Current status of asthma treatment in Korea

2021.09.25

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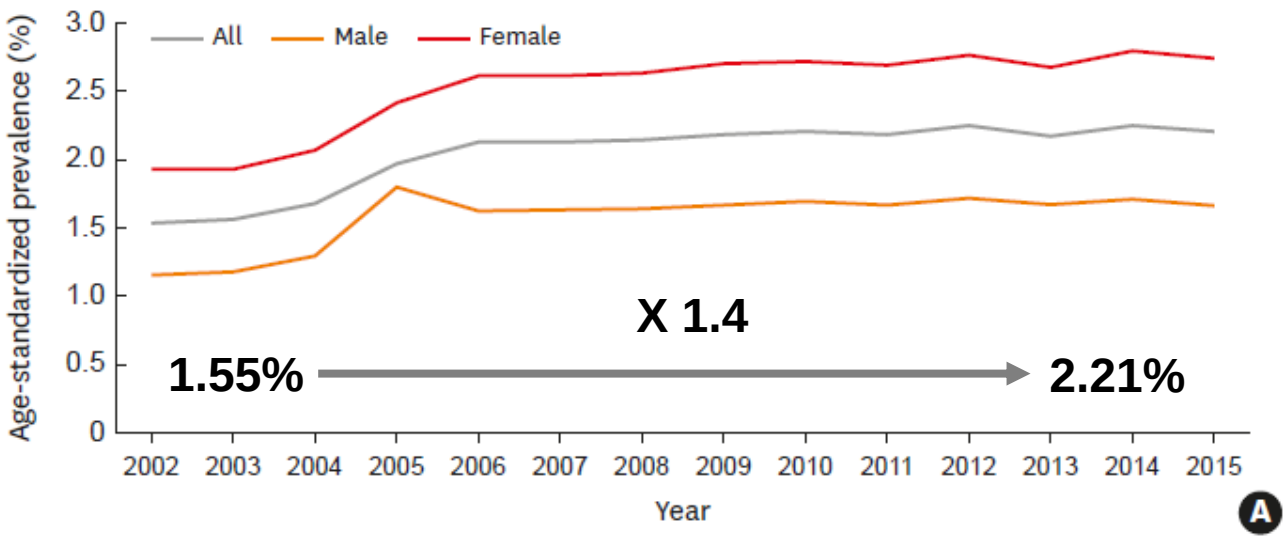
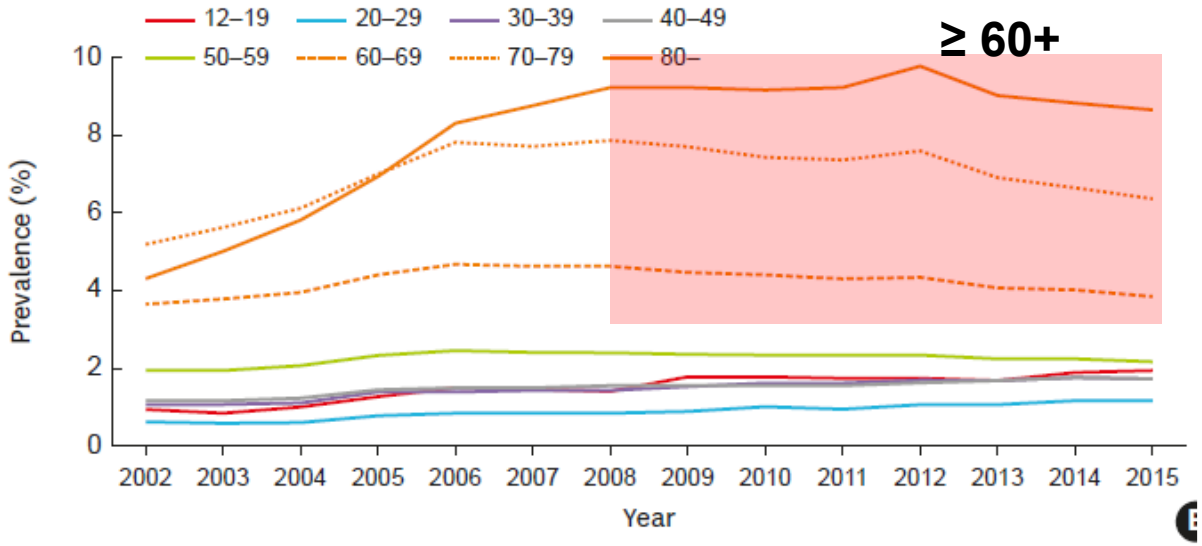
Contents

- Epidemiology
  - Asthma prevalence, asthma-related health care use
- Current asthma treatment
  - Diagnosis – lung function test
  - Asthma medication – Inhalers
- Current status of biologics use

Asthma prevalence in Korea

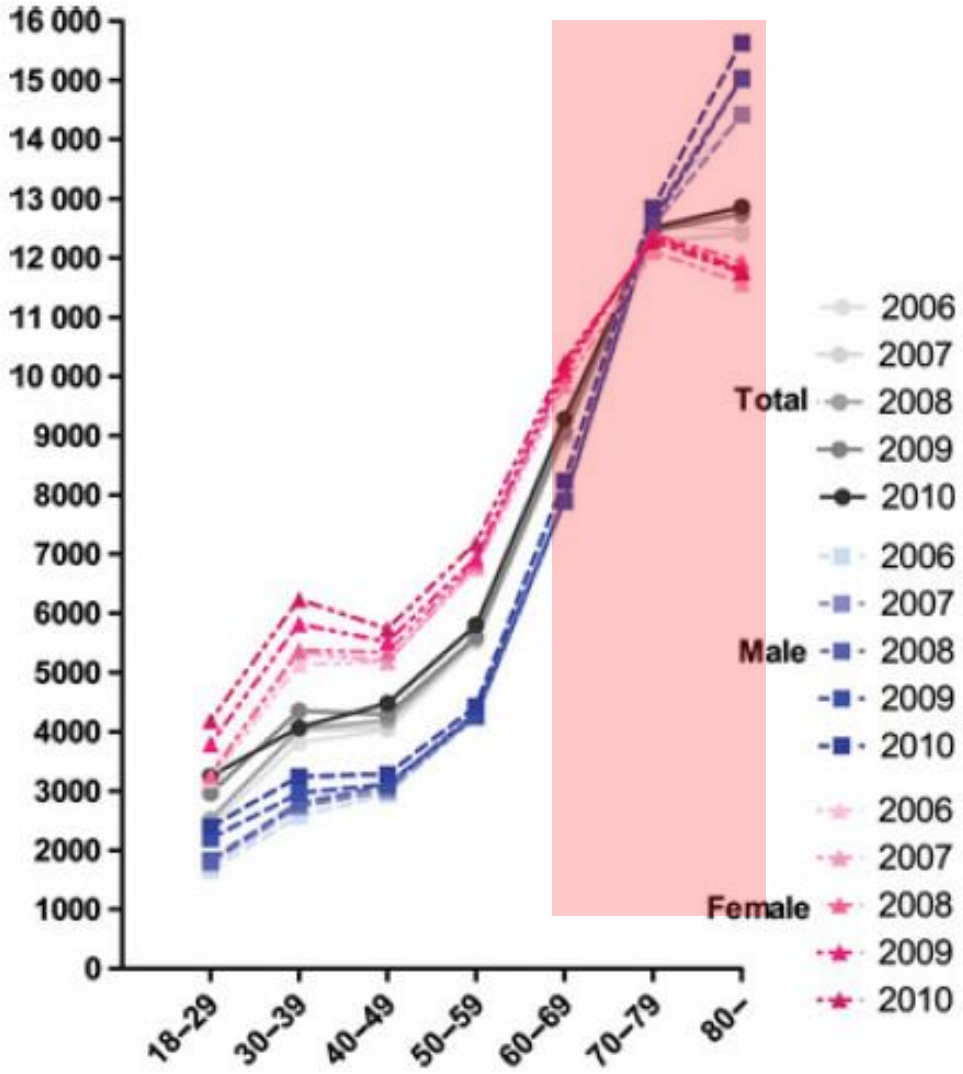
National Health Insurance Sharing Service database from 2002 to 2015





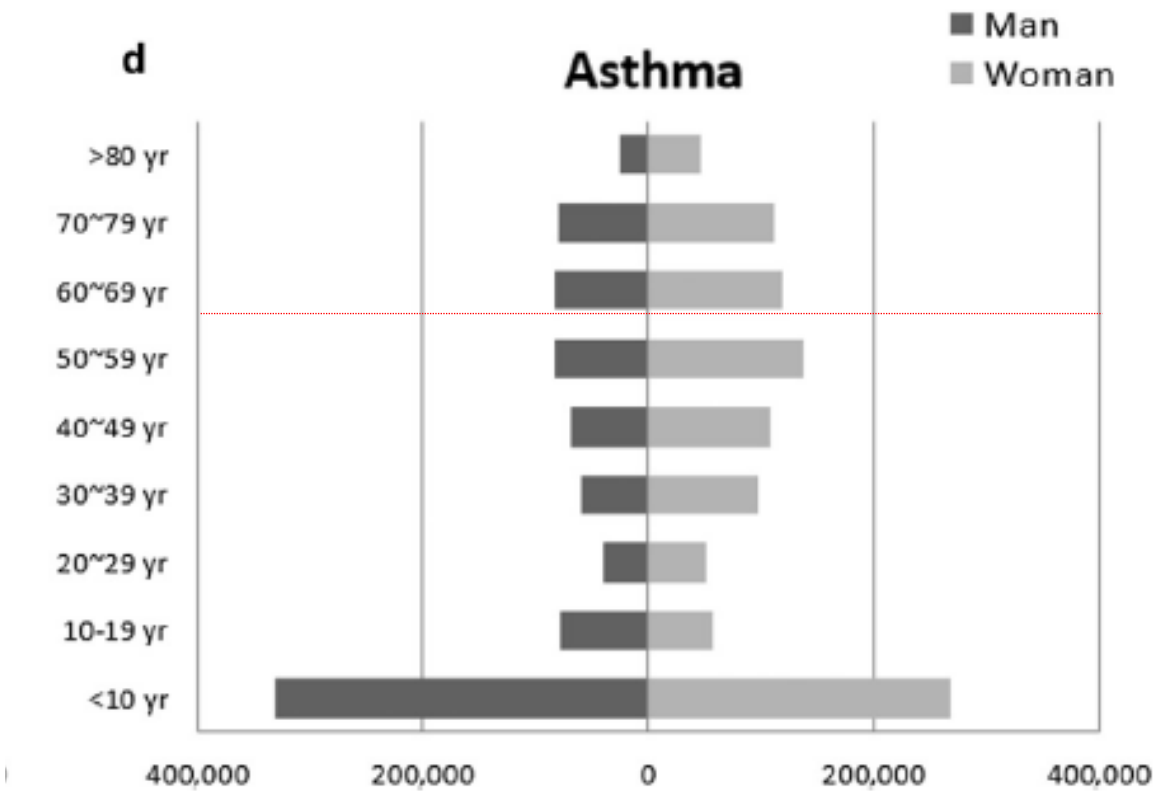
Allergy Asthma Immunol Res. 2020 May;12(3):467-484

National Health Insurance claim records
From 2006 to 2010



Allergy. 2013 Nov;68(11):1435-42

From 2009 to 2014



Allergol Int. 2016 Apr;65(2):186-191

Asthma-related health care use

	2006	2007	2010
Number of subjects	1 857 368	1 916 118	2 256 023
Total visits by type of hospital (%)			
Primary hospital	7 529 854 (85.15%)	6 562 038 (82.06%)	6 137 654 (79.09%)
Secondary hospital	444 600 (4.97%)	443 634 (5.55%)	510 059 (6.57%)
Tertiary hospital	974 077 (10.89%)	991 218 (12.40%)	1 112 919 (14.34%)

Allergy. 2013 Nov;68(11):1435-42

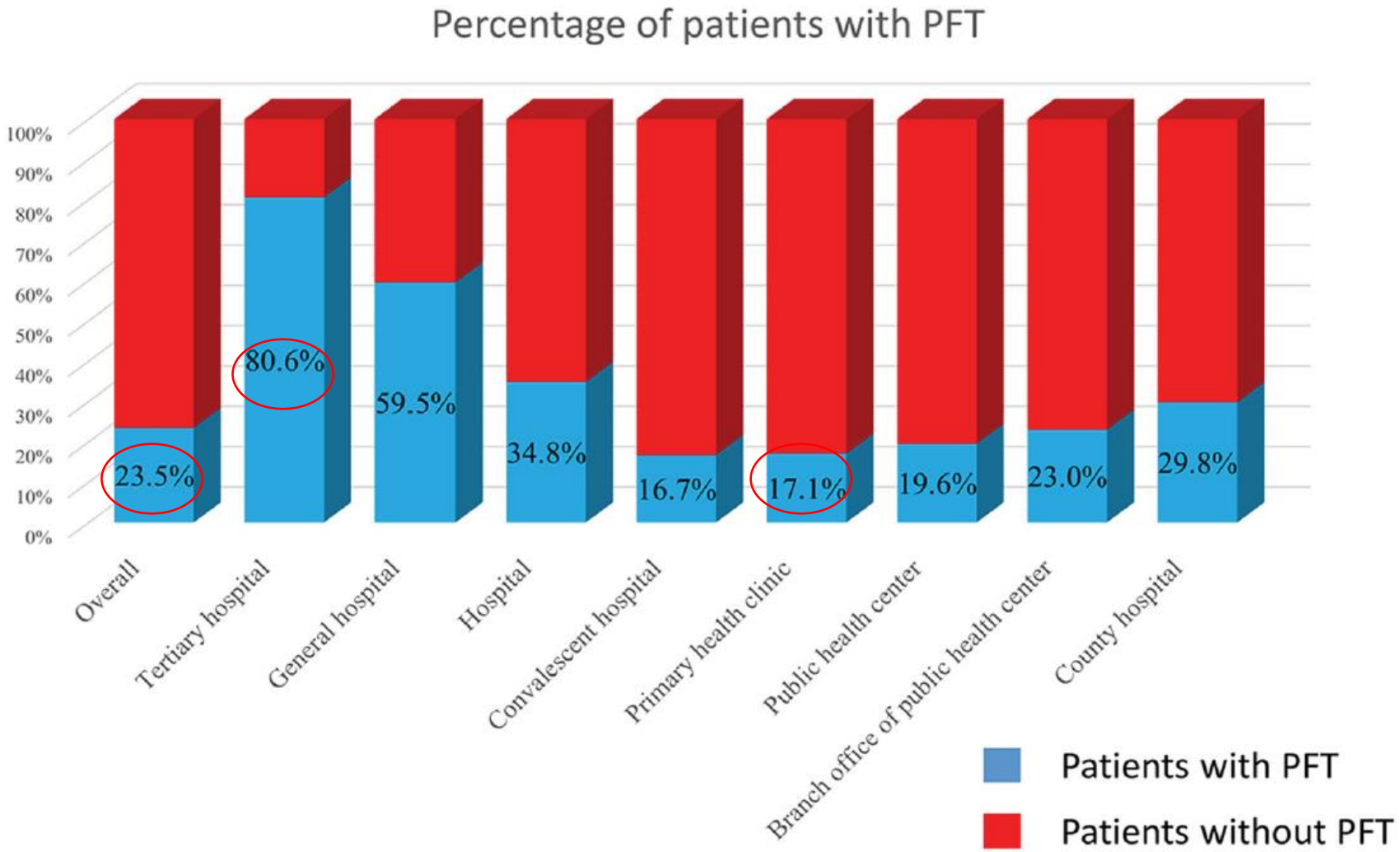
HIRA nationwide database (2013.7~2014.6)

