..
Low (FeNO <20 ppb and eosinophils <0·15 × 10^9/L)	0·68 (0·22–2·14)	0·68 (0·20–2·35)	..	0·17 (0·05–0·65)	0·31 (0·03–3·67)	..
p value (high *vs* low)	0·73	0·20	..	0·18	0·68	..

$p_{interaction}$ refers to the interaction between any treatment effect and the biomarker status. p values between treatment comparisons were only considered further if this interaction was significant. FeNO=fraction of exhaled nitric oxide. ppb=parts per billion.

Table 3: **Exacerbation and severe exacerbation interaction analysis for the change in treatment effect for treatments containing budesonide compared with as-needed salbutamol**

Pavord ID, Lancet Respir Med 2020;8:671-80.

Research letter

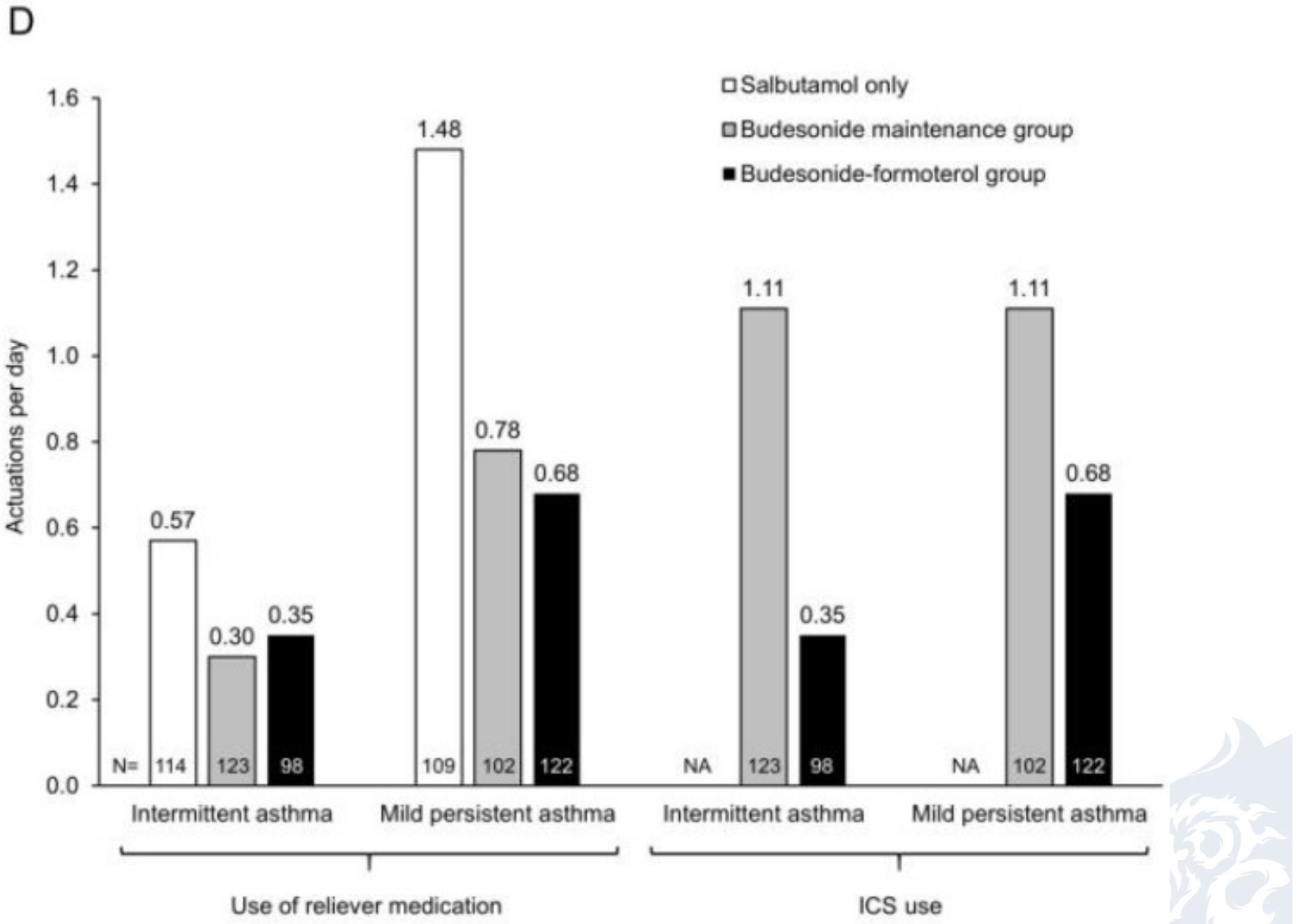
Budesonide-formoterol reliever therapy in intermittent *versus* mild persistent asthma

Alberto Papi, Irene Braithwaite, Stefan Ebmeier, B. Hancox, Tim Harrison, Mark Holliday, Claire Houghton, Luca Morandi, Karen Oldfield, Ian D. Pavord, Helen K. Reddel, Mathew Williams, Mark Weatherall, Richard Beasley

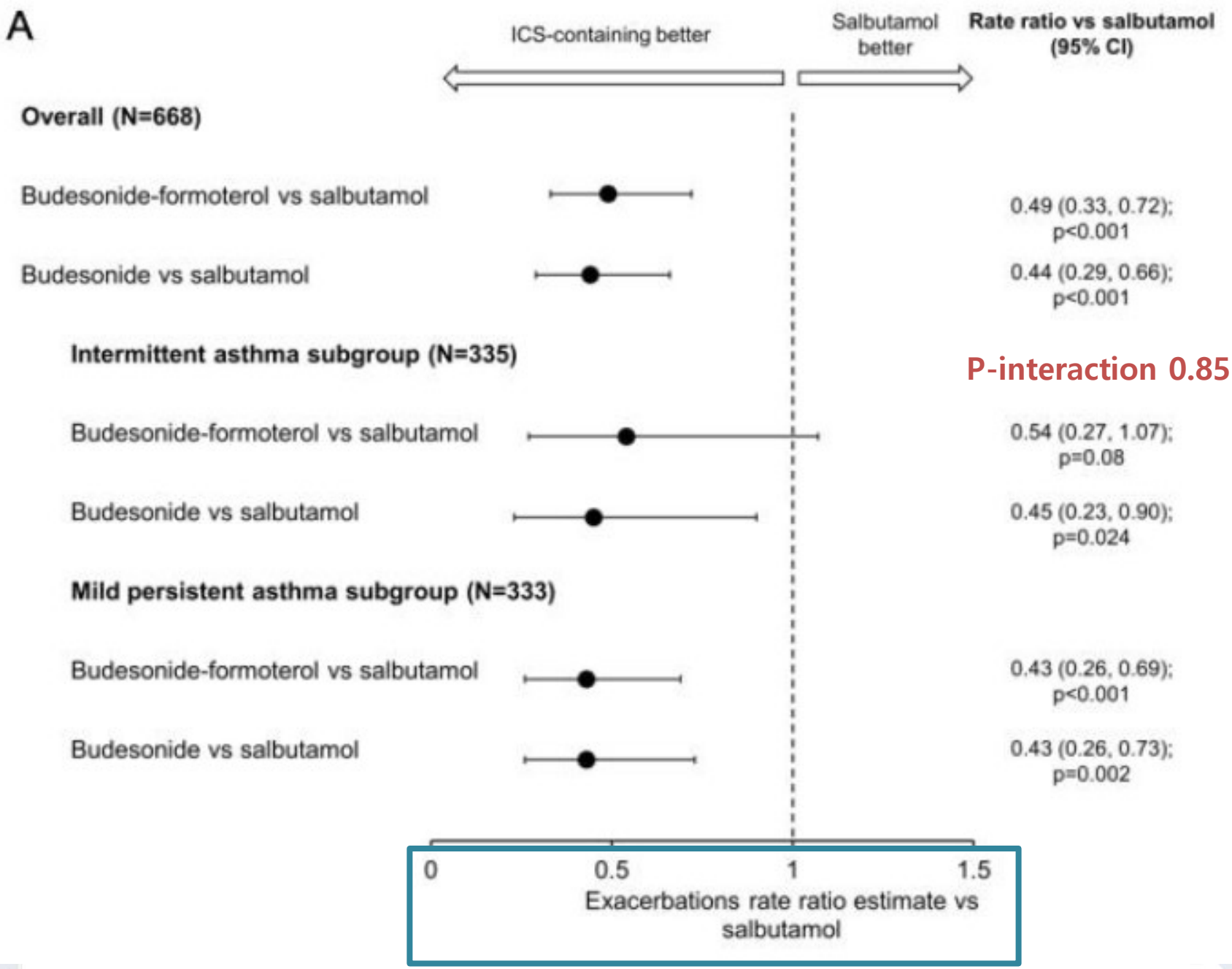
- **post-hoc analyses** of the **Novel START** study
- "**intermittent asthma**" defined as use of SABA-alone on **≤2 occasions/week** in the four weeks before entry, and with no severe exacerbation in the previous year.
- "**mild persistent asthma**", using SABA-alone on **>2 occasions/week** (but less than twice-daily) in the previous four weeks, and/or ≥1 severe exacerbation in the previous year

