

# Chronic cough and QoL in allergic and respiratory diseases measured by a new specific validated tool-CCIQ

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## Summary.

Even though chronic cough (CC) is a bothersome symptom, only a small number of studies have evaluated its specific burden on health-related quality of life (HRQL). The aim of the present study was to assess how the presence of CC interferes with HRQL.

A total of 95 outpatients were enrolled during medical consultation at our “Chronic Cough Center”. A health status measure (SF-36) and a new HRQL questionnaire specific for CC (CCIQ) were administered before the initial visit. Compared to the reference sample, CC patients reported significantly lower scores in 5 of 8 SF-36 domains: Social functioning ( $t=10.292$ ), Physical role limitation ( $t=9.667$ ), Emotional role limitation ( $t=7.712$ ), General health ( $t=5.154$ ) and Vitality ( $t=4.426$ ). The analysis of CCIQ scores showed a disability due to CC, independent of its etiology. The greatest disabilities were observed in the Social relationship (58.33) domain, followed by Sleep/Concentration (54.26), Mood (51.49) and Daily activities (47.69). Sleep, disturbing the partner, and irritability were the three outstanding aspects, affecting 80% of patients.

These results show that CC has a high negative impact on HRQL, and they further suggest that the CCIQ is a useful tool for obtaining a global evaluation including its impact and therapeutic options.

**Keywords:** Chronic cough, quality of life, specific questionnaire.

**Resumen.** A pesar de que la tos crónica (TC) es un síntoma molesto, tan sólo un número reducido de estudios han evaluado su carga específica en la calidad de vida relacionada con la salud (CVRS). El objetivo del presente estudio fue evaluar en qué medida la presencia de TC interfiere en la CVRS.

Se reclutaron un total de 95 pacientes ambulatorios durante la consulta médica en nuestro “Centro de Tos Crónica”. Antes de la visita inicial se suministraron un cuestionario de salud (SF-36) y un nuevo cuestionario de CVRS específico para la TC (CCIQ).

En comparación con la muestra de referencia, los pacientes con TC notificaron puntuaciones significativamente más bajas en 5 de 8 áreas del cuestionario SF-36: funcionamiento social ( $t = 10,292$ ), limitación de tipo físico ( $t = 9,667$ ), limitación de tipo emocional ( $t = 7,712$ ), estado de salud general ( $t = 5,154$ ) y vitalidad ( $t = 4,426$ ). El análisis de las puntuaciones del cuestionario CCIQ mostró una reducción de la calidad de vida para la TC, independientemente de su etiología. Las peores puntuaciones se observaron en el área de las relaciones sociales (58,33) seguido de sueño/concentración (54,26), humor (51,49) y actividades cotidianas (47,69). El sueño, las molestias para la pareja y la irritabilidad fueron los tres aspectos más alterados, afectando a un 80% de los pacientes. Estos resultados muestran que la TC tiene un gran impacto negativo sobre la CVRS, y también indican que el cuestionario CCIQ es una herramienta útil para obtener una evaluación global, incluidos el impacto y las opciones terapéuticas.

**Palabras clave:** tos crónica, calidad de vida, cuestionario específico.

## Introduction

Coughing is a protective reflex and can signal a wide variety of pulmonary and extra-pulmonary diseases. It is the main symptom in respiratory diseases and is one of the most frequent reasons for which patients consult a medical practitioner. In the vast majority of cases (84-98%), it is possible to identify its etiology [1]. Therefore, specific therapy can be undertaken in most cases. Symptomatic treatment is sometimes necessary in idiopathic cough, when the cause cannot be resolved (i.e., cancer), or when the causal treatment cannot suppress symptoms [1-3].

More than 100 causes of chronic cough are recognized to date, although only very limited data are available regarding its impact on health-related quality of life (HRQL) as related to the burden of the illness and its therapy as perceived by the patient [4-9]. The HRQL, along with biomedical parameters, is now accepted as an important outcome measure to achieve a more global approach to management of chronic diseases. The aim of the present study was to assess the impact of CC on patient life, independently of the health status level. For this purpose we adopted a widely used health status measure (SF-36) [10] along with the Chronic Cough Impact Questionnaire (CCIQ) [11], a new specific questionnaire that has been recently validated in accordance with published guidelines [12].