Table 2 Number of patients in each type of medical institution

Type of medical institutions	No. of medical institutions	No. of asthma patients (%)
Overall	16,804	831,613 (100.00)
Tertiary hospital	43	43,471 (5.23)
General hospital	280	83,194 (10.00)
Hospital	910	44,503 (5.35)
Convalescent hospital	379	2,933 (0.35)
Primary health clinic	14,745	686,063 (82.50)
Public health center	212	2,424 (0.29)
Branch office of public health center	222	532 (0.06)
County hospital	13	416 (0.05)

J Thorac Dis. 2017 Sep;9(9):3208-3214

Pulmonary function test rates



Possession rates of PFT equipment

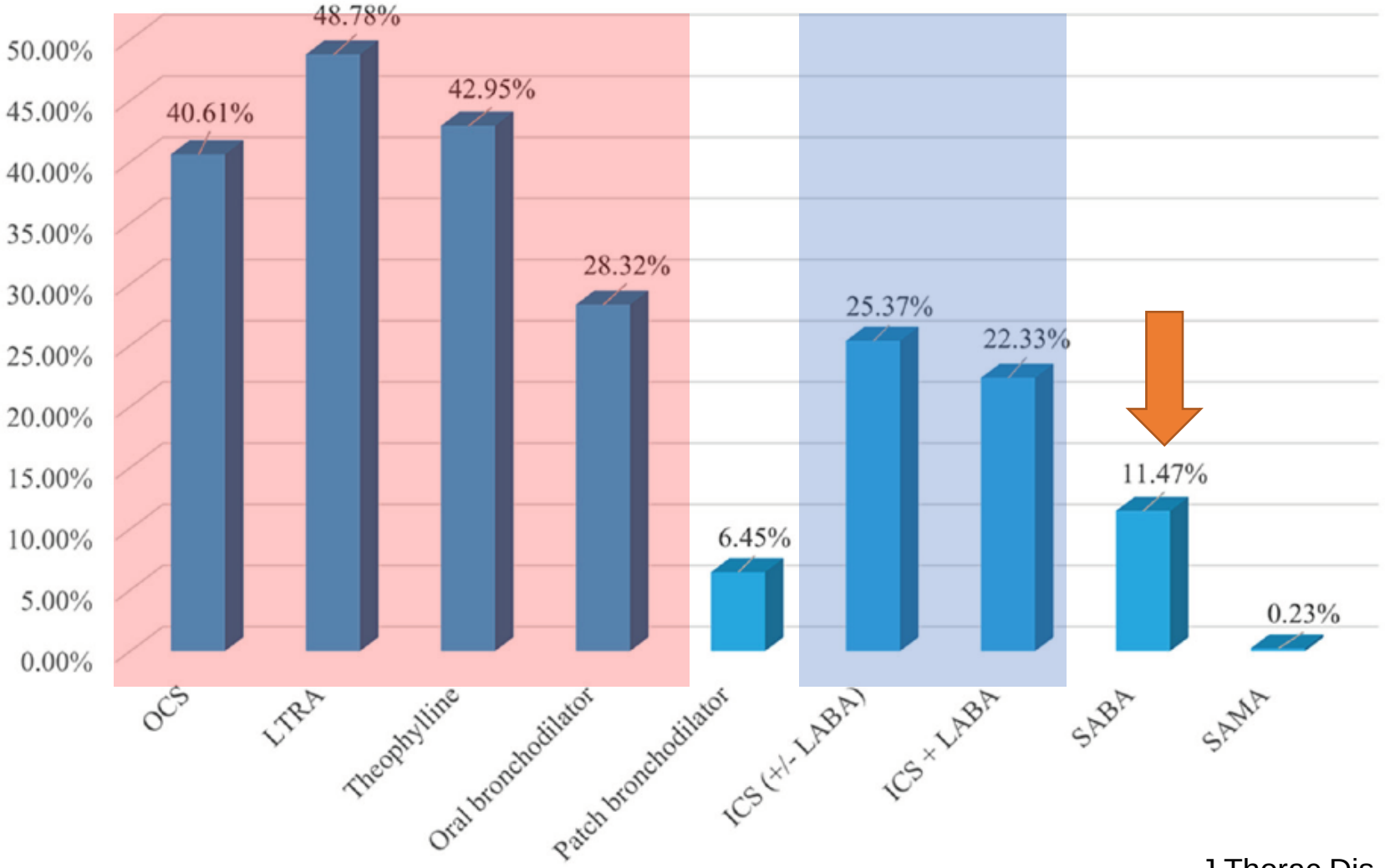
- Primary clinic 51.24%

PFT types

- Spirometry with F-V curve (n=152,639)
- BDR (n=72,486)
- Spirometry w/o F-V curve (n=33,928)
- Bronchial provocation test (n=11,837)

J Thorac Dis. 2018 Jul;10(7):4360-4367

Patterns of asthma medication prescriptions



J Thorac Dis. 2017 Sep;9(9):3208-3214

Table 3. Changes in outcomes of quality assessment of asthma management by the HIRA

Category	Item	Results (%)		
		First report	Second report	Third report
Diagnosis	Performance rate of pulmonary function test	23.47 (17.06)*	24.88 (18.06)	28.34 (20.09)
Treatment	Percentage of visits to same medical institution for asthma management	71.20 (69.28)	71.88 (69.76)	72.02 (69.70)
	Prescription rate of ICS	25.37 (16.42)	27.06 (17.80)	30.62 (20.09)
	Prescription rate of anti-inflammatory controllers for asthma such as leukotriene receptor antagonists and ICS	59.13 (52.69)	61.08 (54.47)	63.65 (56.21)
	Prescription rate of long acting β2-agonists without ICS	16.81 (19.17)	18.26 (21.06)	16.77 (19.91)
	Prescription rate of short acting β2-agonists without ICS	14.34 (16.02)	13.21 (14.87)	12.92 (15.08)
	Prescription rate of oral corticosteroids without ICS	30.36 (34.53)†	29.57 (33.86)†	28.20 (33.07)

*The value in bracket indicates the rate in primary clinics only.

Tuberc Respir Dis 2017;80:221-225

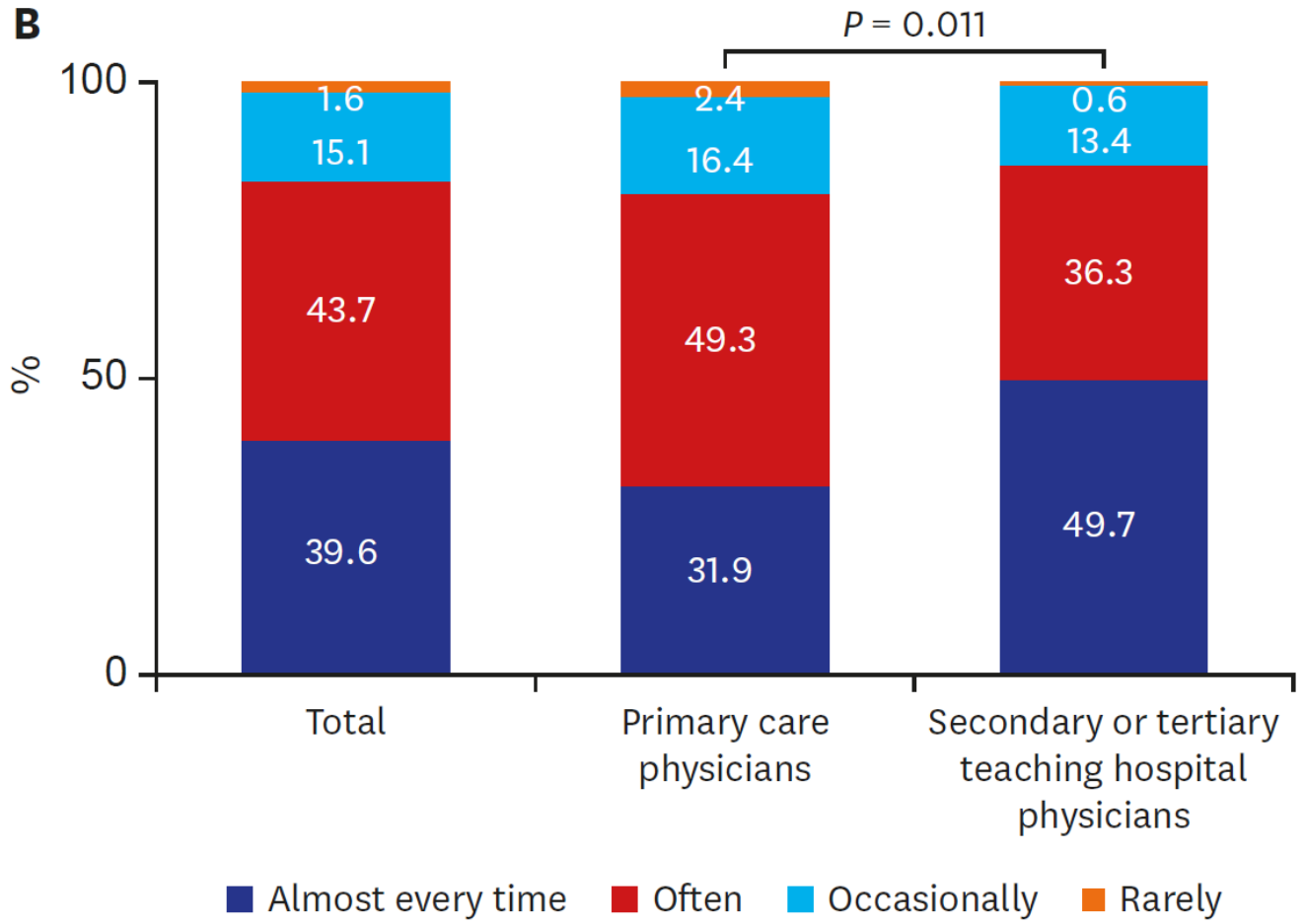
Barriers to ICSs prescription

Physicians' view

Questionnaire survey (2012.3~2012.9)

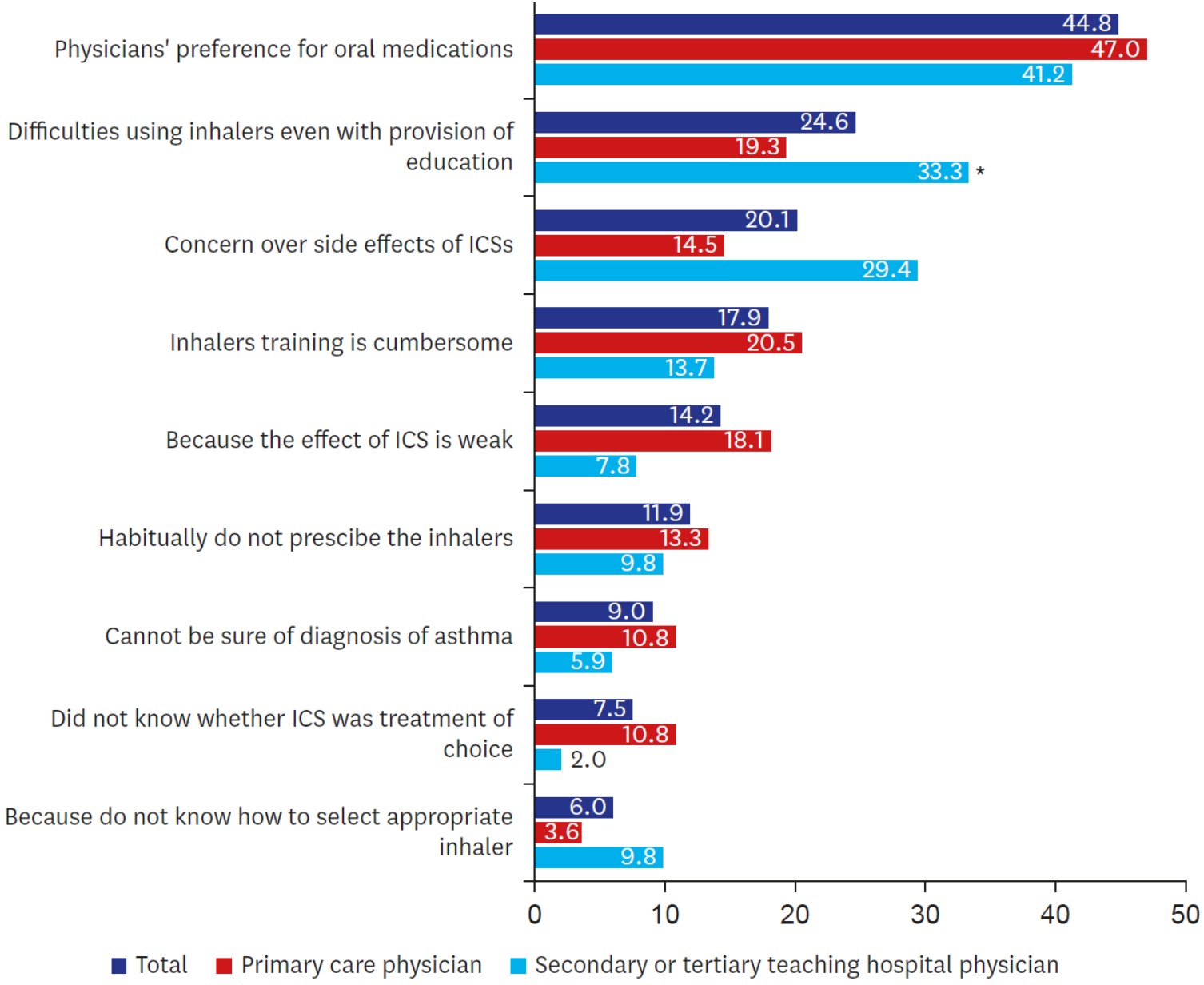
- N= 373 physicians
- 364 (97.6%) were having asthma patients

