

An acute cough-specific quality-of-life questionnaire for children: Development and validation

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Background: Patient-relevant outcome measures are essential for high-quality clinical research, and quality-of-life (QoL) tools are the current standard. Currently, there is no validated children's acute cough-specific QoL questionnaire.

Objective: The objective of this study was to develop and validate the Parent-proxy Children's Acute Cough-specific QoL Questionnaire (PAC-QoL).

Methods: Using focus groups, a 48-item PAC-QoL questionnaire was developed and later reduced to 16 items by using the clinical impact method. Parents of children with a current acute cough (<2 weeks) at enrollment completed 2 validated cough score measures, the preliminary 48-item PAC-QoL, and 3 other questionnaires (the State Trait Anxiety Inventory [STAI], the Short-Form 8-item 24-hour recall Health Survey [SF-8], and the Depression, Anxiety, and Stress 21-item Scale [DASS₂₁]). All measures were repeated on days 3 and 14.

Results: The median age of the 155 children enrolled was 2.3 years (interquartile range, 1.3-4.6). Median cough duration at enrollment was 3 days (interquartile range, 2-5). The reduced 16-item scale had high internal consistency (Cronbach α = 0.95). Evidence for repeatability and criterion validity was shown by significant correlations between the domains and total PAC-QoL scores and the SF-8 (r = -0.36 and -0.51), STAI (r = -0.27 and -0.39), and DASS₂₁ (r = -0.32 and -0.41) scales on days 0 and 3, respectively. The final PAC-QoL questionnaire was sensitive to change over time, with changes significantly relating to changes in cough score measures (P < .001).

Conclusion: The 16-item PAC-QoL is a reliable and valid outcome measure that assesses QoL related to childhood acute cough at a given time point and reflects changes in acute cough-specific QoL over time. (J Allergy Clin Immunol 2014;■■■:■■■-■■■.)

Key words: Children, acute cough, quality of life

Cough is consistently the most common reason for presentation to primary health care services in Australia¹ and internationally.^{2,3} The burden of acute cough in children is reflected by the frequency of these medical presentations,^{4,5} the high use of over-the-counter medications with potential severe adverse events,⁶ and the direct effect of cough on parents and children (eg, sleep disturbance⁷). However, there is a relative paucity of research on acute cough. Also, few validated outcome measures for acute cough in children exist, and this affects the quality of clinical research.

Patient-relevant outcome measures, such as quality-of-life (QoL) tools, are now considered essential for high-quality clinical research,^{8,9} and those relevant to children need pediatric specific measures. It is also increasingly recognized that specific QoL measurements are more sensitive than generic ones.¹⁰ Currently, there is no validated QoL tool specifically for acute cough in children. Although we previously described 2 validated versions of a chronic cough-specific QoL tool for children,¹¹⁻¹³ acute cough might be different from chronic cough in many ways (eg, etiology). Thus chronic cough-specific QoL tools cannot be extrapolated to acute cough without validation studies. There are other scales for measuring the effects of acute respiratory illness, such as the validated Canadian Acute Respiratory Illness and Flu Scale¹⁴; however, this instrument is not specific to acute cough and includes a large number of daily reported items not relating to cough. In adults the Leicester group¹⁵⁻¹⁷ modified their chronic cough QoL for use in patients with acute cough. The adult study reinforces that chronic cough QoL tools cannot be extrapolated to acute cough and highlights the need for a validated and robust outcome measure for acute cough in children.

To address this clinical research gap, we enrolled parents of 155 children. Here we describe the development, item reduction, and validation of a children's acute cough-specific QoL instrument and report on the statistical properties of the final scale. The aim of our study was to develop a valid and reliable Parent-proxy Children's Acute Cough-specific QoL Questionnaire (PAC-QoL) for use by parents of children with acute cough.

METHODS

Written informed consent was obtained from parents (and assent was obtained from children aged ≥ 12 years), and the study was approved by the human

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Abbreviations used

DASS ₂₁ :	Depression, Anxiety and Stress 21-item Scale
IQR:	Interquartile range
MID:	Minimally important difference
PAC-QoL:	Parent-proxy Children's Acute Cough-specific QoL Questionnaire
QoL:	Quality of life
SF-8:	Short-Form 8-item 24-hour recall Health Survey
STAI:	State Trait Anxiety Inventory
VAS:	Visual analog scale
VCD:	Verbal category descriptive

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Development of items for the PAC-QoL

Two focus groups were held, comprising 4 to 5 parents of children with current acute cough or who had recently sought medical assistance for acute cough, to obtain relevant items for the PAC-QoL. Discussions were audio recorded, and verbatim transcripts were independently analyzed by 2 authors (S.A.-J. and P.A.N.) to determine whether discussions had reached an item saturation point.

The resultant draft PAC-QoL questionnaire included 48 items rated with a 7-point Likert-type scale, as previously used.^{11,12} Items referred to a 24-hour recall. Twenty-five items related to the frequency of particular feelings, and 23 items reflected concerns or worries. Lower scores for the scales reflect greater frequency, concerns, or worries, with higher scores therefore reflecting better QoL.

