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Cough in Asthma

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Contents

How does having a cough impact asthma?

Prevalence of respiratory symptoms in the asthmatics

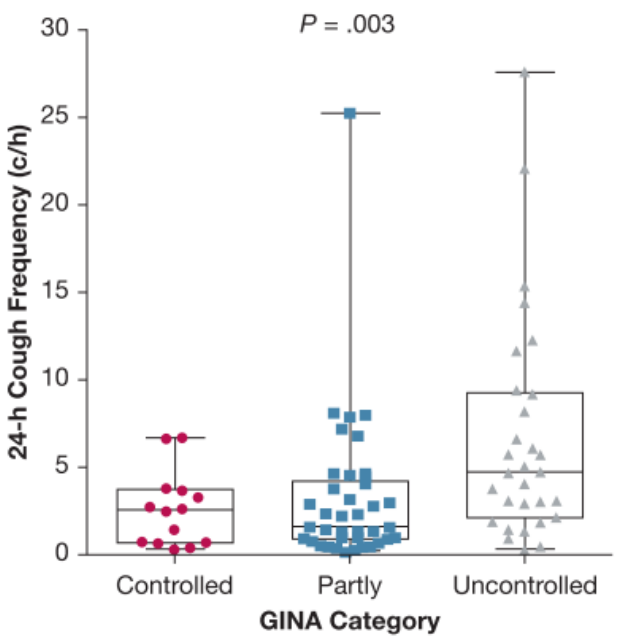
Table 3 Prevalence of respiratory symptoms reported in the last 12 months in the groups of the asthmatics and controls

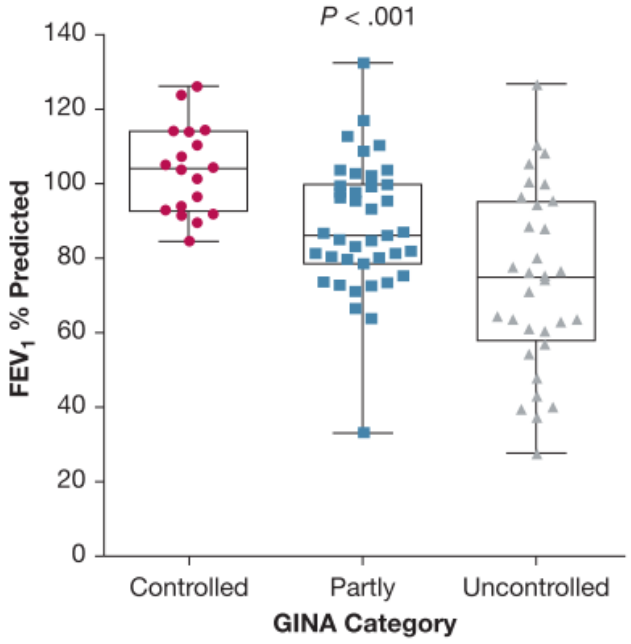
Variables	No	Current asthma No (%)	No	Controls No (%)	P values
Symptoms	744		847		
Longstanding cough		242 (32.5)		94 (11.1)	<0.001
Morning cough		316 (42.5)		131 (15.5)	<0.001
Sputum production		268 (36.1)		57 (6.8)	<0.001
Wheezing		591 (79.4)		78 (9.2)	<0.001
Wheezing with shortness of breath		437 (58.7)		11 (1.3)	<0.001
Shortness of breath		269 (36.1)		21 (2.5)	<0.001
Longstanding cough without other symptoms		14 (1.9)		66 (7.8)	<0.001
Morning cough without other symptoms		23 (3.1)		95 (11.2)	<0.001
Allergic rhinitis and longstanding cough		170 (22.8)		34 (4.0)	<0.001
Allergic rhinitis		548 (73.8)		259 (30.7)	<0.001

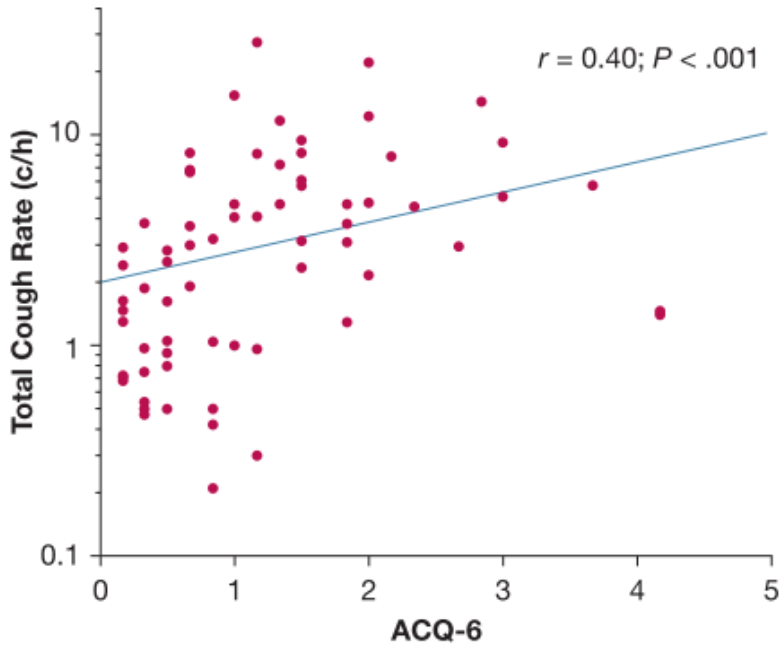
Data are presented as No (%). Chi-square tests are used to make comparisons between individual variables.

