The KAAACI Chronic Cough Registries: Key Findings and Clinical Implications

송우정

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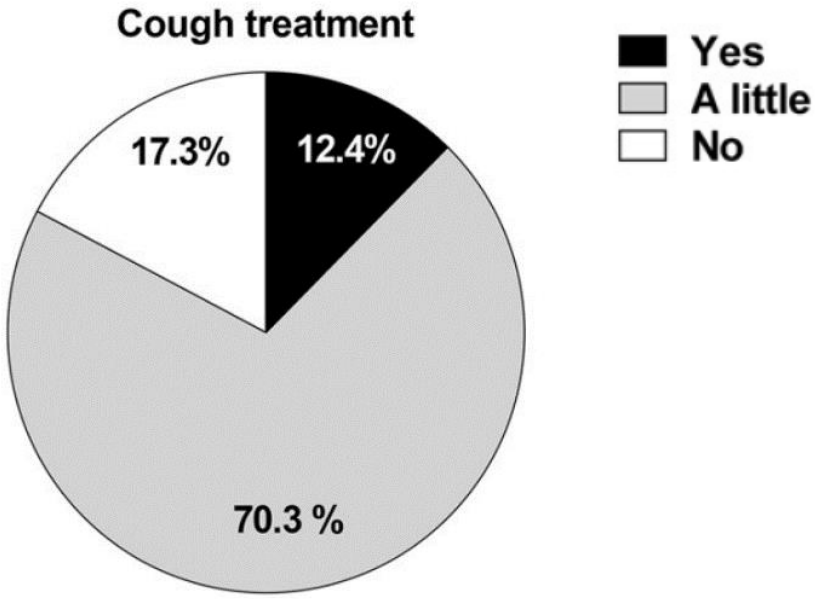
Cough Registry, Why?

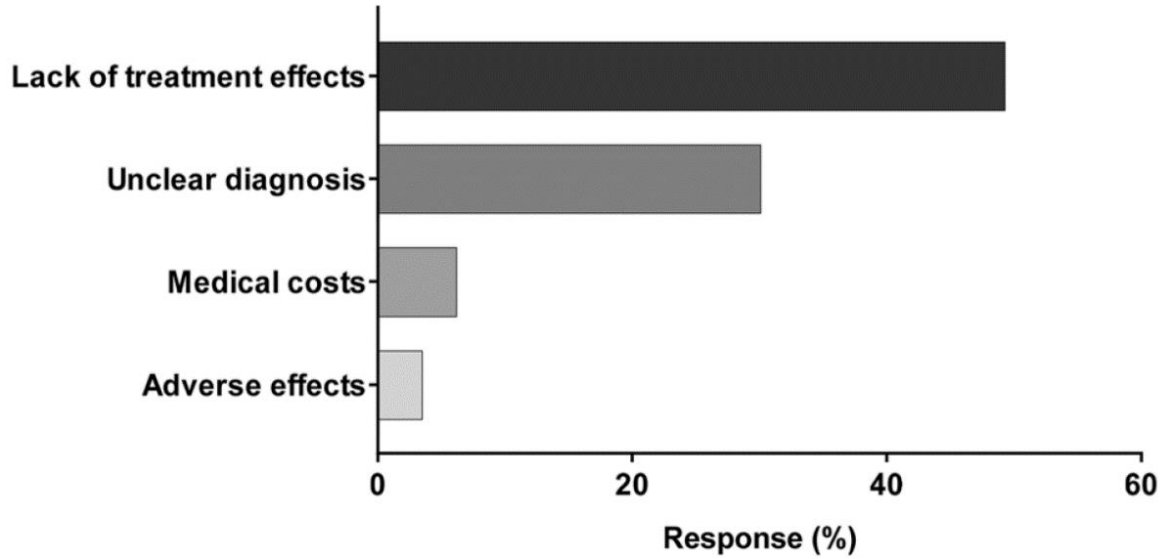
- Chronic cough as a symptom
- Chronic cough as a disease

What are the unmet needs?

- Objective: To identify the disease impact and unmet needs in patients seeking care
- Cross-sectional study of 447 patients recruited from 6 referral hospitals (2016-2018)



Effectiveness of treatment



Unmet needs in chronic cough

Kang SY, Won HK et al. *Lung 2019*

Cough triggers and sensations

- Objective: To describe a symptom profile of cough hypersensitivity and assess its clinical relevance
- Cross-sectional study of 478 patients recruited from 6 referral hospitals (2016-2019)

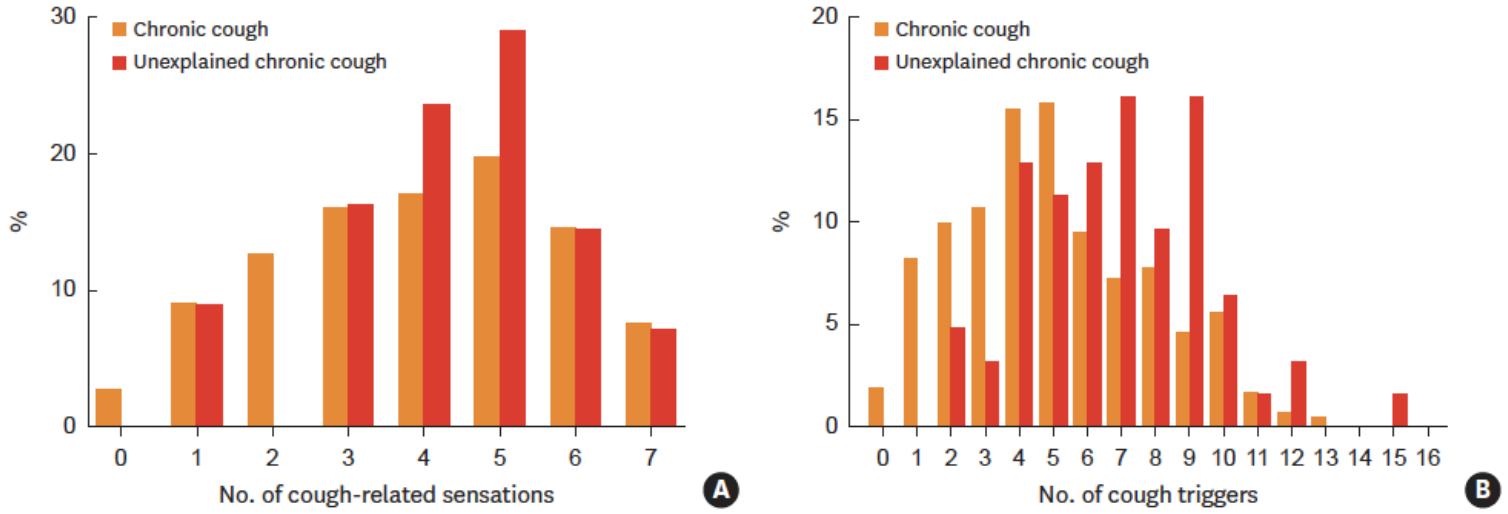
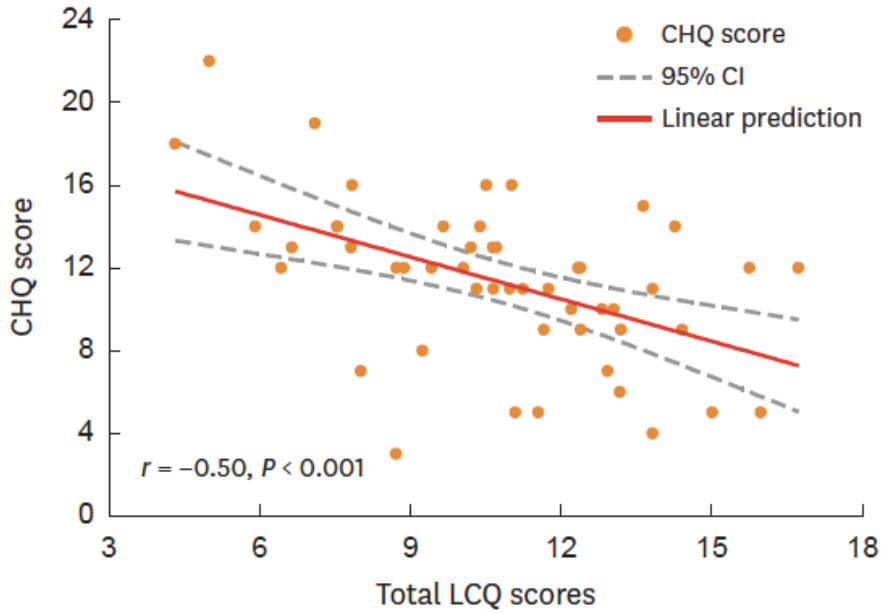


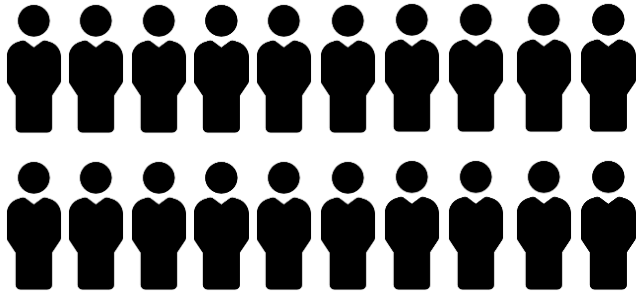
Fig. 1. The number of (A) cough-related laryngeal sensations and (B) cough triggers in patients with chronic cough and unexplained chronic cough.



r= -0.50 (p<0.001)

Won HK, Kang SY et al. *AAIR 2019*

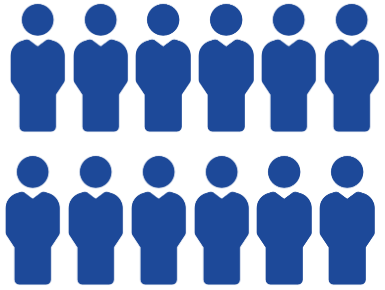
Persistence of chronic cough: Retrospective cohort study



Chronic cough (> 8 weeks), n=323
(mean age: 53 years, female: 71%)

Cough persistence?

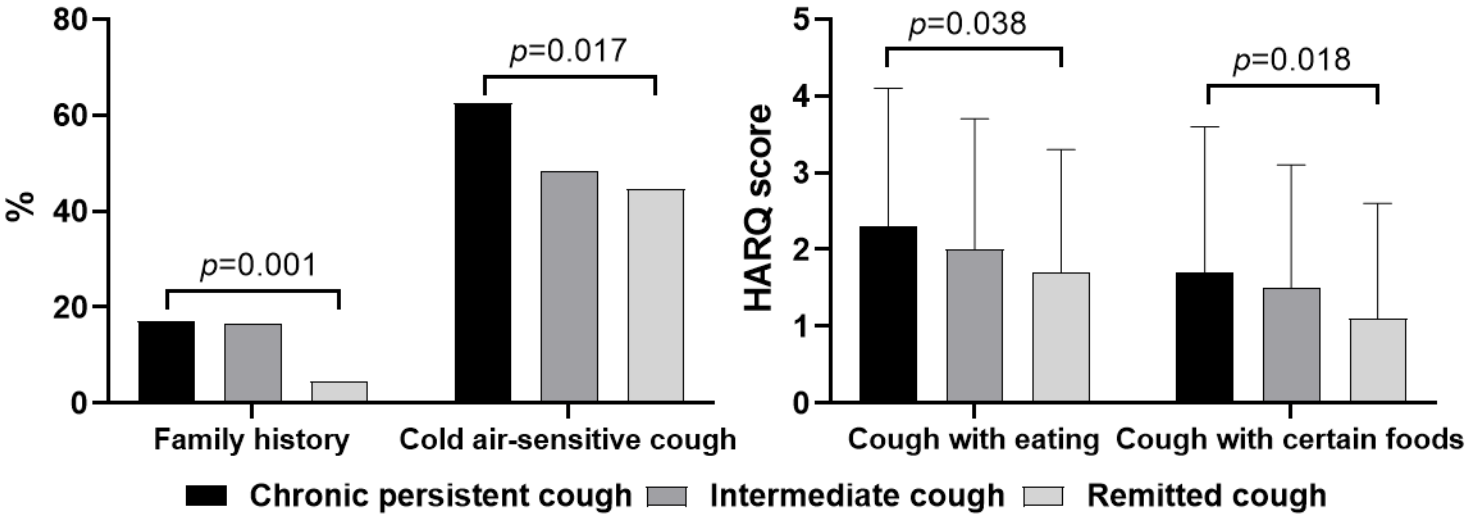
Follow-ups: mean 3.6 years



Remitted cough
(59.8%)

Intermittent cough
(20.4%)

Chronic persistent
cough (19.8%)



Kang SY et al. *Allergology Int 2020*

Korean Chronic Cough Registry: A Prospective Study

- Since 2020
- The primary objectives are:

  (1) to evaluate the clinical characteristics, treatment responses, and longitudinal courses of chronic cough in adults;

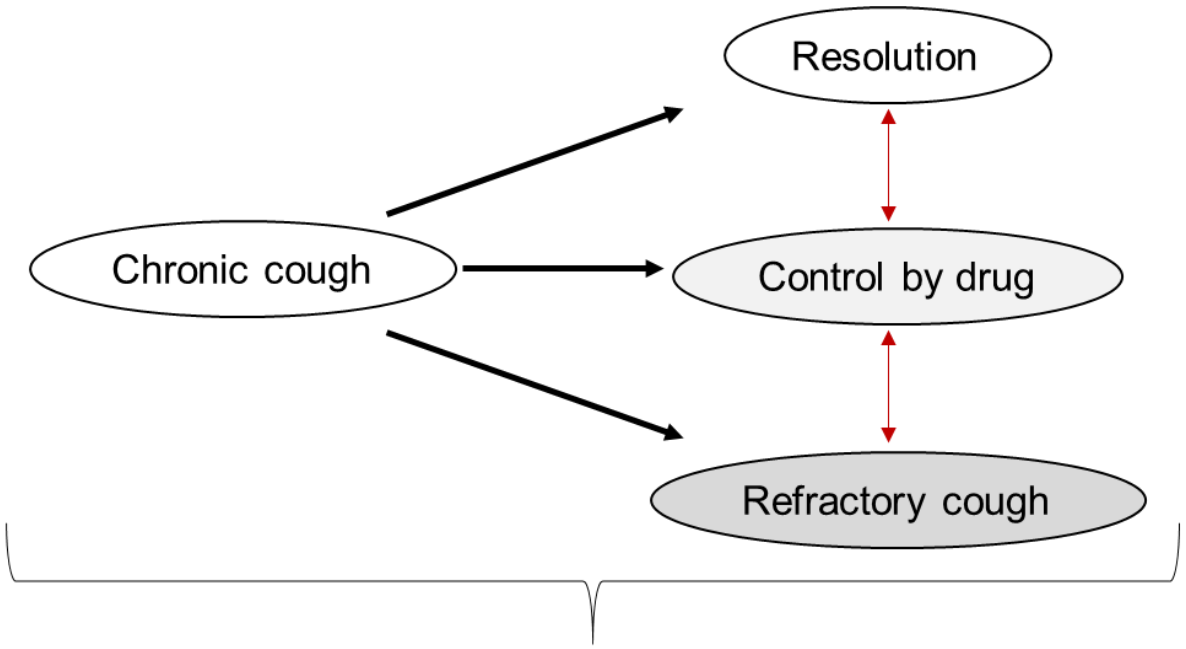
  (2) to quantify the disease burden;