Methods of item reduction for PAC-QoL

The clinical impact method of item reduction, as outlined by Juniper et al,^{9,18,19} was used, based on ranking of the most important items (as detailed in the *Methods* section in this article's Online Repository at www.jacionline.org). For analysis of clinical impact rank, draft PAC-QoL item scales were reverse scored so that higher numbers reflected greater frequency or worry (Table 1). Based on an arbitrary cutoff at a natural break in ranked impact ratings, the 16 highest-impact items were selected. These items were endorsed with a reverse score of at least 3 from the 7-point response scale by greater than 75% of participants.

Domain allocation

We allocated the 16-item instrument into physical, social, and emotional domains based on the World Health Organization's definition of health, as previously done.^{11,12} Face validity of each item was determined based on the expert opinion of a panel of respiratory clinicians and psychologists for allocation to domains.

Procedure for validation

Participants. Parents of generally healthy children aged less than 18 years with an acute coughing illness (cough duration <2 weeks²⁰) at presentation were recruited from the emergency departments of the Royal Children's Hospital and Mater Children's Hospital and community-based health centers in Brisbane, Australia, between September 2011 and September 2013. Exclusion criteria included hospitalized children, pneumonia, and classical asthma. See the *Methods* section in this article's Online Repository for a full list of exclusion criteria.

Procedures. For more details on procedures used, see the *Methods* section in this article's Online Repository. At enrollment, one parent of each child completed 2 validated subjective cough scores (cough verbal category descriptive [VCD] score and visual analog scale [VAS] score)²¹ and the

following 4 questionnaires: the 48-item PAC-QoL questionnaire, the Short-Form 8-item 24-hour recall Health Survey (SF-8),²² the State Trait Anxiety Inventory (STAI),²³ and the Depression, Anxiety, and Stress 21-item Scale (DASS₂₁).²⁴ The PAC-QoL questionnaire was administered by an interviewer (S.A.-J.), and the rest were self-completed. Clinical and demographic data were collected on standardized forms. All measures were repeated on days 3 and 14.

Cough diaries. Both the cough-scoring diaries were previously validated against an objective cough meter, and changes in this subjective cough rating have been shown to reflect changes in cough counts.²¹ In the VCD parents rated their child's cough severity on a 6-point scale. In the VAS parents rated how troublesome their child's cough was on a marked scale of 1 (cough absent) to 10. These 2 cough-scoring diaries were performed together to strengthen the validity of the PAC-QoL in the absence of an objective cough measure, as previously done for validation of our chronic cough PC-QOL.¹²

Description of measures. The SF-8²² is an 8-item shortened version of the 36-item Short-Form Health Survey. The STAI,²³ comprising two 20-item scales, clearly differentiates between the temporary condition of "state anxiety" and the more general and long-standing quality of "trait anxiety." The DASS₂₁ is a 21-item self-report scale that measures the domains of depression, anxiety, and stress.²⁴ Higher scores within all measures reflect greater severity. Further description of these validated scales is provided in the *Methods* section in this article's Online Repository.

Statistical analysis

Nonparametric analyses were used throughout, and descriptive data were presented as medians and interquartile ranges (IQRs). The Mann-Whitney *U* test was used for unpaired comparisons, and the Wilcoxon test was used for paired comparisons. Spearman correlation (r_s) was used for assessing relationships between variables. Cronbach α scores were determined to assess the reliability (internal consistency) of the PAC-QoL full scale and each of the domains. Repeatability and criterion validity were determined by examining correlations over time and relationships with cough measures to determine whether the instrument and its domains were sensitive to change over time. An estimate of the minimally important difference (MID) was determined, combining both distribution and anchor-based methods (see the *Methods* section in this article's Online Repository). A statistical package (IBM SPSS, version 22) was used, and a 2-tailed *P* value of .05 was considered significant. We calculated that a minimum sample size of 60 with complete data was required for a medium impact size ($\beta = 80\%$ and $\alpha = 5\%$, as detailed in the *Methods* section in this article's Online Repository).

RESULTS

Demographics

The median age of the 155 children (87 boys and 68 girls) in the study was 2.17 years (IQR, 1.25-4.58 years); 7 children were aged 12 or more years. Children were enrolled from the emergency department ($n = 120$) and community-based health centers ($n = 35$). Eighty-five (54.8%) children had at least 1 doctor's office visit for their current coughing illness before the enrollment presentation. The median cough duration was 3 days (IQR, 2-5 days). The median parent-reported cough VCD score was 3 (IQR, 2-4), and the median cough VAS score was 6 (IQR, 4-8). Other parent-reported symptoms at enrollment included runny nose, tiredness, and unsettled night. See the *Results* section in this article's Online Repository at www.jacionline.org for a full description of symptoms.

