

## Methods for Creating Condition-Specific Questions<sup>1</sup>

Two basic approaches typically are taken to develop condition-specific questions for Patient-Reported Outcome (PRO) assessments of health:

- Condition attribution and
- Content-validity

The condition-attribution approach is to modify generic PRO questions<sup>2</sup> so that the respondent answers the item only with regard to the condition (Kantz et al., 1992; Ren, Kazis, Lee, & Rogers, 2005; Roland & Morris, 1983). Each item would have an attribution to the condition, for example, by containing the phrase “due to my knee” or “because of my sickle cell disease.” This approach has the advantage of being less costly because the condition-specific questions can be simple modifications of existing questionnaires and patient interviews are not required to generate the item topics or concepts.

According to the content-validity approach, a measure is condition specific when its items are based on aspects of functioning and well-being that persons with the condition have spontaneously offered in semistructured interviews or that are known features of the clinical presentation. That is, the content is condition specific because it has been reported by persons with the condition (de Boer, Wijker, Speelman, & de Haes, 1996; Duncan et al., 1999; Guyatt, Berman, Townsend, Pugsley & Chambers, 1987; Marks, Dunn, & Woolcock, 1992; Sprangers et al., 1996) or is prominent in a review of literature on the condition and endorsed by expert clinical judgment (Calne et al., 1996; Katz et al., 1963; Meenan, Gertman, & Mason, 1980; Wagner et al., 1995). However, the recent FDA draft guidelines (FDA, October 2006) on the development of PROs require that patient interviews be part of the development process, and it is no longer sufficient to rely on literature review or expert consensus alone.

Often condition-specific PRO measures include items generated by both methods either independently or in concert. This hybrid schema for the development of condition-specific PRO measure is comprehensive and multidimensional and the recognized standard for chronic diseases that have a far-reaching impact on the lives of their sufferers (Aaronson, Bullinger, & Ahmedzai, 1988; Vickrey, 1993; Wu et al., 2001).

One might ask why questions are included in the ASCQ-Me<sup>3</sup> that refer to the respondent’s *health* rather than to his or her *sickle cell disease (SCD)*. There are four major reasons:

1. To obtain content-valid content for the items

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<sup>2</sup> Also known as “health-related quality of life (HRQOL)” items or, alternatively, as questions about generic functioning, well-being, and symptoms.

<sup>3</sup> ASCQ-Me = Adult Sickle Cell Quality of Life Measurement Information System

2. To ensure that the previously undocumented effects of SCD on adult lives are more likely to be included in data collections and patient-provider communications
3. To communicate the significance of the ASCQ-Me scores to a variety of audiences
4. To enhance their potential utility to the construction of domain-specific item banks

## **Obtaining Content Valid Items**

The first reason for not attributing aspects of health to a specific condition or disease applies to diseases that are systemic and/or congenital (such as SCD). Persons who have SCD have never known what their functioning and well-being would be like without the disease—not having SCD is a hypothetical state to them. To answer respondents' questions about how much of their functioning and well-being is caused by SCD requires them to entertain a hypothetical state, that of not having SCD. The latest draft guidelines from the FDA state that PROs should not ask respondents to answer with regard to hypothetical states. The attribution technique works well for patients with very localized conditions, such as advanced osteoarthritis of the knee or hip, carpal-tunnel syndrome, or sinusitis, for which a therapy of known efficacy is described (e.g., total knee or hip replacement, carpal tunnel release, sinus surgery, respectively) (Dawson, Fitzpatrick, Murray, & Carr, 1996; Gliklich & Hilinski, 1995). By contrast, the ASCQ-Me is being designed for a condition that is systemic. Because SCD affects the blood, it can change the body at any place that blood travels. Thus, the effects of SCD are pervasive and varied and many may not be consciously attributable to SCD. This fact would compromise the validity of any respondent attribution to SCD.

## **Generating Items That Apply to Effects Not Yet Known or Well-Studied**

The second reason for not attributing aspects of health to a specific condition or disease applies to the measurement of HRQOL for those diseases and conditions for which there is not a complete understanding of health effects or the effects of existing or future treatment. The genesis of the ASCQ-Me project lay in the recognition that the clinical and research community does not understand the experience of adults with SCD and that there is a need for systematic documentation of this experience. If the ASCQ-Me were restricted to content that was known as attributable to SCD, it would be limited in its ability to detect unrecognized effects of the disease. Moreover, patients and scientists alike hope for the development of additional treatments for SCD. However, it is not currently known what the side-effect profile of future treatments might be. Unanticipated and unknown effects are more likely to be picked up if aspects of functioning and well-being are attributed to health, rather than to SCD.

## **Generating Items That Support Comparability between SCD and Other Chronic Conditions**

The third reason for not attributing aspects of health to a specific condition or disease applies to the measurement of HRQOL for all diseases and conditions. Questions referring to health can be answered by anyone, and this is important to the ability to interpret PRO data. Typical scores for

well persons and persons with other chronic diseases are necessary to understand the life burden of SCD.

The most conservative and scientifically defensible approach to developing a condition-specific PRO measure for SCD would be to:

1. Use the attribution approach for items referring to aspects of functioning and well-being that could be due to nothing else (e.g., severe pain episodes that require narcotic therapy with no possible cause external to the body—such as a blow to the head).
2. Address content validity by including all aspects of functioning and well-being that patients have mentioned in their interviews.

This hybrid approach capitalizes on the strengths of the different technologies that it embraces and does not expose the project to the weaknesses inherent in any one methodology.

## **Generating Items That Could Enhance the Utility of Domain-Specific Item Banks in Assessing Adults with Sickle Cell Disease**

When condition-specific questions are based on content mentioned by patients and not disease attributed, they could be of potential value in enhancing the generalizability of a domain-focused measurement system designed to be applied across conditions such as PROMIS. The new items, which are generated for a specific condition, may tap parts of the continuum for which there are currently few questions. For example, given that sickle cell pain is so severe, some of the items in the ASCQ-Me Pain Impact item bank might contribute to the extreme end of the continuum underlying the PROMIS Pain Interference item bank. It is possible to study whether they would do so because the questions were written to address SCD pain but not attributed to SCD.

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