Prescription of ICS as first-line treatments



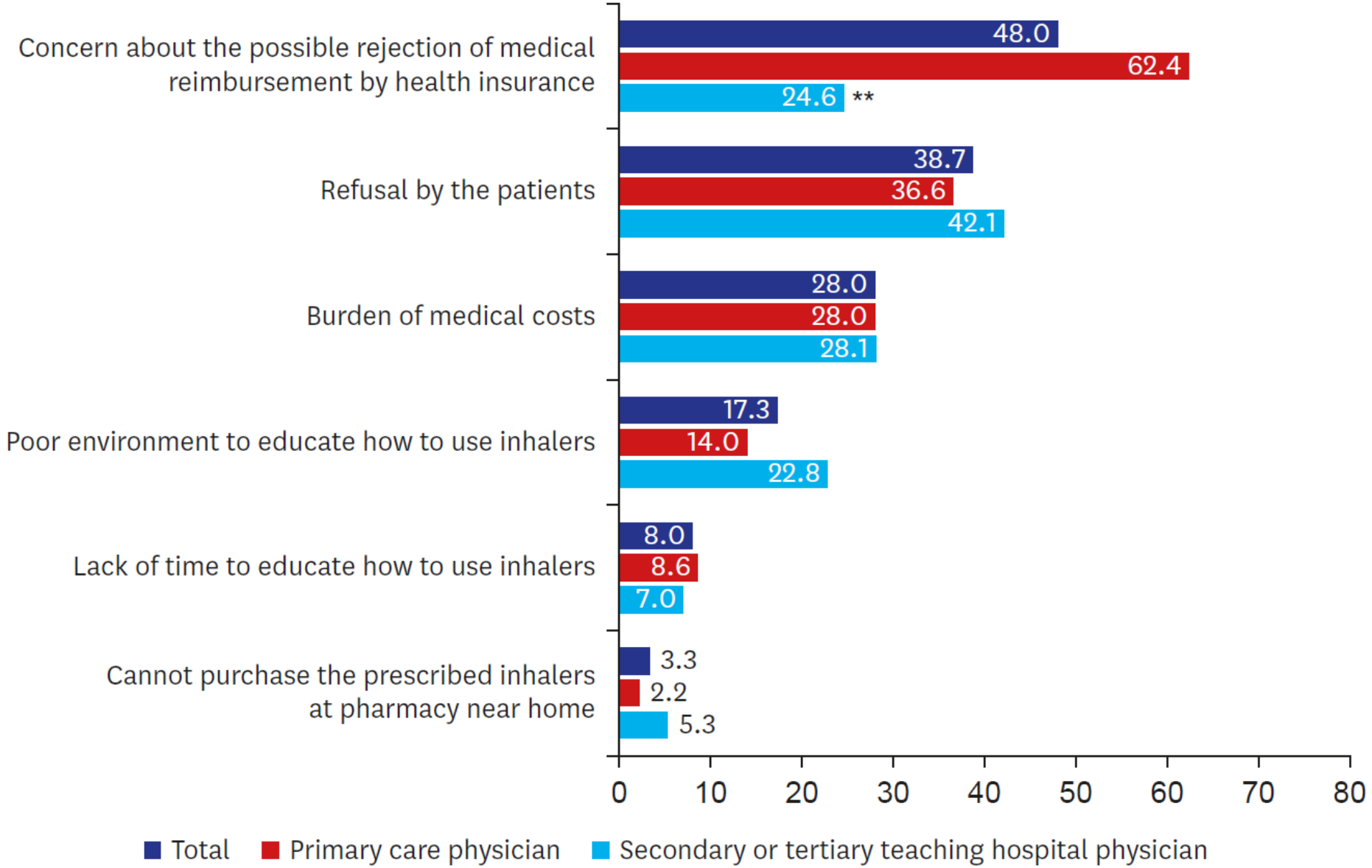
J Korean Med Sci. 2020 Mar 30;35(12):e72

Common internal barriers to ICS prescription



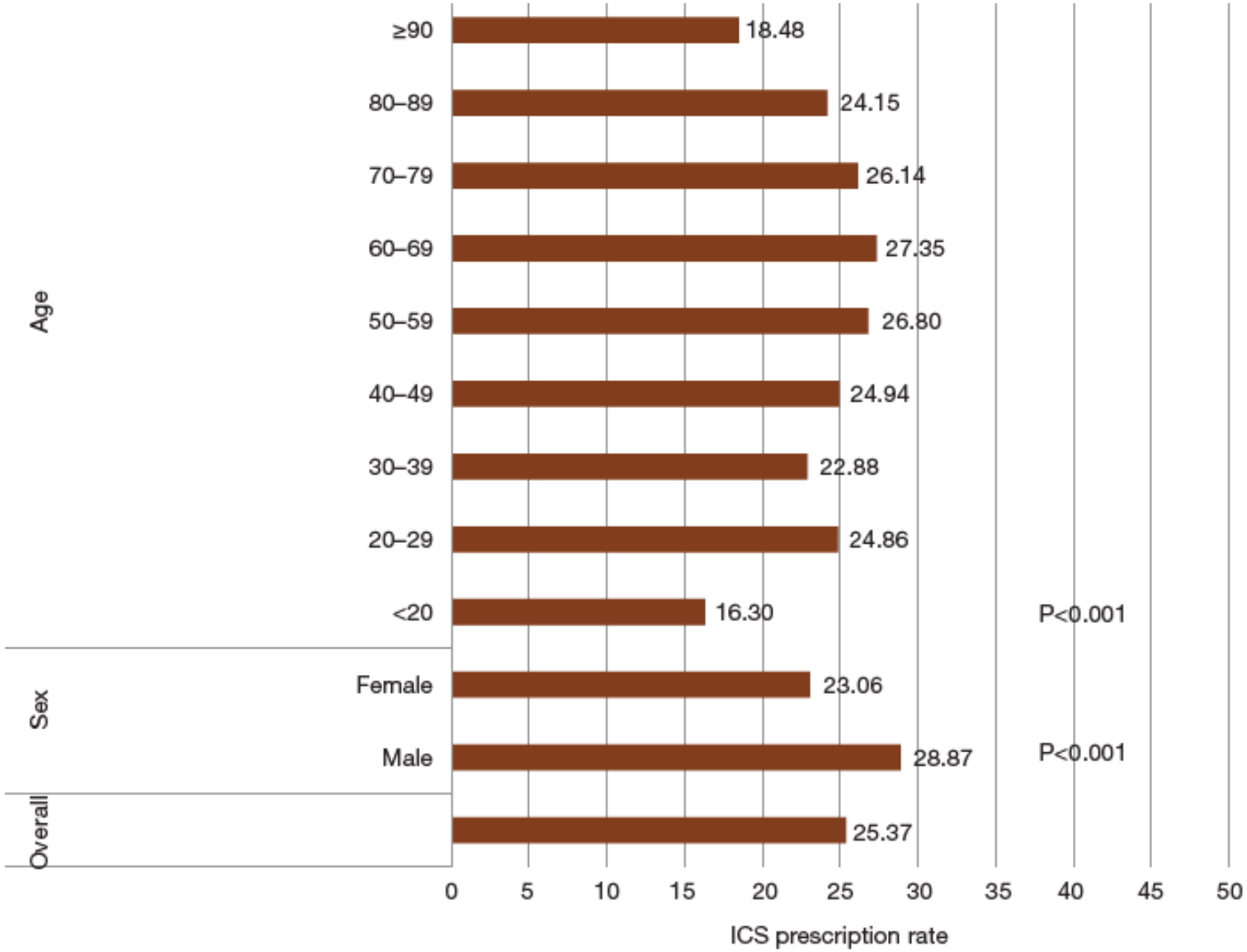
J Korean Med Sci. 2020 Mar 30;35(12):e72

Common external barriers to ICS prescription



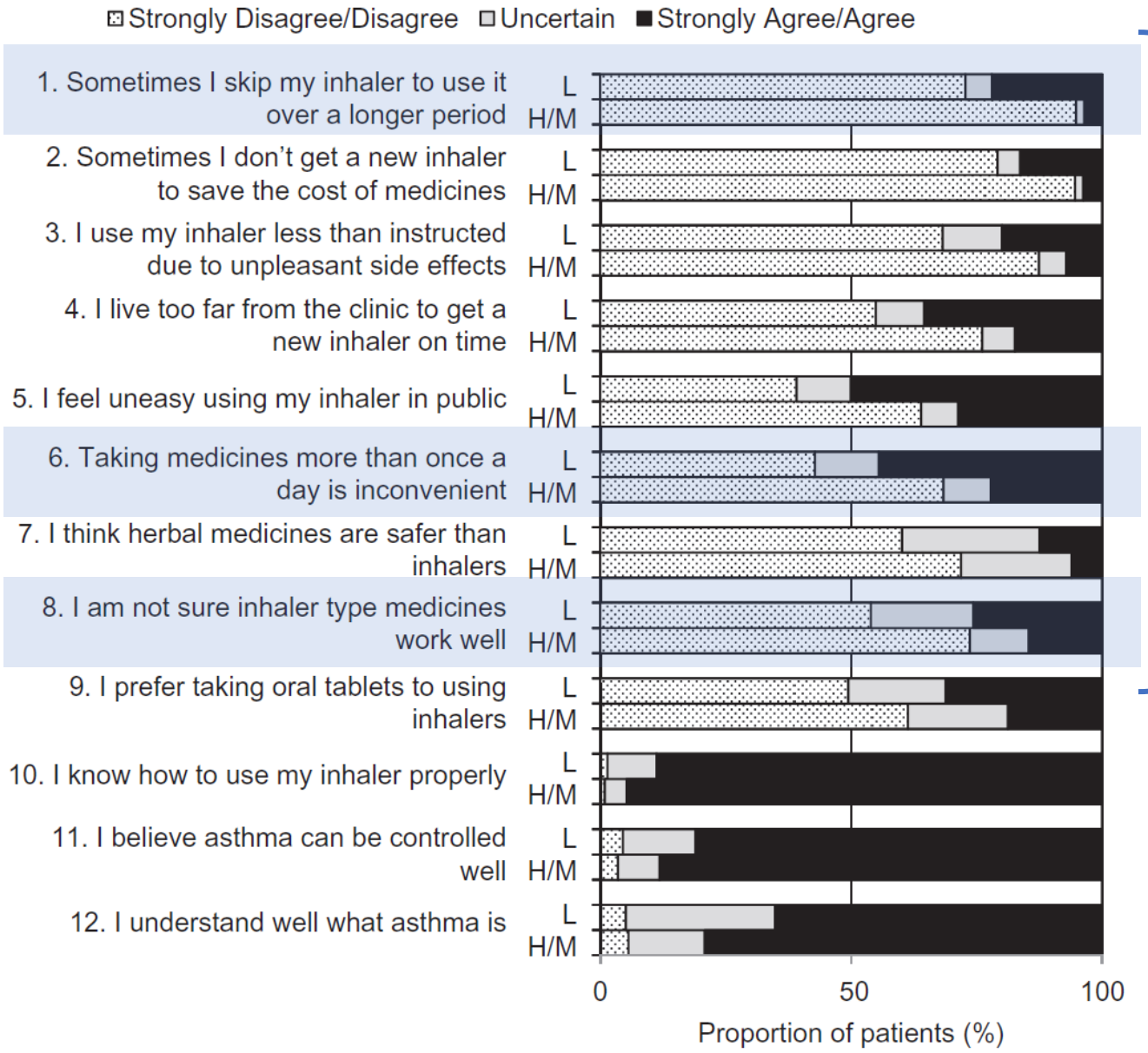
J Korean Med Sci. 2020 Mar 30;35(12):e72

ICS prescription rate by age and sex



J Thorac Dis 2018;10(9):5405-5413

Barriers to ICSs prescription Patients' view



Cross-sectional observational study of adult patients with asthma from specialist clinics in six Asian countries

Patients' acceptance of inhaler medicines

L –low adherence
H/M–high or medium adherence

J Asthma, 2014; 51(6): 652–659

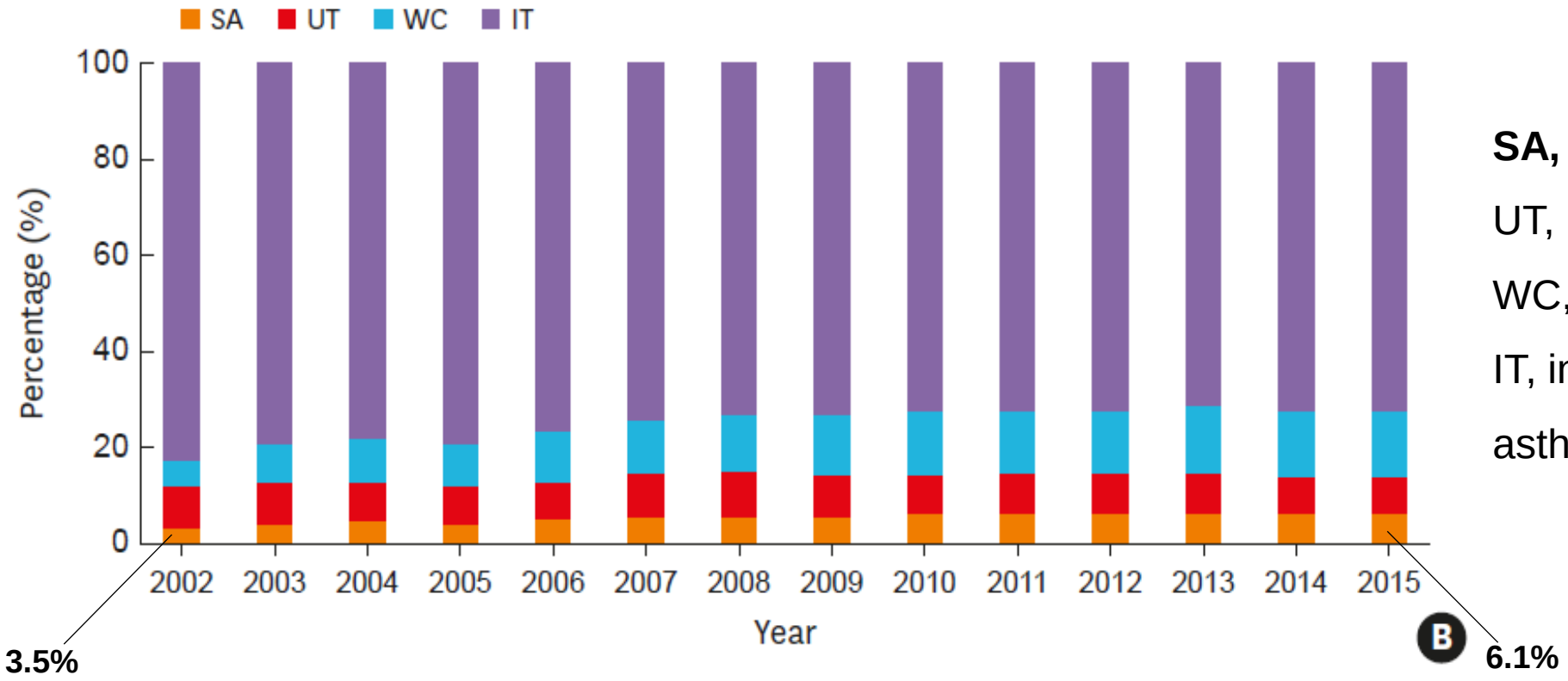
General Types of Nonadherence to Prescribed Aerosol Therapy and Potential Factors

- Unintentional: Patient does not understand therapy correctly
  - Misunderstanding prescribed drug regimen (poor doctor-patient communication)[12]
  - Incorrect aerosol device technique
  - Language barriers
- Intentional: Patient understands therapy but does not adhere correctly
  - Patient beliefs
    - I do not really require regular medication
    - I am not really sick
    - I gain attention from parents, am kept at home (children)
    - The medication is too expensive
    - I have concern about adverse effects
    - I do not perceive effect from the medication
  - Forgetfulness
  - Stress and busy lifestyle
  - Complex, demanding aerosol regimens
  - Psychological factors (eg, depression)[13]

