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Name of Journal: World Journal of Gastroenterology

Manuscript NO: 74705

Manuscript Type: MINIREVIEWS

Current standard values of health utility scores for evaluating cost-effectiveness in

liver disease

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Abstract

Health utility assessments have been developed for various conditions, including

chronic liver disease. Health utility scores are required for socio-economic evaluations,

which can aid the distribution of national budgets. However, the standard health utility

assessment scores for specific health conditions are largely unknown. In this mini-

review, we summarized the health utility scores, including the EQ-5D-5L, EQ-VAS, SF-

36, RAND-36, and Health Utilities Index (HUI)-Mark2/Mark3 scores, for the normal

population and chronic liver disease patients. The EQ-5D-5L is the most popular

questionnaire for health utility assessments. The SF-36 and EQ-5D-5L can be used for

health utility evaluations during antiviral therapy for hepatitis C. HUI-Mark2/Mark3

indicated that the health utility scores of hepatitis B patients are roughly 30% better

than those of hepatitis C patients.

Several concerns regarding current health utility assessments need to be examined

further.

**Key Words:** QOL; EQ-5D-5L; SF-36; RAND-36; HUI-Mark

Ishunuki T, Ota S, Harada K, Kawamoto M, Meguro M, Kutomi G, Tatsumi H, Harada K, Miyanishi K, Kato T, Ohyanagi T, Hui TT, Mizuguchi T. Current standard values of health utility scores for evaluating cost-effectiveness in liver disease. *World J Gastroenterol* 2022; In press

**Core Tip:** This study summarized current knowledge about health utility assessments, including the EQ-5D-5L, EQ-VAS, SF-36, RAND-36, and Health Utilities Index-Mark2/Mark3.

The EQ-5D-5L is the most popular questionnaire for health utility assessments. Health utility assessments need to be used widely and routinely.

#### **INTRODUCTION**

The quality of health is an important factor when assessing medical management rather than simple survival periods<sup>[1, 2]</sup>. Health utility is an important factor in medical assessments and socio-economic politics<sup>[3]</sup>. National health budgets have risen steadily in various countries, and governments need to deeply consider the need to maintain a socio-economic balance<sup>[4]</sup>. Therefore, health benefits should be compared with social costs to avoid national financial collapse.

It is difficult to quantify health quality at regular intervals<sup>[5]</sup>. We are developing wearable devices that can automatically obtain health data, including data regarding mental health. Some health utility assessments require the use of questionnaires, which are associated with low compliance and involve bothersome calculations<sup>[2, 6, 7]</sup>. Before launching our novel health utility assessment tool, we performed this mini-review in order to summarize the currently available health utility assessment tools. The most useful questionnaire for evaluating health status depending on liver disease status or sex is unclear. In addition, no universal health utility assessment values for specific liver diseases or the normal population have been reported. Therefore, we conducted a meta-analysis to estimate health utility assessment values for specific populations.

The EQ-5D-5L is the simplest instrument for evaluating health utility and has been widely translated into various languages with high reliability and validity<sup>[6, 8-10]</sup>. It only involves five questions and five answering levels. The health utility scores produced by the EQ-5D-5L can be used to calculate quality-adjusted life year (QALY) values <sup>[8]</sup>. The Health Utilities Index Mark 2/Mark 3 is another instrument for evaluating health utility scores and can also be used to obtain QALY values<sup>[11]</sup>. However, the Health Utilities Index is complicated, as it involves 45 questions, which take a long time to answer. The Short-Form 36-item (SF-36) is also widely used to evaluate health quality, although it does not directly involve QALY evaluations <sup>[9, 12, 13]</sup>.

There are two types of SF-36, and the copyrights to these tools belong to The RAND Corporation (Santa Monica, CA, USA)<sup>[14]</sup> and QualityMetric (Johnston, RI, USA), respectively<sup>[15]</sup>. However, most researchers do not actively consider which version they use<sup>[12]</sup>. Therefore, the exact method and results of such assessments are not always described in the literature (Table 1).

In this mini-review, we describe the scores obtained with various health utility indexes in normal healthy populations or patients with different types of liver disease (Table 2).

#### EQ-5D-5L

The EQ-5D-5L has been widely investigated as a tool for evaluating general health in normal populations and patients with different stages of liver disease (Table 3)[17, 18, 22, 25-27, 30, 32]. Health utility indices should be affected by age, sex, ethics, religion, and geography. However, the EQ-5D-5L produced similar utility indices for groups with different health statuses (Table 3), such as normal healthy individuals (0.8413±0.1905) and hepatitis C virus (HCV)-infected patients with compensated or decompensated cirrhosis (0.8113±0.2261 and

0.7903±0.2182), HCV-infected patients exhibiting a sustained virologic response (SVR) (0.846±0.1816), and patients with hepatocellular carcinoma 0.8127±0.2084).

