



## Early View

Research letter

# **Sputum production in chronic cough increases the probability of asthma. A cross-sectional questionnaire study**

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**Sputum production in chronic cough increases the probability of asthma. A cross-sectional questionnaire study.**

Revised, third version

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Take home message: Sputum production may suggest asthma as the most probable background disorder maintaining the cough.

*To the editor,*

Cough is the most common symptom why people seek medical attention and therefore, its clinical management is of fundamental importance. Management of chronic cough relies on identification and treatment of the background disorder maintaining the cough. Asthma, upper airway cough syndrome (UACS, previously called postnasal drip syndrome or chronic rhinosinusitis), and gastroesophageal reflux disease (GERD) are the most common background disorders in chronic cough [1].

The extremely high prevalence of cough indicates that its management must usually take place in primary health care where the diagnostic resources are often limited. It would be useful if the characteristics of cough could aid in predicting the most probable cough background disorder. However, they are usually not considered useful in this respect [2]. Cough is often divided to productive and non-productive, according to the presence or absence of sputum production. Sputum production is common in chronic bronchitis, bronchiectasis, cystic fibrosis, and chronic respiratory infections [3]. In the present study, we investigated whether sputum production would be associated with asthma, UACS or GERD among subjects with chronic cough.

This was a cross-sectional study among public service employees of two middle-sized towns in central Finland, altogether 13 980 employees. Details of it have been described earlier [4]. An electronic questionnaire was sent via e-mail to the participants. It included 80 questions with special attention to cough and the cough background disorders. The subjects with current cough filled in the Leicester Cough Questionnaire (LCQ) [5]. The study was approved by the Ethics Committee of Kuopio University Hospital (289/2015).

Chronic cough was defined as current cough with at least eight weeks' duration. Sputum production was defined as alternatives 4 or less to the LCQ question "In the last 2 weeks, have you been bothered by sputum (phlegm) production when you cough? The alternatives were 1: every time, 2: most times, 3: several times, 4: some times, 5: occasionally, 6 rarely, and 7: never. The cut-off value 4 was chosen because it distinguished best the subjects with and without chronic bronchitis, as defined by Medical Research Council [6], when utilizing the receiver operator characteristic curve. Current asthma was defined as a doctor's diagnosis of asthma and wheezing during the last 12 months. Chronic rhinitis was defined as either nasal blockage or nasal discharge (anterior or posterior nasal drip) and either facial pain/pressure or reduction/loss of smell for more than three months [7]. UACS was defined as chronic rhinitis plus current chronic cough. GERD was defined as either a doctor's diagnosis of GERD or heartburn and/or regurgitation on at least one day a week during the last three months [8]. The number of background disorders was calculated as the sum of current asthma, UACS, and GERD. Unexplained chronic cough indicated an absence of all of them as well as an absence of a doctor's diagnosis of chronic obstructive pulmonary disease (COPD, which was present in just four subjects). Chi-Square test and logistic regression analysis were applied when appropriate.

The response rate was 26.4 % (3697 subjects). The proportion of missing values was less than 1 % in all other questions except family income (2.5%) and acetylsalicylic acid intolerance (1.4 %). The present analysis focused on the 415 subjects who suffered from current chronic cough. Their mean (SD) age was 50.5 (10.0) years with 83 % females. Of them, 215 (51.8 %) reported sputum production. There were 102 subjects with current asthma, 157 subjects with UACS, and 113 subjects with GERD. There were 186 subjects with one, 69 subjects with two, and 16 subjects with three background disorders. In addition, there were 144 subjects with unexplained chronic cough. Among subjects with current asthma, UACS, GERD, and unexplained chronic cough, the prevalence of sputum production was 71.6 %, 56.1 %, 55.8 %, and 41.7 %, respectively ( $p < 0.001$ ,  $p = 0.18$ ,  $p = 0.32$ ,  $p = 0.003$ , when compared with subjects without the disorder, respectively). The prevalence of current smoking was low, 8.6 %, and lower among the subjects with GERD than among the rest of the subjects ( $p < 0.019$ ). Table 1 shows the results of the logistic regression analyses about the association of the background disorders with sputum production, adjusted for current smoking, a well-known cause for sputum production.

