

## Validation of a health-related quality of life instrument for primary ciliary dyskinesia: QOL-PCD

Laura Behan, Margaret W Leigh, Sharon D Dell, Audrey Dunn Galvin, Alexandra L. Quittner, Jane S Lucas.

### On line data supplement

#### Methods

#### Materials

At 'baseline' participants completed the prototype adult version of QOL-PCD questionnaire. QOL-PCD was designed to elicit the participant's opinion of his/her health, not someone else's opinion of it, so family, friends or members of staff should not influence the participant's responses; the questionnaires are designed for self-administration. On completion of the questionnaires, the participant was asked to ensure a response had been given to every question. They were also reminded to contact the study team if they have an exacerbation so that they can complete the form whilst unwell.

They also completed a demographic questionnaire and validated generic questionnaires.

Instructions for completion of questionnaires was provided. The generic questionnaires were:

1. The Short-Form 36 Health Survey (SF-36) was derived from the Medical Outcome Study (1), an observational study that began in 1986 among subjects with cardiac impairment. It is a 36-item self-administered questionnaire that includes eight scales, four of which relate to physical health: physical functioning, physical role limitation, bodily pain and general health perception (2). The remaining four scales are related to mental health: emotional role limitation, mental health, social functioning and vitality. Each scale is scored from 0-100. A score of 100 in physical functioning, role physical, bodily pain, social functioning and role emotion indicate the absence of limitations. In general health, mental health and vitality, the best health corresponds to a score of 50. These eight scales provide two component summary scores: mental component summary (MCS) and physical component summary (PCS) in which normal score is  $50 \pm 10$ .
2. The SNOT-20 is a validated disease-specific health-related quality-of-life measure for rhinosinusitis that consists of 20 items, with each item measured on an ordinal Likert scale from 0 to 5. Higher scores indicate worse symptoms. The first 12 items pertain to specific physical sinonasal symptoms including nasal symptoms (numbers 1–6) and ear or pressure symptoms (numbers 7–10). The final 10 items address more systemic and psychological symptoms, with question numbers 11 to 15 pertaining to sleeping difficulty (3).
3. The St George's Respiratory questionnaire-C (SGRQ-C) is a disease-specific instrument designed to measure impact on overall health, daily life, and perceived well-being in patients with obstructive airways disease. This is a shorter 40-item version of the SGRQ, which does not specify a recall period and has been validated specifically for COPD patients. It produces scores equivalent to the longer instrument and the minimally important difference is the same. (4)

Permission was obtained for use of these generic questionnaires where needed. Multi-trait analysis was used to develop the scales; the analyses of the prototype 49-item questionnaire are in

Supplementary Table E1 and the analyses of the final 40 item questionnaire are in the main document, Table 2.

### **Reliability**

For test-retest reliability, a subgroup of  $\geq 20$  participants were asked to repeat the PCD-QOL questionnaire after 10-14 days. They were required to be stable, based on no change in symptoms or change in medication. Participants were asked to contact the study team if they experienced an exacerbation. A respiratory system exacerbation was defined as respiratory tract symptoms leading to prescription of antibiotic treatment by a doctor consulted by the subject (visit at primary care physician or admission to another hospital), irrespective of results of bacterial culture.

### **Validity**

To assess construct validity, several hypotheses were tested. These hypotheses were developed *a priori* to minimise the risk of type 1 errors. For age, we hypothesised that Physical Functioning, Vitality and Upper and Lower Respiratory Symptoms would worsen in older age groups. For patients who have grown pseudomonas aeruginosa in the past, we predicted Physical Functioning and Upper and Lower Respiratory Symptoms would be associated with worse score. For FEV<sub>1</sub> % predicted, we predicted Physical Functioning, Lower Respiratory Symptoms scores would be more closely associated than Upper Respiratory Scores. For gender, we *a priori* examined differences in Social Functioning, Treatment Burden, and Lower Respiratory Symptom scores.