- A total of 668 participants were included, 335 (**50.1%**) with **intermittent asthma.**

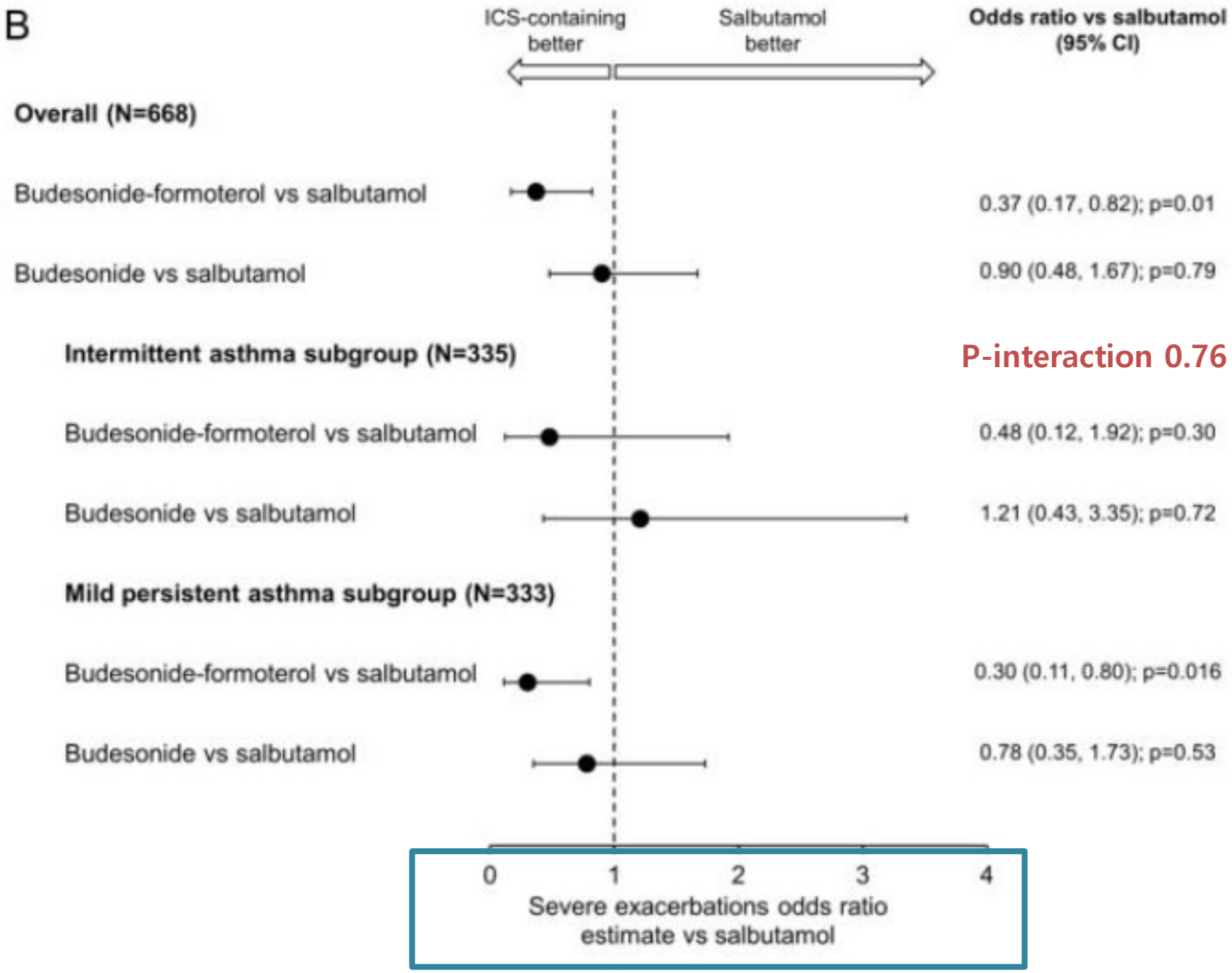
Papi A, Eur Respir J 2020.



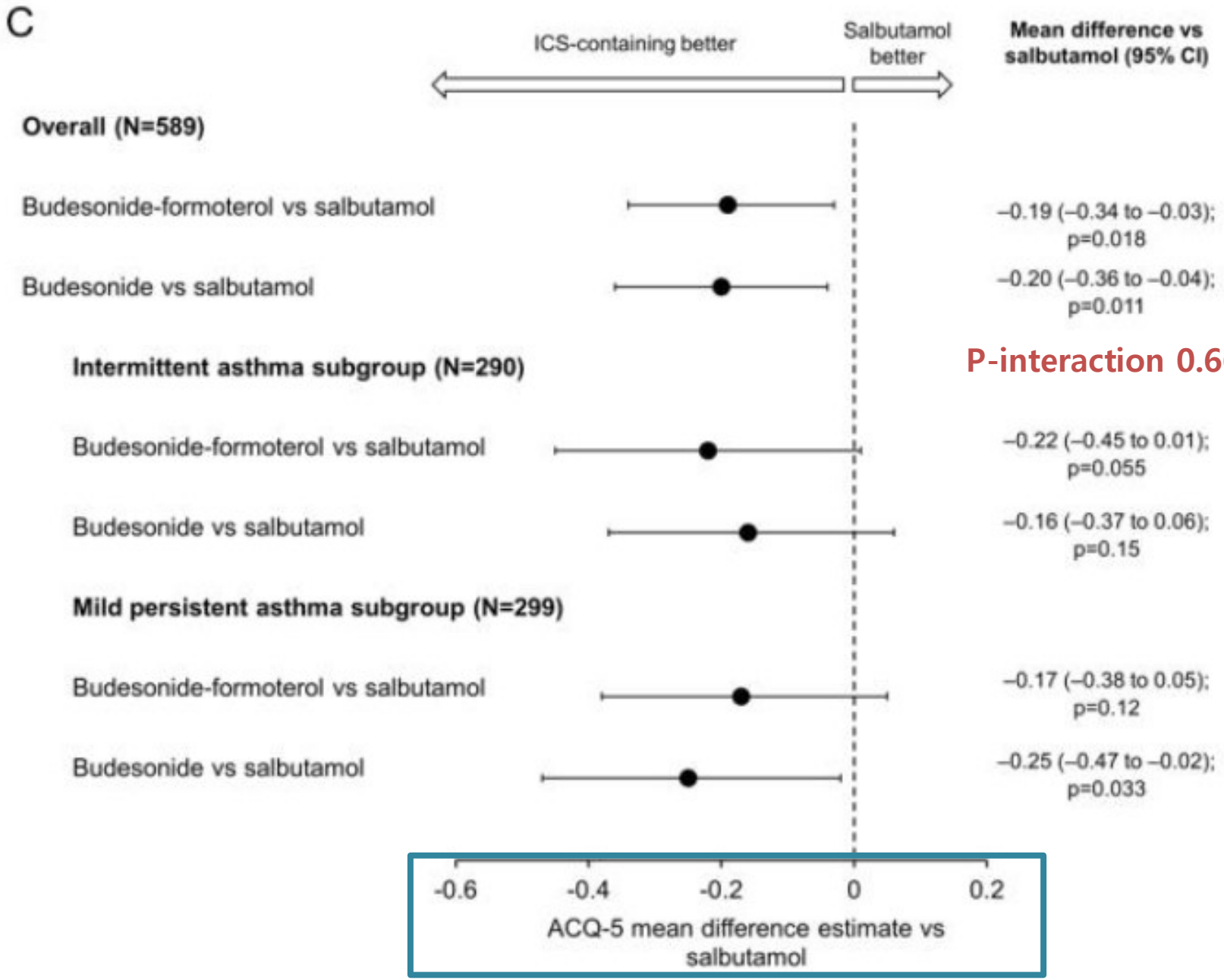
Papi A, Eur Respir J 2020.