Respir Care. 2005 Oct;50(10):1346-56

Prevalence of severe asthma in Korea

National Health Insurance Sharing Service database



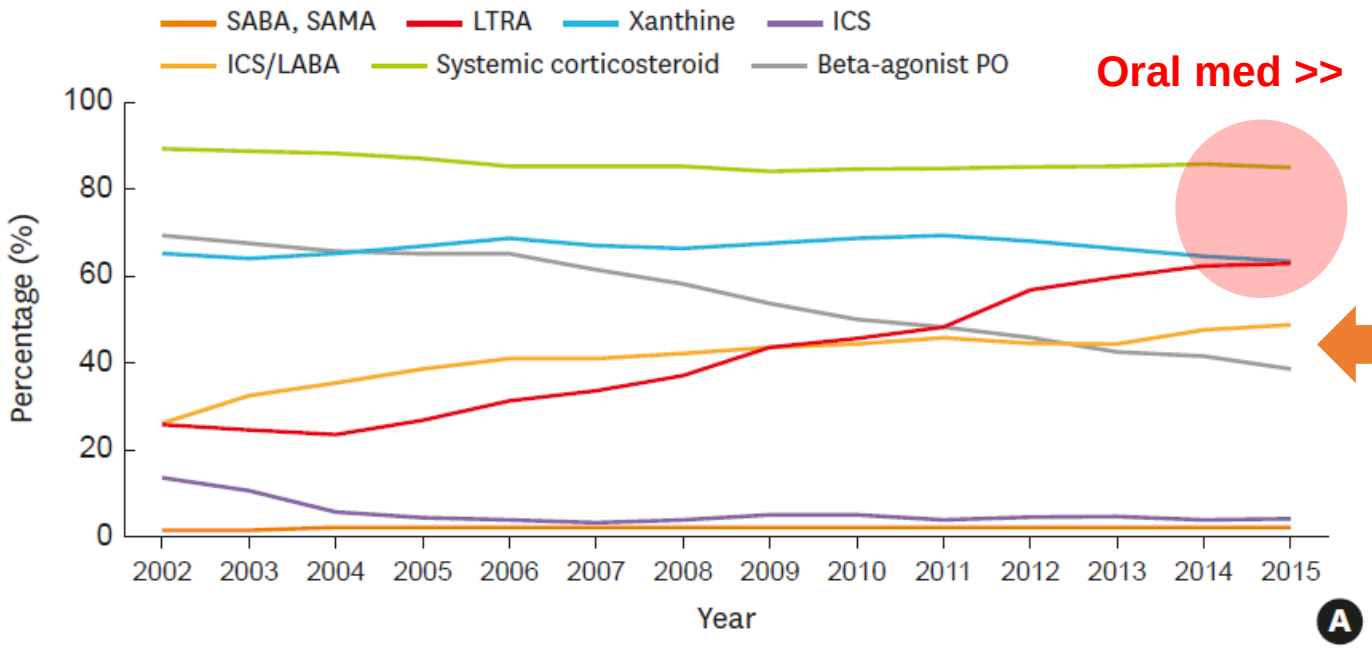
SA, severe asthma

UT, untreated asthma

WC, well-controlled asthma

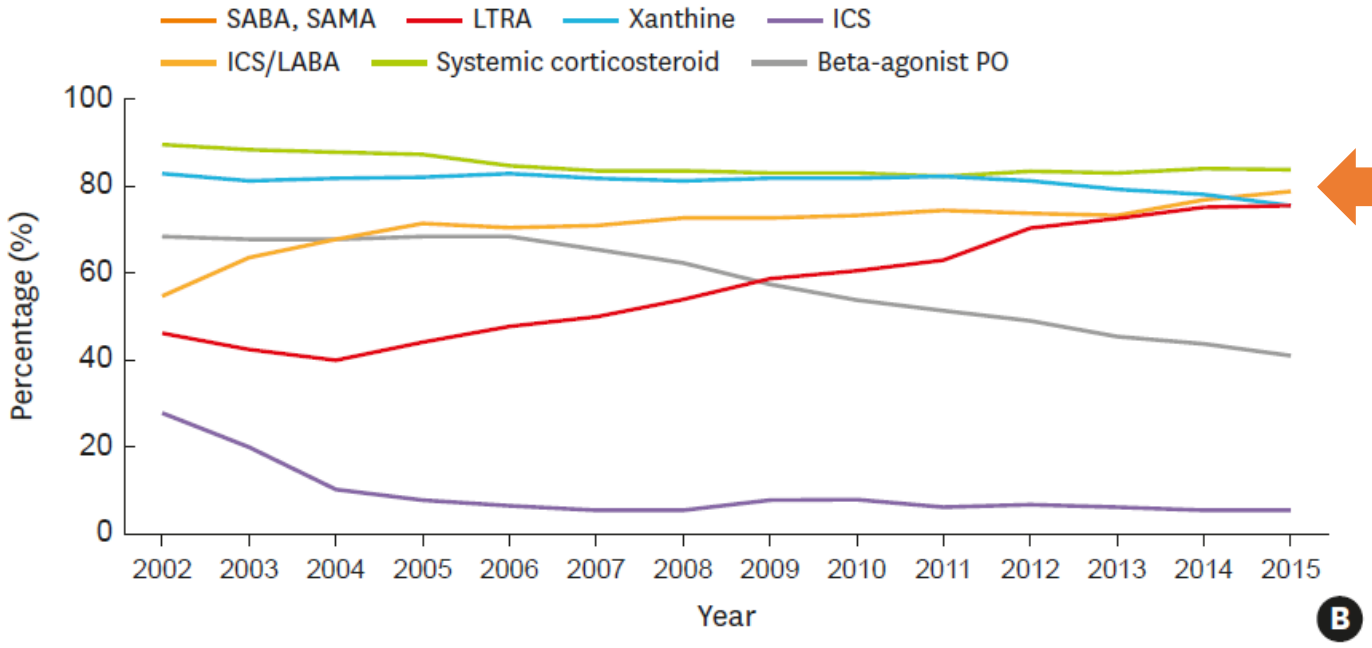
IT, intermittently treated asthma

Allergy Asthma Immunol Res. 2020;12(3):467-484



Uncontrolled asthma:

SABA ≥ 2 canisters per year, SABA nebulizer use for 3 consecutive days ≥2 times per year, systemic corticosteroids burst >2 times per year, or hospital admission for asthma ≥ 1 time per year

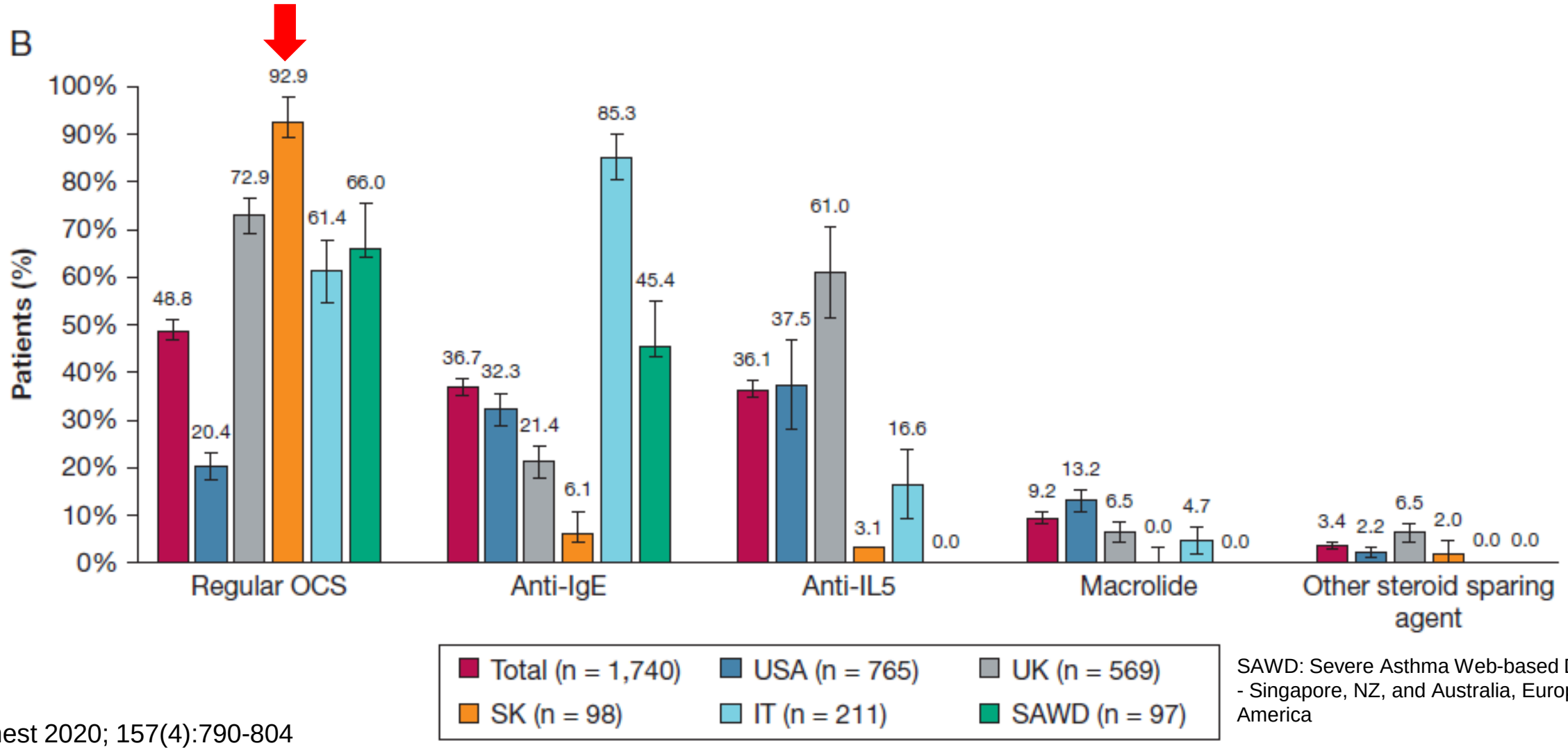


Severe asthma:

defined if asthmatic patients have frequent asthma exacerbations even with regular treatments

Allergy Asthma Immunol Res. 2020 May;12(3):467-484

Prescription patterns in severe asthma

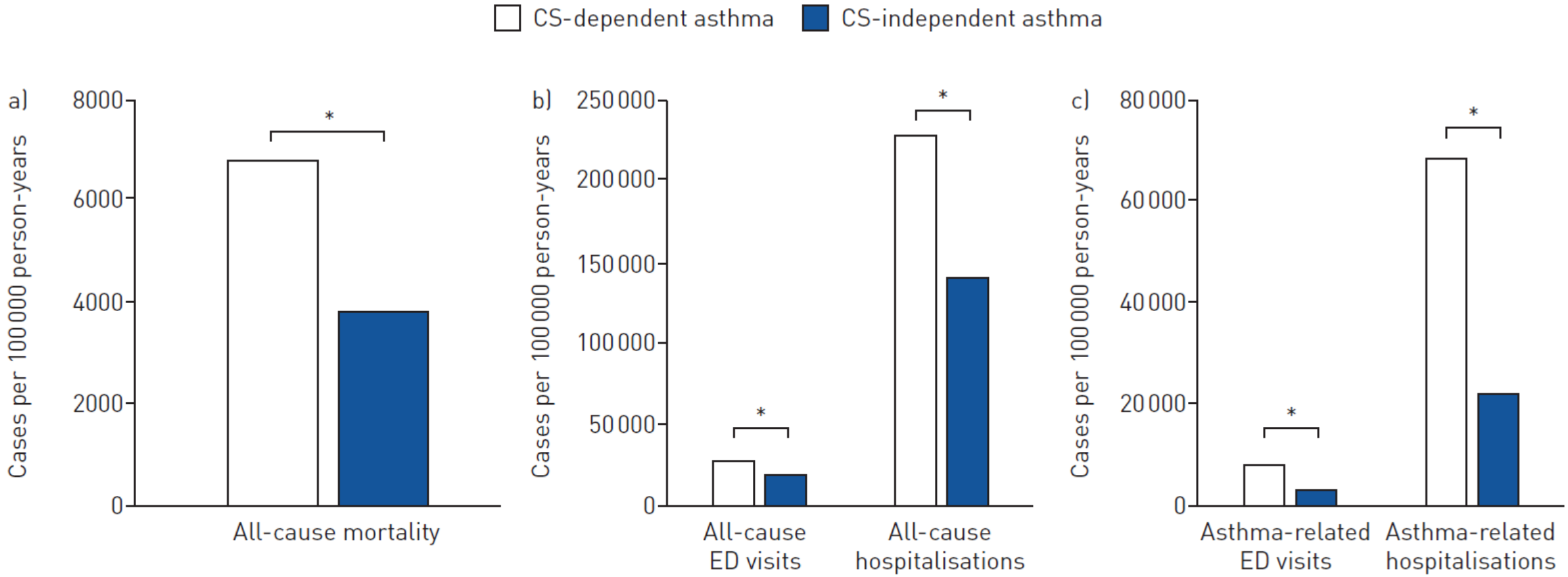


SAWD: Severe Asthma Web-based Database - Singapore, NZ, and Australia, Europe, North America

Chest 2020; 157(4):790-804

Systemic corticosteroid use in asthma

the Korean National Health Insurance Service database from 2005 to 2015



Eur Respir J. 2019 Nov 28;54(5):1900804

Challenges, consequences and proposed solutions for management of asthma in AP region

Sr. no	Identified challenge	Consequences	Proposed solutions
(1)	Stigma Stigma about asthma as a disease/taboo (embarrassment) of using inhaler devices	Impairs diagnosis, non-adherence to medications, use of alternate therapies, use of oral medications	Patient education and disease awareness
(2)	Lower treatment goals Low expectation regarding asthma control/non-compliance to therapy	Poor symptom control	Patient education about disease process and inhaler techniques, asthma management plan
(3)	Suboptimal clinical practice Inappropriate therapy/prescription of OCS/excess use of reliever medication	Inadvertent use leading to adverse effects	Establish uniform local treatment protocols for asthma/educate primary care physicians
(4)	Inappropriate diagnosis/management of severe asthma Regional differences in comorbidities and eosinophil counts Access to biologic medications	High use of OCS There may be higher eosinophil counts owing to helminthic[†] infestations, this may be confounding the phenotyping	Establish region-specific definitions/ diagnosis charters Local data on baseline blood and sputum inflammometry Collaboration with policy makers and payers for improved access
(5)	Variability of access to specialized care There might be easier access to newer therapy in private sector/organized healthcare systems/developed world vis-a-vis the unorganized healthcare systems or developing world	Suboptimal treatment due to lack of resources rather than lack of knowledge	Efforts to align governments and policy makers to establish asthma care as one of the priorities in the healthcare management plan

Respirology (2020) 25, 1235–1242

GINA 2021 update

Track 1

CONTROLLER and **PREFERRED RELIEVER** (Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2
As-needed low dose ICS-formoterol

STEP 3
Low dose maintenance ICS-formoterol

STEP 4
Medium dose maintenance ICS-formoterol

STEP 5
Add-on LAMA
Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R
Consider high dose ICS-formoterol

RELIEVER: As-needed low-dose ICS-formoterol

Track 2

CONTROLLER and **ALTERNATIVE RELIEVER** (Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