  (3) to investigate the prevalence of refractory or unexplained chronic cough (RUCC) among referred chronic cough patients and identify predictive factors;

  (4) to establish an infrastructure for studying novel biomarkers and therapeutic targets

Jo EJ et al. *Lung 2023*

Korean Chronic Cough Registry: Overview



Main outcomes

Cough persistence

Treatment response

Possible associations

Cough characters
Demographics
Clinical factors
?Biomarkers

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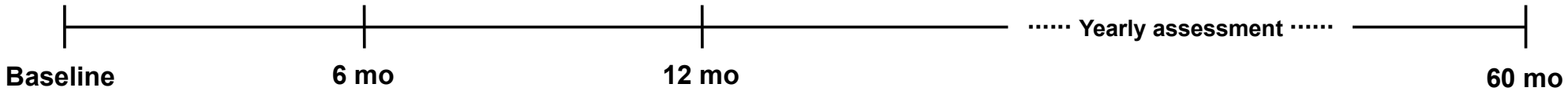
Korean Chronic Cough Registry: Study Protocols

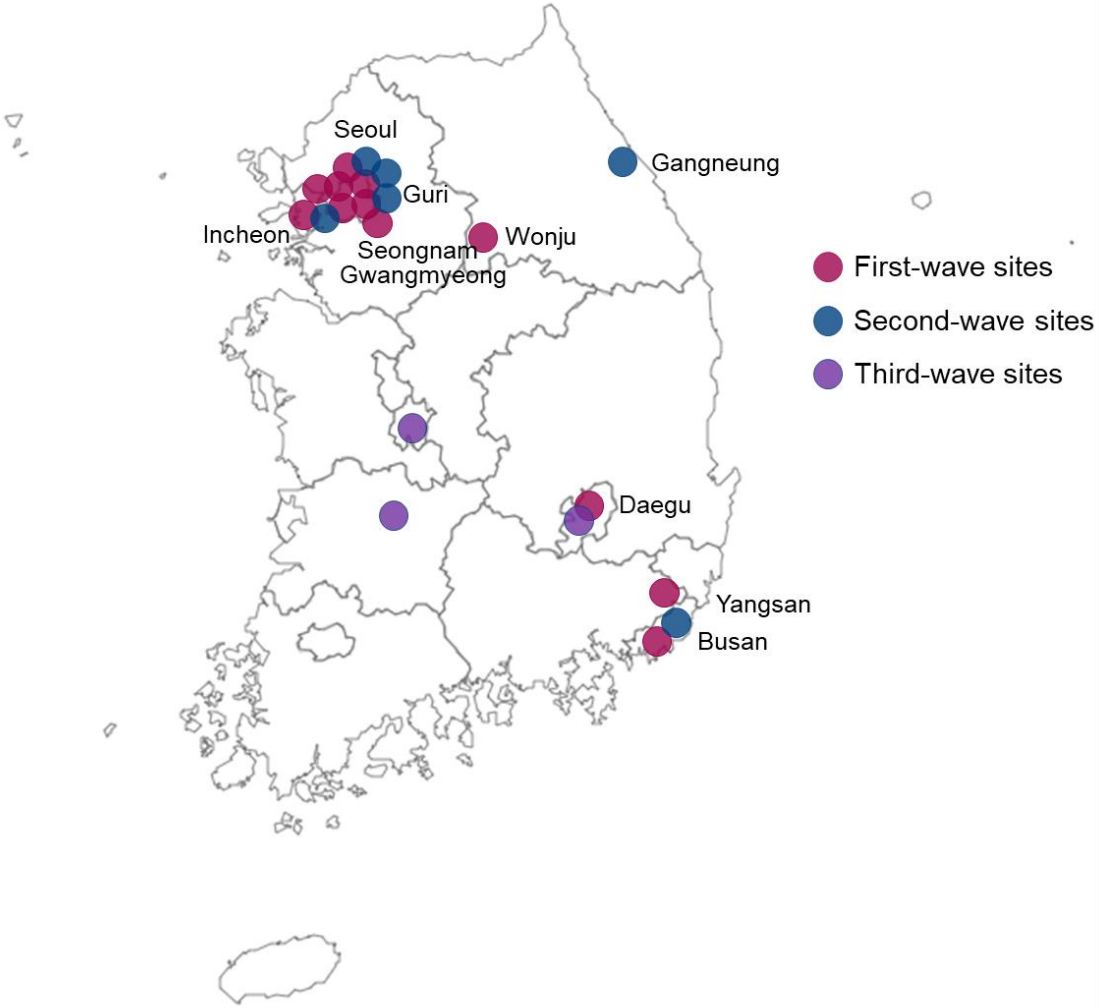


	Baseline visit	Follow-up visits (6, 12, 24, 36, 48, 60 months)
Demographics and clinical information	V	
Cough characteristics	V	V
Patient-reported outcomes		
Cough severity VAS	V	V
LCQ	V	V
CHQ	V	V
EuroQoL	V	V
CES-D	V	V
Physician assessment		
Cough phenotype		V
Physician-assessed treatment response		V
Electronic medical record review	V	V
Blood sample	V	

Jo EJ et al. *Lung 2023*

Korean Chronic Cough Registry: Participation

- 844 patients with chronic cough
- 22 centers



Health-Related Quality of Life and Its Determinants in Chronic Cough: The Korean Chronic Cough Registry Study

Noeul Kang [1], Ha-Kyeong Won [2], Ji-Hyang Lee [3], Ji-Su Shim [4], Sung-Yoon Kang [5], Han-Ki Park [6], Eun-Jung Jo [7], Seung Eun Lee [8], Min-Hye Kim [4], Sang-Heon Kim [9], Sae-Hoon Kim [10], Yoon-Seok Chang [10], Byung-Jae Lee [1], Woo-Jung Song [3*], Min-Woo Jo [11*]

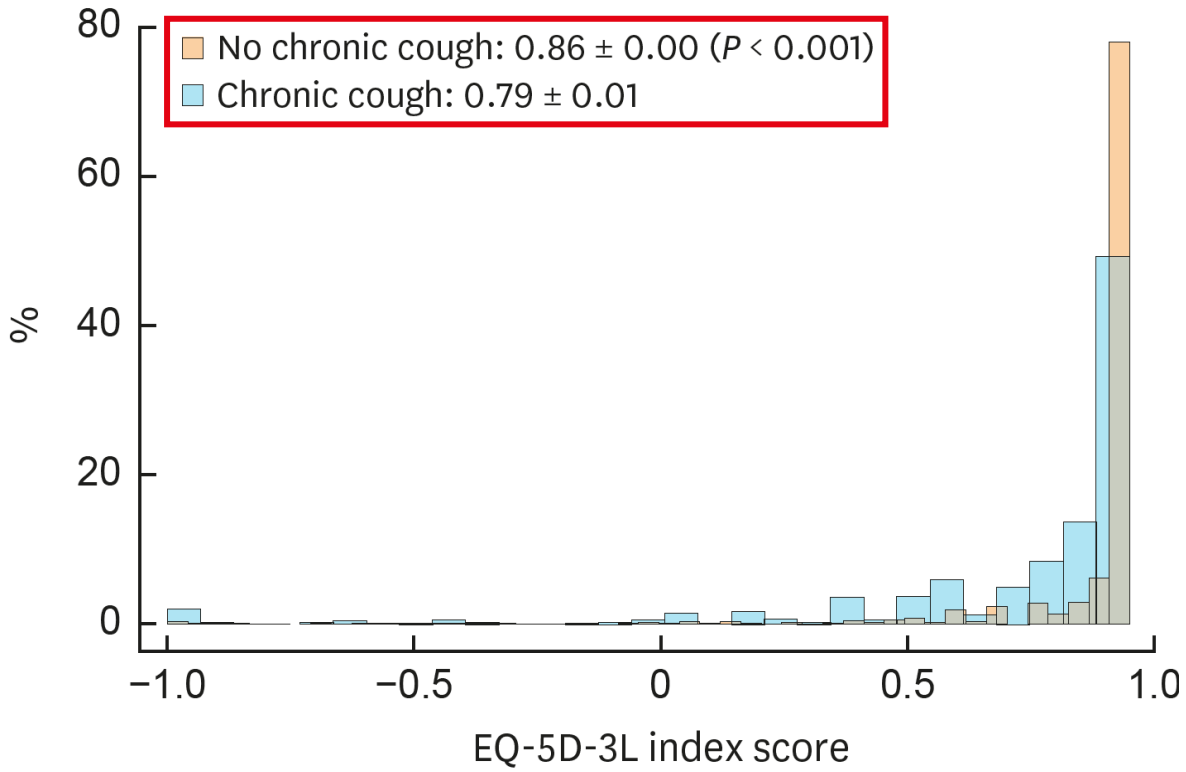
Allergy, Asthma & Immunology Research AAIR

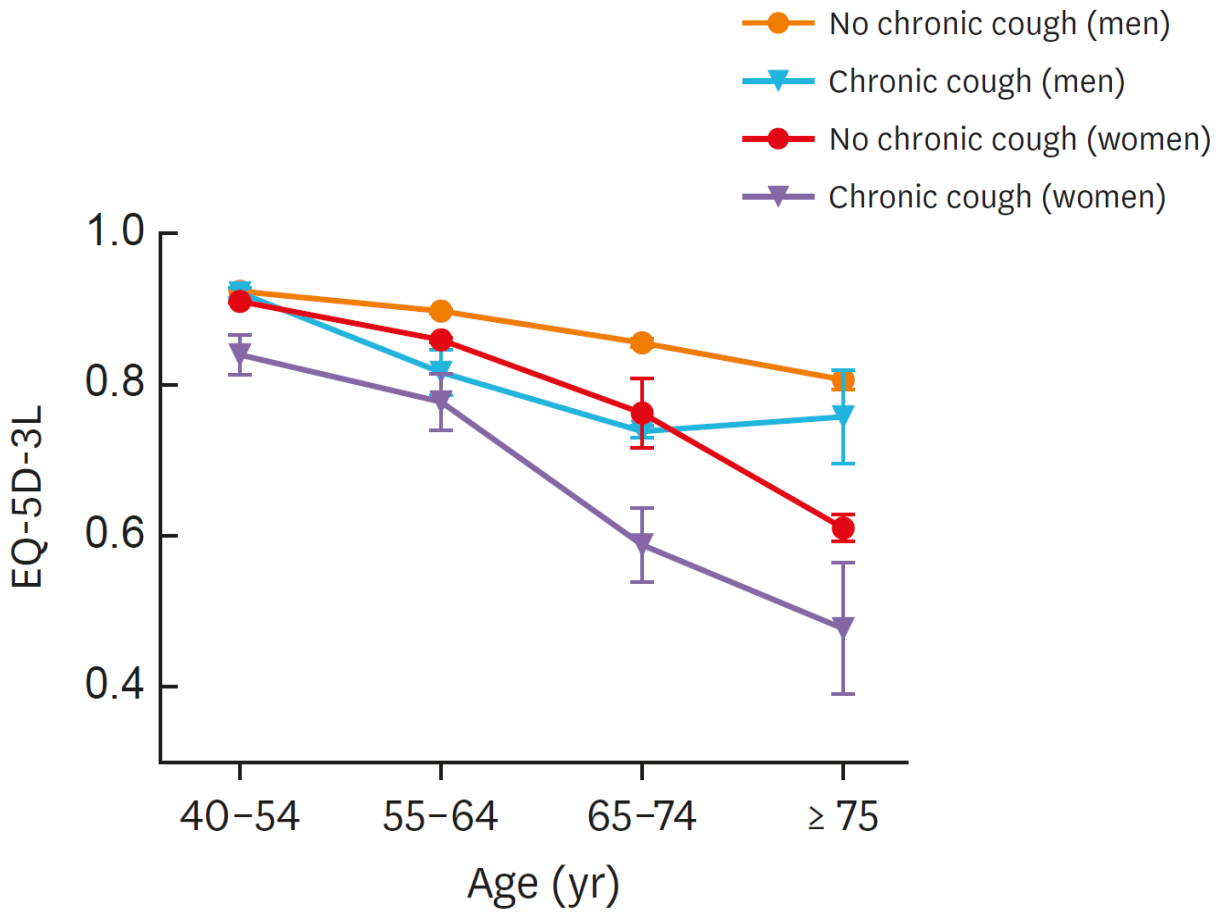
- Objective: To identify HRQoL impairment associated with chronic cough
- Cross-sectional comparison
  - Healthy controls (n=800) & Non-cough controls (n=800) from KNHANES
  - Newly referred chronic cough & refractory chronic cough patients (n=200) from Patient Registry
- Outcome of interest: EQ-5D index

Kang N et al. *AAIR 2022*

Impact of Chronic Cough on Health-Related Quality of Life in the Korean Adult General Population: The Korean National Health and Nutrition Examination Survey 2010–2016