Papi A, Eur Respir J 2020.



Papi A, Eur Respir J 2020.



Papi A, Eur Respir J 2020.

- PRACTICAL -

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

Jo Hardy, Christina Baggott*, James Fingleton, Helen K Reddel, Robert J Hancox, Matire Harwood, Andrew Corin, Jenny Sparks, Daniela Hall, Doñah Sabbagh, Saras Mane, Alexandra Vohlidkova, John Martindale, Mathew Williams, Philippa Shirtcliffe, Mark Holliday, Mark Weatherall, Richard Beasley, on behalf of the PRACTICAL study team†*

- **a 52-week, open-label**, parallel-group, multicentre, superiority, randomised controlled trial (N=**885**)
- adults aged 18–75 years with a self-reported doctor's diagnosis of asthma who were **using SABA for symptom relief** with or without maintenance **low to moderate doses of inhaled corticosteroids** in the previous 12 weeks (=**asthma patients in GINA Step 1 to 3**)
- (1:1) to either
  reliever therapy with budesonide 200 µg–formoterol 6 µg Turbuhaler (one inhalation as needed for relief of symptoms) or
  maintenance budesonide 200 µg Turbuhaler (one inhalation twice daily) plus **terbutaline 250 µg Turbuhaler** (two inhalations as needed)

- Primary outcome : **the number of severe exacerbations per patient per year**

Hardy J, Lancet 2019;394:919-28.

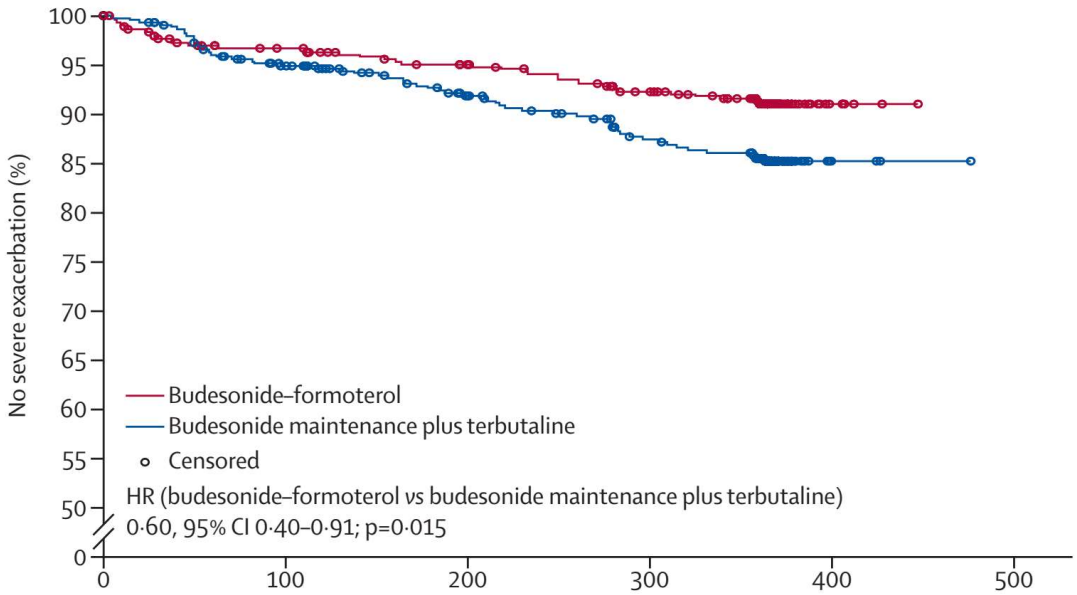
Baseline Characteristics

	Budesonide–formoterol as needed (n=437)	Budesonide maintenance plus terbutaline as needed (n=448)
Age (years)	43·3 (15·2)	42·8 (16·7)
BMI (kg/m^2)	29·4 (7·1)	28·0 (5·8)
Sex		
Female	244 (56%)	241 (54%)
Male	193 (44%)	207 (46%)
Ethnic origin		
Asian	29 (7%)	34 (8%)
European	342 (78%)	357 (80%)
Māori	41 (10%)	31 (7%)
Pacific	20 (5%)	16 (4%)
Other	5 (1%)	10 (2%)
Smoking status		
Current	39 (9%)	24 (5%)
Ex-smoker	123 (28%)	112 (25%)
Never	275 (63%)	312 (70%)
Pack-years (among ever smokers)	4·5 (4·7)	4·6 (4·7)
Age at diagnosis (years)	19·5 (17·7)	18·8 (18·1)
Patient-reported use of inhaled corticosteroids in the 12 weeks before enrolment	305 (70%)	316 (71%)
Patient-reported adherence to inhaled corticosteroids in the 4 weeks before enrolment (percentage of prescribed dose)	54·8% (37·0; n=304)	58·6% (47·3; n=315)
Patient-reported use of inhaled corticosteroids ever	390 (89%)	381 (85%)
Patient-reported SABA use in 4 weeks before enrolment (occasions per week)		
Mean (SD)	4·3 (6·0)	4·9 (7·5)
Median (IQR)	2·0 (1·0–5·5)	2·3 (1·0–6·0)
Range	0–70	0–84
Hospital admissions for asthma during lifetime (number per patient)	0·7 (5·1)	0·5 (2·1)
Severe exacerbation in the previous 12 months		
0	384 (88%)	396 (88%)
1	45 (10%)	41 (9%)
2	5 (1%)	7 (2%)
3	3 (<1%)	3 (<1%)
4	0	1 (<1%)
Any	53 (12%)	52 (12%)
ACQ-5 score*	1·1 (0·8)	1·2 (0·8)
GINA symptom control		
Well controlled	101 (23%)	103 (23%)
Partly controlled	209 (48%)	226 (51%)
Uncontrolled	127 (29%)	119 (27%)
On-treatment FEV_1 (percentage of predicted value†)	87·8% (16·4)	87·4% (16·3)
FENO (parts per billion)	26·0 (15·0–51·0)	30·0 (18·0–62·5)
Blood eosinophil count (×10^9 per L)	0·3 (0·2)	0·3 (0·2)

Hardy J, Lancet 2019;394:919-28.