## Material and methods

The present data were collected during validation of the CCIQ [11]. In particular, 95 consecutive outpatients referring to the Chronic Cough Center of the Allergy & Respiratory Diseases Department at the University of Genoa (Italy) were recruited for the study. Each patient underwent clinical and instrumental evaluation according to the guidelines established by the American College of Chest Physicians for CC [1]. After obtaining informed consent for participation in the study, before the first visit patients were asked to fill out two questionnaires, namely the generic SF-36 [10] and the specific Chronic Cough Impact Questionnaire (CCIQ) [11].

SF-36 is a generic, widely used questionnaire that has also been validated for asthma [13], chronic obstructive pulmonary disease (COPD) [14] and gastroesophageal reflux disease (GERD) [15]. It is composed of 36 items corresponding to 8 domains: Physical function, Role limitation (physical), Bodily pain, General health, Vitality, Social function, Role limitation (emotional), and Mental health. An additional question also investigated self-evaluated changes in health status. Moreover, the SF-36 provides two composite scores, namely the Physical (PCS) and Mental (MCS) component summaries, which compute the physical and mental aggregate scores. A higher score indicates better health status in a 0-100 scale [16].

The CCIQ is a new specific questionnaire developed to measure the specific impact of CC on HRQL. It has

recently been validated in the Italian population. Specifically, the CCIQ met the following standards for validity:

- construct validity: factor analysis revealed a four-dimensional structure, which explained up to 63.06% of total variance; this solution was deemed appropriate on the basis of eigenvalues;
- internal consistency: Chronbach's alpha coefficient showed highly satisfactory levels of internal consistency for sleep/concentration (79.98) and relationship (86.98), and acceptable levels for daily life impact (69.04) and mood (65.41);
- reliability: the Pearson coefficient ranged between 0.67 and 0.88, showing good reliability;
- responsiveness: the ability of the questionnaire to detect significant differences over time in patients whose status has changed has been demonstrated (in a group of 25 patients evaluated before and after treatment, statistically significant differences were recorded in 13 of 16 items, suggesting that the questionnaire is responsive to expected changes in severity of symptoms).

The CCIQ is composed of 16 items divided into 4 areas (Sleep/Concentration, Social Relationship, Mood and Daily Life Impact). Patients indicate on a five-point Likert scale (*not at all/a little/enough/much/very much*) [17] how much they have been troubled by cough during the past two weeks. Numeric values for responses to the CCIQ items are converted to 0-100 point scores, with 100 reflecting the worse health related quality of life. The CCIQ has been shown to be a valid tool for specific assessment of chronic cough and for quantifying the burden of this symptom on QoL [11].

SF-36 domain scores of patients with CC were compared to those of published reference values in 2031 healthy subjects used as controls by an unpaired t-test. Thus, health status was assessed according to the etiology of cough. The specific impact of CC was evaluated by analyzing the CCIQ domain scores and the relative burden of each item. The relationship between CCIQ and SF-36 was evaluated by Pearson correlation coefficients. A statistically significant cut-off value was set at  $p < 0.05$ . All statistical analyses were carried out with the SPSS12.0 statistical package.

*Table 1.* Characteristics of the population under study.

		n (%)
Gender	Male	42 (44)
	Female	53 (56)
Age, years mean (SD)	53.7 ± 11.7	
Disease	Asthma	32 (33.68)
	GERD	27 (28.42)
	PNDS	17 (17.89)
	COPD	19 (20)
Smoking	Current smokers	41 (43.16)
	Ex-smokers	23 (24.21)
	Never smokers	31 (32.63)
Duration of cough, months [mean (SD)]	25.81 (31.71)	

Table 2. Percentage of patient responses on the five-point Likert scale.