Allergy, Asthma & Immunology Research AAIR

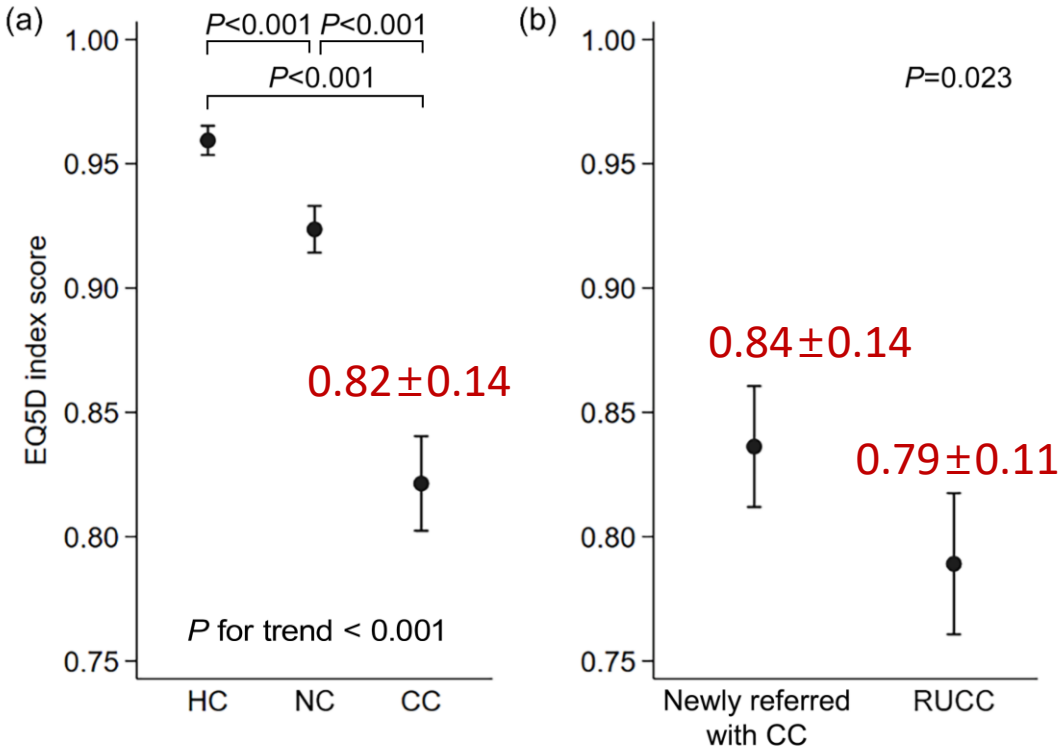


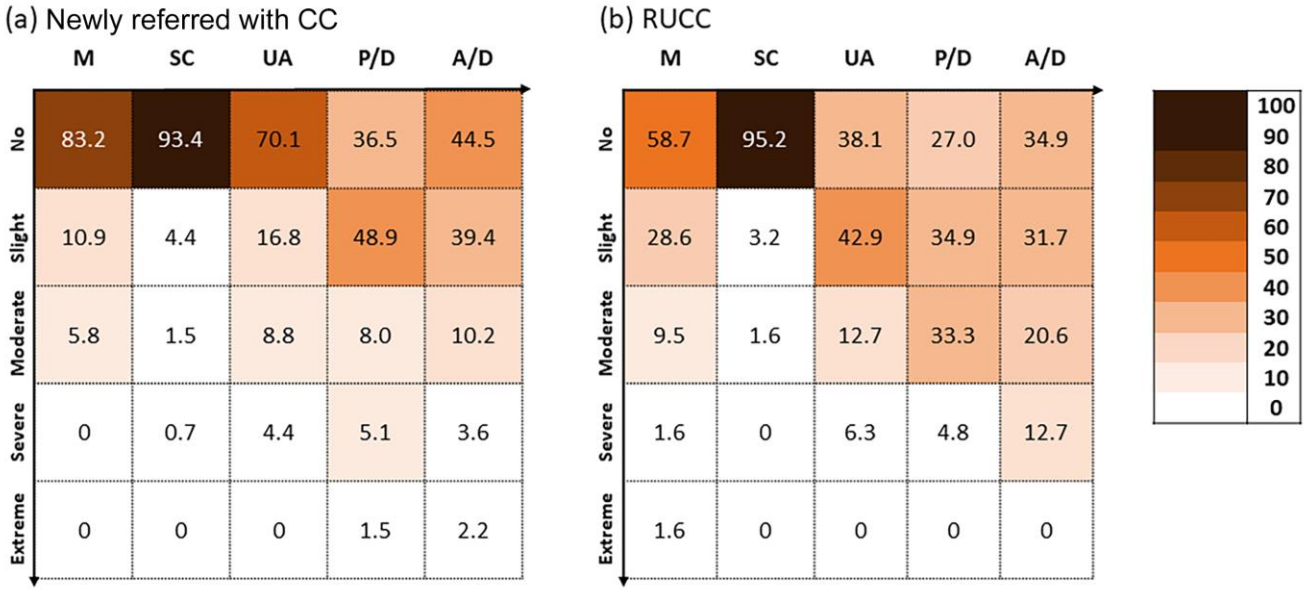


Won HK et al. *AAIR 2020*

Health-Related Quality of Life and Its Determinants in Chronic Cough: The Korean Chronic Cough Registry Study

Noeul Kang,[1] Ha-Kyeong Won,[2] Ji-Hyang Lee,[3] Ji-Su Shim,[4] Sung-Yoon Kang,[5] Han-Ki Park,[6] Eun-Jung Jo,[7] Seung Eun Lee,[8] Min-Hye Kim,[4] Sang-Heon Kim,[9] Sae-Hoon Kim,[10] Yoon-Seok Chang,[10] Byung-Jae Lee,[1] Woo-Jung Song,[3*] Min-Woo Jo [11*]





Mobility (M), self-care (SC), usual activities (UA), pain and discomfort (P/D), and anxiety and depression (A/D)

Kang N et al. *AAIR 2022*

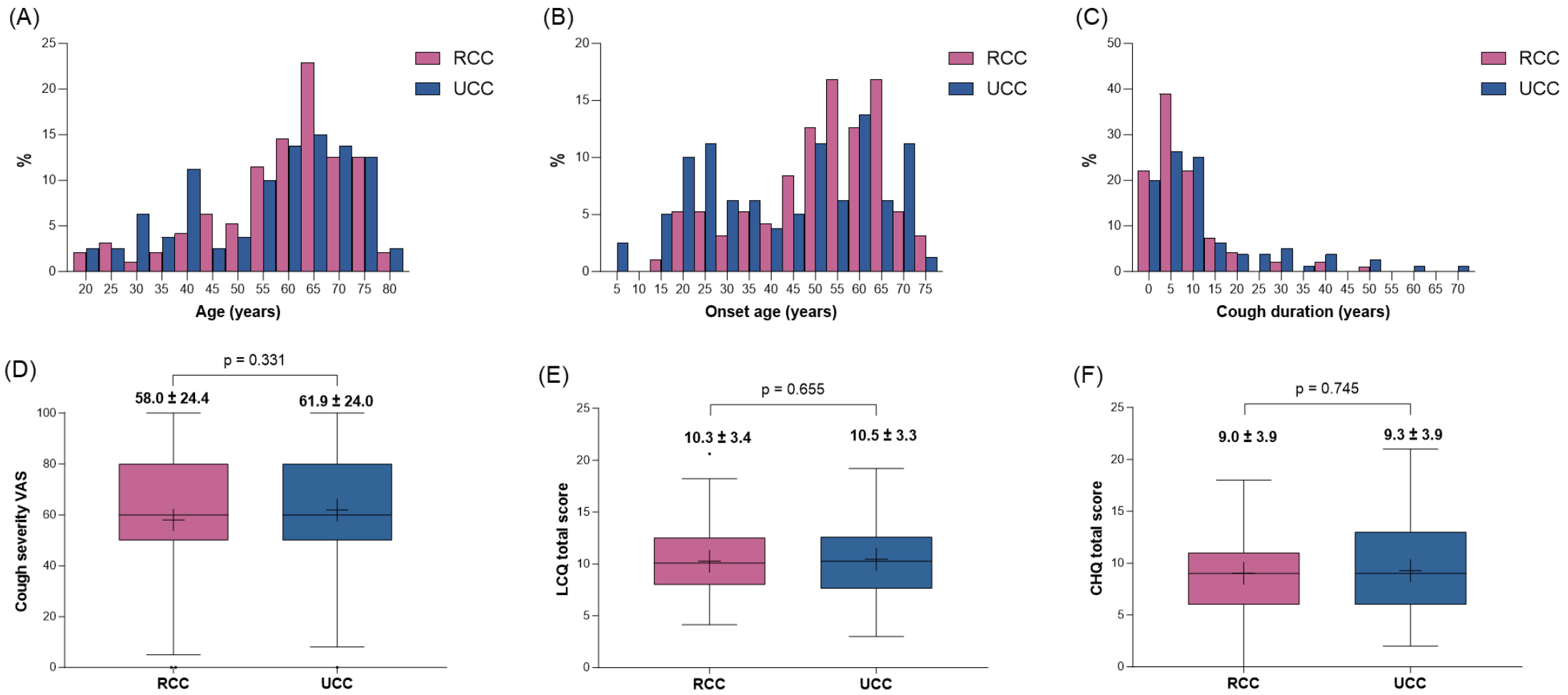
Baseline Cohort Profile of the Korean Chronic Cough Registry: A Multicenter, Prospective, Observational Study

Eun-Jung Jo[1] · Ji-Hyang Lee[2] · Ha-Kyeong Won[3] · Noeul Kang[4] · Sung-Yoon Kang[5] · Seung Eun Lee[1,6] · Ji-Ho Lee[7] · Mi-Yeong Kim[8] · Ji-Su Shim[9] · Jin An[10] · Youngsang Yoo[11] · So-Young Park[12] · Byung-Keun Kim[13] · Ji-Yong Moon[14] · Han-Ki Park[15] · Min-Hye Kim[9] · Hyouk-Soo Kwon[2] · Sae-Hoon Kim[16] · Sang-Heon Kim[14] · Yoon-Seok Chang[16] · Sang-Hoon Kim[17] · Surinder S. Birring[18] · Byung-Jae Lee[4] · Woo-Jung Song[2]

- Objective: To outline the baseline cohort profile and study protocols
- 610 patients (66.9% women; median age 59 years) recruited from 18 centers
- Age at cough onset: 50.1 years (IQR: 34-61)
- Adult-onset CC (≥19 years): 94.4%
- Cough duration: 4 years (IQR: 1-10)

Jo EJ et al. *Lung 2023*

Refractory chronic cough (RCC) or Unexplained chronic cough (UCC)?

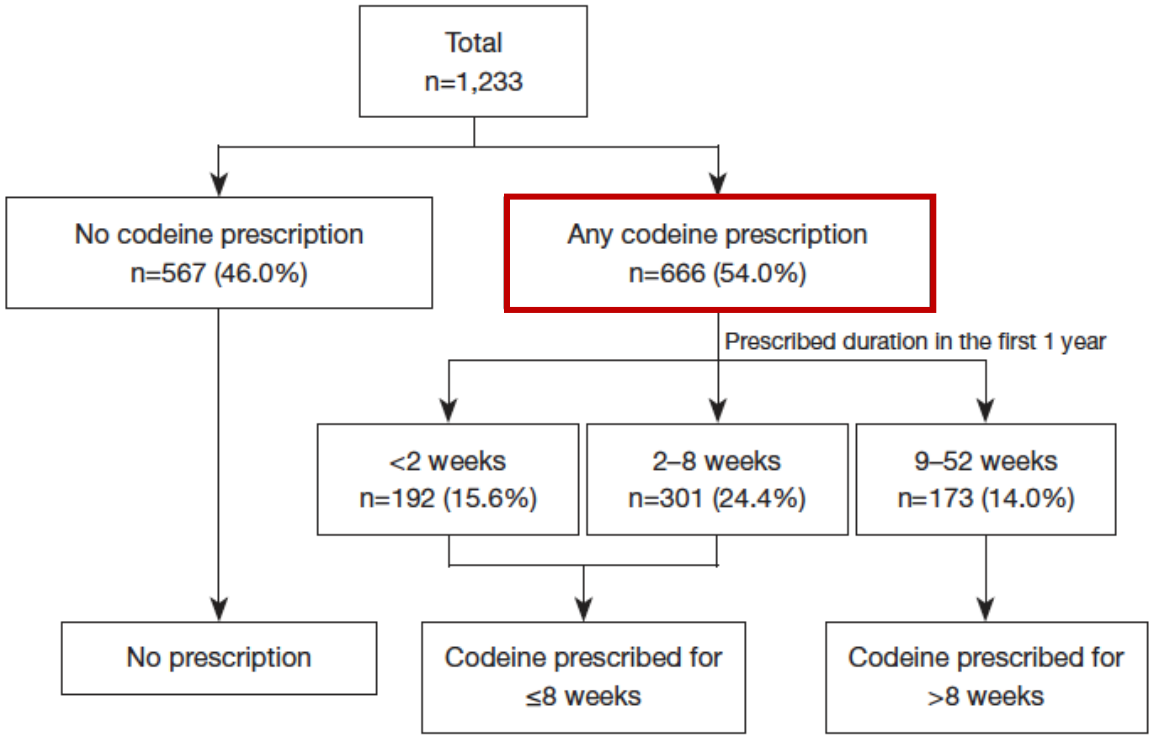


Jo EJ et al. *Lung 2023*

Codeine prescription pattern and treatment responses in patients with chronic cough: a routinely collected institutional database analysis

Ji-Yoon Oh[1^], Yu Ri Kang[1^], Jin An[2^], Eugene Choo[3^], Ji-Hyang Lee[1], Hyouk-Soo Kwon[1], Jae-Seung Lee[4^], Sei Won Lee[4^], Tae-Bum Kim[1^], Yeon-Mok Oh[4^], You Sook Cho[1^], Sang-Do Lee[4], Woo-Jung Song[1^]

- Retrospective cohort of chronic cough patients newly referred to a tertiary clinic (2017-2018)
- Routinely collected data



Oh JY et al. *J Thorac Dis 2023*

Characterization of Codeine Treatment Responders Among Patients with Refractory or Unexplained Chronic Cough: A Prospective Real-World Cohort Study

Ji-Yoon Oh[1] · Sung-Yoon Kang[2] · Noeul Kang[3] · Ha-Kyeong Won[4] · Eun-Jung Jo[5] · Seung-Eun Lee[6] · Ji-Hyang Lee[1] · Ji-Su Shim[7] · Young-Chan Kim[8] · Youngsang Yoo[9] · Jin An[10] · Hwa Young Lee[11] · So-Young Park[12] · Mi-Yeong Kim[13] · Ji-Ho Lee[14] · Byung-Keun Kim[15] · Han-Ki Park[16] · Min-Hye Kim[7] · Sae-Hoon Kim[17] · Sang-Heon Kim[18] · Yoon-Seok Chang[17] · Sang-Hoon Kim[19] · Byung-Jae Lee[3] · Kian Fan Chung[20,21] · Sang-Heon Cho[8] · Woo-Jung Song[1] on behalf of The Korean Chronic Cough Registry Study Group

