

# Health-related Quality of Life—An Introduction

Dinesh Khanna, MD, MS; Joel Tsevat, MD, MPH

## Abstract

Chronic diseases often have a relapsing and remitting course with substantial impact on function and quality of life. Rheumatoid arthritis (RA) is considered a chronic, inflammatory autoimmune disorder that causes disabling and painful inflammation in the joints that can lead to detrimental effects on health-related quality of life (HRQOL). This article provides an overview of HRQOL and a comprehensive description of the attributes of different instruments to measure it. A wide variety of instruments have been created to measure HRQOL using 2 approaches: health status and health utility. Commonly used generic health status instruments in RA are the Medical Outcomes Study 36-Item Short Form (SF-36) and the Health Assessment Questionnaire Disability Index. Health utility measures are divided into 2 categories, direct and indirect. The most common direct health utility measures are the standard gamble, time to trade-off, and rating scale, while the most commonly used indirect measures are EuroQOL, SF-6D, and the Health Utility Index. Different applications of the instruments are analyzed in this article, including their utility to estimate burden of disease, as end points in clinical trials, and to monitor outcomes in clinical practice, as well as their uses in public policy and in individual decision making.

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Chronic diseases often have a relapsing and remitting course with substantial impact on function and quality of life (QOL). For chronic illnesses where there is no cure, it is important to establish that therapy really makes people feel better. Thus, survival per se is no longer perceived to be the only end point; the goal is to improve, restore, or preserve QOL. The World Health Organization (WHO) defines QOL as an “individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns”<sup>1</sup> It is a broad-ranging concept affected by an individual’s physical health, psychological state, level of independence, social relationships, and their relationship to salient features of their environment.<sup>1,2</sup> QOL encompasses the concept of health-related quality of life (HRQOL) and other domains such as environment, family, and work. HRQOL is the extent to which one’s usual or expected physical, emotional, and social well-being are affected by a medical condition or its treatment.<sup>3</sup> The HRQOL measurement therefore attempts to capture QOL in the context of one’s health and illness (Figure 1).<sup>4</sup>

## Assessing Quality of Life

There has been an ongoing interest in developing instruments that capture QOL. Currently, one of the most commonly used QOL instruments is the WHO Quality of Life (WHOQOL) instrument.<sup>5</sup> The WHOQOL-100 is a 100-item self-administered instrument representing 24 or 25 facets organized into 6 domains: physical, psychological, level of independence, social relationships, environment, and spirituality/religion/personal beliefs.

The WHOQOL-100 is designed to be applicable cross-culturally. During its development phase, the instrument was simultaneously developed in different cultures and languages by taking into account individuals’ beliefs and situations in life. Subsequent to that, the WHOQOL-BREF, a 26-item instrument, was derived from the WHOQOL-100.<sup>6</sup> Analysis of the WHOQOL-BREF items supports a 4-factor structure—the physical domain is merged with the level of independence domain, and the psychological domain is merged with the spirituality, religion, and personal beliefs domain. The WHOQOL-BREF contains 1 item from each of the 24 facets of QOL included in

**Address correspondence to:** Dinesh Khanna, MD, MS, Assistant Professor of Medicine, Division of Rheumatology, Department of Medicine, David Geffen School of Medicine, 1000 Veterans Avenue, Rm 32-59 Rehabilitation Building, Los Angeles, CA 90095. E-mail: dkhanna@mednet.ucla.edu.

the WHOQOL-100 plus 2 “benchmark” items from the general facet of overall QOL and general health (not included in the scoring).

**Assessing Health-related Quality of Life**

Work in HRQOL has originated from 2 fundamentally different approaches: health status and health value/preference/utility assessment<sup>7</sup> (Table 1 and Figure 2).<sup>8,9</sup> In general, health status measures describe a person’s functioning in 1 or more domains (eg, physical functioning or mental well-being). Currently, one of the most commonly used generic health status instruments (ie, the concepts are not specific for any age, disease, or treatment group) is the Medical Outcomes Study 36-Item Short Form (SF-36), a 36-item measure encompassing 8 domains—physical functioning, social functioning, mental health, role limitations due to physical problems, role limitations due to emotional problems, vitality (energy and fatigue), bodily pain, and general health perceptions—each of which is scored separately from 0 (worst) to 100 (best) (Table 2).<sup>10</sup> The SF-36 domains can be summarized into physical component summary and mental component summary scores. By comparison, the most commonly used disease-specific instrument in rheumatoid arthritis (RA) is the Health Assessment Questionnaire Disability Index (HAQ-DI)—a self-administered 20-question instrument that assesses a patient’s level of functional ability and includes questions on fine movements of the upper extremities, locomotor activities of the lower extremi-

■ **Figure 1. Quality of Life**



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ties, and activities that involve both the upper and lower extremities.<sup>11</sup> The HAQ-DI score is determined by summing the highest item score in each of the 8 domains and dividing the sum by 8, yielding a score ranging from 0 (no disability) to 3 (severe disability).