Characteristics of the PAC-QoL

The reduced 16-item PAC-QoL scale was internally consistent (Cronbach $\alpha = 0.95$), with a median impact score of 3.36 (IQR,

TABLE I. Impact rank order of the PAC-QoL₄₈ items at enrollment, reflecting the previous 24 hours of child's cough-related illness (n = 155 parents of children with acute cough)

	Item	Item mean	Reverse item mean	SD	Proportion endorsing	Impact
25.	Did you feel sorry for your child because of his/her cough?	2.87	5.13	1.83	0.89	4.56
26.	Were you worried/concerned about your child's cough becoming worse?	3.14	4.86	1.74	0.88	4.27
45.	Were you worried/concerned about your child not sleeping well because of the cough?	3.31	4.69	1.72	0.88	4.11
48.	Were you worried/concerned about whether you should take your child to a doctor or emergency ward because of his/her cough?	3.23	4.77	1.96	0.83	3.97
7.	Were you awakened during the night because of your child's cough?	3.41	4.59	1.98	0.83	3.79
39.	Were you worried/concerned about your child's cough lasting a long time?	3.65	4.35	1.86	0.81	3.50
31.	Were you worried/concerned about the cause of your child's cough?	3.81	4.19	1.85	0.81	3.37
42.	Were you worried/concerned about the effects of your child's cough on him/her?	3.81	4.19	1.85	0.81	3.37
37.	Were you worried/concerned about your child not being able to breathe again after coughing?	3.63	4.37	2.09	0.77	3.35
44.	Were you worried/concerned about your child feeling tired because of the cough?	3.86	4.14	1.85	0.81	3.34
20.	Did you feel tired or exhausted because of your child's cough?	3.77	4.23	2.06	0.77	3.27
27.	Were you worried/concerned about your child's performance of normal activities including feeding and schooling?	3.89	4.11	1.79	0.79	3.26
9.	Were you or your family disturbed by your child's cough?	3.97	4.03	1.80	0.77	3.10
32.	Were you worried/concerned about your child's cough indicating a more serious illness?	3.89	4.11	1.97	0.75	3.07
2.	Did your family need to change plans because of your child's cough?	3.97	4.03	2.08	0.75	3.01
5.	Did you feel upset because of your child's cough?	4.15	3.85	1.78	0.77	2.95
12.	Did you feel stressed because of your child's cough?	4.12	3.88	1.89	0.73	2.83
41.	Were you worried/concerned about your child being contagious to other children?	4.12	3.88	1.89	0.72	2.80
4.	Did your child's cough interfere with your job or work around the house?	4.08	3.92	2.05	0.71	2.79
21.	Did you limit your child's activities because of your child's cough?	4.19	3.81	1.93	0.72	2.73
43.	Were you worried/concerned about the effects of your child's cough on his/her ability to play or do things?	4.21	3.79	1.86	0.72	2.72
10.	Did you feel anxious about your child's cough?	4.29	3.71	1.83	0.71	2.63
14.	Did you feel sad about your child's cough?	4.14	3.86	2.17	0.68	2.62
11.	Did you feel helpless because of your child's cough?	4.19	3.81	2.04	0.67	2.56
34.	Were you worried/concerned about leaving your child with others because of his/her cough?	4.25	3.75	2.14	0.67	2.49
47.	Were you worried/concerned about your child vomiting because of coughing?	4.23	3.77	2.20	0.65	2.46
46.	Were you worried/concerned about the cough causing damage to your child's chest or lungs?	4.24	3.76	2.20	0.63	2.38
33.	Were you worried/concerned about your child choking when coughing?	4.32	3.68	2.06	0.63	2.32
1.	Did you feel frightened when your child experienced cough?	4.57	3.43	1.75	0.67	2.30
40.	Were you worried/concerned about your child worrying about his/her cough?	4.50	3.50	1.99	0.63	2.19
23.	Did you feel powerless because of your child's cough?	4.48	3.52	2.06	0.60	2.11
36.	Were you worried/concerned about your having a sleepless night because of your child's cough?	4.54	3.46	1.96	0.60	2.07
15.	Did you feel scared because of your child's cough?	4.60	3.40	1.95	0.60	2.01
3.	Did you feel frustrated because of your child's cough?	4.61	3.39	1.94	0.59	2.01
22.	Did you feel you were being overprotective because of your child's cough?	4.99	3.01	1.83	0.55	1.65
24.	Did you feel uncomfortable because of your child's cough?	4.92	3.08	1.94	0.52	1.61
19.	Did you feel terrible because of your child's cough?	4.93	3.07	2.08	0.52	1.61
13.	Did you feel guilty about sending your child to (for example) daycare/swimming class when he/she was coughing?	5.08	2.92	2.18	0.48	1.41
38.	Were you worried/concerned about your missing work due to your child's cough?	5.21	2.79	2.08	0.45	1.26
28.	Were you worried/concerned over the side effects of medications your child takes?	5.21	2.79	1.93	0.43	1.21
8.	Would you have liked to call a friend or family member to help you with your child's cough?	5.30	2.70	1.87	0.45	1.20
29.	Were you worried/concerned about being overprotective of your child?	5.32	2.68	1.74	0.45	1.19

(Continued)

TABLE I. (Continued)

	Item	Item mean	Reverse item mean	SD	Proportion endorsing	Impact
30.	Were you worried/concerned about your child being able to lead a normal life?	5.31	2.69	1.90	0.42	1.13
6.	Did your child's cough interfere with family relationships?	5.50	2.50	1.74	0.41	1.02
16.	Did you call a friend/family member to assist you with your child's cough?	5.52	2.48	1.92	0.40	0.99
35.	Were you worried/concerned about other people's reaction to your child's cough?	5.74	2.26	1.64	0.32	0.73
17.	Did you feel others were judging you because of your child's cough?	6.10	1.90	1.40	0.25	0.47
18.	Did you feel others were staring at you because of your child's cough?	6.21	1.79	1.31	0.21	0.37

