Clinical Cough IV: What is the Minimal Important Difference for the Leicester Cough Questionnaire?

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Contents

Abstract *Background:* The Leicester Cough Questionnaire (LCQ) is a valid, reproducible, responsive self-reported cough-specific health status measure. It has been used to assess overall efficacy of treatments for cough, but its threshold for clinical significance, or patient importance, is unknown. The aim of this study was to determine the minimal important difference (MID) of the LCQ for patients with chronic cough; this is the smallest change in quality-of-life score considered to be clinically meaningful.

Methods: The LCQ MID was first estimated by a multidisciplinary panel of experts who reviewed two cases of chronic cough. It was subsequently determined using a standardized method. Fifty-two patients with chronic cough of more than 8 weeks' duration attending a respiratory outpatient clinic were recruited. Participants completed the LCQ at initial evaluation and repeated the LCQ with four Global

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Rating of Change Questionnaires (GRCQ) more than 2 months later. The LCQ total score ranges from 3 to 21 and from 1 to 7 for physical, psychological and social domains; a higher score indicates a better health-related quality of life. The GRCQ, a 15-point scale scored between +7 (a great deal better) and −7 (a great deal worse), was used to record patient ratings of change in cough symptoms. The MID was defined as the change in LCQ health status corresponding to a small change in the GRCQ score.

Results: The mean (standard deviation) LCQ MID corresponding to a small change in the GRCQ score was 1.3 (3.2); the MIDs for domains were as follows: physical 0.2 (0.8), social 0.2 (1.1) and psychological 0.8 (1.5). This MID for LCQ total score was similar to that determined by the expert panel. The global rating of change scores correlated significantly with the change in LCQ total and domain scores ($r = 0.4 - 0.5$; $p < 0.005$).

Conclusion: We have demonstrated that the LCQ MID is 1.3. The LCQ MID should aid clinicians and researchers to make meaningful interpretations of health-related quality-of-life data relating to chronic cough.

1 Introduction

Chronic cough is a common condition that often leads to considerable physical and psychological morbidity (McGarvey et al. 1998; French et al. 2002). We have previously reported the development of the Leicester Cough Questionnaire (LCQ) (Birring et al. 2003), a validated self-reported health-related quality-of-life (QOL) measure specifically for cough. The LCQ is increasingly being used as an outcome measure of cough in clinical trials to assess therapeutic response (Morice et al. 2007; Decalmer et al. 2007). Whilst statistically significant changes in health status are seen after specific therapy for cough (Birring et al. 2003; Morice et al. 2007), the clinical relevance and importance to the patient is not known. Ideally, changes in health status scores should be presented in a context that is meaningful to patients and healthcare professionals. This can be facilitated by determining the minimal important difference (MID) of health status questionnaires. The MID is defined as the smallest change in the health domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects or excessive cost, a change in the patient's management (Jaeschkle et al. 1989). A number of methods are available to determine the MID. These include MID ratings by an expert multidisciplinary panel, anchor-based methods that compare changes in QOL with other measures that assess change in health status, and distribution-based methods such as the standard error of measurement that assess the effect size and the variability of QOL measurements (Jaeschkle et al. 1989; Jones 2002; Wyrwich and Tierry 2002; Guyatt et al. 2002b; Beaton et al. 2002). The aim of this study was to determine the MID for the LCQ, so that clinicians can readily detect clinically significant changes in the health status of patients with chronic cough, both in clinical and in research settings.

2 Methods

2.1 Phase 1

The LCQ MID was determined by two methods. Phase 1 consisted of an estimation of the LCQ MID by a multidisciplinary panel ($n = 4$) consisting of a respiratory physician, a respiratory physiotherapist, a respiratory researcher and a technician, all experienced in administering the LCQ in routine clinical practice to patients with chronic cough. Three members of the panel had been involved in the development of the LCQ. The panel members independently reviewed two hypothetical case scenarios of chronic cough associated with moderate and severely impaired health-related QOL assessed by the LCQ and were asked to indicate the minimal change (positive or negative) in each LCQ item they considered clinically important, resulting from a 3-month trial of proton-pump-inhibitor therapy or inhaled corticosteroids. These changes were used to calculate new LCQ scores for each case scenario; the change in the LCQ score from the baseline was then calculated.