Mincheva et al. Respiratory Research 2014, 15:79

Cough frequency and disease control in asthma

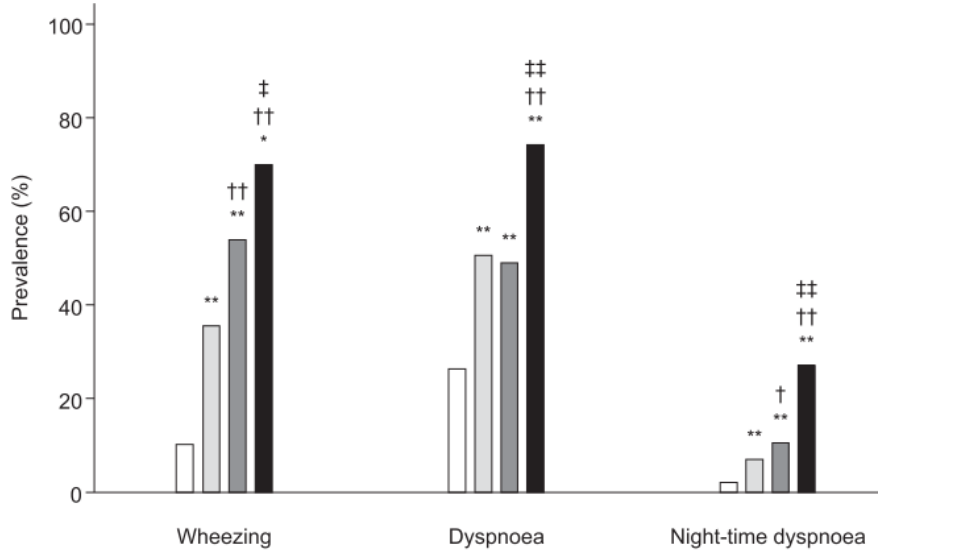


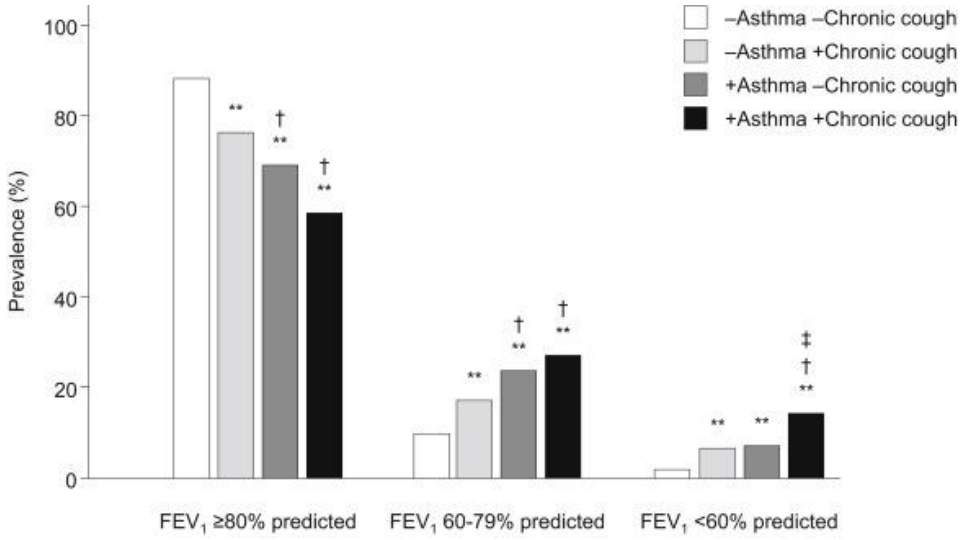


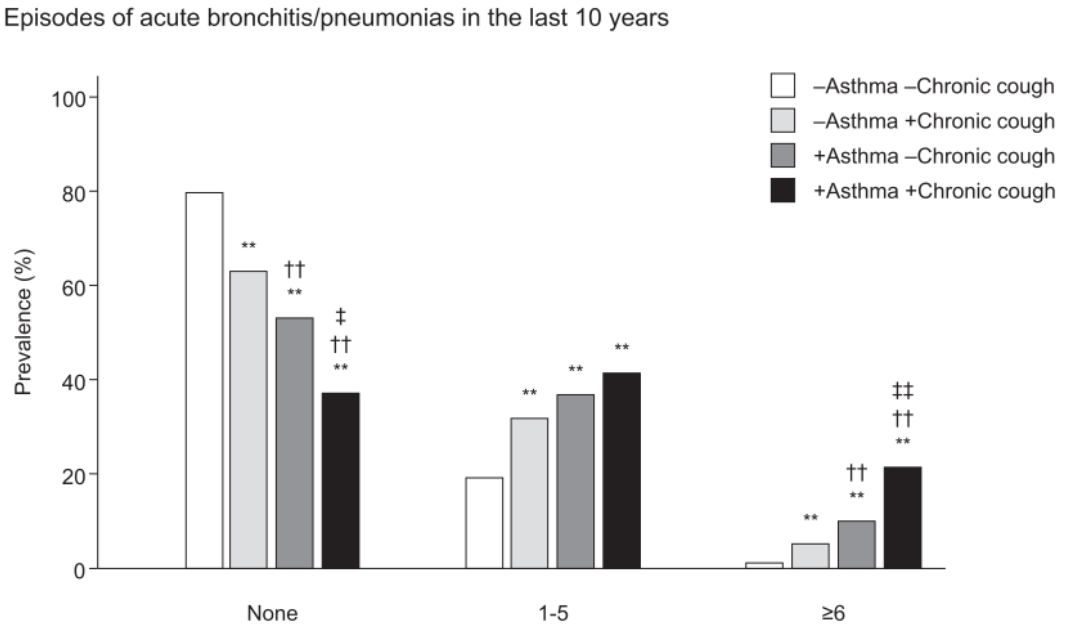


Marsden et al. CHEST 2016; 149(6):1460-1466

Impact of chronic cough in asthmatics from the general population



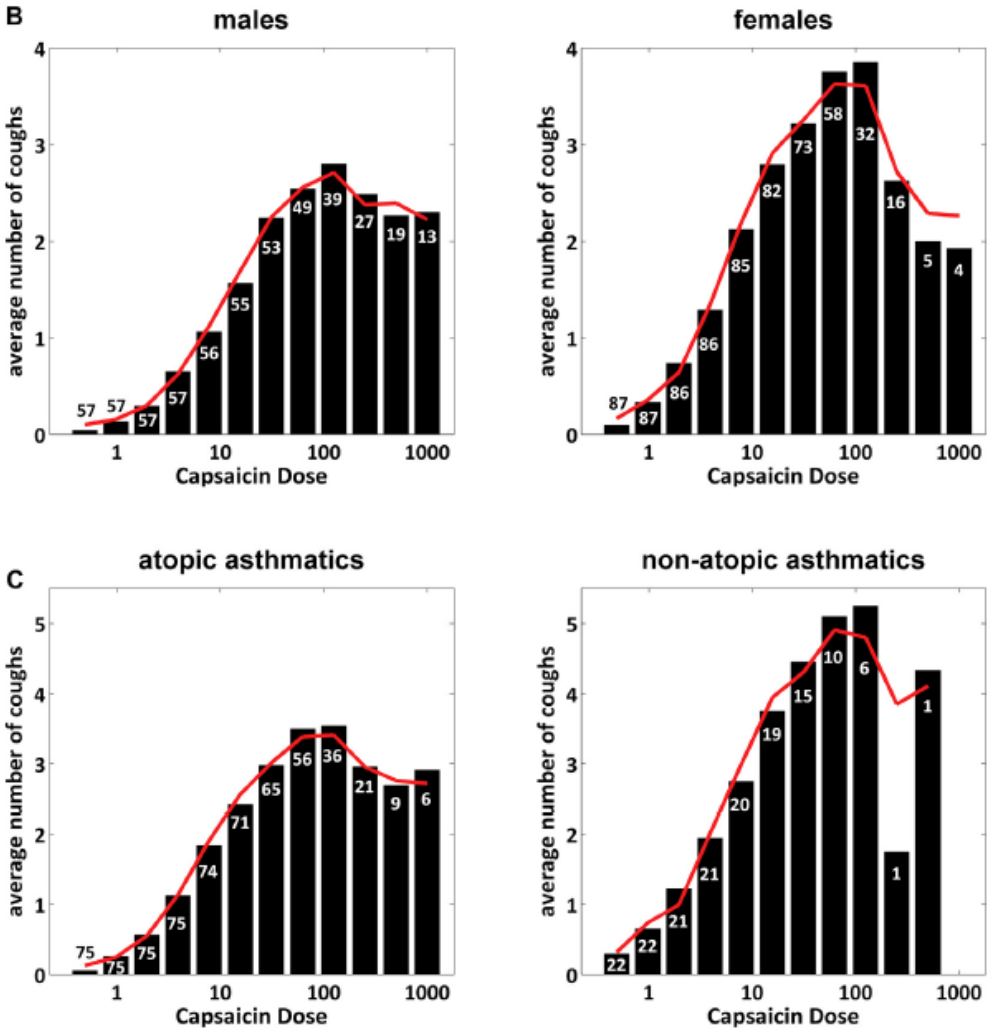


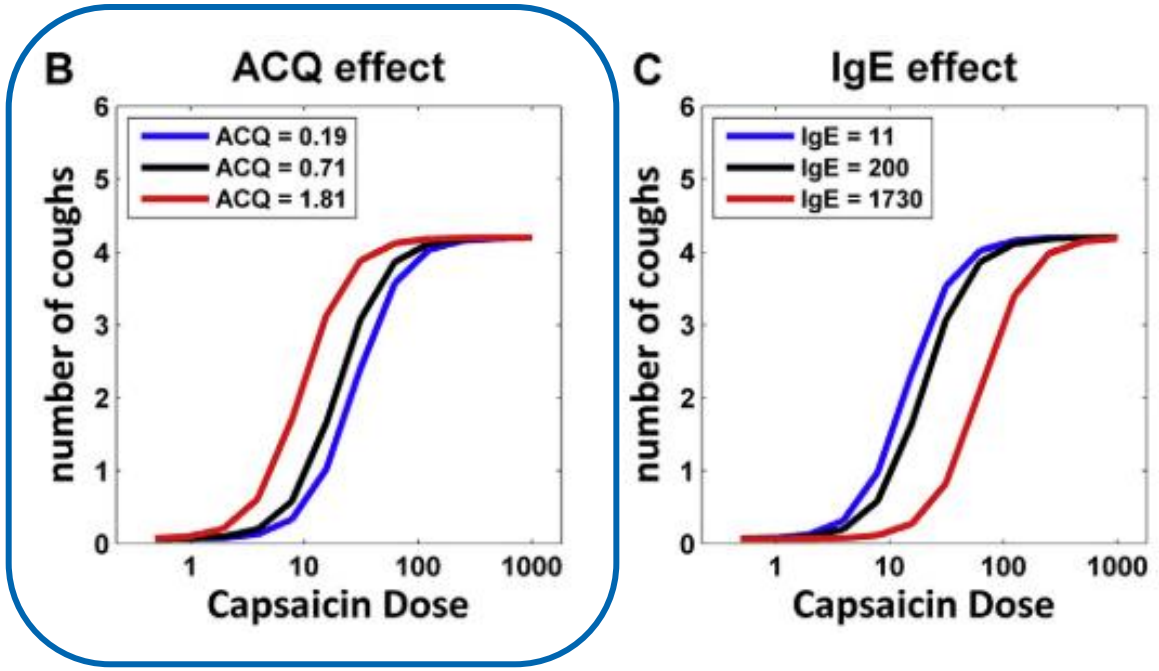


chronic cough /c asthma is associated with a more severe disease phenotype

Çolak et al. J Allergy Clin Immunol Pract 2019;7:1783-92

Capsaicin sensitivity associated with worse asthma control in asthma





female nonatopic asthmatic patients had the highest cough responses to capsaicin

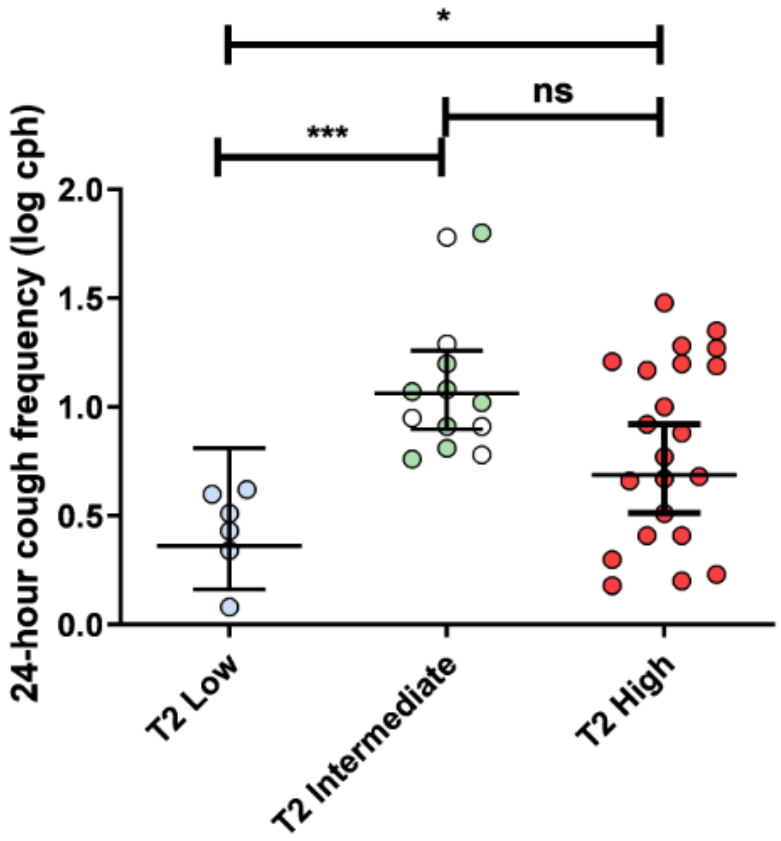
Satia et al. J Allergy Clin Immunol 2017;139:771-9

Capsaicin sensitivity associated with worse asthma control and exacerbation in severe asthma