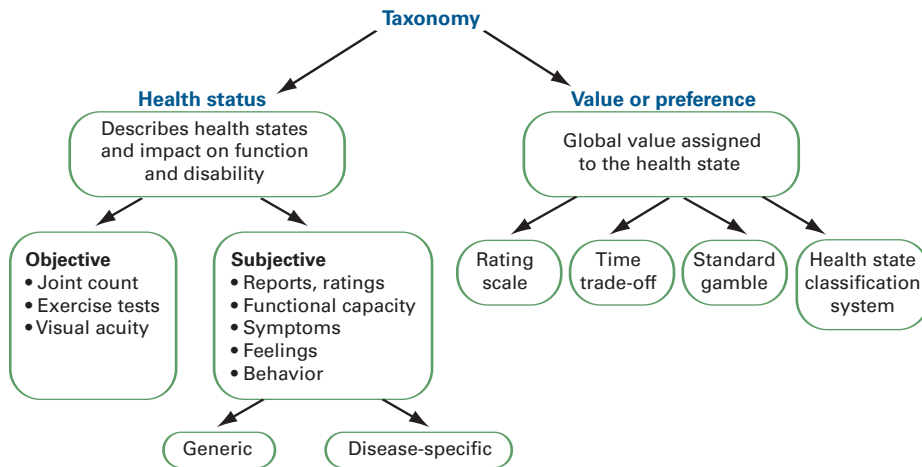
Health value/preference/utility measures, in contrast, assess the *value* or *desirability* of a state of health against an external metric,<sup>12</sup> are generic HRQOL measures, and summarize HRQOL as a single number. There are 2 major families of utility measures, direct and indirect (also known as *multiattribute utilities* or *health state classification systems*) (Table 3).<sup>7,13-16</sup>

■ **Table 1. Health Status Measures**

	Clinical Uses	Advantages	Disadvantages
<b>Generic</b> (eg, WHOQOL-100, SF-36)	Informing and monitoring outcomes in clinical encounters Monitoring population health Estimating the burden of different conditions As end points in clinical trials <sup>7</sup>	Can be used across disease and populations Allows comparison on the same metric across disease, levels of health, and age ranges	May not be as sensitive to change as disease-specific measures Often does not provide a single summary HRQOL score
<b>Disease-specific</b> (eg, HAQ-DI)		More sensitive to smaller differences and smaller changes over time Better face validity for the population under study Can be self-administered	Only applicable to certain diseases or conditions

WHOQOL indicates World Health Organization Quality of Life; SF-36, Medical Outcomes Study 36-Item Short Form; HAQ-DI, Health Assessment Questionnaire-Disability Index; HRQOL, health-related quality of life. Adapted with permission from References 7-9.

■ **Figure 2.** Health-related Quality of Life: Taxonomy



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■ **Table 2.** SF-36 Domain Descriptives

SF-36 Domains	Description
Physical Functioning	Assesses the impact of the health in performing physical activities
Role Physical	Assesses the impact of physical health on vocational and avocational activities
Bodily Pain	Captures the frequency of pain and the extent of interference with normal activities due to pain
General Health	Assesses overall current health status, susceptibility to illness, and one's expectations for health in the future
Vitality	Assesses feelings of energy and fatigue
Social Functioning	Assesses the impact of either physical health or emotional problems on normal or usual social activities
Role Emotional	Assesses the impact of emotional health on vocational and avocational activities
Mental Health	Assesses the frequency of 4 major mental health dimensions: anxiety, depression, loss of behavioral/emotional control, and psychological well-being

SF-36 indicates Medical Outcomes Study 36-Item Short Form. Adapted with permission from Reference 10.