STEP 1
Take ICS whenever SABA taken

STEP 2
Low dose maintenance ICS

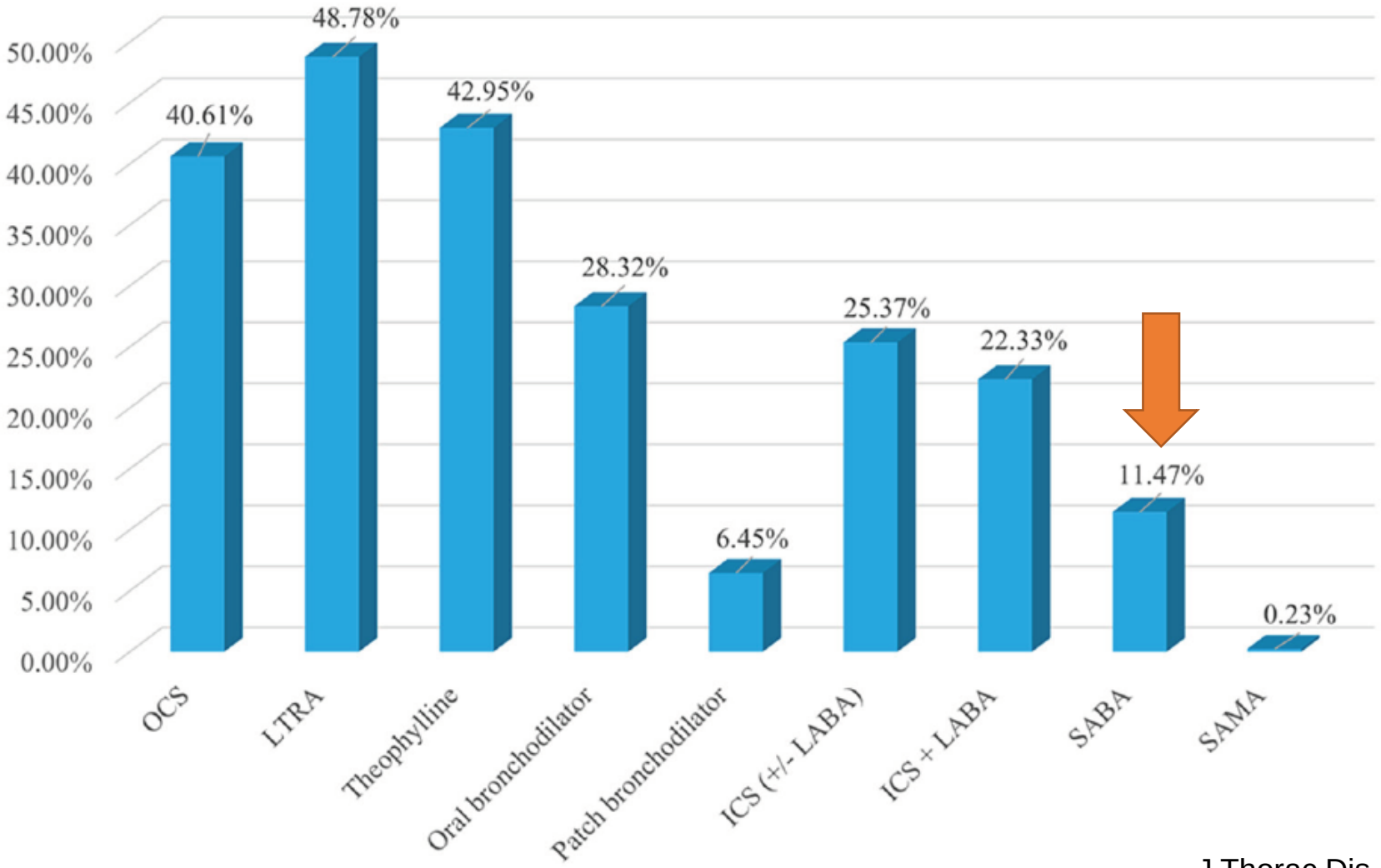
STEP 3
Low dose maintenance ICS-LABA

STEP 4
Medium/high dose maintenance ICS-LABA

STEP 5
Add-on LAMA
Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R
Consider high dose ICS-LABA

RELIEVER: As-needed short-acting β2-agonist

Patterns of asthma medication prescriptions



J Thorac Dis. 2017 Sep;9(9):3208-3214

Short-Acting beta2-Agonist Use in Asthma in Korea: A 10-Year Population-Based Study

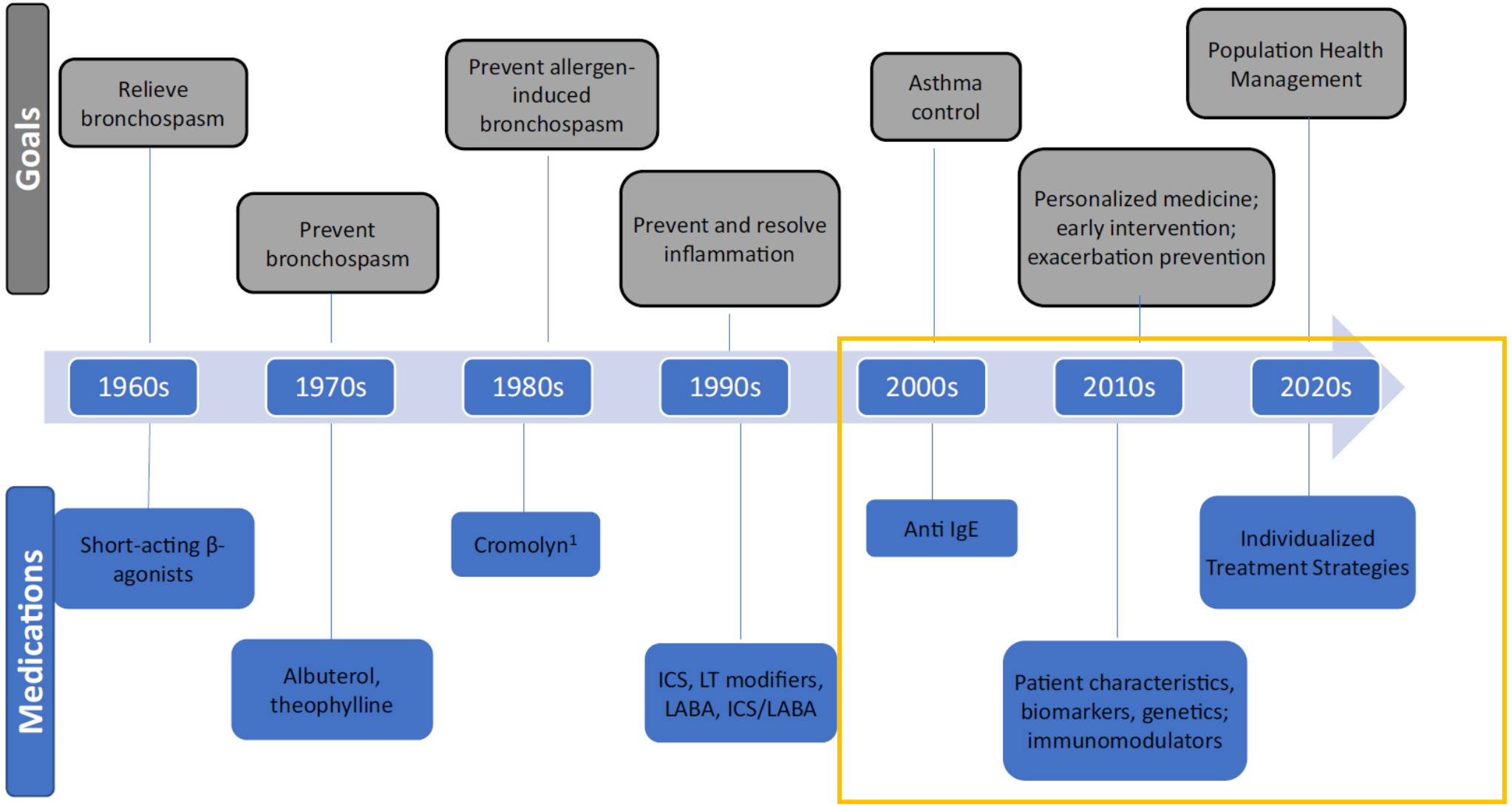
Hyun Lee[1,#], Jiin Ryu[2], Choi Jee Yea[1], Joonkyung Kim[1], Min Ju Jo[1], Sung Jun Chung[1], Yoomi Yeo[1], Dong Won Park[1], Tai Sun Park[1], Ji-Yong Moon[1], Tae Hyung Kim[1], Jang Won Sohn[1], Ho Joo Yoon[1], Sang-Heon Kim[1]*

[1]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea, [2]Biostatistical Consulting and Research Lab, Medical Research Collaborating Center, Hanyang University, Seoul, Korea

Purpose: Short-acting β2 agonist (SABA) use is known to be very lower in Korean asthmatics compared to those in other countries, whilst the rate of asthma exacerbation in Korea is higher compared to other countries. Thus, the epidemiological study on SABA use and the relationship between SABA overuse and treatment outcomes of asthma are needed to be elucidated in Korea.
Methods: We performed a cross-sectional study using the National Health Insurance Service-National Sample Cohort (NHIS-NSC) 2002-2012 database. We evaluated the trend of yearly SABA use and overuse (3 or more SABA canisters/year) and the impact of SABA overuse on increased health care use and mortality.
Results: During the study period, the proportion of asthmatic patients who used SABA ranged about 8%-11%, without significant change in trend. The mean number of annual SABA use in asthmatic patients ranged 0.15-0.22/patient/year, and it ranged 1.93-2.05/patient/year in patients who used SABA ever in a 12-month period. SABA overuse was observed in about 2-4% of asthmatic patients during the study period. SABA overuse generally tended to increase as the age of asthmatic patients increased, with triple peaks in the late twenties (3.3%), late forties (3.1%), and late seventies (3.6%). SABA overuse was associated with increased emergency department visits (odds ratio [OR] = 2.31, 95% CI = 2.19-2.44), hospitalization (OR = 1.75, 95% CI = 1.67-1.84), and mortality (OR = 2.30, 95% CI = 2.19-2.44).
Conclusions: The rate of SABA use in Korean asthmatics was very low in Korean asthmatics between 2002-2012. SABA overuse was found in 2-4% of Korean asthmatics. SABA overuse was associated with an increased risk of health care use and mortality.
This study was funded by the Korea Ministry of Environment (MOE) as "the Environmental Health Action Program (2016001360003)".

2020년 춘계 알레르기학회 초록집

Changes in asthma management



J Allergy Clin Immunol Pract 2021;9:1090-8

Currently approved indications of biologics for severe asthma in Korea

Biologics	Action	Dose	Interval (wk)	Route	Indication
Omalizumab (Xolair®)	Anti-IgE	0.016 mg/kg per IU	2 or 4	SC	≥ 6 years old; positive allergy testing (allergic asthma); IgE: 30–700 IU/mL
Mepolizumab (Nucala®)	Anti-IL5	100 mg	4	SC	≥ 18 years old; AEC ≥ 150 cells/μL or ≥ 300 cells/μL at least once a year
Reslizumab (Cinqair®)	Anti-IL5	3 mg/kg	4	IV	≥ 18 years old; AEC ≥ 400 cells/μL
Benralizumab (Fasenra®)	Anti-IL5R	30 mg	8*	SC	≥ 18 years old; severe eosinophilic asthma
Dupilumab (Dupixent®)	Anti-IL4Rα	200 mg†	2	SC	≥ 12 years old; AEC ≥ 150 cells/μL or FeNO ≥ 25 ppb
		300 mg‡	2	SC	With OCS-dependent or moderate-to-severe atopic dermatitis

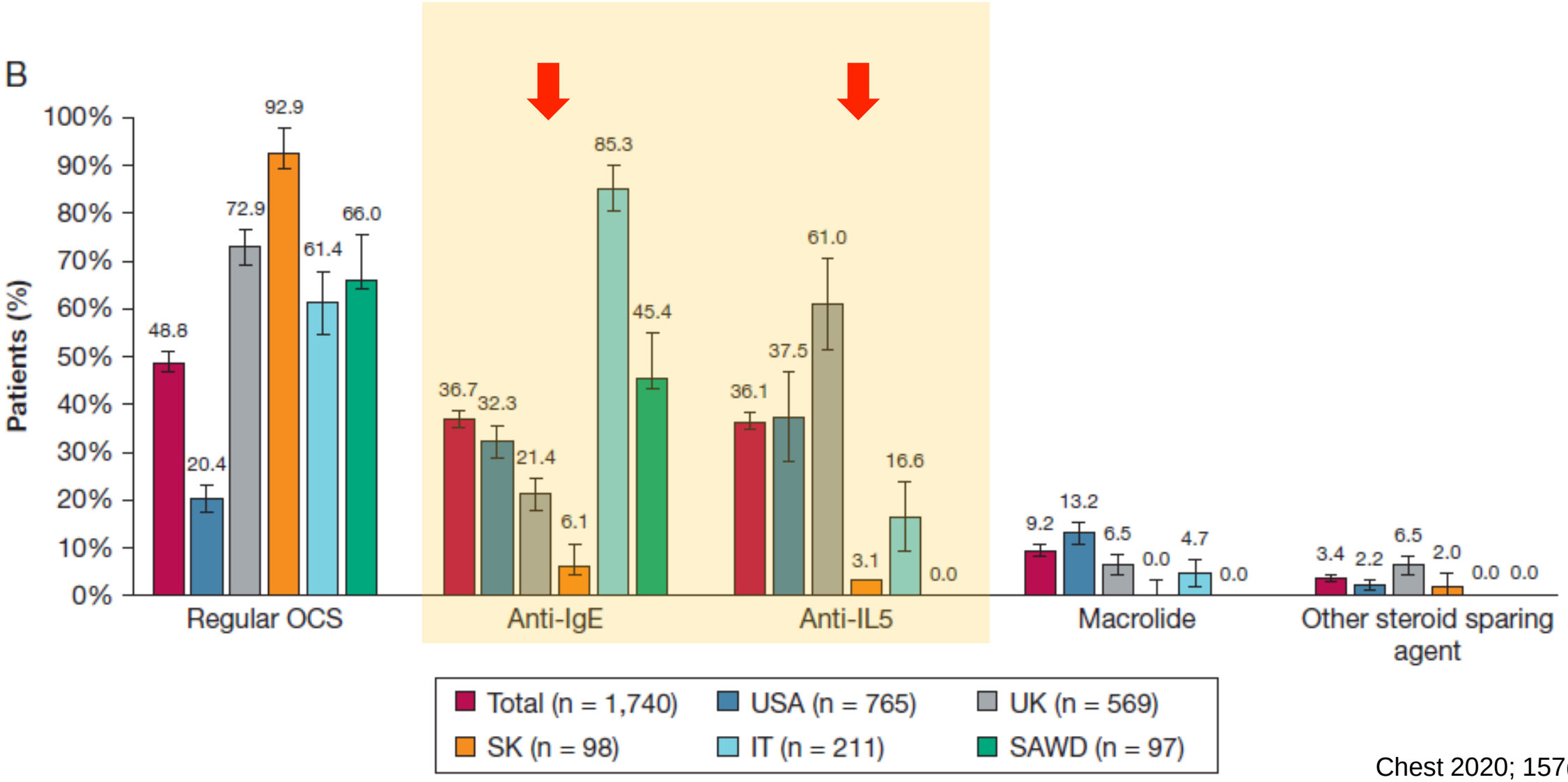
Allergy Asthma Immunol Res. 2020 Nov;12(6):910-933

Efficacy of biologics

Therapy	Asthma Exacerbation	Lung Function	Corticosteroid Weaning
Omalizumab	Reduces by 25%	Minimal or equivocal improvement	Decreases use of ICS, but no data that it helps with OCS weaning
Mepolizumab	Reduces by ~50%	Inconsistent effect	Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (14%)
Reslizumab	Reduces by ~50–60%	Improved	Has not been specifically evaluated for this indication
Benralizumab	Reduces by ~25–60%	Improved	Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (50%)
Dupilumab	Reduces by ~50–70%	Improved	Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (50%)