Case 1: A 35-year-old man with a 6-month history of chronic cough that disturbs sleep a little of the time, who has coughing bouts sometimes during the day, is embarrassed a little of the time, is concerned about what others think a little of the time and has cough that annoys his partner occasionally.

Case 2: A 56-year-old woman with a 6-year history of chronic cough that results in chest or stomach pains a good bit of the time, who is bothered by sputum production most of the time, has coughing bouts several times a day, has 'hardly any energy', is anxious most of the time, is worried about serious illness a good bit of the time, is concerned about what others think most of the time and has cough that interferes with her job and enjoyment most of the time.

2.2 Phase 2

Phase 2 consisted of a prospective study to determine the LCQ MID by validated methods described by other groups (Juniper et al. 1994; Jones 2002; Guyatt et al. 1987). (see Sects. 2.3 to 2.6)

2.3 Subjects

The subjects were 52 consecutive patients with chronic cough referred to a respiratory outpatient clinic. Chronic cough was defined as a cough lasting more than 8 weeks that remained unexplained after assessment by the primary-care physician. The patients underwent investigation and treatment according to a standardized diagnostic protocol described previously (Brightling et al. 1999). Each subject gave informed consent. The study was approved by the local ethics research committee.

2.4 Protocol

All patients completed the LCQ at the first clinic visit and a repeat LCQ and four Global Rating of Change Questionnaires (GRCQ; Appendix 1) more than 2 months later. The repeat questionnaires were either completed at a follow-up clinic visit or posted to patients for completion.

2.5 Leicester Cough Questionnaire

The LCQ is a well-validated, self-completed, cough-specific health status questionnaire that has been shown to be both repeatable and responsive in patients with chronic cough (Birring et al. 2003). The total score range for the LCQ is 3–21 and a higher score indicates a better QOL. A seven-point Likert response scale is used for all 19 LCQ items. The LCQ has three domains: physical, psychological and social (range 1–7). Domain scores are calculated by averaging scores from items in each domain; the total score is the sum of the domain scores. The LCQ can be downloaded from http://thorax.bmjjournals.com/cgi/content/full/58/4/339.

2.6 Global Rating of Change Questionnaire

The GRCQ is a 15-point scale widely used to determine the MID of health-related QOL questionnaires (Juniper et al. 1994). The GRCQ is used to ask patients to make global ratings of changes in their cough over a time interval. The response scale ranges from −7 (a great deal worse) to +7 (a great deal better). All subjects were asked to complete four GRCQs, each relating to one of the LCQ domains and overall health status. The score for each GRCQ was classified as unchanged (scores −1/0/1), a small change (−3, −2, 2, 3), a moderate change (−5, −4, 4, 5) or large change (−7, −6, 6, 7) (Juniper et al. 1994). The MID was defined as the change in LCQ health status corresponding to a small change in GRCQ score as defined by Juniper et al. (1994) and Jaeschkle et al. (1989). The final accepted LCQ MID was determined by phase 2 of this study.

2.7 Statistical Analysis

SPSS version 12 was used for data analysis. Data are presented as the mean (standard deviation) or median (range). The mean change in LCQ score was calculated for each domain. In accordance with previous studies we expressed change of the global rating score as an absolute number, i.e. when the change was negative,

the sign was reversed as was the sign of the change in LCQ score (Jaeschkle et al. 1989; Juniper et al. 1994). Correlations between variables were analysed using Pearson's correlation coefficients (r). Paired t tests were used for group comparisons.