	Asthma Control (*ACT Score < 20*) ($R^2 = 0.31$)			Exacerbations (⩾*2/yr*) ($R^2 = 0.26$)			Admissions (⩾*1/yr*) ($R^2 = 0.36$)			Airflow Limitation (*FEV_1% Predicted < 80%*) ($R^2 = 0.24$)		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value	OR	95% CI	*P* Value	OR	95% CI	*P* Value
General factors												
Sex, F	—	—	—	3.34	0.95–11.7	0.06	—	—	—	0.51	0.19–1.34	0.17
BMI ⩾ 25 kg/m^2	—	—	—	1.79	0.65–4.94	0.26	—	—	—	—	—	—
Nonatopic	2.15	0.97–4.71	0.06	—	—	—	3.13	0.91–10.7	0.07	—	—	—
Ex-smoking status	2.16	0.95–4.91	0.07	—	—	—	6.52	1.89–22.4	0.003	2.07	0.79–5.40	0.14
Biomarkers and FEV_1% predicted												
C5 ⩽ 2.44 μM	4.83	1.97–10.4	0.0004	2.83	1.04–7.71	0.04	3.43	0.91–12.9	0.07	—	—	—
ANC ⩾ 5,000/μl	3.62	0.87–15.1	0.08	2.86	0.74–11.1	0.13	4.55	0.86–24.1	0.07	—	—	—
F_{ENO} ⩾ 25 ppb	—	—	—	—	—	—	—	—	—	1.58	0.63–3.96	0.33
FEV_1% predicted < 80%	2.99	1.13–7.94	0.03	5.42	1.77–16.6	0.003	3.89	0.996–15.2	0.051	N/A	N/A	—

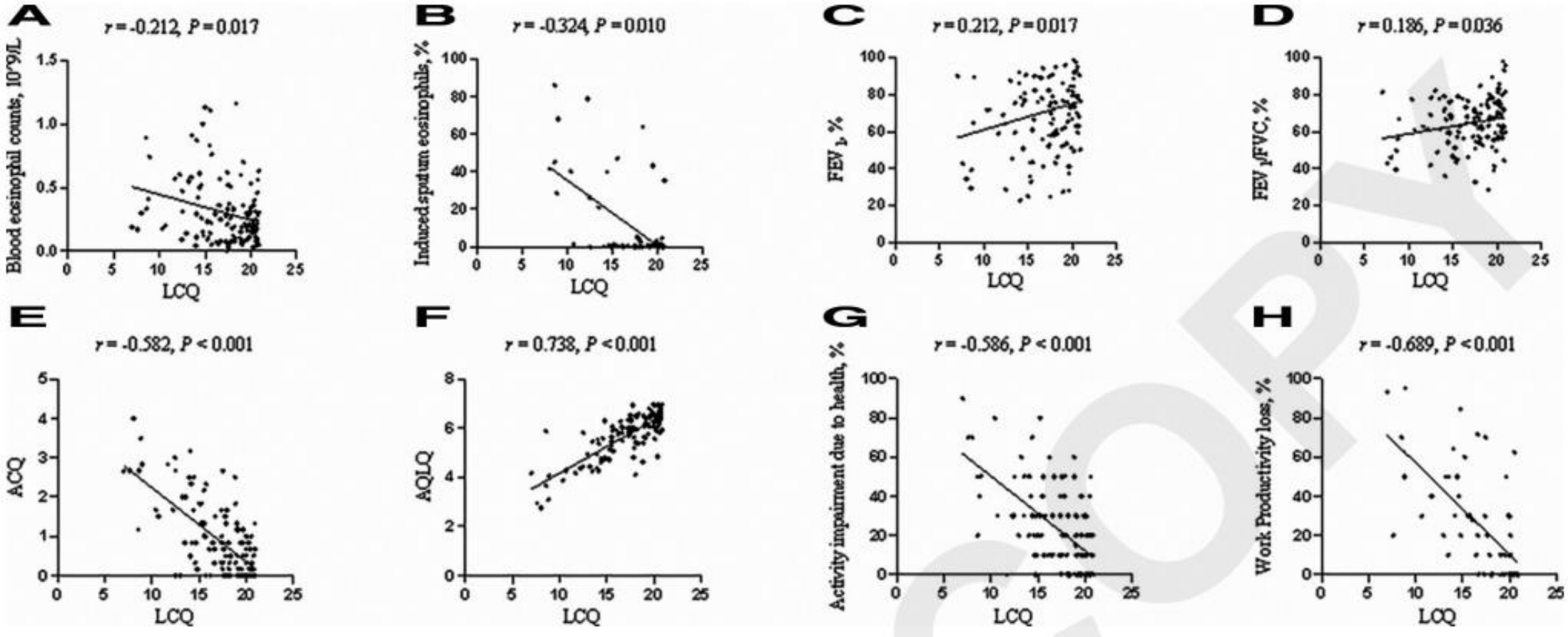
Kanemitus et al. AJRCCM 2020;201:1068-1077

Cough frequency and markers of inflammation in severe asthma



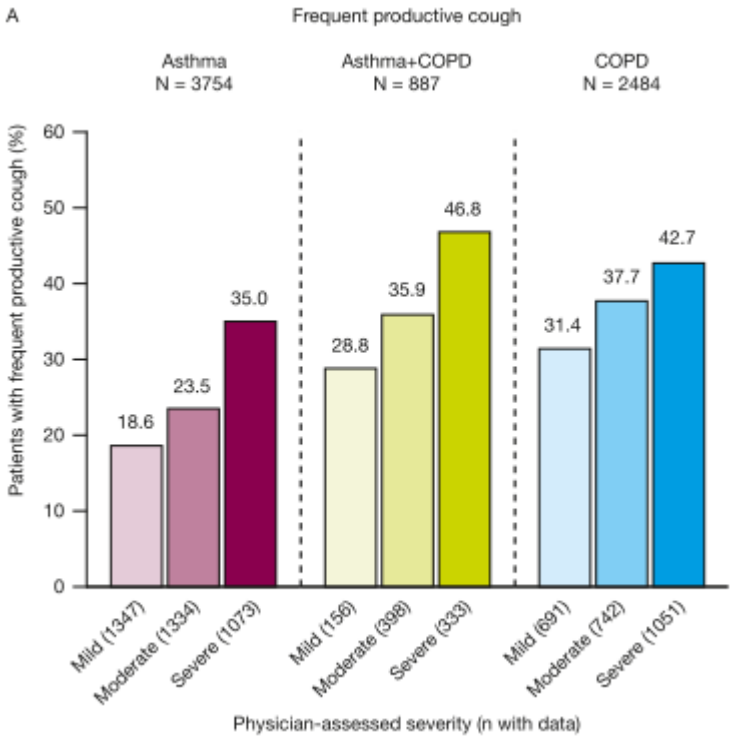
Holmes et al. Eur Respir J 2022; in press