Am J Respir Crit Care Med. 2019 ;199(4):433-445

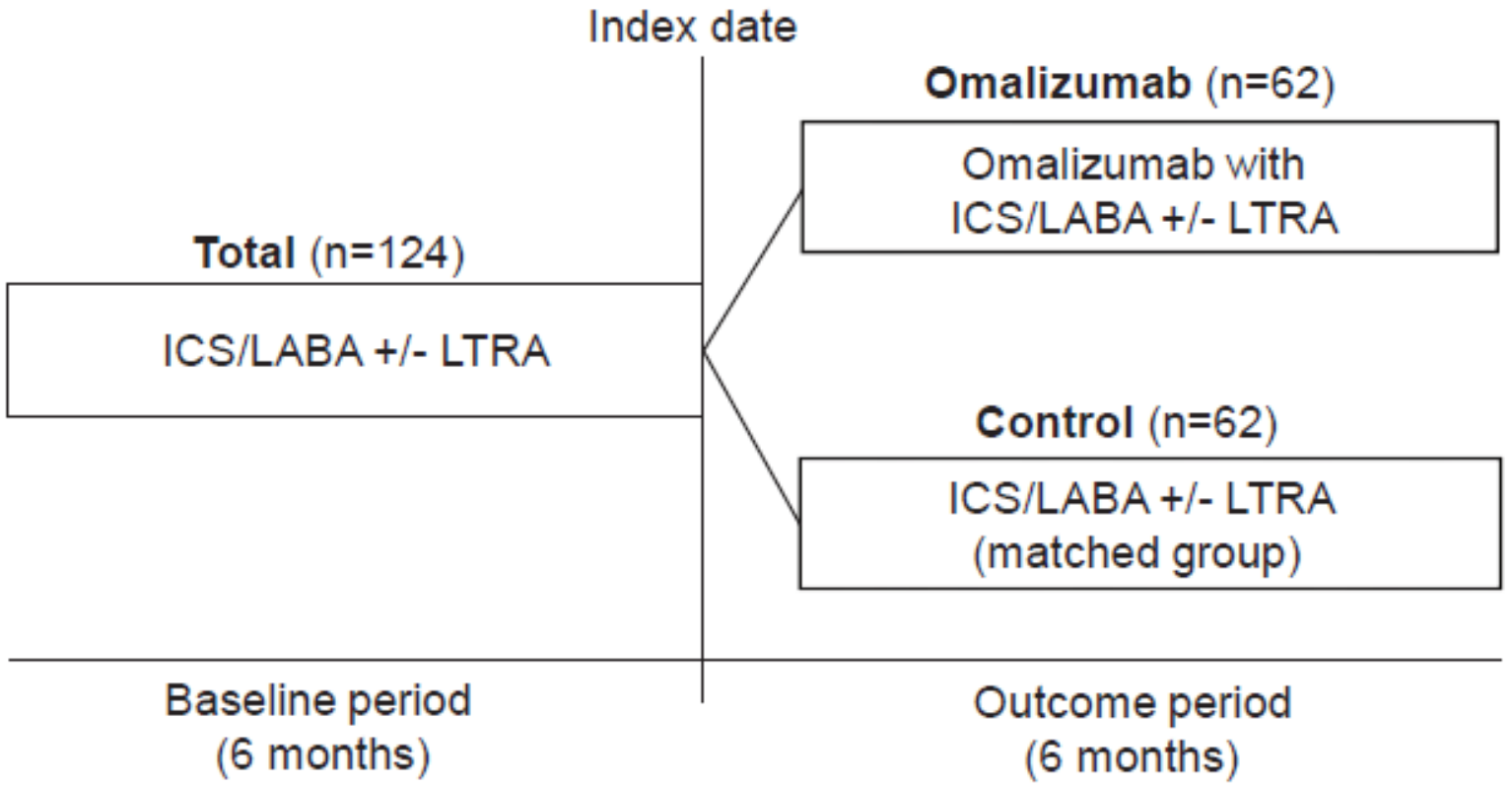
Prescription patterns in severe asthma



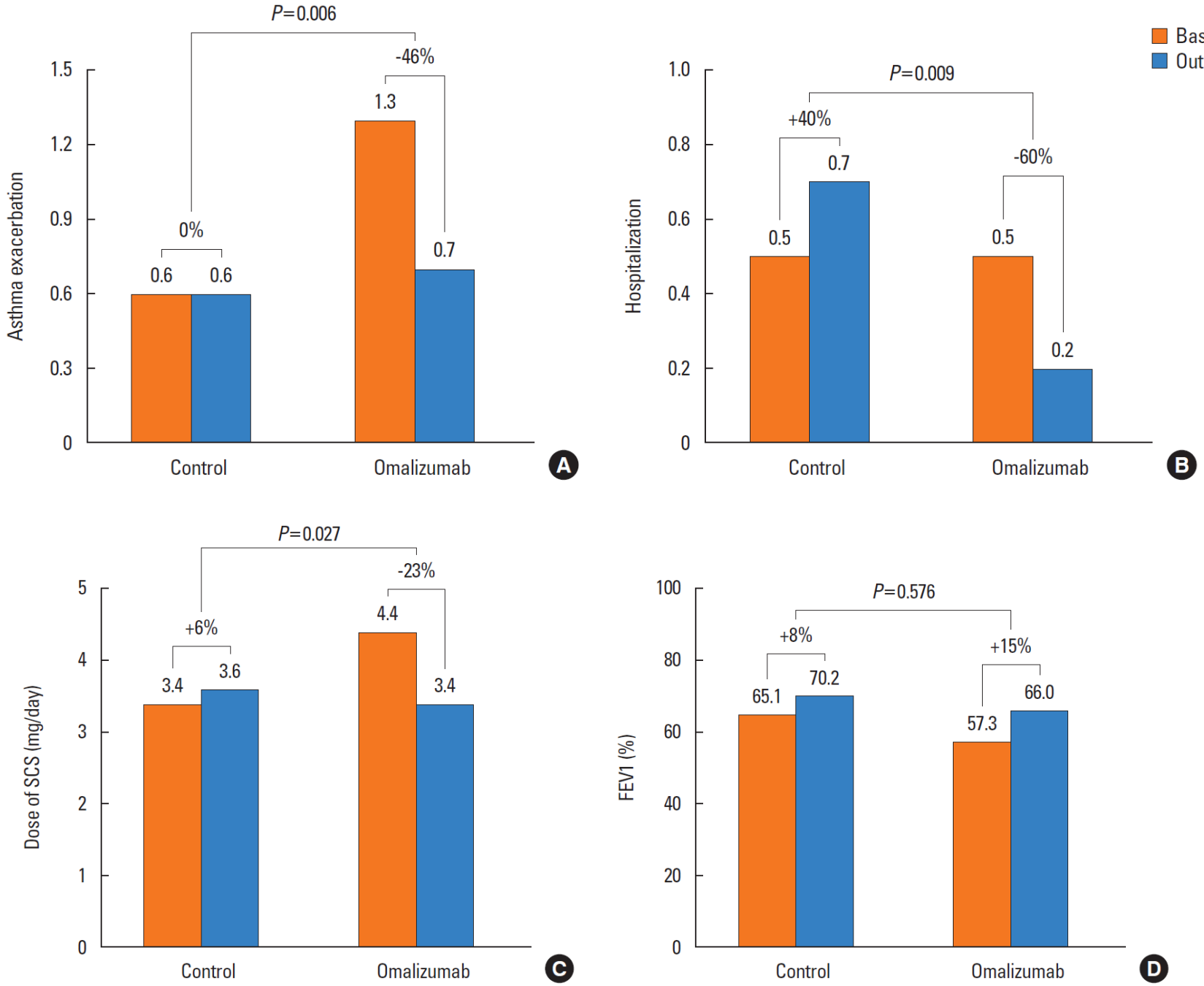
Chest 2020; 157(4):790-804

Therapeutic Effect of Omalizumab in Severe Asthma: A Real-World Study in Korea

A retrospective analysis of electrical medical records between March 2008 and February 2016



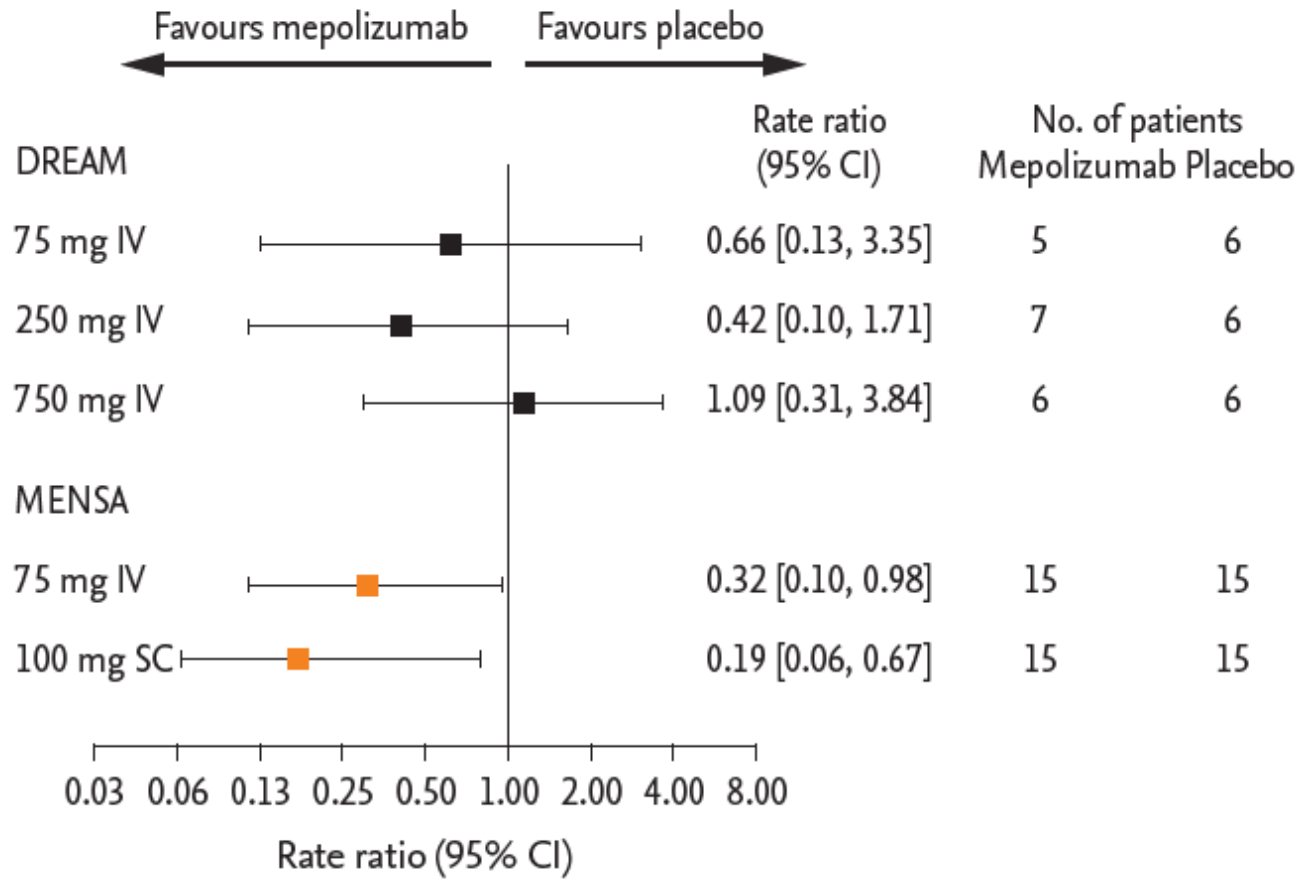
Allergy Asthma Immunol Res. 2018 March;10(2):121-130.



Allergy Asthma Immunol Res. 2018 March;10(2):121-130.

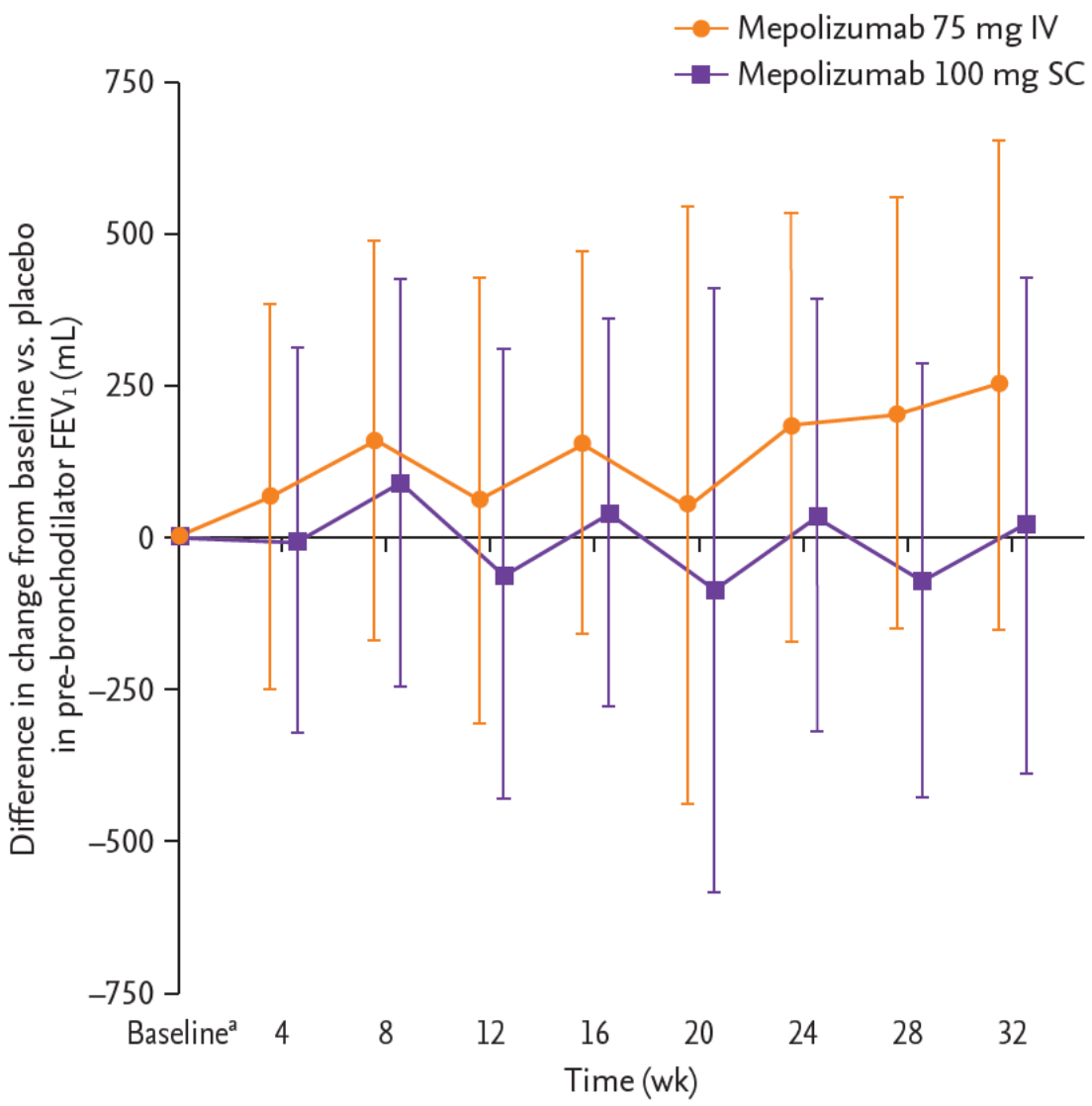
Efficacy and safety of mepolizumab in Korean patients with severe eosinophilic asthma from the DREAM and MENSA studies