TABLE II. Spearman correlations between the subscale and total scores of the PAC-QoL₁₆ (clinical impact analysis) and the dimensions of the STAI, SF-8, DASS₂₁, and cough measures at enrollment (n = 155) and day 3 (n = 103 still coughing)

Scale/dimension	PAC-QoL instrument								Cronbach α	
	Physical domain		Social domain		Emotional domain		Clinical impact total			
	Enrollment	Day 3	Enrollment	Day 3	Enrollment	Day 3	Enrollment	Day 3	Enrollment	Day 3
STAI										
State	-0.52*	-0.50*	-0.38*	-0.44*	-0.46*	-0.46*	-0.52*	-0.49*	0.94	0.95
Trait	-0.28*	-0.40*	-0.16	-0.33*	-0.23*	-0.37*	-0.27*	-0.39*	0.90	0.92
SF-8										
Physical	-0.21*	-0.33*	-0.17†	-0.28*	-0.15	-0.28*	-0.21†	-0.31*	(1 item)	(1 item)
Role physical	-0.16	-0.29*	-0.14	-0.27*	-0.07	-0.22†	-0.15	-0.29*	(1 item)	(1 item)
Bodily pain	-0.18†	-0.36*	-0.14	-0.32*	-0.09	-0.29*	-0.17†	-0.35*	(1 item)	(1 item)
General health	-0.18†	-0.34*	-0.17†	-0.30*	-0.15	-0.27*	-0.20†	-0.33*	(1 item)	(1 item)
Vitality	-0.28*	-0.32*	-0.12	-0.31*	-0.22*	-0.31*	-0.26*	-0.33*	(1 item)	(1 item)
Social	-0.34*	-0.43*	-0.26*	-0.39*	-0.25*	-0.40*	-0.34*	-0.42*	(1 item)	(1 item)
Role emotional	-0.37*	-0.39*	-0.27*	-0.33*	-0.27*	-0.38*	-0.36*	-0.39*	(1 item)	(1 item)
Mental health	-0.38*	-0.45*	-0.26*	-0.38*	-0.31*	-0.44*	-0.38*	-0.44*	(1 item)	(1 item)
Total	-0.36*	-0.52*	-0.26*	-0.46*	-0.27*	-0.47*	-0.36*	-0.51*	0.89	0.90
DASS ₂₁										
Depression	-0.22*	-0.35*	-0.09	-0.35*	-0.17†	-0.37*	-0.21†	-0.35*	0.88	0.92
Anxiety	-0.39*	-0.43*	-0.28*	-0.38*	-0.24*	-0.40*	-0.37*	-0.42*	0.82	0.81
Stress	-0.30*	-0.34*	-0.24*	-0.29*	-0.22*	-0.33*	-0.30*	-0.34*	0.87	0.89
Total	-0.33*	-0.42*	-0.24*	-0.38*	-0.23*	-0.40*	-0.32*	-0.41*	0.93	0.95
VCD cough score	-0.31*	-0.56*	-0.44*	-0.63*	-0.28*	-0.55*	-0.36*	-0.59*	(1 item)	(1 item)
VAS cough score	-0.52*	-0.67*	-0.53*	-0.74*	-0.45*	-0.63*	-0.55*	-0.70*	(1 item)	(1 item)
Cronbach α	0.94	0.96	0.73	0.84	0.72	0.84	0.95	0.97		

Higher scores on the PAC-QoL questionnaire reflect better QoL. Higher scores on the STAI reflect greater severity. Higher scores on the SF-8 reflect worse health states. Higher scores on the DASS₂₁ reflect greater severity. Higher VCD cough scores represent greater interference with usual activities. Higher VAS cough scores represent greater trouble with the cough.

*Correlation is significant at the 0.01 level.

†Correlation is significant at the 0.05 level.

3.14-3.93). Interitem correlations ranged from 0.29 to 0.79. Of these, 11 items were allocated to the physical domain, 3 to the social domain, and 2 to the emotional domain. Cronbach α values for each domain were high (range, 0.72-0.94; Table II). On retesting at day 3, these high internal consistencies were maintained; the Cronbach α value was 0.97, and the intradomain range was 0.84 to 0.96. Interitem correlations ranged from 0.51 to 0.90. These demonstrate little item redundancy within the subscales of the proposed PAC-QoL questionnaire. The final version derived from the clinical impact method of item reduction was therefore shown to be internally reliable.

Validity

Issues of concurrent and criterion validity for the PAC-QoL questionnaire were examined and supported through Spearman correlations with the subscales of the STAI, SF-8, and DASS₂₁ and the cough score measures (Table II). High absolute

correlation values were found between the subscale and total scores of the PAC-QoL questionnaire and the dimensions of all scales at both time points (days 0 and 3), providing strong evidence for criterion validity. The PAC-QoL questionnaire also highly correlated with the VCD and VAS cough score measures at both time points.