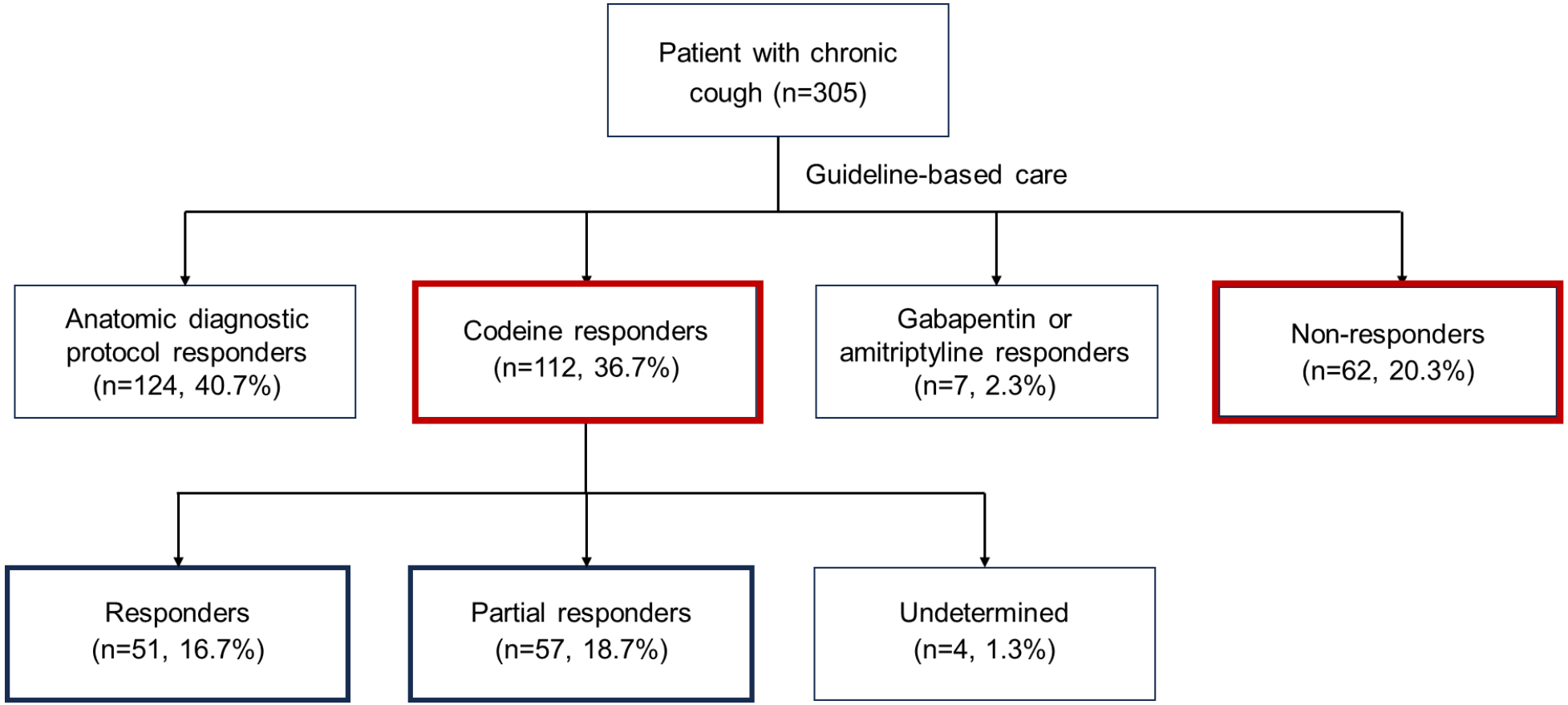
- Objective: To investigate the proportion and characteristics of codeine treatment responders
- 305 patients who completed the 6-month follow-up visits in the prospective registry
- Outcome of interest:

  - Codeine treatment response (determined by a physician)

  - Patient-reported outcomes: VAS, LCQ, CHQ

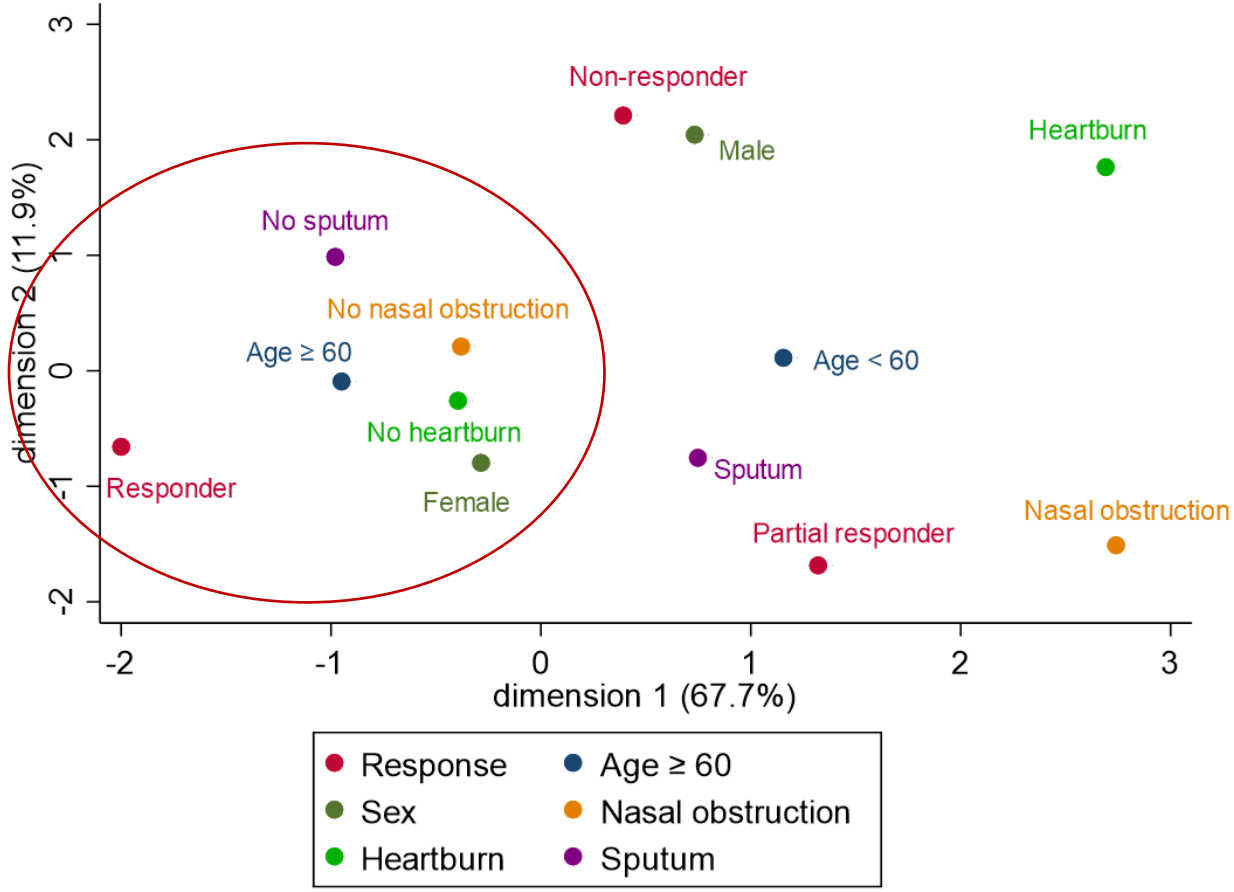
Oh JY et al. *Lung 2024*

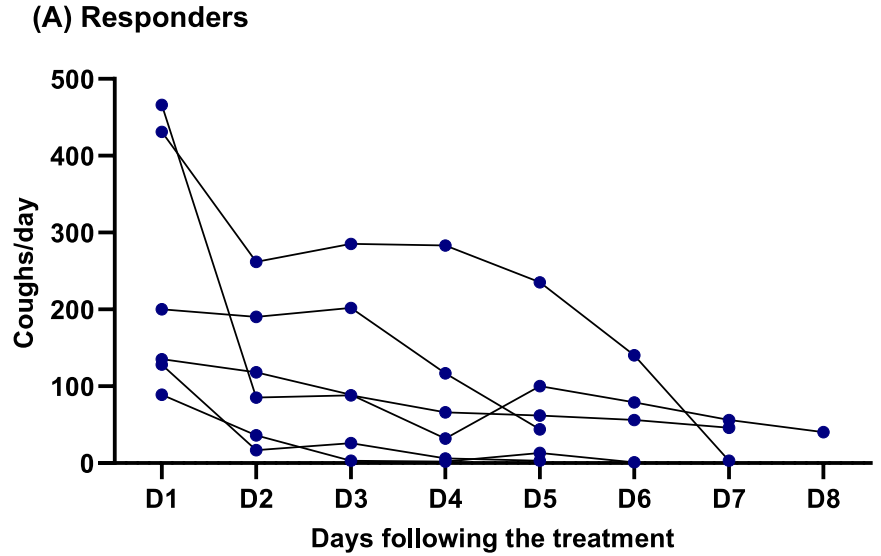
Codeine treatment responders in patients with chronic cough

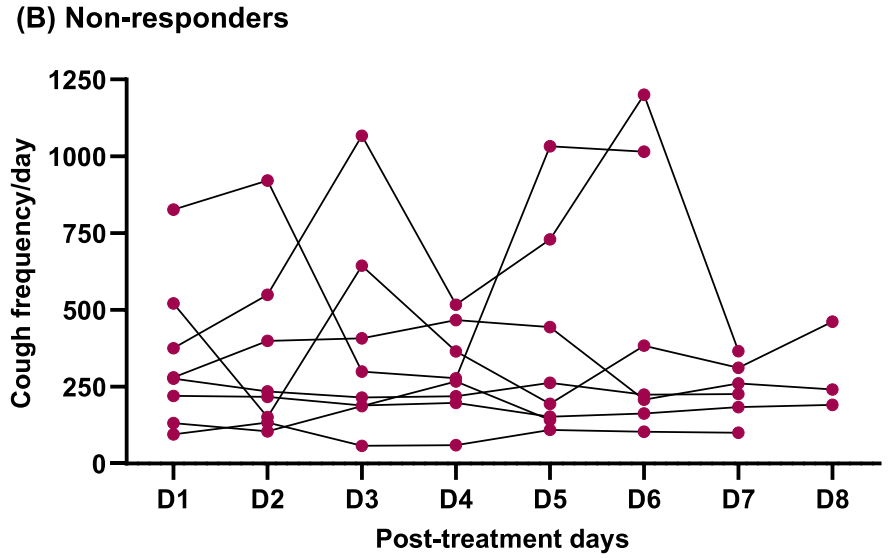


Oh JY et al. *Lung 2024*

Codeine treatment responder characteristics







Oh JY et al. *Lung 2024*

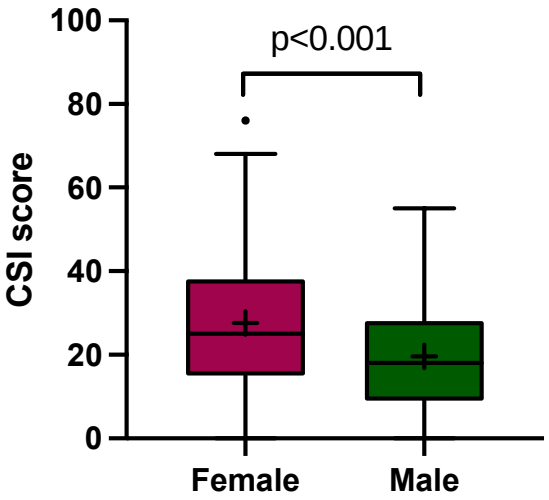
Exploring Traits Associated With Central Sensitization Features in Patients With Chronic Cough

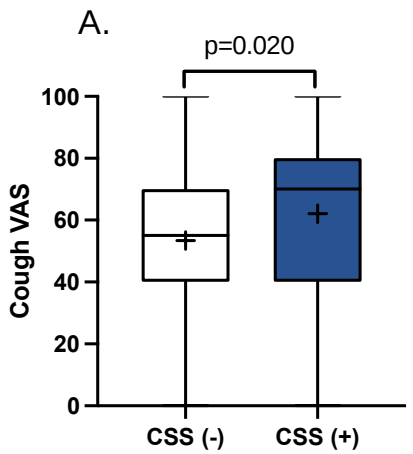
Haesung Jun,[1] Jin Young Park,[1] Ji-Yoon Oh,[2] Ha-Kyeong Won,[3] Sung-Yoon Kang,[4] So-Young Park,[5] Byung-Keun Kim,[6] Mi-Yeong Kim,[7] Young-Chan Kim,[8] Hwa Young Lee,[9] Eun-Jung Jo,[10] Seung-Eun Lee,[10,11] Sae-Hoon Kim,[12] Sang-Heon Kim,[13] Yoon-Seok Chang,[12] Sang-Hoon Kim,[14] Byung-Jae Lee,[15] Kian Fan Chung,[16] Woo-Jung Song,[2*] on behalf of the Korean Chronic Cough Registry Investigators[†]

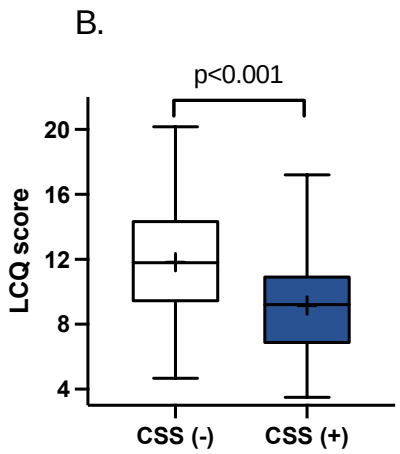
- Objective: To explore patient traits associated with Central Sensitization Inventory (CSI) score
- 317 patients with newly referred chronic cough
- CSI: Screening questionnaire to identify patients with central sensitization pain syndrome
- Outcomes of interest: Baseline patient traits associated with CSI score

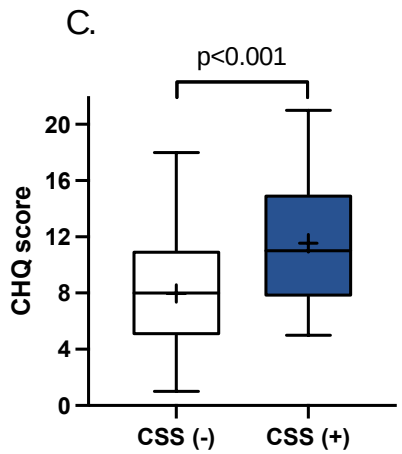
Jun H et al. *AAIR 2024*

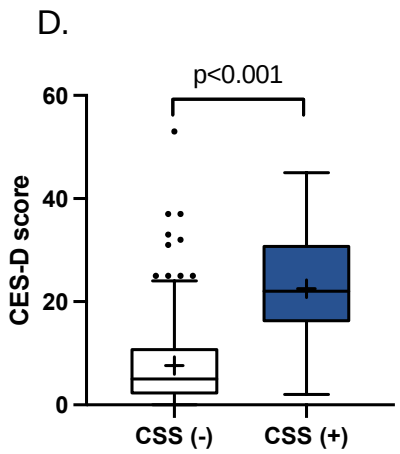
Patient traits associated with central sensitization symptoms