3 Results

3.1 Phase 1

A multidisciplinary panel of four individuals independently reviewed two case scenarios of chronic cough. The mean (standard deviation) LCQ MID determined by the expert multidisciplinary panel for total score was 1.49 (0.32) and for domain scores the MID were as follows: physical 0.52 (0.18), psychological 0.47 (0.14) and social 0.50 (0). There were no significant differences in MID scores between the two cases of chronic cough (Table 1).

3.2 Phase 2

Subject characteristics are shown in Table 2. The causes of cough were asthma (21.2%), eosinophilic bronchitis (9.6%), bronchiectasis (5.8%), gastro-oesophageal reflux disease (5.8%), chronic bronchitis (5.8%), chronic obstructive pulmonary disease (3.8%), chronic enlarged tonsils (3.8%), rhinitis (1.9%), sarcoidosis (1.9%), interstitial lung disease (1.9%) and idiopathic chronic cough (36.5%). The clinical course of patients between visits were investigations (12%), diagnostic trial of therapy (proton-pump inhibitors, inhaled corticosteroids and nasal corticosteroids) (31%), treatment of underlying condition causing cough (29%), chest physiotherapy and speech therapy (18%) and observation only (10%). The median time (range) from the first LCQ to completion of the second LCQ was 43 weeks (9–133 weeks).

Patients with chronic cough had reduced overall health status at baseline; the mean (standard deviation) LCQ total score was 13.6 (4.1); (normal QOL score is 21). Health status was reduced in all domains of QOL (Table 2). The mean change

Table 1 Mean minimal important differences estimated by a multidisciplinary panel for two cases of chronic cough

	Case 1	Case 2	Mean MID (SD) (cases 1 + 2)
MID physical domain	0.63	0.41	0.52 (0.18)
MID psychological domain	0.57	0.37	0.47 (0.14)
MID social domain	0.50	0.50	0.50 (0)
MID LCQ total score	1.70	1.25	1.49 (0.32)

MID minimal important difference, *SD* standard deviation, *LCQ* Leicester Cough Questionnaire

Table 2 Patient baseline characteristics ($n = 52$)

Age (years)	55 (13.9)
Female (n) (%)	29 (56)
FEV_1(% predicted)	95 (4)
Duration of cough (months)	67 (77)
Smoking history	
Ex-smokers (n) (%)	17 (38)
Non-smokers (n) (%)	27 (61)
LCQ scores	
Physical LCQ score	4.8 (1.1)
Psychological LCQ score	4.4 (1.6)
Social LCQ score	4.4 (1.6)
Overall QOL	13.6 (4.1)

Data are presented as the mean (standard deviation).
FEV_1 forced expiratory volume in 1 s, *QOL* quality of life

Table 3 Mean change in Leicester Cough Questionnaire score per global rating category

	Global rating of change category			
	Same (-1/0/1)	Minimal important difference (-3/–2/2/3)	Moderate (–5/–4/4/5)	Large (–7/–6/6/7)
LCQ: total	−1.3 (3.1), $n = 26$	1.3 (3.3), $n = 14$	1.7 (2.3), $n = 10$	2.7 (4.6), $n = 7$
LCQ: physical	−0.6 (0.9), $n = 25$	0.2 (0.8), $n = 14$	0.7 (1), $n = 14$	1.3 (1.2), $n = 4$
LCQ: social	−0.3(1.2), $n = 34$	0.2 (1.1), $n = 6$	0.7 (0.9), $n = 12$	1.3 (2.2), $n = 5$
LCQ: psychological	−0.1(1.1), $n = 28$	0.8 (1.5), $n = 11$	0.5 (0.8), $n = 12$	1.2 (2.1), $n = 6$

