

# Increasing the interpretability of a patient-reported outcomes questionnaire using a mixed methods design: an example in a rare cardiac clinical trial

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## Background

- The Kansas City Cardiomyopathy Questionnaire (KCCQ), a self-administered Patient-Reported Outcomes questionnaire, was selected to measure the health status of patients in a clinical trial.
- The clinical trial was performed in the US and the UK in patients with a rare cardiac disease.
- Given that the KCCQ was originally developed to assess health status in patients with congestive heart failure<sup>1</sup>, it was necessary to check its appropriateness in the current target population.

## Aims

- To validate the Kansas City Cardiomyopathy Questionnaire (KCCQ) in the rare cardiac disease population:
  - Qualitative assessment: content validity documentation
  - Quantitative assessment: preliminary psychometric validation.
- To use mixed method research to support content validity documentation and, in particular, clarify some results of the quantitative component.

## Methods

- Given the scarcity of the target population, the qualitative and quantitative assessments were performed simultaneously.
- The description of KCCQ is presented in Table 1.

**Table 1: Kansas City Cardiomyopathy Questionnaire (KCCQ) description**

Property	Description
<b>Objective</b>	To measure health status in patients with congestive heart failure
<b>Number of items</b>	23
<b>Administration mode</b>	Self-administered
<b>Data collection mode in the study</b>	Paper and pen
<b>Recall period</b>	Over the past two weeks
<b>Domains covered (number of items)</b>	Physical limitations (6); Symptoms stability (1); Symptom frequency (4); Symptom burden (3); Self-efficacy (2); Quality of life (3); Social limitation (4)
<b>KCCQ scores</b>	<ul style="list-style-type: none"> <li>• Sub-scores:                             <ul style="list-style-type: none"> <li>- Available for each domain</li> <li>- Ranging from 0-100. Higher score indicating better health status</li> </ul> </li> <li>• Overall summary score: derived from physical function, symptom (frequency and severity), social function and quality of life domains</li> <li>• Functional status score: combination of physical limitation and symptom domains (excluding symptom stability)</li> <li>• Clinical summary score: combination functional status with quality of life and social limitation domains</li> </ul>

### Qualitative component:

- Cognitive debriefing interviews were conducted with a subgroup of patients who participated in the clinical trial at the end of the trial to assess their comprehension of the KCCQ and its relevance by:
  - Ensuring that the items within the KCCQ cover the aspects of the concept aimed to be measured.
  - Verifying the acceptability of the KCCQ by patients.
  - Collecting feedback from patients on each question of the KCCQ (i.e. perceived patient interpretation of each question, misunderstandings related to any questions and any proposed reformulations of questions put forward by patients).
- Interviews followed a "think-aloud" approach<sup>2</sup>, i.e. patients were asked to report aloud their thinking process when answering the KCCQ questions.
- Interviews were conducted by a trained interviewer using an interview guide specifically developed for the study.
- Patients were asked questions about the instructions, questions, response options and recall period of the KCCQ.
- The following information was extracted into an Excel grid: patients' responses, patients' understanding of the items, patients' assessment of the relevance of the items, and any additional issues mentioned by patients.
- The information in the grid underwent categorical analysis.

### Quantitative component:

- All patients who participated in the clinical trial completed the KCCQ.
- A descriptive analysis of the KCCQ items and domain scores was performed:
  - Quality of completion of the KCCQ: to investigate item properties and the questionnaire's acceptance.
  - Description of the KCCQ domain scores: to investigate distributional properties of the scores.
- A preliminary psychometric analysis was performed, including:
  - Construct validity: to generate evidence that relationships among items, domains and concepts conform to a priori hypotheses concerning logical relationships that should exist with other measures or characteristics of patients and patient groups.
  - Internal consistency reliability: to investigate the degree to which items within a dimension are consistent with each other and measure a single underlying concept.

### Mixed methods research:

- Mixed methods research can be defined as "research in which the investigator collects and analyses data, integrates the findings and draws inferences using both qualitative and quantitative approaches or methods in a single study or program of inquiry."<sup>3</sup>
- Mixed methods research was used to triangulate qualitative and quantitative findings.

## Conclusion

- The qualitative analysis demonstrated that the KCCQ had good content validity in the intended cardiac disease population.
- The quantitative analysis demonstrated that the KCCQ was broadly acceptable but had some limitations in the target population. In particular, ceiling effects were identified for several items.
- Using a convergent design helped explain the causes of some of these ceiling effects and helped improve the use and the interpretation of the KCCQ's results in the clinical trial.