For CSI score	Coefficient (95% CI)	p-value
Age (years)	-0.091 (-0.174 to -0.008)	0.032
Male sex (vs. female)	-0.439 (-7.126 to -1.650)	0.002
LCQ score	-0.579 (-0.977 to -0.181)	0.004
CES-D score	0.832 (0.695 to 0.969)	<0.001

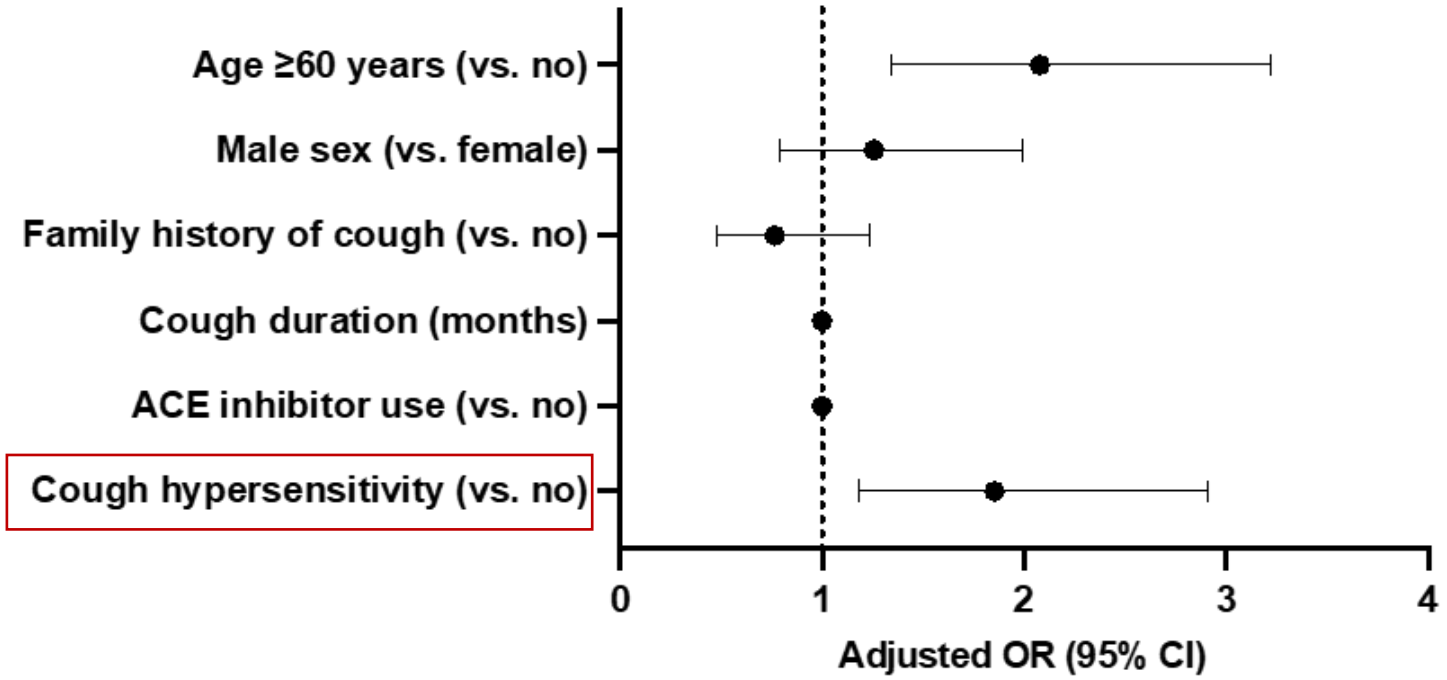
Jun H et al. *AAIR 2024*

Cough persistence predictors?

- Objective: To explore baseline patient traits associated with cough persistence at 1 year
- 426 patients with newly referred chronic cough (female 67.9%; mean age 55.8 years)
- Potential treatable traits measured at baseline
- Outcome of interest: Cough persistence (VAS >20) at follow-up

Kim Y et al. *In revision*

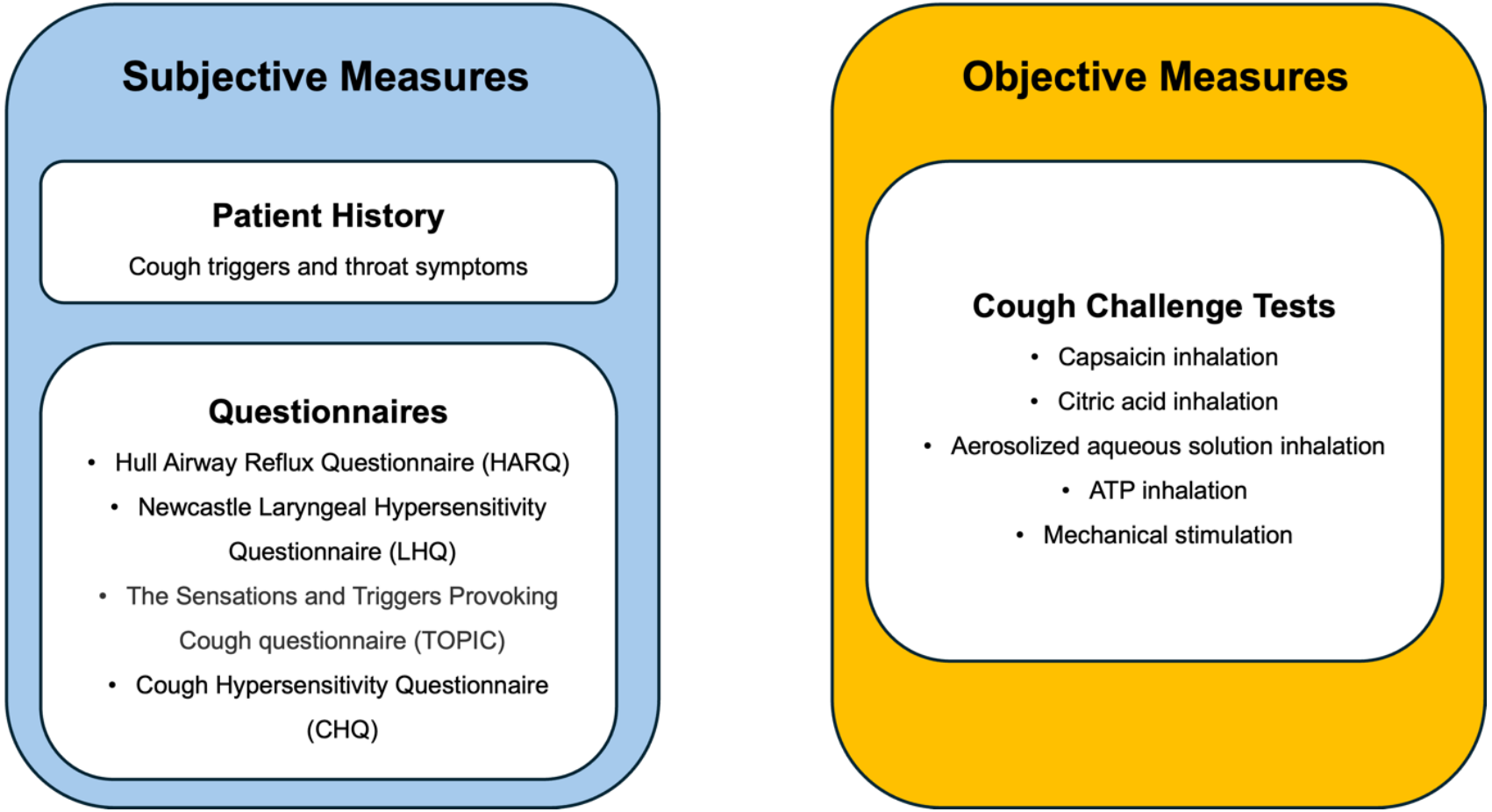
Baseline traits associated with cough persistence at 1 year



At follow-up, patients with persistent cough also had persistently higher CHQ scores (8.4±3.9 vs. 5.2±3.9, p<0.001).

Kim Y et al. *In revision*

How to measure cough hypersensitivity clinically

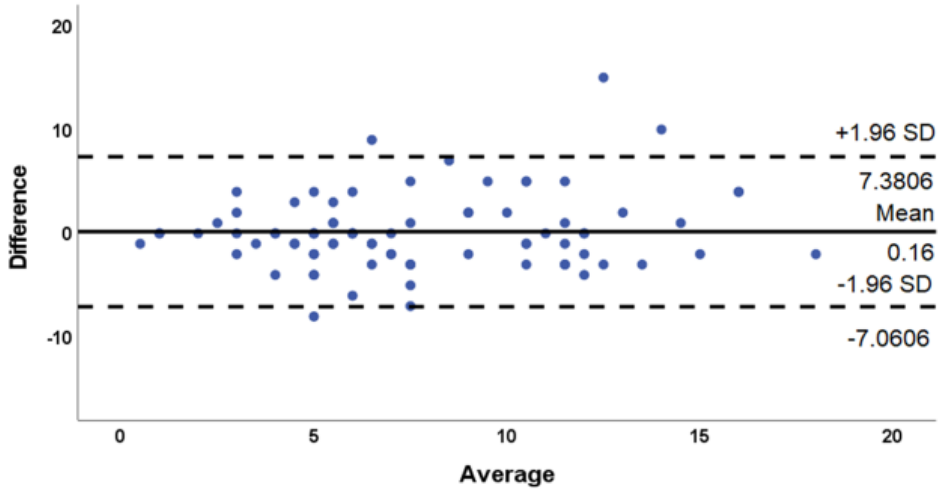


Song WJ et al. *JACI in Pract 2024*

Longitudinal evaluation of Cough Hypersensitivity Questionnaire (CHQ)

- Objective: To evaluate the reliability, longitudinal validity, and responsiveness of CHQ
- 614 patients with chronic cough (331 completed 6-month follow-up)

- Cronbach alpha = 0.792
- Repeatability, ICC = 0.78
- Spearman correlation with LCQ = -0.522 ($p<0.001$)



- Responsiveness to LCQ change, Cohen's D = 0.835 (large effect) with dose response (+)

Kim MY et al. *In submission*

Cough hypersensitivity symptoms are specific to RCC?

- Objective: To compare cough hypersensitivity symptoms between asthmatic cough and RCC
- 365 patients who completed 6-month follow-up visit in the longitudinal cohort
- Outcomes of interest:

  - CHQ score

  - Physician diagnosis of chronic cough: asthmatic cough, RCC

Kim MY et al. *ERJ Open Res 2024*

Cough hypersensitivity symptoms are specific to RCC?

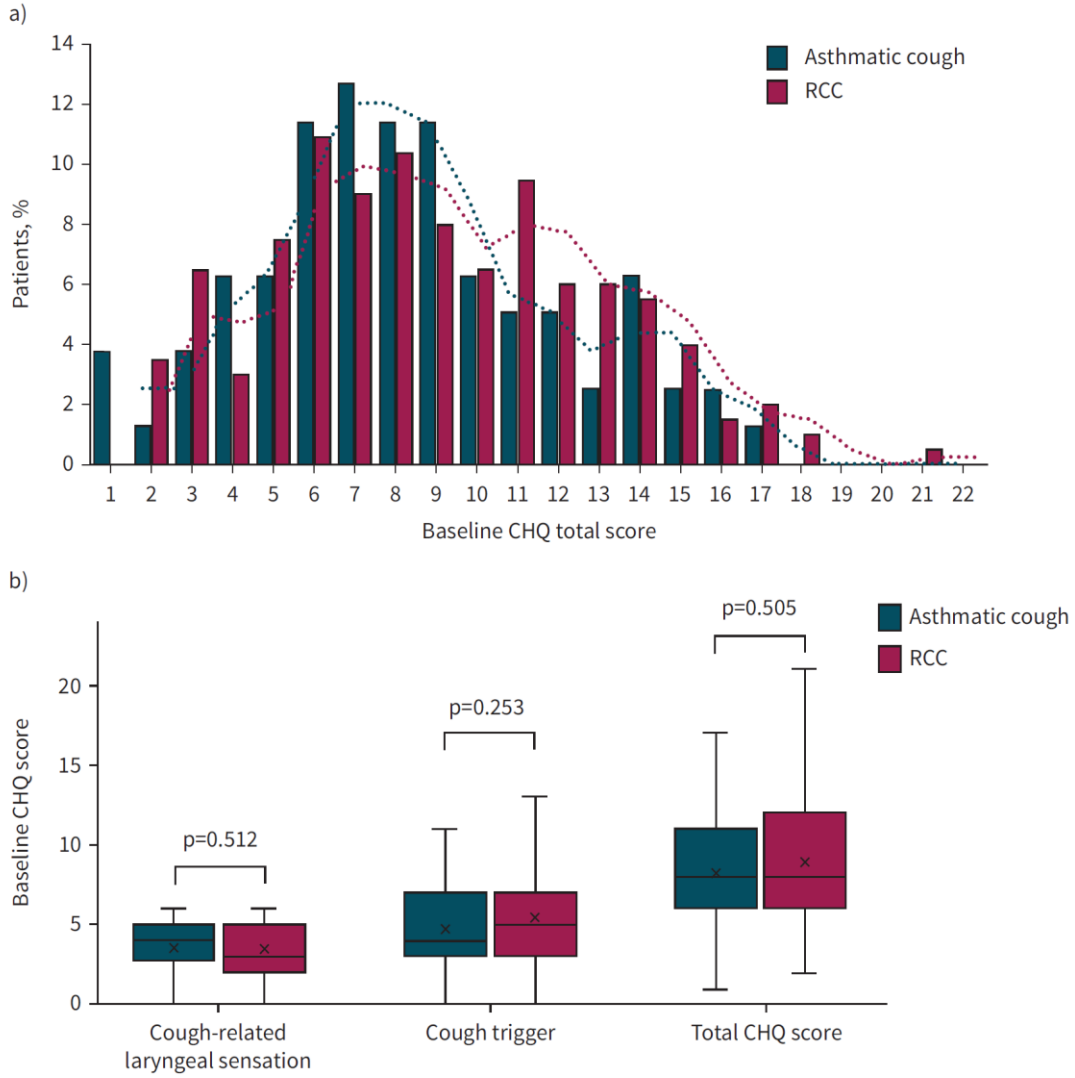


FIGURE 2 a) Comparison of baseline CHQ score distributions in asthmatic cough and RCC and b) Comparison of CHQ scores between asthmatic cough and RCC (box-and-whisker plot). CHQ: Cough Hypersensitivity Questionnaire; RCC: refractory chronic cough.