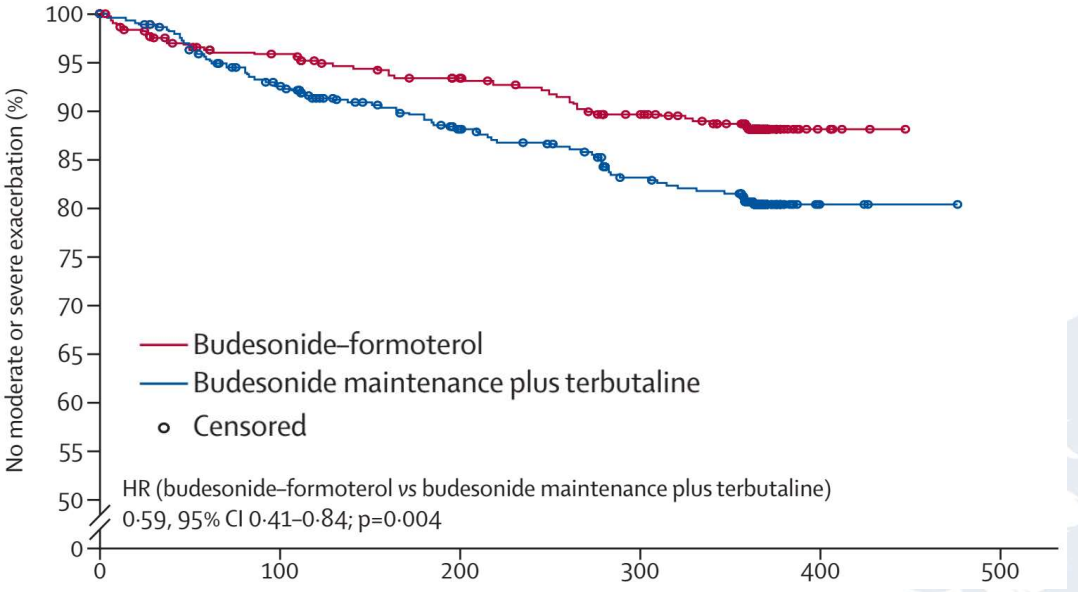
Time to First Severe AE

HR (budesonide–formoterol vs budesonide maintenance plus terbutaline)
0·60, 95% CI 0·40–0·91; p=0·015



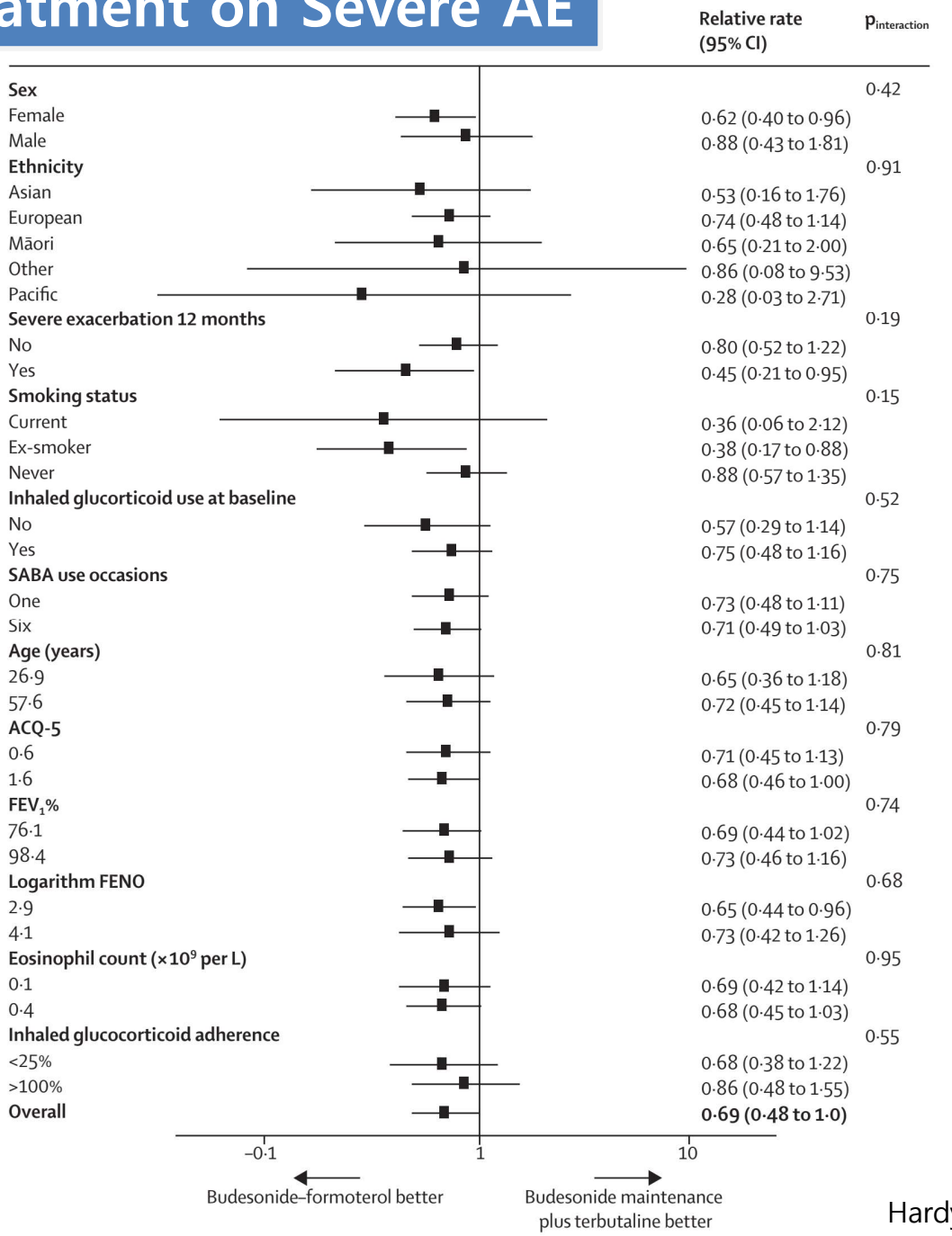
Time to First Moderate or Severe AE

HR (budesonide–formoterol vs budesonide maintenance plus terbutaline)
0·59, 95% CI 0·41–0·84; p=0·004



