Current Situation of Severe Asthma in Korea

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Contents

DEFINITIONS: UNCONTROLLED, DIFFICULT-TO-TREAT, AND SEVERE ASTHMA

Understanding the definitions of difficult-to-treat and severe asthma starts with the concept of uncontrolled asthma.

Uncontrolled asthma includes one or both of the following:

- Poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma)
- Frequent exacerbations (≥2/year) requiring OCS, or serious exacerbations (≥1/year) requiring hospitalization.

Difficult-to-treat asthma is asthma that is uncontrolled despite prescribing of medium- or high-dose ICS with a second controller (usually a LABA) or with maintenance OCS, or that requires high-dose treatment to maintain good symptom control and reduce the risk of exacerbations.[175] It does not mean a 'difficult patient'. In many cases, asthma may appear to be difficult to treat because of modifiable factors such as incorrect inhaler technique, poor adherence, smoking or comorbidities, or because the diagnosis is incorrect.

Severe asthma is a subset of difficult-to-treat asthma (Box 8-1). It means asthma that is uncontrolled despite adherence with maximal optimized high-dose ICS-LABA treatment and management of contributory factors, or that worsens when high-dose treatment is decreased.[175] At present, therefore, 'severe asthma' is a retrospective label. It is sometimes called 'severe refractory asthma',[175] because it is defined by being relatively refractory to high-dose inhaled therapy. However, with the advent of biologic therapies, the word 'refractory' is no longer appropriate.

Asthma is not classified as severe if it markedly improves when contributory factors such as inhaler technique and adherence are addressed.[175]

중증 천식의 정의 (GINA)

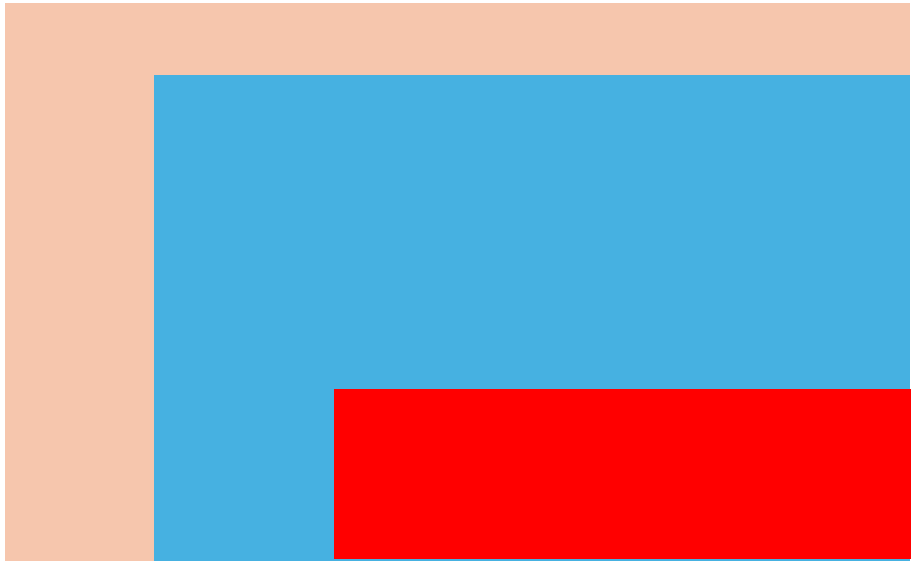
- 조절되지 않는 천식(uncontrolled asthma): 아래의 두가지 항목 중 하나
  - 조절되지 않는 천식 증상 (빈번한 천식 증상 또는 증상 완화제의 사용, 천식으로 인한 활동 제한 또는 야간수면 방해)
  - 년 2회 이상의 경구용 스테로이드가 필요한 천식 악화 또는 년 1회 이상의 입원이 필요한 중증 천식 악화

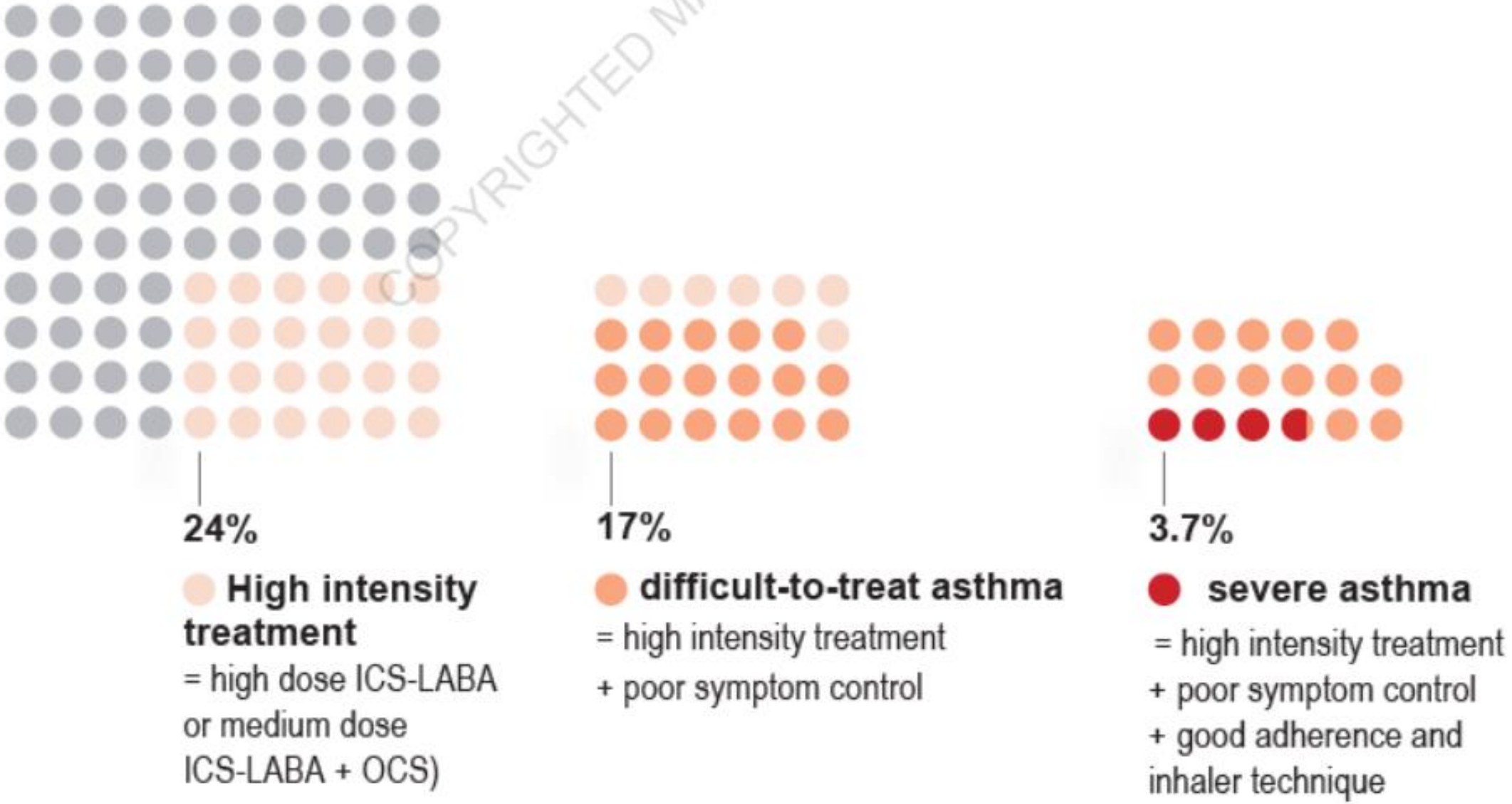
표 3-8. 천식조절평가(GINA 2021)

천식증상조절			천식 증상 조절 정도		
지난 4주 간의 증상			조절 천식	일부 조절 천식	조절되지 않는 천식
- 일주일간 3회 이상의 주간천식 증상	있음 □	없음 □			
- 천식으로 인한 야간수면방해	있음 □	없음 □	4항목 모두 없음	1-2 항목 있음	3-4 항목 있음
- 일주일에 3회 이상 SABA 증상완화제 사용	있음 □	없음 □			
- 천식으로 인한 활동 제한	있음 □	없음 □			

- 조절되지 않는 천식(uncontrolled asthma): 아래의 두가지 항목 중 하나
- 난치성 천식(difficult-to-treat asthma): 아래 중 하나의 경우
  - 중간 또는 고용량의 흡입스테로이드와 다른 조절제 또는 유지 용량의 경구용 스테로이드를 사용하는데도 불구하고 여전히 조절되지 않는 경우
  - 증상 조절 및 악화 위험 감소를 위하여 고용량 흡입스테로이드 이상의 치료가 필요한 경우

- 조절되지 않는 천식(uncontrolled asthma): 아래의 두가지 항목 중 하나
- 난치성 천식(difficult-to-treat asthma): 아래 중 하나의 경우
- 중증 천식(severe asthma): 난치성 천식 중 아래의 경우에 모두 해당하는 경우
  - 치료에 대한 순응도가 좋으며 천식증상의 악화에 기여하는 요인을 모두 치료하고 있음.
  - 고용량 흡입스테로이드-지속형 베타작용제 복합제를 최적화하여 사용하고 있음에도 천식 증상이 조절되지 않거나 치료 용량을 줄이면 악화되는 경우.





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Allergy, Asthma & Immunology Research AAIR

Brief Communication

Specialist Perception of Severe Asthma in Korea: A Questionnaire Survey

Mi-Ae Kim [1], Heung-Woo Park [2*], Byung-Keun Kim [3], So-Young Park [4], Ga-Young Ban [5], Ji-Hyang Lee [6], Jin An [6], Ji-Su Shim [7], Youngsoo Lee [8], Ha-Kyeong Won [9], Hwa Young Lee [10], Kyoung-Hee Sohn [11], Sung-Yoon Kang [12], So Young Park [13], Hyun Lee [14], Min-Hye Kim [7], Jae-Woo Kwon [15], Sun-Young Yoon [16], Jae-Hyun Lee [17], Chin Kook Rhee [10], Ji-Yong Moon [14], Taehoon Lee [18], So Ri Kim [19], Jong Sook Park [20], Sang-Heon Kim [14], Jae Won Jeong [21], Sang-Hoon Kim [13], Young-Il Koh [22], Yeon-Mok Oh [23], An-Soo Jang [20], Kwang Ha Yoo [4], You Sook Cho [6]
on behalf of the Korean Academy of Asthma, Allergy, and Clinical Immunology (KAACI), the Working Group on Severe Asthma

Received: Sep 25, 2020

Table 1. Defining severe asthma

Questions	Value
Q1. Do you agree that the criteria listed below appropriately define severe asthma?	
A fatal exacerbation or at least one episode of mechanical ventilation required because of asthma during the last year	4.69 ± 0.58
At least 2 hospitalizations or ER visits/year	4.31 ± 0.82
Uncontrolled asthma symptoms (at least 3 of daytime symptoms, night awakening, activity limitations, and/or reliever use)	4.30 ± 0.72
At least 2 OCS bursts/year	4.06 ± 0.76
Decreased lung function (FEV1 < 80%)	3.56 ± 0.90
Q2. How many OCS bursts/year appropriately define severe asthma?	
3–4	36 (66.7)
1–2	8 (14.8)
5–6	6 (11.1)
Not a useful criterion	4 (7.5)
More than 7	0 (0)
Q3. What duration of OCS maintenance/year appropriately defines severe asthma?	
6 mon	21 (38.9)
3 mon	16 (29.7)
Not a useful criterion	11 (20.4)
9 mon	4 (7.4)
12 mon	1 (1.9)
No answer	1 (1.9)

Table 2. Considerations prior to diagnosis of severe asthma

Questions	Value
Q4. Do you agree that the tests listed below are appropriate during differential diagnosis of severe asthma?	
Chest CT	4.32 ± 1.07
Anti-*Aspergillus* IgE level	3.18 ± 0.96
Serum ANCA	3.06 ± 1.17
Laryngoscopy	2.98 ± 1.26
Bronchoscopy	2.43 ± 1.06
Q5. Do you agree that the risk factors listed below should be modified prior to diagnosis of severe asthma?	
Chronic rhinosinusitis	4.31 ± 0.87
Obesity	3.91 ± 1.01
Depression/anxiety disorder	3.74 ± 0.89
Gastro-esophageal reflux disease	3.64 ± 1.02
Obstructive sleep apnea	3.47 ± 0.99
Q6. Do you agree that the risk factors listed below should be modified prior to diagnosis of severe asthma?	
Poor inhaler compliance	4.82 ± 0.51
Lack of inhaler skill	4.64 ± 0.68
Stoppage of asthma medication because of side-effects	4.61 ± 0.68
Smoking	4.31 ± 0.93
Exposure to sensitized allergens or nonspecific stimuli that worsen the respiratory symptoms	4.08 ± 0.96

Contents

Review

trd
Tuberculosis & Respiratory Diseases

International Severe Asthma Registry (ISAR): 2017–2024 Status and Progress Update

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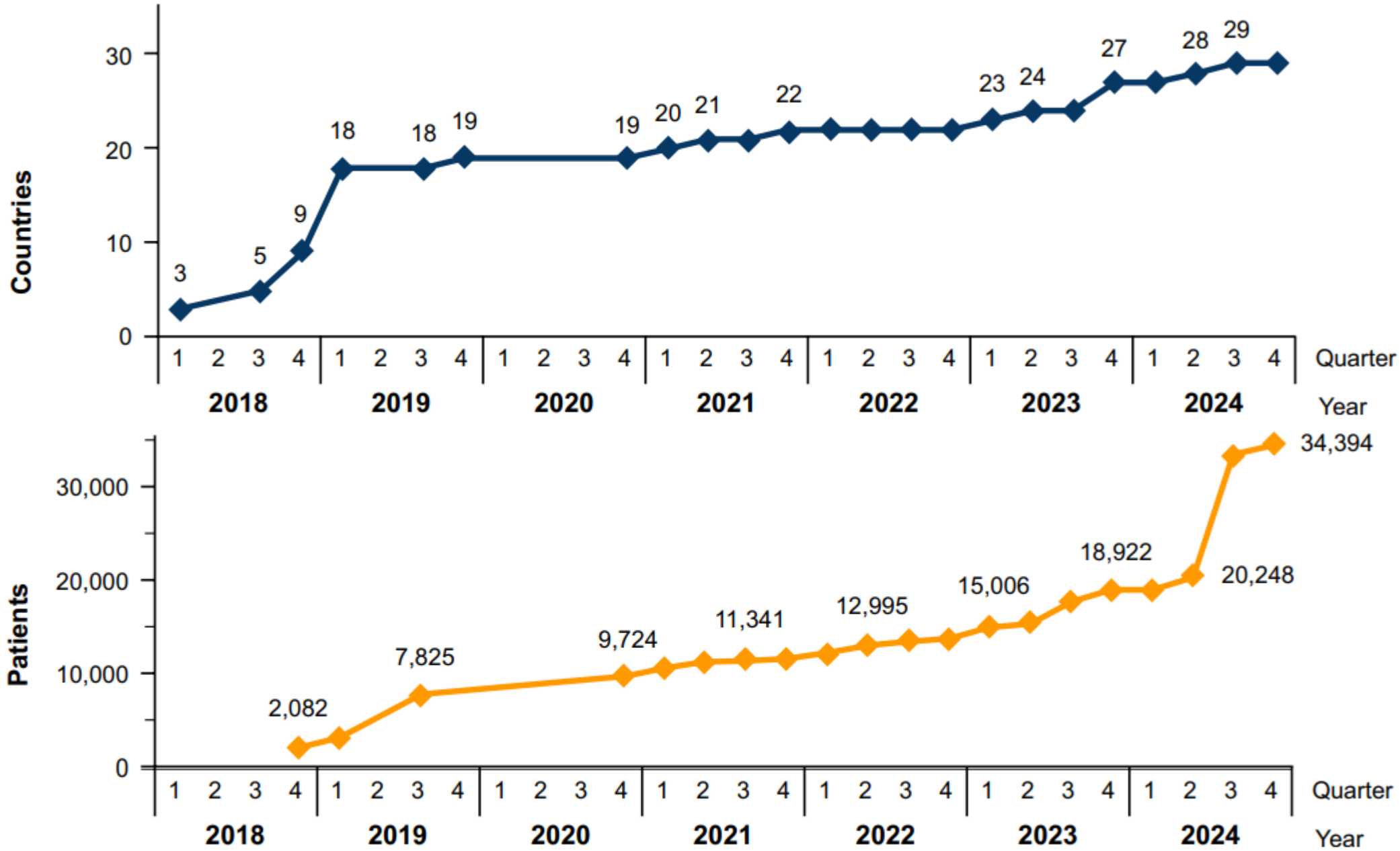
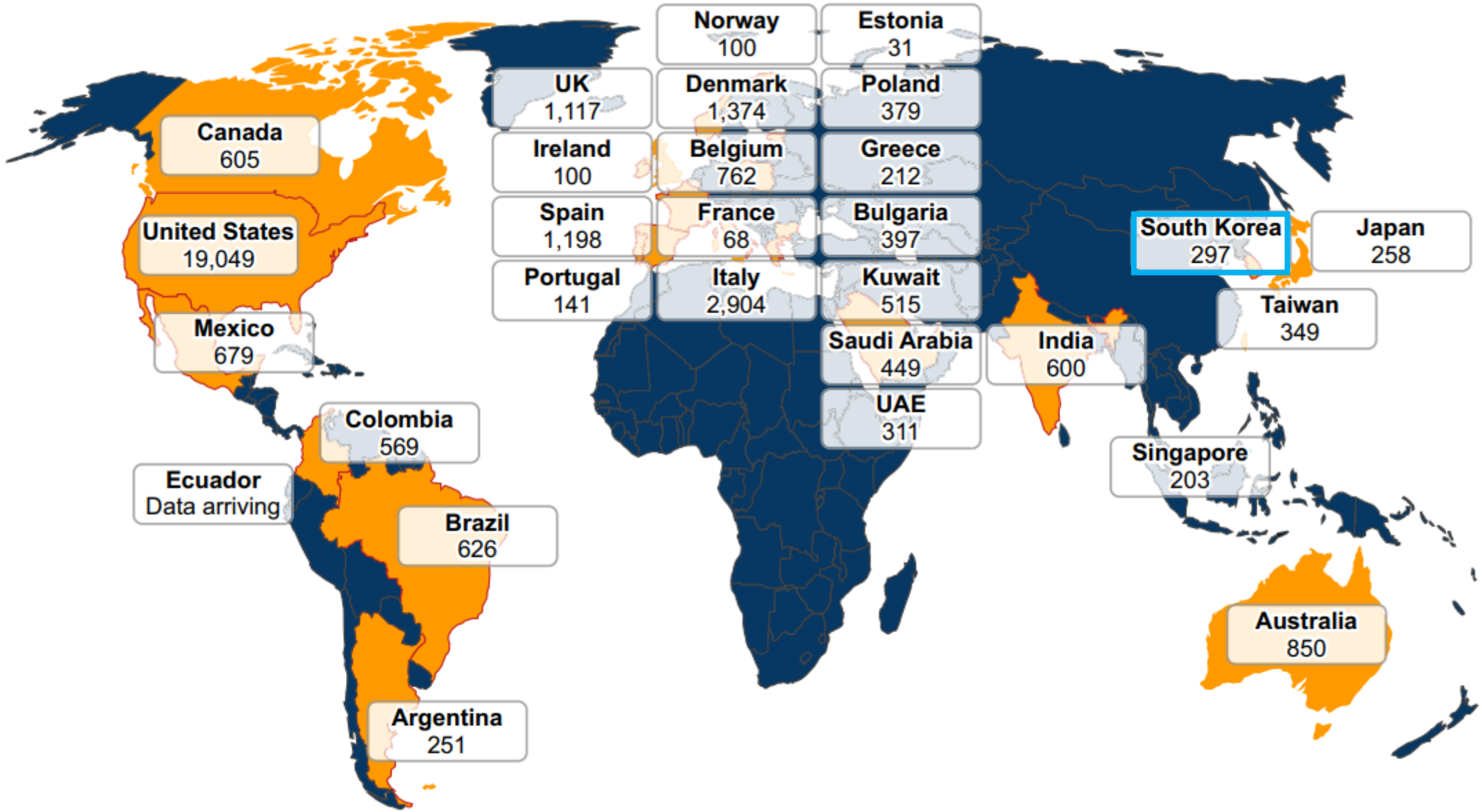
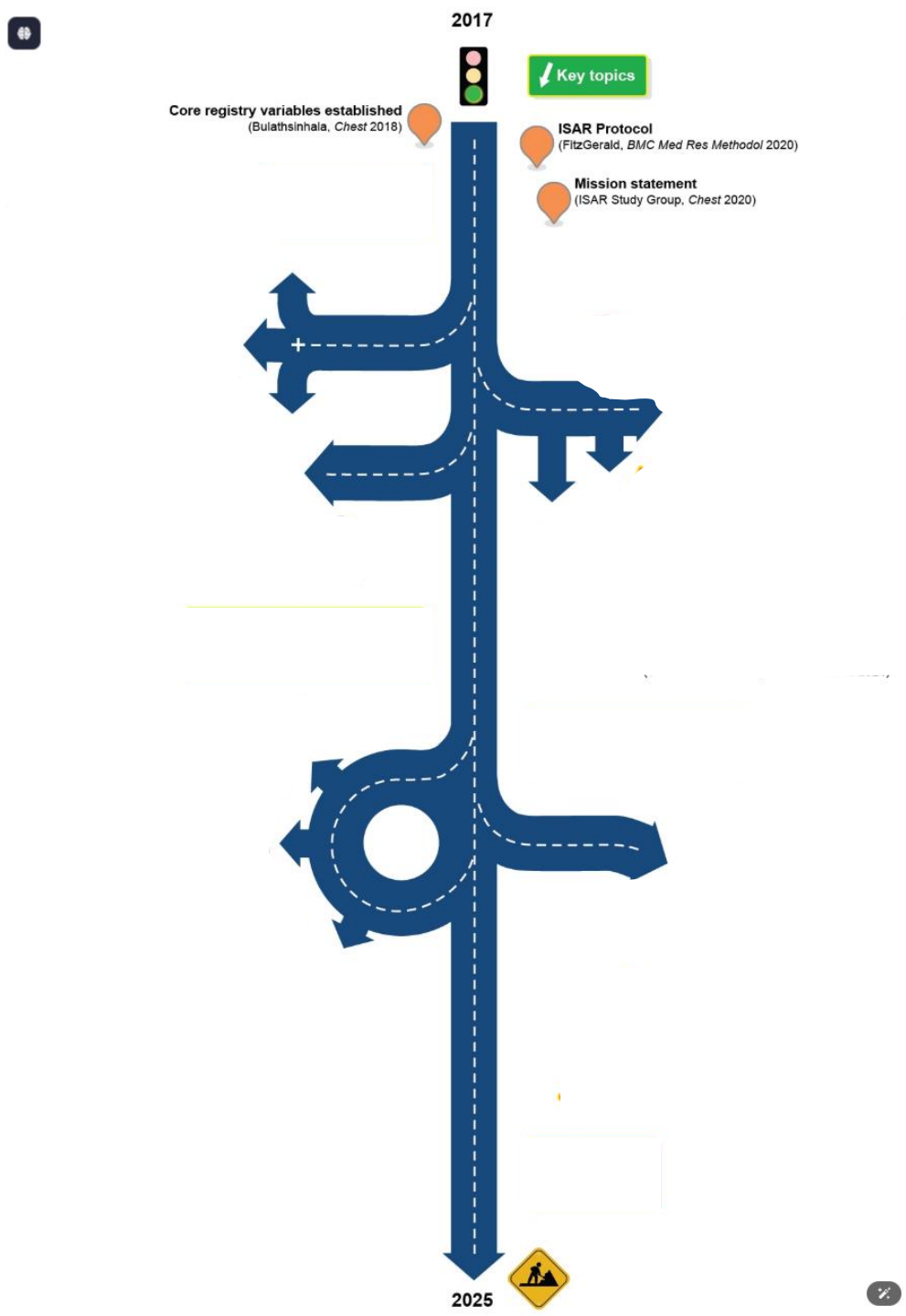

Countries
30
20
10
0
3
5
9
18
18
19
19
20
21
22
23
24
27
28
29
1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4
Quarter
2018
2019
2020
2021
2022
2023
2024
Year
Patients
30,000
20,000
10,000
0
2,082
7,825
9,724
11,341
12,995
15,006
18,922
20,248
34,394
1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4
Quarter
2018
2019
2020
2021
2022
2023
2024
Year



29 countries | **34,394** patients | **>125,000** patient years

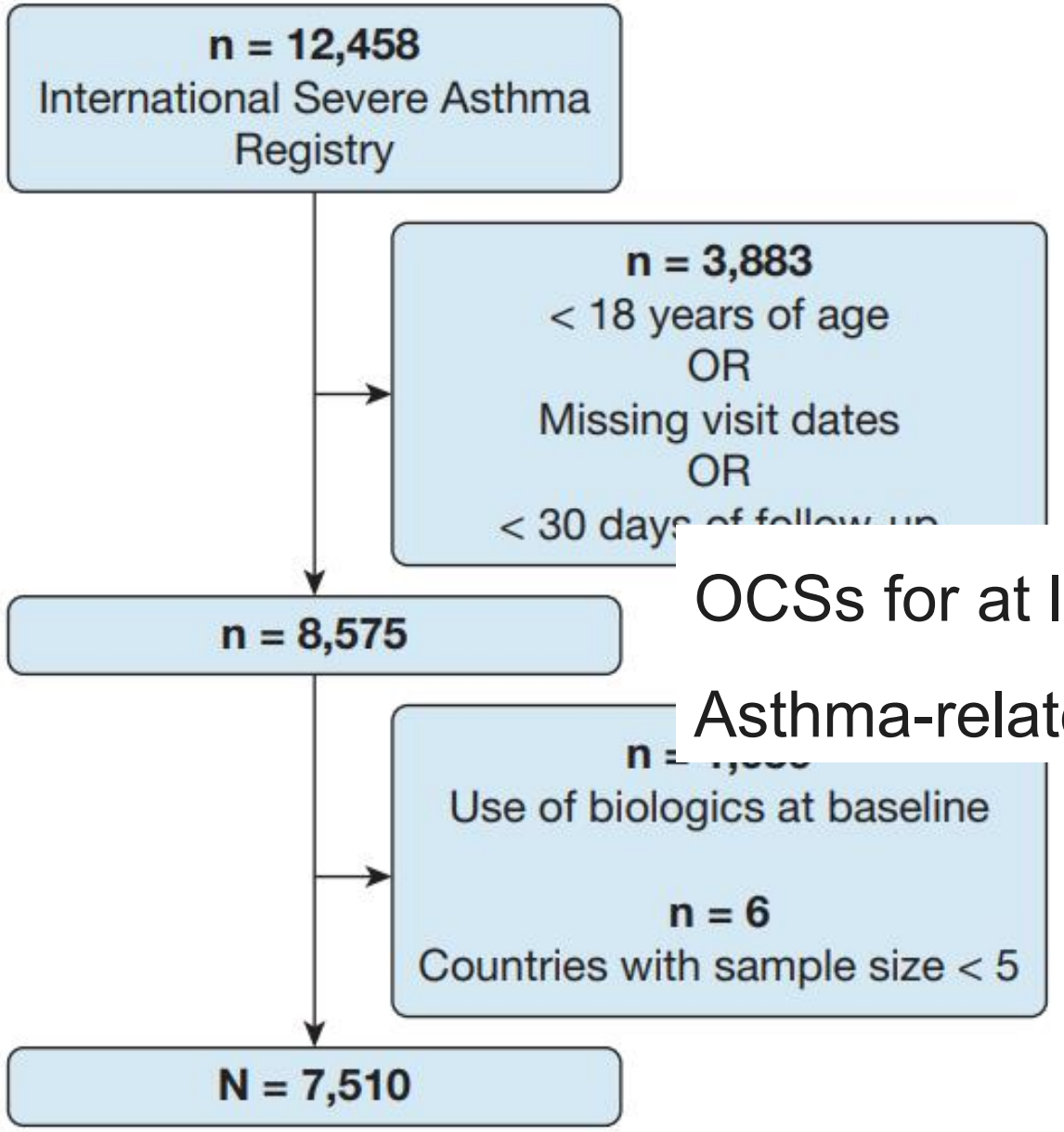

2017
Key topics
Core registry variables established
(Bulathsinhala, *Chest* 2018)
ISAR Protocol
(FitzGerald, *BMC Med Res Methodol* 2020)
Mission statement
(ISAR Study Group, *Chest* 2020)
2025

CHEST

International Variation in Severe Exacerbation Rates in Patients With Severe Asthma

Tae Yoon Lee, MSc; David Price, FRCGP; Chandra Prakash Yadav, PhD; Rupsa Roy, MSc; Laura Huey Mien Lim, MSc; Eileen Wang, MD, PhD; Michael E. Wechsler, MD; David J. Jackson, MBBS, MRCP(UK), PhD; John Busby, PhD; Liam G. Heaney, MD; Paul E. Pfeffer, MRCP(UK), PhD; Bassam Mahboub, MD; Diahn-Warng Perng (Steve), MD, PhD; Borja G. Cosio, MD, PhD; Luis Perez-de-Llano, MD, PhD; Riyad Al-Lehebi, MD; Désirée Larenas-Linnemann, MD; Mona Al-Ahmad, MD; Chin Kook Rhee, MD, PhD; Takashi Iwanaga, MD, PhD; Enrico Heffler, MD, PhD; Giorgio Walter Canonica, MD; Richard Costello, MD; Nikolaos G. Papadopoulos, MD, PhD; Andriana I. Papaioannou, MD, PhD; Celeste M. Porsbjerg, MD, PhD; Carlos A. Torres-Duque, MD; George C. Christoff, MD, PhD, MPH; Todor A. Popov, MD, PhD; Mark Hew, MBBS, PhD; Matthew Peters, MD, PhD; Peter G. Gibson, MBBS; Jorge Maspero, PhD; Celine Bergeron, MD; Saraid Cerda, MD; Elvia Angelica Contreras-Contreras, MD; Wenjia Chen, PhD; and Mohsen Sadatsafavi, MD, PhD

CHEST 2024; 166(1):28-38



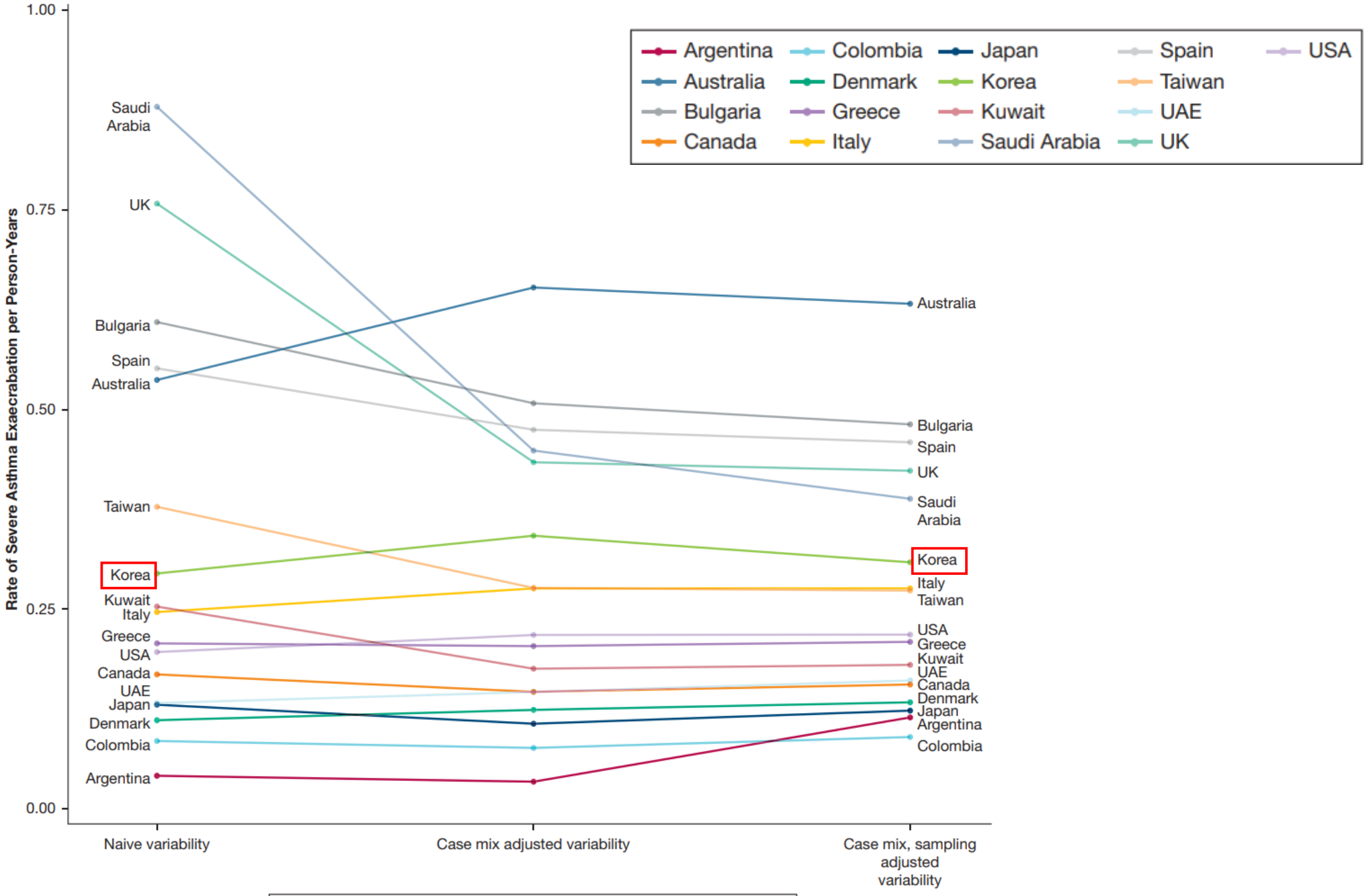
OCSs for at least 3 days

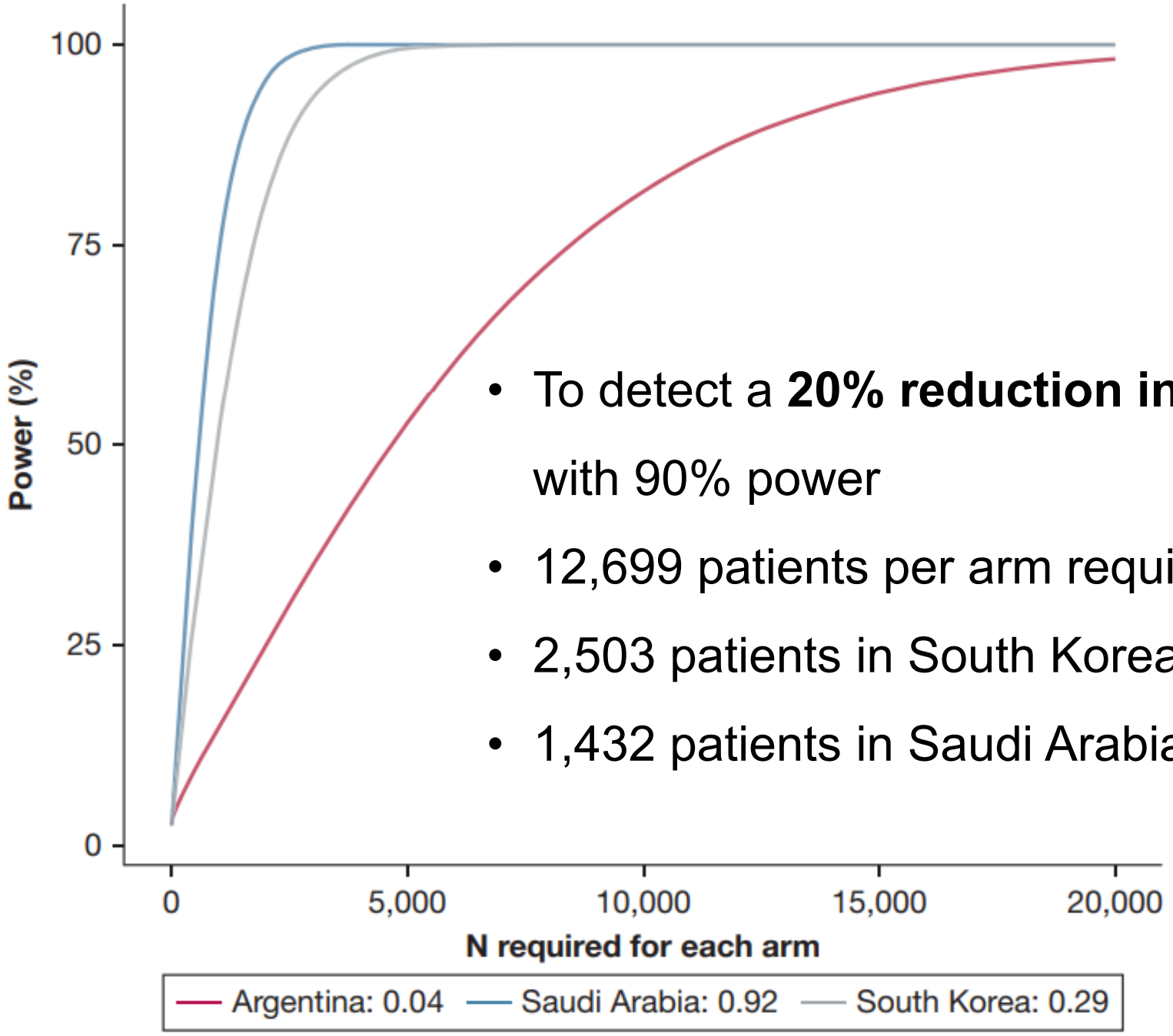
Asthma-related hospitalization or ED visit