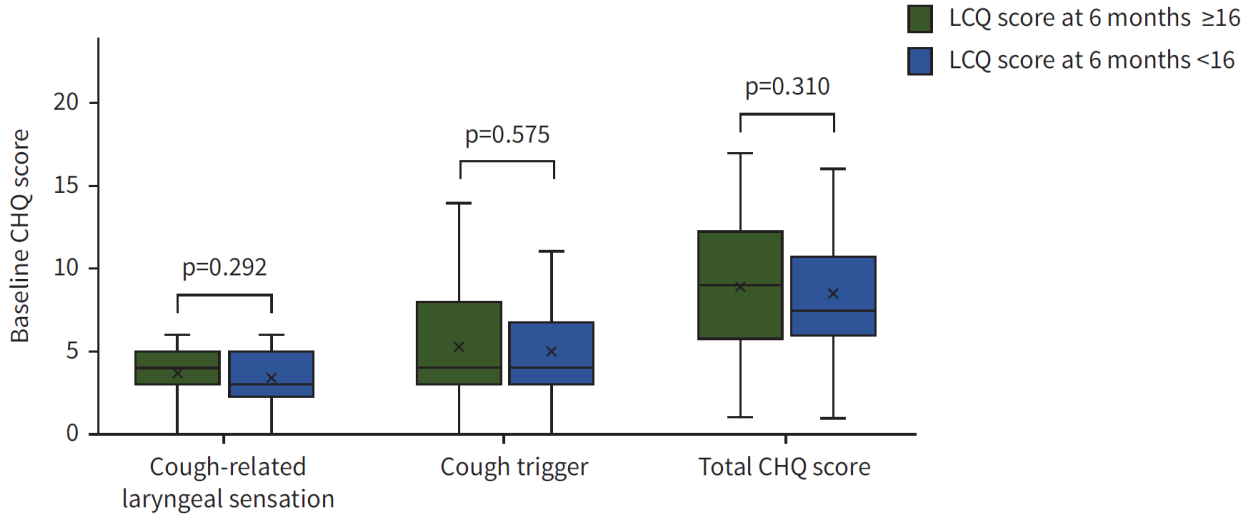


FIGURE 5 Comparison of baseline CHQ scores between patients with 6-months follow-up LCQ score ⩾16 points and <16 points in asthmatic cough. Age, sex and baseline LCQ score were adjusted by ANCOVA (general linear model). CHQ: Cough Hypersensitivity Questionnaire; LCQ: Leicester Cough Questionnaire.

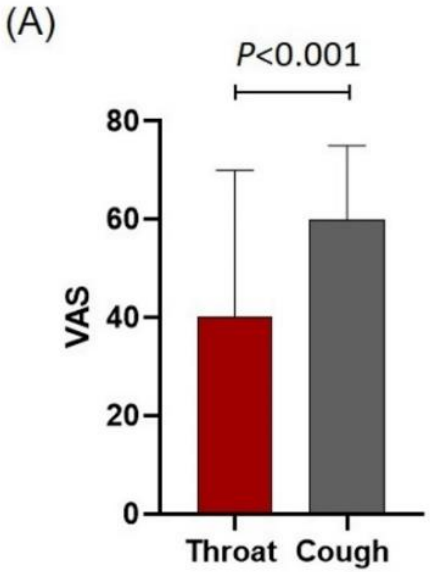
Shareable abstract (@ERSpublications)

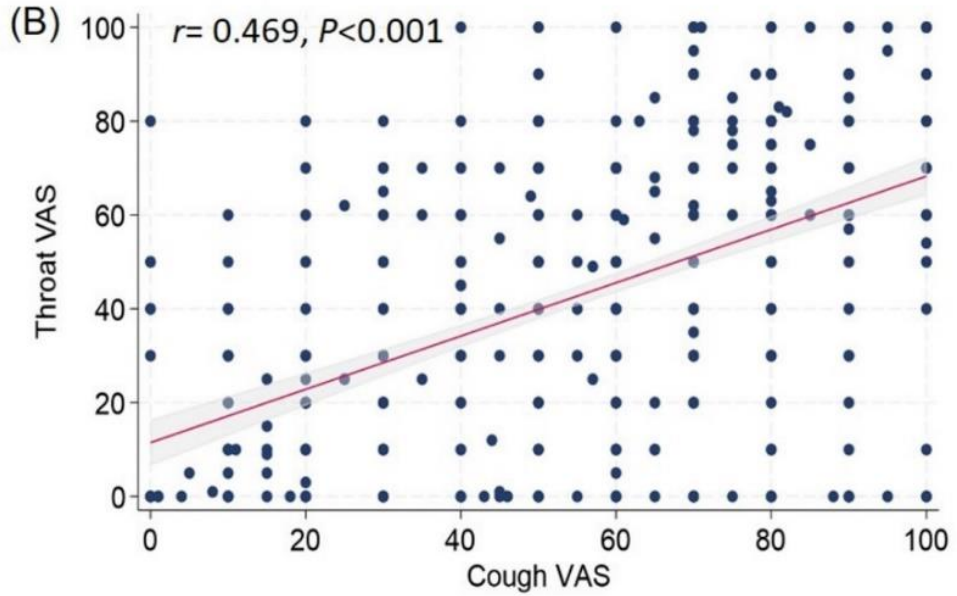
The symptoms of cough hypersensitivity may not distinguish between asthmatic cough and refractory chronic cough. Cough reflex hypersensitivity may underlie chronic cough across different phenotypes, despite having different treatable traits. https://bit.ly/45kgwBm

Kim MY et al. *ERJ Open Res 2024*

Throat sensation in chronic cough

- Objective: To explore the clinical relevance of abnormal throat sensation
- Cross-sectional study of 649 patients with chronic cough
- Throat severity VAS
- Associations with LCQ (cough-specific QoL) and EQ-5D (HRQoL)





Yoo Y, Lee HY et al. *In submission*

Throat sensation in chronic cough

Throat sensation severity VAS tertiles

LCQ score	Coefficient (95% CI)*	*P* value	**EQ-5D index**	Coefficient (95% CI)*	*P* value
T2 vs. T1	-1.03(-1.62 to -0.44)	0.001	T2 vs. T1	-0.01 (-0.05 to 0.03)	0.56
T3 vs. T1	-1.63 (-2.23. to -1.02)	<0.001	T3 vs. T1	-0.06 (-0.09 to 0.02)	0.01

*adjusted for age, sex, smoking history, BMI, number of comorbid symptoms/complications, comorbidities, cough VAS

Yoo Y, Lee HY et al. *In submission*

Clinical Characteristics of Post-COVID-19 Persistent Cough in the Omicron Era

Yu Ri Kang,[1†] Jin-Young Huh,[2,3†] Ji-Yoon Oh,[1] Ji-Hyang Lee,[1] Daegeun Lee,[2]
Hyouk-Soo Kwon,[1] Tae-Bum Kim,[1] Jae Chol Choi,[2,3] You Sook Cho,[1]
Kian Fan Chung,[4] So-Young Park,[2,3*] Woo-Jung Song [1*]

Allergy, Asthma & Immunology Research AAIR

- Objective: To analyze cough and clinical characteristics of post-COVID chronic cough (vs. non-COVID chronic cough)

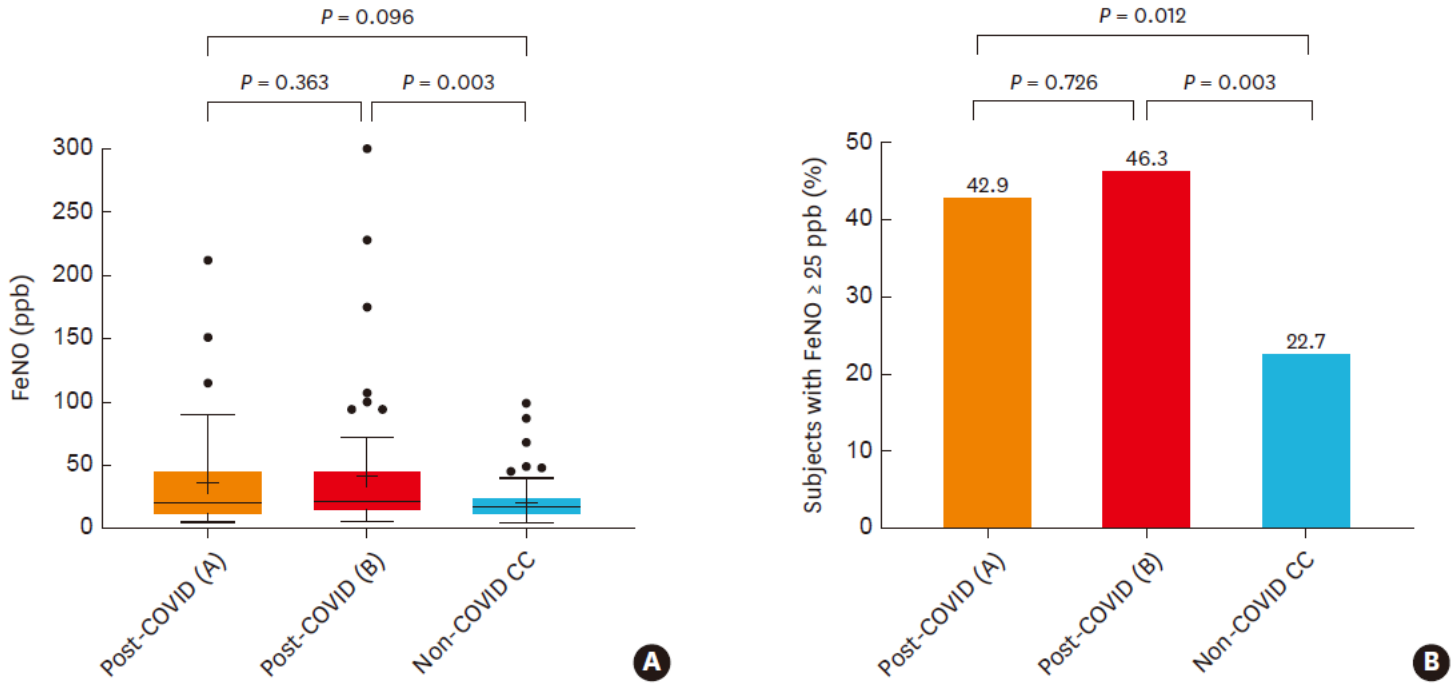
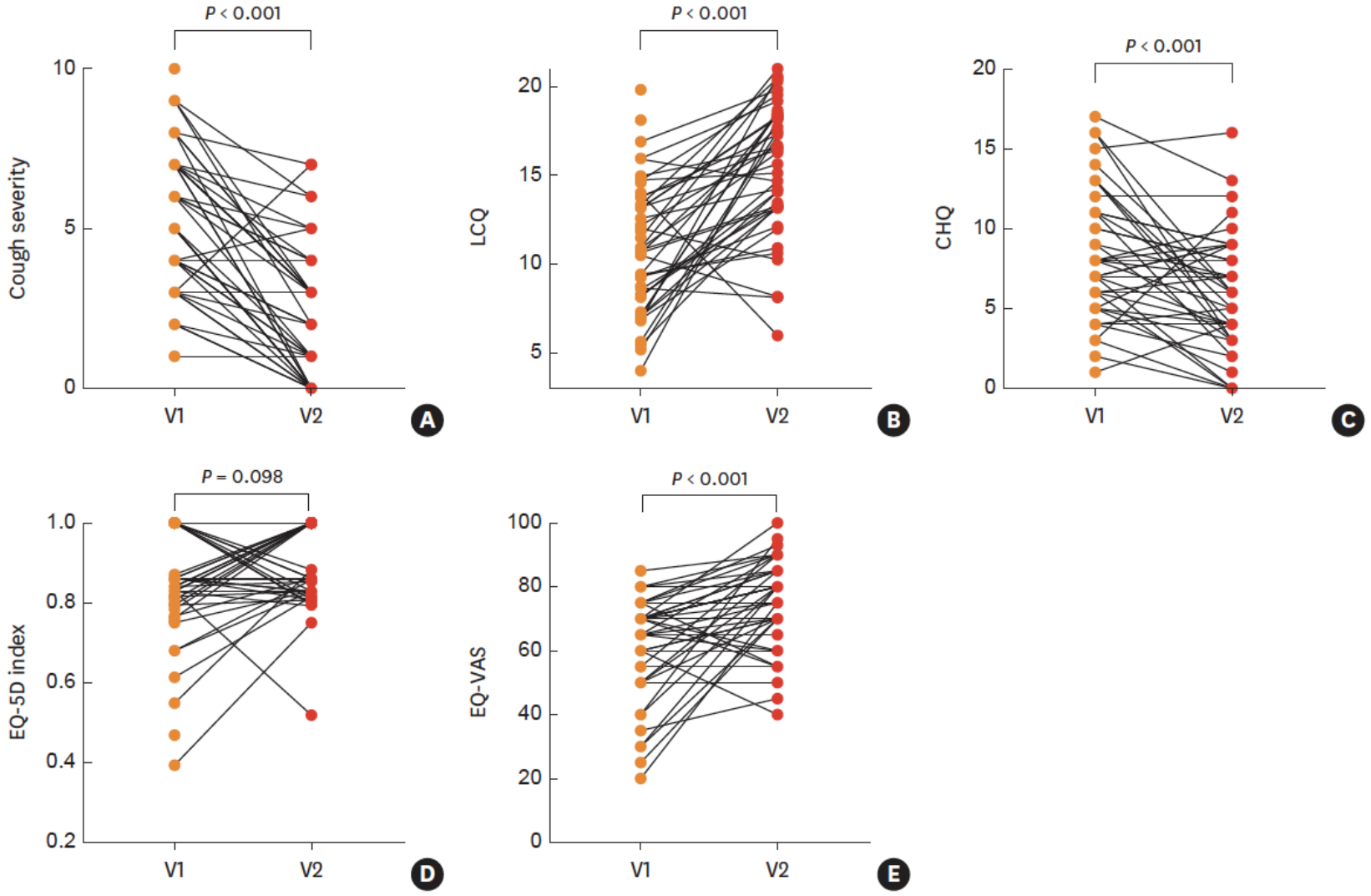


Fig. 1. FeNO levels at study enrollment. (A) FeNO levels; and (B) proportion of subjects with FeNO ≥ 25 ppb. Box indicates the lower and upper quartile; (+) sign, mean value; central line, median value; and points at the ends of the whiskers, upper extreme values. *P* values were determined by the Mann-Whitney *U*-test or the χ^2 test.
FeNO, fractional exhaled nitric oxide; COVID = coronavirus disease.