**Direct Health Utilities.**

Direct health utilities are usually ascertained via face-to-face interviews, with computer-assisted administration being the state of the art. The most common health utility measures are the standard gamble (SG), time to trade-off (TTO), and rating scale (RS).<sup>17-19</sup> The SG determines the risk of (usually) death that one would be willing to take to improve a state of health. The TTO technique asks how many days, months, or years of life one would be willing to give up in exchange for a better health state. Scores on the SG and TTO can range from 0.0 to 1.0,

where 0.0 usually represents dead and 1.0 is excellent or perfect health. A score of 0.7, for example, on the SG indicates a willingness to accept up to a 30% risk of immediate death  $([1.0-0.7] \times 100)$  in exchange for perfect health, and a score of 0.7 on the TTO indicates a willingness to give up 30% of one's life expectancy in exchange for perfect health. The RS, perhaps the simplest of the 3 methods (although not a true measure of utility in a strict sense because it does not involve comparison against an external metric, such as risk or time), asks the subject to rate his or her health on a scale (eg, from 0 to 100), where 0 usually represents dead and 100 is perfect health. Another utility measure is willingness to pay (WTP).<sup>20</sup> WTP measures the value of an improvement in health or a decrease in health risk by determining the maximum amount of money a person would willingly exchange for it. WTP depends on ability to pay (ie, on an individual's wealth and competing demands for their resources).

**Indirect Health Utilities.**

Indirect health utilities use population-assigned weights to calculate utility scores for particular health states from health status instruments. The ease of administration (self-administered) of these indirect measures enables them to be used in national surveys, and they are commonly used as the source of QOL weightings in economic evaluations. Four measures, the EuroQoL EQ-5D, the SF-6D, the Quality of Well Being Self-administered (QWB-SA) Scale, and the Health Utilities Index (HUI), have been used in rheumatology because they are easy to administer and cover domains applicable to arthritides.<sup>21</sup> The EQ-5D has 5

■ **Table 3.** Health Utility Measures

	Uses	Advantages	Disadvantages
<b>Direct health utility measures</b>	<p>As global HRQOL measures in clinical trials<sup>7</sup></p> <p>As “quality-adjustment factors” for calculating QALYs in decision and cost-effectiveness analyses<sup>7,13</sup></p> <p>As an aid in individual-level decision making regarding testing and treatment so that decisions are made from the perspective of the patient’s own value system<sup>14,15</sup></p>	<p>Provides a single HRQOL number</p>	<p>May not be as sensitive to change as health status measures</p> <p>May require face-to-face interview</p> <p>Concepts may be difficult for some subjects to comprehend</p> <p>May depend on patient’s attitude toward money, risk, or time</p>
<b>Indirect health utility measures</b>	<p>As global HRQOL measures in clinical trials<sup>7</sup></p> <p>As “quality-adjustment factors” for calculating QALYs in decision and cost-effectiveness analyses<sup>7,13</sup></p>	<p>Provides a single HRQOL number</p> <p>Considered more appropriate than patients’ direct utilities for public policy because indirect utilities use population-assigned weights<sup>16</sup></p> <p>Does not require face-to-face interview</p>	<p>May not be as sensitive to change as health status measures</p>

HRQOL indicates health-related quality of life; QALYs, quality-adjusted life-years.

domains: mobility, usual activities, self-care, pain, and anxiety, with 3 levels of function for each domain.<sup>22</sup> Possible scores on the EQ-5D range from –0.59 (worse than dead) to 1.00 (perfect health). In RA, the EQ-5D has been found to be reliable and valid.<sup>21</sup> Normative EQ-5D data are available for the US population.<sup>23</sup> The SF-6D<sup>24</sup> derives utility scores from 6 of the 8 SF-36 domains: physical function, role limitations, social function, pain, mental health, and vitality. SF-6D utility scores can range from 0.29 (the worst health state) to 1.00 (perfect or full health). The QWB-SA<sup>25</sup> measure combines 3 scales of functioning (mobility, physical functioning, and social functioning) with a measure of symptoms and problems to produce a single point-in-time expression of well-being that ranges from 0.0 (dead) to 1.0 (perfect health). The QWB-SA has been studied in different arthritides.<sup>26</sup> The HUI consists of 2 separate systems—the HUI2 and HUI3.<sup>27</sup> The HUI3 is recommended for primary analysis; it is comprised of 8 attributes—vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain—and utility scores can range from –0.36 (worse than dead) to 1.00

(perfect or full health). The HUI2 complements the HUI3 and offers independent attributes including self-care, emotion (worry/anxiety), and fertility. The HUI2 and HUI3 have been successfully applied in RA.<sup>21</sup>

