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The risk factors for repetitive doctor's consultations due to cough: A cross-sectional study in a Finnish employed population

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ABSTRACT

Objectives: Cough is the most common symptom prompting people to consult a doctor, thus representing a huge cost to the health care. This burden could be reduced by decreasing the number of repetitive consultations by the same individuals. Therefore, it would be valuable to recognize the factors that associate with repetitive doctor's consultations due to cough.

Design: A cross-sectional, email survey

Setting: Public service employees in two Finnish towns

Participants: The questionnaire was sent to 13 980 subjects; 3695 (26.4 %) replied.

Interventions: The questionnaire sought detailed information about subject characteristics, all disorders diagnosed by a doctor, various symptoms, and doctor's consultations. Those with current cough were inquired about cough characteristics and filled in the Leicester Cough Questionnaire (LCQ).

Primary outcome: Repetitive (≥ 3) doctor's consultations due to cough during the previous 12 months.

Results: There were 205 subjects (5.5 % of the responders) with repetitive consultations. They accounted for 848 out of the 1681 doctor's consultations (50.4 %) due to cough. Among all responders, repetitive consultations were mainly related to the presence of asthma (adjusted odds ratio (aOR) 2.90 (2.01–4.19)) and chronic rhinosinusitis (aOR 2.40 (1.74–3.32)). Among the 975 subjects with current cough, repetitive consultations were mainly related to a low LCQ total score (aOR 3.84 (2.76–5.34) per tertile). Comorbidity, depressive symptoms, and smoking were also associated with repetitive consultations.

Conclusions: A modest proportion of subjects with repetitive consultations is responsible for every second doctor's consultation due to cough. The typical features of these subjects could be identified. These findings can help to focus on certain subpopulations in order to plan interventions to reduce the health care burden attributable to cough.

STRENGTHS AND LIMITATIONS OF THE STUDY

- The results are based on a large community-based sample of 3695 subjects
- The study included a comprehensive list of possible risk factors for repetitive doctor's consultations due to cough
- All subjects had equal and free-of-charge access to doctors, provided by the participating towns' occupational health care organisations. Therefore, supply-related factors do not interfere with the results.
- Only slightly over one in four (26.4 %) of the original population responded
- As all subjects were public service employees, lower social classes and older individuals are underrepresented.

A FUNDING STATEMENT

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A COMPETING INTERESTS STATEMENT

Dr. Koskela reports grants from Kuopion Seudun Hengityssäätiö Foundation, grants from Hengityssairauksien Tutkimussäätiö, during the conduct of the study; personal fees from Mundipharma Ltd, Orion Pharma Ltd, Oy, Eli Lilly Finland Ltd, Boehringer Ingelheim Finland Ltd as payments for giving scientific lectures in gatherings organized by medical companies, personal fees from Takeda Leiras Ltd, Boehringer Ingelheim Ltd, Mundipharma Ltd, and AstraZeneca Ltd, to attend international scientific meetings, in addition to owning shares in Orion Pharma Ltd worth 22 000 euros, outside the submitted work.

Dr. Lätti reports grants from Kuopion Seudun Hengityssäätiö Foundation, grants from Hengityssairauksien Tutkimussäätiö, during the conduct of the study; personal fees from Orion, Boehringer-Ingelheim, Roche to attend international scientific meetings, outside the submitted work.

Dr. Pekkanen has nothing to disclose.

DATA SHARING STATEMENT

De-identified participant data are available upon request from Heikki Koskela ORCID 0000-0002-3386-3262

INTRODUCTION

Cough is the most common symptom prompting individuals to seek medical help from a physician and thus it poses a major health care burden.[1, 2] In the United States, every year there are 21 million outpatient consultations due to cough.[2] Surprisingly, very little is known about the factors that prompt a visit to a doctor due to cough. At present, health care seeking behaviour in coughing patients has been mainly investigated in countries in which there is a high prevalence of tuberculosis, with the goal of improving tuberculosis diagnostics.[3-5] In countries with a low tuberculosis prevalence, the aims may be different. In view of the ageing of the populations in the developed world and the limited health care resources, it would be clearly advantageous if we were able to reduce the number of doctor's consultations due to cough. However, seeking medical help due to the appearance of recent-onset cough must not be discouraged because this would compromise early diagnostics of life-threatening lung disorders like lung cancer, tuberculosis and interstitial lung disorders. Thus, a more reasonable goal might be to decrease the number of repetitive consultations due to cough by the same individual. If we wish to plan interventions to achieve this goal, then it is important that the factors that are associated with repetitive consultations should be clarified. In the present study, these factors were defined in a large population of subjects with equal and free-of-charge access to doctors provided by the participants' occupational health care organisations. The present study report is related to two previous publications, which described the risk factors for cough and the consequences of cough in this population.[6, 7]

METHODS

Population

This was a cross-sectional e-mail study conducted in all public service employees of two towns in central Finland (altogether 13 980 employees, mean 46.6 years with 79.2 % females). All subjects had free-of-charge access to doctors, provided by the participating towns' occupational health care organisations. An invitation to the study and the questionnaire were sent to the employees' e-mail addresses in March - April 2017. Responses were collected via an electronic questionnaire. One reminder message was sent if a subject had not responded within two weeks. The study was approved by the Ethics Committee of Kuopio University Hospital (289/2015). Permission to conduct the study was obtained from the officials of both towns. The invitation letter to participate included detailed information about the study. A subject's decision to reply was considered as informed consent.

Questionnaire

The first part of the questionnaire (57 questions) was filled in by all subjects. All disorders diagnosed by a doctor were inquired, as well as a wide variety of symptoms. Asthma-, rhinosinusitis- and reflux-related symptoms were inquired by questions currently recommended for epidemiologic studies.[8-10] Depressive symptoms were inquired by utilising the Patient Health Questionnaire-2 (PHQ-2).[11] The number of doctor's consultations due to cough during the previous 12 months was inquired from all subjects. The second part of the questionnaire consisted of 23 cough-related questions to be answered by those subjects reporting that they had current cough. It included detailed questions about the cough bout frequency and cough duration, as well as the Leicester Cough Questionnaire (LCQ), which measures the cough-related quality of life.[12] The number of doctor's consultations due to cough was inquired. Many questions were adapted from two previous studies, the Health Behaviour and Health among the Finnish Adult Population study [13] and the Finnish National FINRISK study.[14]

Definitions

The main outcome was repetitive doctor's consultations due to cough. During the last 12 months, 22.5 % of the responders had consulted a doctor due to cough at least once, 11.2 % at least twice, 5.5 % at least three times, 2.7 % at least four times, and 1.4 % at least five times. In the present study, 'repetitive consultations' was arbitrarily defined as at least three doctor's consultations due to cough in the past 12 months.

Current cough was defined as ongoing cough at the time when the survey was conducted. Chronic bronchitis was defined as daily sputum production for at least three months of the year. A cough trigger was defined as the presence of one or more identifiable cough triggers. Current asthma was defined as a doctor's diagnosis of asthma at any age and wheezing during the last 12 months. Chronic rhinosinusitis was present if there was 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.[9] Esophageal reflux disease was present if there had been heartburn and/or regurgitation on at least one day of the week during the last three months.[10] Depressive symptoms were present if the PHQ-2 score was three or more.[11] Allergy was defined as a self-reported allergy to pollens, animals or food. A family history of chronic cough was defined as the presence (now or in the past) of chronic (duration more than eight weeks) cough in parents, sisters or brothers. The disorder sum was defined as the number of medical disorders diagnosed by a doctor. The symptom

sum was defined as the sum of symptoms (other than respiratory symptoms) reported by the subjects.

Patient involvement

Patients were not directly involved in the design, recruitment, or in the conduct of this study. The results will be disseminated to study participants through the Kuopio town and Jyväskylä towns' intranet portals.