Sensitivity to change

The final 16-item PAC-QoL questionnaire resulting from the clinical impact method of item reduction was reproducible, with good test-retest reliability after 3 days (intraclass correlation coefficient, 0.75; 95% CI, 0.63-0.83). Descriptive data (medians with IQRs) along with Wilcoxon signed-rank tests of difference, are presented in Table III, supporting sensitivity to change over time. All total and domain subscales showed significant improvement in PAC-QoL questionnaire scores over time ($P < .001$, Fig 1). Further evidence for discriminant validity and

TABLE III. Clinical impact total and domain scores and cough measures at enrollment and day 3 (*n* = 103 still coughing)*

PAC-QoL	Enrollment	Day 3	<i>z</i> Score†
Physical domain	3.73 (2.45-4.82)	4.66 (3.58-5.83)	−4.88‡
Social domain	4.00 (2.67-5.00)	5.67 (4.00-6.33)	−6.71‡
Emotional domain	3.50 (2.50-5.00)	5.00 (3.50-6.50)	−6.21‡
Clinical impact total	3.81 (2.56-4.88)	5.38 (4.00-6.31)	−7.14‡
VCD cough score	3 (2-4)	2 (2-3)	−5.60‡
VAS cough score	6 (4-7)	4 (2-5)	−5.86‡

Higher scores on the PAC-QoL questionnaire reflect better QoL. Higher VCD cough scores represent greater interference with usual activities. Higher VAS cough scores represent greater trouble with the cough.

*Values are presented as medians (IQRs), unless otherwise indicated.

†*z* Scores are based on the Wilcoxon signed-rank test.

‡*P* < .001, Wilcoxon signed-rank test.

the responsiveness of the PAC-QoL questionnaire to change was shown at time 3 (day 14), at which time parents identified whether their child had ceased coughing. Descriptive data (medians with IQRs) and results of Mann-Whitney *U* tests of difference are presented in Table IV. At enrollment, PAC-QoL questionnaire total and domain scores were not significantly different between the groups of children who were still coughing and those who ceased coughing but were significantly different at day 14, with those parents whose children had not ceased coughing reporting significantly greater frequency of concern and worries than those parents whose children who had ceased coughing. Also, change in PAC-QoL questionnaire scores significantly correlated with change in VAS ($r = -0.49$, $P < .001$) and VCD ($r = -0.58$, $P < .001$) scores.

MID

Results on various possible combinations when using the distribution-based approach to MIDs (see Table E1 in this article's Online Repository at www.jacionline.org) showed that the effect size MIDs ranged from 0.30 to 0.85 for the domains and the overall PAC-QoL questionnaire. By using half SD,²⁵ the MID for the PAC-QoL questionnaire is 0.74. Data on VCD score change classifications for the anchor-based approach are shown in Table E2 in this article's Online Repository at www.jacionline.org. Using a small change (VCD score change = 1) resulted in an MID estimate of 1.18 for overall PAC-QoL questionnaire score change and range of 0.76 to 1.37 for individual domains. Thus the MID of our PAC-QoL questionnaire is between 0.74 and 1.18. Choosing a combination approach (distribution-based within anchor-based approach),²⁶ the estimated MID for the overall PAC-QoL questionnaire was 0.98.

DISCUSSION

In this study we present the first validated children's acute cough-specific QoL questionnaire for parents/caregivers of children with acute cough. The final 16-item PAC-QoL questionnaire, which was derived by using the clinical impact method, had properties of concurrent and criterion validity, reliability, and sensitivity to change measured against cough scores and the STAI, DASS₂₁, and SF-8. The estimated MID of the overall PAC-QoL questionnaire using a combination (distribution-based within anchor-based) approach is 0.98.

Our initial step in the development of the PAC-QoL tool was to obtain appropriate items that were parent derived and reflected issues of relevance to parents. Thereafter, these items were reduced by using the clinical impact method because it has been shown to be superior to the alternative psychometric method for disease- and symptom-specific QoL tools.^{11,19} This method is also consistent with previous validated cough-specific QoL tools in children and adults.^{10,15}

We then examined the properties of our 16-item PAC-QoL tool by comparing responses with previously validated cough severity scores and generic adult QoL instruments (the SF-8, STAI, and DASS₂₁) across 3 time points in parents of children with a current acute coughing illness. We found that the items for our PAC-QoL instrument had excellent internal consistency (ie, all items within the scale were shown to measure the same concept). Also, the PAC-QoL scores significantly correlated to subjective cough score measures and generic adult QoL measures (demonstrating construct validity) and were reproducible and sensitive to change over time; a significant difference was demonstrated when the child's cough resolved. Thus our new PAC-QoL instrument is a valid tool that measures what it is intended to measure, with consistent measurement over time. The findings from the present study endorse the 16-item PAC-QoL instrument as a reliable and valid measure specific to children's acute cough.

A validated acute cough QoL instrument for use in pediatrics is a necessary addition to our understanding of the impact and effects of acute cough on the parent, child, and family. Also, a validated and robust children's acute cough outcome measure is a valuable tool for the evaluation of future treatment and clinical research in children's acute cough, therefore contributing to improving the QoL of children with acute cough and their parents. A chronic cough-specific QoL measure^{11,12} has been shown to be a useful evaluation tool in clinical research studies (including randomized controlled trials) in children with chronic cough-dominated illnesses.²⁷⁻²⁹ Although there are other scales for measuring acute respiratory illness effects, such as the validated Canadian Acute Respiratory Illness and Flu Scale,¹⁴ this instrument is not specific to acute cough and has a large number of daily reported items not specifically relating to cough. An adult-based acute cough QoL tool¹⁷ exists, but because there are significant differences between adults and children, adult-specific QoL measures are not directly transferrable to pediatric research.³⁰ Parental QoL assessments are relevant because parents themselves are affected by their child's medical condition and become proxy assessors for their young children who are unable to adequately verbally express themselves.