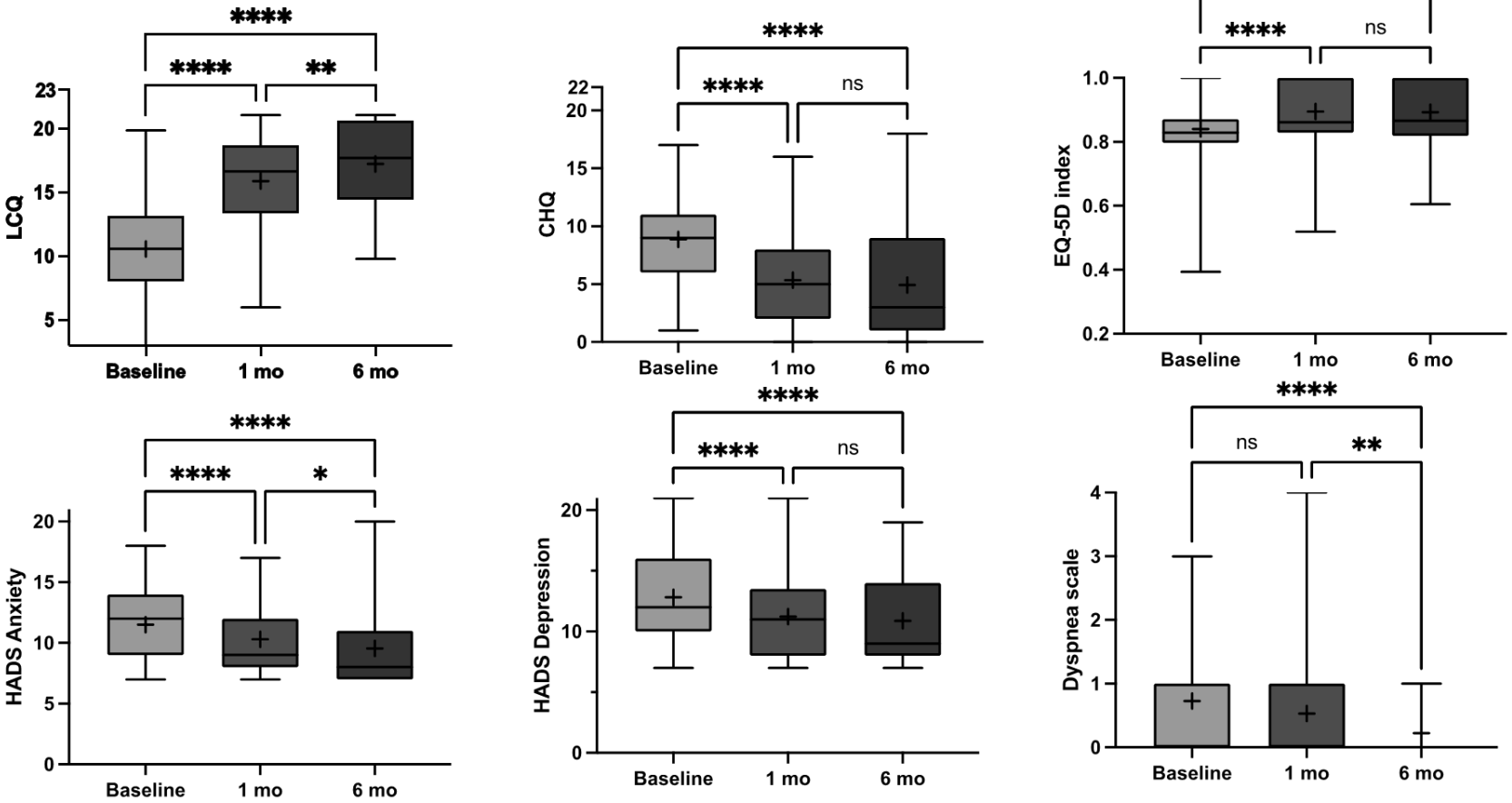
Kang YR, Huh JY et al. *AAIR 2023*

Post-COVID chronic cough: 1-month treatment outcome



Kang YR, Huh JY et al. *AAIR 2023*

Post-COVID chronic cough: 6-month treatment outcome



Asthmatic cough	50%
Refractory chronic cough	20%
Allergic rhinitis or CRS	18%
Spontaneous remission	12%
Interstitial lung disease or fibrosis	2%
Unknown (due to follow-up loss)	9%

Park KE et al., *In submission*

Cough Response to High-Dose Inhaled Corticosteroids in Patients with Chronic Cough and Fractional Exhaled Nitric Oxide Levels ≥ 25 ppb: A Prospective Study

Ji-Ho Lee[1] · Sung-Yoon Kang[2] · Iseul Yu[1] · Kyung Eun Park[3] · Ji-Yoon Oh[4] · Ji-Hyang Lee[4] · So-Young Park[5] · Min-Hye Kim[6] · Eun-Jung Jo[7] · Ji-Yong Moon[8] · Sae-Hoon Kim[9] · Sang-Hoon Kim[10] · Byung-Jae Lee[11] · Woo-Jung Song[3,4] · the Korean Academy of Asthma Allergy, Clinical Immunology Working Group on Chronic Cough

- Objective: To investigate the effects of high-dose ICS on chronic cough patients with FeNO ≥25 ppb
- Single-arm prospective study
- Population: Chronic cough patients with FeNO ≥25 ppb and without other apparent etiology
- Intervention: 3-week high-dose ICS treatment
- Outcome: LCQ score, daily cough severity score, FeNO

Lee JH, Kang SY et al., *Lung 2024*

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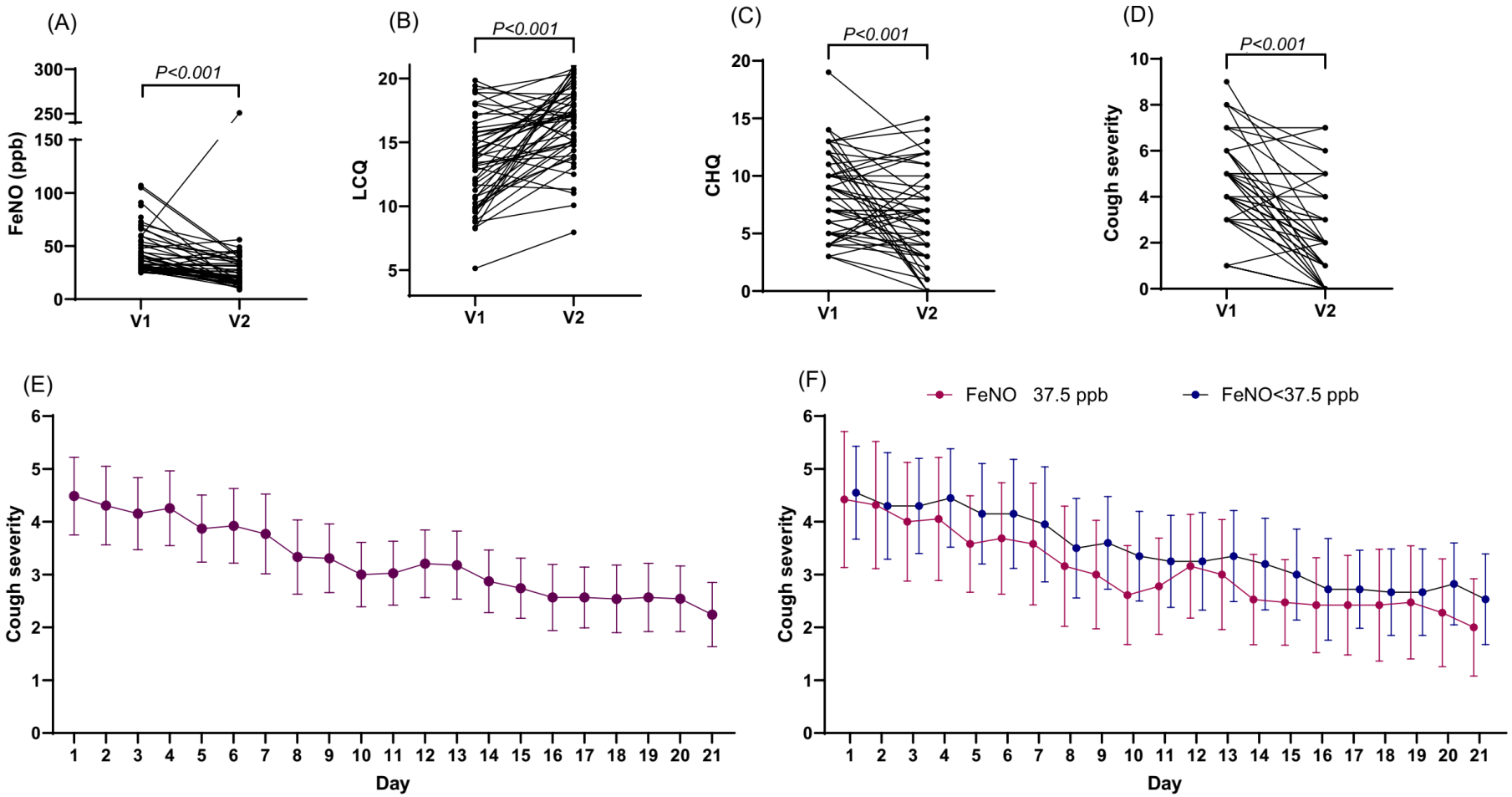
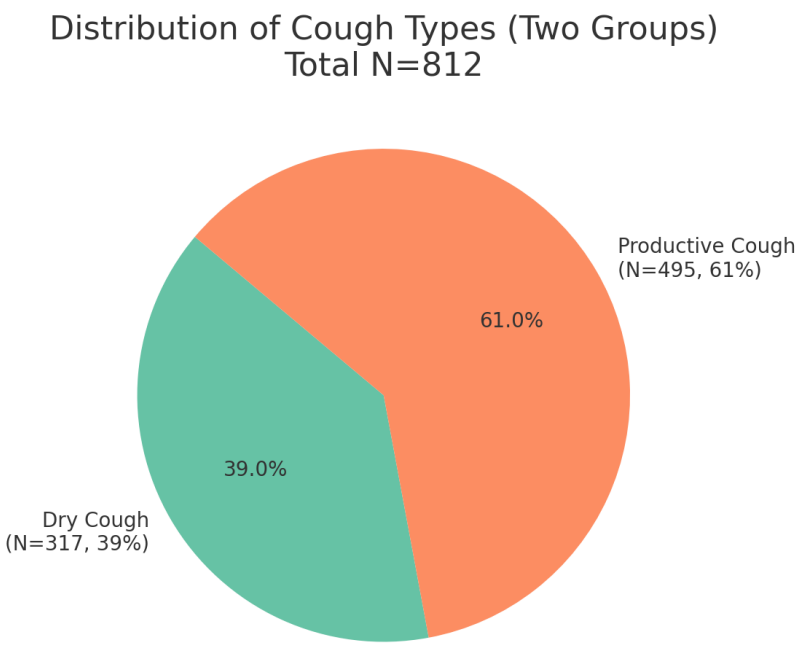
LCQ responder rate: 68%
Gradual improvement
Non-significant correlation between FeNO and cough score



Lee JH, Kang SY et al., *Lung 2024*

Chronic productive cough

- Objective: To explore if chronic productive cough is a distinct phenotype



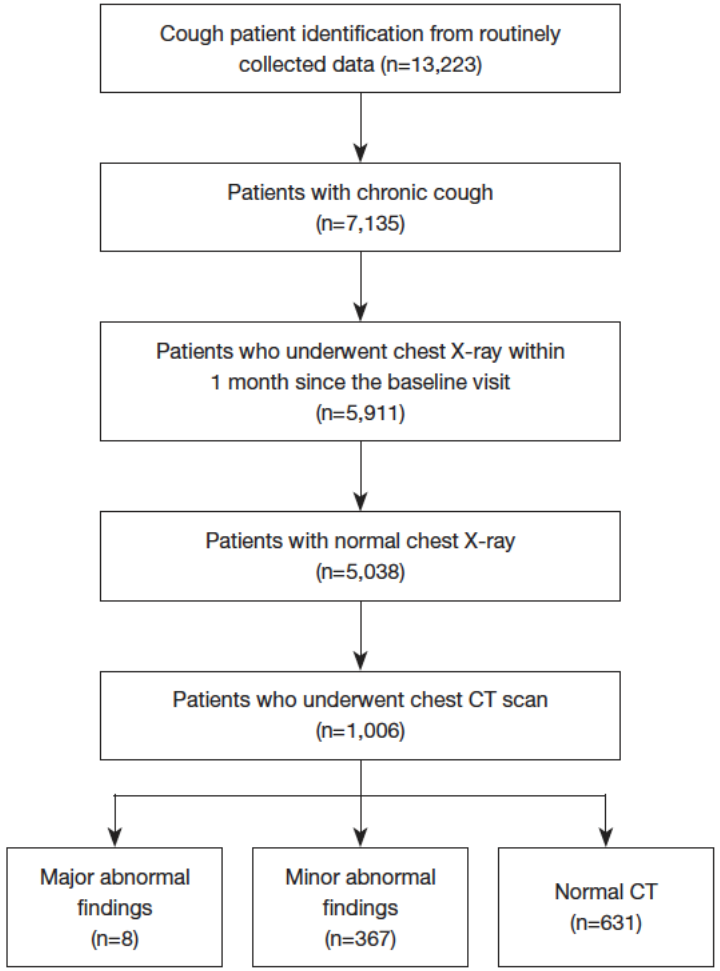
	Dry cough (n=317)	Productive cough (n=495)	P value
Sex, Female, n (%)	63.7%	67.9%	0.251
Age, years	54.7 ± 14.8	53.3 ± 15.5	0.185
Current smoker	3.5%	5.9%	
Chest pain d/t cough	17.5%	33.0%	<0.001
Fatigue d/t cough	29.5%	45.5%	<0.001
Cough VAS	52.3 ± 25.5	60.1 ± 24.5	<0.001
Throat sensation VAS	33.3 ± 29.4	49.9 ± 28.8	<0.001
CHQ score	7.5 ± 3.9	9.3 ± 4.0	<0.001
LCQ score	11.8 ± 3.6	10.6 ± 3.4	< 0.001
CES-D score	7.4 ± 9.6	9.2 ± 11.1	0.015