Figure 1 – *Flow diagram of the International Severe Asthma Registry cohort.*

TABLE 1] Heterogeneity in Patient Characteristics (Average Values) and Severe Exacerbation Rates Between Countries

Country	Sample Size	Severe Exacerbations During Follow-Up	Average Follow-Up, y	Severe Exacerbation Rate (Per y)	Baseline Severe Exacerbation Rate (Per y)	Use of Biologics During Follow-Up, %
Argentina	26	1	0.98	0.04	0.81	0
Australia	394	191	0.94	0.52	0.46	0
Bulgaria	180	74	0.76	0.54	1.08	1
Canada	149	25	1.00	0.17	0.81	7
Colombia	204	17	0.99	0.08	0.82	7
Denmark	229	25	0.99	0.11	0.03	9
Greece	94	18	0.92	0.21	0.67	9
Italy	800	186	0.95	0.25	0.29	13
Japan	107	14	1.00	0.13	0.89	14
South Korea	38	11	0.99	0.29	0.11	32
Kuwait	163	41	1.00	0.25	2.33	25
Saudi Arabia	45	33	0.80	0.92	4.60	11
Spain	209	108	0.94	0.55	1.00	14
Taiwan	141	48	0.93	0.37	0.99	29
United Arab Emirates	117	13	0.88	0.13	0.79	4
United Kingdom	434	328	1.00	0.76	4.86	22
United States	4,180	806	0.98	0.20	0.19	5
Total	7,510	1,939	0.97	0.27	0.67	8


Argentina
Australia
Bulgaria
Canada
Colombia
Denmark
Greece
Italy
Japan
Korea
Kuwait
Saudi Arabia
Spain
Taiwan
UAE
UK
USA
Rate of Severe Asthma Exacerbation per Person-Years
1.00
0.75
0.50
0.25
0.00
Naive variability
Case mix adjusted variability
Case mix, sampling adjusted variability
Saudi Arabia
UK
Bulgaria
Spain
Australia
Taiwan
Korea
Kuwait
Italy
Greece
USA
Canada
UAE
Japan
Denmark
Colombia
Argentina



- To detect a **20% reduction in severe exacerbation rate** with 90% power
- 12,699 patients per arm required in Argentina
- 2,503 patients in South Korea
- 1,432 patients in Saudi Arabia

Journal of Asthma and Allergy Dovepress

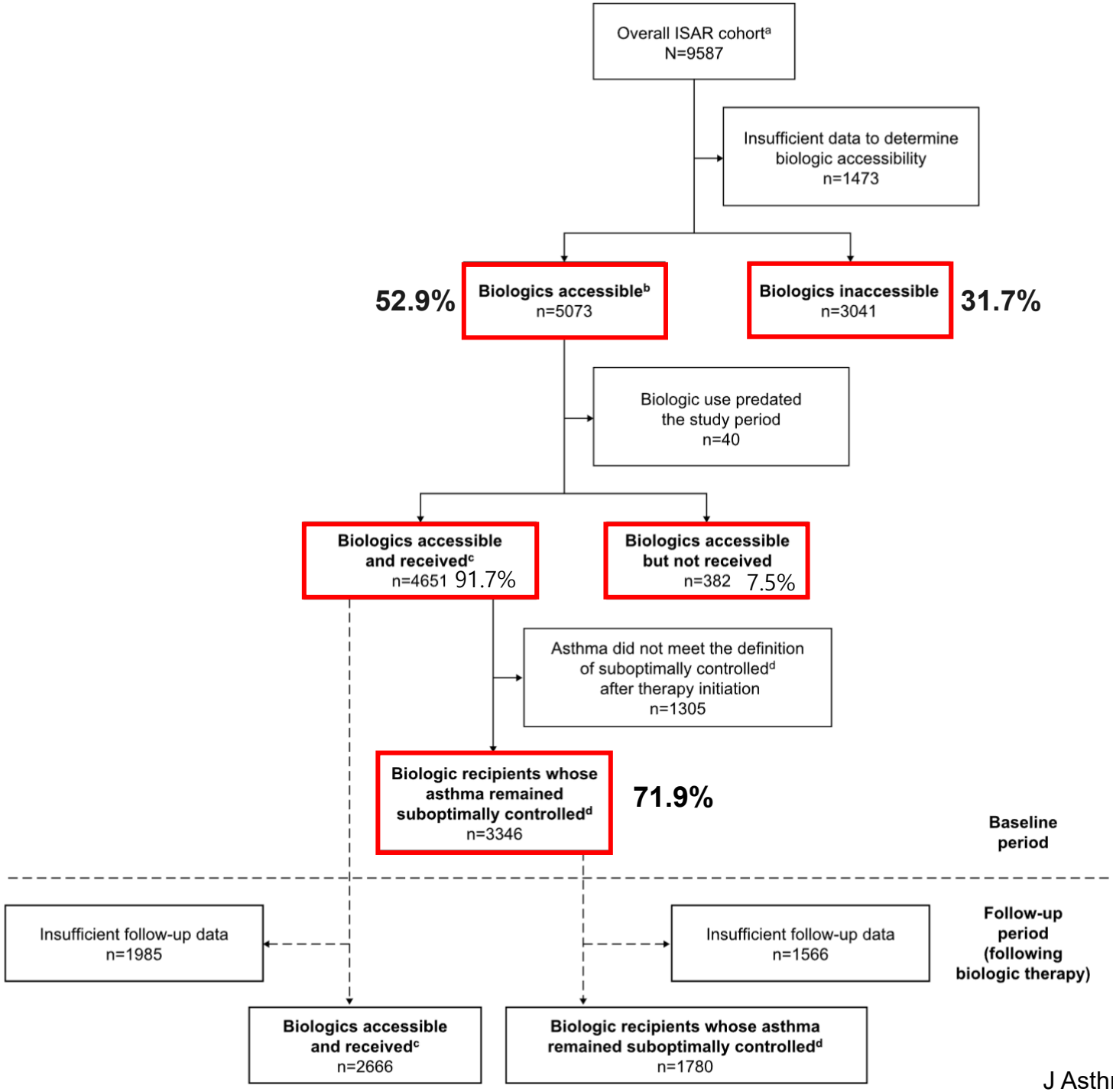
Open Access Full Text Article

ORIGINAL RESEARCH

Disease Burden and Access to Biologic Therapy in Patients with Severe Asthma, 2017–2022: An Analysis of the International Severe Asthma Registry

Tham T Le[1], David B Price[2–4], Clement Erhard[5], Bill Cook[6], Anna Quinton[7], Rohit Katial[8], George C Christoff[9], Luis Perez-de-Llano[10], Alan Altraja[11,12], Celine Bergeron[13], Arnaud Bourdin[14], Mariko Siyue Koh[15,16], Lauri Lehtimäki[17,18], Bassam Mahboub[19], Nikolaos G Papadopoulos[20,21], Paul Pfeffer[22,23], Chin Kook Rhee[24], Victoria Carter[2,3], Neil Martin[25,26], Trung N Tran[1] On behalf of the EVEREST Study Working Group

J Asthma Allergy. 2024 Oct 25:17:1055-1069.



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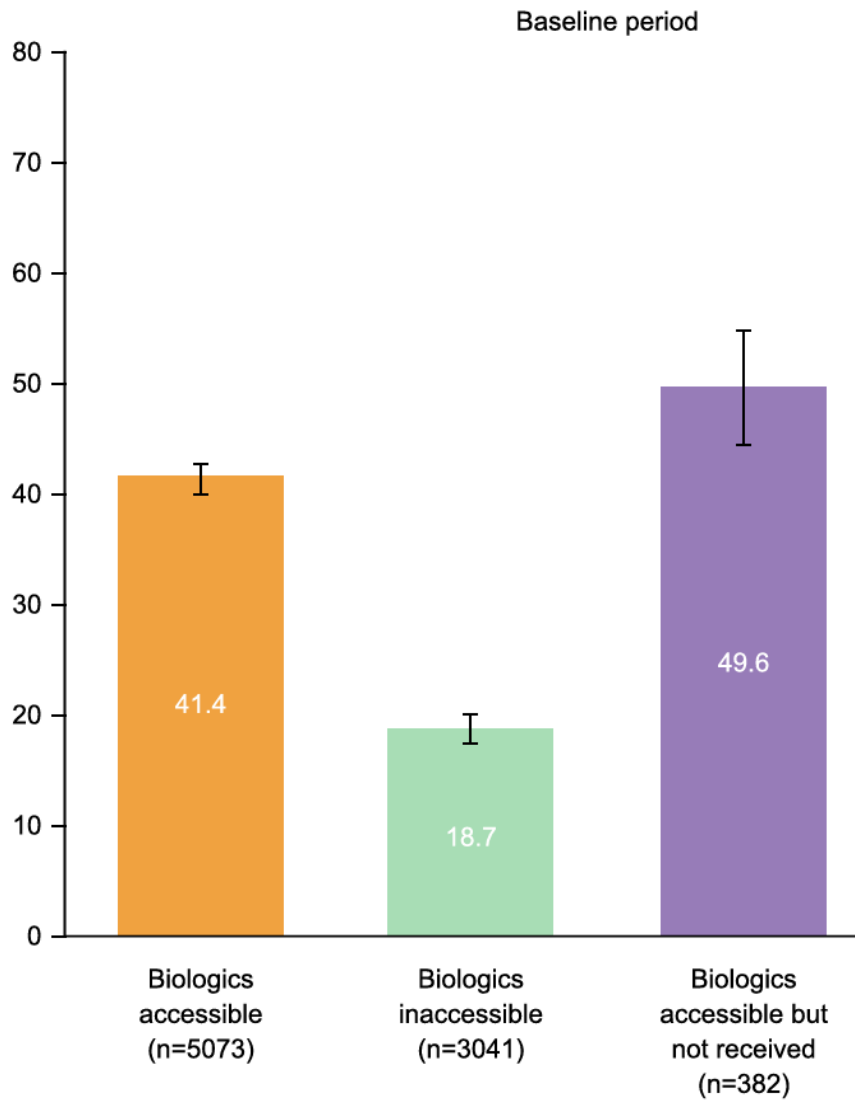
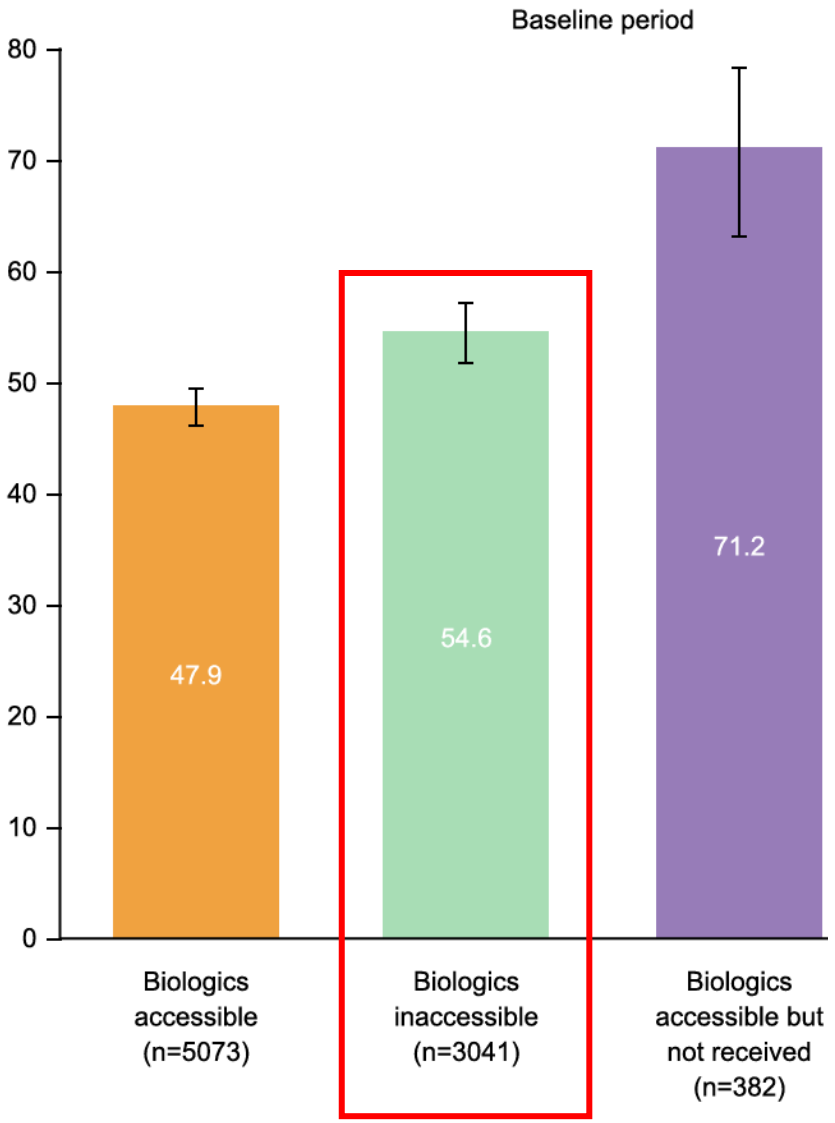
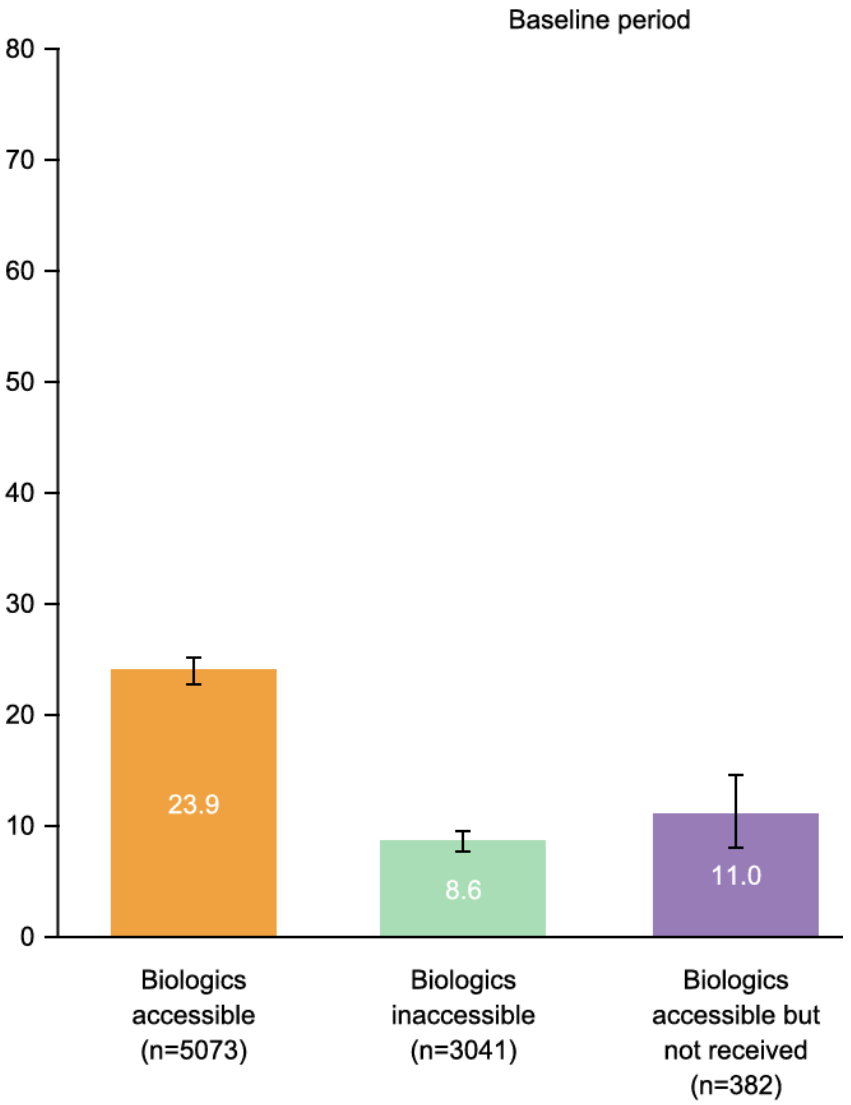


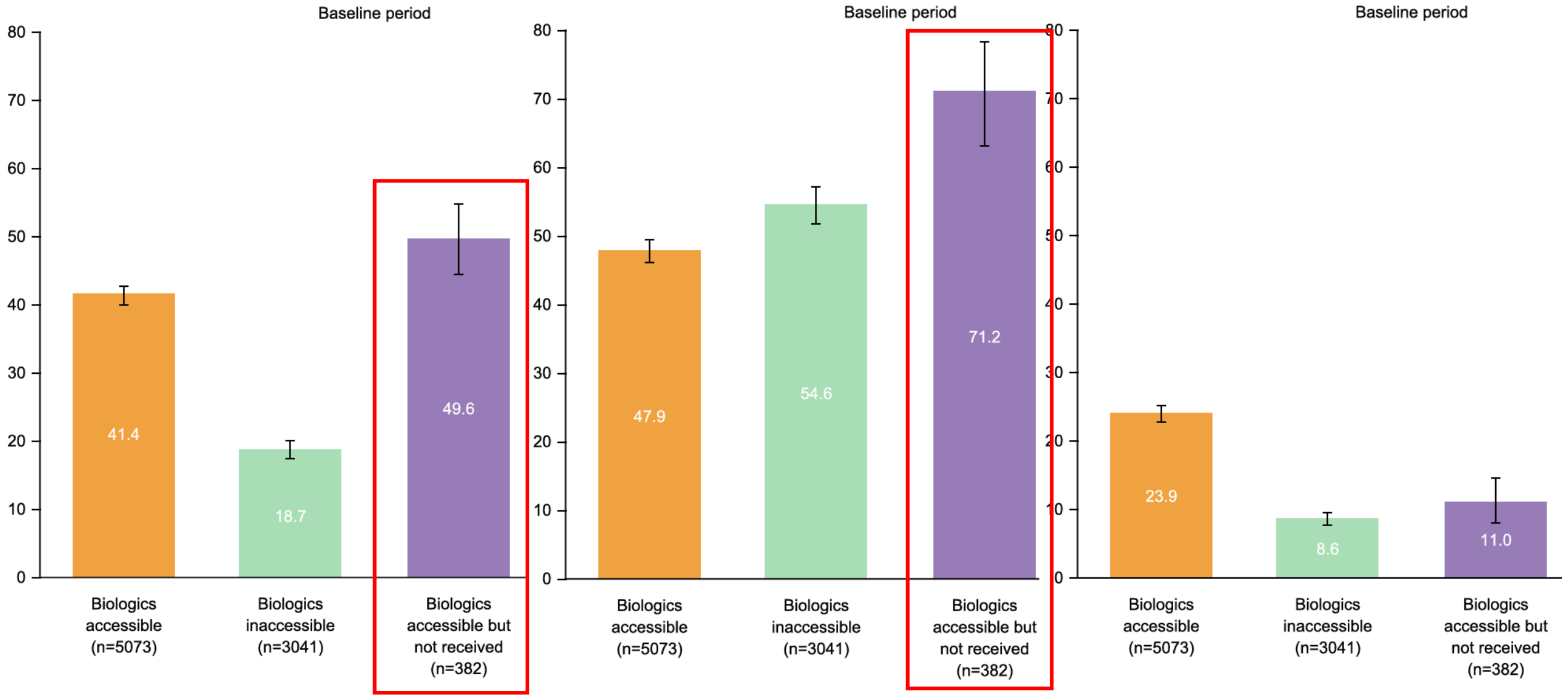
At least 2 exacerbation



Uncontrolled Asthma



LTOCS



At least 2 exacerbation

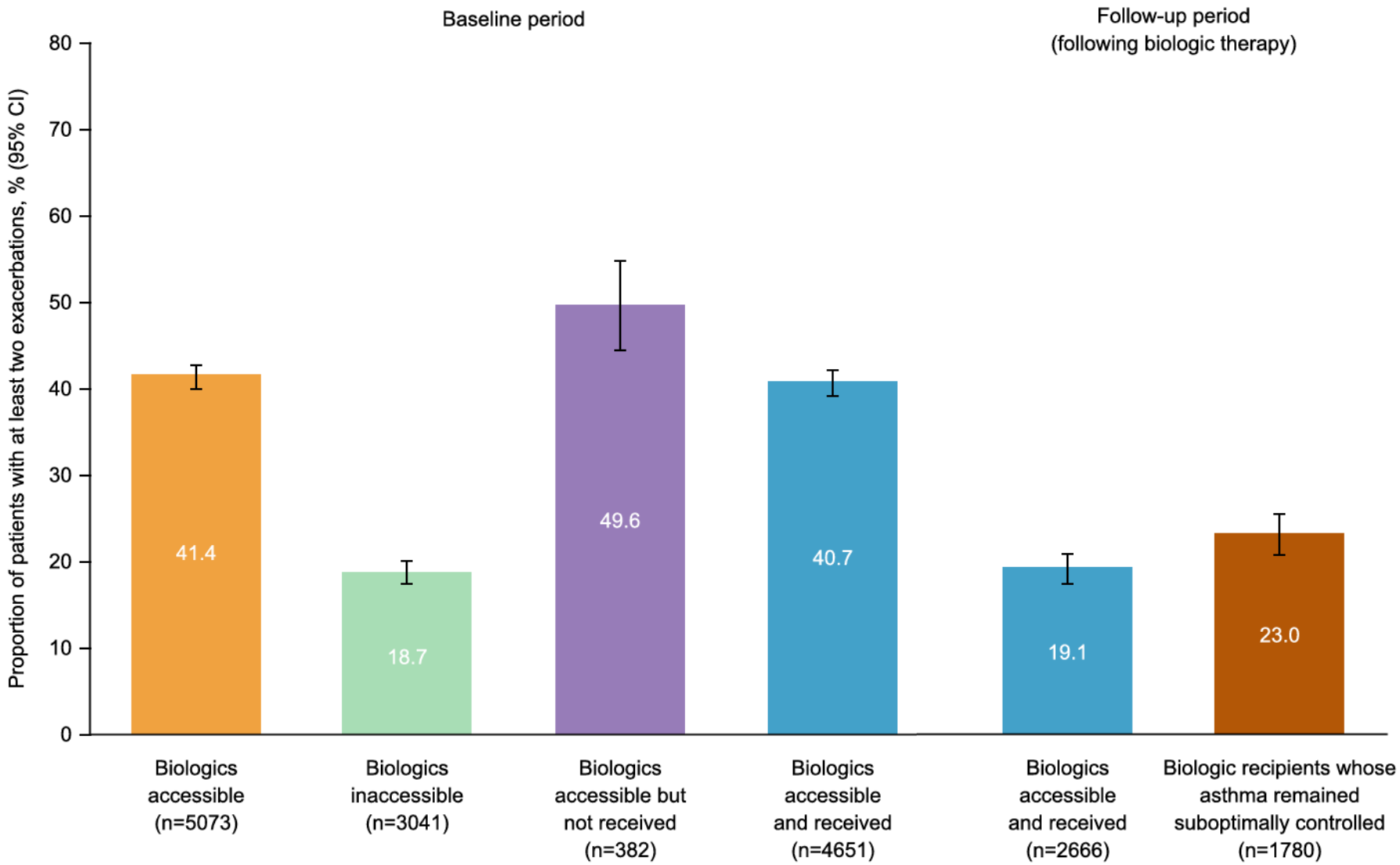
Uncontrolled Asthma

LTOCS

Table 2 Asthma-Related Healthcare Resource Utilization During the Baseline Period and Follow-Up Period (Following Biologic Therapy)

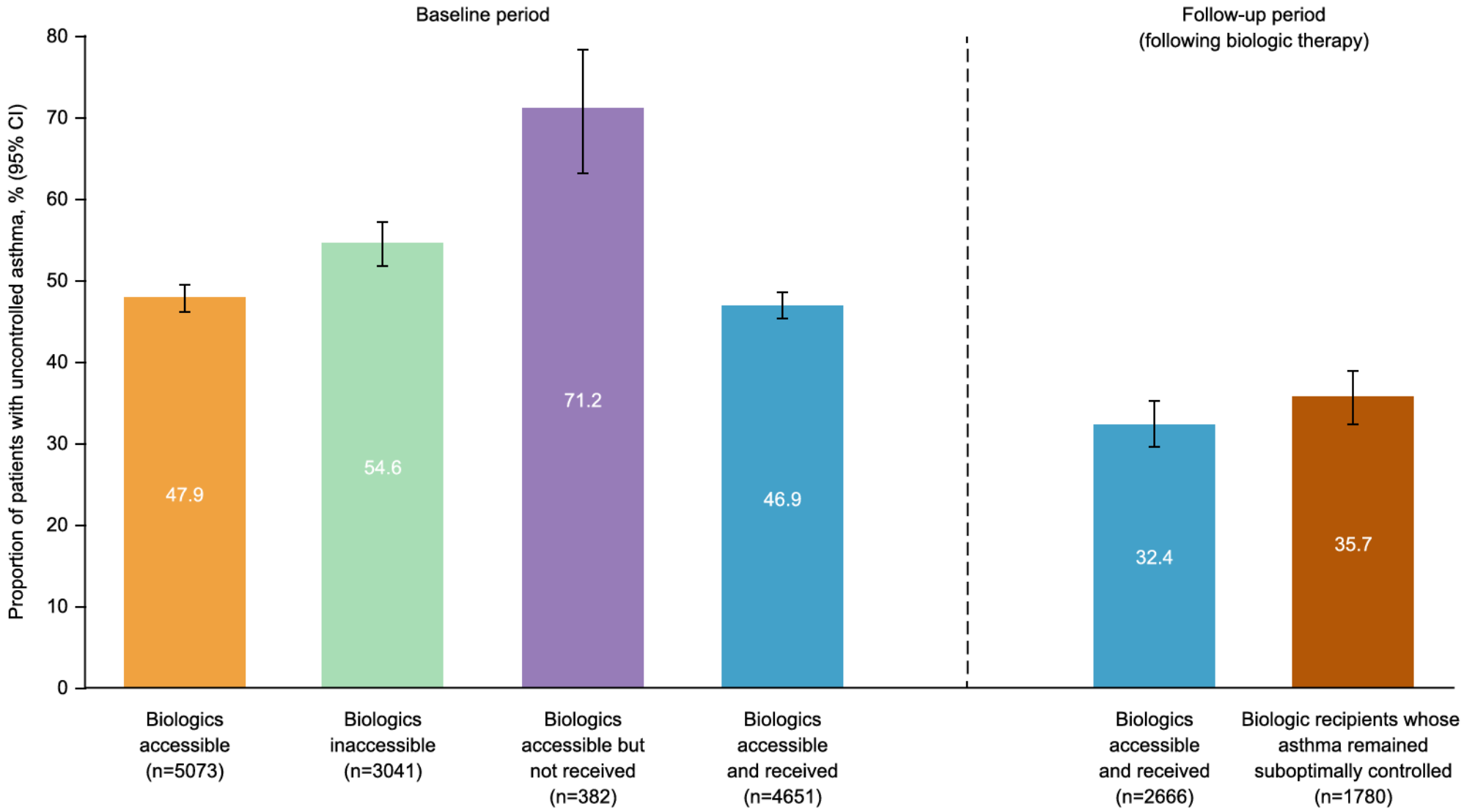
	Baseline Period				Follow-up Period	
	Biologics Accessible (n=5073)	**Biologics Inaccessible (n=3041)**	**Biologics Accessible but Not Received (n=382)**	**Biologics Accessible and Received (n=4651)**	**Biologics Accessible and Received (n=2666)**	**Biologic Recipients Whose Asthma Remained Suboptimally Controlled (n=1780)**
Asthma exacerbations						
Mean (SD)	1.97 (3.16)	0.88 (1.75)	1.69 (1.71)	2.01 (3.27)	0.89 (1.89)	0.99 (1.88)
n (%) [95% CI]						
≥1	2799 (59.0) [57.6–60.4]	1237 (41.0) [39.3–42.8]	265 (69.9) [65.0–74.5]	2520 (58.3 [56.8–59.7]	701 (38.7) [36.5–41.0]	525 (42.2) [39.4–45.0]
≥2	1963 (41.4) [40.0–42.8]	565 (18.7) [17.4–20.2]	188 (49.6) [44.5–54.8]	1761 (40.7) [39.2–42.2]	345 (19.1) [17.3–20.9]	286 (23.0) [20.7, 25.4]
≥4	858 (18.1) [17.0–19.2]	166 (5.5) [4.7–6.4]	47 (12.4) [9.3–16.1]	811 (18.7) [17.6–19.9]	112 (6.2) [5.1–7.4]	92 (7.4) [6.0–9.0]
ER visits						
Mean (SD)	0.53 (2.18)	0.23 (1.19)	0.52 (1.77)	0.54 (2.22)	0.13 (0.82)	0.16 (0.95)
n (%) [95% CI]						
≥1	810 (16.2) [15.2–17.2]	265 (8.8) [7.8–9.9]	55 (14.4) [11.0–18.3]	753 (16.4) [15.4–17.5]	112 (5.9) [4.9–7.1]	90 (6.9) [5.6–8.5]
≥2	466 (9.3) [8.5–10.1]	136 (4.5) [3.8–5.3]	40 (10.5) [7.6–14.0]	425 (9.3) [8.4–10.1]	56 (3.0) [2.2–3.8]	43 (3.3) [2.4–4.4]
≥4	205 (4.1) [3.6–4.7]	45 (1.5) [1.1–2.0]	19 (5.0) [3.0–7.7]	184 (4.0) [3.5–4.6]	16 (0.8) [0.5–1.4]	13 (1.0) [0.5–1.7]
Invasive ventilations						
Mean (SD)	0.03 (0.30)	0.02 (0.59)	0.03 (0.20)	0.03 (0.30)	0.00 (0.06)	0.00 (0.00)
n (%) [95% CI]						
≥1	82 (1.9) [1.5–2.3]	28 (1.0) [0.7–1.4]	6 (1.7) [0.6–3.6]	74 (1.9) [1.5–2.3]	4 (0.2) [0.1–0.6]	0 (0.0) [0.0–0.3]
Hospital admissions						
Mean (SD)	0.25 (1.26)	0.16 (0.56)	0.11 (0.49)	0.26 (1.31)	0.05 (0.61)	0.06 (0.72)
n (%) [95% CI]						
≥1	545 (11.5) [10.6–12.5]	305 (10.5) [9.4–11.7]	22 (6.2) [3.9–9.2]	522 (12.0) [11.1–13.0]	50 (2.7) [2.0–3.6]	36 (2.9) [2.0–3.9]
≥2	223 (4.7) [4.1–5.4]	98 (3.4) [2.8–4.1]	12 (3.4) [1.8–5.8]	211 (4.9) [4.2–5.5]	13 (0.7) [0.4–1.2]	10 (0.8) [0.4–1.5]
≥4	74 (1.6) [1.2–2.0]	13 (0.4) [0.2–0.8]	0 (0.0) [0.0–1.0]	74 (1.7) [1.3–2.1]	1 (0.1) [0.0–0.3]	1 (0.1) [0.0–0.4]

Proportion of patients with at least two exacerbations （F/U）



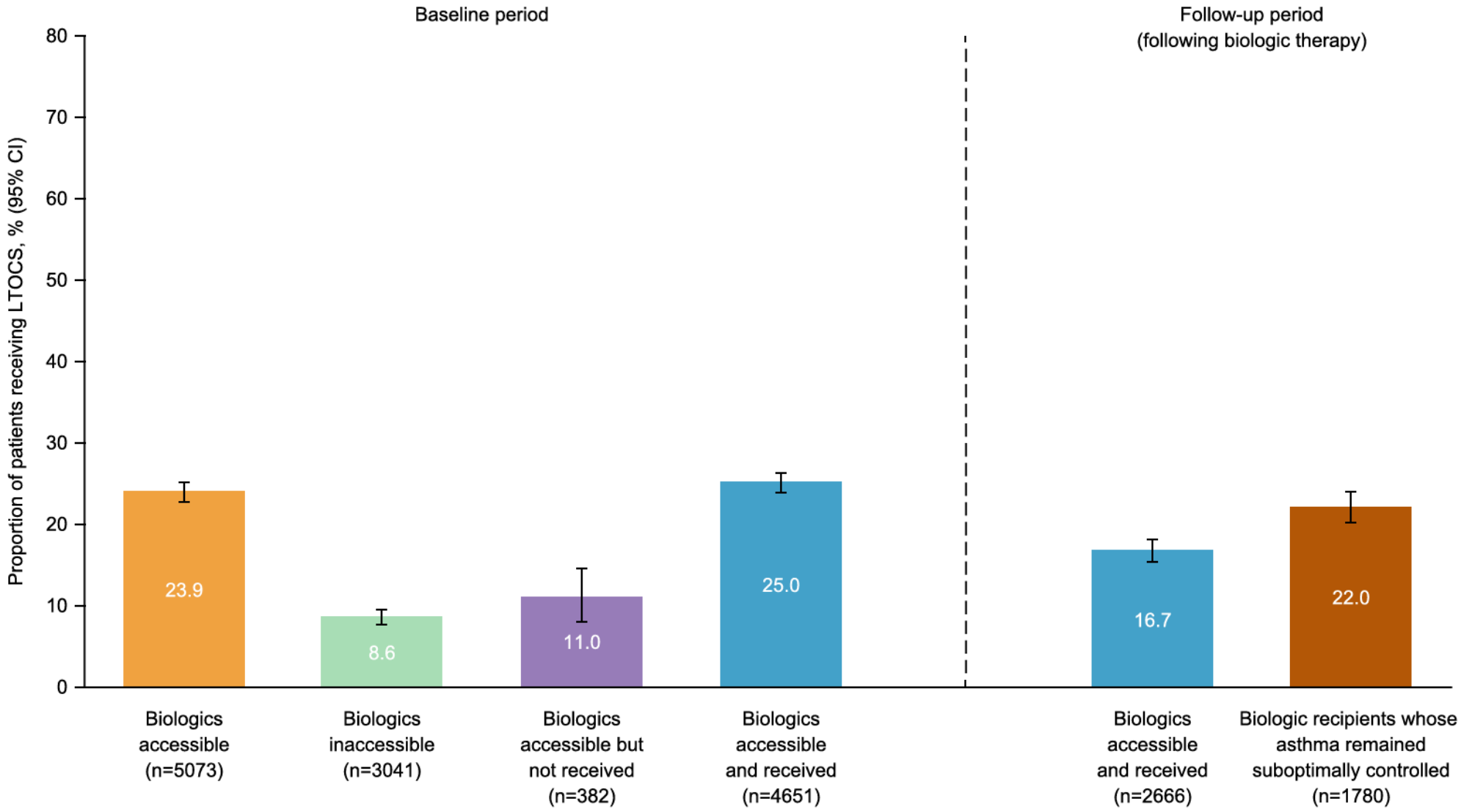
J Asthma Allergy. 2024 Oct 25:17:1055-1069.