Statistical analysis

The descriptive data is shown as means and 95 % confidence intervals (CI) unless otherwise stated. In the participants with current cough, the LCQ total scores (ts) were divided into tertiles. First tertile: 3.0 - 14.1, second tertile: 14.2 to 16.8, and third tertile: 16.9 to 21.0. The cough bout frequency was also divided into tertiles: First tertile: on 2 – 3 days per week or less often, second tertile: on 4 – 6 days per week to once daily, and third tertile: several times daily. The cough episode duration was categorized according to the current guidelines to < 3 weeks (acute cough), 3 – 8 weeks (subacute cough), and > 8 weeks (chronic cough).[15, 16]

The bivariate associations of the following variables with repetitive consultations were analysed: Current asthma, chronic rhinosinusitis, esophageal reflux disease, depressive symptoms, disorder sum, symptom sum, acetylsalicylic acid intolerance, allergy, age, gender, body mass index, years of education, family incomes, professional status, number of family members, pet ownership, moisture damage exposure, smoking history, weekly alcohol doses, level of daily physical exercise, and family history of chronic cough. In addition to these factors, the following variables were included in the analyses among the 975 subjects with current cough: Duration of the current cough episode, current cough bout frequency, LCQ total score (LCQts), chronic bronchitis, and cough trigger.

Mann-Whitney test and chi-square test were applied when appropriate. The variables showing at least a suggestive ($p < 0.1$) association with repetitive consultations in the bivariate analyses were included in the multivariate analyses utilising binary logistic regression analysis with backward directed stepwise process to eliminate non-significant confounders. However, only LCQts was included without its domains due to the presence of strong interrelationships.

A p value less than 0.05 was accepted as the level of statistical significance but in the tables, all factors with at least a suggestive association ($p < 0.1$) are presented. All analyses were performed using SPSS version 22 for the personal computer (SPSS, Inc. Chicago, Illinois, USA).

RESULTS

The response rate was 26.4 % (3695 subjects, mean age 47.8 (47.5 – 48.2) years, 82.6 % females, 31.4 % ever-smokers, table 1). The proportion of missing values was less than 1 % in all other questions except for family income (2.5%) and acetylsalicylic acid intolerance (1.4 %).

Table 1. The basic characteristics and their bivariate associations with repetitive (≥ 3 during the last 12 months) doctor's consultations due to cough in the entire population (N = 3695). The figures are percentages or means and 95 % confidence intervals.

Characteristic	**Subjects without repetitive doctor's consultations due to cough N = 3490**	**Subjects with repetitive doctor's consultations due to cough N = 205**	**P value**
Female gender, %	82.5	85.3	0.30
Age (years)	47.8 (47.4 – 48.2)	48.5 (47.1 – 50.0)	0.35
Body mass index (kg/m^2)	26.5 (26.4 – 26.7)	27.9 (27.0 – 28.7)	< 0.001
Family incomes, income class [a]	1.98 (1.95 – 2.00)	2.06 (1.95 – 2.16)	0.17
Moisture damage exposure, %	25.4	33.7	0.009
Ever smoking, %	31.3	33.2	0.57
Family history of chronic cough, %	34.7	51.0	< 0.001
Acetylsalicylic acid intolerance, %	4.6	9.4	0.002
Allergy, %	17.4	27.8	< 0.001
Depressive symptoms, %	4.9	9.4	0.004
Symptom sum	2.55 (2.48 – 2.62)	3.56 (3.24 – 3.88)	< 0.001
Disorder sum	1.08 (1.04 – 1.13)	2.31 (2.08 – 2.55)	< 0.001
Current asthma, %	8.7	36.6	< 0.001
Chronic rhinosinusitis, %	14.2	40.5	< 0.001
Esophageal reflux disease, %	12.1	21.0	< 0.001

[a] Income classes: 1 = less than 15 000 e/year; 2 = 15 000- 40 000 e; 3 = 40 000 – 70 000 e; 4 = 70 000 – 120 000 e; 5 = over 120 000 e/year. Other definitions, se text.

Among all 3695 responders, there were 205 subjects who reported repetitive doctor's consultations due to cough (5.5 %). They accounted for 848 out of the 1681 doctor's consultations due to cough (50.4 %) during the previous 12 months.

There were 975 participants with current cough (mean age 48.7 (48.0 – 49.3) years, 83.8 % females, 31.4 % ever-smokers). Among them, there were 135 subjects (13.8 % of the subjects with current cough) with repetitive doctor's consultations due to cough. They accounted for 573 out of the 926 doctor's consultations due to cough (61.9 %) among the subjects with a current cough.

In addition to the other baseline characteristics, table 1 shows all variables for which there was at least a suggestive association with repetitive consultations in bivariate analyses among all 3695 responders. Table 2 shows the results of the multivariate analyses in these individuals. The most important factors were the presence of current asthma and chronic rhinosinusitis. Table 3 shows the results of the bivariate analyses among the 975 subjects with current cough and table 4 displays the results of the multivariate analysis in these individuals. Among the subjects with current cough, the LCQts was the most important determinant of repetitive doctor's consultations. The proportions of subjects with repetitive doctor's consultations due to cough within each LCQts tertile are illustrated in figure 1.

Table 2. The characteristics that associated with repetitive doctor's consultations due to cough in the entire population (3695 subjects). Multivariate analysis with adjusted odds ratios (aOR) and confidence intervals (CI).

Characteristic	**aOR (95 % CI)**	**P value**
Current asthma	2.90 (2.01 – 4.19)	< 0.001
Chronic rhinosinusitis	2.40 (1.74 – 3.32)	< 0.001
Disorder sum [a]	1.33 (1.20 – 1.47)	< 0.001
Depressive symptoms [b]	1.72 (1.01 – 2.92)	0.046
Family history of chronic cough	1.38 (1.02 – 1.87)	0.039

[a] aOR calculated for every doctor's diagnosed disorder. [b] Patient Health Questionnaire-2 score three or more

Table 3. The basic characteristics and their bivariate associations with repetitive (≥ 3 during the last 12 months) doctor's consultations due to cough among the subjects with current cough (N = 975). The figures are percentages or means and 95 % confidence intervals unless otherwise stated.

Characteristic	**Subjects without repetitive doctor's consultations due to cough. N = 840**	**Subjects with repetitive doctor's consultations due to cough. N = 135**	**P value**
Female gender, %	83.9	83.6	0.93
Age (years)	48.5 (47.8 – 49.2)	49.6 (47.8 – 51.3)	0.40
Body mass index (kg/m^2)	27.1 (26.8 – 27.5)	27.7 (26.8 – 28.7)	0.18
Family incomes, income class [a]	2.03 (1.98 – 2.08)	2.04 (1.90 – 2.17)	0.89
Moisture damage exposure, %	32.5	38.5	0.17
Ever smoking, %	30.4	37.8	0.085
Family history of chronic cough, %	46.3	53.0	0.15
Acetylsalicylic acid intolerance, %	5.4	9.8	0.049
Allergy, %	23.8	26.7	0.47
Depressive symptoms, %	5.4	6.7	0.56
Symptom sum	3.18 (3.03 – 3.32)	3.69 (3.28 – 4.10)	0.017
Disorder sum	1.50 (1.40 – 1.60)	2.33 (2.04 – 2.62)	< 0.001
Chronic bronchitis, %	32.5	56.7	< 0.001
Current asthma, %	16.1	40.0	< 0.001
Chronic rhinosinusitis, %	26.5	45.9	< 0.001
Esophageal reflux disease, %	16.5	23.0	0.068
Cough trigger, %	73.6	88.9	< 0.001
Duration of the cough episode (median, range)	3 – 8 weeks (some days-over 10 yrs)	2 – 12 months (some days-over 10 yrs)	< 0.001
Cough bout frequency (median, range)	Daily (less than weekly – several times a day)	Several times a day (less than weekly – several times a day)	< 0.001
LCQ total score	15.7 (15.5 – 15.9)	12.3 (11.8 – 12.8)	< 0.001
LCQ physical domain	5.06 (5.00 – 5.12)	4.08 (3.92 – 4.23)	< 0.001
LCQ psychological domain	5.18 (5.10 – 5.25)	3.96 (3.78 – 4.13)	< 0.001
LCQ social domain	5.45 (5.38 – 5.53)	4.25 (4.05 – 4.44)	< 0.001
Number of doctor's consultations due to cough during the last 12 months (median, range)	0 (0 – 2)	3 (3 – 20)	< 0.001

[a] Income classes: 1 = less than 15 000 e/year; 2 = 15 000- 40 000 e; 3 = 40 000 – 70 000 e; 4 = 70 000 – 120 000 e; 5 = over 120 000 e/year. Other definitions, se text.