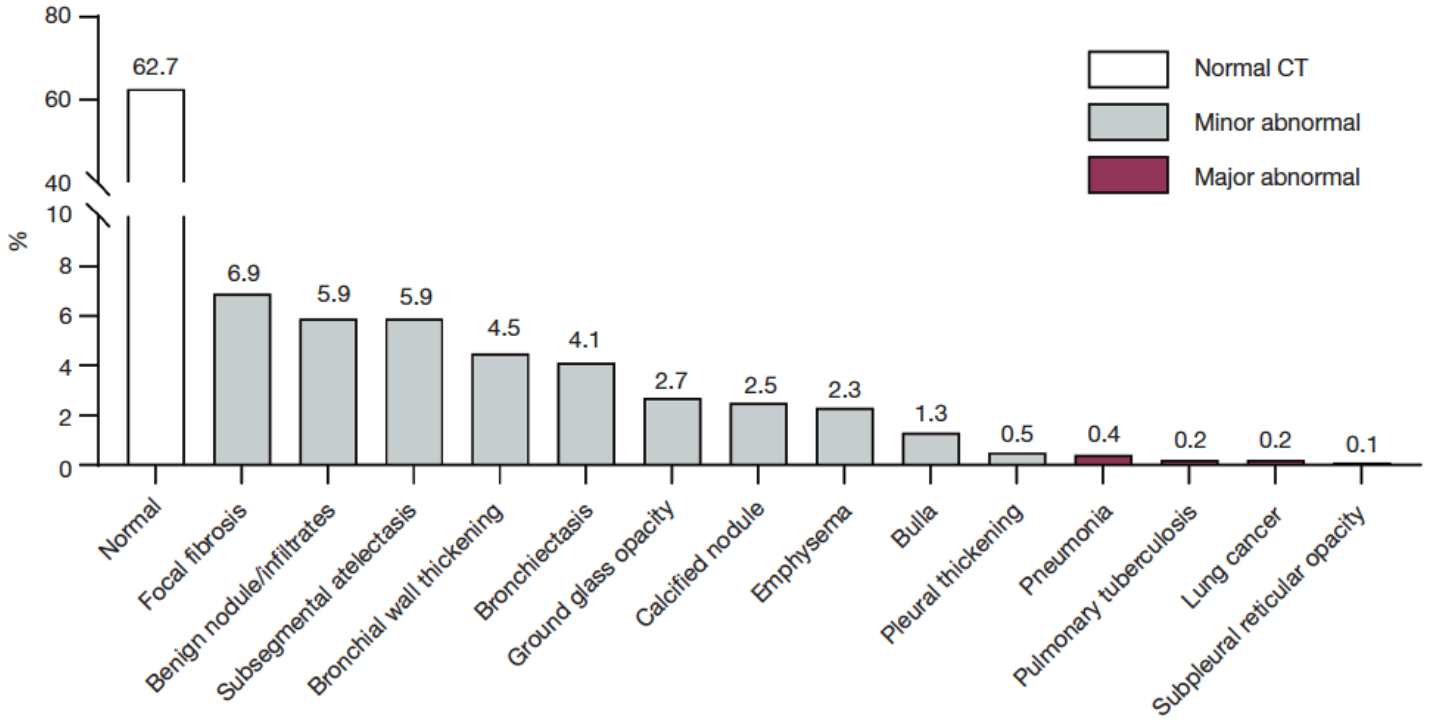
Park SY et al. *In submission*

Chest computed tomography scan utilization and diagnostic outcomes in chronic cough patients with normal chest X-rays: analysis of routinely collected data of a tertiary academic hospital

Jin An[1], Ji-Hyang Lee[2], Youngsang Yoo[3], Hyouk-Soo Kwon[2], Jae-Seung Lee[4], Sei Won Lee[4], Tae-Bum Kim[2], Yeon-Mok Oh[4], You Sook Cho[2], Sang-Do Lee[4], Woo-Jung Song[2]^

- Routinely collected data analysis

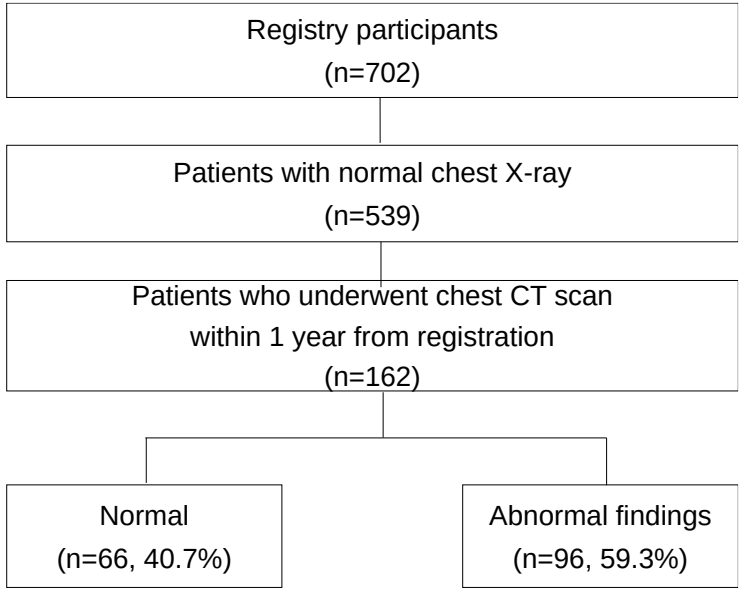


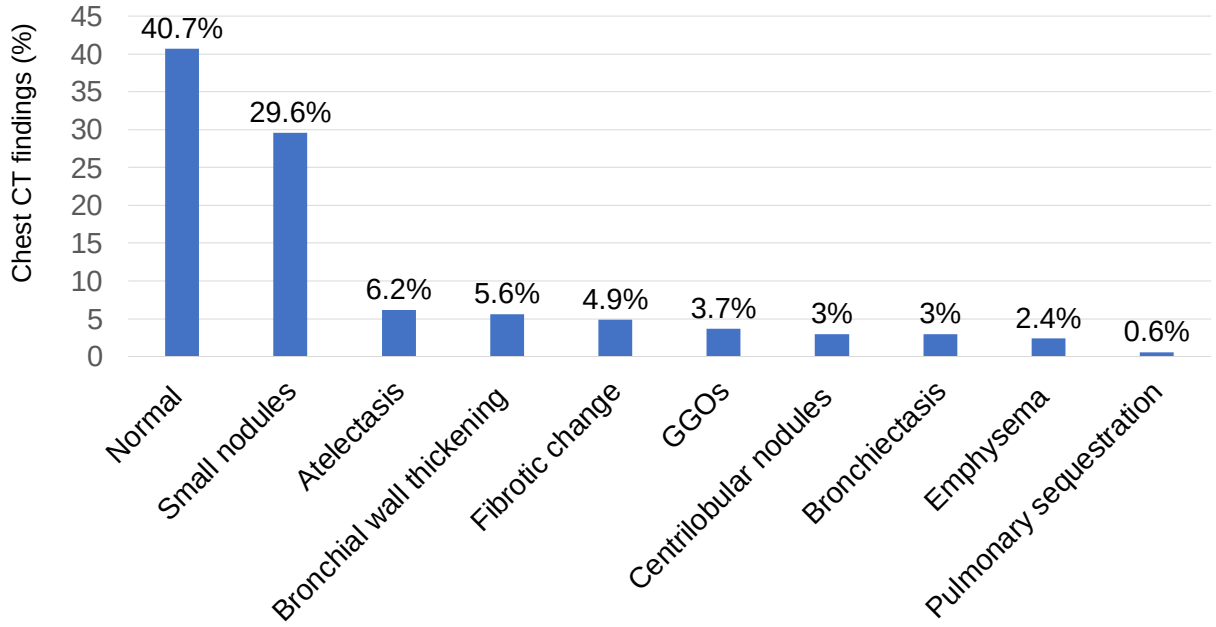


An J et al. *J Thorac Dis 2023*

Role of chest CT scan in patients with normal chest X-rays

- Prospective cohort analysis
- Outcome: Clinical impact of CT scan





CT findings	Additional tests	Treatment change	Treatment response
Benign nodules (n=5)	Chest CT follow-up	No	-
GGOs (n=2)	Sputum culture	Yes (Pneumonia: antibiotics)	Improved
Centrilobular nodules (n=1)	Sputum AFB stain	No	-

An J et al. In submission

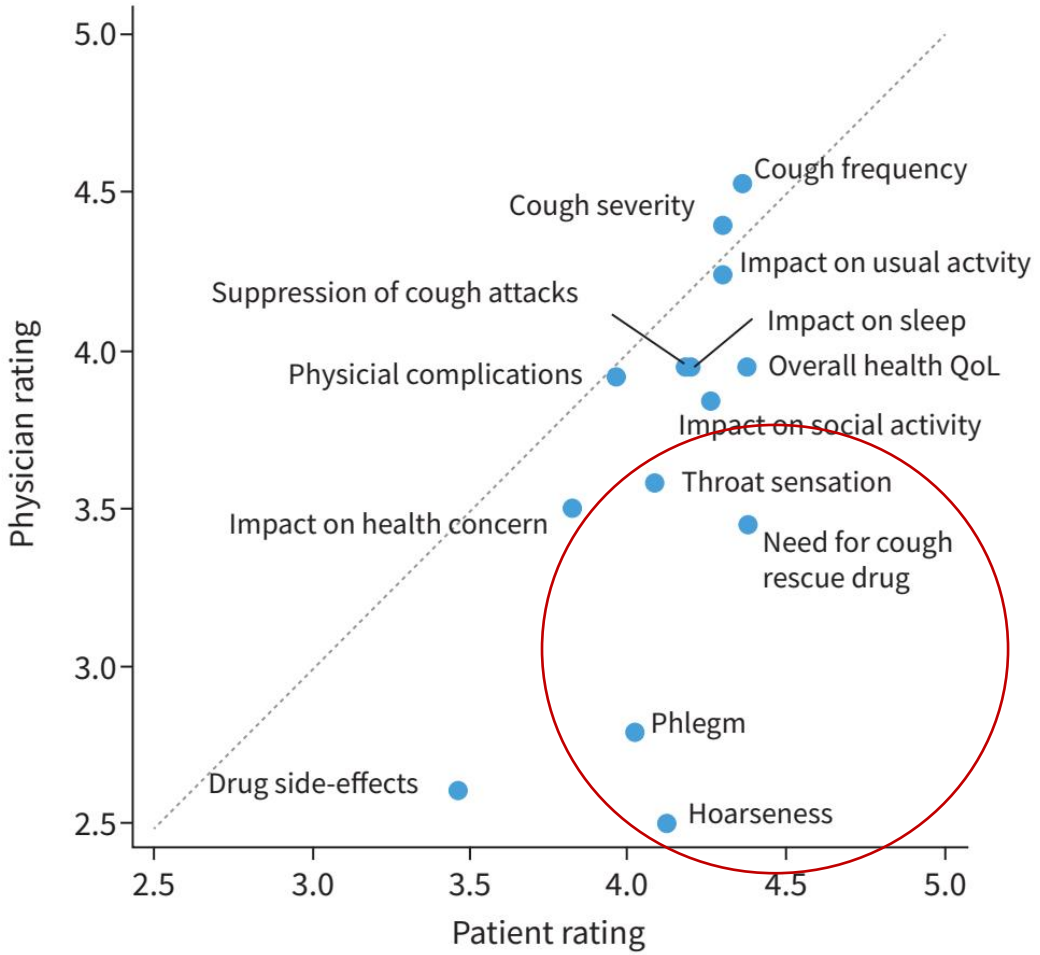
Exploring the concept of disease control in chronic cough

Jin Young Park[1], Haesung Jun[1], Seung-Eun Lee[2], Ha-Kyeong Won[3], Sung-Yoon Kang[4], Noeul Kang[5], Ji-Yoon Oh[6,7], Young-Chan Kim[8], So-Young Park[9], Jin An[10], Youngsang Yoo[11], Mi-Yeong Kim[12], Hwa Young Lee[13], Ji-Su Shim[14], Min-Hye Kim[14], Sae-Hoon Kim[15], Sang-Heon Kim[16], Yoon-Seok Chang[15], Sang-Hoon Kim[17], Byung-Jae Lee[5], Surinder S. Birring[18] and Woo-Jung Song[6], on behalf of the Korean Chronic Cough Registry Investigators

- Disease control vs. Disease severity?
- Objective: To provide a conceptual exploration of patient-reported cough control in chronic cough
- Registry data (1): Correlation between patient-reported cough control (1-5) and conventional cough PROs
- Survey of items pertinent to cough control (2): 50 patients and 38 clinicians

Park JY et al. *ERJ Open Res 2024*

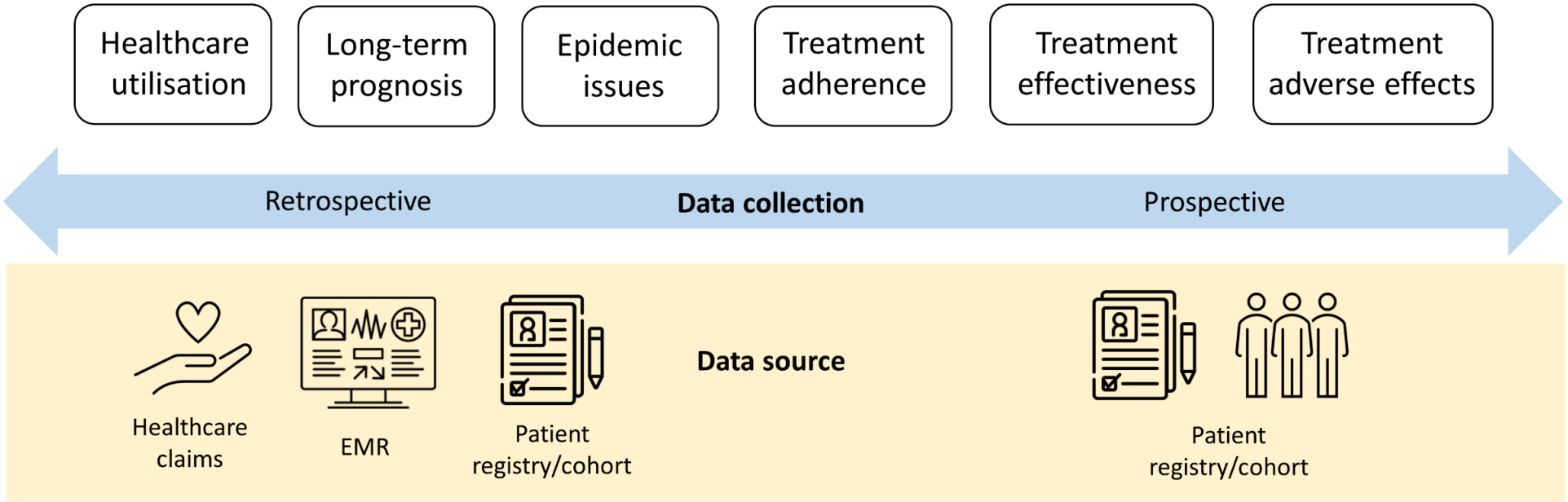
Concept of disease control in chronic cough: patient's perspectives?



Park JY et al. *ERJ Open Res 2024*

Roles of real-world patient registries

Which real-world data are "fit for purpose" to address a specific question?



Lee Y et al. *ERJ Open Res 2022*

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  - Seung-Eun Lee (Pusan National University Yangsan Hospital)
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  - Ji-Su Shim (Ewha Womans University Mokdong Hospital)
  - Sang-Heon Kim (Hanyang University Hospital)
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