How Do We Define a Meaningful Change in Quality of Life for Patients with Sarcoidosis?

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A key characteristic of any outcome metric—whether imaging, physiological, or patient reported—is validity. In lay-person's parlance, a metric has validity if it measures what it purports to measure. For example, consider forced vital capacity (FVC): We would all agree FVC is a valid measure of lung capacity among patients with interstitial lung disease (including sarcoidosis). Why? Because FVC correlates with other measures of lung capacity, such as the size of the lungs on chest imaging, and anthropometric measures closely tied to lung capacity, such as height. These correlations and other performance characteristics of FVC have convinced us that it is indeed a sound measure of lung capacity. We trust it; we know what it's telling us, and we have a good sense of what patients "look like" at a given FVC and, at least generally, what they are like if FVC changes (improves or declines) by a given amount.

An important aspect of a metric's validity centers on the meaning or implications of change. The minimal clinical important difference (MCID) is the smallest amount of change that is relevant to patients and would indicate the success or detriment of an intervention or warrant changes in the care plan (1). Without knowledge of a metric's MCID (or similar characteristics, such as responder thresholds), we are left to rely on statistical significance, which fails to provide any patient-centered context or relevance to the outcome and does little to bolster validity (2).

One outcome valued by people in the general population and patients alike is quality of life (QoL), an abstract construct, typically measured using questionnaires, that comprises an individual's perspective on the status of multiple dimensions of their lives (3). As with any other outcome, knowing the MCID for a questionnaire that assesses QoL is a key aspect of its validity, and, more importantly, it allows determination of whether a change in score (perhaps in response to an intervention) is clinically meaningful at the group level.

MCID estimates are typically triangulated using anchor- and distribution-based methods. In the anchor-based approach, change in the outcome of interest is compared with change in an "anchor"—another metric that either directly measures (e.g., a gold standard) or is closely linked to the construct of interest (4)—that correlates (0.3 or greater) with the metric under study and whose MCID has already been established (importantly, in the population of interest) (5). The distribution-based approach uses any number of calculations run on statistics for the metric of interest derived in the study cohort. This method is sometimes criticized because of its reliance on sample statistics alone without taking into account patients' perceptions (6).

In this issue of *AnnalsATS*, Baughman and colleagues (pp. 477–485) describe their study aimed at deriving the MCID for the Kings Sarcoidosis Questionnaire (KSQ) (7), a multidimensional instrument developed to assess QoL in sarcoidosis patients (8). The authors calculated MCIDs for two major domains of the KSQ (the general health and pulmonary-specific [KSQ lung] domains) and for a patient global assessment question. At the initial visit and 6-month follow up, participants completed the KSQ and questionnaires that have previously undergone validation testing in Sarcoidosis (St. George's Respiratory Questionnaire [SGRQ], the Short Form-36 [SF-36], and the Fatigue Assessment Score [FAS]). The MCID was calculated using anchor- and distribution-based methods: the SGRQ, SF-36, and FAS were anchors, and the investigators used the 0.5 standard deviation of baseline KSQ scores for their distribution-based method. The means and 90th percentiles for the MCIDs for improvement or worsening were calculated.

There were 321 patients with sarcoidosis in the study, with 83% (271) completing both study visits. More than 90% of patients had lung involvement. There were very weak (and not statistically significant) correlations between change in KSQ scores and change in any of the physiological parameters (FVC, forced expiratory volume in 1 second, and 6-minute walking distance), and, appropriately, none were used as anchors. Ultimately, triangulation of methods yielded the following MCID estimates (the same for improvement or worsening): KSQ general health = 8, KSQ lung = 4, and patient global assessment = 2.

We commend the authors for their work. This is a significant advancement of knowledge about QoL measurement in sarcoidosis. Study design, choice of anchors, and the analyses they performed were all appropriate. Like other investigators, they identified very weak correlations between KSQ scores and physiological (FVC) and functional (6-minute-walk test [6MWT]) measures of (lung) sarcoidosis severity; the weak correlations meant the investigators could not use either FVC or 6MWT as an anchor in their analyses. However, the absence of strong correlation between those measures and KSQ scores reassures us that the KSQ yields information about

DOI: 10.1513/AnnalsATS.202010-1241ED

sarcoidosis patients' experiences that FVC and 6MWT do not.