Item	Not at all	A little	Enough	Much	Very Much
<b>Daily Life Impact</b>					
Work	13	19	43	20	5
Physical activities	11	23	34	22	10
Spare time	6	32	41	16	5
Social life	6	27	37	26	3
<b>Sleep/Concentration</b>					
Night sleep	2	16	35	28	19
Do you have difficulties in falling asleep?	9	21	37	28	5
Do you wake up during the night?	2	11	28	40	19
Do you feel tired during the day because of your bad night's sleep?	4	33	37	20	6
Do you have difficulties in concentrating?	11	24	44	18	3
<b>Mood</b>					
Do you feel nervous?	3	15	45	25	12
Do you feel in a bad mood?	17	31	26	19	7
Do you feel anxious about your health conditions?	3	24	36	22	15
<b>Social Relationship</b>					
Are you afraid of annoying your partner?	4	13	29	34	19
Are you afraid of annoying your family?	7	16	27	32	18
Are you afraid of annoying your friends?	7	13	36	26	18

## Results

The study population was composed of 42 females and 53 males with a mean age of  $53.7 \pm 11.7$  years (range 23-86 years), with cough lasting 25 months on average; 43% were smokers and 24% were former smokers (Table 1). The etiology of cough was asthma (33.7%), GERD (28.4%), post-nasal drip syndrome (PNDS) (17.9%) and COPD (20%).

## SF-36 analysis

Compared to the reference population, CC patients reported significantly lower scores in 5 of 8 domains: social functioning ( $t=10.292$ ), physical role limitation ( $t=9.667$ ), emotional role limitation ( $t=7.712$ ), general health ( $t=5.154$ ) and vitality ( $t=4.426$ ). After diagnosis, we noticed a significant difference ( $p<0.05$ ) between

Table 3. Items listed according to the percentage of patients who reported an impact (answers: «Enough», «Much» or «very much»).

Item	Domain	(%)
Night sleep	Sleep/Concentration	82
Are you afraid of annoying your partner?	Social Relationship	82
Do you feel nervous?	Mood	82
Do you wake up during the night	Sleep/Concentration	80
Are you afraid of annoying your friends?	Social Relationship	80
Are you afraid of annoying your family?	Social Relationship	77
Do you feel anxious about your health conditions?	Mood	73
Do you have difficulties in falling asleep?	Sleep/Concentration	70
Work	Daily Life impact	68
Physical activities	Daily Life impact	66
Social life	Daily Life impact	66
Do you have difficulties in concentrating?	Sleep/Concentration	65
Do you feel tired during the day because of a bad night of sleep?	Sleep/Concentration	63
Spare time	Daily Life impact	62
Do you feel in a bad mood?	Mood	52

Table 4. Correlations between SF-36 domains and CCIQ factors.

	Sleep/ Concentration	Social Relationship Impact	Daily Life Impact	Mood
Physical Functioning	.072	-.048	.281*	-.055
Role Physical	.122	.067	.134	-.047
Bodily Pain	.141	.036	.367*	.010
General Health	.157	.191	.183	.041
Vitality	.027	.044	.291*	.061
Social Functioning	-.009	-.002	-.008	-.220
Emotional Role	.103	.117	.067	-.113
Mental Health	.124	.151	.094	-.039
Physical Component Summary	.147	.029	.333*	.005
Mental Component Summary	.074	.129	.026	-.149

\*  $p < .01$ 

patients with COPD and GERD (concerning the domain of physical role limitation), and between patients with COPD and asthma (concerning vitality domain). In both cases, patients with COPD always had lower scores.

### CCIQ analysis

The analysis of CCIQ scores showed that the most negative impact of cough was on the Social Relationship domain ( $58.33 \pm 25.21$ ), followed by Sleep/Concentration ( $54.26 \pm 18.84$ ), Mood ( $51.49 \pm 20.96$ ) and Daily Life Impact ( $47.69 \pm 18.93$ ). Neither etiology, gender nor age had any influence on the degree of impairment, as shown by analysis of covariance. Table 2 reports the percentage of patients referring the entity of impairment for each item. In the Sleep/Concentration domain, the most compromised items were night sleep and night awakenings; in fact, about 80% of patients referred that they were *enough/much or very much* affected in these domains. In the Mood domain, the most burdened items were "Do you feel nervous?" and "Do you feel anxious about your health condition?" affecting 82% and 73% of patients, respectively. In the Daily Life Impact domain, work, physical activities and social life were impaired in more than 65% of patients. Analysis of the Social relationships domain showed that cough significantly impaired relationships with partners (82%), friends (80%) and family (77%). The three most impaired aspects in the questionnaire, affecting 4 of 5 patients, were sleep, disturbing partner and irritability, while tiredness, spare time and bad mood had the least impact (Table 3).