Proportion of patients with uncontrolled asthma （F/U）



J Asthma Allergy. 2024 Oct 25:17:1055-1069.

Proportion of patients receiving LTOCS （F/U）



J Asthma Allergy. 2024 Oct 25:17:1055-1069.

Schleich et al. World Allergy Organization Journal (2025) 18:101066
http://doi.org/10.1016/j.waojou.2025.101066

WORLD ALLERGY ORGANIZATION JOURNAL

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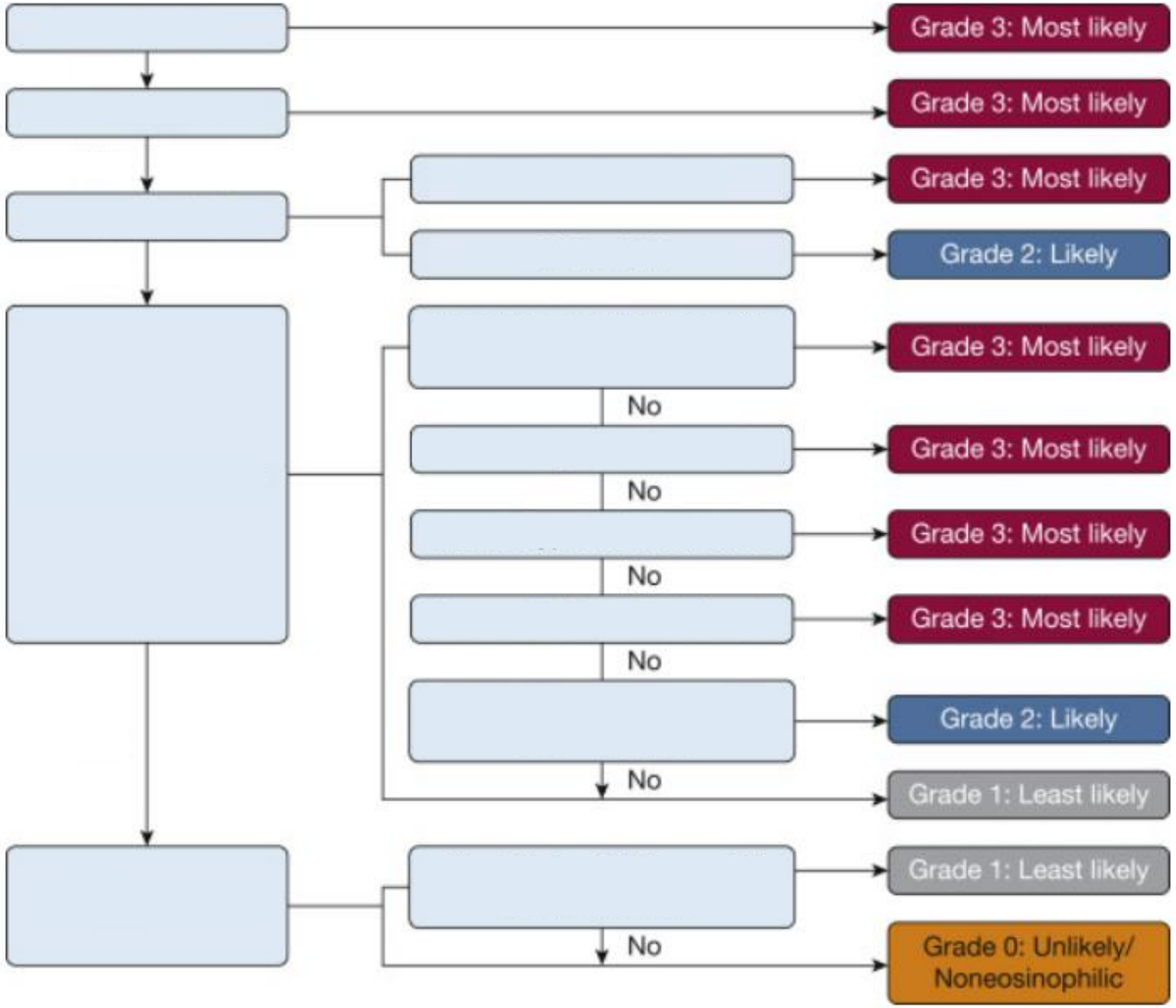
Biomarker profile and disease burden associated with intermittent and long-term oral corticosteroid use in patients with severe asthma prior to biologic initiation in real-life (STAR)

Eosinophilic and Non-eosinophilic Asthma

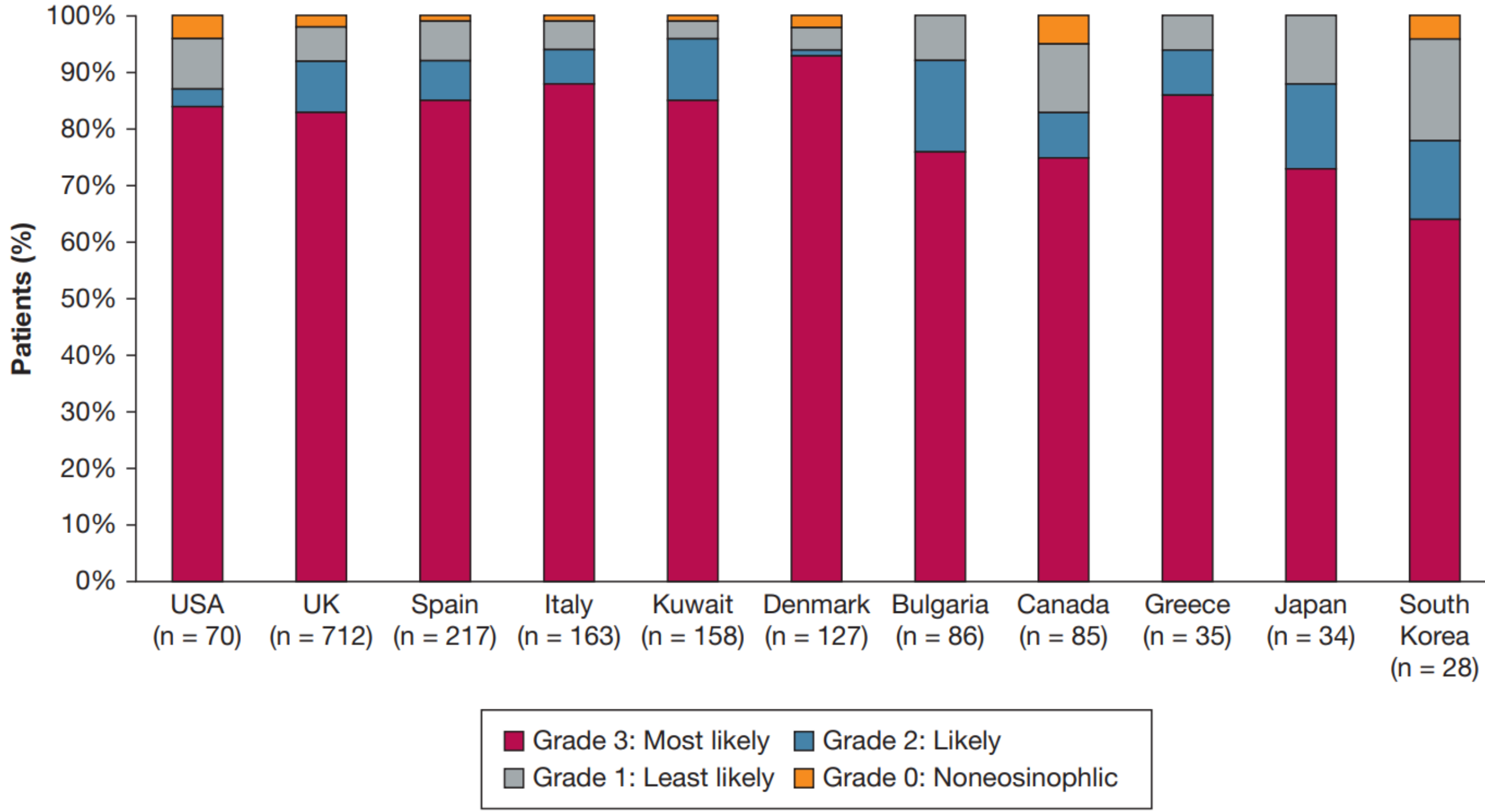


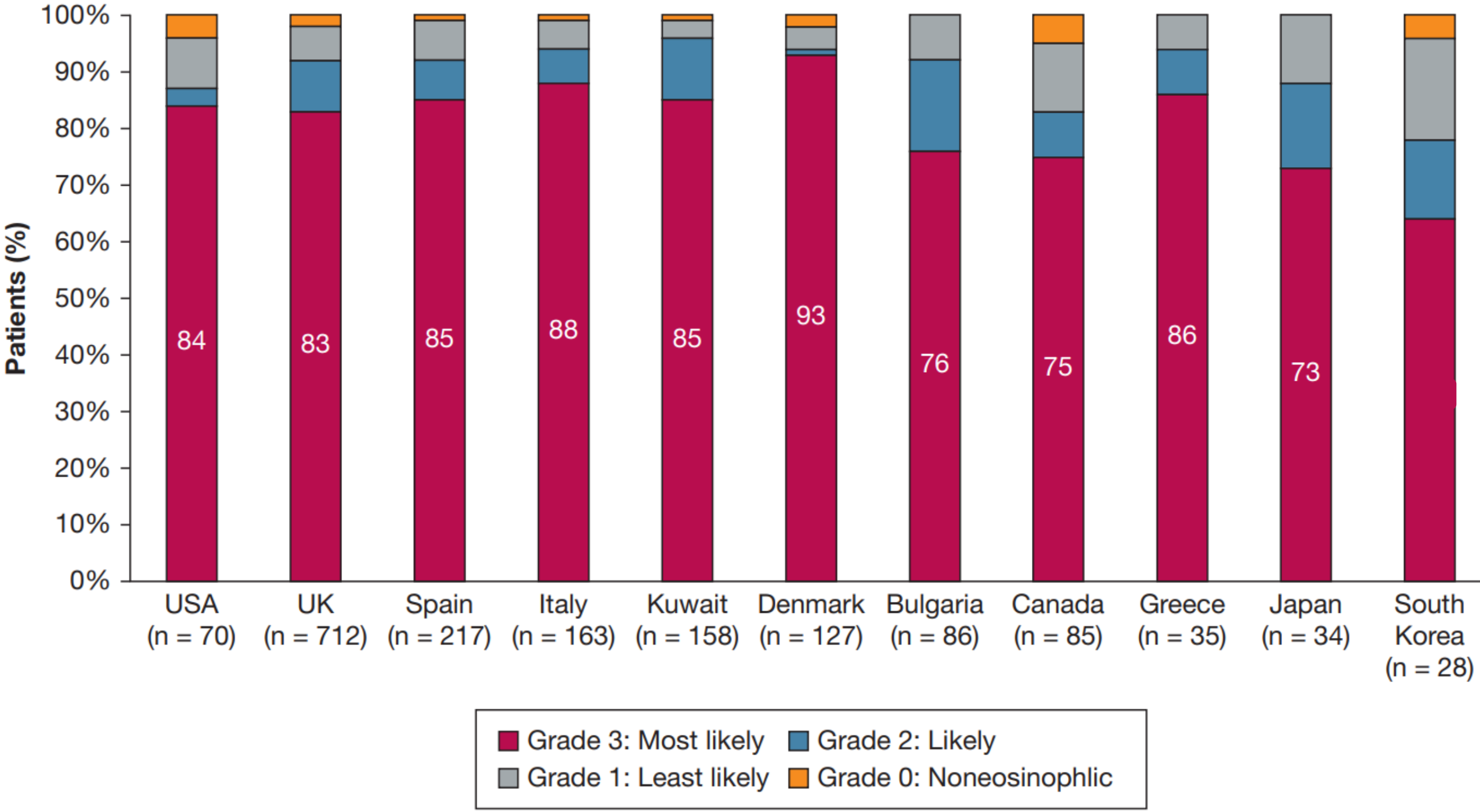
Chest. 2021 Sep;160(3):814-830

Eosinophilic and Non-eosinophilic Asthma: An Expert Consensus Framework to Characterize Phenotypes in a Global Real-Life Severe Asthma Cohort

TABLE 1] Characterization of Eosinophilic and Noneosinophilic Phenotypes and the Proportion of Patients With Severe Asthma With These Phenotypes in ISAR

Highest BEC Available (cells/μL)[a]	Treatment or Clinical Characteristic	Eosinophilic Phenotype	Prospective ISAR Population (N = 1,716) [Original Algorithm]		Prospective ISAR Population (N = 1,716) [Original Algorithm Minus Age of Onset]		Prospective ISAR Population (N = 1,716) [Original Algorithm Minus FENO]	
			No. (%)	(%)	No. (%)	%	No. (%)	%
≥ 300		Grade 3: most likely						
Anti-IL5		Grade 3: most likely						
≥ 150-< 300	Long-term OCS	Grade 3: most likely						
	Presence of ≥ 2 of the following: NP, FENO ≥ 25 ppb, or adult onset[c] (no long-term OCS)	Grade 3: most likely						


Patients (%)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
USA (n = 70)
UK (n = 712)
Spain (n = 217)
Italy (n = 163)
Kuwait (n = 158)
Denmark (n = 127)
Bulgaria (n = 86)
Canada (n = 85)
Greece (n = 35)
Japan (n = 34)
South Korea (n = 28)
Grade 3: Most likely
Grade 2: Likely
Grade 1: Least likely
Grade 0: Noneosinophlic


Patients (%)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
84
83
85
88
85
93
76
75
86
73
USA (n = 70)
UK (n = 712)
Spain (n = 217)
Italy (n = 163)
Kuwait (n = 158)
Denmark (n = 127)
Bulgaria (n = 86)
Canada (n = 85)
Greece (n = 35)
Japan (n = 34)
South Korea (n = 28)
Grade 3: Most likely
Grade 2: Likely
Grade 1: Least likely
Grade 0: Noneosinophlic

Contents lists available at ScienceDirect

Respiratory Medicine

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The effects of oral corticosteroids on lung function, type-2 biomarkers and patient-reported outcomes in stable asthma: A systematic review and meta-analysis

John Busby [a,*], Esther Khoo [a], Paul E. Pfeffer [b], Adel H. Mansur [c], Liam G. Heaney [a]

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[c] *University Hospitals Birmingham NHS Foundation Trust, University of Birmingham, UK*

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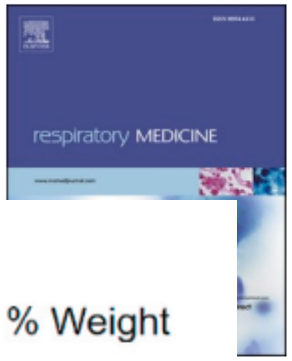
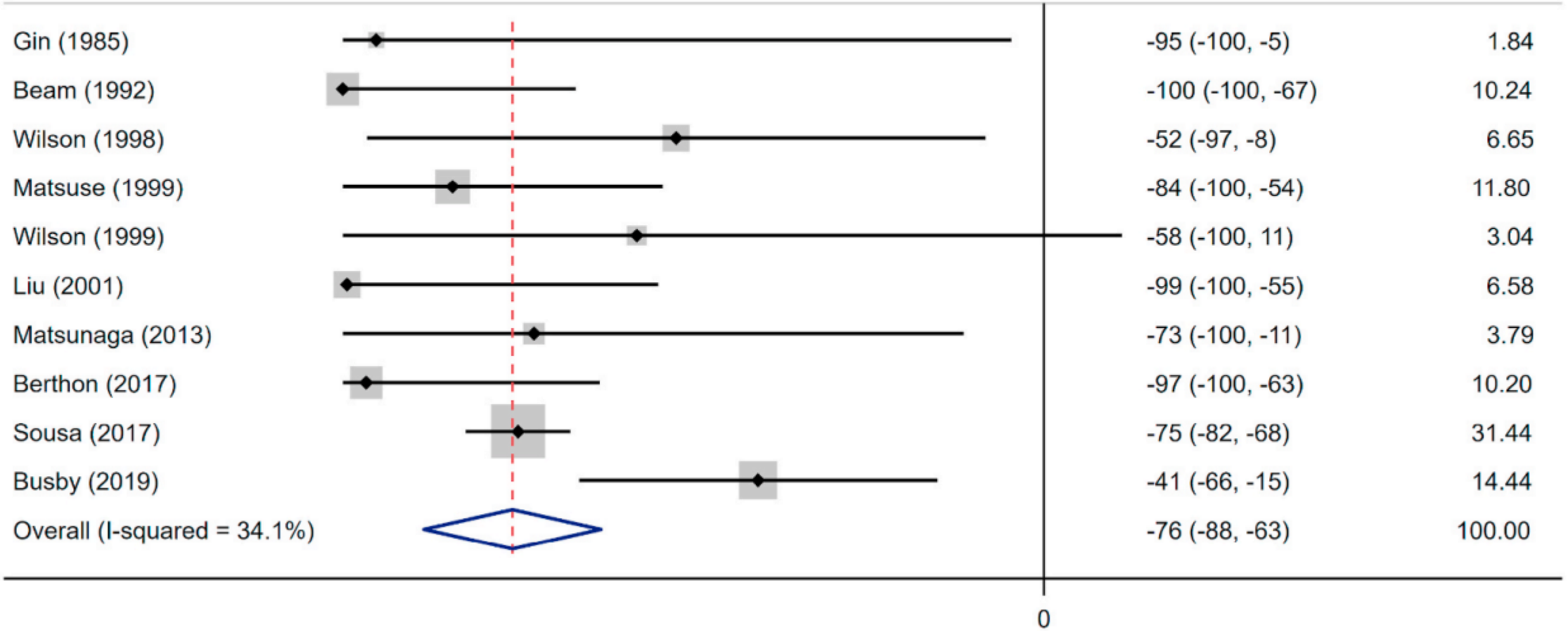
Respiratory Medicine



Blood Eosinophils



Schleich et al. World Allergy Organization Journal (2025) 18:101066
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WORLD ALLERGY ORGANIZATION JOURNAL

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Biomarker profile and disease burden associated with intermittent and long-term oral corticosteroid use in patients with severe asthma prior to biologic initiation in real-life (STAR)

	No OCS N = 215	iOCS[a] N = 2330	LTOCS[a] N = 1760	Total N = 4305	iOCS vs LTOCS P-value
Demographic characteristics					
Sex		N = 2329		N = 4304	
Female, n (%)	130 (60.5)	1424 (61.1)	1070 (60.8)	2624 (61.0)	0.822
Age at biologic initiation					
Mean (SD)	52.5 (14.2)	51.9 (14.5)	53.0 (14.1)	52.4 (14.3)	0.011
BMI, kg/m²				= 3846	
Median (IQR)				24-32)	0.732
Underweight, n (%)				(1.8)	0.106
Normal, n (%)				7 (28.3)	
Overweight, n (%)				3 (32.8)	
Obese (≥30), n (%)				5 (37.1)	
Smoking status				= 3627	
Current smoker, n (%)				0 (3.0)	0.523
Ex-smoker, n (%)				1 (30.6)	
Never smoked, n (%)				5 (66.3)	
Biomarkers					
BEC cells/μL	N = 150	N = 1460	N = 1288	N = 2898	
Mean (SD)	569.9 (615.3)	531.5 (525.7)	490.4 (547.0)	515.2 (540.5)	
Median (IQR)	460 (210-700)	400 (200-700)	310 (100-695)	400 (180-700)	<0.001
FeNO (ppb)	N = 126	N = 1044	N = 939	N = 2109	
Mean (SD)	45.3 (42.9)	49.3 (47.1)	58.0 (54.5)	53.0 (50.5)	
Median (IQR)	36 (17-61)	34 (17-65)	40 (20-77)	36 (18-70)	<0.001
IgE, IU/ml	N = 145	N = 1272	N = 778	N = 2195	
Mean (SD)	530.8 (796.5)	494.7 (1747.6)	397.2 (818.9)	462.5 (1432.1)	
Median (IQR)	295 (121-608)	206 (83-486)	154 (53-389)	190 (74-463)	<0.001
Disease characteristics					
Asthma onset age, yrs	N = 160	N = 1494	N = 1105	N = 2759	
Mean (SD)	30.8 (18.3)	30.0 (19.0)	29.4 (19.1)	29.8 (19.0)	0.418
<18 yrs, n (%)	43 (26.9)	454 (30.4)	345 (31.2)	842 (30.5)	0.649
≥18 yrs, n (%)	117 (73.1)	1040 (69.6)	760 (68.8)	1917 (69.5)	
Asthma duration, yrs	N = 160	N = 1470	N = 1081	N = 2711	
Mean (SD)	21.1 (15.2)	22.2 (16.4)	23.9 (16.9)	22.8 (16.5)	0.010
Eosinophil phenotype[b]	N = 176	N = 1936	N = 1586	N = 3698	
Non eosinophilic, n (%)	5 (2.8)	77 (4.0)	0 (0.0)	82 (2.2)	<0.001
Least likely, n (%)	12 (6.8)	117 (6.0)	0 (0.0)	129 (3.5)	
Likely, n (%)	7 (4.0)	69 (3.6)	126 (7.9)	202 (5.5)	
Most likely, n (%)	152 (86.4)	1673 (86.4)	1460 (92.1)	3285 (88.8)	

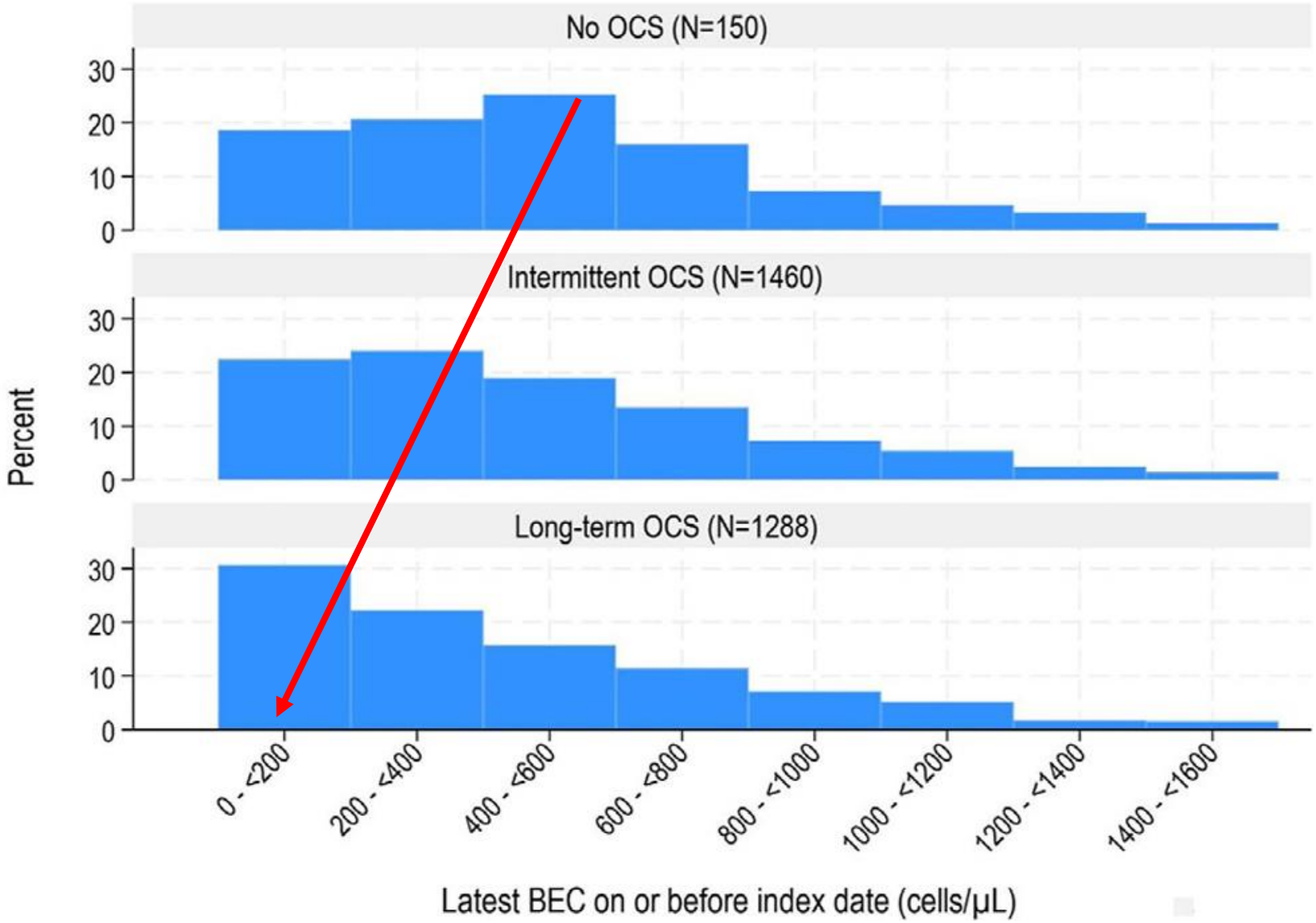
No OCS = 215 (5.0%)

Intermittent OCS = 2330 (54.1%)

Long term OCS = 1760 (40.9%)

World Allergy Organ J 2025;18:101066

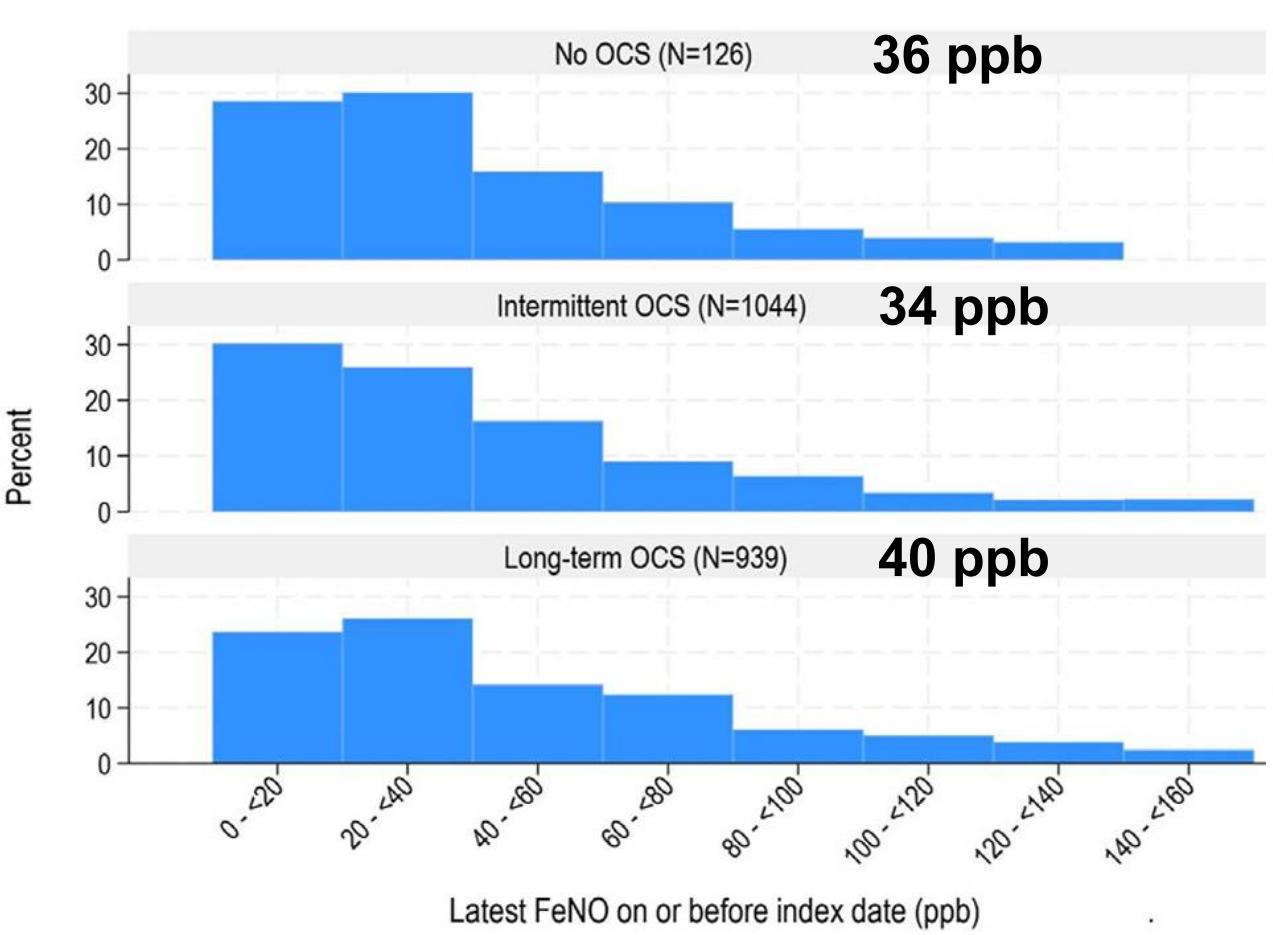
BEC distribution by OCS treatment pattern

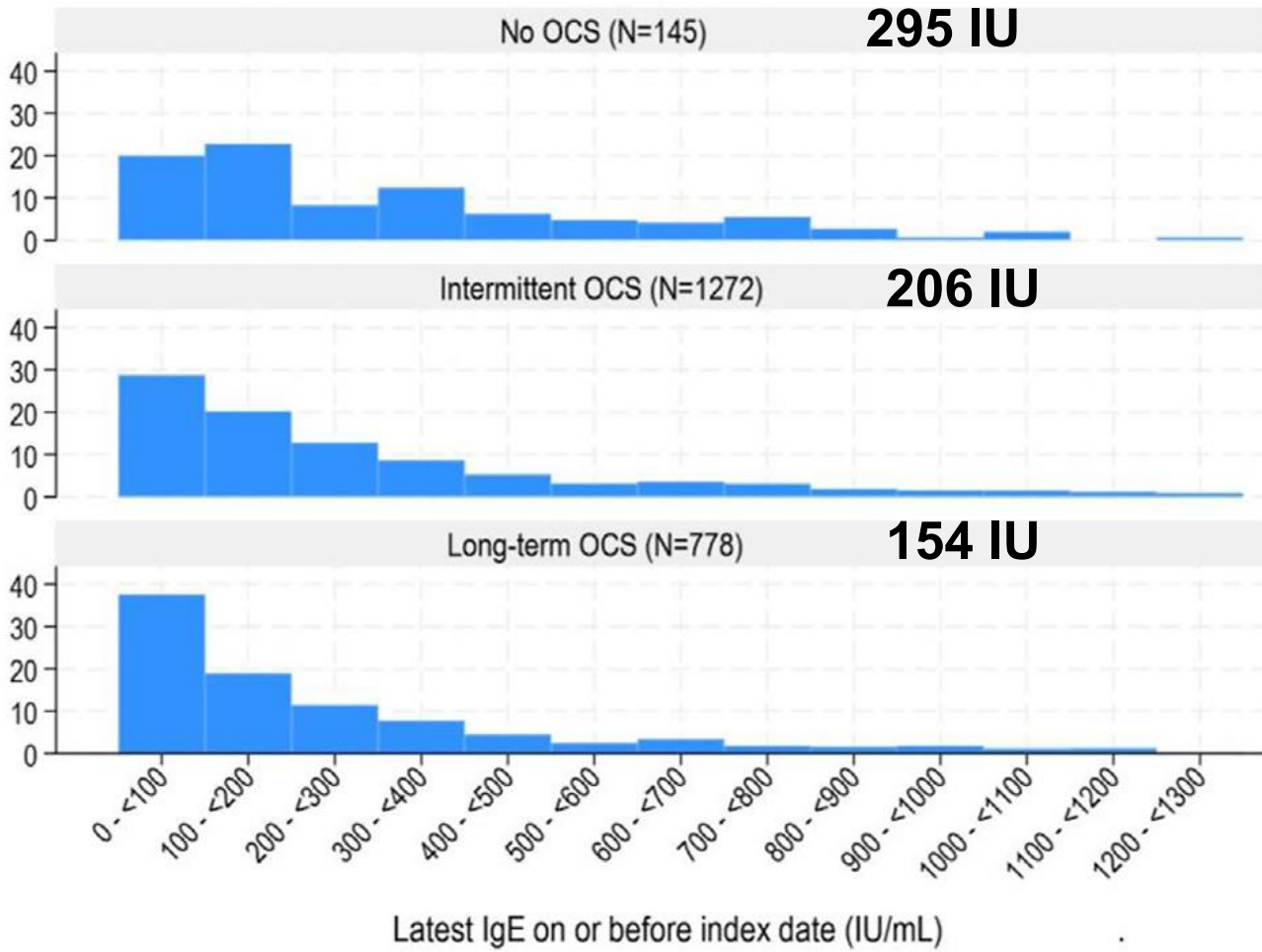


	Median BEC	BEC < 150
No OCS (N=150)	460 cells/uL	14.0%
Intermittent OCS (N=1460)	400 cells/uL	19.5%
Long-term OCS (N=1288)	310 cells/uL	28.6%

