

Prior Specialist Consultations and Treatments in a Refractory Chronic Cough Population Enrolled In a Phase 2b Study of the P2X3 Antagonist BLU-5937

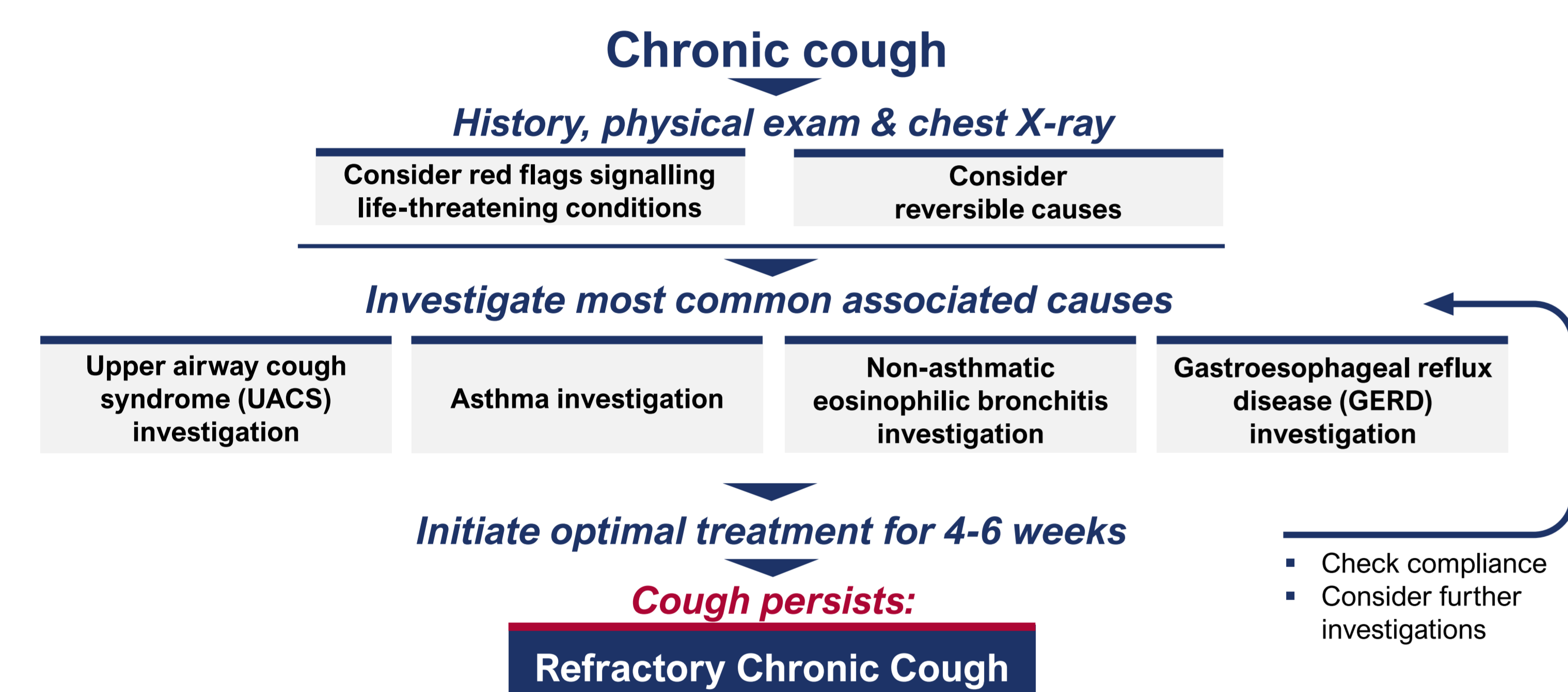
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Introduction

- Refractory Chronic Cough (RCC) is a cough that persists for 8 weeks or more despite adequate treatment of all identifiable associated diseases or without identifiable cause^{1,2}. RCC can impose a significant physical, psychological and social burden on patients².
- Guided by patient history, the diagnostic journey of patients with chronic cough may involve multiple medical consultations, diagnostic investigations and trials of therapy to lead to a diagnosis of refractory chronic cough (Fig.1). These cycles of consultations, tests and trials of ineffective treatments for RCC patients further add to the burden on RCC patients.