Convergent validity was assessed by calculating the correlation coefficients between relevant scales of QOL-PCD with the generic questionnaires. Validity was further assessed by examining relationships between scales of QOL-PCD and the generic questionnaire that were not measuring similar constructs (divergent validity).

### References for online supplementary file

1. Ware Jr JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Medical care*. 1992 Jun 1:473-83.
2. Maruish ME (2011) User's manual for the SF-36v2 Health Survey (3rd ed.). Lincoln, RI: QualityMetric Incorporated.
3. Meguro M, Barley EA, Spencer S, Jones PW. Development and validation of an improved, COPD-specific version of the St. George Respiratory Questionnaire. *CHEST Journal*. 2007 Aug 1;132(2):456-63.
4. Piccirillo JF, Merritt MG, Richards ML. Psychometric and clinimetric validity of the 20-item Sino-Nasal Outcome Test (SNOT-20). *Otolaryngology-head and neck surgery*. 2002 Jan 31;126(1):41-7.

Supplementary Table E1: Multi-trait analysis of 49 items from prototype version of QOL-PCD into conceptualised scales, item to scale correlations and Cronbach's alpha for each scale are reported: Physical Functioning, Emotional Functioning, Treatment Burden, Social Functioning, Role Functioning, Health Perception, Vitality, Upper Respiratory Symptoms, Lower Respiratory Symptoms and Ear and Hearing (n = 72, adults $\geq$ 18 years). Correlations between each item and its intended scale are shaded. These analyses informed the development of the 40 item QOL-PCD which underwent full psychometric analyses; the items that were deleted during this process\*\* are detailed in the footnote.

	<b>Physical</b>	<b>Emotional</b>	<b>Treatment</b>	<b>Social</b>	<b>Role</b>	<b>Health</b>	<b>Vitality</b>	<b>Upper Respiratory</b>	<b>Lower Respiratory</b>	<b>Hearing</b>
<b>Cronbach's <math>\alpha</math></b>	0.940	0.837	0.750	0.703	0.870	0.868	0.803	0.839	0.883	0.784
q1	0.795	0.604	0.563	0.642	0.691	0.749	0.572	0.430	0.758	0.517
q2	0.895	0.483	0.468	0.583	0.716	0.692	0.474	0.270	0.633	0.394
q3	0.876	0.492	0.468	0.557	0.607	0.683	0.575	0.257	0.673	0.361
q4	0.858	0.403	0.399	0.442	0.560	0.563	0.435	0.266	0.620	0.370
q5**	0.391	0.504	0.494	0.457	0.478	0.650	0.620	0.354	0.498	0.369
q6	0.468	0.669	0.534	0.413	0.426	0.612	0.76	0.390	0.497	0.341
q7	0.503	0.576	0.395	0.393	0.469	0.597	0.502	0.345	0.447	0.244
q8	0.391	0.431	0.409	0.519	0.506	0.638	0.541	0.277	0.388	0.369
q9	0.567	0.558	0.657	0.412	0.606	0.637	0.666	0.312	0.513	0.370
q10	0.416	0.711	0.423	0.479	0.420	0.519	0.440	0.334	0.496	0.346
q11	0.307	0.680	0.360	0.317	0.342	0.424	0.392	0.299	0.365	0.222
q12**	0.397	0.538	0.598	0.485	0.517	0.533	0.595	0.335	0.470	0.442