World Allergy Organ J 2025;18:101066

FeNO and IgE distribution by OCS treatment pattern





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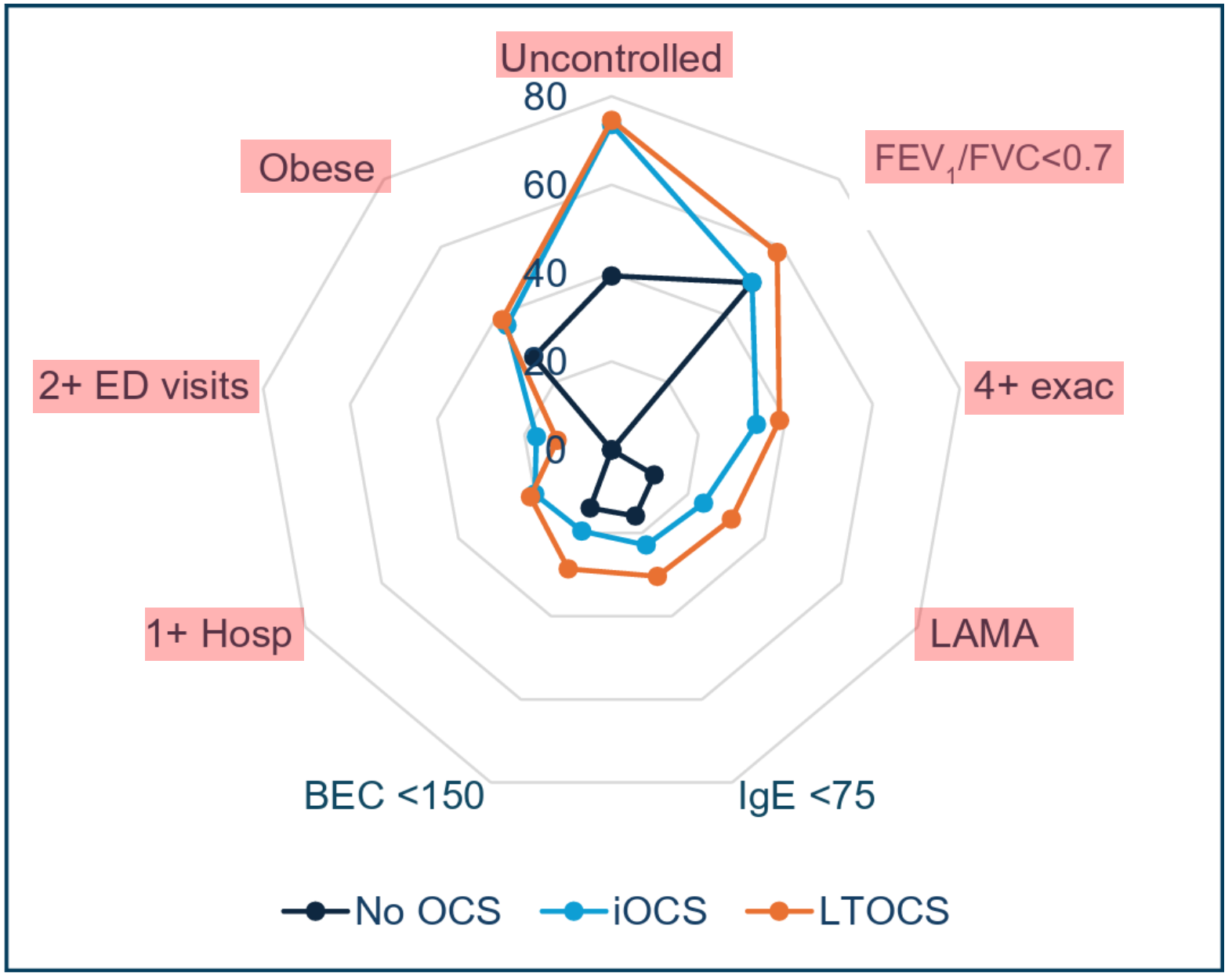
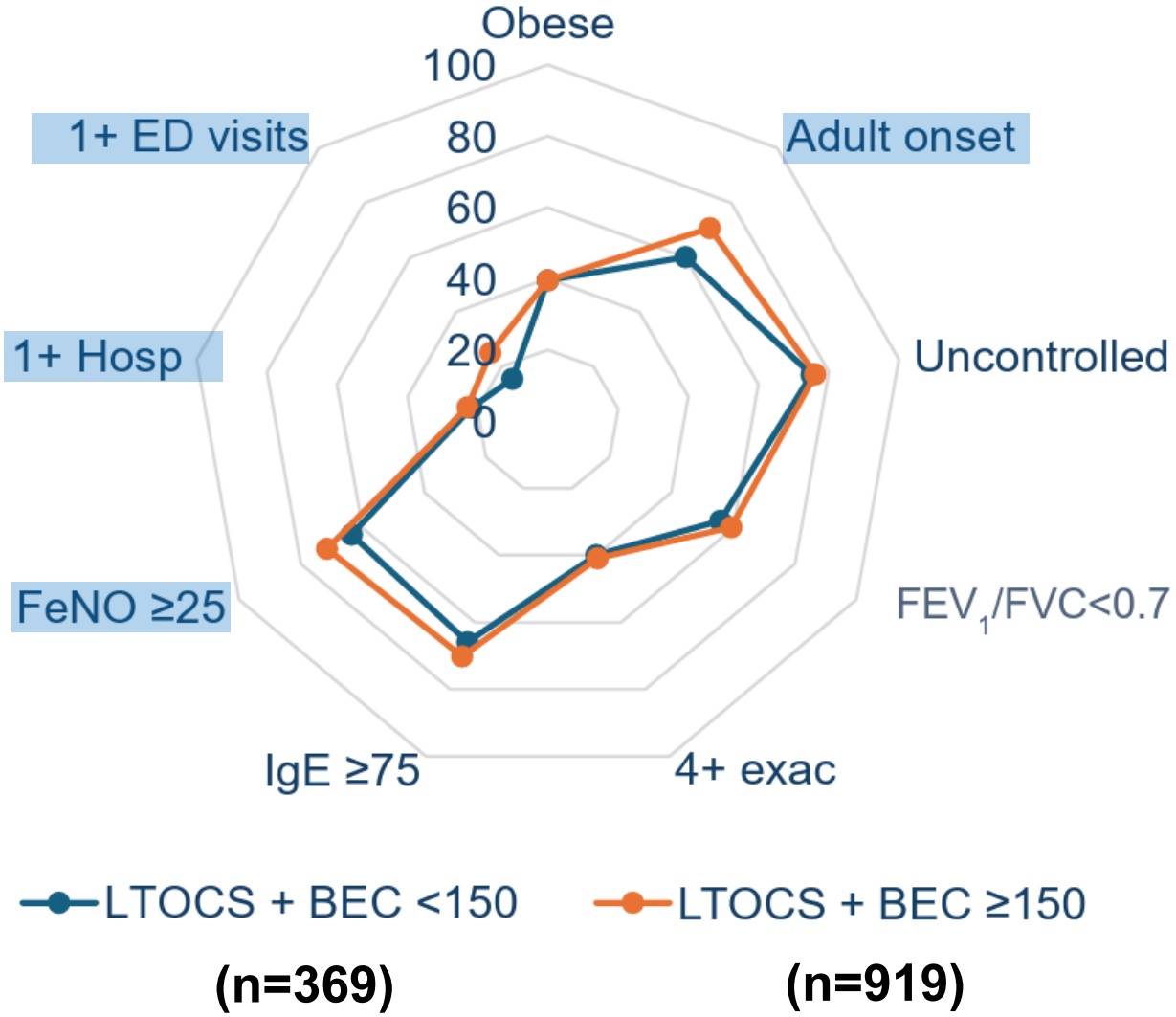
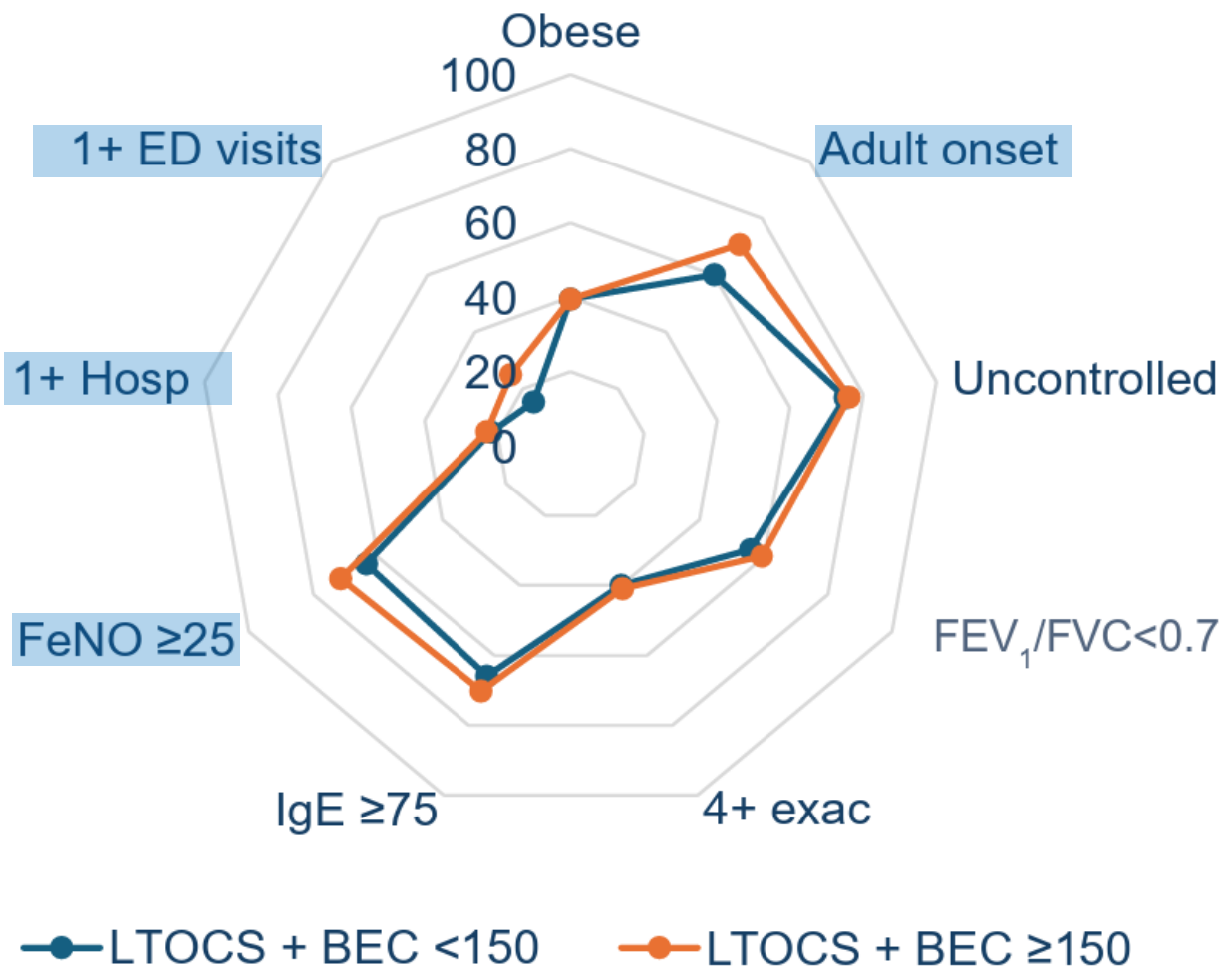


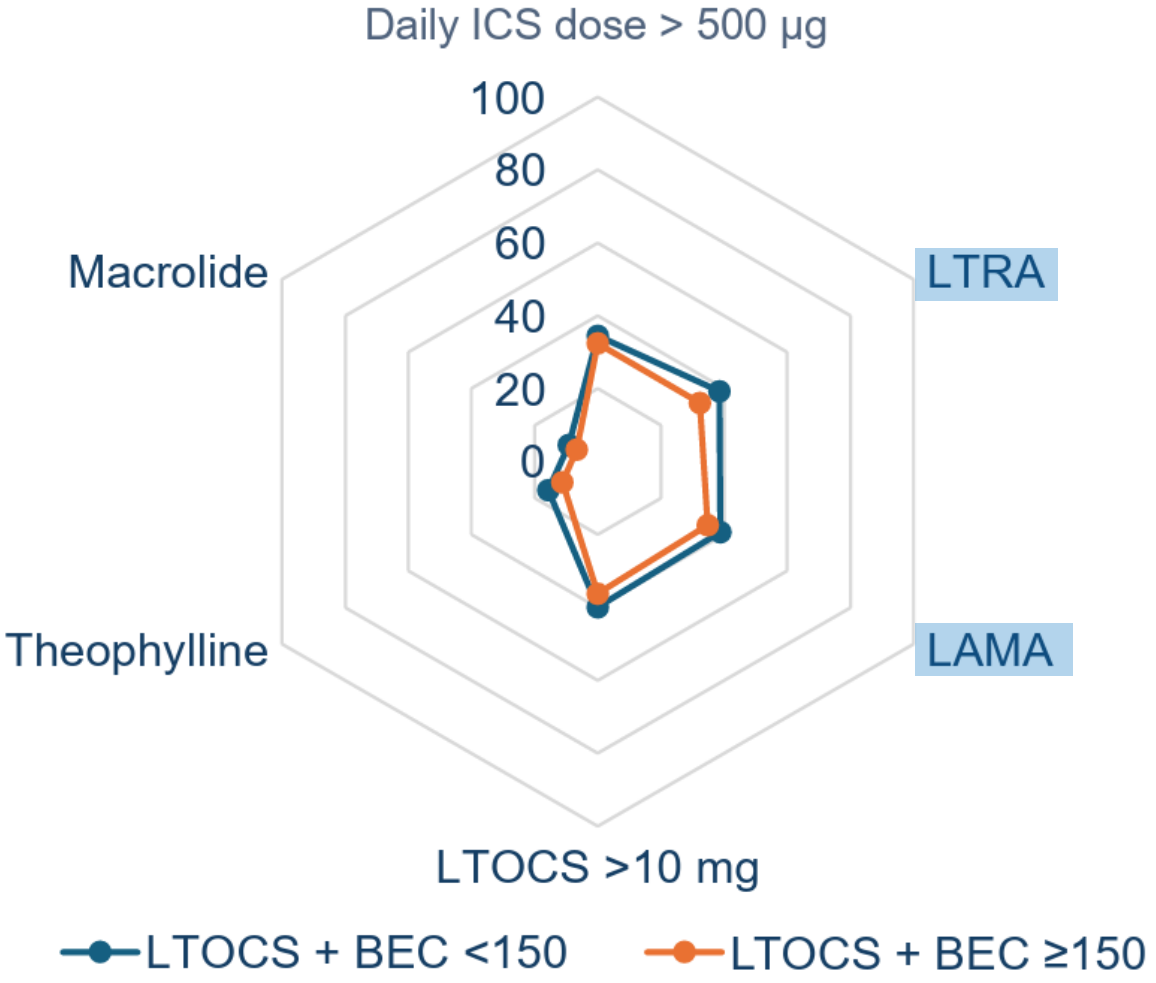
World Allergy Organ J 2025;18:101066


Obese
100
80
60
40
20
0
Adult onset
Uncontrolled
FEV1/FVC<0.7
4+ exac
IgE ≥75
FeNO ≥25
1+ Hosp
1+ ED visits
LTOCS + BEC <150
LTOCS + BEC ≥150

(n=369) **(n=919)**


Obese
100
80
60
40
20
0
Adult onset
Uncontrolled
FEV1/FVC<0.7
4+ exac
IgE ≥75
FeNO ≥25
1+ Hosp
1+ ED visits
LTOCS + BEC <150
LTOCS + BEC ≥150

(n=369) **(n=919)**


Daily ICS dose > 500 µg
100
80
60
40
20
0
LTRA
LAMA
LTOCS >10 mg
Theophylline
Macrolide
LTOCS + BEC <150
LTOCS + BEC ≥150

Original Article

Impact of Biologics Initiation on Oral Corticosteroid Use in the International Severe Asthma Registry and the Optimum Patient Care Research Database: A Pooled Analysis of Real-World Data

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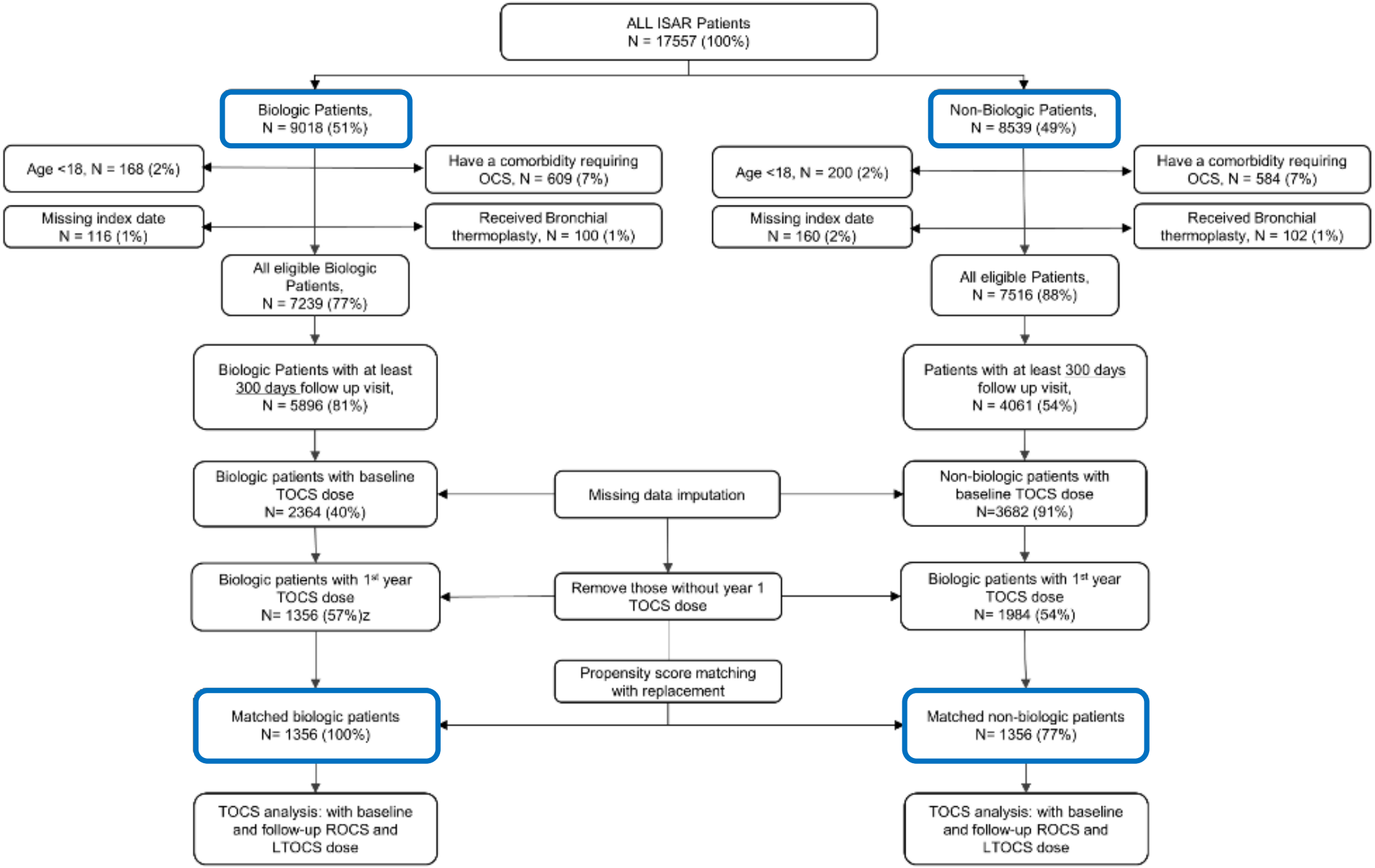
J Allergy Clin Immunol Pract. 2025 Apr 26:S2213-2198(25)00390-3.


ALL ISAR Patients
N = 17557 (100%)
Biologic Patients,
N = 9018 (51%)
Non-Biologic Patients,
N = 8539 (49%)
Age <18, N = 168 (2%)
Have a comorbidity requiring OCS, N = 609 (7%)
Missing index date
N = 116 (1%)
Received Bronchial thermoplasty, N = 100 (1%)
Age <18, N = 200 (2%)
Have a comorbidity requiring OCS, N = 584 (7%)
Missing index date
N = 160 (2%)
Received Bronchial thermoplasty, N = 102 (1%)
All eligible Biologic Patients,
N = 7239 (77%)
All eligible Patients,
N = 7516 (88%)
Biologic Patients with at least 300 days follow up visit,
N = 5896 (81%)
Patients with at least 300 days follow up visit,
N = 4061 (54%)
Biologic patients with baseline TOCS dose
N= 2364 (40%)
Missing data imputation
Non-biologic patients with baseline TOCS dose
N=3682 (91%)
Biologic patients with 1st year TOCS dose
N= 1356 (57%)z
Remove those without year 1 TOCS dose
Biologic patients with 1st year TOCS dose
N= 1984 (54%)
Propensity score matching with replacement
Matched biologic patients
N= 1356 (100%)
Matched non-biologic patients
N= 1356 (77%)
TOCS analysis: with baseline and follow-up ROCS and LTOCS dose
TOCS analysis: with baseline and follow-up ROCS and LTOCS dose

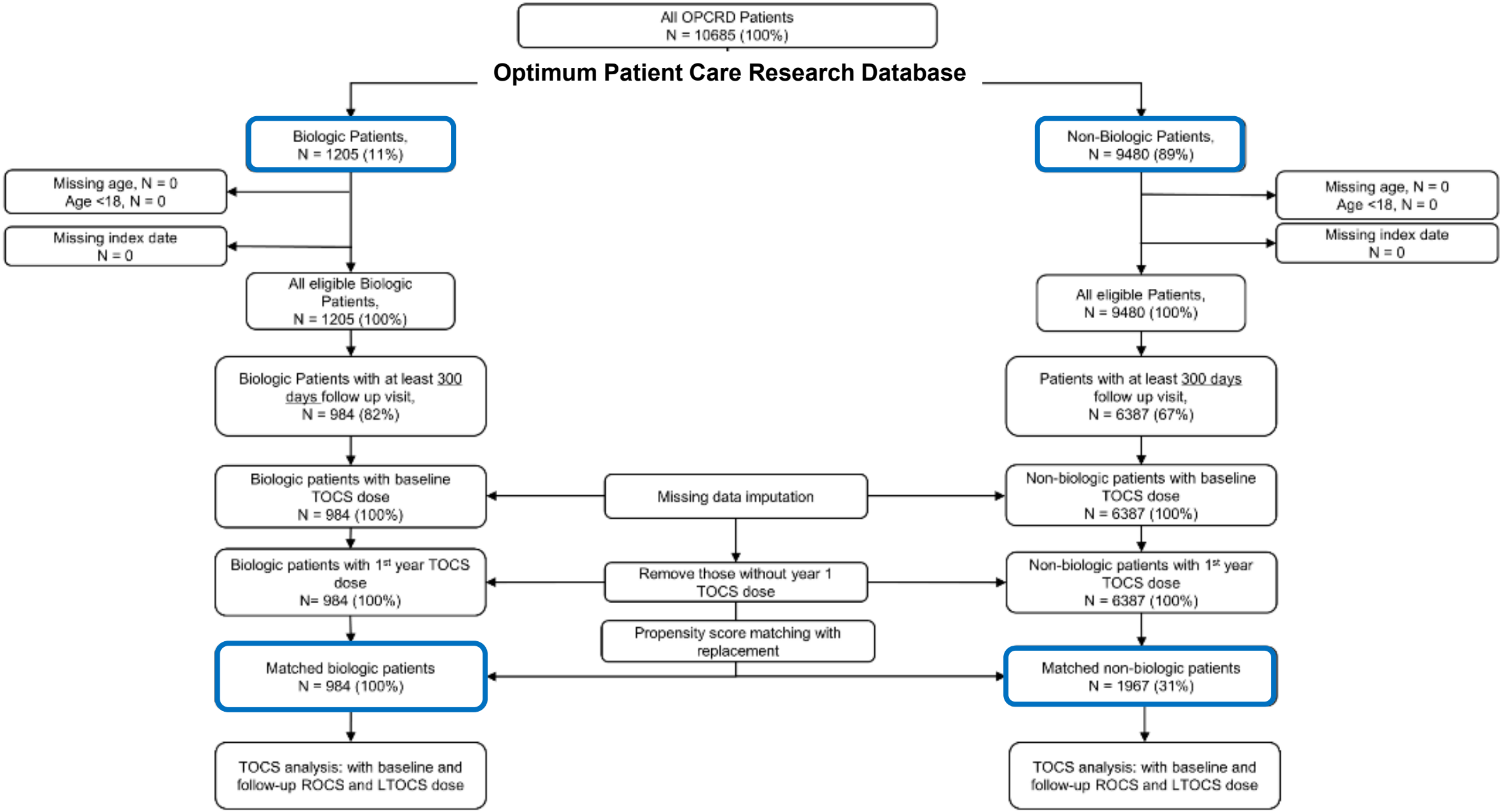
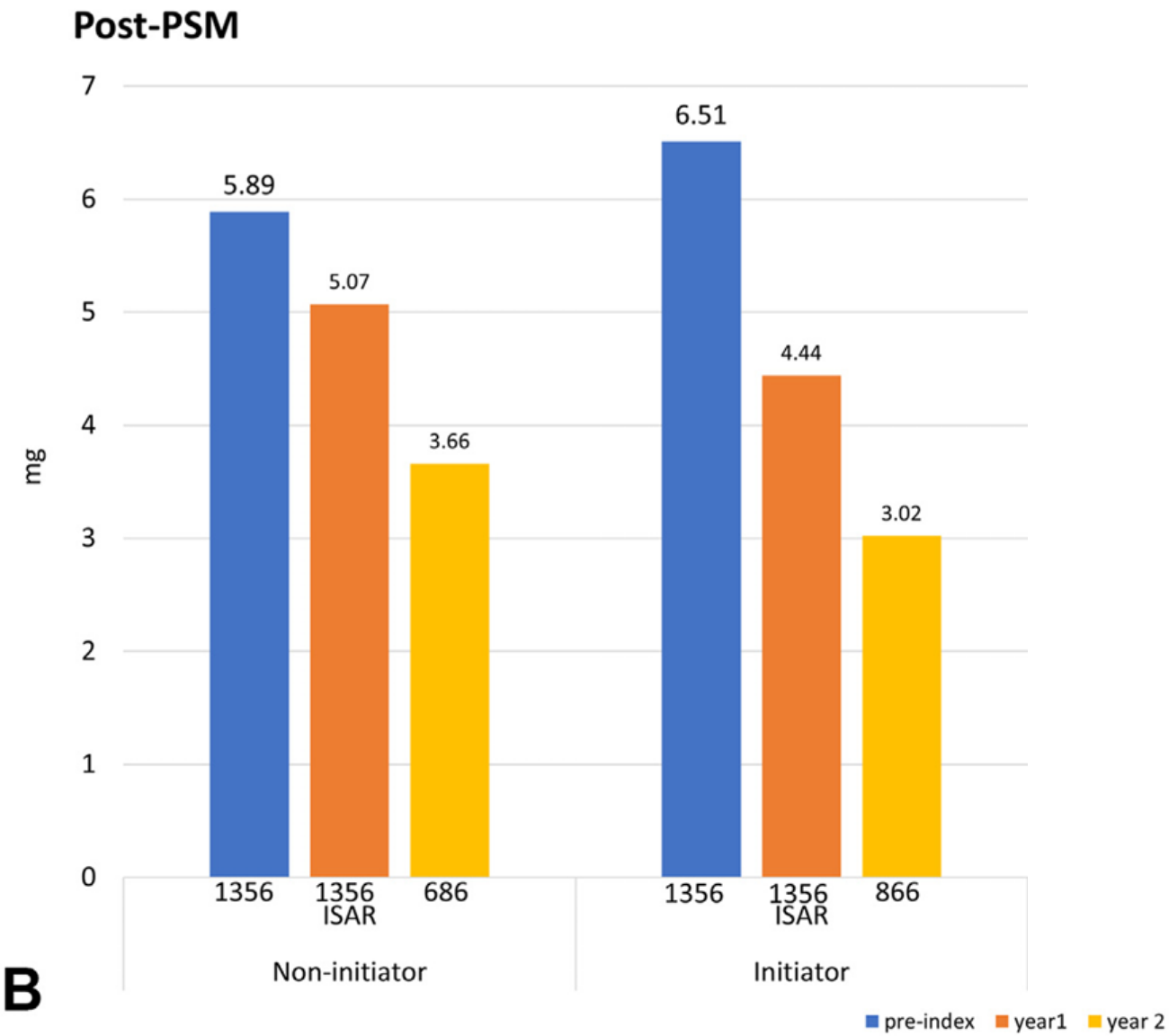

All OPCRD Patients
N = 10685 (100%)
Optimum Patient Care Research Database
Biologic Patients,
N = 1205 (11%)
Missing age, N = 0
Age <18, N = 0
Missing index date
N = 0
All eligible Biologic Patients,
N = 1205 (100%)
Biologic Patients with at least 300 days follow up visit,
N = 984 (82%)
Biologic patients with baseline TOCS dose
N = 984 (100%)
Biologic patients with 1st year TOCS dose
N= 984 (100%)
Matched biologic patients
N = 984 (100%)
TOCS analysis: with baseline and follow-up ROCS and LTOCS dose
Missing data imputation
Remove those without year 1 TOCS dose
Propensity score matching with replacement
Non-Biologic Patients,
N = 9480 (89%)
Missing age, N = 0
Age <18, N = 0
Missing index date
N = 0
All eligible Patients,
N = 9480 (100%)
Patients with at least 300 days follow up visit,
N = 6387 (67%)
Non-biologic patients with baseline TOCS dose
N = 6387 (100%)
Non-biologic patients with 1st year TOCS dose
N = 6387 (100%)
Matched non-biologic patients
N = 1967 (31%)
TOCS analysis: with baseline and follow-up ROCS and LTOCS dose

TABLE I. Post-matching patient characteristics* for ISAR and OPCRD cohorts

	ISAR cohort			OPCRD cohort		
Demographics and disease characteristics	**Biologic not initiated (n = 1,356)**	**Biologic initiated (n = 1,356)**	**Standardized mean difference**	**Biologic not initiated (n = 1,967)**	**Biologic initiated (n = 984)**	**Standardized mean difference**
Age, y (mean [SD])	54.1 (15.7)	53.4 (13.8)	0.05	49.4 (16.8)	50.2 (15.4)	−0.05
Sex, n (%)			0.04			0.02
Male	533 (39.3%)	561 (41.4%)		767 (39.0%)	392 (39.8%)	
Female	823 (60.7%)	795 (58.6%)		1,200 (61.0%)	592 (60.2%)	
Body mass index, kg/m^2 (mean [SD])	28.8 (6.3)	28.4 (5.9)	0.08	29.8 (7.9)	29.9 (8.2)	−0.01
Symptom control in past 4 wk, n (%)			0.08			0.06
Well controlled	148 (10.9%)	183 (13.5%)		96 (4.9%)	36 (3.7%)	
Partially controlled	220 (16.2%)	225 (16.6%)		683 (34.7%)	343 (34.9%)	
Uncontrolled	989 (72.9%)	948 (69.9%)		1,188 (60.4%)	605 (61.5%)	
Blood eosinophil count (highest), mL (mean [SD])	510.6 (429.1)	586.3 (494.8)	−0.16	838.8 (556.3)	825.7 (518.2)	−0.02
FEV_1 % predicted (mean [SD])	73.2 (23.5)	73.3 (22.8)	0.00	74.5 (23.7)	74.7 (22.8)	−0.01
FEV_1/FVC ratio (mean [SD])	0.7 (0.1)	0.7 (0.1)	0.04	0.7 (0.2)	0.7 (0.2)	0.04
Nasal polyps, n (%)	508 (37.5%)	551 (40.6%)	0.06	380 (19.3%)	204 (20.7%)	0.04
Use of leukotriene receptor antagonists, n (%)	354 (26.1%)	332 (24.5%)	0.04	53 (2.7%)	24 (2.4%)	0.02
Use of long-acting muscarinic antagonists, n (%)	338 (24.9%)	287 (21.2%)	0.09	867 (44.1%)	464 (47.2%)	0.06
Use of long-term OCS, n (%)	654 (48.2%)	555 (40.9%)	0.15	437 (44.2%)	438 (44.5%)	0.01
Use of antibiotics, n (%)	—	—	—	1,400 (71.2%)	697 (70.8%)	0.01
Exacerbations in past 12 mo (mean [SD])	2.7 (2.9)	2.9 (2.8)	−0.04	2.8 (2.3)	3.1 (2.6)	−0.11
Asthma-related emergency department visits or hospitalizations in past 12 mo (mean [SD])	0.7 (1.7)	0.6 (1.4)	0.09	0.2 (0.5)	0.2 (0.5)	0.01
Pre-index total daily OCS use (mean [SD]), mg	5.9 (6.9)	6.5 (7.0)	−0.09	4.6 (5.1)	6.0 (7.0)	−0.23
First year total daily OCS use, mg (mean [SD])	5.2 (7.5)	4.7 (8.0)	0.07	3.5 (4.9)	4.6 (7.0)	−0.18
Second year total daily OCS use, mg (mean [SD])	3.7 (6.3)	3.3 (7.2)	0.07	3.1 (6.3)	4.0 (6.8)	−0.16

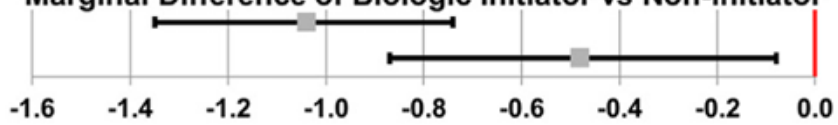
B


Post-PSM
mg
7
6
5
4
3
2
1
0
5.89
5.07
3.66
6.51
4.44
3.02
1356
1356 ISAR
686
1356
1356 ISAR
866
Non-initiator
Initiator
pre-index
year1
year 2

Association of biologic initiation on daily TOCS (absolute change)

Original Result

		No Bx, mg/d [95%CI]	Bx, mg/d [95%CI]	Marginal Difference of Biologic Initiator vs Non-initiator	MD (Bx vs Non-Bx) [95% CI]	P-value
Absolute Change	1st year	-1.40 [-1.57,-1.22]	-2.44 [-2.70,-2.18]		-1.04 [-1.35,-0.74]	<0.001
	2nd year	-2.64 [-2.95,-2.33]	-3.12 [-3.40,-2.84]		-0.48 [-0.87,-0.08]	0.017

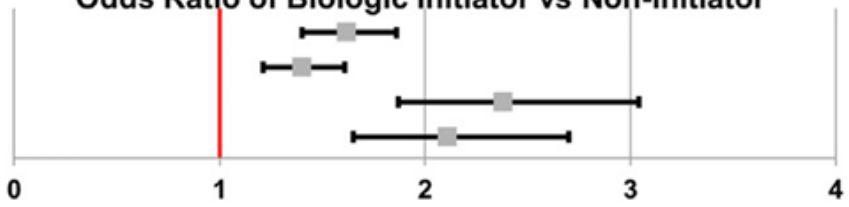


A

Association of biologic initiation on daily TOCS

Original Result

		No Bx, Pr [95%CI]	Bx, Pr [95%CI]	OR (Bx vs Non-Bx) [95% CI]	P-value
Low Dose (0-5mg)	1st year	0.63 [0.62,0.65]	0.70 [0.68,0.72]	1.62 [1.40,1.86]	<0.001
	2nd year	0.71 [0.69,0.73]	0.73 [0.71,0.75]	1.40 [1.21,1.61]	<0.001
Zero Dose (0mg)	1st year	0.19 [0.17,0.21]	0.28 [0.26,0.30]	2.38 [1.87,3.04]	<0.001
	2nd year	0.25 [0.23,0.27]	0.33 [0.31,0.35]	2.11 [1.65,2.70]	<0.001

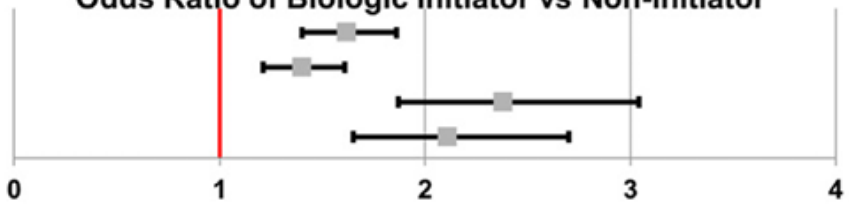


A

Association of biologic initiation on daily TOCS

Original Result

		No Bx, Pr [95%CI]	Bx, Pr [95%CI]	OR (Bx vs Non-Bx) [95% CI]	P-value
Low Dose (0-5mg)	1st year	0.63 [0.62,0.65]	0.70 [0.68,0.72]	1.62 [1.40,1.86]	<0.001
	2nd year	0.71 [0.69,0.73]	0.73 [0.71,0.75]	1.40 [1.21,1.61]	<0.001
Zero Dose (0mg)	1st year	0.19 [0.17,0.21]	0.28 [0.26,0.30]	2.38 [1.87,3.04]	<0.001
	2nd year	0.25 [0.23,0.27]	0.33 [0.31,0.35]	2.11 [1.65,2.70]	<0.001