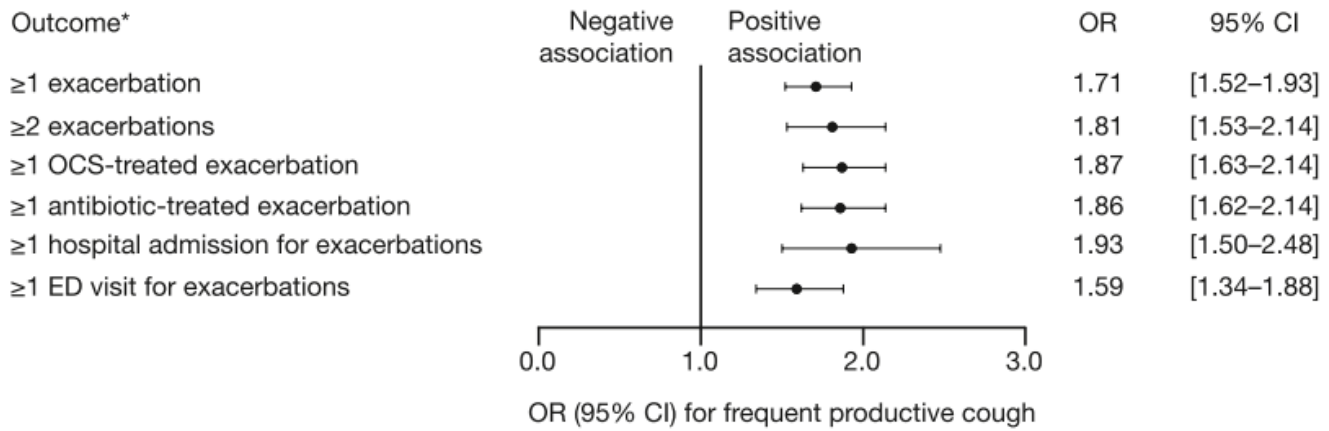
Chronic cough in asthma is associated with increased airway inflammation, more comorbidities, and worse clinical outcomes



Deng SJ et al. Allergy Asthma Proc 43:209–219, 2022

Frequent productive cough:
Symptom burden and future exacerbation risk among patients with asthma

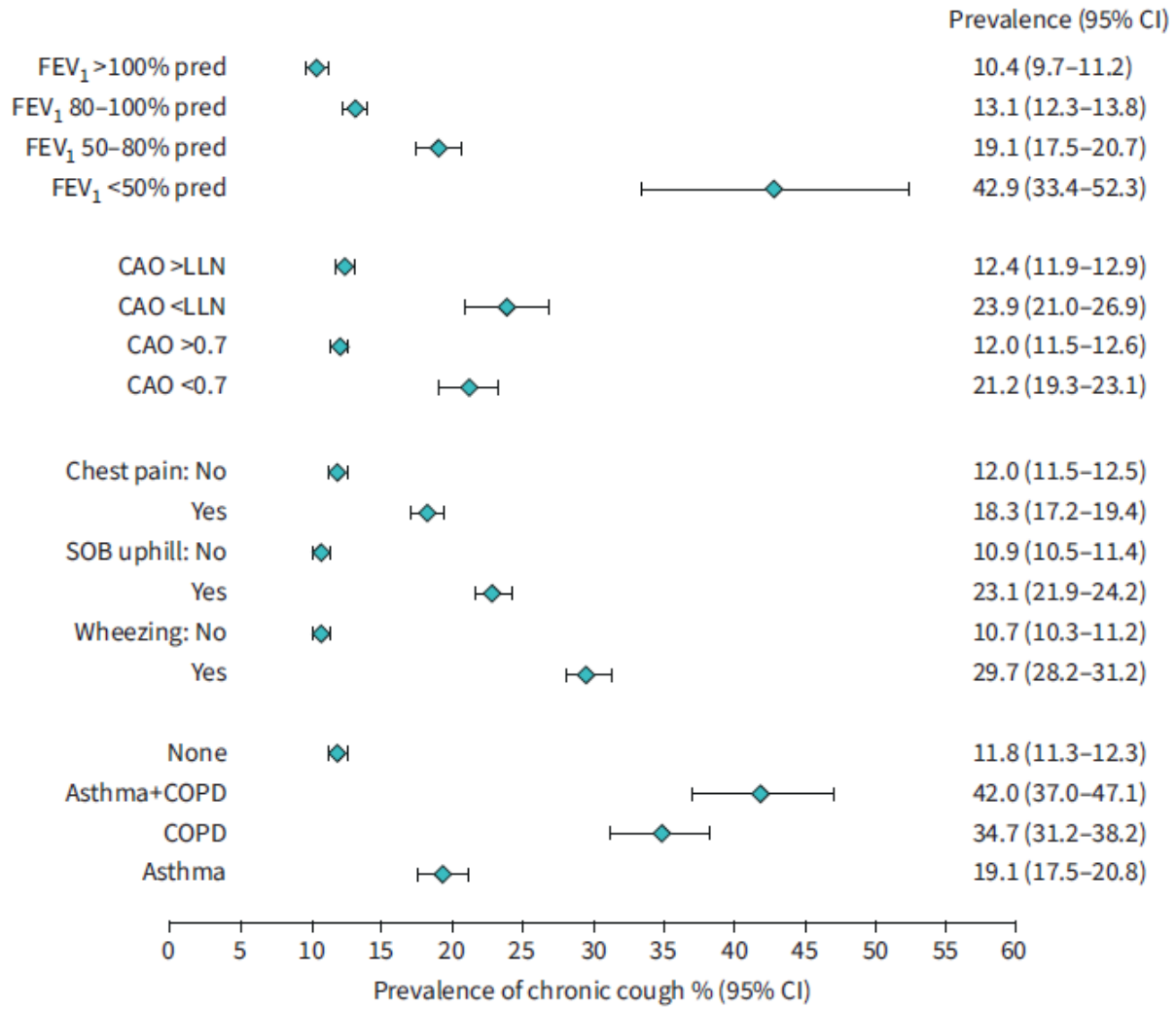




R. Hughes et al. Respiratory Medicine 2022;200

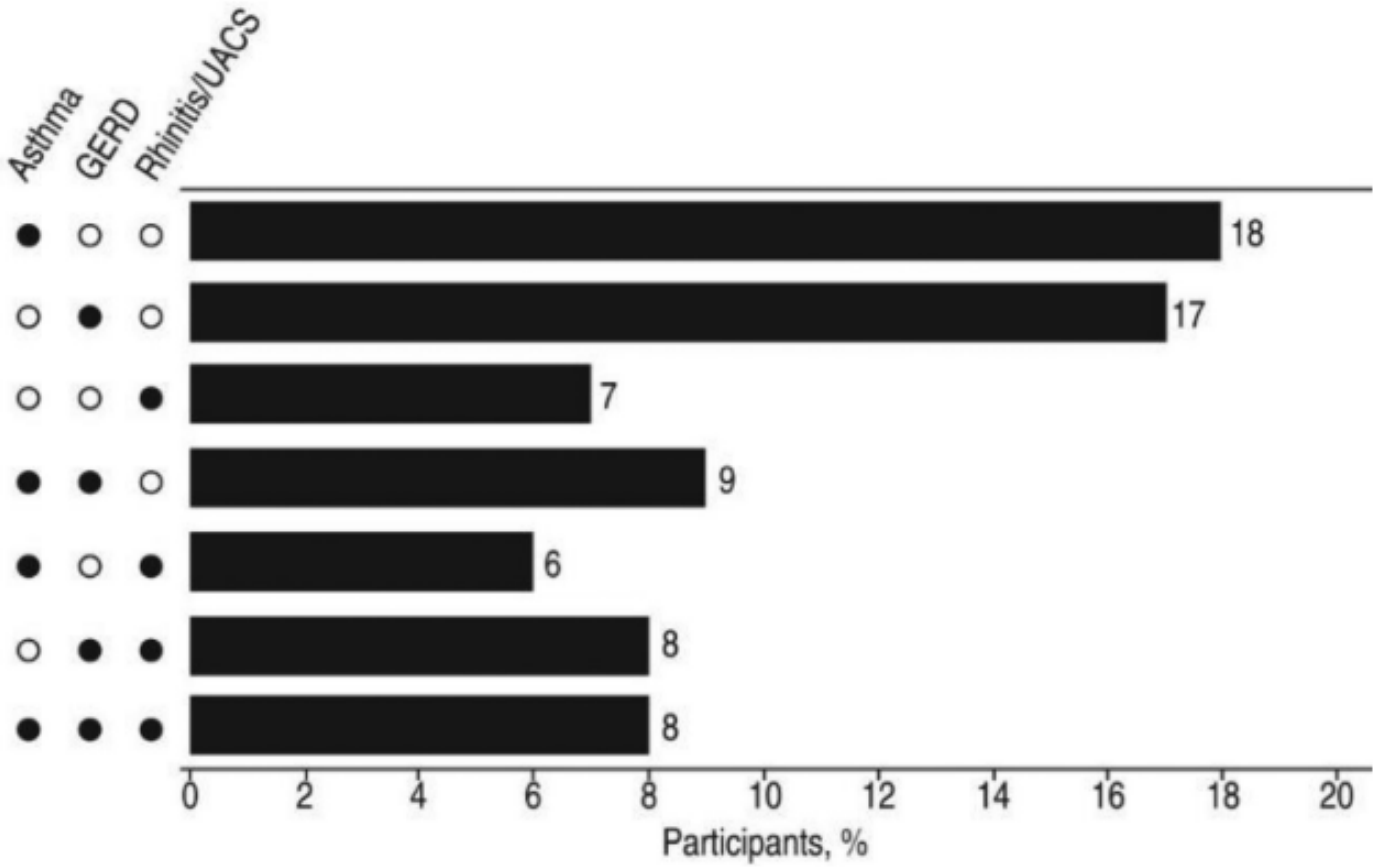
How does having asthma impact cough outcomes?