q13	0.399	0.34	0.386	0.377	0.635	0.493	0.223	0.275	0.341	0.179
q14	0.377	0.525	0.665	0.487	0.618	0.586	0.524	0.327	0.474	0.388
q15	0.303	0.51	0.643	0.322	0.419	0.429	0.571	0.398	0.415	0.382
q16	0.475	0.518	0.519	0.512	0.515	0.655	0.621	0.536	0.590	0.274
q17**	0.644	0.547	0.558	0.452	0.772	0.690	0.499	0.359	0.559	0.328
q18	0.245	0.254	0.285	0.485	0.324	0.481	0.311	0.102	0.192	0.049
q19	0.519	0.381	0.456	0.411	0.604	0.511	0.266	0.445	0.511	0.406
q20	0.414	0.694	0.480	0.408	0.395	0.528	0.409	0.433	0.416	0.370
q21	0.189	0.288	0.261	0.474	0.246	0.397	0.379	0.033	0.188	0.013
q22**	0.362	0.483	0.401	0.305	0.458	0.433	0.227	0.490	0.466	0.251
q23	0.407	0.214	0.183	0.494	0.385	0.441	0.323	0.120	0.159	0.262
q24	0.674	0.454	0.645	0.647	0.819	0.759	0.542	0.355	0.589	0.373
q25**	0.516	0.580	0.633	0.621	0.686	0.655	0.579	0.338	0.568	0.277
q26	0.682	0.568	0.629	0.671	0.836	0.775	0.537	0.429	0.587	0.420
q27	0.758	0.645	0.652	0.623	0.769	0.737	0.640	0.450	0.695	0.432
q28	0.541	0.534	0.543	0.667	0.633	0.611	0.528	0.387	0.462	0.240
q29	0.529	0.554	0.471	0.585	0.682	0.634	0.474	0.408	0.650	0.409
q30	0.640	0.611	0.639	0.679	0.720	0.830	0.672	0.315	0.565	0.414
q31	0.372	0.614	0.473	0.357	0.427	0.528	0.591	0.469	0.521	0.403
q32	0.639	0.505	0.528	0.581	0.596	0.670	0.602	0.357	0.649	0.394

q33	0.483	0.479	0.464	0.451	0.489	0.550	0.377	0.509	0.71	0.431
q34**	0.217	0.163	0.183	0.135	0.087	0.243	0.231	0.297	0.443	0.252
q35	0.452	0.520	0.397	0.359	0.446	0.509	0.467	0.423	0.567	0.669
q36	0.281	0.299	0.276	0.297	0.295	0.324	0.204	0.656	0.418	0.292
q37	0.238	0.453	0.490	0.302	0.402	0.448	0.372	0.719	0.457	0.431
q38	0.515	0.460	0.426	0.391	0.541	0.530	0.414	0.503	0.655	0.418
q39	0.317	0.064	0.266	0.331	0.343	0.322	0.151	0.242	0.411	0.264
q40	0.362	0.259	0.346	0.464	0.371	0.441	0.321	0.263	0.523	0.289
q41**	0.528	0.490	0.483	0.429	0.446	0.526	0.319	0.470	0.569	0.266
q42	0.802	0.479	0.570	0.551	0.760	0.739	0.527	0.424	0.693	0.447
q43	0.487	0.479	0.392	0.403	0.438	0.460	0.406	0.497	0.668	0.503
q44	0.213	0.317	0.295	0.241	0.276	0.302	0.289	0.599	0.335	0.311
q45**	0.630	0.548	0.559	0.471	0.624	0.640	0.556	0.396	0.701	0.421
q46	0.745	0.609	0.511	0.528	0.632	0.695	0.538	0.499	0.74	0.426
q47**	0.409	0.561	0.575	0.444	0.451	0.578	0.407	0.516	0.620	0.288
q48	0.371	0.289	0.326	0.241	0.307	0.317	0.281	0.416	0.402	0.669
q49	0.219	0.344	0.412	0.336	0.360	0.382	0.271	0.747	0.451	0.467

**Supplementary Table E2:** Multi-trait analysis of QOL-PCD scales showing item to scale correlations: Physical Functioning, Emotional Functioning, Treatment Burden, Social Functioning, Role Functioning, Health Perception, Vitality, Upper Respiratory Symptoms, Lower Respiratory symptoms and Ear and Hearing Symptoms (n = 72, adults $\geq$ 18 years). We required item to scale correlations  $\geq$ 0.40 with the intended scale (shaded) and much lower correlations with the competing scales.