Data are presented as the mean (standard deviation).
n number of patients

in LCQ score for each GRCQ category at follow-up visit is given in Table 3. The LCQ MID, corresponding to a small change in the GRCQ score was 1.3 and the MIDs of the health domains were as follows: physical 0.2(0.8), social 0.2(1.1) and psychological 0.8(1.5) (Table 3). Patients reporting a positive change in global rating (+1 to +7) had improved health status (median change in LCQ score of 1.6; $n = 17$) compared with those reporting a negative change (median LCQ change of –1.3; $n = 22$; $p = 0.5$). The global rating of change scores correlated significantly with the change in the LCQ total and domain scores ($r = 0.4 - 0.5$; all $p < 0.005$). This was higher than correlation of global rating scores with post-LCQ scores ($r = -0.2$ to -0.3) and pre-LCQ scores ($r = 0$ to 0.2). The post-LCQ total and domain scores were significantly higher than the baseline LCQ scores in those patients who indicated an improvement on the global rating scale (mean difference in the LCQ

total score of 2.7; $p = 0.01$; physical $p = 0.007$; psychological $p = 0.04$; social $p = 0.04$). There were no statistically significant differences in the change in LCQ scores when they were analysed per global rating category. The LCQ total score MID was 1.2 when patients with a global rating change of –1/+1 were included in the MID group.

4 Discussion

The LCQ is a brief, well-validated self-completed cough-specific health status questionnaire that has been shown to be repeatable and responsive. The purpose of this study was not to validate the LCQ, which has previously been done, but to determine the MID. We have demonstrated that the MID for the LCQ total health status score is 1.3 and the MID for LCQ health status domains ranges from 0.2 to 0.8. This study represents an advance in the clinical utility of cough severity outcome measures and should aid clinicians and researchers in making meaningful interpretations of health-related QOL data relating to chronic cough.

We determined the LCQ MID by two methods that assessed the patients' and healthcare professionals' perception of change in health status and found them to be very similar. The expert panel consensus method is simple and brief and provides an estimation of the MID from a clinicians' perspective (Jaeschkle et al. 1989; Jones et al. 1991). We chose the anchor-based method of Juniper et al. (Juniper et al. 1994) and Jaeschke et al. (Jaeschkle et al. 1989) as the main determinant of the LCQ MID, since this is the most widely used and published method and emphasizes the patients' opinion (Juniper et al. 1994). Distribution methods such as those based on the standard deviation are being used increasingly since they are easier to generate than anchor based methods (Guyatt et al. 2002b). Their limitations are the dependence on heterogeneity of the population being studied and the arbitrary nature of the units of measure (Guyatt et al. 2002b). These problems are minimized by using the standard error of measurement method, which has been found to correlate well with anchor-based methods.(Wyrwich et al. 1999) We chose multiple methods to determine the MID to enhance the interpretability of our QOL questionnaire and overcome the limitations of individual methods (Guyatt et al. 2002b; Beaton et al. 2002).

The GRCQ has been used to determine the MID for a wide range of QOL questionnaires, in which patients quantify the magnitude of the change in health status. We chose to include patients with a global rating score of –1/+1 in the unchanged category to be consistent with others (Juniper et al. 1994). It is possible that some patients in this group may have experienced a minimal important change in health status but there was little change in the LCQ MID when patients with GRCQ scores of –1/+1 were included in the MID group. The LCQ MID applies to patients whose health improved or deteriorated. We found a similar change in LCQ health status score in those scoring an improvement in their global rating of change to those with deterioration. It is possible that patients with deteriorating health may have a

different LCQ MID from those experiencing an improvement. Studies with larger numbers of patients with deterioration in health status would be required to determine a separate MID value for deteriorating health status.