Asthma associated with increased prevalence of chronic cough



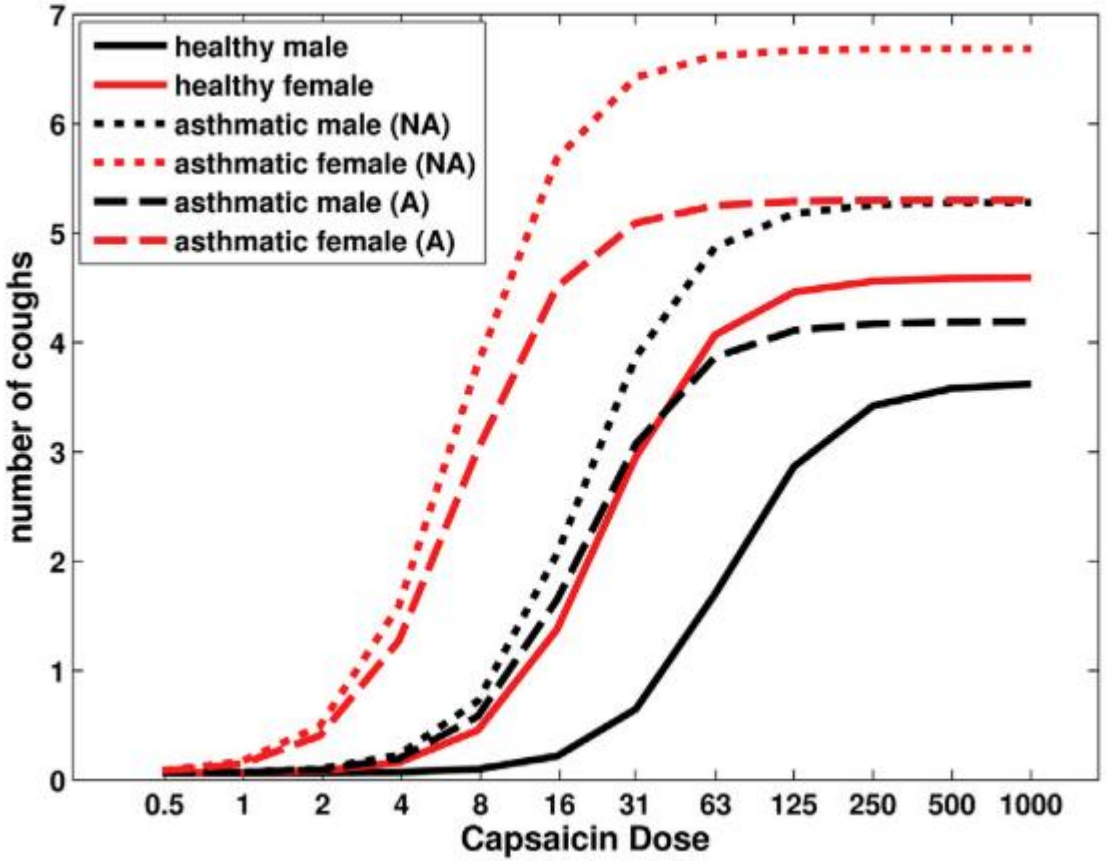
Satia et al. ERJ Open Res 2021; 7

Refractory chronic cough secondary to asthma in clinical trials



P.V. Dicpinigaitis et al. Ann Allergy Asthma Immunol (2022) 1−7

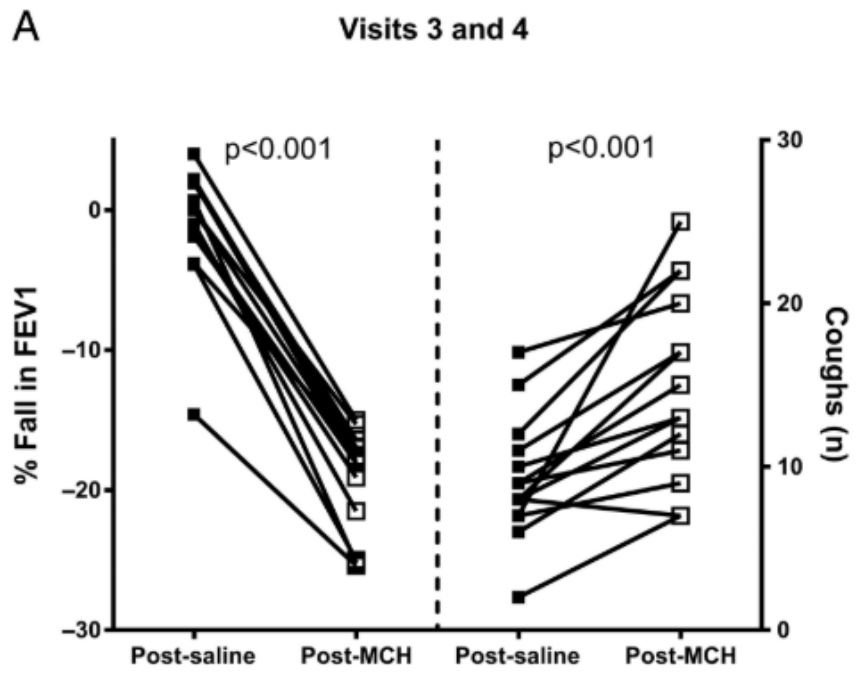
Asthma, sex, and atopic status affect capsaicin-evoked cough responses

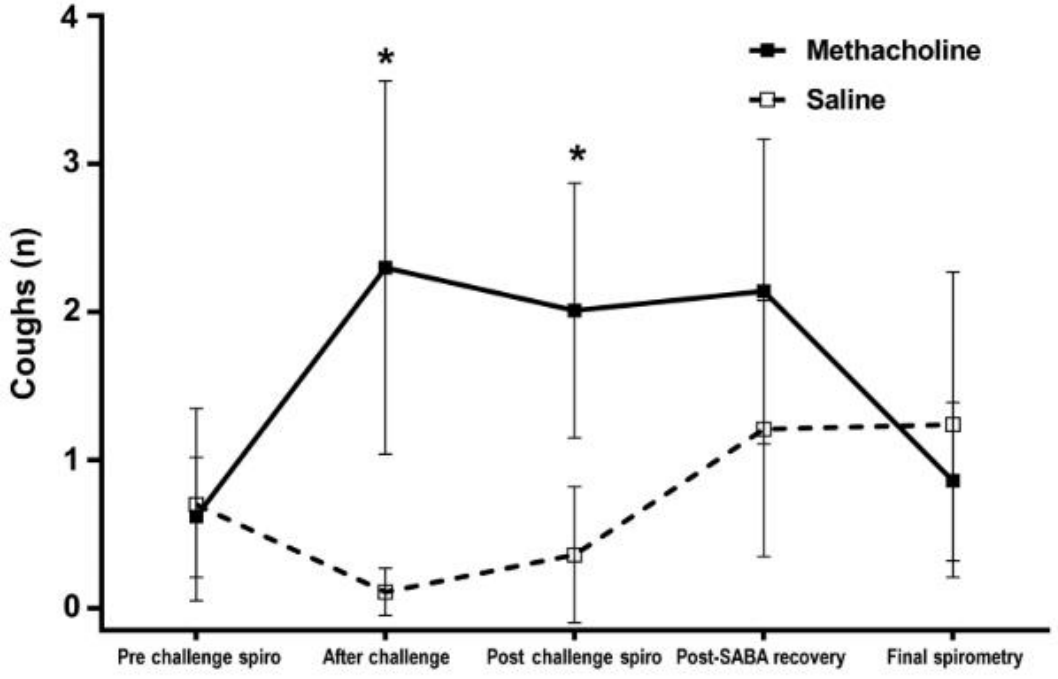


- Healthy male > the lowest cough responses
- Female nonatopic asthmatics > the highest cough responses