### Correlations between SF-36 and CCIQ

Significant correlations were found between CCIQ and SF-36 ( $p < 0.05$ ) in the Daily life domain in CCIQ and Physical function, Bodily pain, General health, Vitality, in SF-36. A significant correlation was also observed between the Mood domain in CCIQ and Social functioning in SF-36 (Table 4).

### Discussion

Cough is the major symptom in respiratory diseases

and one of the most frequent reasons for which patients consult a medical practitioner. The importance of this symptom comes from epidemiological data, which have shown that cough is a common aggravation for patients with respiratory disease, with an incidence of up to 40%. This is also reflected by the strong impact of cough on health expenses. The etiology can be either single (38-82%) or multiple (18-62%). The most frequent causes are PNDS (40%), bronchial asthma (25%), and GERD (20%). In fact, these 3 causes are known as the pathogenetic triad of chronic cough. Other less frequent causes are ACE-inhibitors cough, chronic bronchitis, lung cancer, congestive heart failure, interstitial lung disease, bronchiectasis, chronic pulmonary infection, and psychogenic disorders. Thus, CC may be due to curable causes or to incurable pathologies and accordingly, either complete or partial resolution of symptoms may be achieved.

Despite the high incidence of cough observed in clinical practice, little it is known about the impact of coughing from the patient perspective, and only a few studies have described HRQL in coughers on the basis of diagnosis. We used a generic widely employed questionnaire (SF-36) and a validated specific tool for HRQL assessment in chronic cough (CCIQ) in an outpatient population undergoing medical examination in our Chronic Cough Center. The results demonstrated a high burden of this symptom on HRQL. The generic questionnaire identified a different profile of health status according to the severity of the cause inducing CC. Furthermore, in each disease group (asthma, GERD, PNDS, COPD), a poorer HRQL profile was found compared to the control population. The presence of chronic disease, as expected, causes a considerable impact on both physical and mental functioning. Analysis of CCIQ scores indicates that, independently of health status, the presence of cough interferes with several aspects of life.

CC has a detrimental effect on relationships with partners, family and friends. A high percentage of coughers also have disturbed sleep. This specific aspect should always be evaluated in a clinical setting, especially for choice of the most appropriate treatment. Irritability and anxiety are also significant. The impact on daily life is the domain that was affected less and may be due to the patient's coping resources.

Table 5. SF-36 scores according to diagnosis.

Domains	SF-36											
	ASTHMA			COPD			GERD			PNDS		
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
Physical Function	86.6	15.71	90.0	78.6	12.8	80.0	91.9	19.22	100.0	100.0	21.66	100.0
Role Limitation (Physical)	39.1	32.96	25.0	6.6	11.3	0.0	54.6	33.99	50.0	75.0	33.21	75.0
Bodily Pain	80.9	18.16	84.0	60.9	20.9	62.0	64.9	21.26	62.0	84.0	19.65	84.0
General Health	58.8	19.24	56.6	34.9	14.7	40.0	55.4	18.12	57.0	67.0	18.42	67.0
Vitality	56.6	13.47	55.0	40.5	10.7	40.0	52.0	17.33	50.0	55.0	1.47	55.0
Social Function	55.1	15.87	50.0	44.5	18.6	37.5	50.5	21.22	50.0	50.0	14.74	50.0
Role Limitation (Emotional)	50.8	31.1	35.4	21.0	25.3	0.0	45.6	29.4	33.3	66.6	30.9	66.6
Mental Health	70.8	11.43	72.0	56.2	8.9	56.0	59.6	14.26	60.0	64.0	14.42	64.0
Physical component summary	47.3	7.18	47.5	40.1	6.0	42.0	49.0	7.04	51.0	54.0	8.86	54.0
Mental component summary	42.1	6.36	42.0	34.3	5.6	32.0	37.3	8.98	39.0	42.0	6.77	42.0

Table 6. CCIQ scores according to diagnosis.