The GRCQ has limitations that may lead to some imprecision in determining the MID; it is a subjective instrument with arbitrary scales and categories, and individual patients may interpret the wording of GRCQ questions differently, leading to variability in GRCQ scoring. This may have contributed to the variability seen in the LCQ MID, but this is probably true for all QOL instruments (Decalmer et al. 2007). The GRCQ is subject to recall bias, particularly if patients are unable to recall their prior health status and may reflect current health status in some subjects (Guyatt et al. 2002b; Beaton et al. 2002). This may have been a particular problem for some of our patients who completed the repeat LCQ several months after the first. The long duration for repeat questionnaires for some patients reflects the prolonged treatment trials and follow-up that are often required for patients with chronic cough. The fact that the LCQ was administered only once before and patients were asked to recall this visit may have improved the performance of the GRCQ and minimized recall bias. Despite these limitations, the LCQ MID is similar to the MID of other QOL questionnaires and is consistent with the observations by Juniper et al. that QOL questionnaires utilizing a seven-point Likert response scale have a MID of approximately 0.5 points per item or question (Redelmeier et al. 1996; Guyatt et al. 1987; Guyatt et al. 1989). A change of LCQ score of 0.5 per question equates to a change in LCQ domain of 0.5 and LCQ overall score change of 1.5. We found significant correlations between global rating of change scores and the change in LCQ scores and weaker correlations with post-LCQ and pre-LCQ scores, in keeping with findings of Guyatt et al. (2002a), supporting the use of the global rating of change scale. We generally found a stepwise increase in the change in LCQ scores across GRCQ categories (with the exception of the psychological domain), which suggests that this instrument was able to discriminate between patients with small and large changes in health status related to chronic cough. Furthermore, the LCQ MID of 1.3 is consistent with our clinical experience of using the LCQ in routine clinical practice over the past 5 years.

We found an overall reduction in LCQ score in patients with chronic cough who indicated their cough remained unchanged on the GRCQ. This group included patients scoring +1/-1 on the GRCQ (hardly any change), so it is possible that some patients may have experienced more appreciable changes in health status in this category. Another unexpected finding was a higher LCQ psychological domain MID score than that of patients indicating moderate change in their psychological domain. Further review of our data revealed that this was due to three patients with large improvements in psychological domain scores who rated themselves as slightly changed in the global rating. This may reflect that for some patients perception of overall psychological status is not easily captured with a single global rating of change question and requires specific psychological questionnaires.

We were unable to perform a subanalysis to determine whether the LCQ MID varied according to age, gender or cause of cough owing to the small number of patients studied. The change in LCQ scores within individual global rating of change

categories was not statistically significant, a finding also likely to have been influenced by the small number of subjects in the subgroup analysis. Larger studies are required to address this and it is hoped that the findings of this study will be used to determine the sample size of future studies to demonstrate both statistically and clinically significant differences. The findings of this study should be considered preliminary since the MID is likely to be refined by further studies and experience with the LCQ. Our study represents a useful starting point for interpreting QOL data and should stimulate further studies. The MID for acute cough may differ from that of chronic cough and needs to be determined. Objective cough assessment tools, such as 24-h ambulatory cough monitors, may allow further refinement of the MID for health status questionnaires.

Chronic cough frequently impacts on QOL and often profoundly. Health-related QOL questionnaires are increasingly being used as end points in clinical trials as they provide a standardized method to quantify the impact of cough on health status (Morice et al. 2007). It is of critical importance that health status data are interpreted in the correct context. The LCQ MID will facilitate this and aid interpretation of health status data when used in outpatient clinics as well as assessing risk–benefit profiles of new medicines and their cost-effectiveness. The MIDs for other measures of cough severity, such as cough reflex sensitivity, diary scores and cough frequency measurement, are not known and future studies should address this.

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Appendix 1: Global Rating of Change Questionnaire

Question 1: Since your last clinic visit, has there been any change in the impact of your cough-related symptoms?
Question 2: Since your last clinic visit, has there been any change in your feelings (e.g. anxiety, embarrassment) as a consequence of your cough?
Question 3: Since your last clinic visit, has there been any change in the impact your cough has had on your work or social life?
Question 4: Since your last clinic visit, has there been any change in the impact your cough has had on your overall quality of life?

Please circle the response that best applies to you, for each question.
–7 A very great deal worse
–6 A great deal worse
–5 A good deal worse
–4 Moderately worse
–3 Somewhat worse
–2 A little worse
–1 Almost the same, hardly any worse at all
0 No change
1 Almost the same, hardly any better at all
2 A little better
3 Somewhat better
4 Moderately better
5 A good deal better
6 A great deal better
7 A very great deal better