Similar to the existing children's chronic cough^{11,12} and pediatric asthma⁹ QoL instruments, PAC-QoL items reflect both worry and frequency of parental concerns and can be reliably divided into the domains of physical, social, and emotional concerns. Twelve of the 16 items of greatest impact relate to the physical domain, reflecting the acute physical nature of this common problem, in contrast to the equal numbers of physical and emotional items within the children's chronic cough QoL.^{11,12} This suggests that the extent of emotional impact might increase as cough persists and highlights an area for future research.

Our findings are limited by several factors. First, we did not use an objective measure, such as a cough counter. In the absence of a

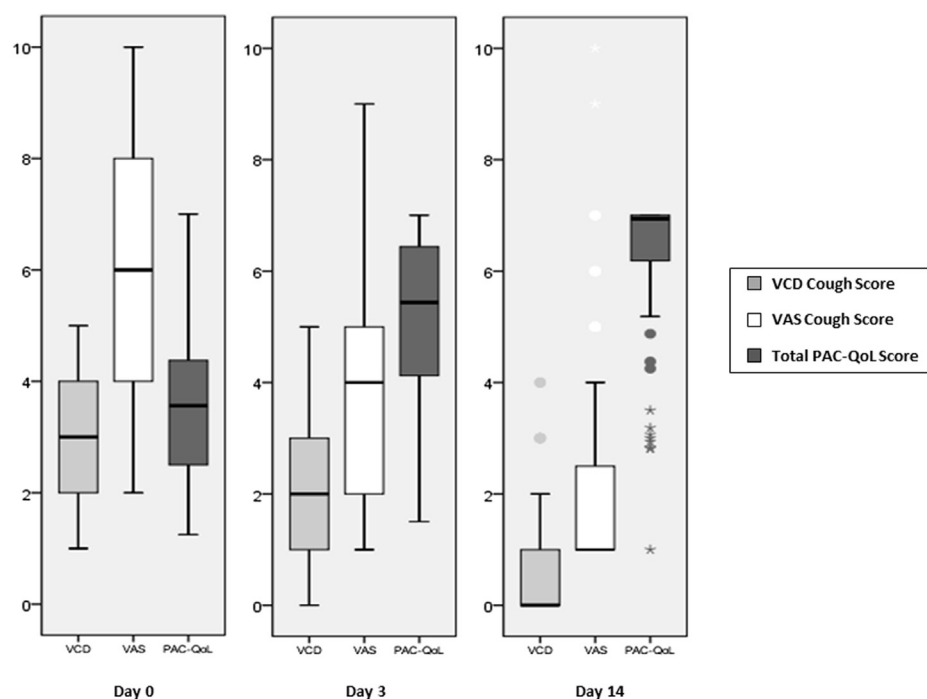


FIG 1. Median total PAC-QoL scores and 2 cough scores across 3 time points. Higher scores on the PAC-QoL questionnaire reflect better QoL. Higher VCD cough scores represent greater interference with usual activities. Higher VAS cough scores represent greater trouble with the cough.

TABLE IV. Clinical impact total and domain scores and cough measures at enrollment and day 14 grouped according to whether children were or were not still coughing at day 14 (n = 106)*

PAC-QoL score	Still coughing at day 14		P value†
	No	Yes	
Physical domain			
Enrollment	3.77 (2.45-4.82)	3.64 (2.43-4.48)	.47
Day 14	6.42 (6.42-6.42)	5.58 (4.27-6.25)	.0001
Social domain			
Enrollment	4.33 (3.00-5.33)	3.67 (2.25-4.67)	.06
Day 14	7.00 (7.00-7.00)	6.33 (5.33-7.00)	.0001
Emotional domain			
Enrollment	4.00 (2.50-5.00)	3.25 (2.50-4.13)	.18
Day 14	7.00 (7.00-7.00)	5.57 (4.50-7.00)	.0001
Clinical impact total			
Enrollment	4.06 (2.52-4.98)	3.53 (2.58-4.47)	.25
Day 14	7.00 (6.95-7.00)	6.09 (4.75-6.88)	.0001
VCD cough score			
Enrollment	3 (2-4)	3 (2-4)	.52
Day 14	0 (0-0)	1 (1-3)	.0001
VAS cough score			
Enrollment	5.5 (4-7.75)	6 (4-7)	.74
Day 14	1 (1-1)	3 (2-5)	.0001

Higher scores on the PAC-QoL questionnaire reflect better QoL. Higher VCD cough scores represent greater interference with usual activities. Higher VAS cough scores represent greater trouble with the cough.

*Values are presented as medians (IQRs), unless otherwise indicated.

†Mann-Whitney U test.

commercial cough counter for children and the large number of children tested in our study, use of cough counters was not feasible. However, cough counters measure cough frequency but

not cough impact, which is a more important patient-oriented outcome.