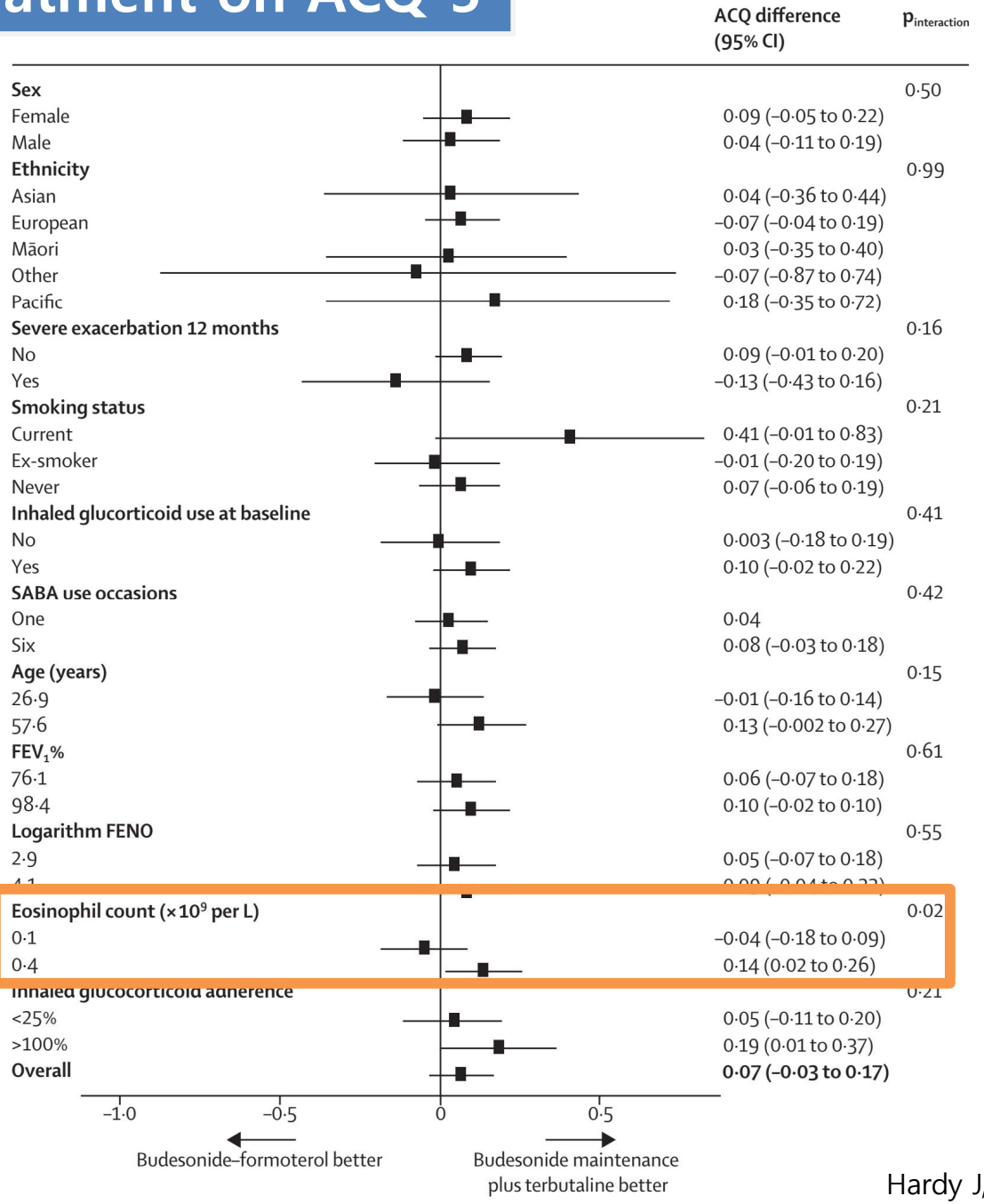
Hardy J, Lancet 2019;394:919-28.

Effect of Treatment on Severe AE



Hardy J, Lancet 2019;394:919-28.

Effect of Treatment on ACQ-5



Hardy J, Lancet 2019;394:919-28.

Medication Outcomes in Electronic Monitoring Subgroups

	Budesonide–formoterol as needed (n=55)	Budesonide maintenance plus terbutaline as needed (n=55)
Inhaled corticosteroid use		
Number of budesonide-containing actuations per day		
Mean (SD)	0·9 (0·7)	1·5 (0·4)
Median (IQR)	0·8 (0·4–1·3)	1·6 (1·2–1·8)
Range†	0·0–3·4	0·1–2·3
Daily budesonide dose (μg)		
Mean (SD)	176·0 (143·0)	302·5 (84·8)
Median (IQR)	164·3 (74·0–251·7)	328·3 (245·8–364)
Range‡	6·7–682·5	26·8–458·1
β_2-agonist use		
Number of β_2-agonist-containing actuations per day		
Mean (SD)	0·9 (0·7)	0·5 (0·6)
Median (IQR)	0·8 (0·4–1·3)	0·3 (0·1–0·6)
Range†	0·0–3·4	0·0–2·7

Hardy J, Lancet 2019;394:919-28.

Self-titration of inhaled corticosteroid and β_2-agonist in response to symptoms in mild asthma: a pre-specified analysis from the PRACTICAL randomised controlled trial

Christina Baggott [1,2], Jo Hardy [1,2], Jenny Sparks [1], Mark Holliday [1], Daniela Hall [1], Alexandra Vohlidkova [1], Robert J. Hancox [3], Mark Weatherall [4], James Fingleton [1] and Richard Beasley [1,2] on behalf of the PRACTICAL Study Team

- The aim of this pre-specified analysis of the PRACTICAL study was **to investigate the patterns of ICS and β2-agonist use,** in order to better understand the **31%** reduction in severe exacerbation risk observed in this study with as-needed budesonide–formoterol compared with maintenance budesonide plus as-needed terbutaline.

- Within the PRACTICAL study, a total of **890** patients were randomised at 15 sites. Among these, a subgroup of **110** participants at two sites had **electronic inhaler monitors** (**Adherium**, Auckland, New Zealand) incorporated onto all their study inhalers.

Baggott C, Eur Respir J 2020;56.

TABLE 1 Patient demographics

	Budesonide–formoterol as needed	Maintenance budesonide
Patients	55	55
Age years	48.1±14	51.4±14
Age at diagnosis years	23.1±20	23.3±19.2
Female	28 (51)	28 (51)
Ethnicity		
Asian	1 (2)	2 (4)
European	45 (82)	46 (84)
Māori	4 (7)	3 (6)
Other	1 (2)	2 (4)
Pacific	4 (7)	2 (4)
Smoking status		
Current smoker	1 (2)	2 (4)
Ex-smoker	13 (24)	20 (36)
Never-smoker	41 (75)	33 (60)
Pack-years (ever-smoker)	4.9±4.8	6.2±5.9
ICS use ever[#]	51 (93)	47 (86)
ICS use at randomisation[#]	36 (66)	37 (67)
Self-reported adherence to ICS % prescribed dose[¶]	50.4±34.8	60.1±33.8
Weekly SABA use occasions		
Mean	3.7±4.9	3.3±4.1
Median	2 (1–5)	2 (1– 5)
Severe exacerbation in year prior to randomisation	0.1±0.3	0.1±0.3
ACQ-5 score at randomisation[+]	1.1±0.9	0.9±0.7
Eosinophil count at randomisation $\times 10^9$ L^{-1}	0.3±0.2	0.2±0.2
FEV_1 % pred at randomisation[§]	87.4±15.3	88.4±14.4
F_{ENO} ppb	23 (14–63)	19 (12–31)

Baggott C, Eur Respir J 2020;56.