Annual rate of clinically significant exacerbations
with mepolizumab versus placebo in Korean patients

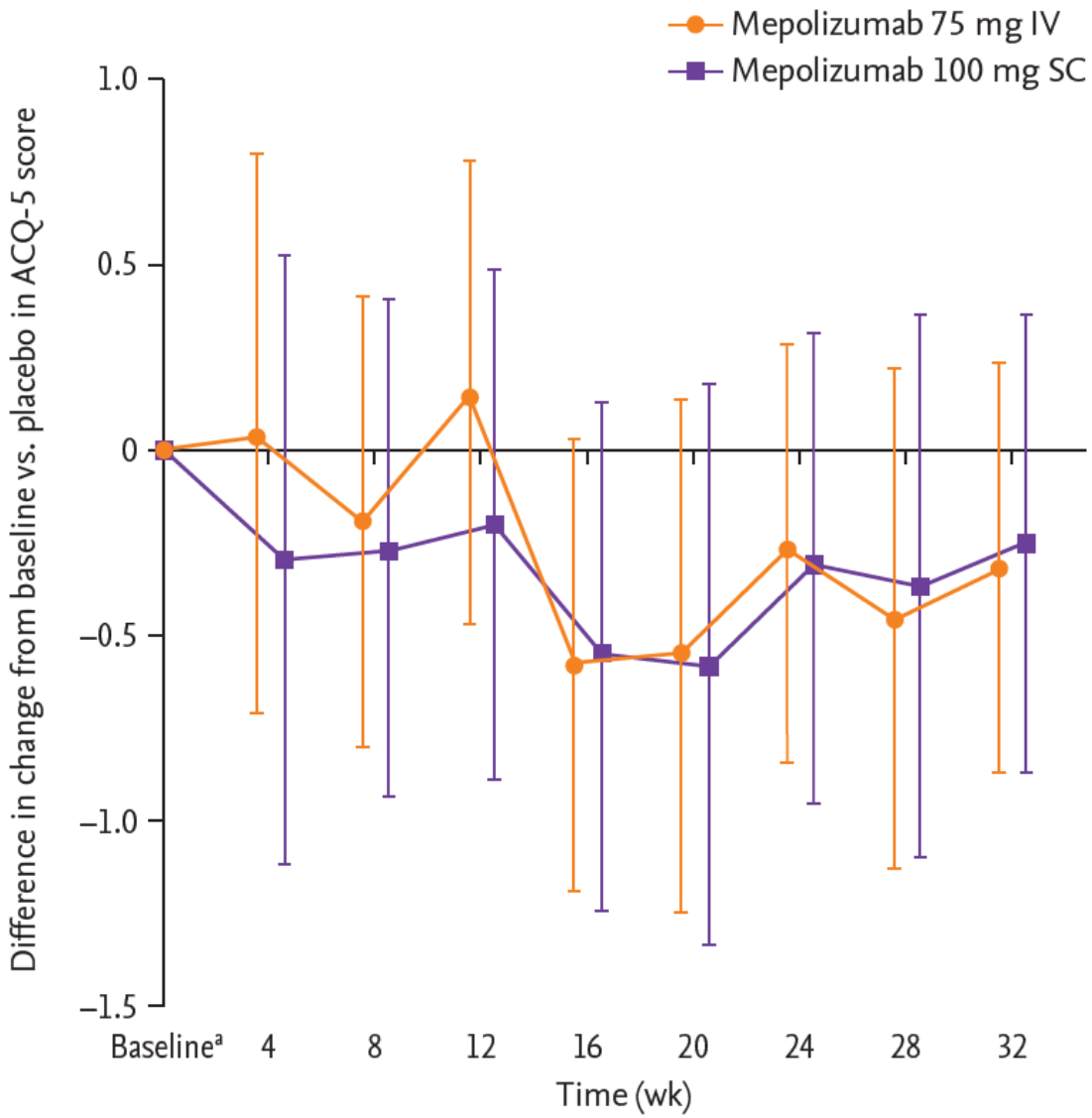


Korean J Intern Med 2021;36:362-370

FEV1

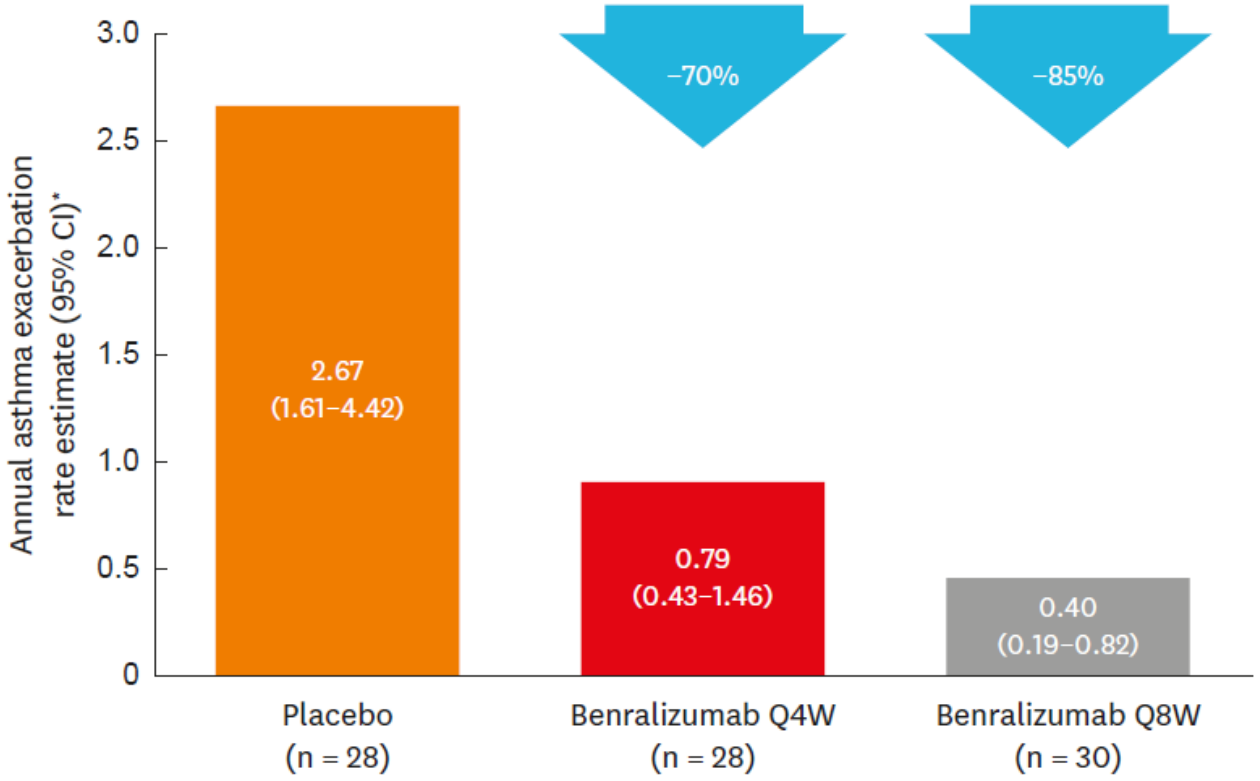


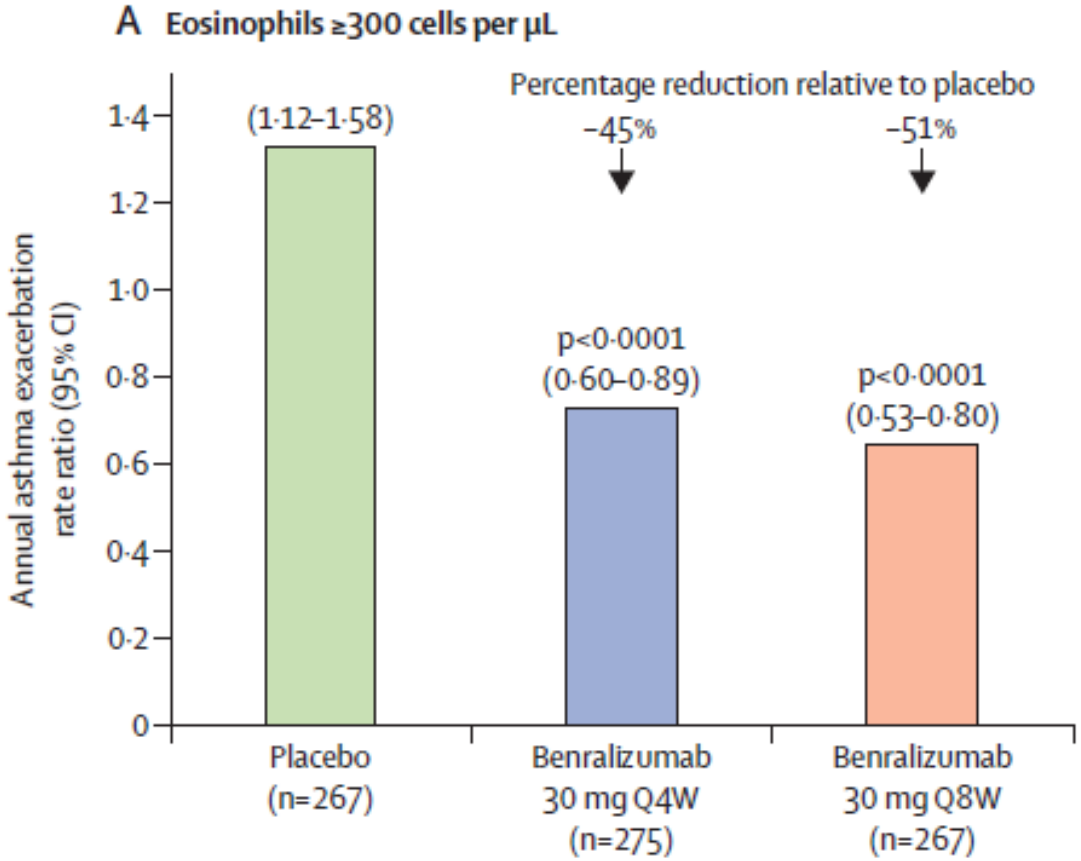
ACQ-5



Korean J Intern Med 2021;36:362-370

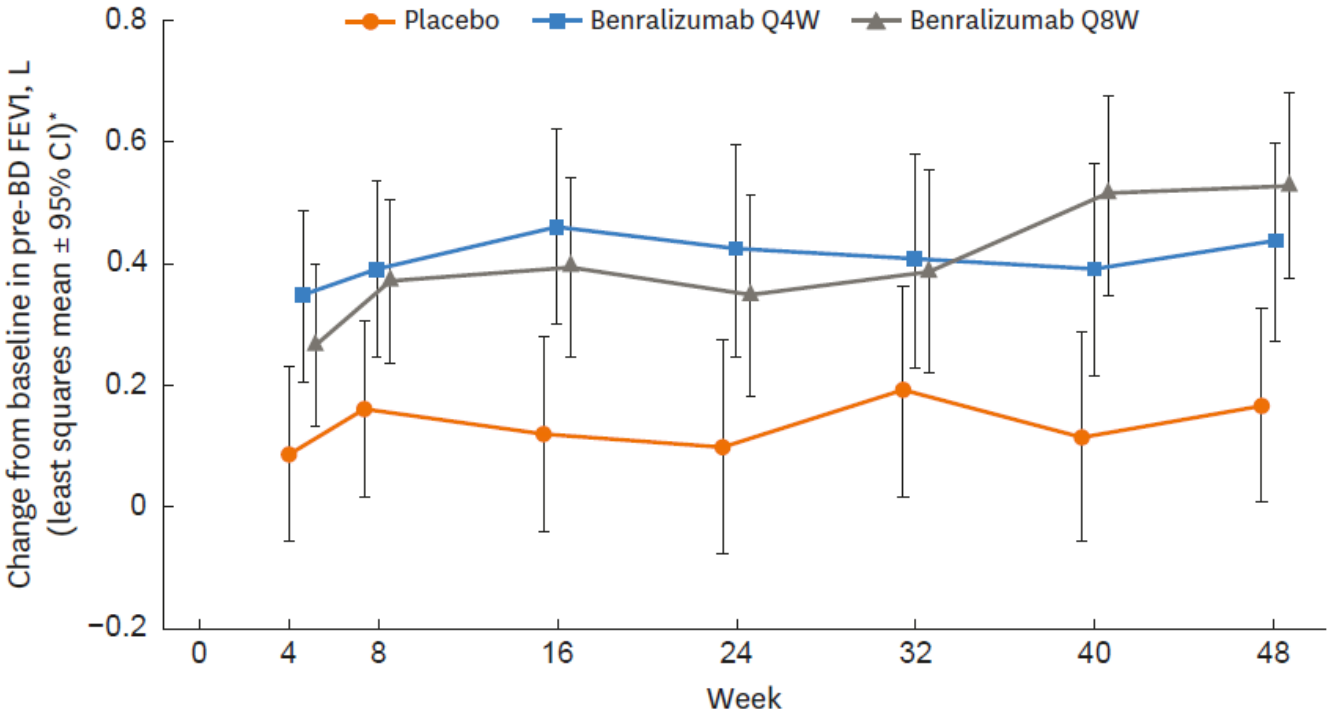
Efficacy and Safety of Benralizumab for Korean Patients With Severe, Uncontrolled Eosinophilic Asthma

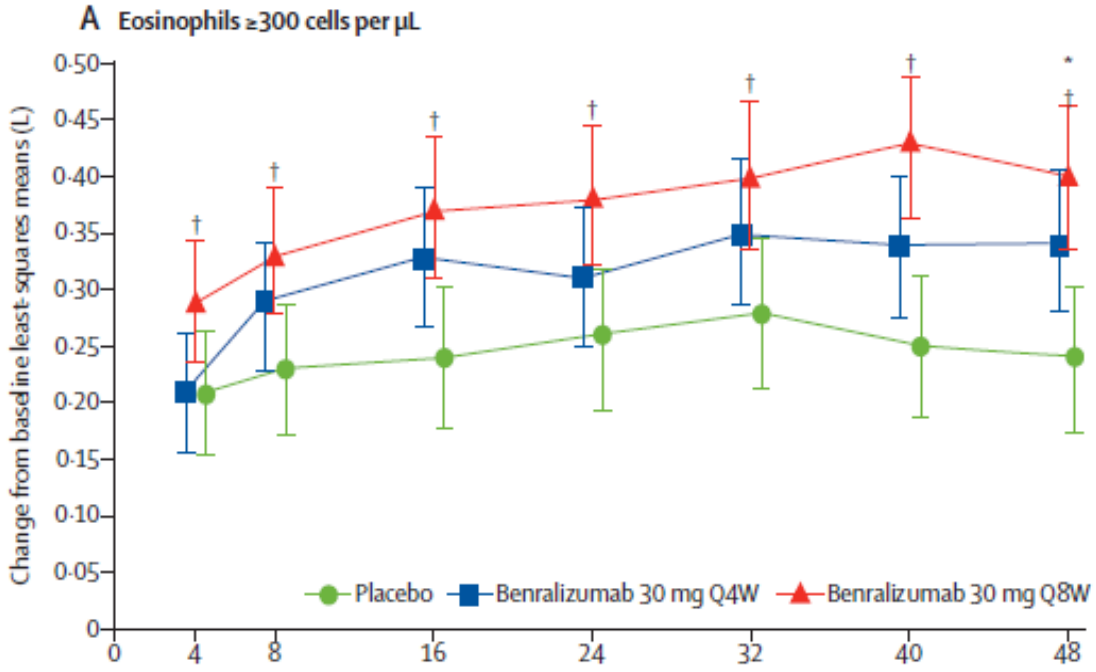




Allergy Asthma Immunol Res. 2019 Jul;11(4):508-518
Lancet 2016; 388: 2115–27

Efficacy and Safety of Benralizumab for Korean Patients With Severe, Uncontrolled Eosinophilic Asthma





Allergy Asthma Immunol Res. 2019 Jul;11(4):508-518
Lancet 2016; 388: 2115–27

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section **3** (including inhaler technique, adherence, comorbidities)

6b Consider ***add-on biologic Type 2*** targeted treatments

- Consider add-on Type 2-targeted biologic for patients with exacerbations or poor symptom control on high dose ICS-LABA, who:
  - have eosinophilic or allergic biomarkers, or
  - need maintenance OCS
- Consider **local payer eligibility criteria** and **predictors of response** when choosing between available therapies
- Also consider cost, dosing frequency, route (SC or IV), patient preference

Which biologic is appropriate to start first?