Table 4. The characteristics that associated with repetitive doctor's consultations due to cough among 975 subjects with current cough. Multivariate analysis with adjusted odds ratios (aOR) and confidence intervals (CI).

Characteristic	aOR (95 % CI)	P value
LCQ total score [a]	3.84 (2.76 – 5.34)	< 0.001
Current asthma	1.85 (1.16 – 2.94)	0.010
Duration of cough episode [b]	1.50 (1.17 – 1.93)	0.001
Smoking ever	1.50 (0.98 – 2.29)	0.059
Disorder sum [c]	1.13 (0.99 – 1.29)	0.061

[a] aOR calculated per one less LCQ total score tertile. [b] aOR calculated per one duration step (< 3 weeks, 3 – 8 weeks, > 8 weeks). [c] aOR calculated for every doctor's diagnosed disorder

The associations of each of the nineteen LCQ questions with repetitive doctor's consultation were analysed and ranked according to the Mann-Whitney test z-score. According to the rank order of association, the LCQ questions with the closest associations were; number 6 (psychological domain: "In the last 2 weeks, my cough has made me feel anxious."), 16 (psychological: "In the last 2 weeks, have you worried that your cough may indicate a serious illness?"), 13 (psychological: "In the last 2 weeks, my cough has made me feel fed up"), 3 (physical: "In the last 2 weeks, have you been tired because of your cough?"), and 17 (psychological: In the last 2 weeks, have you been concerned that other people think something is wrong with you, because of your cough?").

DISCUSSION

The present study in an employed, working-age population revealed that a modest proportion (5.5 %) of subjects with repetitive doctor's consultations was responsible for about every second consultation to the doctor because of cough. In the entire population, the list of factors underpinning the repetitive consultations resembled that of the common causes of chronic cough[15, 16] i.e. it was predominated by current asthma and chronic rhinosinusitis. The analysis among the 975 subjects with current cough included more detailed information about the characteristics of their cough. In this analysis, the dominant factor behind the repetitive consultations was the severity of the impairment in the cough-related quality of life.

It is well known that a small proportion of individuals account for the majority of health care utilisation and spending. Most of the studies about these "high cost users" have concentrated on the most expensive forms of health care, such as inpatient care, emergency consultations, and

operations, and have not been concerned with primary care consultations.[17-20] These “high cost users” are often found to be elderly, have a low socio-economic status, and suffer from several comorbid illnesses including mental illnesses or addictions. Accordingly, in the present population, it was found that the number of comorbid illnesses, the presence of depressive symptoms and smoking were associated with repetitive consultations. However, age did not show an independent association. This discrepancy may be attributable to the homogeneous nature of our study population i.e. all subjects were of working-age. Nonetheless, most of the known characteristics of “high cost users” could be taken into account in the present analyses.

The present population may not represent well the general population since elderly and unemployed subjects were missing. However, this study has one feature, which makes it especially enlightening: All subjects had equal and free-of-charge access to doctors, provided by the participating towns’ occupational health care organisations. Apart from need-related factors, health care utilisation is also supply-dependent; this is associated with the nature of the health care system.[21] In the present study, supply-related factors did not influence the results as all the respondents could obtain medical help from their occupational health care centre.

Asthma and chronic rhinosinusitis are important background diseases of chronic cough [15, 16] and therefore it is not surprising that they were clearly associated with repetitive doctor’s consultations in the entire population. It may be fair to say that three or more yearly consultations due to cough by a subject with chronic rhinosinusitis or asthma indicates that there is inadequate control of these disorders. A better understanding of the association of these disorders with cough as well as their more efficient management might effectively decrease the number of doctor’s consultations due to cough. Esophageal reflux disease was not associated with repetitive consultations though it is also considered as an important background disease to chronic cough.[15, 16] We have previously reported that for some reason in our study population, esophageal reflux disease is much less clearly associated with chronic cough than asthma and chronic rhinosinusitis.[6] In the present study, the diagnoses of chronic rhinosinusitis and esophageal reflux disease relied purely on self-reported symptoms, a factor which must be borne in mind when considering the associations of these disorders with repetitive doctor’s consultations.

The analysis among subjects with current cough included much more information than the analysis gathered from the entire population. Therefore, different factors were evident. Among these subjects, the major factor behind repetitive doctor’s consultations due to cough seems to be the level of impairment in the cough-related quality of life. Subjects with cough are often dissatisfied with the therapy prescribed by physicians, which may lead to another consultation as the cough

continues.[22] It is noteworthy that the length of the cough episode was also associated with repetitive doctor's consultations. Therefore, repetitive doctor's consultations due to cough could be decreased by more effective clinical management of cough on the first consultation which would make repetitive consultations unnecessary. Further education of general practitioners may be needed to achieve this goal. However, new, effective medications for the long-standing hypersensitivity of the cough reflex arch are also urgently needed.[23]

The quality of life was measured by the LCQ and the LCQts were divided into tertiles. Given that the present 975 subjects with current cough represent an unselected, community-based population, we suggest that the first tertile (3.0 - 14.1) represents severe cough, the second tertile (14.2 – 16.8) represents individuals with moderate cough and those in the third tertile (16.9 – 21) have mild cough. The respective proportions of subjects with repetitive doctor's consultations were 31 %, 8 % and 2 %, highlighting the dominant role of the quality of life impairment. Though LCQ is a well validated questionnaire,[12] we are unaware of any previous attempts to grade it in a clinically meaningful way. The grading of LCQts utilized here may have several applications in everyday clinical cough management as well as in epidemiologic studies. It could also be applied to create meaningful inclusion criteria for clinical drug trials.

LCQ is a very comprehensive questionnaire with nineteen questions covering multiple characteristics of cough. Interestingly, the most important questions with respect to repetitive consultations belonged to the psychological domain. It seems that the crucial factor leading to the decision to seek medical attention is not the symptom per se but the feelings that the symptom induces. This finding suggests that the patient's concerns may differ significantly from those of the doctor. The latter may be more interested if there are serious symptoms, like haemoptysis, or if there are symptoms suggestive of possible background diseases behind the cough, like wheezing or regurgitation.

There are several shortcomings in the present study. As mentioned, the population may not represent well the general population because elderly and unemployed subjects were missing. In addition, the majority of the participants were female. These facts decrease the applicability of the data to the general population. The participation rate to the survey was relatively low. However, the responders and non-responders did not differ with respect to age and sex distribution. Furthermore, it is unlikely that the low response rate could affect the associations of various features with repetitive doctor's consultations. The authors did not have access to individual patient files, for example to investigate physician-patient relationships, the accuracy of diagnoses, or treatment details. The information gained is based on self-reports in a cross-sectional design with the

associated problems of recall bias, biased reporting and the lack of any possibility to separate associations from causality.

In conclusion, a modest proportion of subjects with repetitive doctor's consultations is responsible for half of all doctor's consultations due to cough. This finding may help to focus on certain subpopulations in whom interventions to reduce the number of doctor's consultations due to cough could be targeted, without compromising early diagnostics of life-threatening lung disorders. In the whole population, repetitive consultations were mainly associated with asthma and chronic rhinosinusitis. A more widespread understanding about the association of these disorders with cough and more efficient management of these disorders might effectively reduce the number of doctor's consultations due to cough. From the patient's point of view, the level of impairment in the cough-related quality of life and the prolongation of the cough episode increased the probability of repetitive consultations. Doctor's consultations due to cough could thus also be decreased by more effective clinical management of cough on the first consultation which would make repetitive consultations unnecessary. Awareness of the psychological nature of the patient's main concerns may help physicians to better understand the patient complaining of a cough.