The KSQ was developed using sound methodology and is now available in several languages (9, 10). Despite this, it has yet to be enthusiastically adopted by the sarcoidosis research community (11), mainly because its MCID has yet to be established (12). This study provides a missing piece. However, as validation is a never-ending process, there is work to be done on the KSQ. Patients with any and all manifestations of sarcoidosis were included in the analysis. Although this is certainly appropriate (as even those without lung involvement can experience dyspnea or limitations in physical functioning) (13), the MCID estimates may not apply to a cohort with only lung involvement.

For any anchor-based MCID analysis, estimates of the MCID are only as good as the anchors selected and only as good as the MCID estimates for the anchors. The authors state the anchors they chose (the generic SF-36, the airway disease–specific SGRQ, and the fatigue-specific FAS) all have MCIDs of 4; however, these MCIDs are not specific to sarcoidosis and may not be applicable here. All distribution-based methods have been criticized because they depend on the patient population and conditions of the study, they ignore the patient perspective, and they do not distinguish between improvement and deterioration (14). These are challenges encountered by all researchers conducting such validity analyses.

Recognizing these challenges and the need for additional research on the KSQ in sarcoidosis, the authors have provided us with reasonable MCID values for the KSQ for a general sarcoidosis population. Moving forward, we believe it would be reasonable for other investigators to include it as an outcome in their studies of patients with sarcoidosis. Such data could be used to conduct additional analyses to further support the validity of the KSQ that the current study has built. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

References

1 McGlothlin AE, Lewis RJ. Minimal clinically important difference: defining what really matters to patients. *JAMA* 2014;312: 1342–1343.
2 Sedaghat AR. Understanding the Minimal Clinically Important Difference (MCID) of patient-reported outcome measures. *Otolaryngol Head Neck Surg* 2019;161:551–560.
3 The WHOQOL Group. The World Health Organization Quality of Life assessment (WHOQOL): position paper from the World Health Organization. *Soc Sci Med* 1995;41:1403–1409.
4 Rai SK, Yazdany J, Fortin PR, Aviña-Zubieta JA. Approaches for estimating minimal clinically important differences in systemic lupus erythematosus. *Arthritis Res Ther* 2015;17:143.
5 Revicki D, Hays RD, Cella D, Sloan J. Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. *J Clin Epidemiol* 2008;61:102–109.
6 Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. *Med Care* 2003;41:582–592.
7 Baughman RP, Judson MA, Beaumont JL, Maier LA, Sweiss NJ, Culver DA, *et al*. Evaluating the minimal clinically important difference of the King's Sarcoidosis Questionnaire in a multicenter prospective study. *Ann Am Thorac Soc* 2021;18:477–485.
8 Patel AS, Siegert RJ, Creamer D, Larkin G, Maher TM, Renzoni EA, *et al*. The development and validation of the King's Sarcoidosis Questionnaire for the assessment of health status. *Thorax* 2013;68: 57–65.
9 Farin E, Heyduck K, Frye BC, Birring SS, Müller-Quernheim J, Schupp JC. Translation and psychometric properties of the King's Sarcoidosis Questionnaire (KSQ) in German language. *Health Qual Life Outcomes* 2019;17:62.
10 Van Manen MJ, Wapenaar M, Strookappe B, Drent M, Elfferich M, de Vries J, *et al*. Validation of the King's Sarcoidosis Questionnaire (KSQ) in a Dutch sarcoidosis population. *Sarcoidosis Vasc Diffuse Lung Dis* 2016;33:75–82.
11 Baughman RP, Sweiss N, Keijsers R, Birring SS, Shipley R, Saketkoo LA, *et al*. Repository corticotropin for chronic pulmonary sarcoidosis. *Lung* 2017;195:313–322.
12 Judson MA, Mack M, Beaumont JL, Watt R, Barnathan ES, Victorson DE. Validation and important differences for the sarcoidosis assessment tool: a new patient-reported outcome measure. *Am J Respir Crit Care Med* 2015;191:786–795.
13 Baughman RP, Teirstein AS, Judson MA, Rossman MD, Yeager H Jr, Bresnitz EA, *et al*.; Case Control Etiologic Study of Sarcoidosis (ACCESS) research group. Clinical characteristics of patients in a case control study of sarcoidosis. *Am J Respir Crit Care Med* 2001; 164:1885–1889.
14 Wright A, Hannon J, Hegedus EJ, Kavchak AE. Clinimetrics corner: a closer look at the minimal clinically important difference (MCID). *J Manual Manip Ther* 2012;20:160–166.