Anti-IgE

*Is the patient eligible for **anti-IgE** for severe allergic asthma?*

- Sensitization on skin prick testing or specific IgE
- Total serum IgE and weight within dosage range
- Exacerbations in last year

What factors may predict good asthma response to anti-IgE?

- Blood eosinophils ≥260/µl ++
- FeNO ≥20 ppb +
- Allergen-driven symptoms +
- Childhood-onset asthma +

no / *no*

Anti-IL5 / Anti-IL5R

*Is the patient eligible for **anti-IL5 / anti-IL5R** for severe eosinophilic asthma?*

- Exacerbations in last year
- Blood eosinophils ≥300/µl

What factors may predict good asthma response to anti-IL5/5R?

- Higher blood eosinophils +++
- More exacerbations in previous year +++
- Adult-onset of asthma ++
- Nasal polyposis ++

no / *no*

Anti-IL4R

*Is the patient eligible for **anti-IL4R***

... for severe eosinophilic/Type 2 asthma?

- Exacerbations in last year
- Blood eosinophils ≥150/µl or FeNO ≥25 ppb

... or because of need for maintenance OCS?

What factors may predict good asthma response to anti-IL4R?

- Higher blood eosinophils +++
- Higher FeNO +++

Anti-IL4R may also be used to treat

- Moderate/severe atopic dermatitis
- Nasal polyposis

Eligible for none?
Return to section **6a**

TEC, 400/µl
FENO >50
Atopy

..overlapping

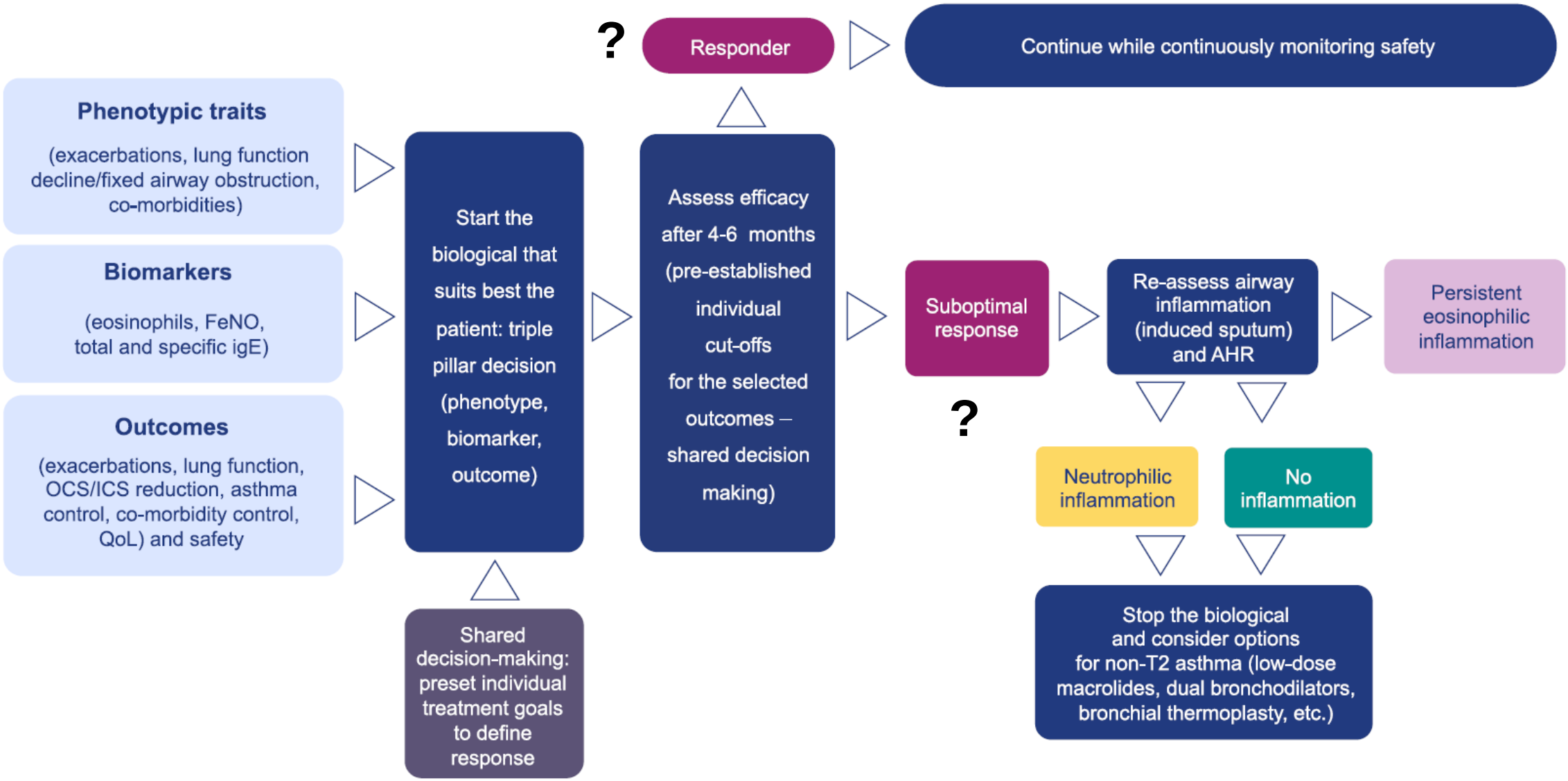
different Type
argeted therapy,
f eligible

no

Little/no response to T2-targeted therapy

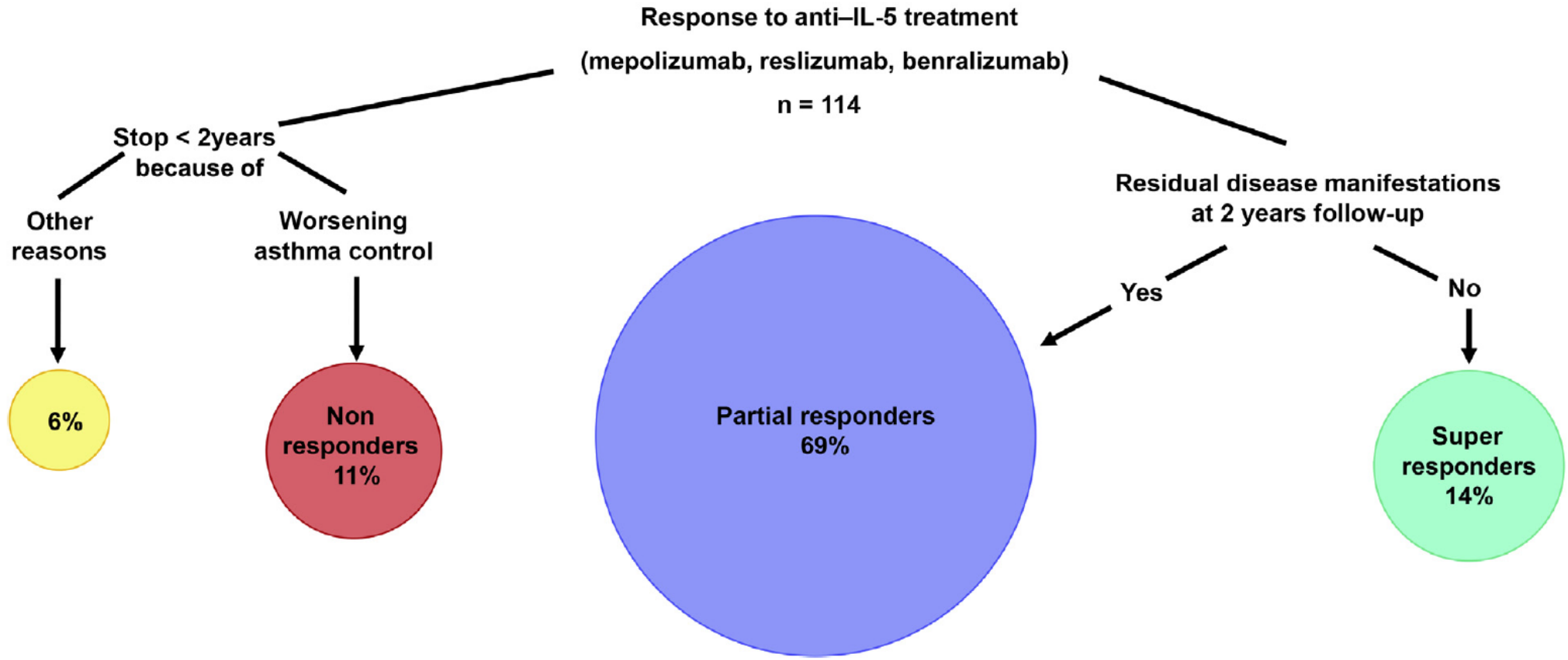
Check local eligibility criteria for specific biologic therapies as these may vary from those listed

Decision tree guiding biological use



Allergy. 2021 Jan;76(1):14-44.

Long-Term Therapy Response to AntieIL-5 Biologics in Severe Asthma—A Real-Life Evaluation



- Super responders: no residual disease at 2 year follow up
  (no OCS, ACQ <1.5, FEV1 ≥80%, FENO<50ppb, control of comorbidities (CRSwNP, AD, etc)
- Partial responders
- Non-responders: discontinue anti IL-5/5R d/t clinical worsening

J Allergy Clin Immunol Pract 2021;9:1194-200

Gaps in evidence for the use of biologicals in severe asthma

- Standardizing the use of biologicals in clinical practice
  - Criteria for responders and suboptimal response (early stopping rules)
  - Switching rules
  - Duration of treatment in responders (late stopping rules)
  - Long-term treatment regimen in responders
  - Identification of factors related to failure
  - Efficacy in cases of prior failure to other biologicals
  - Routine measurement of ADA
- Long-term safety data
- Assess the long-term efficacy/disease-modifying effect of biologicals in severe asthma (after treatment cessation)
- Cost-effectiveness of biologicals in severe asthma
- Identification of clinically relevant biomarkers in order to select responders to the current available biologicals

Allergy 2020;75(2):311-325

The Korean Severe Asthma Registry (KoSAR)

KoSAR-Biologics registry (KoSAR-BIO)

Characteristics of Severe Asthma Patients Treated with Biologics in Real-World: Findings From Korean Severe Asthma Registry (KoSAR)

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Severe asthma has high morbidity and healthcare utilization. However, treatment options for these patients are limited. Recently, a new paradigm for severe asthma treatment is emerging with introduction of novel biologics. Currently, several biologics such as mepolizumab, reslizumab, and omalizumab have been approved in Korea and began to be prescribed for severe asthma. The aim of this study is to figure out the current status of biologics use in real-world clinics in Korea.

Korea Severe Asthma Registry (KoSAR), the largest representative severe asthma cohort in Korea, was established in 2011 and the patients were enrolled from 28 university hospitals nationwide in Korea (n=495). Severe asthma was defined according to modified European Respiratory Society/American Thoracic Society criteria. Among them, independent Biologic Registry (BR) was established to evaluate clinical features of the patients treated with biologics (n=41). In this study, we analyzed various clinical characteristics and courses of the patients treated with biologics in real-world clinics in Korea.

Mepolizumab was prescribed in 31 patients and reslizumab in 10 patients in BR. The mean age of the patients was 51.2±12.8 years, which was lower than that of whole patients in KoSAR (62.3±14.0). The asthma onset age was 35.7±18.3 years, which was also lower than that of whole KoSAR (44.8 ±16.3). The number of exacerbations over the past year was 1.1±1.7. Mean FVC, FEV1 and FEV1/FVC values were 74.5±15.6%, 66.8±18.4% and 70.2±11.4%, respectively. Mean blood eosinophil count was 695.2±823.3. There were no reported side effects except mild burning sensation in only one case.

It is important to know the status of biologic treatment for severe asthma in Korea not only because the medical environment can vary in each country but also because analyzing the characteristics of the patients may be helpful to improve the management of severe asthma in real-world clinical practice.

2019년 춘계 알레르기학회 초록집

Category	Information
Demographics	Age, sex, height, weight, body mass index Smoking status and past smoking Previous and current occupation Living area Owning a pet
Diagnosis	Physician (specialist) diagnosis of asthma Onset and duration of asthma Treatment period of asthma Family history of allergic diseases (asthma, allergic rhinitis, and atopic dermatitis) Combined COPD
Exacerbations	Frequency of exacerbations and OCS bursts Use of healthcare facilities: visits to outpatient department and emergency department, hospitalization and use of ICU
Asthma control and quality of life	Level of symptom control Asthma Control Test® Quality of Life Questionnaire for Adult Korean Asthmatics
Environmental factors	Work exacerbated asthma Aspirin hypersensitivity Aggravation during menstruation period
Comorbidities	Current or previous history of diagnosis and time Current treatment Allergic rhinitis: severity, comorbid sinusitis and nasal polyp, treatment atopic dermatitis, allergic conjunctivitis, GERD, sleep apnea, depression, anxiety disorder, diabetes mellitus, hypertension, heart failure, arrhythmia, cardiovascular disease, osteoporosis, and bronchiectasis
Asthma medications	Controllers including inhalers and biologics OCS and immunosuppressant Adherence to medications Use of SABA
Lung function tests	Spirometry Bronchodilator response Lung volume Bronchial provocation test
Laboratory tests	Skin prick test to aeroallergens Peripheral blood eosinophils Total IgE Induced sputum analysis Exhaled nitric oxide

OCS long-term complication (infection, osteoporosis, etc.)

Patient centered outcomes

Adherence – objective measurement

Biologics – safety (preg. Malignancy)
- *co-morbidities (CRSwNP, AD in detail)*

Summaries

- A considerable gap between asthma management guidelines and real practice in Korea
  - Lack of pulmonary function measurement
  - Low rate of inhaler prescription
  - Low rate of SABA overuse

- Severe asthma
  - Hight rate of OCS use, low rate of biologics use in severe asthma than other countries
  - Severe asthma registry-based real-world studies would be needed
    - Biomarkers (patient-selection, treatment response)
    - Long-term safety and efficacy
    - Independent head-to-head comparison, etc.
    - To define nonT2 asthma

경청해주셔서 감사합니다