Domains	CCIQ											
	ASTHMA			COPD			GERD			PNDS		
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
Daily Life	51.14	21.28	50.00	42.76	20.33	43.75	46.06	16.73	43.75	49.26	15.76	43.75
Sleep/ Concentration	55.00	18.32	50.00	56.84	19.16	65.00	51.85	19.86	50.00	53.82	19.00	50.00
Mood	48.70	22.31	45.84	56.14	13.28	50.00	55.25	22.42	50.00	45.59	16.95	41.67
Social Relationship	63.28	27.09	66.67	50.88	27.06	50.00	53.39	23.49	50.00	65.20	19.59	66.67

On the basis of our results, the burden of cough on night time sleep, partner annoyance and mood are the three main aspects that should be considered. The use of quality of life questionnaires can provide useful information for evaluating the impact of disease and treatment on health status and well-being as related to a specific disease symptom. In CC due to incurable diseases, it may permit the selection of treatment priorities based on preferred medication (i.e., antitussive drugs with sedating effects in sleep disturbed patients). In CC related to diseases that are symptomatically treated, such as COPD and asthma, questionnaires can provide information about the level of control achieved and the eventual presence of cough related drug problems (i.e., tightness of bronchial secretions in anticholinergic treatment).

We found that the presence of cough itself induces specific alterations in the life of patients that might be modifiable with treatment. In our opinion, the use of a specific questionnaire should be part of the routine evaluation of outcomes in pharmacological trials.

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### References

1. Irwin RS, Boulet LP, Cloutier MM, Fuller R, Gold PM, Hoffstein V, Ing AJ, McCool FD, O'Byrne P, Poe RH, Prakash UB, Pratter MR, Rubin BK. . Managing cough as a defence mechanism and as a symptom: a consensus panel report of the American College of Chest Physicians. *Chest* 1998;114:133-181.
2. Fuller RW, Jackson DM. Physiology and treatment of cough. *Thorax* 1990; 45:425-430.
3. Irwin RS, Madison JM. Diagnosis and treatment of cough. *N Engl J Med* 2000; 343:1715-1721.
4. Schipper H, Clinch J, Olweny CLM. Quality of life studies: definitions and conceptual issues. In: Spilker B, ed. *Quality of Life and Pharmacoeconomics in Clinical Trials*. Philadelphia: Lippincot-Raven Press 1990: pp.11-23.
5. French CT, Irwin RS, Curley FJ, Krikorian CJ. Impact of Chronic Cough on Quality of Life. *Arch Intern Med* 1998;158:1657-1661.
6. French CT, Irwin RS, Fletcher KE, Adams TM. Evaluation of a Cough-Specific Quality-of-Life Questionnaire. *Chest* 2002;121:1123-1131.
7. Irwin RS, French CT, Fletcher KE. Quality of life in coughers. *Pulm Pharmacol Ther* 2002;15:283-286.
8. Birring SS, Pudon B, Carr AJ, Morgan MDL, Pavord ID. Development of a symptom specific health status measure for patients with chronic cough: Leicester Cough Questionnaire (LCQ). *Thorax* 2003; 58:339-343.
9. French CT, Fletcher KE, Irwin RS. Gender differences in Health-Related Quality of Life in patients complaining of chronic cough. *Chest* 2004; 125:482-488.
10. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care* 1993 Mar;31(3):247-63.

11. Baiardini I, Braido F, Fassio O, Tarantini F, Pasquali M, Tarchino F, Berlendis A, Canonica GW. A new tool to assess and monitor the burden of chronic cough on quality of life: Chronic Cough Impact Questionnaire. *Allergy* 2005; 60:482-488
12. Guyatt GH, Kirshner B, Jaeschke R. Measuring health status: what are the necessary measurement properties? *J Clin Epidemiol* 1992;45:1341-1345.
13. Leynaert B, Neukirch C, Liard R, Bousquet J, Neukirch F. Quality of life in allergic rhinitis and asthma. A population-based study of young adults. *Am J Respir Crit Care Med* 2000;162:1391-1396.
14. Wyrwich KW, Tierney WM, Babu AN, Kroenke K, Wolinsky FD. A comparison of clinically important differences in health-related quality of life for patients with chronic lung disease, asthma, or heart disease. *Health Serv Res.* 2005;40:577-591
15. Velanovich V. Using quality-of-life measurements to predict patient satisfaction outcomes for antireflux surgery. *Arch Surg* 2004; 139:621-625
16. Ware JE Jr, Kosinski M, Bayliss MS, Mc Horney CA, Rogers WH, Raczek A. Comparison of methods for the scoring and statistical analysis of SF-36 health profile and summary measures: summary of results from the Medical Outcomes Study. *Med Care* 1995;33:AS264-279.
17. Likert R. A technique for the measurement of attitudes. *Arch Psychol* 1932;140:5-55.

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