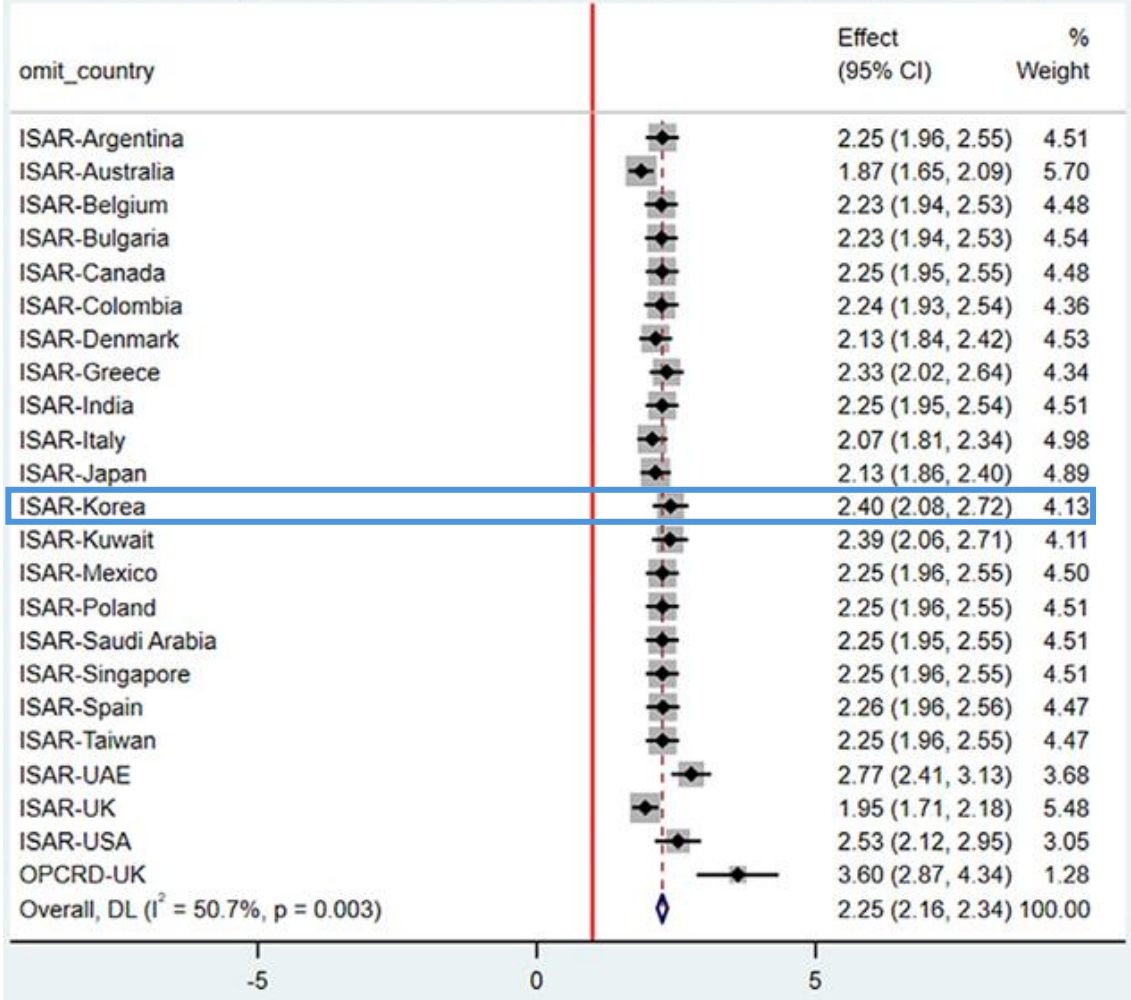
A

Association of biologic initiation on daily TOCS

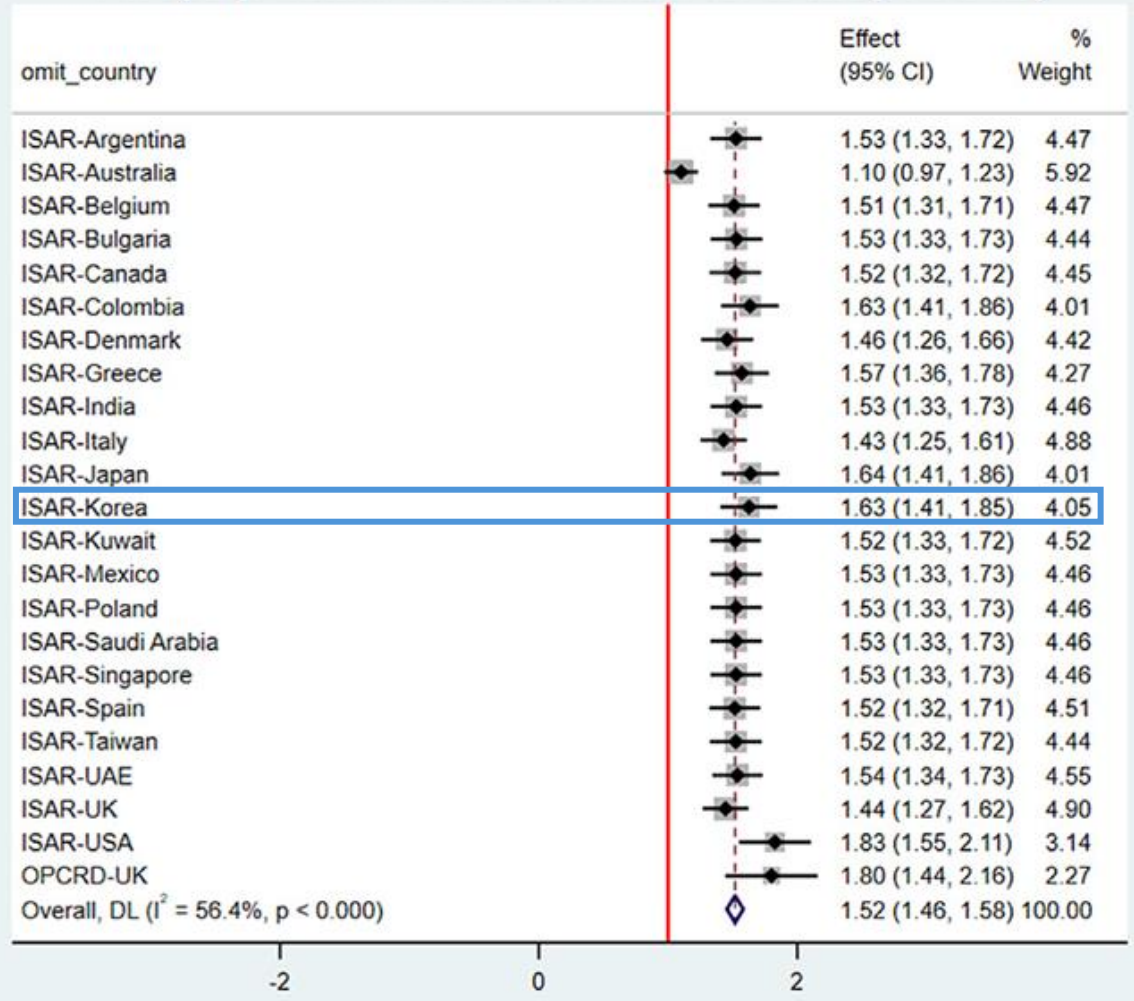
Original Result

		No Bx, Pr [95%CI]	Bx, Pr [95%CI]	OR (Bx v Non-Bx) [95% CI]	P-value
Any Reduction*	1st year	0.68 [0.66,0.70]	0.76 [0.73,0.78]	**1.13 [1.09,1.19]**	**<0.001**
	2nd year	0.79 [0.76,0.81]	0.78 [0.76,0.80]	1.00 [0.96,1.05]	0.896
Optimal Reduction*	1st year	0.21 [0.19,0.23]	0.37 [0.35,0.40]	**2.35 [2.06,2.68]**	**<0.001**
	2nd year	0.37 [0.34,0.40]	0.46 [0.44,0.49]	**1.53 [1.35,1.73]**	**<0.001**

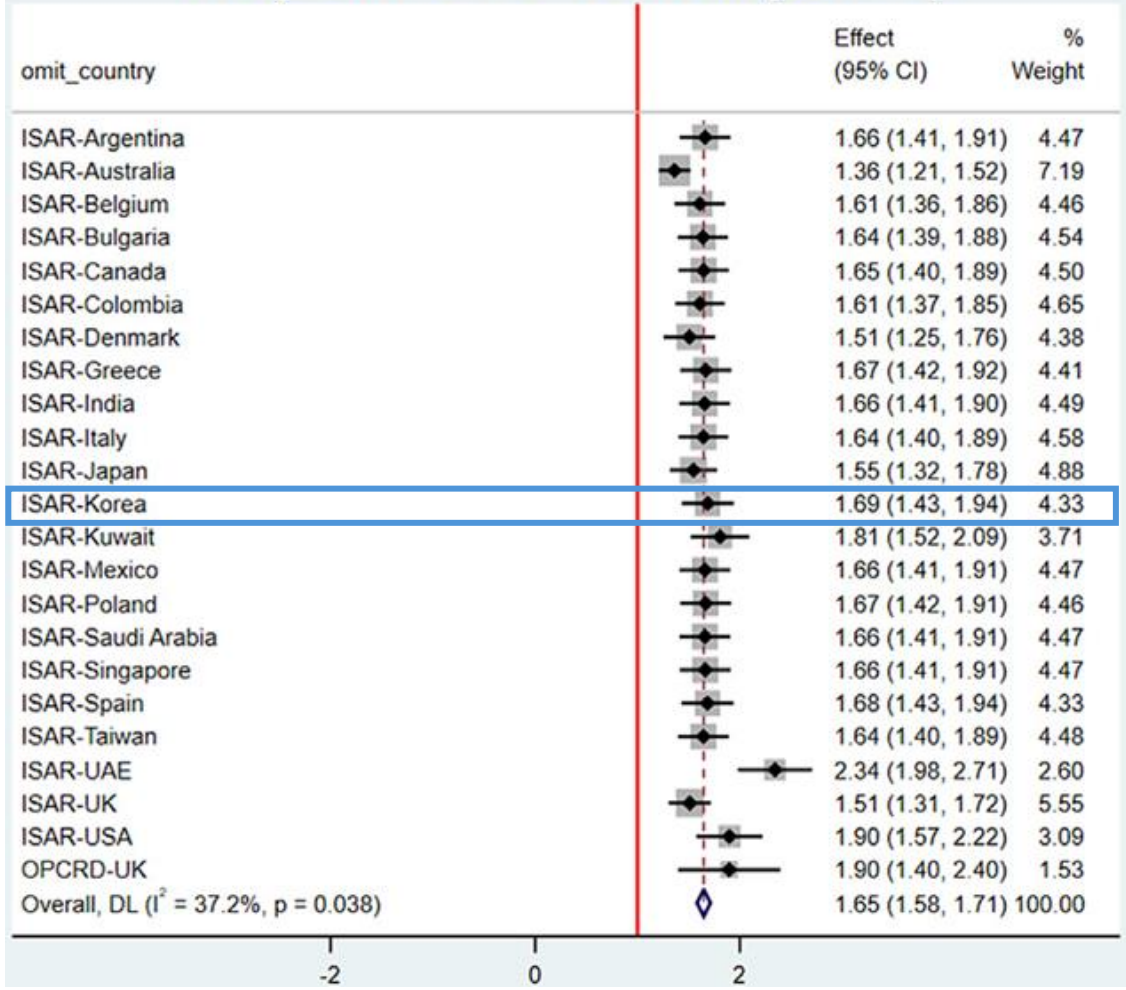
RR(Optimal OCS reduction in year 1)



RR(Optimal OCS reduction in year 2)



RR(Zero OCS dose in year 1)



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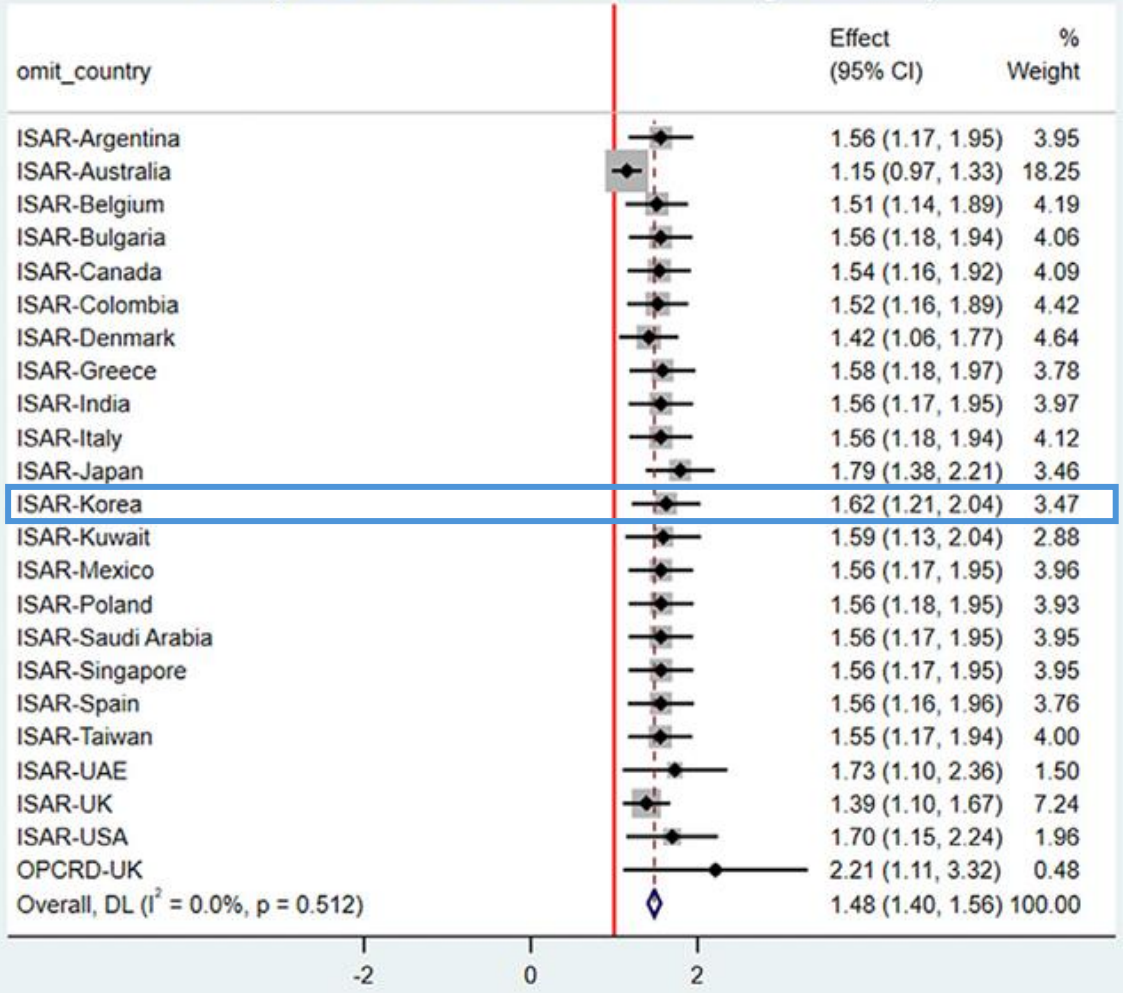

ORIGINAL ARTICLE

Prevention of Cardiovascular and Other Systemic Adverse Outcomes in Patients with Asthma Treated with Biologics

Mohsen Sadatsafavi[1], Trung N. Tran[4], Ghislaine Scelo[5,6], Ming-Ju Tsai[7,8], John Busby[9], Benjamin Emmanuel[4], Liam G. Heaney[10], Christine Jenkins[11,12], Flavia Hoyte[13], Giorgio Walter Canonica[15,16], Rohit Katial[13], Enrico Heffler[15,16], Eileen Wang[13,17], Francesca Puggioni[15], Michael E. Wechsler[14], Ledit R. F. Ardusso[18], Jorge Máspero[19,20], Martin Sivori[21], Cathy Emmas[22], Andrew N. Menzies-Gow[22,23], Neda Stjepanovic[24], Sinthia Z. Bosnic-Anticevich[25,26,27], Belinda Cochrane[28,29], Eve Denton[30,31], Peter G. Gibson[33,34], Mark Hew[30,32], Peter G. Middleton[35], Matthew J. Peters[26,36], Guy G. Brusselle[37,38,39], Renaud Louis[40], Florence Schleich[40], George C. Christoff[41], Todor A. Popov[42], Celine Bergeron[2,43], Mohit Bhutani[44], Kenneth R. Chapman[45], Andréanne Côté[46], Simon Couillard[47], Delbert R. Dorscheid[3], Libardo Jiménez-Maldonado[48,49], Ivan Solarte[51,52], Carlos A. Torres-Duque[50,53], Susanne Hansen[54,55], Celeste M. Porsbjerg[56], Charlotte Suppli Ulrik[57], Alan Altraja[58], Arnaud Bourdin[59], Konstantinos P. Exarchos[60], Athena Gogali[60], Konstantinos Kostikas[60], Michael P. Makris[61], Andriana I. Papaioannou[62], Patrick D. Mitchell[63], Takashi Iwanaga[64], Tatsuya Nagano[65], Yuji Tohda[66], Mona S. Al-Ahmad[67,68], Désirée Larenas-Linnemann[69], Bernt Bøgvald Aarli[70,71], Piotr Kuna[72], Cláudia Chaves Loureiro[73,74], Riyad Al-Lehebi[75,76], Adeeb A. Bulkhi[77], Wenjia Chen[78], Yah Ru Juang[78], Mariko Siyue Koh[79,80], Anqi Liu[78], Chin Kook Rhee[81], Borja G. Cosio[82], Luis Perez-de-Llano[83,84], Diahn-Warng Perng[85,86], Chau-Chyun Sheu[7,8], Hao-Chien Wang[87], Bassam Mahboub[88,90], Laila Salameh[88,89], David J. Jackson[91], Pujan H. Patel[92], Paul E. Pfeffer[93,94], Njira Lugogo[95], Roy Alton Pleasants[95,96], Aaron Beastall[5,6], Lakmini Bulathsinhala[5,6], Victoria Carter[5,6], Nevaashni Eleangovan[5,6], Kirsty Fletton[5,6], John Townend[5,6], Ruth B. Murray[5,6], and David B. Price[5,6,97]; on behalf of the ISAR SOLAR II Working Group

Am J Respir Crit Care Med. 2025 Jul;211(7):1165-1174.

ORIGINAL ARTICLE

Comorbidity in severe asthma requiring systemic corticosteroid therapy: cross-sectional data from the Optimum Patient Care Research Database and the British Thoracic Difficult Asthma Registry

Joan Sweeney,[1] Chris C Patterson,[2] Andrew Menzies-Gow,[3] Rob M Niven,[4] Adel H Mansur,[5] Christine Bucknall,[6] Rekha Chaudhuri,[7] David Price,[8] Chris E Brightling,[9] Liam G Heaney,[1] on behalf of the British Thoracic Society Difficult Asthma Network

Thorax 2016;71:339–346.

Table 1 Demographic details of the OPCRD cohorts (for list of steroid-induced morbidities see online supplementary table E1)

Demographics	All (n=7195)	Severe asthma (n=808)	Mild/moderate asthma (n=3975)	Non-asthma controls (n=2412)	p Value
Female, n (%)	4503 (63)	507 (63)	2515 (63)	1481 (61)	–
Age (years)*	58±17	59±17	58±16	58±17	–
Geographical region, n (%)					
London	597 (8)	55 (7)	344 (9)	198 (8)	0.06
South of England	903 (13)	93 (12)	477 (12)	333 (14)	
East of England	1064 (15)	115 (14)	616 (15)	333 (14)	
Midlands	2146 (30)	248 (31)	1213 (31)	685 (28)	
North of England	1648 (23)	193 (24)	874 (22)	581 (24)	
Scotland/NI/Wales/unknown	837 (12)	104 (13)	451 (11)	282 (12)	
Number of corticosteroid-related comorbidities† n (%)					
0	1790 (25)			864 (36)	<0.001
1	1754 (24)			574 (24)	
2	1382 (19)			404 (17)	
≥3	2269 (32)			570 (24)	

Thorax 2016;71:339–346.

Table 2 Prevalence rates of potential systemic corticosteroid-induced comorbidity and comparisons by groups in the OPCRD dataset

Morbidity	Severe asthma (%) (n=808)	Mild/moderate asthma (%) (n=3975)	OR (95% CI)*	p Value*	Non-asthma controls (%) (n=2412)	OR (95% CI)*	p Value*
Type II diabetes	82 (10)	281 (7)	1.46 (1.11 to 1.91)	0.006	149 (6)	1.76 (1.30 to 2.38)	<0.001
Obesity (BMI >30 kg/m^2)	339 (42)	1385 (35)	1.36 (1.16 to 1.59)	<0.001	561 (23)	2.04 (1.74 to 2.39)	<0.001
Osteopenia	78 (10)	85 (2)	5.26 (3.75 to 7.37)	<0.001	41 (2)	6.68 (4.28 to 10.43)	<0.001
Osteoporosis	126 (16)	162 (4)	5.23 (3.97 to 6.89)	<0.001	74 (3)	6.53 (4.63 to 9.21)	<0.001
Fracture	41 (5)	134 (3)	1.54 (1.06 to 2.22)	0.022	88 (4)	1.65 (1.14 to 2.39)	0.007
Dyspeptic disorders	524 (65)	1331 (34)	3.99 (3.37 to 4.72)	<0.001	578 (24)	4.88 (4.11 to 5.79)	<0.001
Glaucoma	32 (4)	137 (3)	1.12 (0.75 to 1.68)	0.58	67 (3)	1.41 (0.89 to 2.25)	0.15
Cataract	70 (9)	195 (5)	1.89 (1.39 to 2.56)	<0.001	105 (4)	2.42 (1.70 to 3.43)	<0.001
Cardiovascular disease	77 (10)	277 (7)	1.36 (1.02 to 1.81)	0.035	168 (7)	1.57 (1.14 to 2.15)	0.005
Hypertension	276 (34)	1145 (29)	1.35 (1.12 to 1.61)	0.001	596 (25)	1.76 (1.44 to 2.14)	<0.001
Psychiatric conditions/anxiety/ depression	310 (38)	1238 (31)	1.43 (1.22 to 1.69)	<0.001	607 (25)	1.67 (1.42 to 1.97)	<0.001
Hypercholesterolaemia	124 (15)	561 (14)	1.15 (0.92 to 1.44)	0.21	258 (11)	1.61 (1.25 to 2.08)	<0.001
Sleep disorder	33 (4)	99 (2.5)	1.70 (1.13 to 2.53)	0.010	40 (2)	2.21 (1.46 to 3.35)	<0.001
Chronic kidney disease	110 (14)	342 (9)	1.80 (1.39 to 2.32)	<0.001	167 (7)	2.41 (1.81 to 3.21)	<0.001

Thorax 2016;71:339–346.

Table 4 Prevalence rates of corticosteroid-induced morbidity and comparisons between cohorts in the BTS Registry

Disease/adverse event	Severe corticosteroid-dependent asthma (442) n (%)	Severe non-corticosteroid-dependent asthma (328) n (%)	OR (95% CI)*	OR (95% CI)†	OR (95% CI)‡	p Value
Endocrine disorder						
IDDM	2 (0.5)	1 (0.3)	–	–	–	1.00
NIDDM	64 (14)	15 (5)	3.55 (1.98 to 6.35)	3.50 (1.94 to 6.24)	3.48 (1.94 to 6.26)	<0.001
Cardiac disease						
Hypertension	98 (22)	49 (15)	1.61 (1.11 to 2.36)	1.59 (1.07 to 2.36)	1.59 (1.07 to 2.37)	0.012
Cardiovascular disease	27 (6)	25 (8)	0.78 (0.44 to 1.37)	0.74 (0.41 to 1.33)	0.71 (0.39 to 1.30)	0.41
Hypercholesterolaemia	76 (17)	24 (7)	2.61 (1.60 to 4.23)	2.64 (1.60 to 4.37)	2.59 (1.57 to 4.30)	<0.001
Osteoporosis and bone disease						
Osteoporosis	57/319 (18)	18/122 (15)	1.26 (0.71 to 2.24)	1.27 (0.71 to 2.28)	1.21 (0.67 to 2.17)	0.44
Osteopenia	117/319 (37)	39/122 (32)	1.22 (0.78 to 1.90)	1.23 (0.79 to 1.92)	1.15 (0.73 to 1.81)	0.36
Fracture	13 (3)	1 (0.3)	–	–	–	0.007
Obesity (BMI > 30 kg/m^2)	237 (54)	147 (45)	1.43 (1.07 to 1.91)	1.41 (1.06 to 1.88)	1.47 (1.10 to 1.97)	0.016
Weight gain	55 (12)	3 (1)	–	–	–	<0.001
Sleep disorders						
Sleep disturbance	18 (4)	2 (1)	–	–	–	0.003
Obstructive sleep apnoea	51 (12)	13 (4)	3.14 (1.68 to 5.89)	3.07 (1.64 to 5.77)	2.80 (1.48 to 5.29)	<0.001
Eye disease						
Cataracts	25 (6)	0 (0)	–	–	–	0.002
Glaucoma	8 (2)	6 (2)	0.97 (0.33 to 2.83)	0.93 (0.31 to 2.74)	0.83 (0.28 to 2.50)	0.98
Dyspeptic disorders	283 (64)	157 (48)	2.00 (1.49 to 2.68)	1.94 (1.44 to 2.61)	1.96 (1.45 to 2.64)	<0.001
Psychiatric disorders						
Depression/anxiety/low mood	125 (28)	46 (14)	2.36 (1.62 to 3.44)	2.39 (1.64 to 3.49)	2.57 (1.76 to 3.76)	<0.001
Skin conditions	16 (4)	1 (0.3)	–	–	–	0.002
Corticosteroid-related diseases						
Cushingoid symptoms	27 (6)	1 (0.3)	–	–	–	<0.001
Adrenal insufficiency	12 (3)	1 (0.3)	–	–	–	0.010
Corticosteroid-induced proximal myopathy	1 (0.2)	0	–	–	–	1.00

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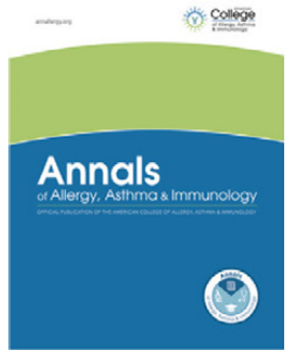
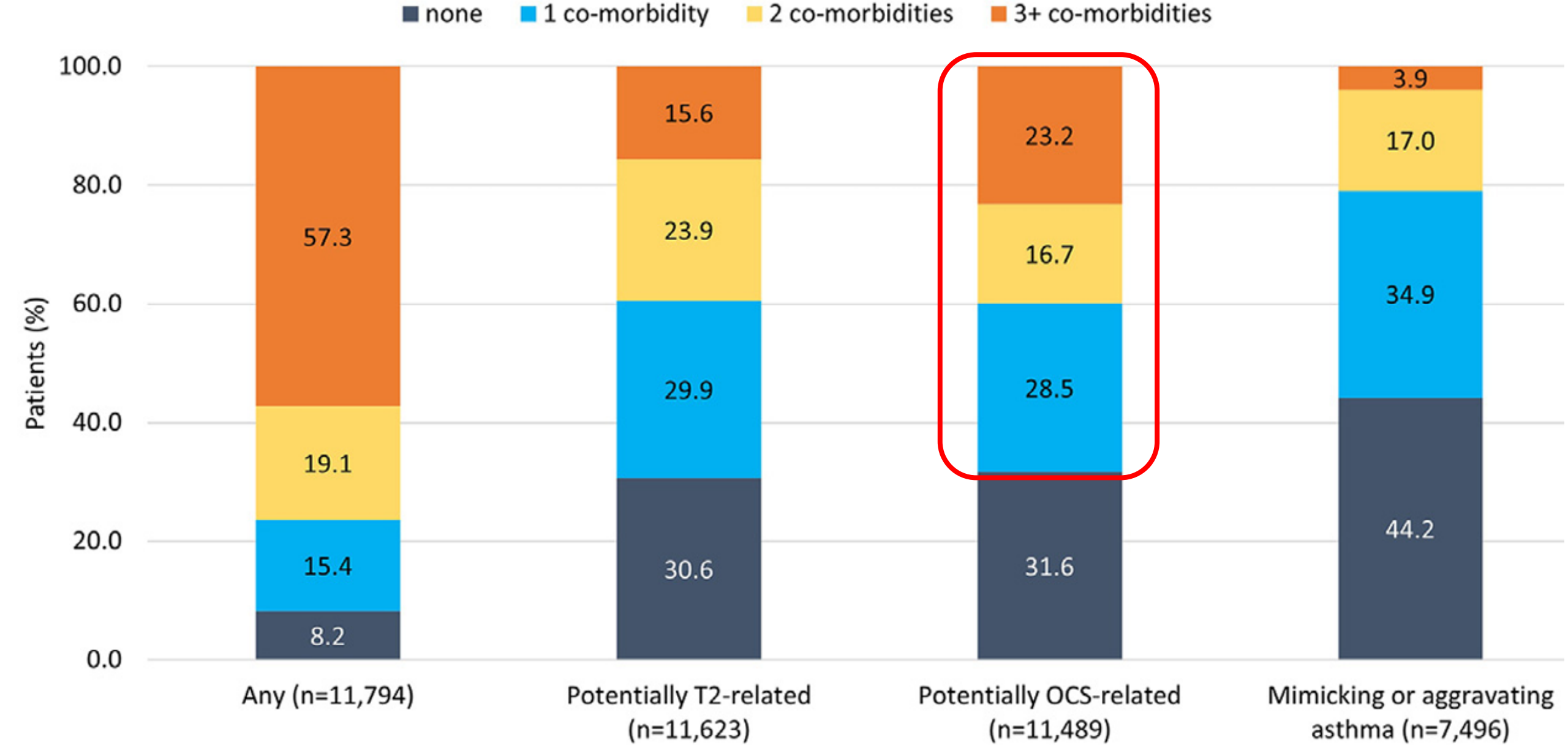
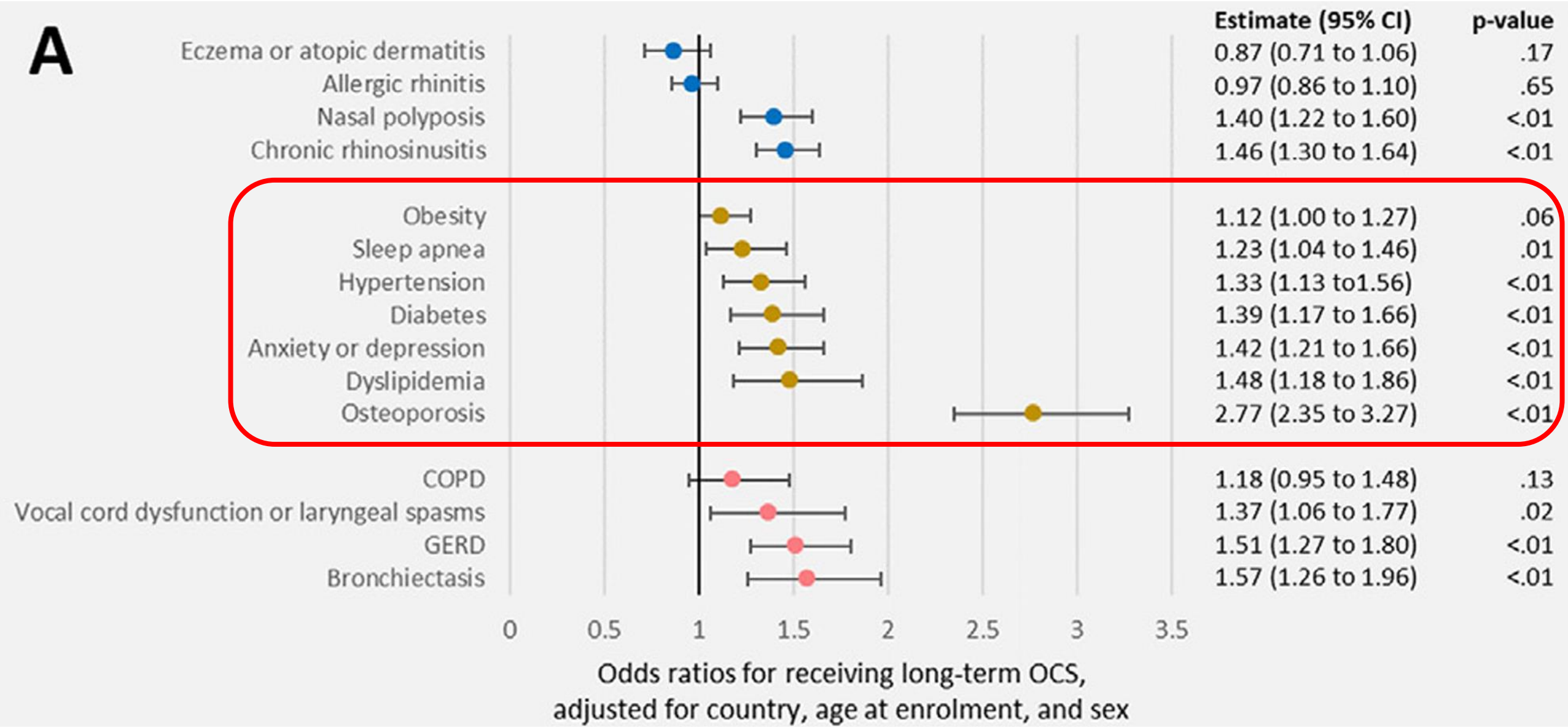
Contents lists available at ScienceDirect



Original Article

Analysis of comorbidities and multimorbidity in adult patients in the International Severe Asthma Registry


none
1 co-morbidity
2 co-morbidities
3+ co-morbidities
Patients (%)
100.0
80.0
60.0
40.0
20.0
0.0
57.3
19.1
15.4
8.2
15.6
23.9
29.9
30.6
23.2
16.7
28.5
31.6
3.9
17.0
34.9
44.2
Any (n=11,794)
Potentially T2-related (n=11,623)
Potentially OCS-related (n=11,489)
Mimicking or aggravating asthma (n=7,496)