Adapted from: Irwin RS et al. (2018) CHEST 153 (1): 196-209.

FIGURE 1. Diagnostic Algorithm of Refractory Chronic Cough²

- The development of P2X3 antagonists³⁻⁵ for the treatment of RCC and approvals in Japan and Switzerland have opened an avenue to alleviate the burden of RCC.
- To better understand the current experience of RCC patients, we report the prior specialty consultations, clinical tests and treatments in a RCC population enrolled in a phase 2b study of BLU-5937, a selective P2X3 antagonist.

Methods

- SOOTHE (NCT04678206) was a multi-center phase 2b, randomized, placebo-controlled, parallel arm clinical dose-finding study in participants diagnosed with
 - Persistent Cough for ≥ 1 year and Awake cough frequency ≥ 25 coughs/h.
 - Patients included also had to report a cough severity of at least 40 mm on a 100 mm visual analog scale.
 - A FEV1/FVC score of at least 60% was also necessary for inclusion. Patients with a diagnosis of COPD, bronchiectasis or IPF were excluded from the study.
 - Prohibited medications during the study included anti-tussive therapy, gabapentin, pregabalin, baclofen, tricyclic antidepressants, systemic corticosteroids and ACE inhibitors.
- Following a single-blind run-in period, 249 participants were randomized 1:1:1:1 to the three active treatment arms of BLU-5937 (12.5, 50 and 200 mg BID) or placebo for 4 weeks of double-blind treatment.

Results

- Overall, the RCC populations randomized in SOOTHE (Tab. 1) had characteristics representative of those reported for RCC elsewhere³⁻⁶.
- The SOOTHE main population (n=249) presented a higher percentage of women (82%), a mean age of 60.9 \pm 10.6 years a mean BMI above average. (Tab. 1).

TABLE 1. Baseline Demographics And Characteristics

Participants, (n)	249	
Female, n (%)	204 (82%)	
Age, mean (SD)	60.9 (10.6)	
BMI (kg/m ²), mean (SD)	28.1 (6.0)	
FEV ₁ /FVC, mean (SD)*	0.77 (0.07)	
Race, n (%)	White	240 (96%)
	Black	3 (1%)
	Asian	4 (2%)
	American Indian/ Alaska Native	2 (1%)
	Cough-associated disease	
	Asthma	76 (31%)
	GERD	115 (46%)
	UACS	64 (26%)
	Unexplained	86 (35%)

* Measured at Day -16 (screening) or within 2 years prior to screening and after the onset of cough

- Pulmonologists were the specialists most often consulted, with 78% of participants having seen at least one. Moreover, 59% had consulted with an ENT specialist, 50% with an allergist/ or immunologist (Fig. 2).
- Patients enrolled in the main population of SOOTHE had received an average of 5.2 \pm 3.1 treatments related to their cough prior to the start of the trial.
- The most common prior medications included acid reducers (76%), inhaled bronchodilators (56%) and oral antihistamines (51%).
- The most common tests performed reflected the range of conditions associated with chronic cough: allergy testing (56%), upper GI endoscopy (42%), upper airway imaging (42%), rhinoscopy (39%) and sinus imaging (34%).
- Interestingly, 73% tried at least one prior treatment for asthma, but 31% were diagnosed with the condition; 77% tried at least one prior treatment for GERD, but 46% were diagnosed with the condition; 70% tried at least one prior treatment for UACS, but 26% were diagnosed with the condition.
- Overall, over half of participants had either consulted with 3 or more specialists, underwent 3 or more investigational tests or tried 3 or more therapies.

Conclusions

- The broad range of specialists seen by patients reflects the evaluation currently needed to establish the diagnosis of RCC.
- The large number of specialists consulted, diagnostic tests performed, and treatments attempted, demonstrate the burden on patients and healthcare systems by the lack of approved treatments for RCC.