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Authors' contributions

Dr Koskela has made substantial contributions to the conception and design of the work, the acquisition, analysis, and interpretation of data for the work, and drafting the work. He has mainly written the manuscript. He has provided the final approval of the version to be published and has consented 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. He was involved in the analysis and interpretation of the data; in the writing of the report; and in the decision to submit the paper for publication.

Dr Lätti has made substantial contributions to the conception and design of the work, the acquisition, analysis, and interpretation of data for the work, and drafting the manuscript. She has given her final approval of the version to be published and has provided an 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.

Dr Pekkanen has made substantial contributions to the conception and design of the work, and interpretation of data for the work, and drafting the manuscript. He has provided a final approval of the version to be published and has given his approval 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.

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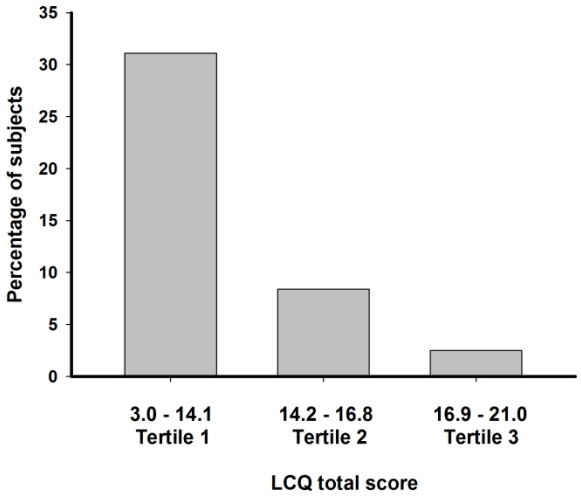

Percentage of subjects with repetitive (≥ 3 during 12 months) doctor's consultations due to cough in each Leicester Cough Questionnaire (LCQ) total score tertile. N = 975, subjects with current cough. Low LCQ total score indicates poor cough-related quality of life.

209x296mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 2	Title and abstract, design: A cross-sectional, email survey
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	See the abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	Thus, a more reasonable goal might be to decrease the number of repetitive consultations due to cough by the same individual. If we wish to plan interventions to achieve this goal, then it is important that the factors that are associated with repetitive consultations should be clarified.
Objectives	3	State specific objectives, including any prespecified hypotheses	4	If we wish to plan interventions to achieve this goal, then it is important that the factors that are associated with repetitive consultations should be clarified.
Methods				
Study design	4	Present key elements of study design early in the paper	4	This was a cross-sectional e-mail study conducted in all public service employees of two towns in central Finland

Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4	An invitation to the study and the questionnaire were sent to the employees' e-mail addresses in March - April 2017. Responses were collected via an electronic questionnaire
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4	This was a cross-sectional e-mail study among all public service employees of two towns in central Finland.
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5, 6	The main outcome was repetitive doctor's consultations due to cough. In the present study, 'repetitive consultations' was arbitrarily defined as at least three doctor's consultations due to cough in the past 12 months.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5	See the paragraph "Questionnaire".
Bias	9	Describe any efforts to address potential sources of bias	12	The participation rate to the survey was relatively low. It is possible that subjects with current cough were more interested to participate than

				those without. However, the responders and non-responders did not differ with respect to age and sex distribution.
Study size	10	Explain how the study size was arrived at	4, 7	This was a cross-sectional e-mail study among all public service employees of two towns in central Finland (altogether 13 980 employees, mean 46,6 years with 79.2 % females). The response rate was 26.4 % (3695 subjects, mean age 47.8 (47.5 – 48.2) years, 82.6 % females, 31.4 % ever-smokers, table 1).

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6	See the chapter 'statistical analysis'
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6	See the chapter 'statistical analysis'
		(*b*) Describe any methods used to examine subgroups and interactions		
		(*c*) Explain how missing data were addressed	7	The proportion of missing values was less than 1 % in all other questions except family income (2.5%) and acetylsalicylic acid intolerance (1.4 %).
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	6	See the chapter 'statistical analysis'
		(*e*) Describe any sensitivity analyses	5, 7	The main outcome was repetitive doctor's consultations due to cough. During the last 12 months, 22.5 % of the responders had consulted a doctor due to cough at least once, 11.2 % at least twice, 5.5 % at least three times, 2.7 % at least four times, and 1.4 % at least five times. See also the chapter 'statistical analysis'
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4, 7	This was a cross-sectional e-mail study among all public service employees of two towns in central Finland (altogether 13 980 employees, mean 46,6 years with 79.2 % females).

				The response rate was 26.4 % (3695 subjects, mean age 47.8 (47.5 – 48.2) years, 82.6 % females, 31.4 % ever-smokers, table 1).
		(b) Give reasons for non-participation at each stage	NA	
		(c) Consider use of a flow diagram	NA	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	7	The proportion of missing values was less than 1 % in all other questions except family income (2.5%) and acetylsalicylic acid intolerance (1.4 %). (2.5%) and acetylsalicylic acid intolerance (1.4 %).
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA	
		Cross-sectional study—Report numbers of outcome events or summary measures	7	Among the responders, there were 205 subjects (5.5 % of the responders) with repetitive doctor's visits due to cough.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables 1, 2, 3, 4, text page 6	The variables showing at least a suggestive ($p < 0.1$) association with repetitive consultations in the bivariate analyses were included in the multivariate analyses utilising binary logistic regression analysis with backward directed stepwise process to eliminate non-significant confounders.

	(*b*) Report category boundaries when continuous variables were categorized	6	The LCQ total scores (ts) were divided into tertiles. First tertile: 3.0 - 14.1, second tertile: 14.2 to 16.8, and third tertile: 16.9 to 21.0. The cough bout frequency was also divided into tertiles: First tertile: on 2 – 3 days per week or less often, second tertile: on 4 – 6 days per week to once daily, and third tertile: several times daily. The cough episode duration was categorized according to the current guidelines to < 3 weeks (acute cough), 3 – 8 weeks (subacute cough), and > 8 weeks (chronic cough).
	(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6	There were 975 subjects with current cough
Discussion				
Key results	18	Summarise key results with reference to study objectives	9	In the whole population, the list of factors behind repetitive visits resembled that of the common causes of chronic cough, predominated by current asthma and chronic rhinosinusitis. The analysis in the 975 subjects with current cough included more detailed information. Among them, the dominant factor behind repetitive doctor's visits was the severity of the impairment in the cough-related quality of life.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11	There are several shortcomings in the present study...
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11	
Generalisability	21	Discuss the generalisability (external validity) of the study results	9	The present population may not represent well the general population since elderly and unemployed subjects were missing.
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3	The study was funded by grants from Kuopion Hengityssäätiö and Hengityssairauksien Tutkimussäätiö foundations.

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The risk factors for repetitive doctor's consultations due to cough: A cross-sectional study in a Finnish employed population

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The risk factors for repetitive doctor's consultations due to cough: A cross-sectional study in a Finnish employed population

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ABSTRACT

Objectives: Cough is the most common symptom prompting people to consult a doctor, thus representing a huge cost to the health care. This burden could be reduced by decreasing the number of repetitive consultations by the same individuals. Therefore, it would be valuable to recognize the factors that associate with repetitive doctor's consultations due to cough.

Design: A cross-sectional, email survey

Setting: Public service employees in two Finnish towns

Participants: The questionnaire was sent to 13 980 subjects; 3695 (26.4 %) participated.