### Minimum Clinically Important Differences

An important advance in HRQOL research is the concept of *minimum clinically important difference* (MCID), defined as the smallest difference in score on an HRQOL instrument that patients perceive as beneficial and that would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient’s management.<sup>28</sup> Differences in scores smaller than the MCID are considered unimportant, regardless of whether statistical significance is reached. For example, although an average change of 0.15 point on the HAQ-DI may be statistically significant in a clinical trial, it may not be perceived as meaningful by study subjects, so it would not meet MCID criteria. The MCID for the HAQ-DI in RA is 0.22 point<sup>29,30</sup>; for various arthritides, the MCID for the SF-36 summary scores is 2.5 to 5.0 points, and on the

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individual SF-36 domain scores, the MCID is 5.0 to 10.0 points.<sup>30-32</sup> For indirect health utilities, MCIDs are generally 0.01 to -0.10.<sup>33</sup> MCID estimates of HRQOL measures have influenced designs of subsequent clinical trials aimed at improving HRQOL.<sup>34</sup>

### Applications of HRQOL Instruments

**To Estimate Burdens of Different Diseases.** Health status instruments can be used to assess the impact of different diseases on HRQOL. As an example, Hays et al<sup>35</sup> compared SF-36 physical functioning scores of people with asymptomatic human immunodeficiency virus (HIV) infection versus those of the US general population and of patients with other chronic diseases; for adults with asymptomatic HIV disease physical functioning was similar to the US population (mean standard deviation [SD]: 92 [16] vs 90 [17]), but for those with symptomatic HIV disease (76 [28]) or acquired immunodeficiency syndrome (AIDS) (58 [31]) it was much worse. In their study, patients with AIDS had worse physical functioning than patients with other chronic medical diseases (eg, epilepsy or gastroesophageal reflux disease).

**As an End Point in Clinical Trials.** Generic (health status and health utility) and disease-specific measures complement each other as measures of HRQOL in clinical trials (Tables 1 and 3). Before incorporating an HRQOL measure in a clinical trial, one should assess its responsiveness to change (ie, whether HRQOL scores change in the right direction when the underlying construct it is measuring changes). For example, for the HAQ-DI to be a valuable HRQOL measure in an RA clinical trial, scores should improve (rather than worsen) when joint count and patient global ratings improve. In addition, the improvement in HAQ-DI scores should be greater in the improved group than in the no-change group. In fact, the SF-36 and the HAQ-DI have been found to be responsive to change in RA and are therefore used in RA clinical trials. In addition, a global health utility scale was used in a 6-month, double-blind, placebo-controlled RA clinical trial of auranofin therapy<sup>36</sup>; auranofin was found to be superior to placebo according to the health utility measure.

**To Monitor Outcomes in Clinical Practice.** HRQOL measures can be used in day-to-day practice. Extensive research in RA has shown that the HAQ-DI is a powerful predictor of mortality even after adjusting for sociodemographic and clinical features.<sup>37</sup>

**In Public Policy.** Direct and indirect health utility scores serve as “quality-adjustment factors” or quality weights for

calculating quality-adjusted life-years (QALYs). QALYs take into account both quantity and QOL in a single metric, calculated as the arithmetic product of life expectancy and the QOL of the remaining life-years.<sup>38</sup> A year of perfect health is worth 1.0 QALY, a year of life in less than perfect health is worth less than 1.0 QALY, and being dead is worth 0.0 QALY. At a policy level, QALYs are incorporated into decision analysis and cost-effectiveness (cost-utility) analyses of healthcare interventions.

**In Individual Decision Making.** On an individual level, one’s own health utilities may be used to help make decisions regarding testing and treatment.<sup>7</sup> Because medical decision making inherently involves multiple uncertain outcomes, valuing health states can be particularly relevant in healthcare.<sup>14,15</sup>

### Conclusion

HRQOL is key in chronic (and acute) diseases. As such, HRQOL is considered an important outcome in arthritis clinical trials, and the US Food and Drug Administration (FDA) requires a sustained improvement in the HRQOL scores to file for an “improvement in HRQOL” claim. The FDA acknowledges that “not enough information is available on the performance of general HRQOL measures in longer-term arthritis trials (and) the incorporation of such measures in planned trials is encouraged.”<sup>39</sup> Similarly, further research and applications of HRQOL stand to improve patient care and benefit health policy.

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