Second, only 7 children were aged greater than 12 years. Older children's perceived burden might be different to the burden felt by their parents, and thus the PAC-QoL questionnaire is a parent-proxy tool and not a child-answered QoL questionnaire. Because of the young median age of our sample, our findings are likely most representative of parents with young children. A supplemental questionnaire from the perspective of the older child is an avenue for future research.

Third, recruitment from emergency departments and the relatively long recruitment period might have biased our results. However, sampling across seasons arguably also improves generalizability.

Finally, although we have shown that the PAC-QoL instrument fulfills the criteria of a validated QoL measure for use in pediatrics, a second data set is required to confirm the reliability, validity, and MID of this instrument.

The clinical usefulness of the PAC-QoL instrument is evident as a valid and reliable patient-relevant outcome measure for evaluating interventions in much-needed clinical research in children with acute cough. QoL measures are also being increasingly used in policy-making and funding decisions. We have shown the PAC-QoL instrument to be a valid and robust measure, which can be completed quickly and easily by parents. Further research to confirm its reliability with a second data set and specific relationship to an objective cough measure would strengthen the validity of this clinical research tool.

We thank the parents and children who participated in this study. We also thank Samantha Gardiner, Joanne Tuppin, and Helen Petsky for their assistance with data collection.

Key messages

- The burden to families of children with acute cough is demonstrated by frequent medical presentations and high use of over-the-counter medications.
- Measuring QoL is important for the understanding of the burden of illness and evaluating interventions in clinical research relating to acute cough in children.
- The 16-item PAC-QoL questionnaire is a valid, reliable, and responsive tool that measures the burden of acute cough in children.

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METHODS

Methods of item reduction for the PAC-QoL questionnaire

The clinical impact method of item reduction, as outlined by Juniper et al,^{E1-E3} was used. This method includes ranking of items based on a product of the item mean (“importance”) and the proportion of respondents endorsing the item (“frequency”), arriving at an impact figure seen as a marker of the item’s disease-specific relevance. Parents either reported the item as “once in a while” or higher (frequency items) or as “a little worried/concerned” or higher (worry items) to be included in the proportion endorsing. The 48 items were then ranked according to the strength of their clinical impact (Table I). For analysis of clinical impact rank, draft PAC-QoL item scales were reverse scored so that higher numbers reflected greater frequency or worry. Based on an arbitrary cutoff at a natural break in ranked impact ratings, the 16 highest-impact items were selected. These items were endorsed with a reverse score of at least 3 from the 7-point response scale by greater than 75% of participants.

Participants

Parents of generally healthy children aged less than 18 years with an acute coughing illness (cough duration <2 weeks^{E4}) at presentation were recruited from the emergency departments of the Royal Children’s Hospital and Mater Children’s Hospital and community-based health centers in Brisbane, Australia, between September 2011 and September 2013. The exclusion criteria were as follows: hospitalized children; pneumonia; presence of physician-confirmed underlying chronic respiratory illnesses (eg, classical asthma defined as recurrent episodes of wheeze or dyspnea clinically responsive to salbutamol, cystic fibrosis, bronchiectasis, tracheomalacia, aspiration lung disease, and chronic neonatal lung disease); cerebral palsy or severe neurodevelopmental abnormality; congenital heart disease; or current treatment for any oncology condition.

Procedures

At enrollment, 1 parent of each child completed 2 validated subjective cough scores (cough VCD score and VAS score)^{E5} and the following 4 questionnaires: the 48-item PAC-QoL questionnaire, SF-8,^{E6} STAI,^{E7} and DASS₂₁.^{E8} The PAC-QoL questionnaire was administered by an interviewer (S.A.-J.), and the rest were self-completed. Clinical and demographic data were collected on standardized forms. All measures were repeated on days 3 and 14.

Description of materials

Cough diaries. Both the cough-scoring diaries were previously validated against an objective cough meter, and changes in this subjective cough rating have been shown to reflect changes in cough counts.^{E5} In the VCD parents rated their child’s cough on a 6-point scale (0 = no cough to 5 = severe cough and cannot perform activities), with higher scores reflecting greater interference with usual activities. In the VAS parents rated how troublesome their child’s cough was on a marked scale of 1 to 10, with 10 representing the presence of the most severe troublesome cough and 1 representing the absence of cough.

SF-8. A shortened version of the 36-item Short Form Health Survey, the SF-8, provides a single item for each of the 8 domains: physical functioning, role limitations as a result of physical health problems, role limitations as a result of emotional problems, mental health, bodily pain, general health perceptions, vitality, and social functioning.^{E6} Higher scores reflect greater burden and worse health states.

STAI. The STAI is considered the definitive instrument for measuring anxiety in adults, comprising two 20-item scales.^{E7} The STAI clearly differentiates between the temporary condition of “state anxiety” and the more general and long-standing quality of “trait anxiety.” The essential qualities evaluated by the STAI anxiety scale are feelings of apprehension, tension, nervousness, and worry. Higher scores reflect greater severity.

DASS₂₁. This self-report scale measures the domains of depression, anxiety, and stress.^{E8} Seven items explore each of these domains, and

participants respond to each item on a 4-point severity scale from 0 (“did not apply to me”) to 3 (“applied to me very much or most of the time”). Higher scores reflect greater severity. The DASS₂₁ has been shown to be a reliable and valid measure and is reported to be easier to use in clinical settings than the 42-item version of the depression anxiety stress scale.^{E8} In the present study the DASS₂₁ has been modified to a 24-hour reference time point.