Interventions: The questionnaire sought detailed information about participant characteristics, all disorders diagnosed by a doctor, various symptoms, and doctor's consultations. Those with current cough were inquired about cough characteristics and filled in the Leicester Cough Questionnaire (LCQ).

Primary outcome: Repetitive (≥ 3) doctor's consultations due to cough during the previous 12 months.

Results: There were 205 participants (5.5 % of the participants) with repetitive consultations. They accounted for 848 out of the 1681 doctor's consultations (50.4 %) due to cough. Among all participants, repetitive consultations were mainly related to the presence of asthma (adjusted odds ratio (aOR) 2.90 (2.01–4.19)) and chronic rhinosinusitis (aOR 2.40 (1.74–3.32)). Among the 975 participants with current cough, repetitive consultations were mainly related to a low LCQ total score (aOR 3.84 (2.76–5.34) per tertile). Comorbidity, depressive symptoms, and smoking were also associated with repetitive consultations.

Conclusions: A modest proportion of subjects with repetitive consultations is responsible for every second doctor's consultation due to cough. The typical features of these subjects could be identified. These findings can help to focus on certain subpopulations in order to plan interventions to reduce the health care burden attributable to cough.

STRENGTHS AND LIMITATIONS OF THE STUDY

- The results are based on a large community-based sample of 3695 participants
- The study included a comprehensive list of possible risk factors for repetitive doctor's consultations due to cough
- All participants had equal and free-of-charge access to doctors, provided by the participating towns' occupational health care organisations. Therefore, supply-related factors do not interfere with the results.
- Only slightly over one in four (26.4 %) of the original population participated
- As all participants were public service employees, lower social classes and older individuals are underrepresented.

A FUNDING STATEMENT

The study was funded by grants from Kuopion Seudun Hengityssäätiö and Hengityssairauksien Tutkimussäätiö Foundations. They had no input in the development of the research or in the preparation of this manuscript.

A COMPETING INTERESTS STATEMENT

Dr. Koskela reports grants from Kuopion Seudun Hengityssäätiö Foundation, grants from Hengityssairauksien Tutkimussäätiö, during the conduct of the study; personal fees from Mundipharma Ltd, Orion Pharma Ltd, Oy, Eli Lilly Finland Ltd, Boehringer Ingelheim Finland Ltd as payments for giving scientific lectures in gatherings organized by medical companies, personal fees from Takeda Leiras Ltd, Boehringer Ingelheim Ltd, Mundipharma Ltd, and AstraZeneca Ltd, to attend international scientific meetings, in addition to owning shares in Orion Pharma Ltd worth 22 000 euros, outside the submitted work.

Dr. Lätti reports grants from Kuopion Seudun Hengityssäätiö Foundation, grants from Hengityssairauksien Tutkimussäätiö, during the conduct of the study; personal fees from Orion, Boehringer-Ingelheim, Roche to attend international scientific meetings, outside the submitted work.

Dr. Pekkanen has nothing to disclose.

DATA SHARING STATEMENT

De-identified participant data are available upon request from Heikki Koskela ORCID 0000-0002-3386-3262

INTRODUCTION

Cough is the most common symptom prompting individuals to seek medical help from a physician and thus it poses a major health care burden.[1, 2] In the United States, every year there are 21 million outpatient consultations due to cough.[2] Surprisingly, very little is known about the factors that prompt a visit to a doctor due to cough. At present, health care seeking behaviour in coughing patients has been mainly investigated in countries in which there is a high prevalence of tuberculosis, with the goal of improving tuberculosis diagnostics.[3-5] In countries with a low tuberculosis prevalence, the aims may be different. In view of the ageing of the populations in the developed world and the limited health care resources, it would be clearly advantageous if we were able to reduce the number of doctor's consultations due to cough. However, seeking medical help due to the appearance of recent-onset cough must not be discouraged because this would compromise early diagnostics of life-threatening lung disorders like lung cancer, tuberculosis and interstitial lung disorders. Thus, a more reasonable goal might be to decrease the number of repetitive consultations due to cough by the same individual. If we wish to plan interventions to achieve this goal, then it is important that the factors that are associated with repetitive consultations should be clarified. The present study was conducted to define the factors associated with repetitive doctor's consultations due to cough in a large population of subjects with equal and free-of-charge access to doctors provided by the participants' occupational health care organisations. The present study report is related to two previous publications, which described the risk factors for cough and the consequences of cough in this population.[6, 7]

METHODS

Population

This was a cross-sectional e-mail study conducted in all public service employees of two towns in central Finland (altogether 13 980 employees, mean 46.6 years with 79.2 % females). All participants had free-of-charge access to doctors, provided by the participating towns' occupational health care organisations. An invitation to the study and the questionnaire were sent to the employees' e-mail addresses in March - April 2017. Responses were collected via an electronic questionnaire. One reminder message was sent if a subject had not responded within two weeks. The study was approved by the Ethics Committee of Kuopio University Hospital (289/2015). Permission to conduct the study was obtained from the officials of both towns. The invitation letter to participate included detailed information about the study. A participant's decision to reply was considered as informed consent.

Questionnaire

The first part of the questionnaire (57 questions) was filled in by all participants. All disorders diagnosed by a doctor were inquired, as well as a wide variety of symptoms. Asthma-, rhinosinusitis- and reflux-related symptoms were inquired by questions currently recommended for epidemiologic studies.[8-10] Depressive symptoms were inquired by utilising the Patient Health Questionnaire-2 (PHQ-2).[11] The number of doctor's consultations due to cough during the previous 12 months was inquired from all participants. The second part of the questionnaire consisted of 23 cough-related questions to be answered by those participants reporting that they had current cough. It included detailed questions about the cough bout frequency and cough duration, as well as the Leicester Cough Questionnaire (LCQ), which measures the cough-related quality of life.[12] Many questions were adapted from two previous studies, the Health Behaviour and Health among the Finnish Adult Population study [13] and the Finnish National FINRISK study.[14]

Definitions

The main outcome was repetitive doctor's consultations due to cough. During the last 12 months, 22.5 % of the responders had consulted a doctor due to cough at least once, 11.2 % at least twice, 5.5 % at least three times, 2.7 % at least four times, and 1.4 % at least five times. In the present study, 'repetitive consultations' was arbitrarily defined as at least three doctor's consultations due to cough in the past 12 months.

Current cough was defined as ongoing cough at the time when the survey was conducted. Chronic bronchitis was defined as daily sputum production for at least three months of the year. A cough trigger was defined as the presence of one or more identifiable cough triggers. Current asthma was defined as a doctor's diagnosis of asthma at any age and wheezing during the last 12 months. Chronic rhinosinusitis was present if there was 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.[9] Esophageal reflux disease was present if there had been heartburn and/or regurgitation on at least one day of the week during the last three months.[10] Depressive symptoms were present if the PHQ-2 score was three or more.[11] Allergy was defined as a self-reported allergy to pollens, animals or food. A family history of chronic cough was defined as the presence (now or in the past) of chronic (duration more than eight weeks) cough in parents, sisters or brothers. The disorder sum was defined as the number of medical disorders diagnosed by a doctor. The symptom sum was defined as the sum of symptoms (other than respiratory symptoms) reported by the participants.

Patient involvement

Patients were not directly involved in the design, recruitment, or in the conduct of this study. The results will be disseminated to study participants through the Kuopio town and Jyväskylä towns' intranet portals.