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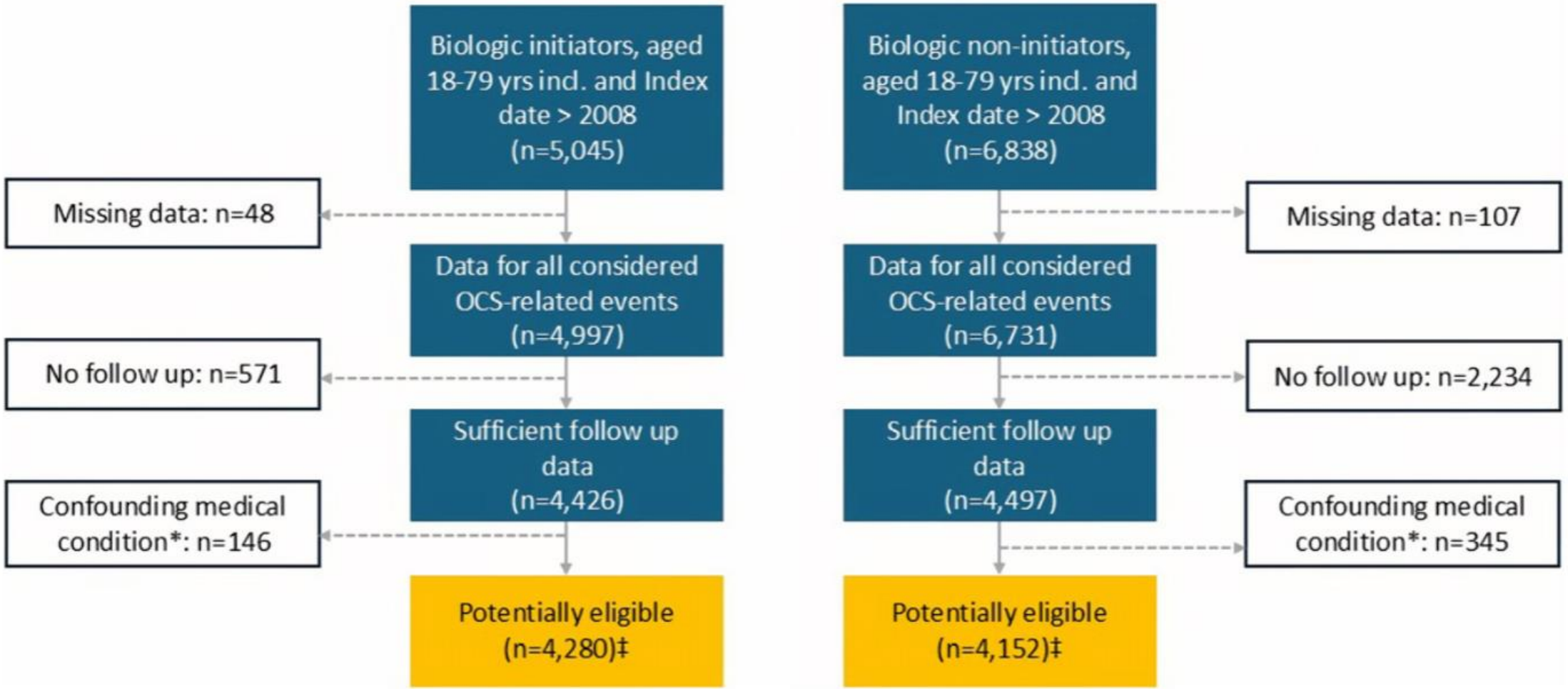

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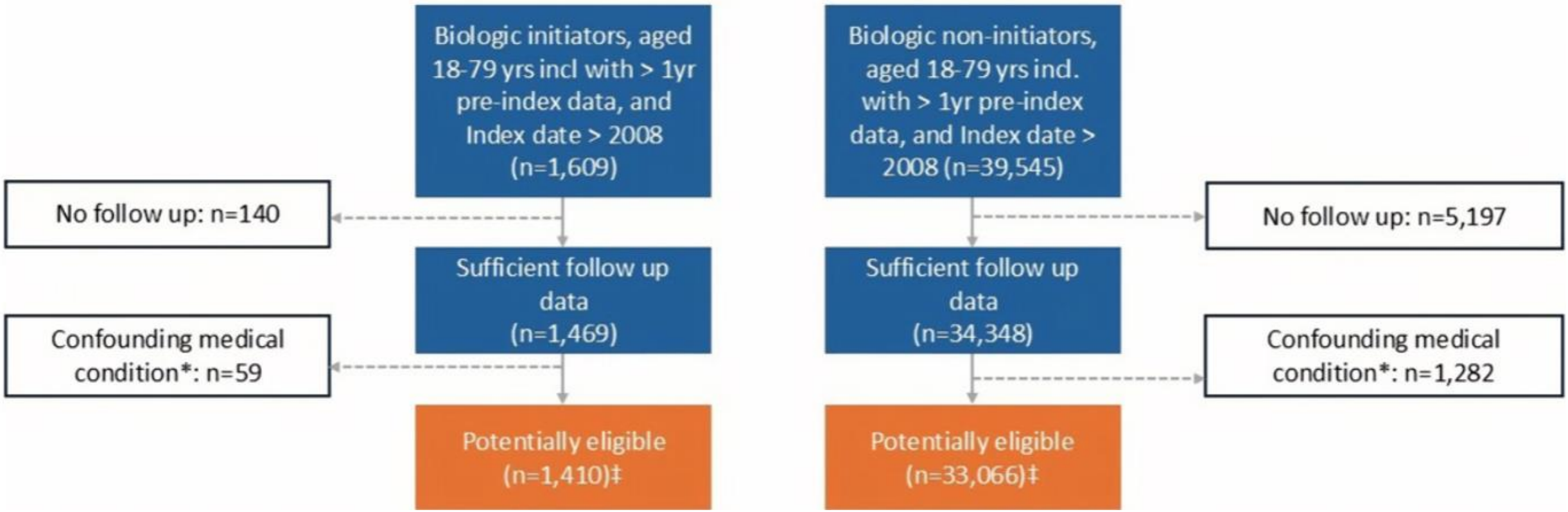
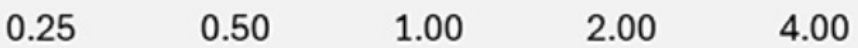

Biologic initiators, aged 18-79 yrs incl with > 1yr pre-index data, and Index date > 2008 (n=1,609)
No follow up: n=140
Sufficient follow up data (n=1,469)
Confounding medical condition*: n=59
Potentially eligible (n=1,410)‡
Biologic non-initiators, aged 18-79 yrs ind. with > 1yr pre-index data, and Index date > 2008 (n=39,545)
No follow up: n=5,197
Sufficient follow up data (n=34,348)
Confounding medical condition*: n=1,282
Potentially eligible (n=33,066)‡

Characteristics	Biologic Initiators (*N* = 5,690)	Noninitiators (*N* = 37,218)
Age, yr, mean (SD)	51.3 (14.4)	48.9 (15.7)
Sex, female	3,532 (62.1)	24,808 (66.7)
Smoking status, *N*	5,309	36,195
Current smoker	273 (5.1)	8,314 (23.0)
Ex-smoker	1,403 (26.4)	11,150 (30.8)
Never-smoker	3,633 (68.4)	16,731 (46.2)
BMI, kg/m^2, *N*	5,580	36,129
Mean (SD)	28.7 (6.7)	30.2 (7.8)
<25	1,779 (31.9)	9,633 (26.7)
25–<30	1,858 (33.3)	10,353 (28.7)
⩾30	1,943 (34.8)	16,143 (44.7)
LTOCS use, *N*	4,279	36,814
n (%)	1,168 (27.3)	1,728 (4.7)
LTOCS daily dose in users, mg/d, *N*	1,076	1,698
Mean (SD)	10.2 (9.8)	6.2 (7.1)
Median (Q1, Q3)	7.5 (4.4, 12.3)	4.6 (2.0, 7.6)
Exacerbations, *N*	3,712	35,068
AAER, mean (SD)	2.2 (2.6)	0.7 (1.1)
0	1,019 (27.5)	20,144 (57.4)
1	889 (23.9)	7,100 (20.2)
2–5	1,483 (40.0)	7,688 (21.9)
⩾6	321 (8.6)	136 (0.4)
Asthma control, *N*	4,314	31,104
Uncontrolled	1,925 (44.6)	7,936 (25.5)
Partly controlled	1,419 (32.9)	17,313 (55.7)
Well controlled	970 (22.5)	5,855 (18.8)
$ppFEV_1$, %, *N*	3,543	19,124
Mean (SD)	75.5 (22.4)	76.7 (22.7)
<80%	2,058 (58.1)	10,085 (52.7)
FEV_1/FVC ratio, *N*	3,312	17,821
Mean (SD)	0.69 (0.13)	0.72 (0.14)
<0.70	1,555 (47.0)	6,568 (36.9)
Highest BEC, 10^9 cells/L, *N*	3,894	33,534
Median (Q1, Q3)	600 (300, 960)	400 (220, 600)
Latest IgE, IU/ml, *N*	2,453	4,666
Median (Q1, Q3)	201 (73, 543)	101 (28, 301)
Latest F_{ENO}, ppb, *N*	1,338	1,952
Median (Q1, Q3)	38 (18, 75)	23 (13, 47)
Biologic class initiated at index date (first biologic)		
Anti-IL5/5R	2,588 (45.5)	—
Anti-IgE	2,261 (39.7)	—
Anti-IL4Rα	807 (14.2)	—
Anti-TSLP	34 (0.6)	—

Characteristics	Biologic Initiators (*N* = 5,690)	Noninitiators (*N* = 37,218)
Country		
Argentina	27 (0.5)	6 (<0.1)
Australia	260 (4.6)	121 (0.3)
Bulgaria	50 (0.9)	164 (0.4)
Canada	387 (6.8)	46 (0.1)
Colombia	179 (3.1)	151 (0.4)
Greece	77 (1.4)	31 (0.1)
Italy	1,381 (24.3)	251 (0.7)
Japan	130 (2.3)	72 (0.2)
Kuwait	217 (3.8)	12 (<0.1)
Mexico	228 (4.0)	8 (<0.1)
Saudi Arabia	118 (2.1)	45 (0.1)
Singapore	44 (0.8)	91 (0.2)
South Korea	37 (0.7)	44 (0.1)
Taiwan	99 (1.7)	139 (0.4)
United Arab Emirates	117 (2.1)	103 (0.3)
United States	929 (16.3)	2,868 (7.7)
United Kingdom	1,410 (24.8)	33,066 (88.8)

Association between biologic initiation and risk of OCS-related adverse outcomes

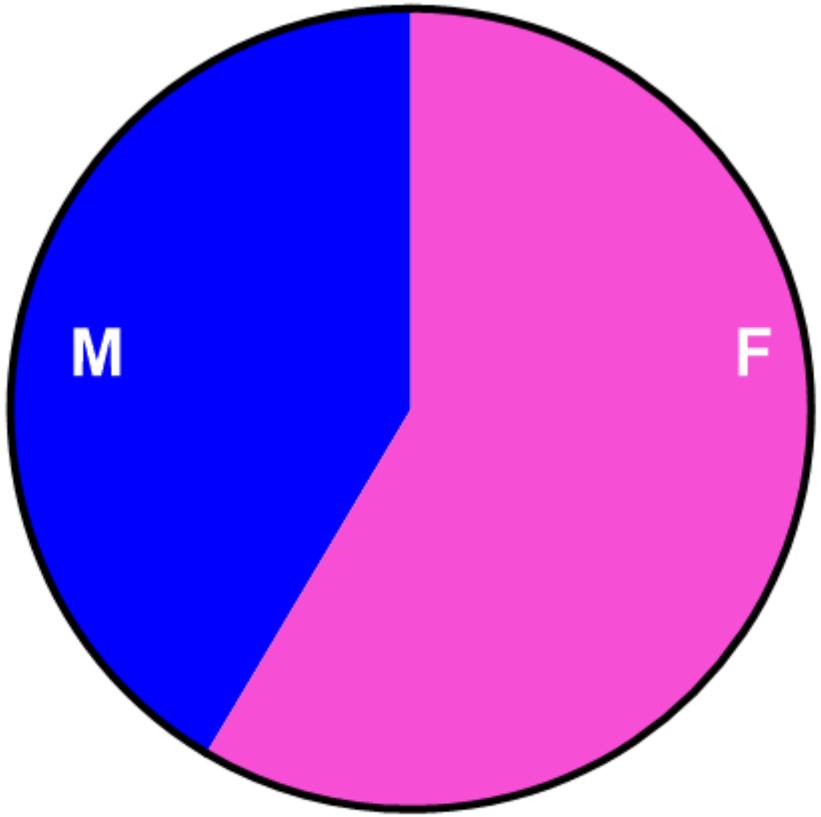
	Group	N (total)	N (events)	HR (95% CI)	p-value
Any event	Non-initiators	36,845	7,062	Ref.	0.002
	Bx initiators	5,633	736	0.82 (0.72-0.93)	



Hazard ratios (and 95% CIs) of new-onset events

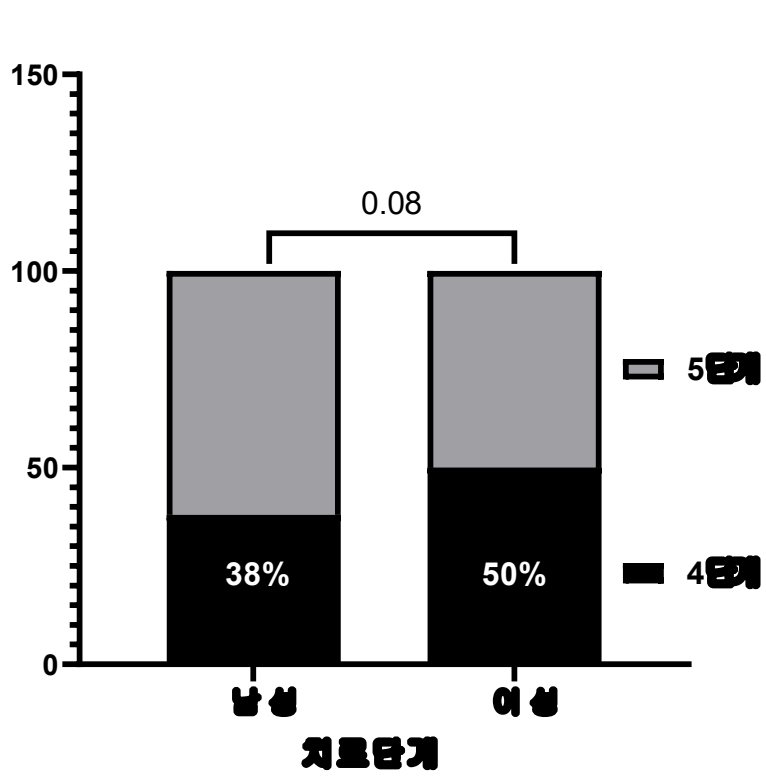
Contents

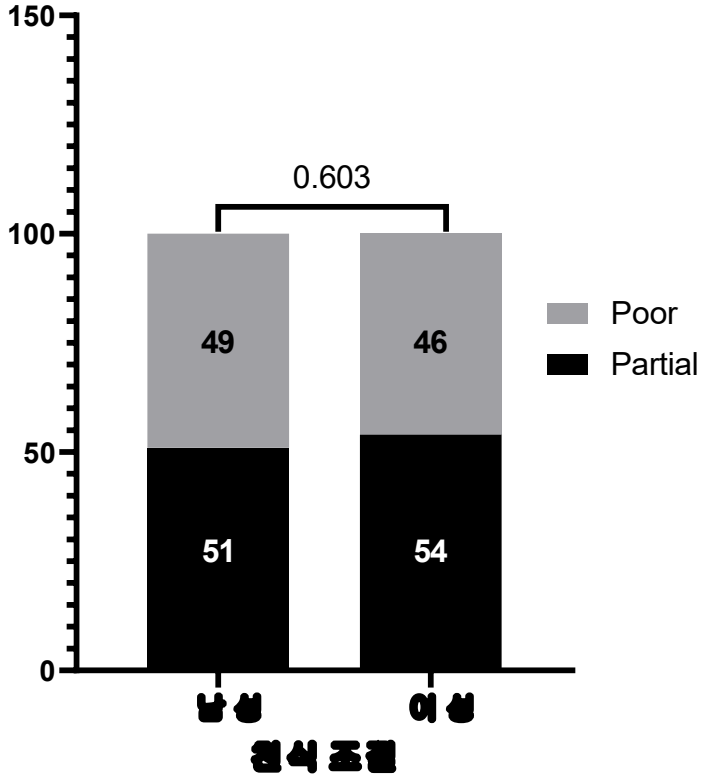
Baseline chracteristics

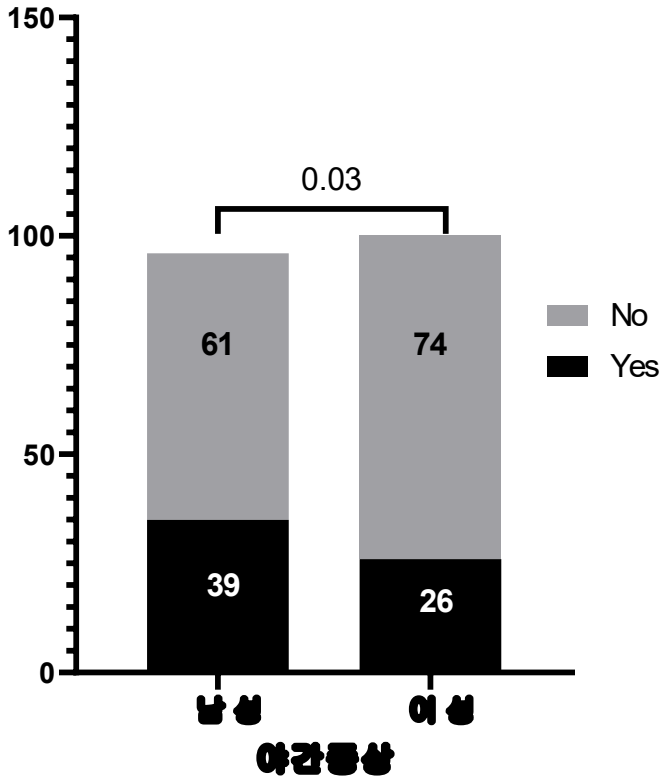


Total=205, male=85(41.5), female 120 (58.5)

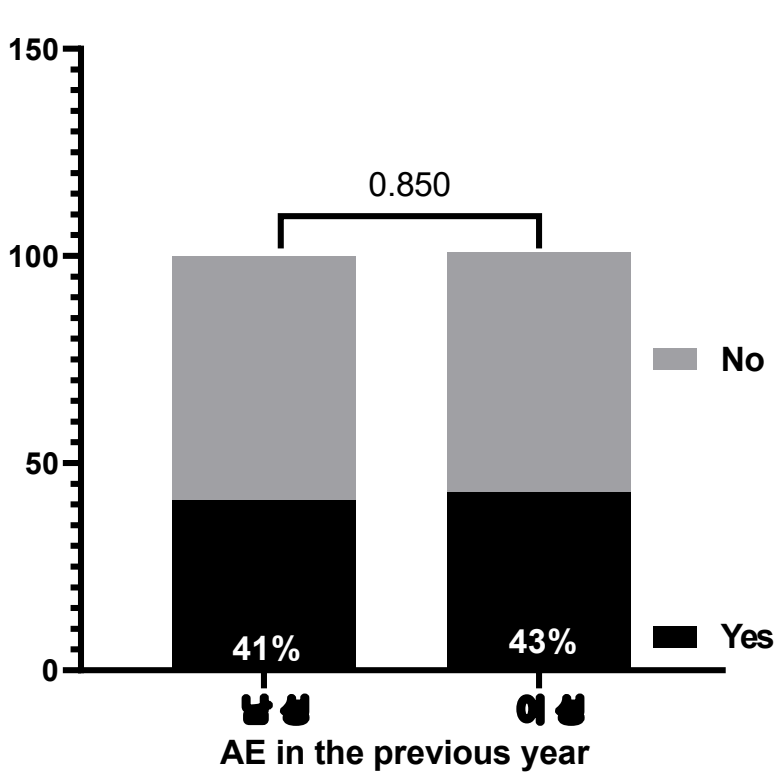
Sex and Athma control

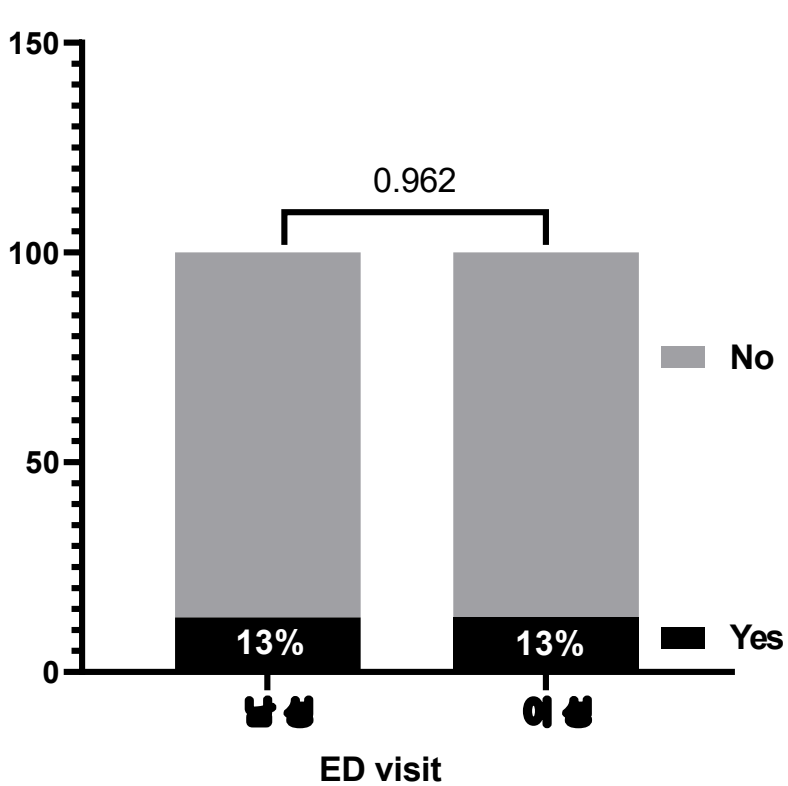


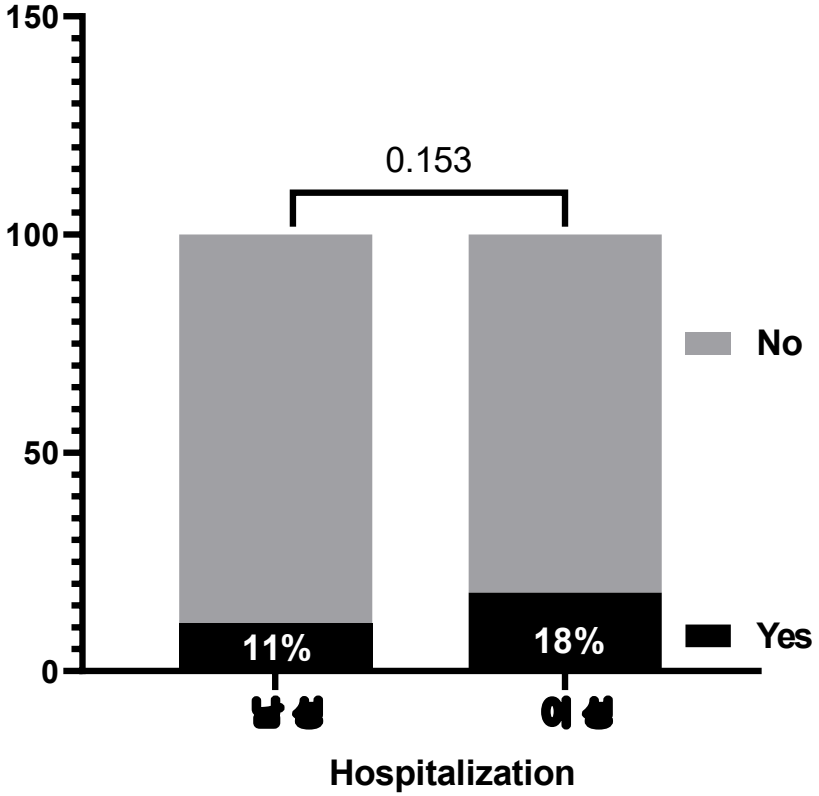




Sex and Acute Exacerbation



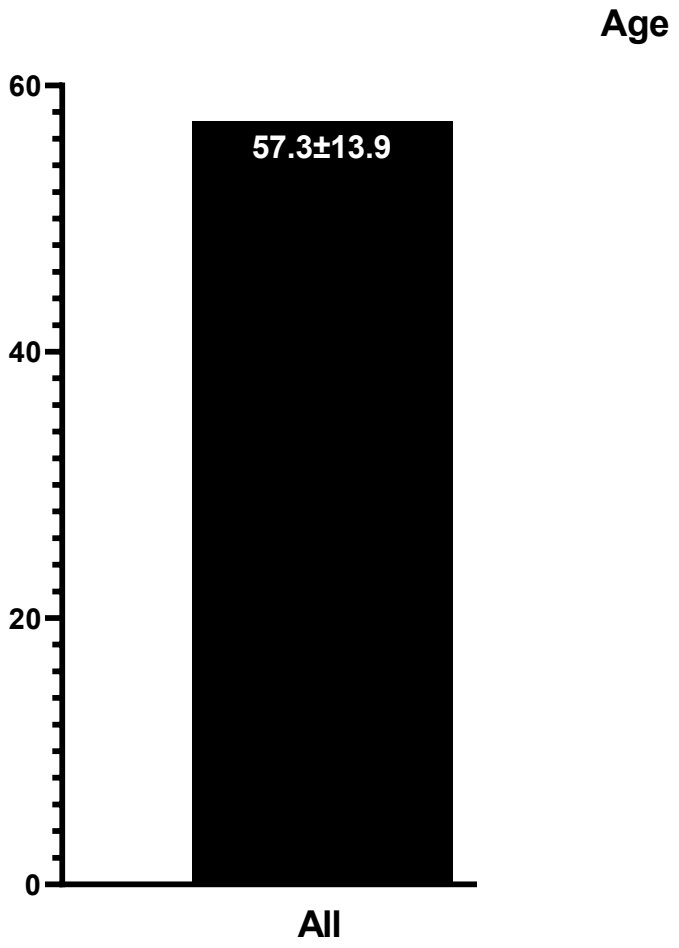




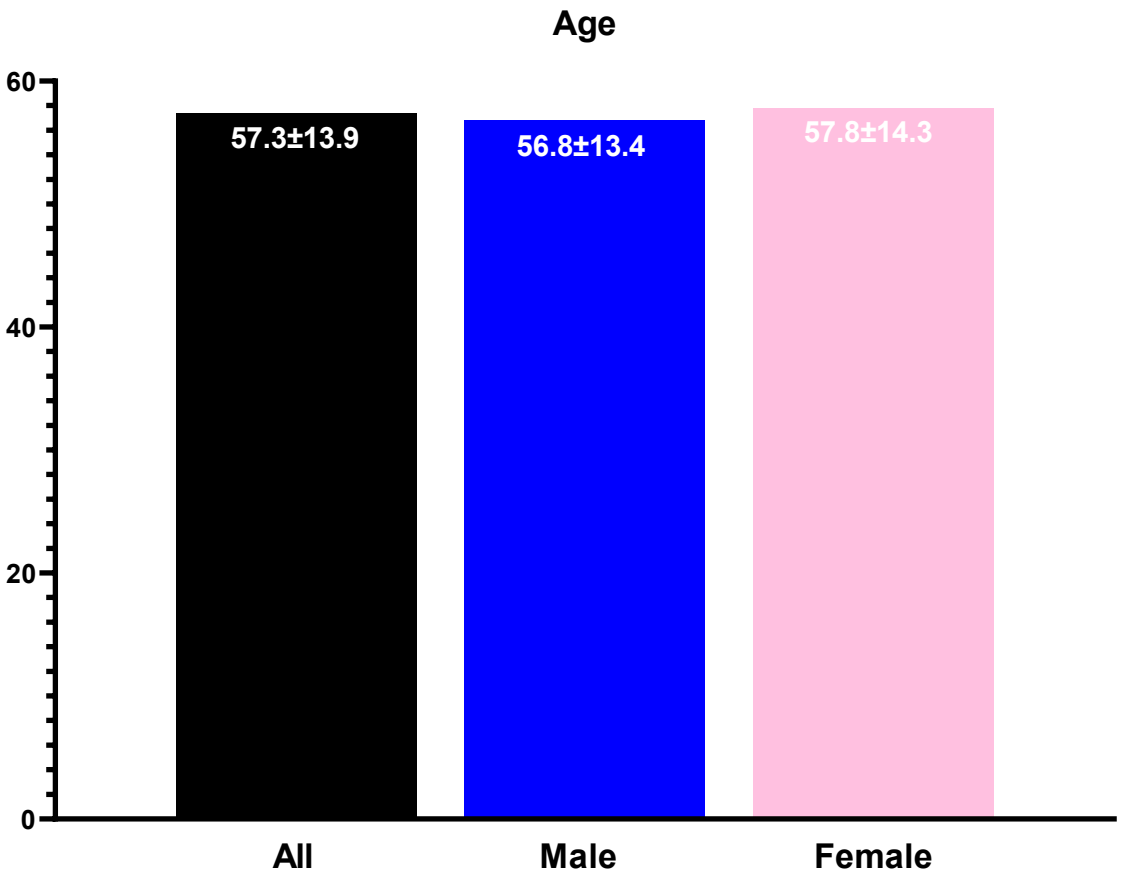
Sex and Pulmonary function Test

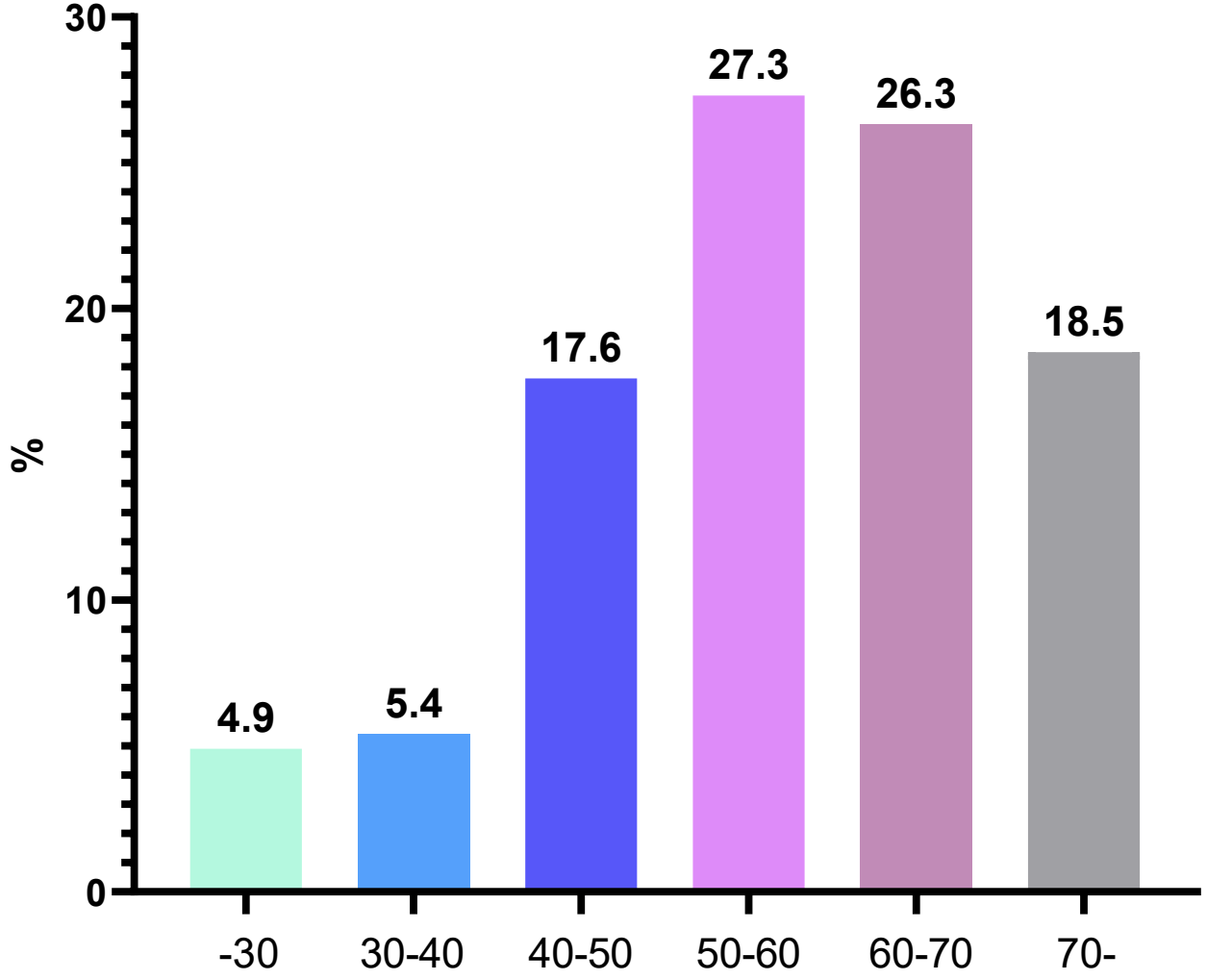
	Pre-bronchodilator			Post bronchodilator		
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC
Sex						
Male (83)	**67.3±21.3**	**92.1±15.2**	**58.3±15.6**	**68.2±20.6**	**92.2±15.2**	**59.4±15.6**
Female (115)	**79.6±22.9**	**102.5±20.3**	**64.7±13.2**	**81.2±22.9**	**102.9±20.9**	**65.9±13.8**
	<0.001	<0.001	<0.002	<0.001	0.001	0.006