MID

Distribution-based methods for calculating MIDs link meaningful change to the statistical characteristics, most commonly the effect size,^{E9} the standard error of measurement,^{E10} and the SD^{E11} of the scale. The effect size represents a standardized measure of change and is found by dividing the difference between pretest and posttest scores by the SD at pretest. The standard error of measurement is calculated as the SD of a measure multiplied by the square root of 1 minus its reliability coefficient. It is not sample dependent because the algorithm includes the sample’s reliability and variability. Recent research indicates that one-half SD might also signify an MID.^{E12}

The anchor-based method examined changes in scores over time against changes in an external but meaningful anchor.^{E13} In this study cough severity measured by using the VCD score. Change in domain scores, as well as overall PAC-QoL questionnaire scores for each participant, were calculated as differences in scores across the time interval (days 0-3). Cough was classified as unchanged if the change in VCD cough score was 0. A small change in the VCD cough score, which was defined as an absolute change in VCD score of 1, was considered equivalent to an MID. An absolute change in VCD score of 2 was considered a moderate change, and an absolute change in VCD score of 3 or greater was considered a large change. This classification system is based on an MID of a noticeable difference and follows previous research.^{E13,E14} The mean PAC-QoL questionnaire score for participants in the small-change group was determined to be an estimate of the MID. A combination approach, combining both distribution and anchor-based approaches,^{E15,E16} was chosen as the most plausible estimate of the MID.

Sample size estimation

Based on the item reduction and validation of the children’s chronic cough PC-QoL,^{E17,E18} a minimum of 60 participants with complete follow-up data at day 14 were required for analysis by using the clinical impact method. Our sample size calculation was based on a medium effect size (ie, time 1-time 2: $r = 0.3$), an α value of 0.05, and a power of 80%. This effect size is considered equivalent to a “noticeable difference,”^{E19} and as such, would be of clinical significance. On the basis of these criteria, a minimum of 60 participants was required to limit type II error.

RESULTS

Demographics

The median duration of current cough was 3 days (IQR, 2-5 days). The median parent-reported cough VCD score was 3 (IQR, 2-4), and the median cough VAS score was 6 (IQR, 4-8). Other parent-reported symptoms at enrollment included runny nose ($n = 126$ [81.3%]), wheeze or whistle ($n = 96$ [61.9%]), fever ($n = 109$ [70.3%]), shortness of breath ($n = 97$ [62.6%]), inability to play or exercise ($n = 84$ [54.2%]), irritability ($n = 107$ [69%]), tiredness ($n = 128$ [82.6%]), unsettled night ($n = 133$ [85.8%]), missed school or child care ($n = 73$ [47.1%]), and sore throat ($n = 66$ [42.6%]). Thirty-five children were school-aged, 75 regularly attended child care, and 45 did not attend child care. One hundred twelve (72.3%) of the participating families had more than 1 child. All parents were English speaking and were of varied socioeconomic status.

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TABLE E1. Calculation of the MID using the distribution-based method^{E9-E11}

Sample statistic	Time 1 (day 0)					Time 2 (day 3)				
	VCD	Total PAC-QoL	Physical	Social	Emotional	VCD	Total PAC-QoL	Physical	Social	Emotional
Mean	3.22	3.80	3.78	3.98	3.66	2.29	5.06	4.61	5.27	4.91
SD	1.08	1.48	1.56	1.57	1.59	1.13	1.56	1.47	1.55	1.77
Cronbach α		0.96	0.95	0.78	0.74					
MID calculations										
Effect size		0.85	0.53	0.82	0.79					
SEM		0.30	0.35	0.74	0.81					
One-half SD		0.74	0.78	0.79	0.80					
One-third SD		0.49	0.52	0.52	0.53					

Distribution characteristics of the VCD (range, 0-5) and PAC-QoL questionnaire (range, 1-7) at time 1 and time 2, along with estimates of distribution-based measures of the MID (n = 108 with repeated measures at day 3).

SEM, Standard error of measurement.

TABLE E2. Calculation of the MID using the anchor-based method (mean change [SD], effect size)^{E13}

QoL scale	VCD score change rating (day 3 – day 0)			
	No change, 0 (n = 26)	Small change, ± 1 (n = 41)	Moderate change, ± 2 (n = 30)	Large change, ± 3 (n = 11)
Total PAC-QoL	0.81 (1.22), 0.49	1.18 (1.26), 0.98	1.23 (1.33), 0.71	2.67 (1.66), 2.34
Physical	0.38 (1.32), 0.22	0.76 (1.21), 0.61	0.79 (1.34), 0.43	2.28 (1.50), 1.98
Social	0.73 (1.14), 0.43	1.37 (1.67), 0.93	1.21 (1.31), 0.72	2.58 (2.05), 2.21
Emotional	1.04 (1.41), 0.59	0.97 (1.68), 0.63	1.40 (1.52), 0.86	2.36 (2.23), 1.69

Changes in total PAC-QoL questionnaire and domain scores against changes in VCD cough score ratings were used for the anchor-based approach to MID. A small change in VCD score was considered equivalent to an MID.