Statistical analysis

The descriptive data is shown as means and 95 % confidence intervals (CI) unless otherwise stated. In the participants with current cough, the LCQ total scores (ts) were divided into tertiles. First tertile: 3.0 - 14.1, second tertile: 14.2 to 16.8, and third tertile: 16.9 to 21.0. The cough bout frequency was also divided into tertiles: First tertile: on 2 – 3 days per week or less often, second tertile: on 4 – 6 days per week to once daily, and third tertile: several times daily. The cough episode duration was categorized according to the current guidelines to < 3 weeks (acute cough), 3 – 8 weeks (subacute cough), and > 8 weeks (chronic cough).[15, 16]

The bivariate associations of the following variables with repetitive consultations were analysed: Current asthma, chronic rhinosinusitis, esophageal reflux disease, depressive symptoms, disorder sum, symptom sum, acetylsalicylic acid intolerance, allergy, age, gender, body mass index, years of education, family incomes, professional status, number of family members, pet ownership, moisture damage exposure, smoking history, weekly alcohol doses, level of daily physical exercise, and family history of chronic cough. In addition to these factors, the following variables were included in the analyses among the 975 participants with current cough: Duration of the current cough episode, current cough bout frequency, LCQ total score (LCQts), chronic bronchitis, and cough trigger.

Mann-Whitney test and chi-square test were applied when appropriate. The variables showing at least a suggestive ($p < 0.1$) association with repetitive consultations in the bivariate analyses were included in the multivariate analyses utilising binary logistic regression analysis with backward directed stepwise process to eliminate non-significant confounders. However, only LCQts was included without its domains due to the presence of strong interrelationships.

A p value less than 0.05 was accepted as the level of statistical significance but in the tables, all factors with at least a suggestive association ($p < 0.1$) are presented. All analyses were performed using SPSS version 22 for the personal computer (SPSS, Inc. Chicago, Illinois, USA).

RESULTS

The response rate was 26.4 % (3695 participants, mean age 47.8 (47.5 – 48.2) years, 82.6 % females, 31.4 % ever-smokers, table 1). The proportion of missing values was less than 1 % in all other questions except for family income (2.5%) and acetylsalicylic acid intolerance (1.4 %).

Table 1. The basic characteristics and their bivariate associations with repetitive (≥ 3 during the last 12 months) doctor's consultations due to cough in all participants (N = 3695). The figures are percentages or means and 95 % confidence intervals.

Characteristic	**Participants without repetitive doctor's consultations due to cough N = 3490**	**Participants with repetitive doctor's consultations due to cough N = 205**	**P value**
Female gender, %	82.5	85.3	0.30
Age (years)	47.8 (47.4 – 48.2)	48.5 (47.1 – 50.0)	0.35
Body mass index (kg/m^2)	26.5 (26.4 – 26.7)	27.9 (27.0 – 28.7)	< 0.001
Family incomes, income class [a]	1.98 (1.95 – 2.00)	2.06 (1.95 – 2.16)	0.17
Moisture damage exposure, %	25.4	33.7	0.009
Ever smoking, %	31.3	33.2	0.57
Family history of chronic cough, %	34.7	51.0	< 0.001
Acetylsalicylic acid intolerance, %	4.6	9.4	0.002
Allergy, %	17.4	27.8	< 0.001
Depressive symptoms, %	4.9	9.4	0.004
Symptom sum	2.55 (2.48 – 2.62)	3.56 (3.24 – 3.88)	< 0.001
Disorder sum	1.08 (1.04 – 1.13)	2.31 (2.08 – 2.55)	< 0.001
Current asthma, %	8.7	36.6	< 0.001
Chronic rhinosinusitis, %	14.2	40.5	< 0.001
Esophageal reflux disease, %	12.1	21.0	< 0.001

[a] Income classes: 1 = less than 15 000 e/year; 2 = 15 000- 40 000 e; 3 = 40 000 – 70 000 e; 4 = 70 000 – 120 000 e; 5 = over 120 000 e/year. Other definitions, se text.

Among all 3695 responders, there were 205 participants who reported repetitive doctor's consultations due to cough (5.5 %). They accounted for 848 out of the 1681 doctor's consultations due to cough (50.4 %) during the previous 12 months.

There were 975 participants with current cough (mean age 48.7 (48.0 – 49.3) years, 83.8 % females, 31.4 % ever-smokers). Among them, there were 135 participants (13.8 % of the participants with current cough) with repetitive doctor's consultations due to cough. They accounted for 573 out of the 926 doctor's consultations due to cough (61.9 %) among the participants with a current cough.

In addition to the other baseline characteristics, table 1 shows all variables for which there was at least a suggestive association with repetitive consultations in bivariate analyses among all 3695 responders. Table 2 shows the results of the multivariate analyses in these individuals. The most important factors were the presence of current asthma and chronic rhinosinusitis. Table 3 shows the results of the bivariate analyses among the 975 participants with current cough and table 4 displays the results of the multivariate analysis in these individuals. Among the participants with current cough, the LCQts was the most important determinant of repetitive doctor's consultations. The proportions of participants with repetitive doctor's consultations due to cough within each LCQts tertile are illustrated in figure 1.

Table 2. The characteristics that associated with repetitive (≥ 3 during the last 12 months) doctor's consultations due to cough in all partcipants (3695 subjects). Multivariate analysis with adjusted odds ratios (aOR) and confidence intervals (CI).

Characteristic	**aOR (95 % CI)**	**P value**
Current asthma	2.90 (2.01 – 4.19)	< 0.001
Chronic rhinosinusitis	2.40 (1.74 – 3.32)	< 0.001
Disorder sum [a]	1.33 (1.20 – 1.47)	< 0.001
Depressive symptoms [b]	1.72 (1.01 – 2.92)	0.046
Family history of chronic cough	1.38 (1.02 – 1.87)	0.039

[a] aOR calculated for every doctor's diagnosed disorder. [b] Patient Health Questionnaire-2 score three or more

Table 3. The basic characteristics and their bivariate associations with repetitive (≥ 3 during the last 12 months) doctor's consultations due to cough among the participants with current cough (N = 975). The figures are percentages or means and 95 % confidence intervals unless otherwise stated.

Characteristic	**Participants without repetitive doctor's consultations due to cough. N = 840**	**Participants with repetitive doctor's consultations due to cough. N = 135**	**P value**
Female gender, %	83.9	83.6	0.93
Age (years)	48.5 (47.8 – 49.2)	49.6 (47.8 – 51.3)	0.40
Body mass index (kg/m^2)	27.1 (26.8 – 27.5)	27.7 (26.8 – 28.7)	0.18
Family incomes, income class [a]	2.03 (1.98 – 2.08)	2.04 (1.90 – 2.17)	0.89
Moisture damage exposure, %	32.5	38.5	0.17
Ever smoking, %	30.4	37.8	0.085
Family history of chronic cough, %	46.3	53.0	0.15
Acetylsalicylic acid intolerance, %	5.4	9.8	0.049
Allergy, %	23.8	26.7	0.47
Depressive symptoms, %	5.4	6.7	0.56
Symptom sum	3.18 (3.03 – 3.32)	3.69 (3.28 – 4.10)	0.017
Disorder sum	1.50 (1.40 – 1.60)	2.33 (2.04 – 2.62)	< 0.001
Chronic bronchitis, %	32.5	56.7	< 0.001
Current asthma, %	16.1	40.0	< 0.001
Chronic rhinosinusitis, %	26.5	45.9	< 0.001
Esophageal reflux disease, %	16.5	23.0	0.068
Cough trigger, %	73.6	88.9	< 0.001
Duration of the cough episode (median, range)	3 – 8 weeks (some days-over 10 yrs)	2 – 12 months (some days-over 10 yrs)	< 0.001
Cough bout frequency (median, range)	Daily (less than weekly – several times a day)	Several times a day (less than weekly – several times a day)	< 0.001
LCQ total score	15.7 (15.5 – 15.9)	12.3 (11.8 – 12.8)	< 0.001
LCQ physical domain	5.06 (5.00 – 5.12)	4.08 (3.92 – 4.23)	< 0.001
LCQ psychological domain	5.18 (5.10 – 5.25)	3.96 (3.78 – 4.13)	< 0.001
LCQ social domain	5.45 (5.38 – 5.53)	4.25 (4.05 – 4.44)	< 0.001
Number of doctor's consultations due to cough during the last 12 months (median, range)	0 (0 – 2)	3 (3 – 20)	< 0.001

[a] Income classes: 1 = less than 15 000 e/year; 2 = 15 000- 40 000 e; 3 = 40 000 – 70 000 e; 4 = 70 000 – 120 000 e; 5 = over 120 000 e/year. Other definitions, se text.