## Results

### Description of study sample:

- Twelve patients completed the cognitive debriefing interviews. Twenty-six patients (inclusive of the twelve interviewed patients) completed the questionnaire.
- The description of demographic characteristics of the two samples is presented in Table 2.

**Table 2. Description of the study samples who were included in the qualitative assessment and the quantitative assessment**

Demographic characteristic	Cognitive debriefing sample (n = 12)	Questionnaire completion sample (n = 26)
<b>Age (Years)</b>	Median	68.5
	Min - Max	60.0 - 78.0
<b>Gender [n(%)]</b>	Male / Female	11 (91.7) / 1 (0.08)
		23 (88.5) / 3 (11.5)
<b>Country of origin [n(%)]</b>	USA / UK	4 (33.3) / 8 (66.6)
		16 (61.5) / 10 (38.5)

### Qualitative results:

- The KCCQ covered all themes patients with rare cardiac disease deemed important.
- Item 3, about swelling in feet, legs or ankles in the morning, was considered irrelevant by patients because the symptom occurred in the evening.
- Patients found the recall period (the past two weeks) too short and not always adapted to the study context.

### Quantitative results:

- Overall, the KCCQ had good distributional properties.
- Some items had a ceiling effect:
  - Item 3: "Over the past 2 weeks, how many times did you have swelling in your feet, ankles or legs when you woke up in the morning?"
  - Item 4: "Over the past 2 weeks, how much has swelling in your feet, ankles or legs bothered you?"
  - Item 7: "Over the past 2 weeks, on average, how many times has shortness of breath limited your ability to do what you wanted?"
  - Item 9: "Over the past 2 weeks, on average, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of shortness of breath?"
  - Item 10: "Heart failure can worsen for a number of reasons. How sure are you that you know what to do, or whom to call, if your heart failure gets worse?"
  - Item 15C: "How much does your heart failure affect your lifestyle? Please indicate how your heart failure may have limited your participation in the following activities over the past 2 weeks – visiting family or friends out of your home."
- Excellent results for quality of completion:
  - No missing items per patient and no missing data per patient.
- Good internal consistency reliability for five KCCQ domain scores out of nine with Cronbach's alpha coefficients above the recommended 0.70 threshold for good reliability<sup>4</sup>:
  - Physical limitation (0.73); Quality of life (0.84); Social limitation (0.79); Overall summary (0.90) and Clinical summary (0.80)
- The construct validity of the KCCQ was confirmed:
  - Moderate to high correlations between the KCCQ domain scores and EQ-5D VAS score (except for the 'Symptom stability' score)
  - Moderate correlations between Karnofsky score and the 'Physical limitation', 'Social limitation' and 'Overall summary' scores
  - Expected trends for all KCCQ domain scores and EQ-5D items (lower score for the category 'Some problems' compared to 'No problem')
  - Expected trend for all KCCQ domain scores and NYHA classification (lower score along with higher class)

### Mixed methods results:

- Several of the items which showed a ceiling effect (items 3, 4, 7 and 9) could be interpreted using qualitative findings: the interpretative process is summarized in Figure 1.

**Figure 1. Mixed method research based on triangulation of qualitative and quantitative results: qualitative findings to help explain and/or clarify quantitative findings**

KCCQ Item	Quantitative results	Qualitative results	Mixed methods results
<b>Item 3</b> : Swelling in your feet, ankles or legs in the morning	Around 70% of patients answered they never had this symptom	During interviews, patients described this symptom as being a problem in the evenings	Patients understood the item but <b>timeframe is inappropriate</b>
<b>Item 4</b> : Swelling in feet, ankles or legs bothersome	Over 60% of patients answered that they were not bothered by swelling	During interviews, some patients <b>did not understand the term "bothered"</b>	Patients might have been bothered by swelling but <b>did not accurately understand the item</b>
<b>Item 7</b> : Shortness of breath limiting ability to do what patient wants	Over 40% of patients answered that shortness of breath never limited their ability and/or limited their ability less than once a week to do what they wanted	Two patients reported <b>changing their lifestyle</b> to avoid shortness of breath	Patients may not have experienced shortness of breath because they engaged in <b>avoidance behaviors</b>
<b>Item 9</b> : Forced to sleep sitting because of shortness of breath?	Over 80% of patients answered that they had never been forced to sleep sitting up because of shortness of breath	During the interviews, <b>no patients reported being affected</b> by this symptom	This symptom was <b>not relevant to patients</b>

### References

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