Satia et al. JACI 2017;139(3);771-779

The effect of bronchoconstriction on capsaicin-evoked coughs and spontaneous coughs





Satia et al. Thorax 2017;72:1144–1146

ECP/EDN and cough in asthma

		ECP		EDN	
	Subjects, n	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)
Current asthma (vs never asthma)	941	**1.56 (1.27 to 1.92)**	**1.69 (1.35 to 2.12)**	**2.04 (1.72 to 2.41)***	**2.12 (1.76 to 2.57)***
Among participants with current asthma					
Uncontrolled or partly controlled (vs controlled asthma)	350	**1.39 (1.05 to 1.83)**	**1.35 (1.02 to 1.81)**	**1.31 (1.00 to 1.71)**	**1.38 (1.04 to 1.84)**
Asthma attacks in past 12 months	373	1.11 (0.83 to 1.47)	1.13 (0.85 to 1.51)	**1.34 (1.02 to 1.76)***	**1.50 (1.13 to 1.99)***
Exacerbations in past 12 months	368	1.14 (0.77 to 1.70)	1.11 (0.74 to 1.66)	1.10 (0.76 to 1.59)	1.23 (0.84 to 1.81)
Wheezing and breathlessness in past 12 months	373	1.18 (0.86 to 1.62)	1.23 (0.89 to 1.69)	**1.34 (1.04 to 1.73)***	**1.38 (1.05 to 1.80)***
Nocturnal symptoms					
Shortness of breath	373	1.19 (0.85 to 1.65)	1.15 (0.83 to 1.61)	1.13 (0.86 to 1.49)	1.25 (0.93 to 1.66)
Chest tightness	374	1.19 (0.88 to 1.62)	1.19 (0.88 to 1.62)	1.15 (0.89 to 1.49)	1.24 (0.95 to 1.62)
Cough	374	0.96 (0.70 to 1.30)	0.92 (0.67 to 1.27)	**0.75 (0.58 to 0.99)**	0.80 (0.60 to 1.06)
Chronic cough†	354	**1.60 (1.05 to 2.45)**	1.59 (0.99 to 2.55)	1.36 (0.72 to 1.90)	1.37 (0.92 to 2.03)
Chronic phlegm†	355	1.40 (0.95 to 2.04)	1.38 (0.87 to 2.17)	1.44 (0.98 to 2.10)	1.20 (0.87 to 1.97)
Chronic bronchitis†	371	**1.70 (1.13 to 2.55)**	**1.70 (1.09 to 2.64)**	**1.46 (1.04 to 2.06)**	**1.48 (1.03 to 2.13)**
Dyspnoea grade 3	372	1.32 (0.92 to 1.89)	1.28 (0.88 to 1.87)	0.94 (0.68 to 1.31)	1.14 (0.79 to 1.63)
Any asthma treatments in past 12 months‡	374	**1.58 (1.13 to 2.20)**	**1.55 (1.09 to 2.20)**	**1.81 (1.32 to 2.50)***	**1.91 (1.37 to 2.68)***
Use of ICS in past 12 months	371	**1.50 (1.10 to 2.03)**	**1.41 (1.02 to 1.95)**	**1.53 (1.18 to 1.97)***	**1.54 (1.17 to 2.02)***
Positive skin test§	374	1.16 (0.83 to 1.63)	1.34 (0.94 to 1.90)	1.15 (0.83 to 1.61)	1.17 (0.82 to 1.69)
Adult-onset asthma¶	357	1.24 (0.90 to 1.72)	1.23 (0.88 to 1.70)	1.13 (0.86 to 1.48)	1.21 (0.91 to 1.60)
FEV_1 <80% pred	373	1.43 (0.99 to 2.07)	1.38 (0.95 to 2.00)	1.23 (0.90 to 1.68)	1.15 (0.82 to 1.61)
Methacholine challenge** PD_{20} ≤4 mg	241	1.41 (0.98 to 2.02)	**1.48 (1.04 to 2.12)**	**1.73 (1.21 to 2.47)***	**2.03 (1.38 to 2.97)***

Vanessa granger et al. Thorax 2022;77:552-562

Characteristics of different asthma phenotypes associated with cough

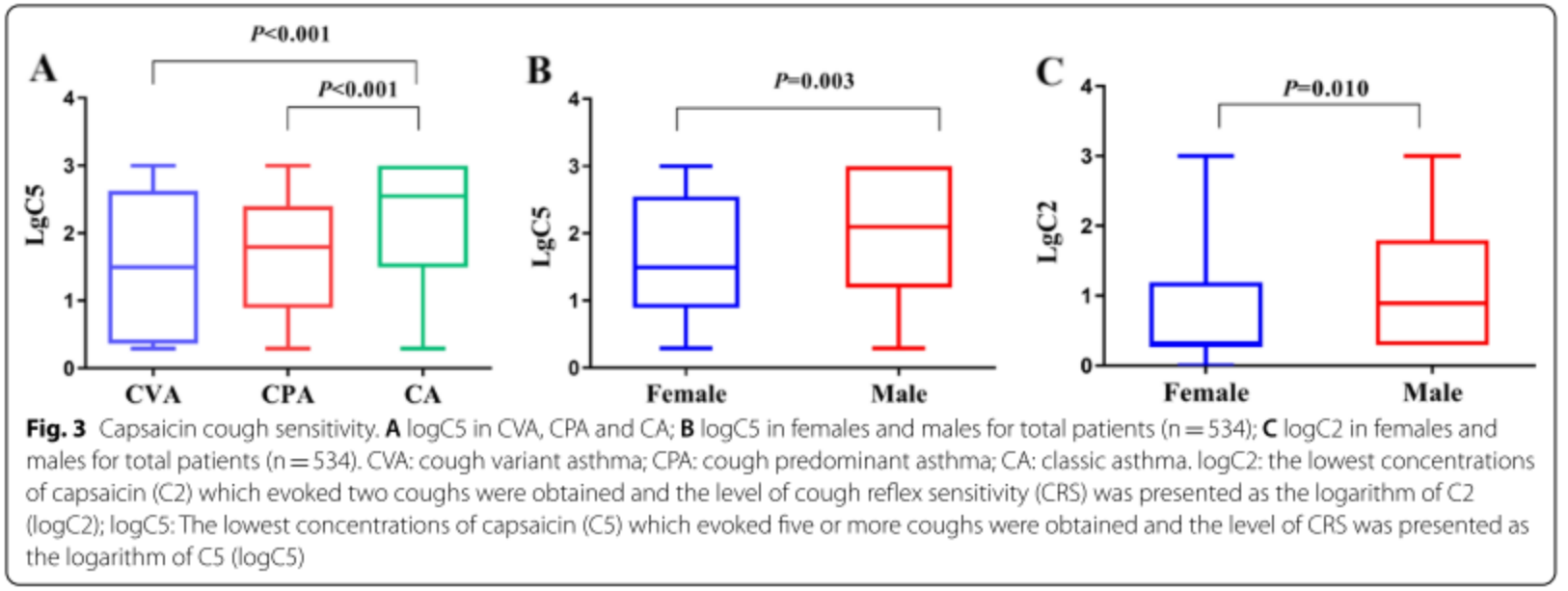
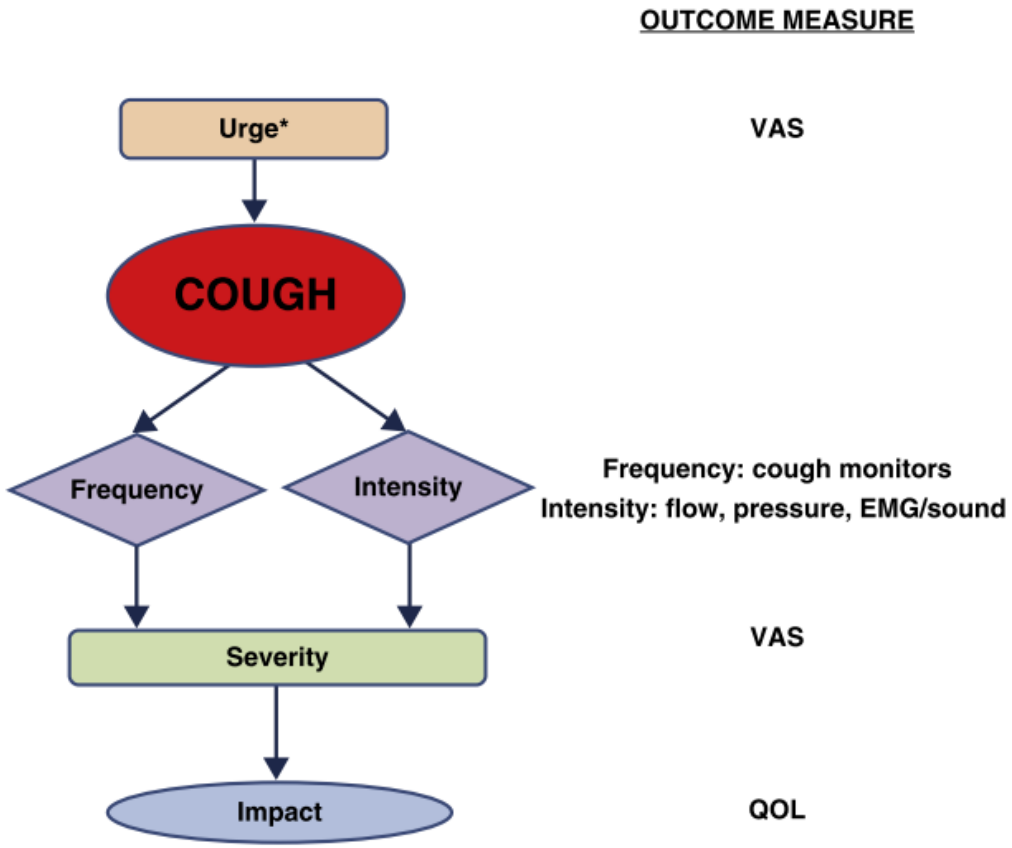