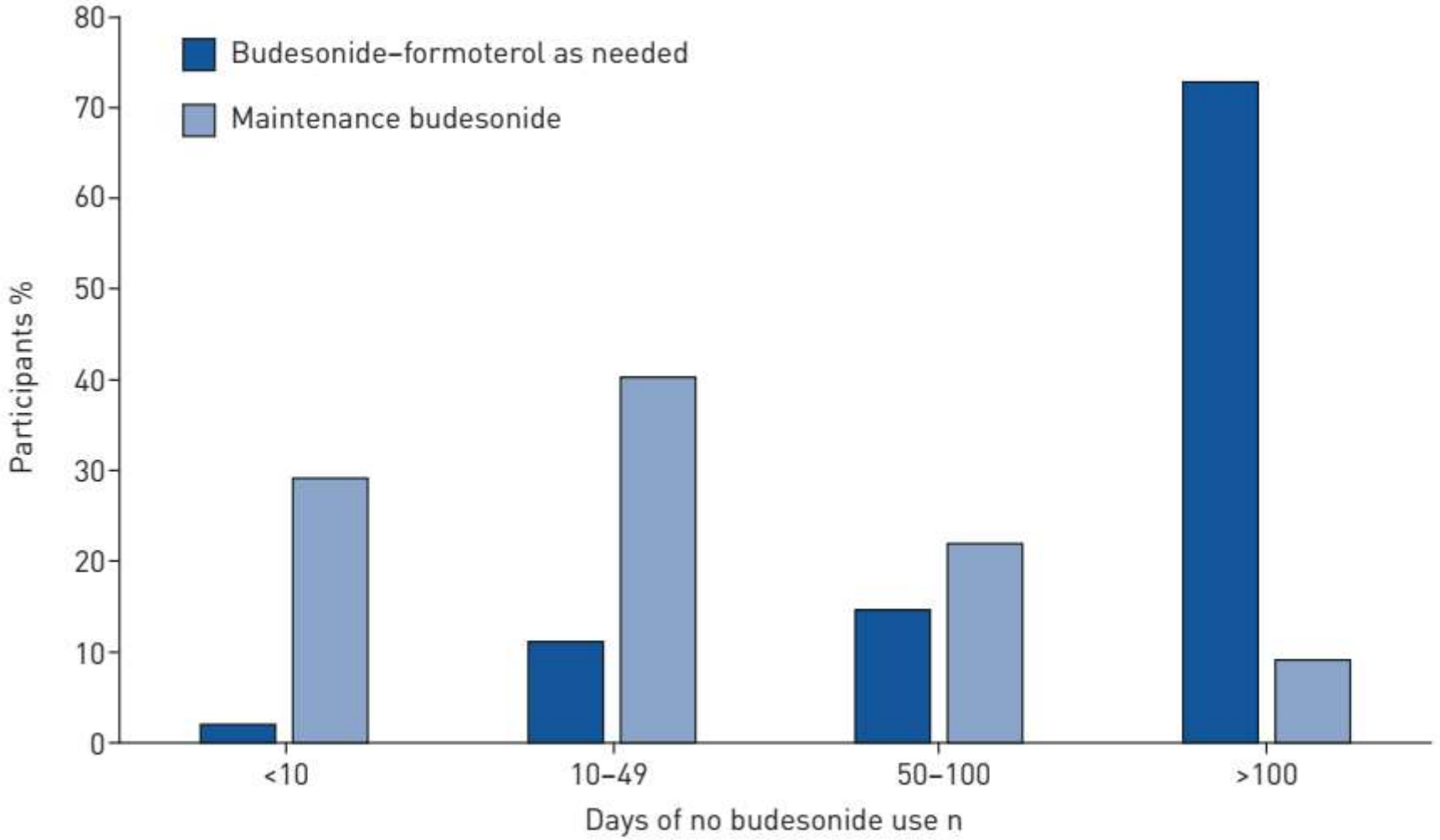


FIGURE 1 Total number of days of no budesonide use.

Baggott C, Eur Respir J 2020;56.

TABLE 4 Actuations per day before and after an asthma exacerbation

	Budesonide–formoterol as needed	Maintenance budesonide with terbutaline as needed
Patients	12	15
Budesonide use actuations		
Use in the 14 days before an exacerbation		
Mean±SD	2.1±1.7	1.7±0.3
Median (IQR)	1.5 (0.9–2.4)	1.7 (1.5–2.0)
Range (minimum–maximum)	0.4–6.0	1.1–2.2
Use in the 5 days before an exacerbation		
Mean±SD	2.4±1.6	2.0±0.4
Median (IQR)	1.7 (1.2–3.7)	2.0 (1.8–2.2)
Range (minimum–maximum)	0.8–5.2	1.2–2.4
Use in the 14 days after an exacerbation		
Mean±SD	1.2±0.8	1.7±0.9
Median (IQR)	1.0 (0.9–1.3)	1.9 (1.4–1.9)
Range (minimum–maximum)	0.0–3.4	0.4–4.1
Use in the 5 days after an exacerbation		
Mean±SD	1.5±0.7	1.9±1.2
Median (IQR)	1.5 (1.1–2.0)	1.8 (1.1–1.9)
Range (minimum–maximum)	0.0–2.4	0.4–5.4

Baggott C, Eur Respir J 2020;56.

TABLE 4 Actuations per day before and after an asthma exacerbation

	Budesonide–formoterol as needed	Maintenance budesonide with terbutaline as needed
Patients	12	15
β_2-agonist use actuations		
Use in the 14 days before an exacerbation		
Mean±SD	2.1±1.7	1.9±1.6
Median (IQR)	1.5 (0.9–2.4)	1.8 (0.7–2.9)
Range (minimum–maximum)	0.4–6.0	0.0–5.9
Use in the 5 days before an exacerbation		
Mean±SD	2.4±1.6	2.8±1.8
Median (IQR)	1.7 (1.2–3.7)	2.8 (1.6–3.8)
Range (minimum–maximum)	0.8–5.2	0.0–6.2
Use in the 14 days after an exacerbation		
Mean±SD	1.2±0.8	1.6±1.4
Median (IQR)	1.0 (0.9–1.3)	1.1 (0.4–2.8)
Range (minimum–maximum)	0.0–3.4	0.0–4.1
Use in the 5 days after an exacerbation		
Mean±SD	1.5±0.7	2.2±2.0
Median (IQR)	1.5 (1.1–2.0)	2.0 (0.5–3.3)
Range (minimum–maximum)	0.0–2.4	0.0–6.0

IQR: interquartile range.

Baggott C, Eur Respir J 2020;56.

TABLE 5 Patterns of β_2-agonist use

	Budesonide–formoterol as needed	Maintenance budesonide
Patients	55	55
β_2-agonist	Formoterol 6 µg	Terbutaline 250 µg
Daily β_2-agonist actuations#		
Mean±SD	0.9±0.7	0.5±0.6
Median (IQR)	0.8 (0.4–1.3)	0.3 (0.1–0.6)
Range (minimum–maximum)	0.0–3.4	0.0–2.7
Maximum actuations in a single day		
Mean±SD	6.0±2.9	8.0±10.9
Median (IQR)	5 (4–8)	6 (3–9.5)
Range (minimum–maximum)	1–13	0–80
Days ⩾2 actuations of formoterol or ⩾4 actuations of terbutaline		
Total days across all participants in the whole study n	4175	694
Mean±SD	75.9±72.8	12.6±23.5
Median (IQR)	48 (15–114)	3 (0–14.5)
Range (minimum–maximum)	0–329	0–139
Days ⩾4 actuations of formoterol or ⩾8 actuations of terbutaline		
Total days across all participants in the whole study n	675	94
Mean±SD	12.3±26.0	1.7±3.9
Median (IQR)	4 (1–10)	0 (0–2)
Range (minimum–maximum)	0–153	0–21

IQR: interquartile range. #: data previously reported in the main publication of the PRACTICAL study [21] but presented again here for illustrative purposes.

Baggott C, Eur Respir J 2020;56.

TABLE 6 PRACTICAL study outcomes by inclusion in the electronic monitoring substudy or not

	Budesonide–formoterol as needed		Maintenance budesonide		$p_{interaction}$ between inclusion in electronic monitoring substudy and outcome
	Electronic monitoring subgroup	Not in electronic monitoring subgroup	Electronic monitoring subgroup	Not in electronic monitoring subgroup	
Patients	55	382	55	393	
Severe exacerbations	8	40	11	57	
Rate of severe exacerbations per participant per year	0.15	0.11	0.21	0.17	0.92
F_{ENO} ppb end of study	23 (15–48)	26 (16–45) (n=346)	18 (13–32)	27 (16–41) (n=351)	0.89
ACQ-5# end of study	0.87±0.69	0.86±0.76 (n=348)	0.64±0.72	0.82±0.88 (n=351)	0.50

Data are presented as n, median (interquartile range) or mean±SD. F_{ENO}: exhaled nitric oxide fraction; ACQ-5: five-item Asthma Control Questionnaire. #: the ACQ-5 consists of five questions that assess asthma symptoms in the previous week, each of which is scored on a 7-point scale that ranges from 0 (no impairment) to 6 (maximum impairment), and averaged, in which a 0.5-unit change represents the minimal clinically important difference.