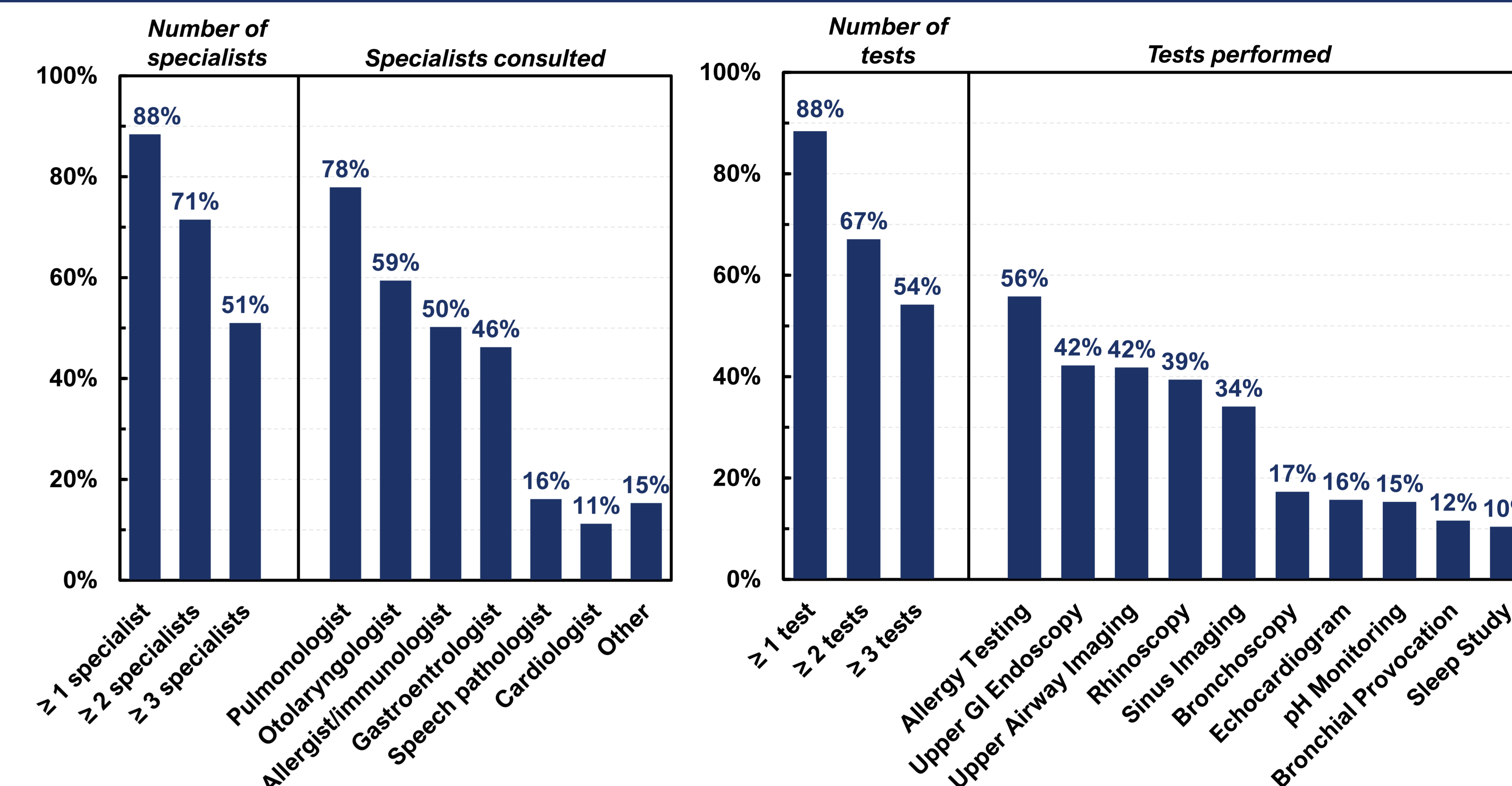
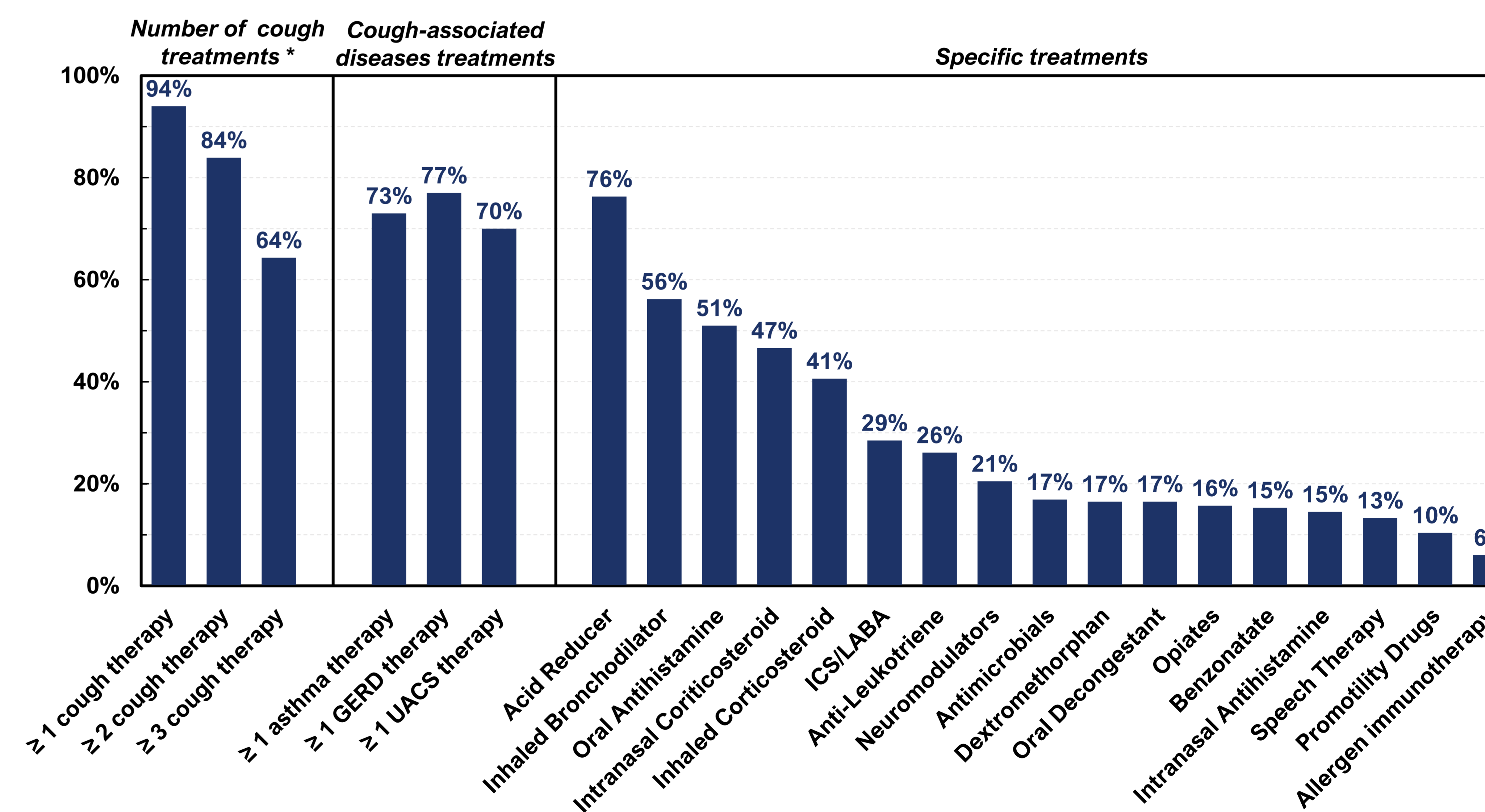


FIGURE 2. Percentage of Participants Who Consulted Specialists Prior To SOOTHE

FIGURE 3. Percentage of Participants With Tests Performed Prior To SOOTHE



* Including anti-tussives, neuromodulators and therapies for cough associate conditions

FIGURE 4. Percentage of Participants Who Underwent Trials of Therapy Prior To SOOTHE

References

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