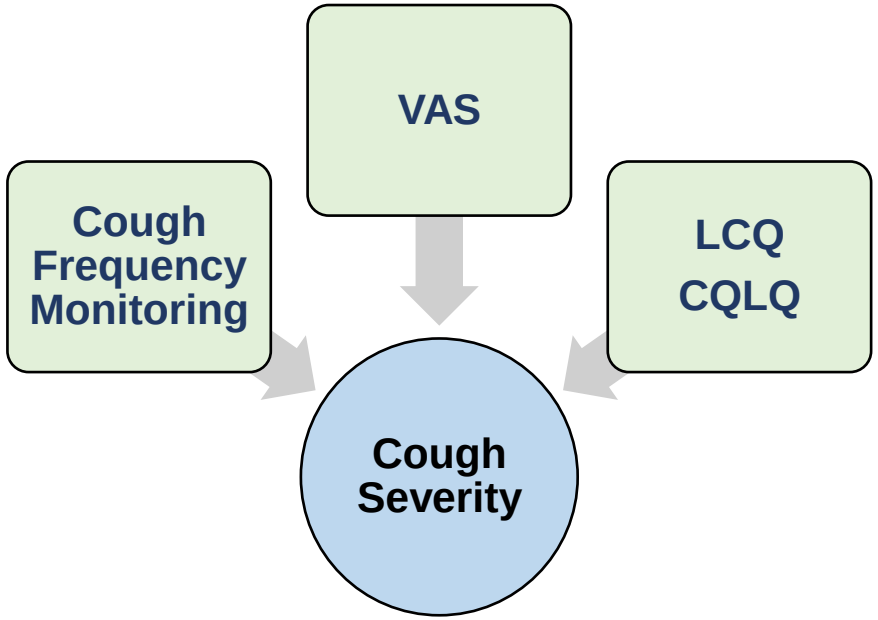
Fig. 3 Capsaicin cough sensitivity. **A** logC5 in CVA, CPA and CA; **B** logC5 in females and males for total patients (n = 534); **C** logC2 in females and males for total patients (n = 534). CVA: cough variant asthma; CPA: cough predominant asthma; CA: classic asthma. logC2: the lowest concentrations of capsaicin (C2) which evoked two coughs were obtained and the level of cough reflex sensitivity (CRS) was presented as the logarithm of C2 (logC2); logC5: The lowest concentrations of capsaicin (C5) which evoked five or more coughs were obtained and the level of CRS was presented as the logarithm of C5 (logC5)

Zhou et al. Respiratory Research (2022) 23:243

How best to measure cough severity in asthmatics?

How best to measure cough severity in chronic cough





Birring, s. s. et al. Current Opinion in Pharmacology 2015, 22:37–40

Cough assessment tools

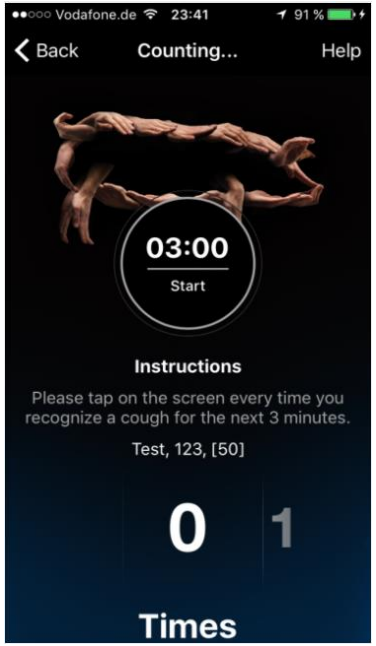
Subjective	Objective
Symptoms	Cough reflex sensitivity
Visual analogue scales (VAS)	Capsaicin
Cough severity score (CSS)	Cough monitors
Cough severity diary (CSD)	Leicester cough monitor (LCM)
Health related quality of life (HRQOL)	VitaloJak
Leicester cough questionnaire (LCQ)	
Cough-specific quality of life questionnaire (CQLQ)	

Cough frequency monitoring device

VitaloJak

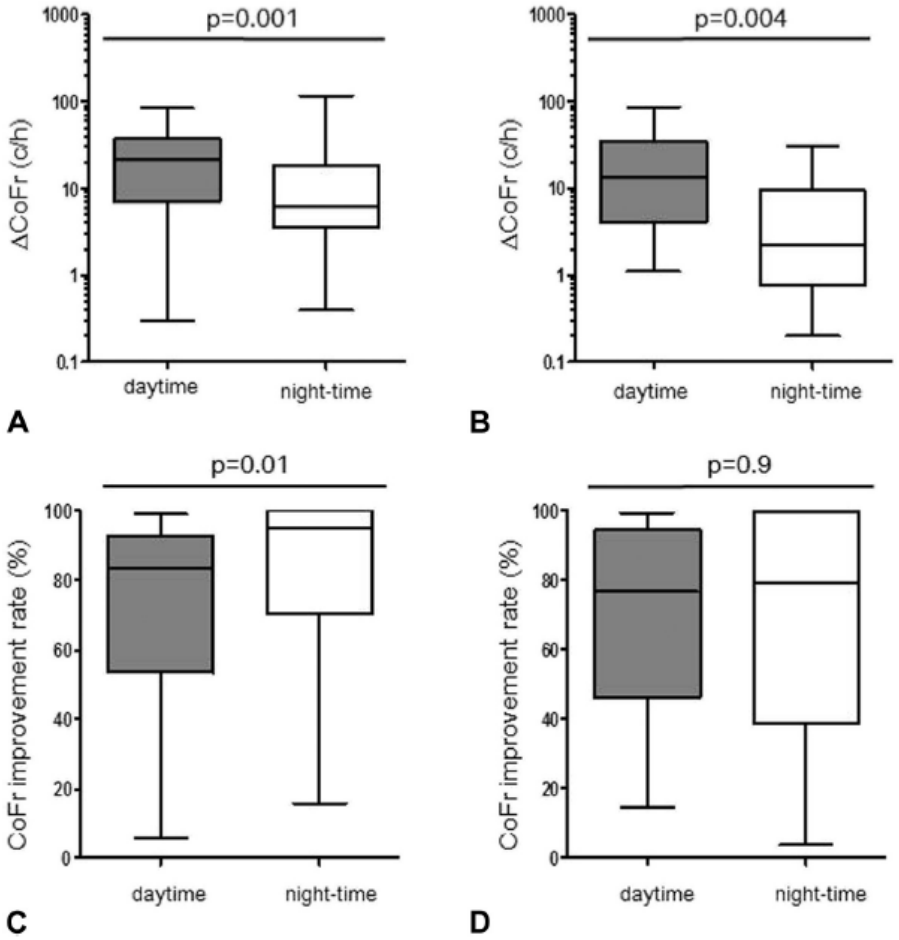
Leciester Cough Monitor

Hyfe Cough Tracker



Cough Index App

Valuable cough monitoring in patients with asthma



In patients with asthma

- ΔCoFr, ΔLCQ, and ΔVAS

  : significant correlations

  (p < .001, not in nonasthmatic pt.)