Baseline chracteristics: Age

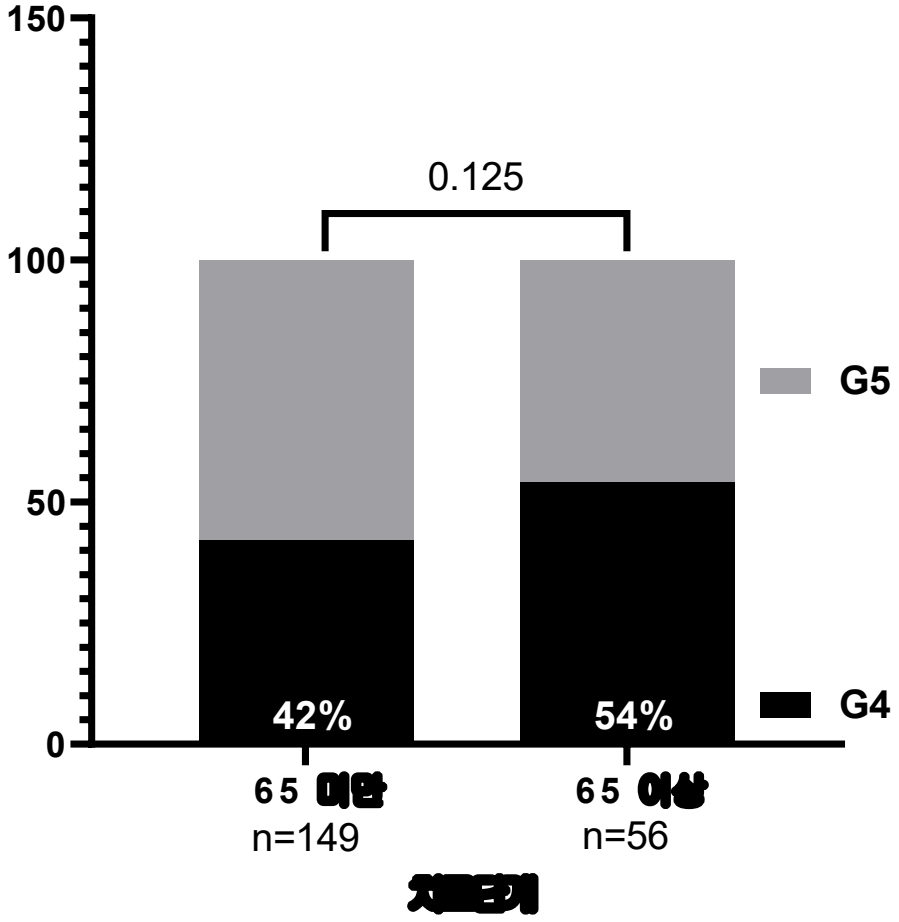


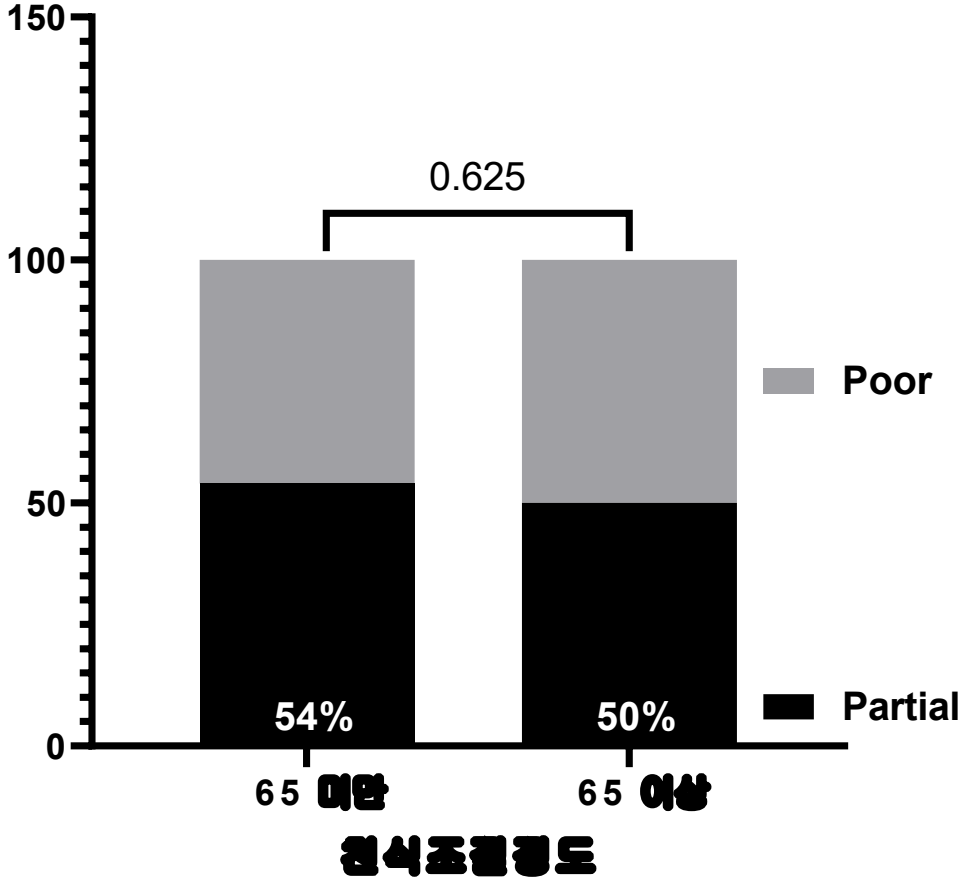
Baseline chracteristics: Age



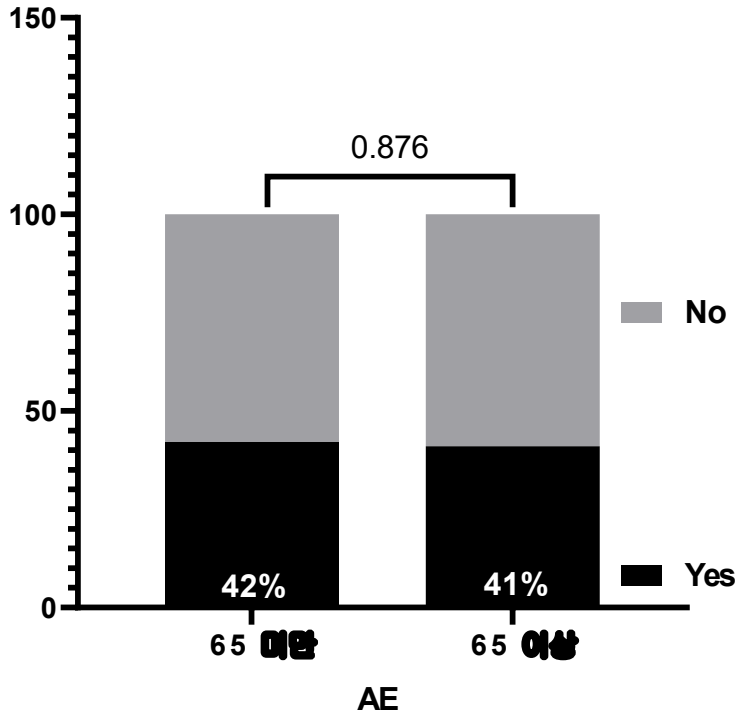


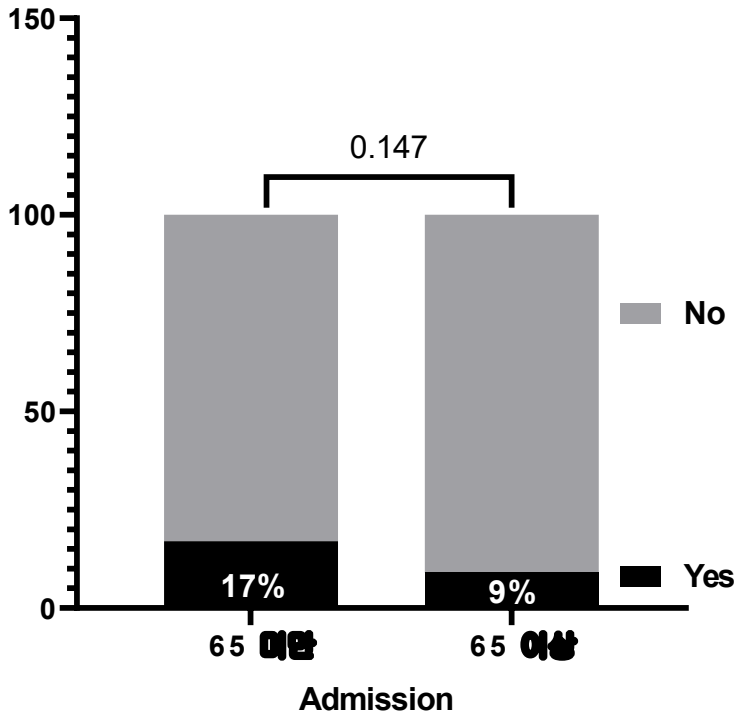
Elederly and Asthma Control

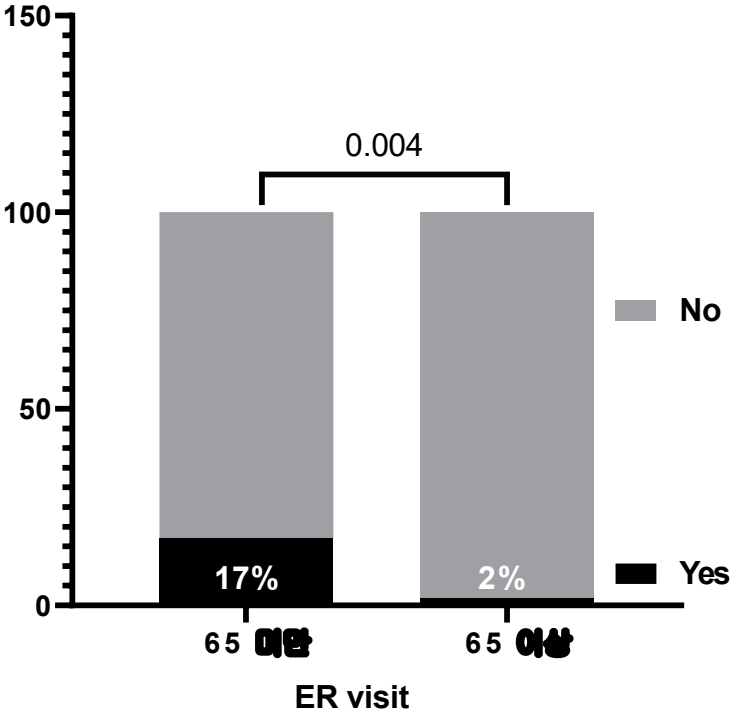




Elederly and Acute Exacerbation

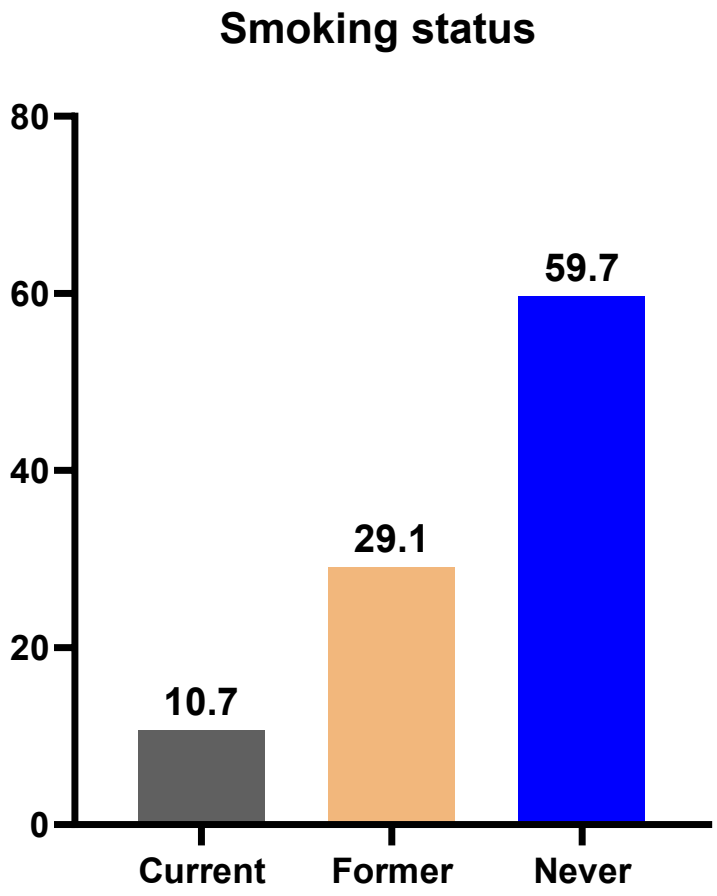


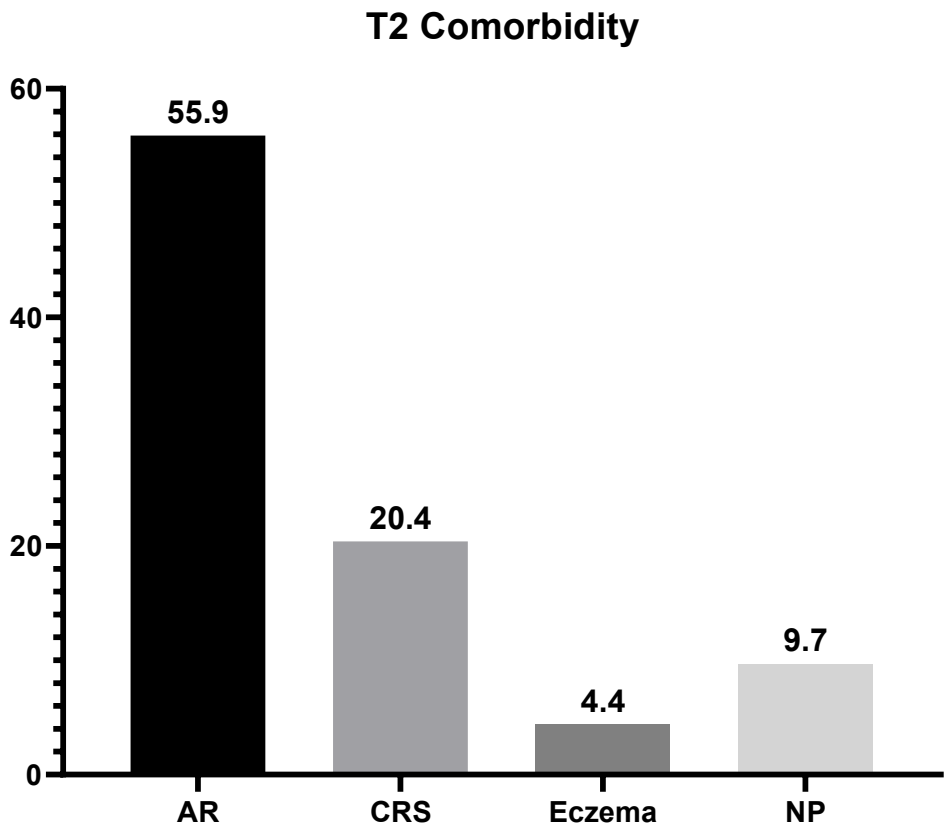




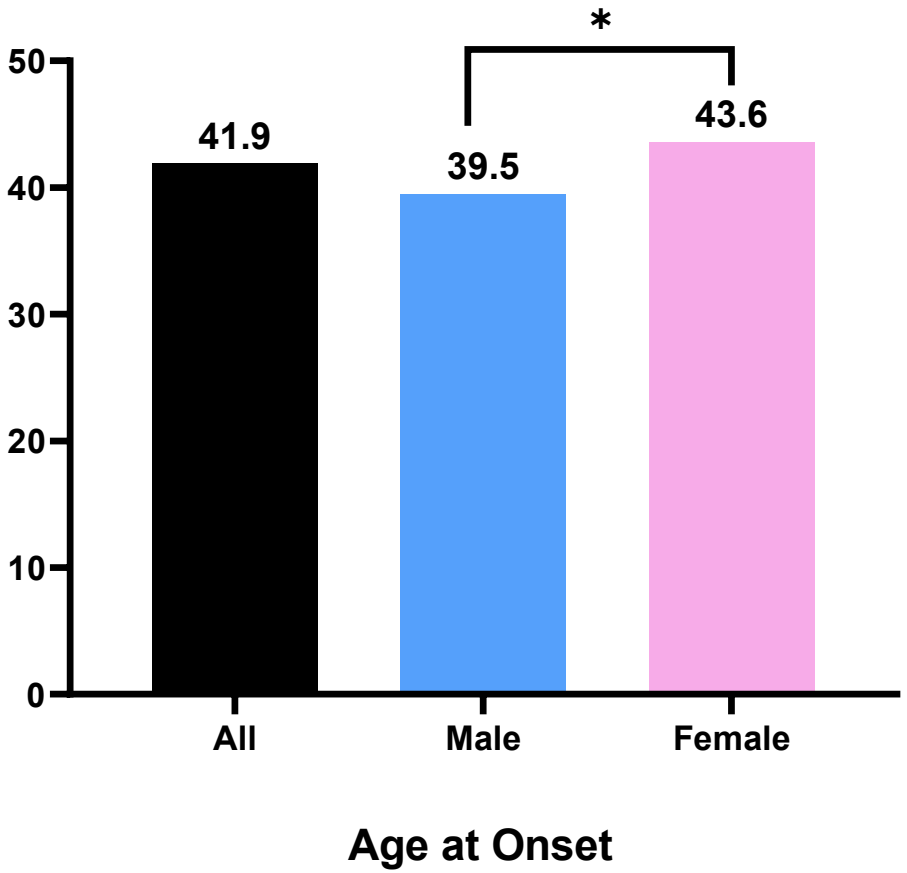
Elederly and Pulmonary function test

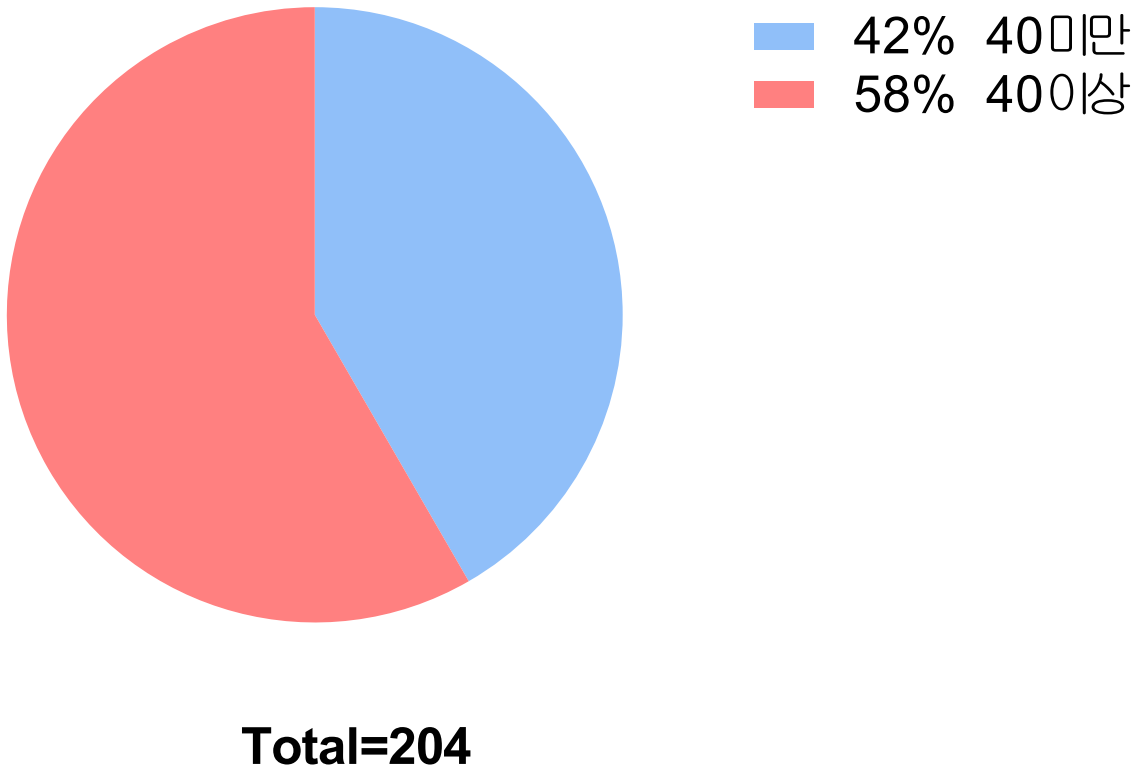
	Pre-bronchodilator			Post bronchodilator		
	FEV_1	**FVC**	**FEV_1/FVC**	**FEV_1**	**FVC**	**FEV_1/FVC**
Age						
<65 (100)	76.4±22.9	100.6±18.3	62.2±15.0	77.4±22.7	100.4±18.7	63.5±15.6
≥65 (94)	**69.1±22.7**	**91.2±19.6**	61.5±13.4	71.6±23.2	**92.8±21.0**	62.7±12.6
	0.050	0.003	0.779	0.164	0.030	0.759


Smoking status
80
60
40
20
0
10.7
29.1
59.7
Current
Former
Never

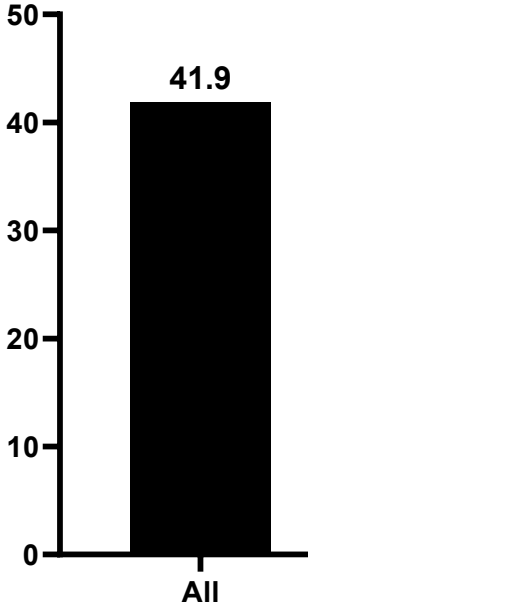

T2 Comorbidity
60
40
20
0
55.9
20.4
4.4
9.7
AR
CRS
Eczema
NP

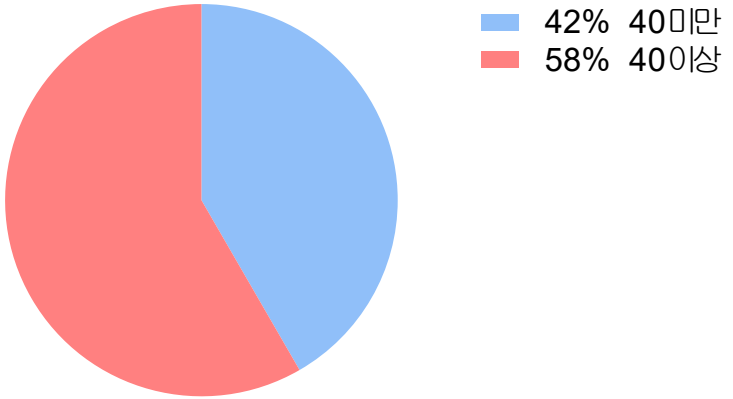
Age at onset of asthma

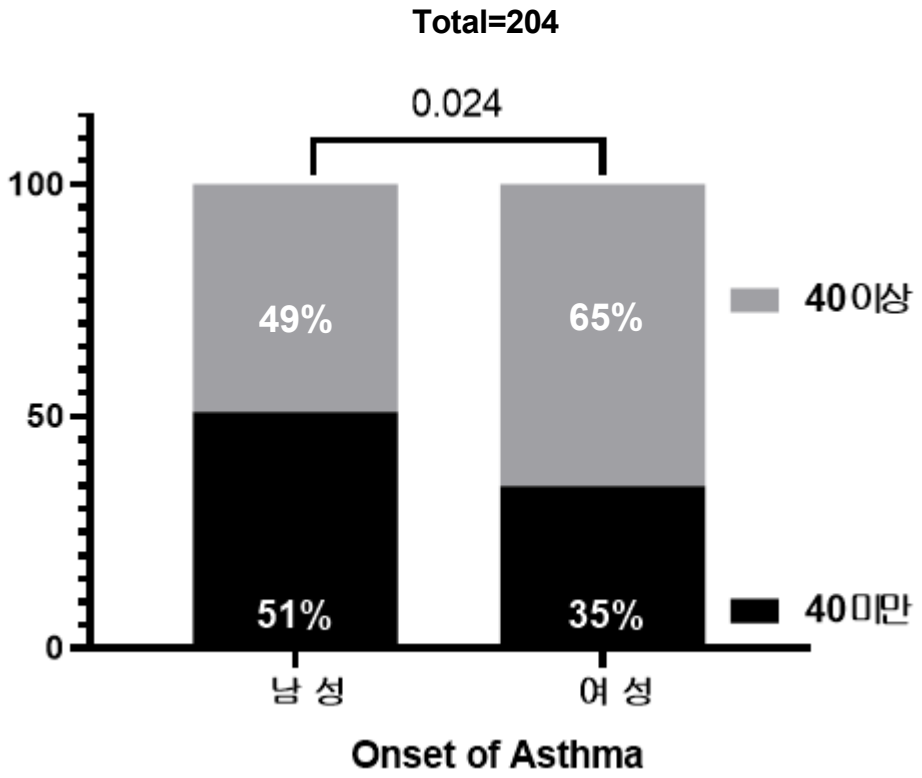




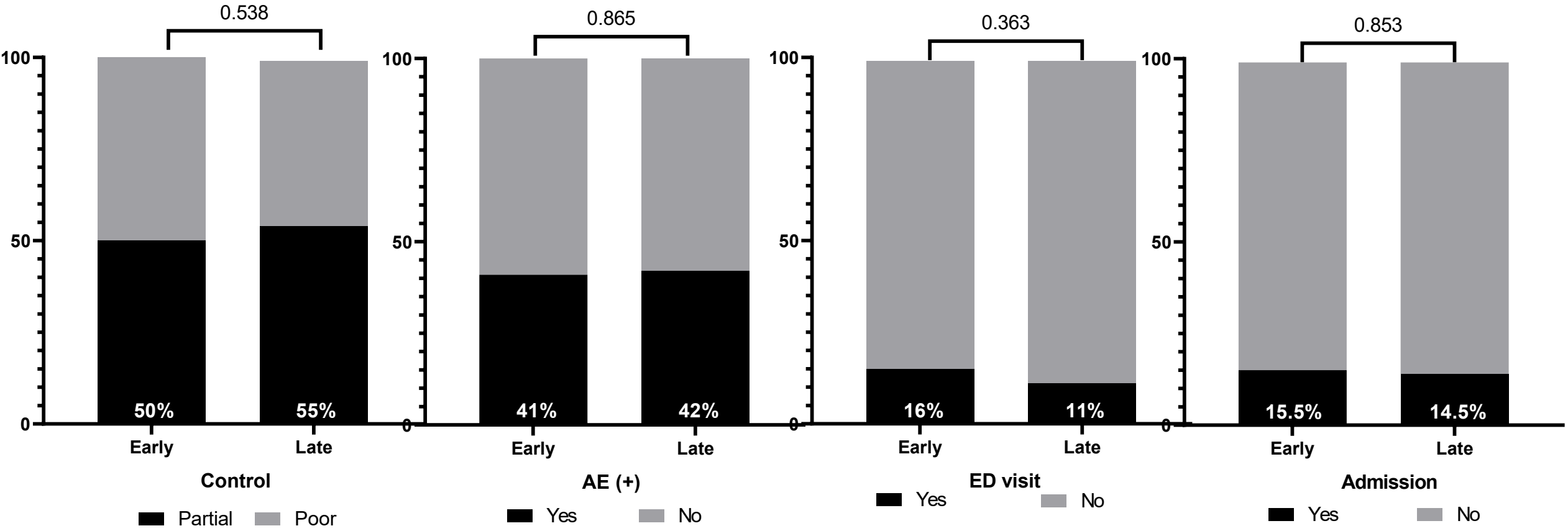
Age at onset of asthma







Age at onset of asthma

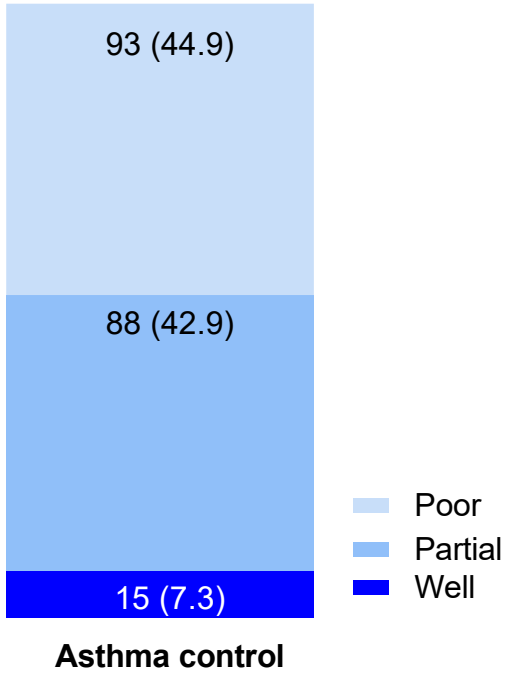


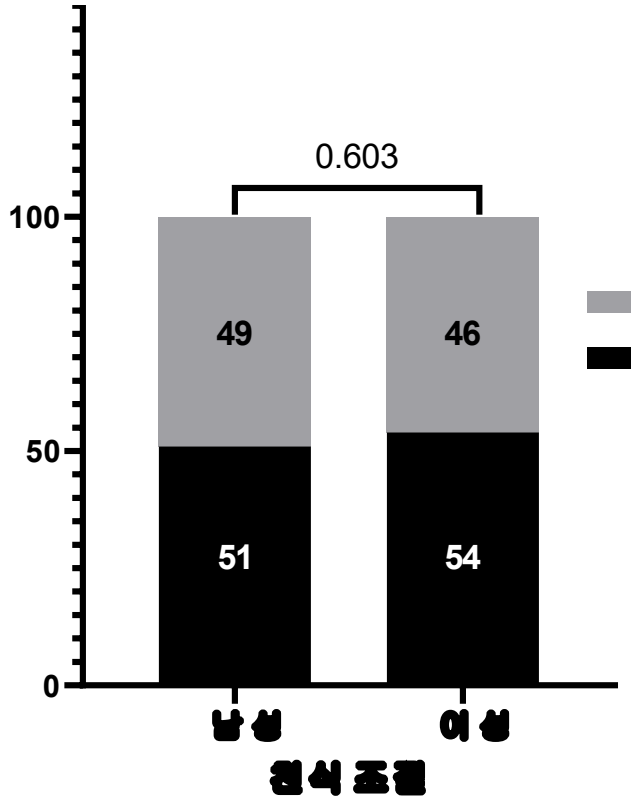
Asthma control status

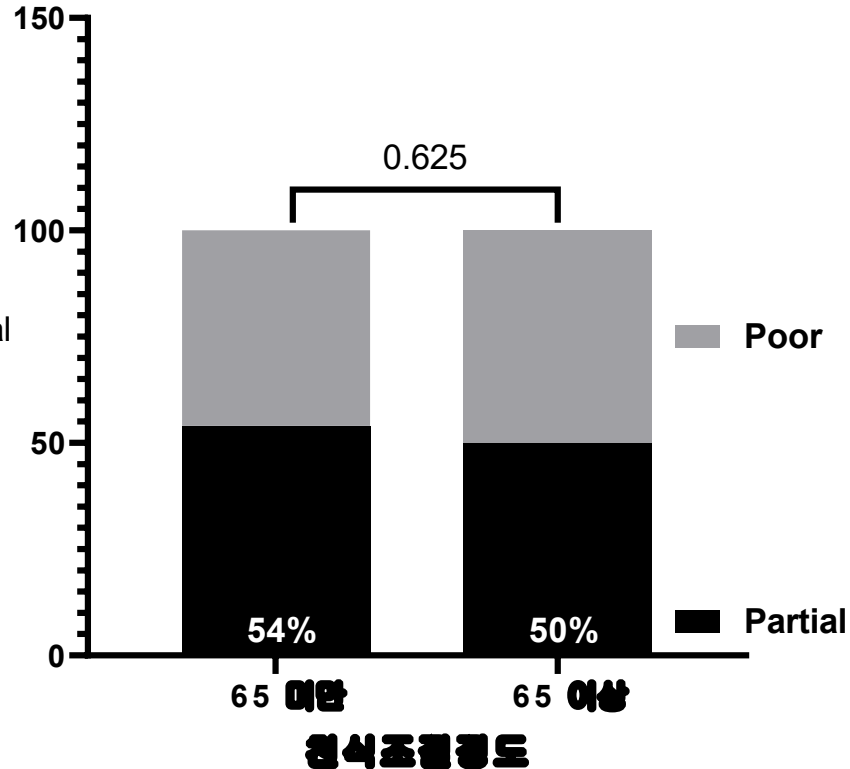
A. Recent asthma symptom control (but also ask the patient/caregiver about the whole period since last review#)

In the past 4 weeks, has the patient had:

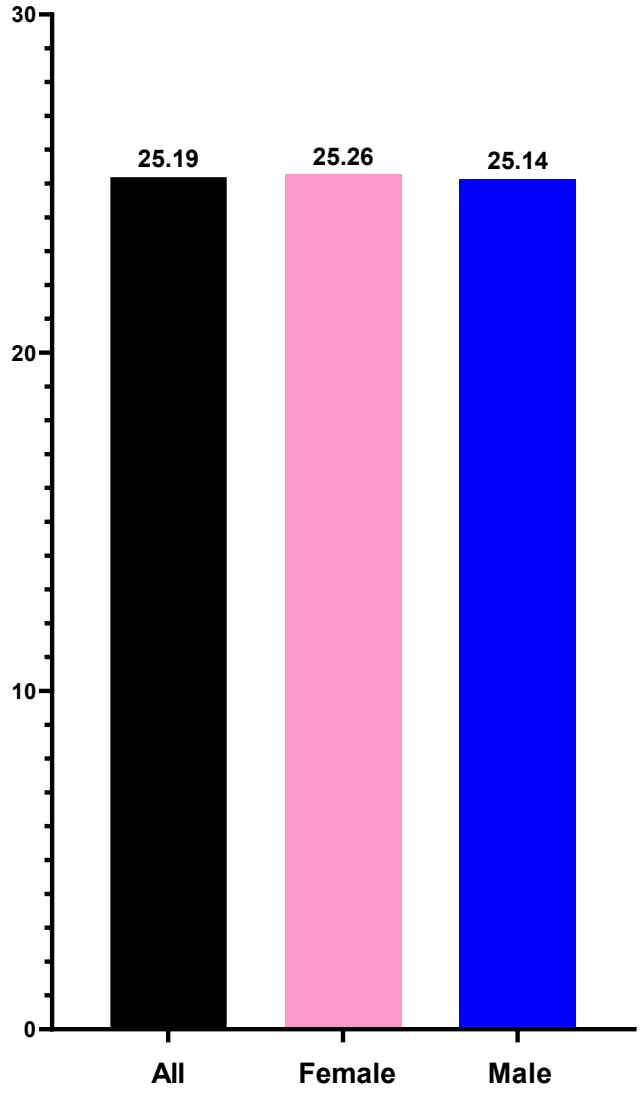
		Well controlled	Partly controlled	Uncontrolled
• Daytime asthma symptoms more than twice/week?	Yes☐ No☐			
• Any night waking due to asthma?	Yes☐ No☐	None of these	1–2 of these	3–4 of these
• SABA* reliever for symptoms more than twice/week?	Yes☐ No☐			
• Any activity limitation due to asthma?	Yes☐ No☐			