	Physical	Emotional	Treatment	Social	Role	Health	Vitality	Upper Respiratory	Lower Respiratory	Hearing
Physical 1	0.880	0.502	0.463	0.408	0.705	0.728	0.527	0.387	0.715	0.474
Physical 2	0.873	0.471	0.445	0.393	0.762	0.688	0.465	0.243	0.542	0.364
Physical 3	0.863	0.445	0.424	0.328	0.629	0.672	0.508	0.229	0.590	0.315
Physical 4	0.801	0.323	0.315	0.266	0.562	0.528	0.371	0.154	0.461	0.359
Physical 5	0.906	0.515	0.573	0.196	0.742	0.711	0.471	0.430	0.659	0.395
Emotional 1	0.495	0.766	0.343	0.247	0.523	0.623	0.514	0.299	0.402	0.239
Emotional 2	0.428	0.782	0.281	0.316	0.408	0.466	0.374	0.267	0.453	0.300
Emotional 3	0.309	0.723	0.281	0.121	0.361	0.452	0.390	0.265	0.273	0.196
Emotional 4	0.307	0.629	0.366	0.220	0.404	0.450	0.295	0.368	0.306	0.345
Emotional 5	0.418	0.757	0.444	0.161	0.416	0.527	0.539	0.471	0.512	0.330
Treatment 1	0.397	0.198	0.598	0.137	0.542	0.497	0.244	0.217	0.259	0.164

Treatment 2	0.423	0.330	0.805	0.236	0.527	0.550	0.409	0.288	0.414	0.333
Treatment 3	0.280	0.308	0.730	0.211	0.407	0.312	0.462	0.381	0.318	0.313
Treatment 4	0.368	0.505	0.736	0.262	0.522	0.596	0.628	0.445	0.472	0.239
Social 1	0.273	0.161	0.284	0.814	0.357	0.452	0.324	0.055	0.286	0.055
Social 2	0.151	0.231	0.220	0.861	0.185	0.306	0.367	0.015	0.138	-0.006
Social 3	0.431	0.206	0.157	0.710	0.447	0.364	0.327	0.100	0.193	0.250
Role 1	0.562	0.336	0.434	0.204	0.731	0.431	0.225	0.432	0.498	0.389
Role 2	0.741	0.508	0.668	0.305	0.868	0.774	0.594	0.359	0.535	0.354
Role 3	0.647	0.493	0.588	0.406	0.899	0.751	0.521	0.382	0.541	0.417
Role 4	0.717	0.548	0.598	0.314	0.812	0.746	0.629	0.372	0.664	0.395
Health 1	0.529	0.506	0.563	0.541	0.628	0.808	0.580	0.328	0.427	0.263
Health 2	0.608	0.563	0.435	0.293	0.686	0.784	0.442	0.388	0.666	0.386
Health 3	0.697	0.642	0.662	0.391	0.725	0.923	0.678	0.307	0.585	0.396
Health 4	0.704	0.524	0.560	0.301	0.582	0.781	0.653	0.364	0.628	0.386
Vitality 1	0.577	0.576	0.458	0.382	0.394	0.533	0.893	0.337	0.410	0.269