- CoFr with FeNO and FEV1

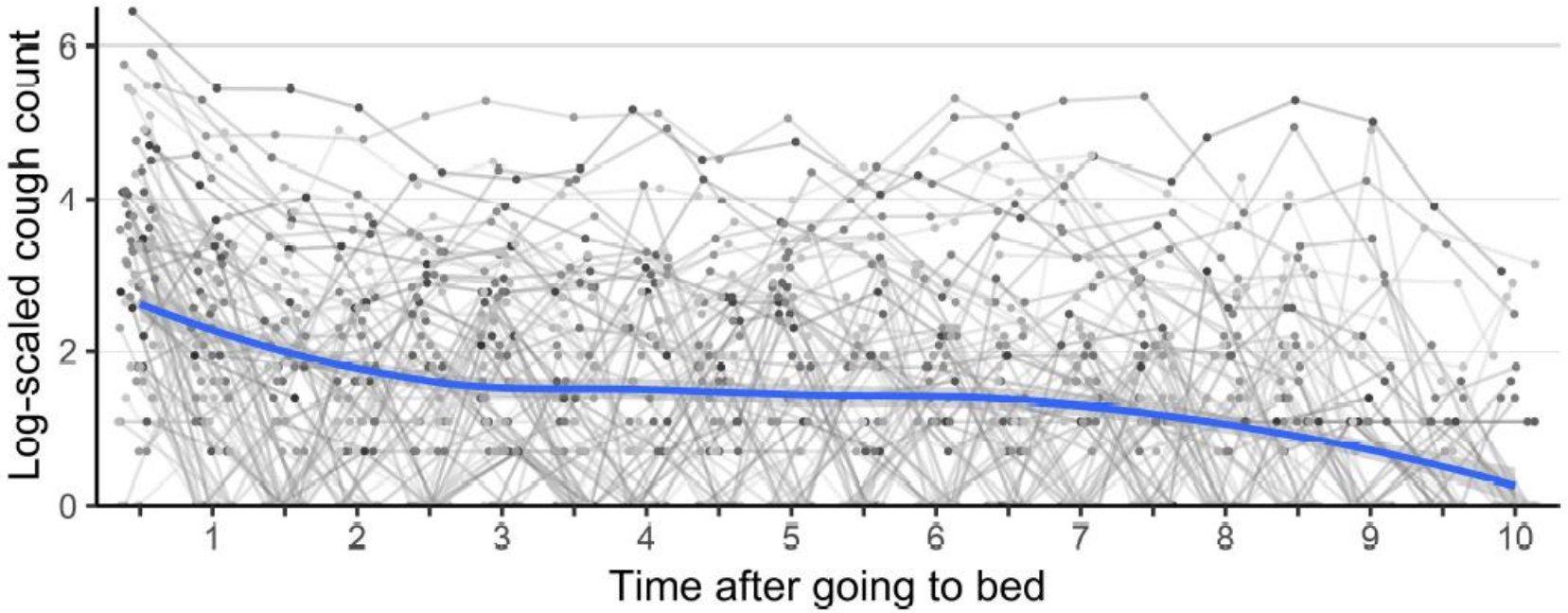
  : no correlations

- Dmin and ACT score

  : weak but significant correlations

Fukuhara et al. J Allergy Clin Immunol Pract, 2020, 8(2), 654-661

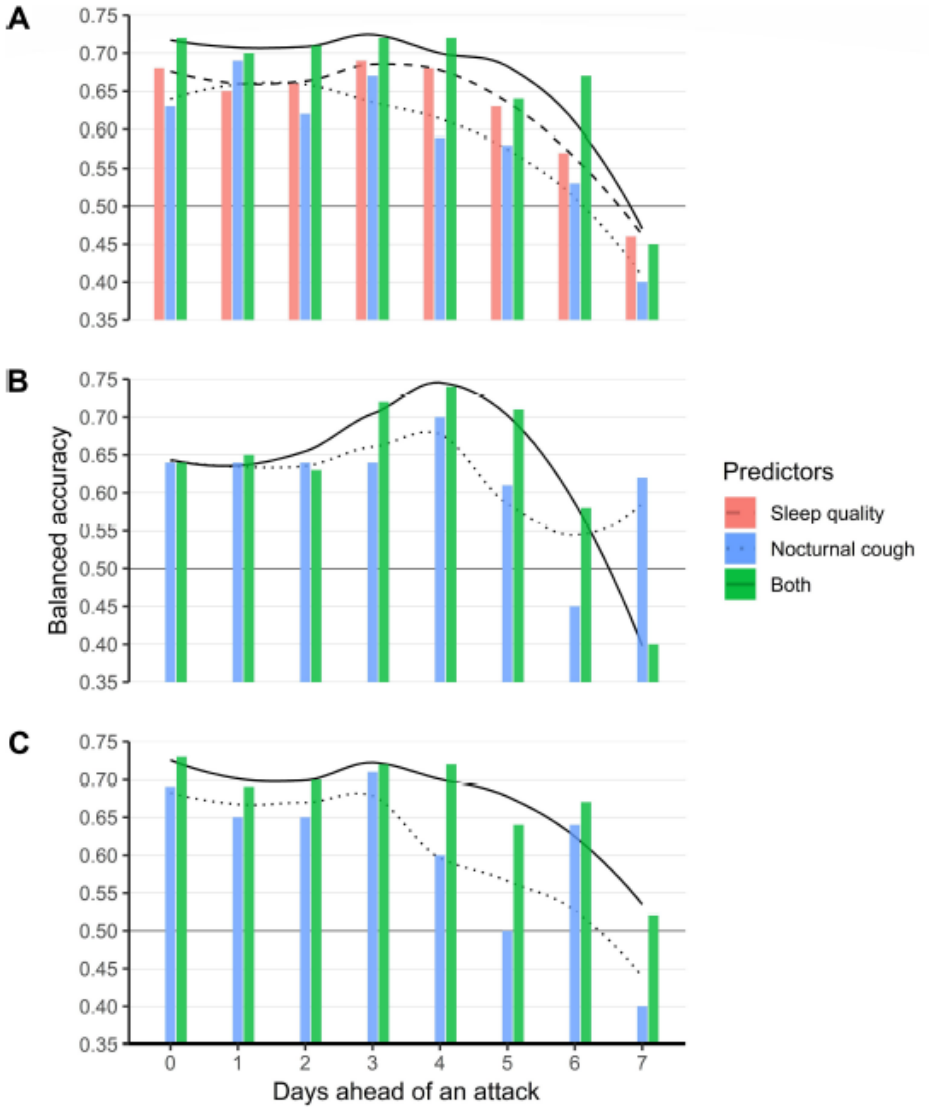
Characteristics of asthma-related nocturnal cough: a potential new digital biomarker



- Highest counts in the first 30 min in bed (4.5-fold higher than the rest of the night)
- Significant correlation between nocturnal cough rate and FEV1

Rassouli et al. Journal of Asthma and Allergy 2020:13 649–657

Nocturnal Cough to Assess Asthma Control



- nocturnal cough and sleep quality were statistically significantly associated with asthma control on a between- and within-patient level

- Cut-offs using both markers predicted asthma attacks up to five days ahead with BACs between 70% and 75%

Tinschert et al. Journal of Asthma and Allergy 2020:13

Managing Chronic Cough Due to Asthma and NAEB in Adults and Adolescents

CHEST Guideline and Expert Panel Report

- Q1. What is the role of non-invasive measurements of airway inflammation in the evaluation of cough associated with asthma?
- Q2. How is cough due to asthma best treated?

- 56 studies in asthma

Côté, A. et al. Chest 2020;158(1), 68-96

Cough assessment tools and outcomes in asthma studies

Assessment tools	Studies, n
Cough severity score, cough score, day cough score, night cough score	50
Cough frequency score	3
Cough severity VAS	2
Cough sensitivity test	2
Days with cough	1
LCQ	1

Côté, A. et al. Chest 2020;158(1), 68-96

How is cough due to asthma best treated?

- 4 RCT of ICS vs placebo (n = 277)
- 2 studies LTRA vs placebo (n = 22)

  > reduction in cough score

- 2 studies inhaled beta agonist (n = 168)
- Poor quality, old studies /c theophylline, mast cell stabilizers and H1RA

  > showed some benefit

Côté, A. et al. Chest 2020;158(1), 68-96

Cough assessment with asthma in clinic

- Cough severity-VAS
- Asthma Control Questionnaire

➢ Q2. On average, during the past week, how bad were your **asthma symptoms** when you woke up in the morning?

- Asthma Control Test

➢ Q4. During the past 4 weeks, how often did your **asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain)** wake you up at night, or earlier than usual in the morning?

Summary

- Chronic cough in asthma is associated with a more severe disease phenotype, worse control status, and higher exacerbation risk.
- Asthma associated with increased prevalence of chronic cough, higher cough frequency, and capsaicin cough responses.
- In asthma, the same as chronic cough, cough severity can be evaluated with VAS, LCQ, and cough frequency monitoring devices.
- If there is an assessment tool that considers the characteristic cough pattern of asthma patients, it may be helpful for asthma control and research.