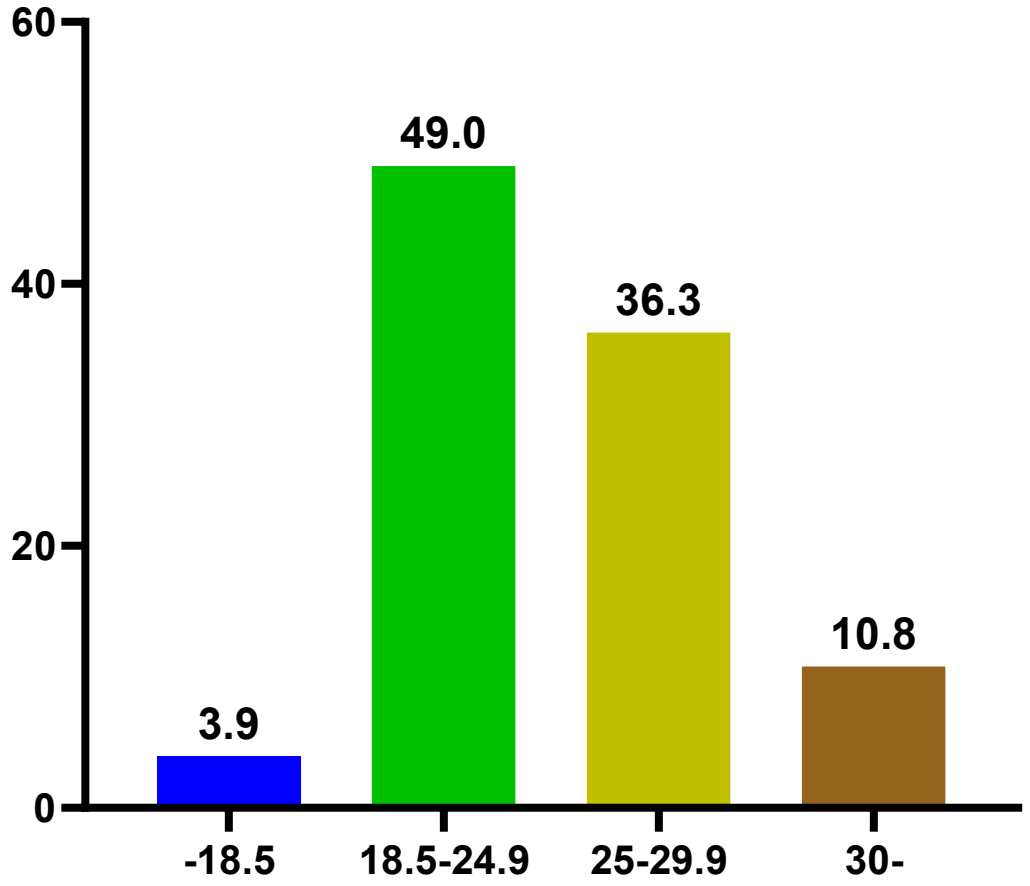




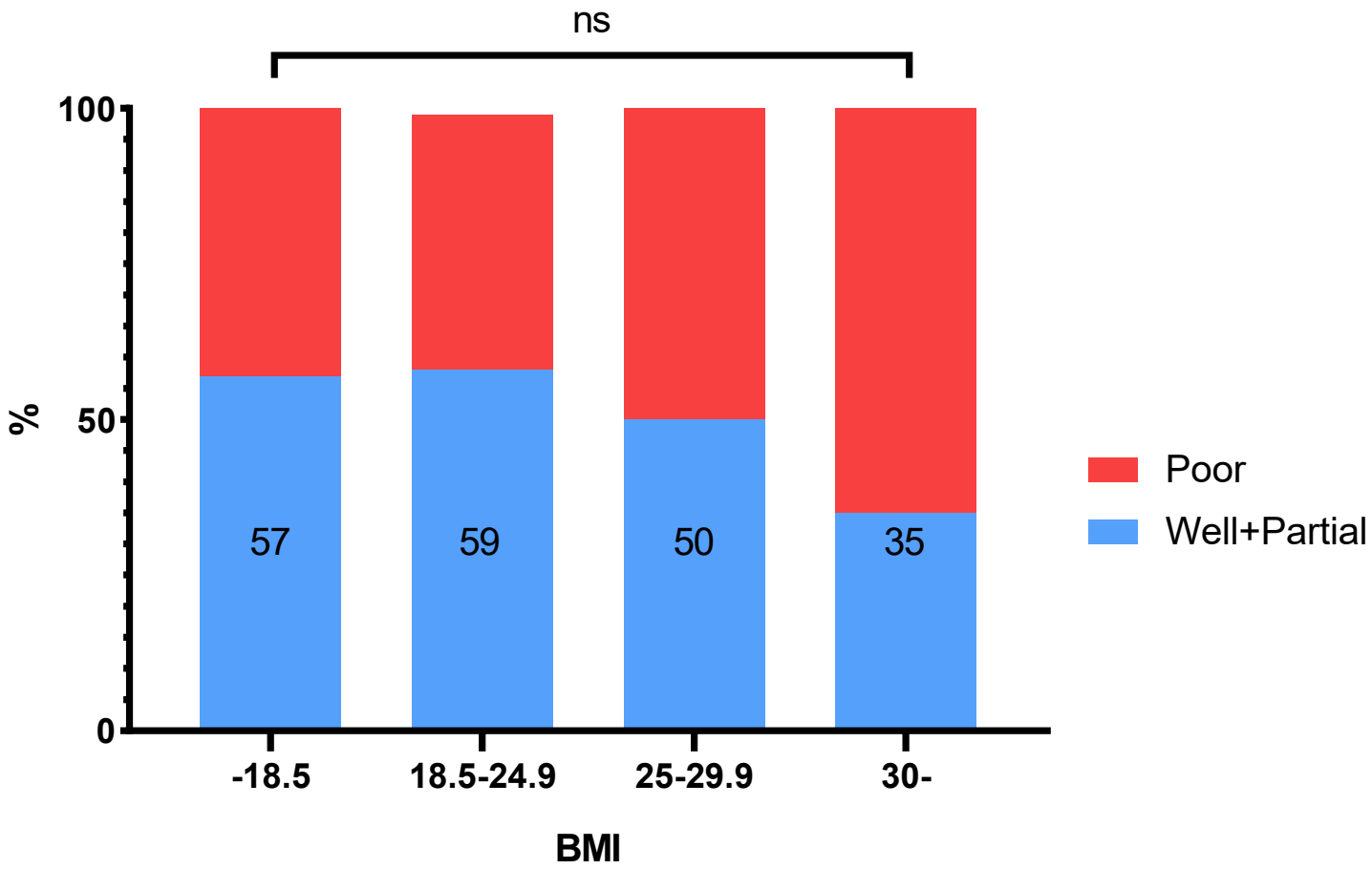
Asthma control and BMI



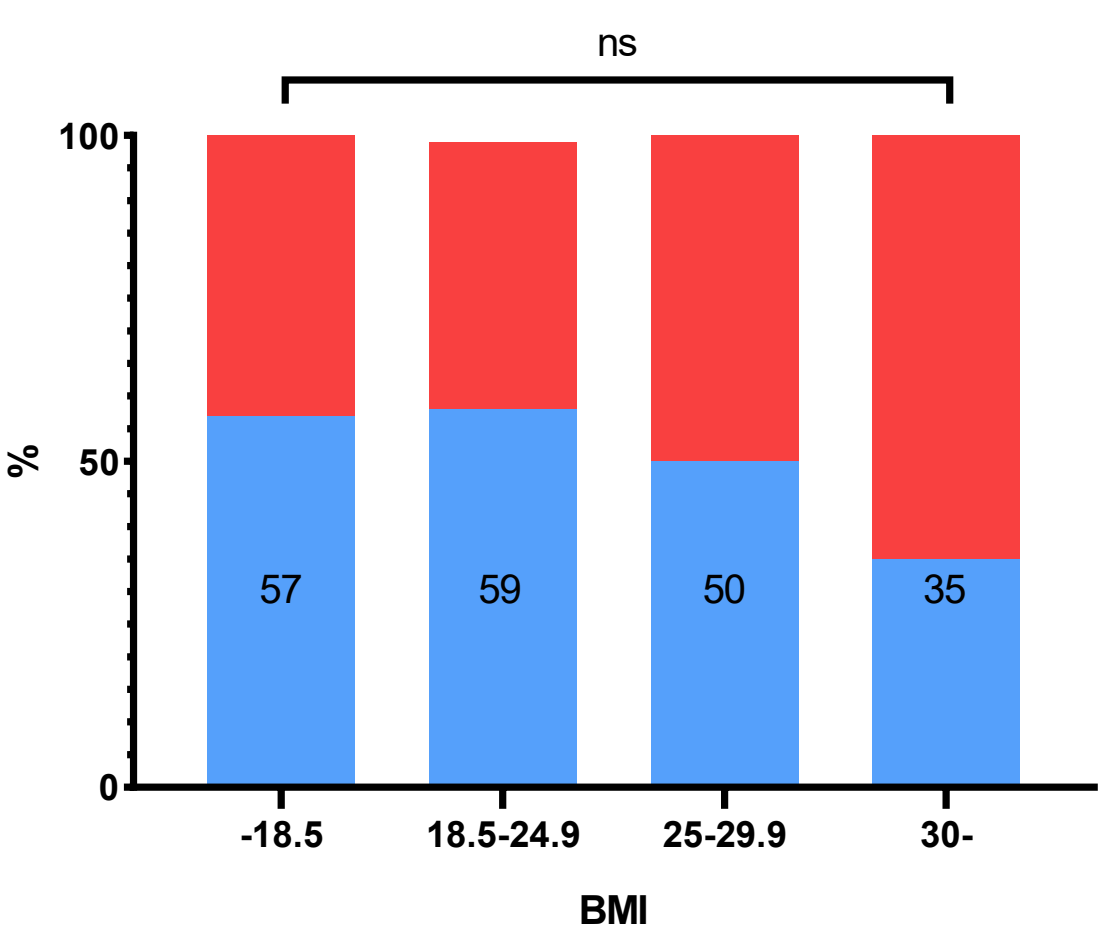
BMI

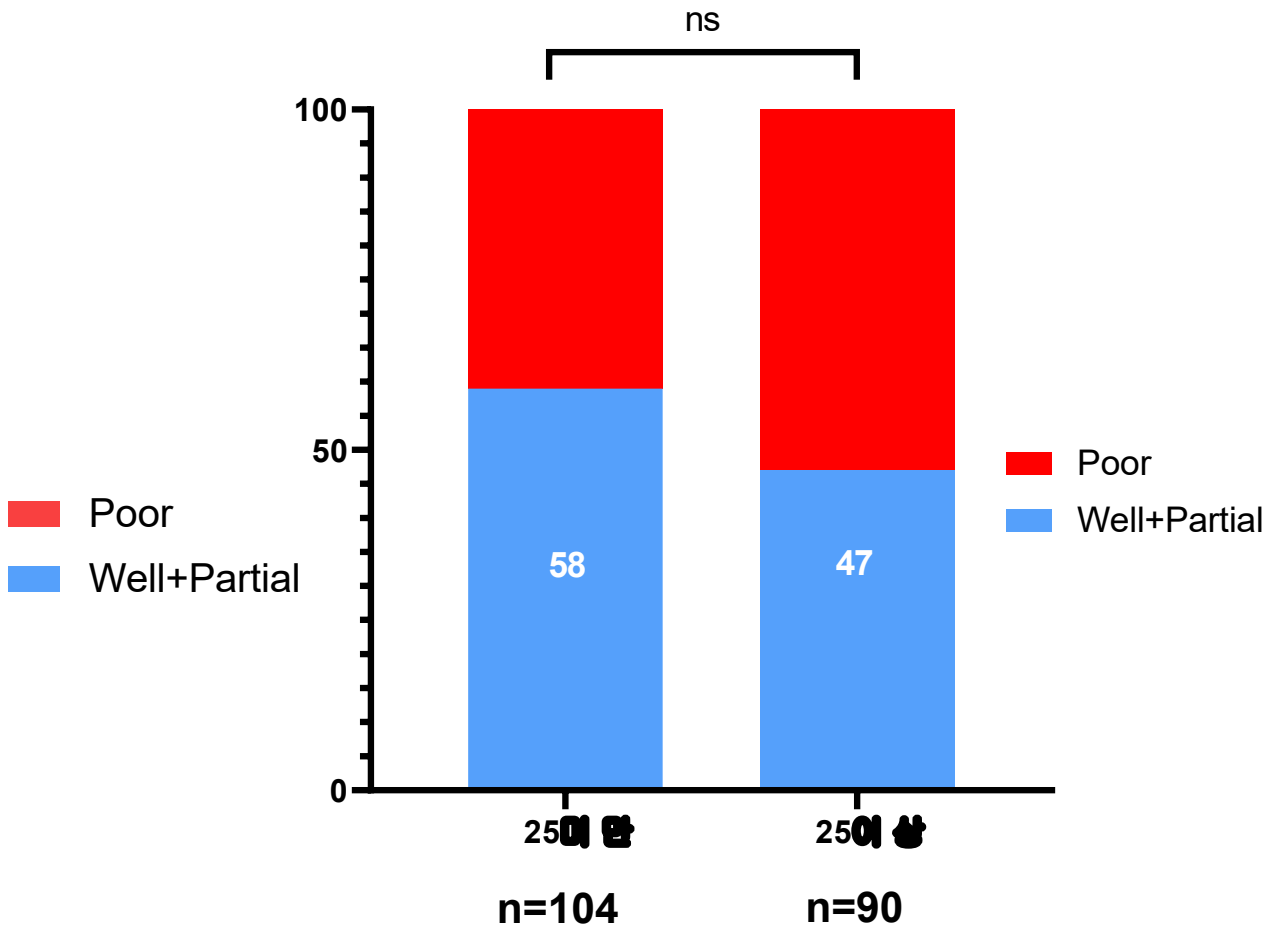


Asthma control and BMI

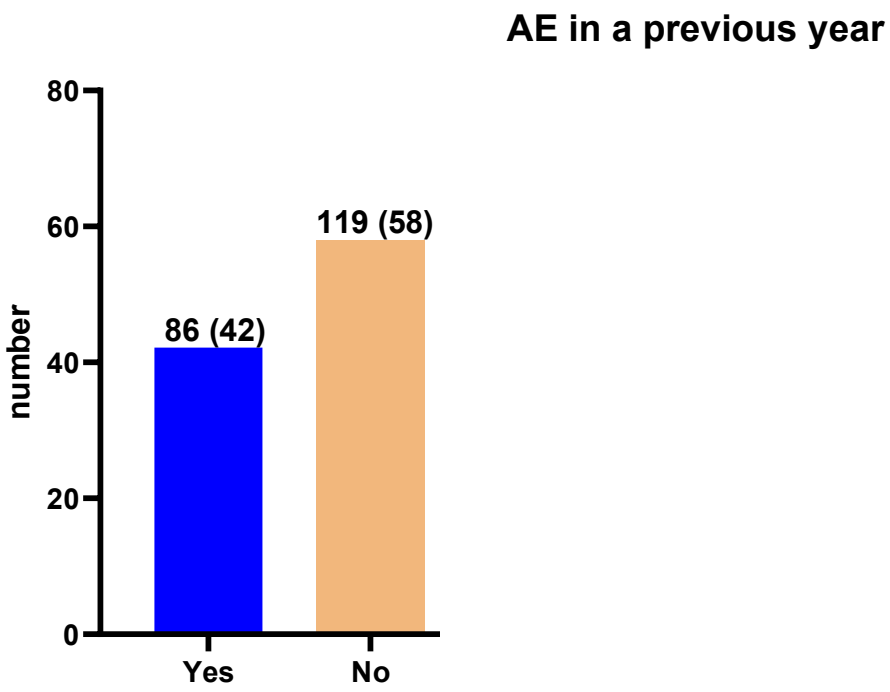


Asthma control and BMI

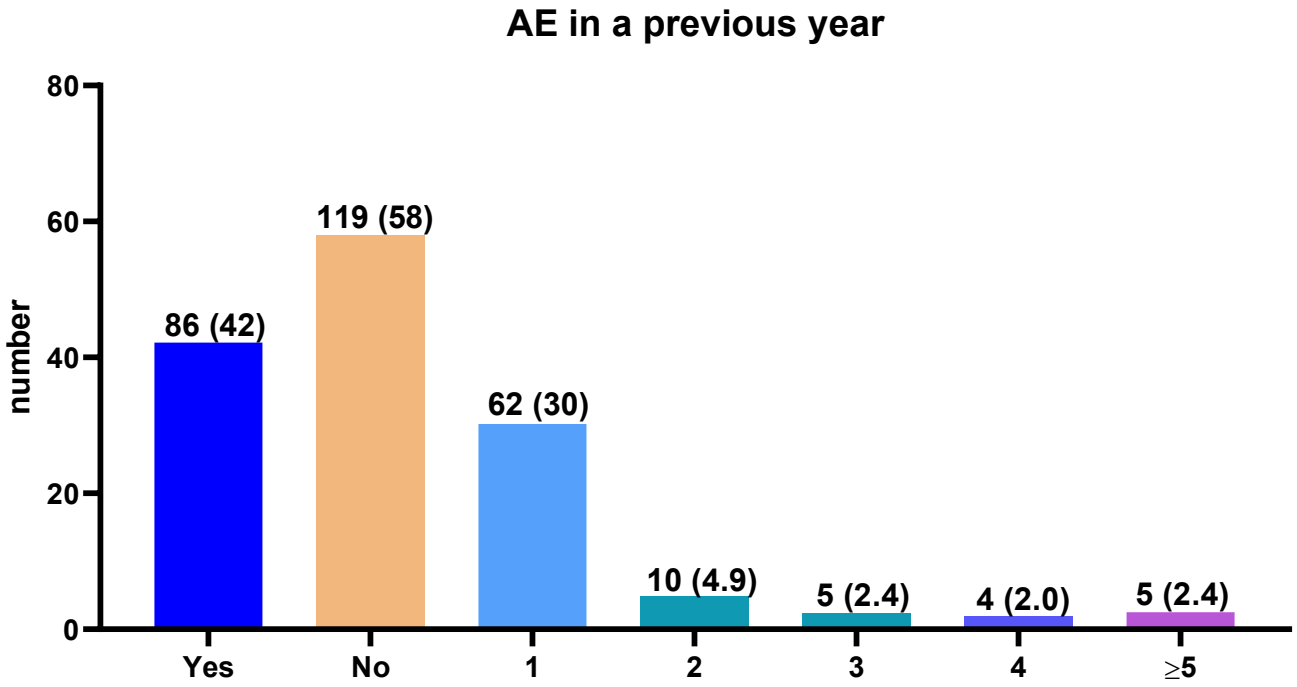


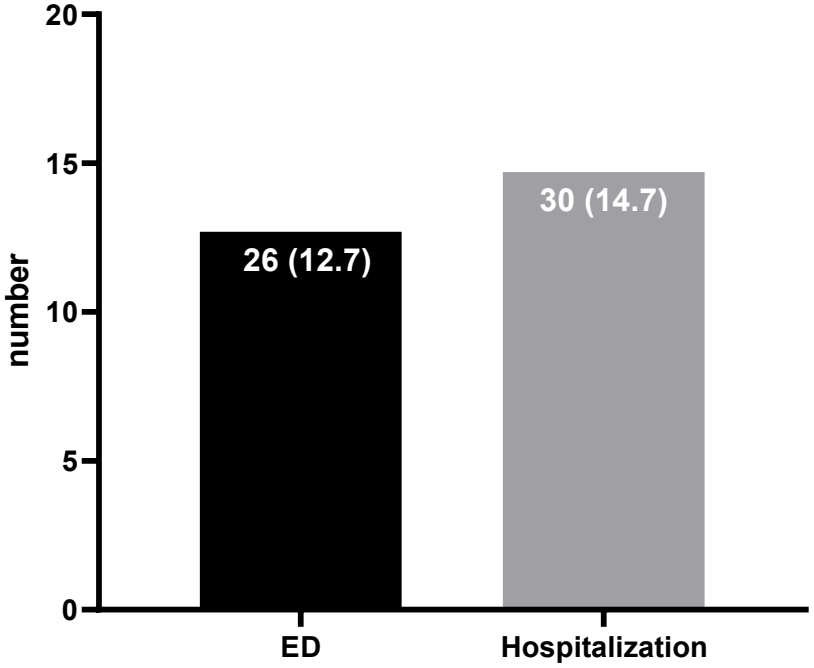


Asthma and AE



Asthma and AE





Asthma and Lung function

	Pre-bronchodilator			Post bronchodilator		
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC
All	74.5±23.0	98.1±19.1	62.0 ±14.6	75.9±22.9	98.5±19.5	63.3±14.8
Step						
GINA 4 (89)	77.5±22.6	100.5±18.7	63.2±14.3	77.0±22.3	100.8±20.1	63.0±15.0
GINA 5(109)	72.0±23.1	96.2±19.3	61.0±14.8	75.1±23.3	96.9±18.9	63.5±14.8
	0.092	0.115	0.279	0.596	0.208	0.855
Smoking						
Ever (80)	**69.7±24.8**	96.1±17.9	**58.0±15.9**	**70.3±23.8**	96.0±18.2	**59.2±15.9**
Never (117)	**77.8±21.3**	99.6±19.8	**64.7±13.0**	**79.9±21.6**	100.4±20.2	**66.1±13.5**
	0.016	0.199	0.002	0.008	0.158	0.004
Sex						
Male (83)	**67.3±21.3**	**92.1±15.2**	**58.3±15.6**	**68.2±20.6**	**92.2±15.2**	**59.4±15.6**
Female (115)	**79.6±22.9**	**102.5±20.3**	**64.7±13.2**	**81.2±22.9**	**102.9±20.9**	**65.9±13.8**
	<0.001	<0.001	<0.002	<0.001	0.001	0.006
Control						
Well or partial (102)	**78.1±21.5**	100.9±18.4	63.6±14.4	76.8±21.1	99.5±18.0	63.6±15.1
Poor (86)	**69.9±25.0**	94.6±20.2	59.9±15.1	74.1±25.4	97.1±21.7	62.5±15.1
	0.017	0.027	0.081	0.466	0.453	0.624
BMI						
<25 (100)	**71.2±22.7**	96.7±20.2	60.7±15.1	72.9±22.9	97.98±21.3	61.5±15.4
≥25 (94)	**78.1±22.9**	99.7±17.8	63.4±14.0	79.3±22.5	99.13±17.3	65.3±14.0
	0.035	0.261	.0160	0.078	0.708	0.106
Age						
<65 (100)	76.4±22.9	100.6±18.3	62.2±15.0	77.4±22.7	100.4±18.7	63.5±15.6
≥65 (94)	**69.1±22.7**	**91.2±19.6**	61.5±13.4	71.6±23.2	**92.8±21.0**	62.7±12.6
	0.050	0.003	0.779	0.164	0.030	0.759

Asthma and Lung function

	Pre-bronchodilator			Post bronchodilator		
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC
All	74.5±23.0	98.1±19.1	62.0 ±14.6	75.9±22.9	98.5±19.5	63.3±14.8
Step						
GINA 4 (89)	77.5±22.6	100.5±18.7	63.2±14.3	77.0±22.3	100.8±20.1	63.0±15.0
GINA 5(109)	72.0±23.1	96.2±19.3	61.0±14.8	75.1±23.3	96.9±18.9	63.5±14.8
	0.092	0.115	0.279	0.596	0.208	0.855
Smoking						
Ever (80)	**69.7±24.8**	96.1±17.9	**58.0±15.9**	**70.3±23.8**	96.0±18.2	**59.2±15.9**
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	0.016	0.199	0.002	0.008	0.158	0.004
Sex						
Male (83)	**67.3±21.3**	**92.1±15.2**	**58.3±15.6**	**68.2±20.6**	**92.2±15.2**	**59.4±15.6**
Female (115)	**79.6±22.9**	**102.5±20.3**	**64.7±13.2**	**81.2±22.9**	**102.9±20.9**	**65.9±13.8**
	<0.001	<0.001	<0.002	<0.001	0.001	0.006
Control						
Well or partial (102)	**78.1±21.5**	100.9±18.4	63.6±14.4	76.8±21.1	99.5±18.0	63.6±15.1
Poor (86)	**69.9±25.0**	94.6±20.2	59.9±15.1	74.1±25.4	97.1±21.7	62.5±15.1
	0.017	0.027	0.081	0.466	0.453	0.624
BMI						
<25 (100)	**71.2±22.7**	96.7±20.2	60.7±15.1	72.9±22.9	97.98±21.3	61.5±15.4
≥25 (94)	**78.1±22.9**	99.7±17.8	63.4±14.0	79.3±22.5	99.13±17.3	65.3±14.0
	0.035	0.261	.0160	0.078	0.708	0.106
Age						
<65 (100)	76.4±22.9	100.6±18.3	62.2±15.0	77.4±22.7	100.4±18.7	63.5±15.6
≥65 (94)	**69.1±22.7**	**91.2±19.6**	61.5±13.4	71.6±23.2	**92.8±21.0**	62.7±12.6
	0.050	0.003	0.779	0.164	0.030	0.759

Asthma and Lung function

	Pre-bronchodilator			Post bronchodilator		
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC
All	74.5±23.0	98.1±19.1	62.0 ±14.6	75.9±22.9	98.5±19.5	63.3±14.8
Step						
GINA 4 (89)	77.5±22.6	100.5±18.7	63.2±14.3	77.0±22.3	100.8±20.1	63.0±15.0
GINA 5(109)	72.0±23.1	96.2±19.3	61.0±14.8	75.1±23.3	96.9±18.9	63.5±14.8
	0.092	0.115	0.279	0.596	0.208	0.855
Smoking						
Ever (80)	**69.7±24.8**	96.1±17.9	**58.0±15.9**	**70.3±23.8**	96.0±18.2	**59.2±15.9**
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	0.016	0.199	0.002	0.008	0.158	0.004
Sex						
Male (83)	**67.3±21.3**	**92.1±15.2**	**58.3±15.6**	**68.2±20.6**	**92.2±15.2**	**59.4±15.6**
Female (115)	**79.6±22.9**	**102.5±20.3**	**64.7±13.2**	**81.2±22.9**	**102.9±20.9**	**65.9±13.8**
	<0.001	<0.001	<0.002	<0.001	0.001	0.006
Control						
Well or partial (102)	**78.1±21.5**	100.9±18.4	63.6±14.4	76.8±21.1	99.5±18.0	63.6±15.1
Poor (86)	**69.9±25.0**	94.6±20.2	59.9±15.1	74.1±25.4	97.1±21.7	62.5±15.1
	0.017	0.027	0.081	0.466	0.453	0.624
BMI						
<25 (100)	**71.2±22.7**	96.7±20.2	60.7±15.1	72.9±22.9	97.98±21.3	61.5±15.4
≥25 (94)	**78.1±22.9**	99.7±17.8	63.4±14.0	79.3±22.5	99.13±17.3	65.3±14.0
	0.035	0.261	.0160	0.078	0.708	0.106
Age						
<65 (100)	76.4±22.9	100.6±18.3	62.2±15.0	77.4±22.7	100.4±18.7	63.5±15.6
≥65 (94)	**69.1±22.7**	**91.2±19.6**	61.5±13.4	71.6±23.2	**92.8±21.0**	62.7±12.6
	0.050	0.003	0.779	0.164	0.030	0.759

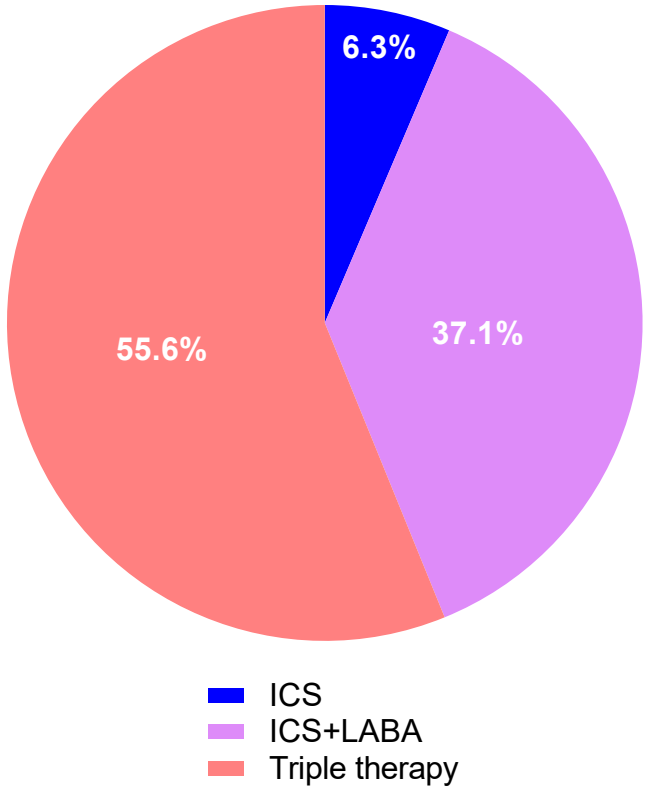
Asthma and Lung function

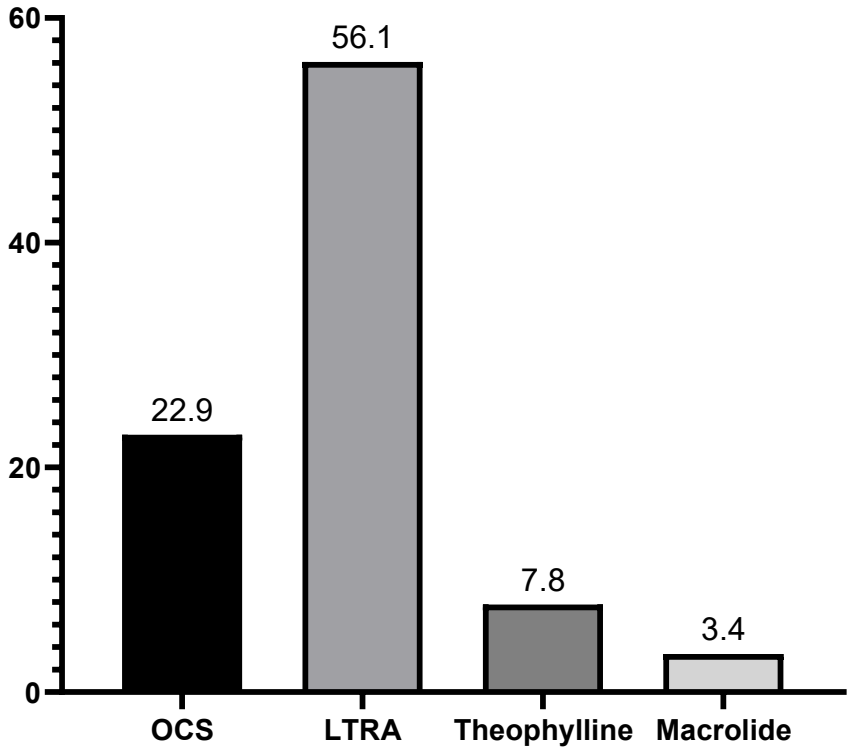
	Pre-bronchodilator			Post bronchodilator		
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC
All	74.5±23.0	98.1±19.1	62.0 ±14.6	75.9±22.9	98.5±19.5	63.3±14.8
Step						
GINA 4 (89)	77.5±22.6	100.5±18.7	63.2±14.3	77.0±22.3	100.8±20.1	63.0±15.0
GINA 5(109)	72.0±23.1	96.2±19.3	61.0±14.8	75.1±23.3	96.9±18.9	63.5±14.8
	0.092	0.115	0.279	0.596	0.208	0.855
Smoking						
Ever (80)	**69.7±24.8**	96.1±17.9	**58.0±15.9**	**70.3±23.8**	96.0±18.2	**59.2±15.9**
Never (117)	**77.8±21.3**	99.6±19.8	**64.7±13.0**	**79.9±21.6**	100.4±20.2	**66.1±13.5**
	0.016	0.199	0.002	0.008	0.158	0.004
Sex						
Male (83)	**67.3±21.3**	**92.1±15.2**	**58.3±15.6**	**68.2±20.6**	**92.2±15.2**	**59.4±15.6**
Female (115)	**79.6±22.9**	**102.5±20.3**	**64.7±13.2**	**81.2±22.9**	**102.9±20.9**	**65.9±13.8**
	<0.001	<0.001	<0.002	<0.001	0.001	0.006
Control						
Well or partial (102)	**78.1±21.5**	**100.9±18.4**	63.6±14.4	76.8±21.1	99.5±18.0	63.6±15.1
Poor (86)	**69.9±25.0**	**94.6±20.2**	59.9±15.1	74.1±25.4	97.1±21.7	62.5±15.1
	0.017	**0.027**	0.081	0.466	0.453	0.624
BMI						
<25 (100)	**71.2±22.7**	96.7±20.2	60.7±15.1	72.9±22.9	97.98±21.3	61.5±15.4
≥25 (94)	**78.1±22.9**	99.7±17.8	63.4±14.0	79.3±22.5	99.13±17.3	65.3±14.0
	0.035	0.261	.0160	0.078	0.708	0.106
Age						
<65 (100)	76.4±22.9	100.6±18.3	62.2±15.0	77.4±22.7	100.4±18.7	63.5±15.6
≥65 (94)	**69.1±22.7**	**91.2±19.6**	61.5±13.4	71.6±23.2	**92.8±21.0**	62.7±12.6
	0.050	0.003	0.779	0.164	0.030	0.759

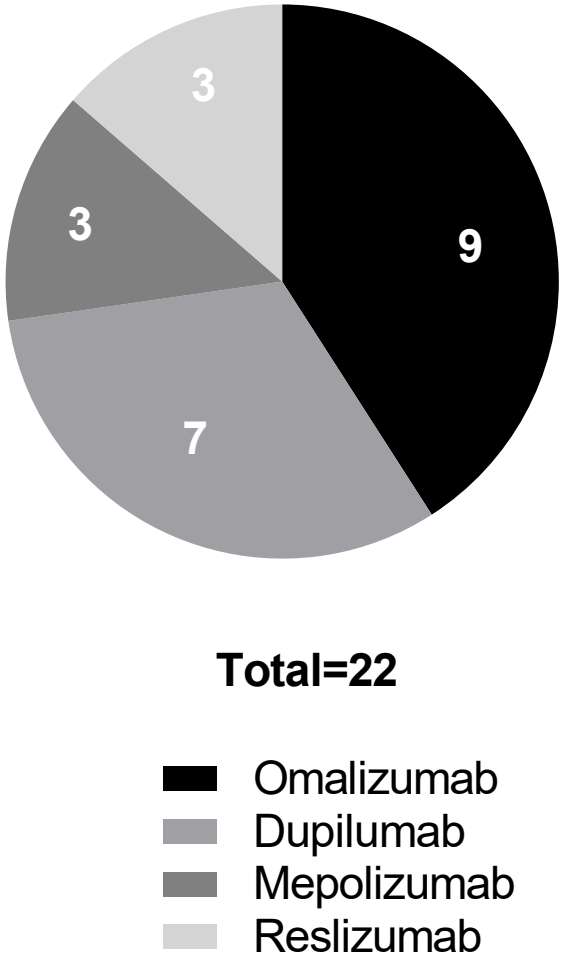
Asthma and Lung function

	Pre-bronchodilator			Post bronchodilator		
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC
All	74.5±23.0	98.1±19.1	62.0 ±14.6	75.9±22.9	98.5±19.5	63.3±14.8
Step						
GINA 4 (89)	77.5±22.6	100.5±18.7	63.2±14.3	77.0±22.3	100.8±20.1	63.0±15.0
GINA 5(109)	72.0±23.1	96.2±19.3	61.0±14.8	75.1±23.3	96.9±18.9	63.5±14.8
	0.092	0.115	0.279	0.596	0.208	0.855
Smoking						
Ever (80)	**69.7±24.8**	96.1±17.9	**58.0±15.9**	**70.3±23.8**	96.0±18.2	**59.2±15.9**
Never (117)	**77.8±21.3**	99.6±19.8	**64.7±13.0**	**79.9±21.6**	100.4±20.2	**66.1±13.5**
	0.016	0.199	0.002	0.008	0.158	0.004
Sex						
Male (83)	**67.3±21.3**	**92.1±15.2**	**58.3±15.6**	**68.2±20.6**	**92.2±15.2**	**59.4±15.6**
Female (115)	**79.6±22.9**	**102.5±20.3**	**64.7±13.2**	**81.2±22.9**	**102.9±20.9**	**65.9±13.8**
	<0.001	<0.001	<0.002	<0.001	0.001	0.006
Control						
Well or partial (102)	**78.1±21.5**	100.9±18.4	63.6±14.4	76.8±21.1	99.5±18.0	63.6±15.1
Poor (86)	**69.9±25.0**	94.6±20.2	59.9±15.1	74.1±25.4	97.1±21.7	62.5±15.1
	0.017	0.027	0.081	0.466	0.453	0.624
BMI						
<25 (100)	**71.2±22.7**	96.7±20.2	60.7±15.1	72.9±22.9	97.98±21.3	61.5±15.4
≥25 (94)	**78.1±22.9**	99.7±17.8	63.4±14.0	79.3±22.5	99.13±17.3	65.3±14.0
	0.035	0.261	.0160	0.078	0.708	0.106
Age						
<65 (100)	76.4±22.9	100.6±18.3	62.2±15.0	77.4±22.7	100.4±18.7	63.5±15.6
≥65 (94)	**69.1±22.7**	**91.2±19.6**	61.5±13.4	71.6±23.2	**92.8±21.0**	62.7±12.6
	0.050	0.003	0.779	0.164	0.030	0.759

Asthma and Medication







Summary

Definition

Acute exacerbation

Disease burden

OCS: T2 biomarker, biologics, comorbidity

Severe asthma in Korea