Baggott C, Eur Respir J 2020;56.

Contents

GINA 2020 & SABA Overuse

ICS-formoterol as-needed

Patient Preferences

Patient preferences for symptom-driven or regular preventer treatment in mild to moderate asthma: findings from the PRACTICAL study, a randomised clinical trial

Christina Baggott[1], Helen K. Reddel[2], Jo Hardy[1], Jenny Sparks[1], Mark Holliday[1], Andrew Corin[3], Barney Montgomery[4], Jim Reid[5], Davitt Sheahan[6], Robert J. Hancox[7,8], Mark Weatherall[9], Richard Beasley[1,10] and James Fingleton[1,10] on behalf of the PRACTICAL study team

- A subgroup of participants in the PRACTICAL study
- a survey on treatment preferences, satisfaction, beliefs and experience at their final study visit

- 306 (75%) out of 407 eligible participants completed the survey

Baggott C, Eur Respir J 2020;55.

TABLE 2 Participant characteristics by randomised treatment and regimen preference

	Randomised treatment			
	Budesonide–formoterol as needed		Maintenance budesonide plus as-needed terbutaline	
	Preferred treatment		Preferred treatment	
	Combined preventer and reliever inhaler taken as needed	Preventer inhaler taken twice a day with a reliever inhaler as needed	Combined preventer and reliever inhaler taken as needed	Preventer inhaler taken twice a day with a reliever inhaler as needed
Baseline characteristics				
Participants	135	15	63	93
Age years	45.6±14.5	44.1±23.2	41.8±16.1	47.7±17.1
Female	78 (58)	10 (67)	33 (52)	50 (54)
Age at diagnosis years				
Mean±SD	19.7±17.9	23.9±26.9	18.7±18.7	24.1±20.1
Median (IQR)	14 (4–31.5)	7 (4–42)	12 (5–25.5)	18 (6–40)
Self-reported frequency of SABA use in 4 weeks prior to randomisation				
Mean±SD	3.9±5.1	4.4±5.9	4.2±4.9	3.9±5.5
Median (IQR)	2 (1–5)	2 (0.5–5)	2 (1–5)	2 (1–4)
Self-reported ICS use in the 12 weeks prior to randomisation	93 (69)	11 (73)	39 (62)	72 (77)
Self-reported ICS adherence#	53.1 (36.7)	67.5 (33.3)	53.3 (38.2)	62.6 (33.7)
Self-reported ICS use ever	119 (88)	14 (93)	51 (81)	80 (86)
Participants with ⩾1 lifetime hospital admissions for asthma	20 (15)	2 (13)	8 (13)	10 (11)
Participants with ⩾1 severe exacerbation in the 12 months prior to study entry	12 (9)	1 (7)	7 (11)	8 (9)
Ever-smoker	42 (31)	4 (27)	20 (32)	26 (28)
Pack-years (among ever-smokers)	5.2±4.3	5.8±7.8	6.5±5.9	5.2±5.2
GINA level of asthma symptom control at randomisation				
Well controlled	28 (21)	7 (47)	12 (19)	29 (31)
Part controlled	68 (50)	4 (27)	35 (56)	44 (47)
Uncontrolled	39 (29)	4 (27)	16 (25)	20 (22)

Baggott C, Eur Respir J 2020;55.

TABLE 2 Participant characteristics by randomised treatment and regimen preference

	Randomised treatment			
	Budesonide–formoterol as needed		Maintenance budesonide plus as-needed terbutaline	
	Preferred treatment		Preferred treatment	
	Combined preventer and reliever inhaler taken as needed	Preventer inhaler taken twice a day with a reliever inhaler as needed	Combined preventer and reliever inhaler taken as needed	Preventer inhaler taken twice a day with a reliever inhaler as needed
Baseline characteristics				
Participants	135	15	63	93
End-of-study characteristics				
Final visit ACQ-5[¶]	0.84±0.64	1.00±0.76	0.82±0.84	0.62±0.73
Final visit F_{eNO} ppb	22 (15–38.5)	22 (15–47.5)	22 (13–36.5)	23 (15–40)
Final visit on treatment FEV_1 % predicted[+]	89.5±14.8	92.6±17.6	89.7±14.4	88.0±14.9
Participants who experienced ⩾1 exacerbation or severe exacerbation during the study	16 (12)	1 (7)	12 (19)	18 (19)
Early withdrawal	3 (2)	4 (27)	6 (10)	7(8)

Data are presented as n, mean±SD, n (%) or median (interquartile range (IQR)), unless otherwise stated. SABA: short-acting β_2-agonist; ICS: inhaled corticosteroid; GINA: Global Initiative for Asthma; ACQ-5: five-item Asthma Control Questionnaire; F_{eNO}: exhaled nitric oxide fraction; FEV_1: forced expiratory volume in 1 s. [#]: patient-reported adherence to ICS in the 4 weeks prior to enrolment (% prescribed dose); [¶]: five questions that assess asthma symptoms in the previous week, each of which is scored on a seven-point scale that ranges from 0 (no impairment) to 6 (maximum impairment), and averaged, in which a 0.5-unit change represents the minimal clinically important difference; [+]: participants received no specific instruction to withhold use of their bronchodilator before measurement of FEV_1 [21].

Baggott C, Eur Respir J 2020;55.

TABLE 3 Regimen preference

	Subjects n	Preferred treatment		Preference for combined *versus* regular treatment OR (95% CI)	p-value
		Combined[#] preventer and reliever inhaler taken as needed	Preventer inhaler[¶] taken twice a day with a reliever inhaler[+] as needed		
Budesonide–formoterol	150	135 (90)	15 (10)		
Maintenance budesonide	156	63 (40)	93 (60)		
Total	306	198 (65)	108 (35)	13.3 (7.1–24.7)	<0.001
After adjustment for ICS use prior to randomisation				13.6 (7.3–25.5)	<0.001

Data are presented as n (%), unless otherwise stated. Descriptions given to participants prior to starting the survey were as follows (full details are given in the supplementary material). [#]: in the study, you may have been using Symbicort (red) as a combined preventer and reliever when you had asthma symptoms; [¶]: contains a corticosteroid to reduce inflammation. This type of inhaler is normally used regularly twice a day to prevent asthma symptoms and reduce the risk of flare-ups. In the study you may have been using Pulmicort (brown) inhaler twice a day as your preventer. Other preventer inhalers you may have taken before the study are Beclazone (brown) or Flixotide (orange); [+]: used when you are getting symptoms of asthma such as breathlessness, wheeze, tight-chested or cough. You may have been on a Ventolin or Respigen inhaler as your reliever before the study. In the study you would have used either Bricanyl (blue) or Symbicort (red) inhaler as your reliever inhaler.

- Most patients **preferred as-needed corticosteroid–formoterol** therapy if they had experienced it

Baggott C, Eur Respir J 2020;55.

ORIGINAL RESEARCH

What matters most to patients when choosing treatment for mild–moderate asthma? Results from a discrete choice experiment

Christina Baggott [1], Paul Hansen,[2] Robert J Hancox [3,4], Jo Katherine Hardy [1], Jenny Sparks [1], Mark Holliday [1], Mark Weatherall [5], Richard Beasley [1,6], Helen K Reddel [7], James Fingleton [1,6] on behalf of the PRACTICAL discrete choice experiment study team

- At their final **PRACTICAL** study visit, a subgroup of participants indicated their preferred treatment and completed a **discrete choice experiment (DCE)** using the Potentially All Pairwise RanKings of all possible Alternatives method and 1000minds software.