Table 4. The characteristics that associated with repetitive (≥ 3 during the last 12 months) doctor's consultations due to cough among 975 participants with current cough. Multivariate analysis with adjusted odds ratios (aOR) and confidence intervals (CI).

Characteristic	**aOR (95 % CI)**	**P value**
LCQ total score [a]	3.84 (2.76 – 5.34)	< 0.001
Current asthma	1.85 (1.16 – 2.94)	0.010
Duration of cough episode [b]	1.50 (1.17 – 1.93)	0.001
Smoking ever	1.50 (0.98 – 2.29)	0.059
Disorder sum [c]	1.13 (0.99 – 1.29)	0.061

[a] aOR calculated per one less LCQ total score tertile. [b] aOR calculated per one duration step (< 3 weeks, 3 – 8 weeks, > 8 weeks). [c] aOR calculated for every doctor's diagnosed disorder

The associations of each of the nineteen LCQ questions with repetitive doctor's consultations were analysed and ranked according to the Mann-Whitney test z-score. The five questions with the closest associations are presented in table 5. Most of these belonged to the psychological domain of the LCQ.

Table 5. The five Leicester cough questionnaire (LCQ) questions, which showed the closest associations with repetitive (≥ 3 during the last 12 months) doctor's consultations among participants with current cough (N = 975), according to the Mann-Whitney test z score. The question with the strongest association is uppermost. Domain indicates the LCQ domain (psy = psychological, phy = physical, soc = social). The scale in each question is 1 – 7 with a lower value indicating more severe impairment. The figures are means and 95 % confidence intervals. $p < 0.001$ between the subgroups in all presented questions.

Question	LCQ question number, domain	Participants without repetitive doctor's consultations due to cough. N = 840	Participants with repetitive doctor's consultations due to cough. N = 135	Z score
In the last 2 weeks, my cough has made me feel anxious.	LCQ 6, psy	5.37 (5.28 – 5.46)	3.83 (3.60 – 4.06)	-11.2
In the last 2 weeks, have you worried that your cough may indicate a serious illness?	LCQ 16, psy	5.70 (5.61 – 5.79)	4.34 (4.10 – 4.57)	-10.3
In the last 2 weeks, my cough has made me feel fed up.	LCQ 13, psy	4.49 (4.37 – 4.61)	2.88 (2.62 – 3.14)	-9.5
In the last 2 weeks, have you been tired because of your cough?	LCQ 3, phy	5.29 (5.19 – 5.39)	3.99 (3.76 – 4.23)	-9.3
In the last 2 weeks, have you been concerned that other people think something is wrong with you, because of your cough?	LCQ 17, psy	5.91 (5.83 – 6.00)	4.70 (4.45 – 4.96)	-9.2

DISCUSSION

The present study in an employed, working-age population revealed that a modest proportion (5.5 %) of participants with repetitive doctor's consultations was responsible for about every second consultation to the doctor because of cough. In the entire population, the list of factors underpinning the repetitive consultations resembled that of the common causes of chronic cough[15, 16] i.e. it was predominated by current asthma and chronic rhinosinusitis. The analysis

among the 975 participants with current cough included more detailed information about the characteristics of their cough. In this analysis, the dominant factor behind the repetitive consultations was the severity of the impairment in the cough-related quality of life.

It is well known that a small proportion of individuals account for the majority of health care utilisation and spending. Most of the studies about these “high cost users” have concentrated on the most expensive forms of health care, such as inpatient care, emergency consultations, and operations, and have not been concerned with primary care consultations.[17-20] These “high cost users” are often found to be elderly, have a low socio-economic status, and suffer from several comorbid illnesses including mental illnesses or addictions. Accordingly, in the present population, it was found that the number of comorbid illnesses, the presence of depressive symptoms and smoking were associated with repetitive consultations. However, age did not show an independent association. This discrepancy may be attributable to the homogeneous nature of our study population i.e. all participants were of working-age. Nonetheless, most of the known characteristics of “high cost users” could be taken into account in the present analyses.

The present population may not represent well the general population since elderly and unemployed subjects were missing. However, this study has one feature, which makes it especially enlightening: All participants had equal and free-of-charge access to doctors, provided by the participating towns’ occupational health care organisations. Apart from need-related factors, health care utilisation is also supply-dependent; this is associated with the nature of the health care system.[21] In the present study, supply-related factors did not influence the results as all the respondents could obtain medical help from their occupational health care centre.

Asthma and chronic rhinosinusitis are important background diseases of chronic cough [15, 16] and therefore it is not surprising that they were clearly associated with repetitive doctor’s consultations in the entire population. It may be fair to say that three or more yearly consultations due to cough by a patient with chronic rhinosinusitis or asthma indicates that there is inadequate control of these disorders. A better understanding of the association of these disorders with cough as well as their more efficient management might effectively decrease the number of doctor’s consultations due to cough. Esophageal reflux disease was not associated with repetitive consultations though it is also considered as an important background disease to chronic cough.[15, 16] We have previously reported that for some reason in our study population, esophageal reflux disease is much less clearly associated with chronic cough than asthma and chronic rhinosinusitis.[6] In the present study, the diagnoses of chronic rhinosinusitis and esophageal reflux disease relied purely on self-reported

symptoms, a factor which must be borne in mind when considering the associations of these disorders with repetitive doctor's consultations.

The analysis among participants with current cough included much more information than the analysis gathered from the entire population. Therefore, different factors were evident. Among these participants, the major factor behind repetitive doctor's consultations due to cough seems to be the level of impairment in the cough-related quality of life. Patients with cough are often dissatisfied with the therapy prescribed by physicians, which may lead to another consultation as the cough continues.[22] It is noteworthy that the length of the cough episode was also associated with repetitive doctor's consultations. Therefore, repetitive doctor's consultations due to cough could be decreased by more effective clinical management of cough on the first consultation which would make repetitive consultations unnecessary. Further education of general practitioners may be needed to achieve this goal. However, new, effective medications for the long-standing hypersensitivity of the cough reflex arch are also urgently needed.[23]

The quality of life was measured by the LCQ and the LCQts were divided into tertiles. Given that the present 975 participants with current cough represent an unselected, community-based population, we suggest that the first tertile (3.0 - 14.1) represents severe cough, the second tertile (14.2 – 16.8) represents individuals with moderate cough and those in the third tertile (16.9 – 21) have mild cough. The respective proportions of participants with repetitive doctor's consultations were 31 %, 8 % and 2 %, highlighting the dominant role of the quality of life impairment. Though LCQ is a well validated questionnaire,[12] we are unaware of any previous attempts to grade it in a clinically meaningful way. The grading of LCQts utilized here may have several applications in everyday clinical cough management as well as in epidemiologic studies. It could also be applied to create meaningful inclusion criteria for clinical drug trials.

LCQ is a very comprehensive questionnaire with nineteen questions covering multiple characteristics of cough. Interestingly, the most important questions with respect to repetitive consultations belonged to the psychological domain. It seems that the crucial factor leading to the decision to seek medical attention is not the symptom per se but the feelings that the symptom induces. This finding suggests that the patient's concerns may differ significantly from those of the doctor. The latter may be more interested if there are serious symptoms, like haemoptysis, or if there are symptoms suggestive of possible background diseases behind the cough, like wheezing or regurgitation.

There are several shortcomings in the present study. As mentioned, the population may not represent well the general population because elderly and unemployed subjects were missing. In

addition, the majority of the participants were female. These facts decrease the applicability of the data to the general population. The participation rate to the survey was relatively low. However, the responders and non-responders did not differ with respect to age and sex distribution. Furthermore, it is unlikely that the low response rate could affect the associations of various features with repetitive doctor's consultations. The authors did not have access to individual patient files, for example to investigate physician-patient relationships, the accuracy of diagnoses, or treatment details. The information gained is based on self-reports in a cross-sectional design with the associated problems of recall bias, biased reporting and the lack of any possibility to separate associations from causality.