Vitality 2	0.681	0.377	0.428	0.400	0.549	0.647	0.749	0.271	0.463	0.396
Vitality 3	0.354	0.526	0.618	0.240	0.526	0.594	0.836	0.322	0.380	0.290
Upper Resp 1	0.311	0.316	0.274	0.041	0.366	0.307	0.221	0.836	0.484	0.281
Upper Resp 2	0.315	0.406	0.462	0.085	0.402	0.373	0.352	0.827	0.452	0.439
Upper Resp 3	0.210	0.322	0.227	-0.074	0.321	0.222	0.267	0.762	0.374	0.287
Upper Resp 4	0.249	0.342	0.366	0.129	0.347	0.380	0.288	0.821	0.456	0.470
Lower Resp 1	0.513	0.428	0.467	0.194	0.543	0.599	0.391	0.472	0.821	0.429
Lower Resp 2	0.463	0.460	0.380	0.079	0.522	0.501	0.362	0.507	0.717	0.414
Lower Resp 3	0.343	0.127	0.323	0.162	0.400	0.352	0.230	0.250	0.649	0.267
Lower Resp 4	0.367	0.240	0.314	0.351	0.336	0.458	0.298	0.281	0.679	0.286
Lower Resp 5	0.461	0.488	0.355	0.144	0.443	0.452	.346	0.503	0.751	0.496
Lower Resp 6	0.711*	0.546	0.490	0.263	0.615	0.643	0.467	0.455	0.694	0.448
Ear and Hear 1	0.416	0.415	0.315	0.107	0.443	0.478	0.424	0.434	0.538	0.931
Ear and Hear 2	0.364	0.232	0.292	0.073	0.357	0.289	0.221	0.408	0.435	0.886

\* item correlation with competing scale higher than its correlation with its own scale.



Footnote: Reasons for deleting items\*\*

**Item**

- Q5: You felt well
- Q12: You were frustrated about doing your treatment
- Q17: I have to stay home more than I want to
- Q22: It is difficult to be intimate with a partner (kissing, hugging, sexual activity)
- Q25: How often were you absent from work, school, or unable to complete daily activities because of your illness or treatments?
- Q34: You coughed during the day
- Q41: You had trouble sleeping because of coughing
- Q45: Your chest hurt
- Q47: You had trouble sleeping due to congestion

**Reason for removing item**

- Overlap with Q30. Endorsement better in Q30
- Poor endorsement alpha not affected by removal.
- Did not fit with a conceptual scale, Endorsement <20%
- Did not fit with a conceptual scale, endorsement <20%
- Low endorsement <20% and multiple cross-loadings
- Similar questions more discriminatory, did not improve conceptual scale.
- Did not fit with a conceptual scale, endorsement <20%
- Low endorsement <20%
- Low endorsement <20% and did not fit with a conceptual scale,

**Supplementary Table E3:** Responsiveness to change was measured, paired t-tests compared scores (SD) for each scale in 10 patients who completed QOL-PCD whilst stable and during an exacerbation.

	<b>Stable</b>	<b>Exacerbation</b>	<b>Mean Difference</b>	<b>P-value</b>
			<b>(95% CI)</b>	
<b>Physical</b>	41.33 (37.55)	26.00 (34.20)	15.33 (1.47-29.20)	0.03
<b>Emotional</b>	67.33 (27.12)	63.33 (23.63)	4.00 (-6.35-14.35)	0.41
<b>Treatment</b>	49.16 (26.77)	39.16 (23.58)	10.00 (0.05-20.05)	0.05
<b>Social</b>	38.88 (26.31)	43.33 (21.24)	-4.44 (-20.42-11.54)	0.54
<b>Role</b>	45.83 (36.05)	31.66(30.63)	14.16 (4.41-23.92)	0.01
<b>Health</b>	38.33 (27.8)	27.50 (20.80)	10.83 (20.58-1.08)	0.03

<b>Vitality</b>	45.55 (25.89)	27.77 (22.98)	17.77 (3.66-31.91)	0.02
<b>Upper respiratory</b>	45.83 (22.65)	36.66 (26.11)	9.16 (0.34-18.67)	0.05
<b>Lower respiratory</b>	38.88 (24.14)	28.33 (19.67)	10.56 (0.74-20.37)	0.03
<b>Ears and Hearing</b>	41.66 (29.65)	43.33 (28.54)	-1.66 (-14.78 - -11.45)	0.78