- Treatment attributes and their levels were selected from measurable study outcomes, and included:
  - **treatment regimen**
  - **shortness** of **breath**
  - **steroid dose**
  - **likelihood** of asthma **flare-up**

Baggott C, Thorax 2020;75:842-8.

Table 1 Attributes and levels

Attribute	Participant's stated ranking of levels, in as-needed-preference DCE	Participant's stated ranking of levels, in maintenance-preference DCE
Type of asthma treatment	A preventer inhaler taken twice a day every day, with a reliever inhaler taken as needed	A combined preventer and reliever inhaler, taken as needed
	A combined preventer and reliever inhaler, taken as needed	A preventer inhaler taken twice a day every day, with a reliever inhaler taken as needed
Attribute	**Inherent ranking of levels, in as-needed-preference DCE**	**Inherent ranking of levels, in maintenance-preference DCE**
The dose of your steroid inhaler	Medium	Medium
	Low	Low
	Very low	Very low
Likelihood of a flare-up in your asthma severe enough that you need to see a doctor	20 out of 100 people in a year (20%)	20 out of 100 people in a year (20%)
	10 out of 100 people in a year (10%)	10 out of 100 people in a year (10%)
	5 out of 100 people in a year (5%)	5 out of 100 people in a year (5%)
In an average week you will be short of breath because of asthma	A moderate amount or more	A moderate amount or more
	A little	A little
	Not at all	Not at all

Each attribute's levels are presented within the table in increasing order of preference (ie, the lowest ranked level is listed first).
DCE, discrete choice experiment.

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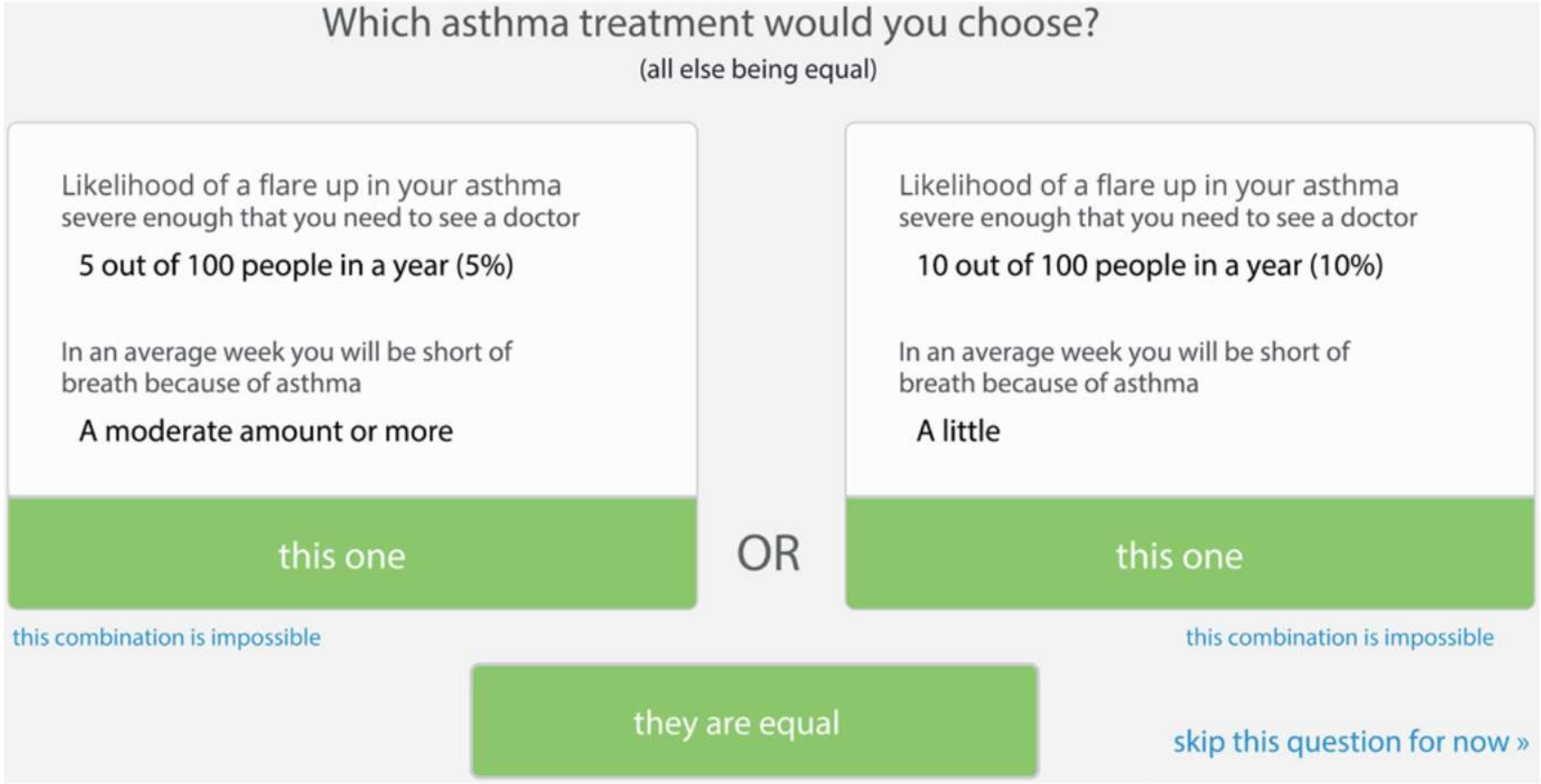
Example of a tradeoff question from the 1000minds software



Baggott C, Thorax 2020;75:842-8.

Table 3 Mean preference weights and ranking for the attributes and levels in each discrete choice experiment (DCE)

Attribute	Level	Mean weight (SD)	Attribute rank
As-needed-preference DCE, n=185			
Treatment regimen	A preventer inhaler taken two times a day every day, with a reliever inhaler taken as needed	0	
	A combined preventer and reliever inhaler, taken as needed	**0.24** (0.11)	3
Dose of steroid	Medium	0	
	Low	0.10 (0.08)	
	Very low	**0.17** (0.11)	4
Likelihood of asthma flare-up severe enough to need to see your doctor	20 out of 100 people in a year (20%)	0	
	10 out of 100 people in a year (10%)	0.14 (0.07)	
	5 out of 100 people in a year (5%)	**0.25** (0.09)	2
Shortness of breath in an average week	A moderate amount or more	0	
	A little	0.20 (0.09)	
	Not at all	**0.33** (0.12)	1

Baggott C, Thorax 2020;75:842-8.

Table 3 Mean preference weights and ranking for the attributes and levels in each discrete choice experiment (DCE)

Attribute	Level	Mean weight (SD)	Attribute rank
Maintenance-preference DCE, n=103			
Treatment regimen	A combined preventer and reliever inhaler, taken as needed	0	
	A preventer inhaler taken twice a day every day, with a reliever inhaler taken as needed	**0.18** (0.12)	4
Dose of steroid	Medium	0	
	Low	0.11 (0.08)	
	Very low	**0.19** (0.10)	3
Likelihood of asthma flare-up severe enough to need to see your doctor	20 out of 100 people in a year (20%)	0	
	10 out of 100 people in a year (10%)	0.16 (0.08)	
	5 out of 100 people in a year (5%)	**0.30** (0.12)	2
Shortness of breath in an average week	A moderate amount or more	0	
	A little	0.19 (0.09)	
	Not at all	**0.34** (0.12)	1

Baggott C, Thorax 2020;75:842-8.

Summary of Clinical Trials