In conclusion, a modest proportion of subjects with repetitive doctor's consultations is responsible for half of all doctor's consultations due to cough. This finding may help to focus on certain subpopulations in whom interventions to reduce the number of doctor's consultations due to cough could be targeted, without compromising early diagnostics of life-threatening lung disorders. In the whole population, repetitive consultations were mainly associated with asthma and chronic rhinosinusitis. A more widespread understanding about the association of these disorders with cough and more efficient management of these disorders might effectively reduce the number of doctor's consultations due to cough. From the patient's point of view, the level of impairment in the cough-related quality of life and the prolongation of the cough episode increased the probability of repetitive consultations. Doctor's consultations due to cough could thus also be decreased by more effective clinical management of cough on the first consultation which would make repetitive consultations unnecessary. Awareness of the psychological nature of the patient's main concerns may help physicians to better understand the patient complaining of a cough.

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Authors' contributions

Dr Koskela has made substantial contributions to the conception and design of the work, the acquisition, analysis, and interpretation of data for the work, and drafting the work. He has mainly written the manuscript. He has provided the final approval of the version to be published and has consented 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. He was involved in the analysis and interpretation of the data; in the writing of the report; and in the decision to submit the paper for publication.

Dr Lätti has made substantial contributions to the conception and design of the work, the acquisition, analysis, and interpretation of data for the work, and drafting the manuscript. She has given her final approval of the version to be published and has provided an 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.

Dr Pekkanen has made substantial contributions to the conception and design of the work, and interpretation of data for the work, and drafting the manuscript. He has provided a final approval of the version to be published and has given his approval 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.

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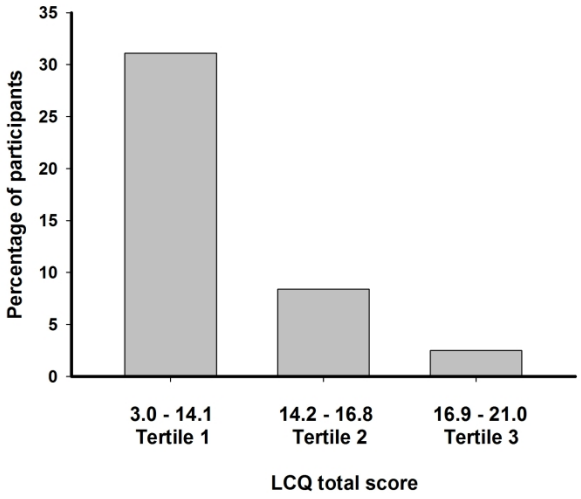
FIGURE LEGENDS

Figure 1. Percentage of participants with repetitive (≥ 3 during 12 months) doctor's consultations due to cough in each Leicester Cough Questionnaire (LCQ) total score tertile. N = 975, participants with current cough. Low LCQ total score indicates poor cough-related quality of life.



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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 2	Title and abstract, design: A cross-sectional, email survey
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	See the abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	Thus, a more reasonable goal might be to decrease the number of repetitive consultations due to cough by the same individual. If we wish to plan interventions to achieve this goal, then it is important that the factors that are associated with repetitive consultations should be clarified.
Objectives	3	State specific objectives, including any prespecified hypotheses	4	If we wish to plan interventions to achieve this goal, then it is important that the factors that are associated with repetitive consultations should be clarified.
Methods				
Study design	4	Present key elements of study design early in the paper	4	This was a cross-sectional e-mail study conducted in all public service employees of two towns in central Finland

Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4	An invitation to the study and the questionnaire were sent to the employees' e-mail addresses in March - April 2017. Responses were collected via an electronic questionnaire
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4	This was a cross-sectional e-mail study among all public service employees of two towns in central Finland.
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5, 6	The main outcome was repetitive doctor's consultations due to cough. In the present study, 'repetitive consultations' was arbitrarily defined as at least three doctor's consultations due to cough in the past 12 months.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5	See the paragraph "Questionnaire".
Bias	9	Describe any efforts to address potential sources of bias	12	The participation rate to the survey was relatively low. It is possible that subjects with current cough were more interested to participate than

				those without. However, the responders and non-responders did not differ with respect to age and sex distribution.
Study size	10	Explain how the study size was arrived at	4, 7	This was a cross-sectional e-mail study among all public service employees of two towns in central Finland (altogether 13 980 employees, mean 46,6 years with 79.2 % females). The response rate was 26.4 % (3695 subjects, mean age 47.8 (47.5 – 48.2) years, 82.6 % females, 31.4 % ever-smokers, table 1).

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6	See the chapter 'statistical analysis'
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6	See the chapter 'statistical analysis'
		(*b*) Describe any methods used to examine subgroups and interactions		
		(*c*) Explain how missing data were addressed	7	The proportion of missing values was less than 1 % in all other questions except family income (2.5%) and acetylsalicylic acid intolerance (1.4 %).
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	6	See the chapter 'statistical analysis'
		(*e*) Describe any sensitivity analyses	5, 7	The main outcome was repetitive doctor's consultations due to cough. During the last 12 months, 22.5 % of the responders had consulted a doctor due to cough at least once, 11.2 % at least twice, 5.5 % at least three times, 2.7 % at least four times, and 1.4 % at least five times. See also the chapter 'statistical analysis'
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4, 7	This was a cross-sectional e-mail study among all public service employees of two towns in central Finland (altogether 13 980 employees, mean 46,6 years with 79.2 % females).

				The response rate was 26.4 % (3695 subjects, mean age 47.8 (47.5 – 48.2) years, 82.6 % females, 31.4 % ever-smokers, table 1).
		(b) Give reasons for non-participation at each stage	NA	
		(c) Consider use of a flow diagram	NA	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	7	The proportion of missing values was less than 1 % in all other questions except family income (2.5%) and acetylsalicylic acid intolerance (1.4 %). (2.5%) and acetylsalicylic acid intolerance (1.4 %).
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA	
		Cross-sectional study—Report numbers of outcome events or summary measures	7	Among the responders, there were 205 subjects (5.5 % of the responders) with repetitive doctor's visits due to cough.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables 1, 2, 3, 4, text page 6	The variables showing at least a suggestive ($p < 0.1$) association with repetitive consultations in the bivariate analyses were included in the multivariate analyses utilising binary logistic regression analysis with backward directed stepwise process to eliminate non-significant confounders.

	(*b*) Report category boundaries when continuous variables were categorized	6	The LCQ total scores (ts) were divided into tertiles. First tertile: 3.0 - 14.1, second tertile: 14.2 to 16.8, and third tertile: 16.9 to 21.0. The cough bout frequency was also divided into tertiles: First tertile: on 2 – 3 days per week or less often, second tertile: on 4 – 6 days per week to once daily, and third tertile: several times daily. The cough episode duration was categorized according to the current guidelines to < 3 weeks (acute cough), 3 – 8 weeks (subacute cough), and > 8 weeks (chronic cough).
	(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6	There were 975 subjects with current cough
Discussion				
Key results	18	Summarise key results with reference to study objectives	9	In the whole population, the list of factors behind repetitive visits resembled that of the common causes of chronic cough, predominated by current asthma and chronic rhinosinusitis. The analysis in the 975 subjects with current cough included more detailed information. Among them, the dominant factor behind repetitive doctor's visits was the severity of the impairment in the cough-related quality of life.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11	There are several shortcomings in the present study...
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11	
Generalisability	21	Discuss the generalisability (external validity) of the study results	9	The present population may not represent well the general population since elderly and unemployed subjects were missing.
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3	The study was funded by grants from Kuopion Hengityssäätiö and Hengityssairauksien Tutkimussäätiö foundations.

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.