The present analysis in a large population-based sample demonstrates that the presence of sputum production in chronic cough increases the probability of current asthma by three-fold. Another large population-based study corroborates this finding [9]. In that study, 59 % of subjects with asthma and chronic cough reported sputum production, significantly more often than other subjects with chronic cough. Previous studies reveal also other typical characteristics of cough in asthma. It is associated with nocturnal cough [10], cold air as a cough trigger [4,11,12], and multiple triggers of cough [4]. These features may help physicians to recognize asthma as a potential cough background disorder even among subjects lacking the classical asthma symptoms namely shortness of breath and wheezing.

Sputum production was not associated statistically significantly with UACS or GERD in the present study. In a previous large Japanese study, both were statistically significantly associated with sputum production [13]. Different populations may explain this discrepancy. All subjects in the present study suffered from chronic cough but the previous study investigated apparently healthy subjects. In our study, sputum production was more common in UACS and GERD than in unexplained chronic cough. Therefore, we think that the two studies are not conflicting.

The prevalence of sputum production was lowest among the subjects with unexplained chronic cough. A similar association has been reported earlier [14]. Furthermore, our study showed that the number of cough background disorders is associated with sputum production. These findings, alongside with the findings of the previously mentioned Japanese study [13], suggests that a presence of sputum production in a patient with chronic cough should encourage a clinician to seek especially carefully treatable cough background disorders.

There are many shortcomings in the present study. The response rate was rather low, which is common in electronic surveys. However, this does probably not affect the main results of the present study. There were

no elderly and unemployed subjects in the present population, which may decrease the generalizability of the results. GERD is difficult to recognize in a questionnaire study since as many as 40 – 75 % of subjects with GERD-associated cough do not exhibit the classic symptoms of GERD [15]. Thus, the number of GERD patients in the present population may be underestimated. The causative relationships between the background disorders and chronic cough are uncertain without confirmation by treatment response. All of the information used in the present analyses are based on self-reports in a cross-sectional design with the associated problems of biased reporting. The strengths of the present study include the large, unselected, and well-characterized sample. The background disorders were clearly defined. Especially, the doctor's diagnosis of asthma in Finland is always based on objective evidence of variable airway obstruction [4].

In conclusion, the presence of sputum production increases the probability of current asthma as the cough background disorder. It also increases the probability of multiple background disorders. On the contrary, dry cough may suggest unexplained chronic cough. These findings may aid the physicians in predicting the most probable cough background disorder.

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### **Author contributions**

Substantial contributions to the conception and design of the work: All authors. Acquisition, analysis or interpretation of data for the work: All authors. Drafting the article or revising it critically for important intellectual content: All authors. Final approval of the version to be published: All authors. Agreement to be accountable for all aspects of the work, in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: All authors

### **Other contributions**

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Table 1. Logistic regression analyses about the associations of the background disorders with sputum production. In each disorder, the control group was those with chronic cough but without that background disorder. Several subjects had more than one background disorder.

Disorder	N	Adjusted <sup>#</sup> Odds Ratio (95 % CI)	p value
Current asthma	102	3.04 (1.87 – 4.94)	< 0.001
Upper airway cough syndrome	157	1.32 (0.88 – 1.96)	0.18
Gastroesophageal reflux disease	113	1.24 (0.80 – 1.92)	0.34
Unexplained chronic cough	144	0.54 (0.36 – 0.81)	0.003
Number of background disorders <sup>†</sup>	415	1.62 (1.26 – 2.08)	< 0.001

<sup>#</sup> adjusted for current smoking; <sup>†</sup> Number of background disorders was calculated as the sum of current asthma, upper airway cough syndrome, and gastroesophageal reflux disease. The Odds Ratio was calculated per one background disorder.