In general, the EQ-5D-5L produces significantly higher scores in males than in females (Figure 1) (0.8267±0.229 vs. 0.7922±0.239; P<0.001). The mean total EQ-VAS score for the

general population was found to be 79.796±17.614 in two independent studies (Table 4)[26, 30].

#### SHORT FORM (SF)-36

The SF-36 consists of eight scales, including physical functioning (PF) (85.07±15.40); role limitations due to physical health problems (RP)(82.50±25.15); bodily pain (BP) (77.62±17.55); general health perceptions (GH) (63.37±14.16); vitality, energy, or fatigue (VT) (63.37±14.16); social functioning (SF) (86.97±15.13); role limitations due to emotional problems (RE) (83.94±23.57); and general mental health (MH) (63.37±14.16). Although the eligible healthy controls differed among countries and age groups, the health utility scores produced by each scale were similar (Table 5)[16, 17, 22, 23].

#### COMPENSATED LIVER CIRRHOSIS VS. SUSTAINED VIROLOGIC RESPONSE

Patients with hepatitis C had achieved an SVR exhibited significantly better health utility scores for each SF-36 scale (Figure 2)<sup>[22, 29, 31]</sup> and the EQ-5D-5L (Figure 3)<sup>[18, 19, 22, 32]</sup> than those with compensated liver cirrhosis (Table 6)<sup>[18, 19, 22, 29, 31, 32]</sup>. In particular, significant differences in the scores for RP (61.5±31.6 vs. 73.3±27.3), GH (64.8±20.9 vs. 74.8±18.5), VT (70.5±24.0 vs. 78.1±18.4), RE (56.8±32.0 vs. 68.1±27.3), and the EQ-5D-5L (0.6863±0.3065 vs. 0.846±0.1816) were seen between these groups. These results indicate that health utility indices improve by 10-20% after patients with hepatitis C achieve an SVR.

#### THE HEALTH UTILITY INDEX (HUI MARK-2/MARK-3)

Hepatitis B and C are the main causes of viral-associated chronic liver disease (Figure 4)<sup>[20, 21]</sup>. The health utility scores of hepatitis B patients were significantly better than those of hepatitis C patients (0.6312±0.2867 vs. 0.8186±0.1886); i.e., there was a roughly 30% difference between the scores of these patients.

## WHICH HEALTH UTILITY INDEX SHOULD BE USED FOR NORMAL POPULATIONS OR PATIENTS WITH CHRONIC LIVER DISEASE?

In this mini-review, we summarized the findings of previous studies examining health utility evaluations in patients with chronic liver disease. Various questionnaires have been used to evaluate health utility in different populations/at different times. The EQ-5D-5L is the most popular of the questionnaires used to examine health utility scores internationally<sup>[17]</sup>.

One of the concerns regarding the application of health utility scores is their sensitivity<sup>[33]</sup>. For example, the health utility scores produced by the EQ-5D-5L for patients with compensated cirrhosis and decompensated cirrhosis did not differ significantly (Table 3). On the other hand, the health utility scores for hepatitis C patients with compensated liver cirrhosis and those who achieved an SVR differed significantly according to both the SF-36 and EQ-5D-5L (Table 6). This indicated that both questionnaires are suitable for evaluating health utility in hepatitis C patients after viral elimination. Although the health utility scores derived from the EQ-5D-5L were calculated from 5 questions, the score range of the EQ-5D-5L (123.3%) was greater than that of the SF-36 (105.8-119.2%). Therefore, the EQ-5D-5L could be suitable for evaluating health utility scores in this specific disease state. On the other hand, EQ-5D-5L-derived health utility scores are based on only five personal factors, mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Therefore, their sensitivity and any ceiling effects should be validated in each language and ethnic group.

It is well known that the prevailing subtype of viral hepatitis differs depending on the geographic region<sup>[34]</sup>. Hepatitis B is the prevailing subtype in East Asia<sup>[13]</sup>, whereas hepatitis C is the most common in Western countries<sup>[35]</sup>. Both types of hepatitis can be controlled by nucleic acid analogs<sup>[36]</sup>. In this mini-review, the HUI scores of hepatitis C patients were roughly 30% lower than those of hepatitis B patients. The differences between hepatitis B and hepatitis C need to be investigated using the EQ-5D-5L and SF-36 in future.

The second concern regarding the use of questionnaires for health assessments relates to the number of questions in each questionnaire. The EQ-5D-5L consists of only five questions<sup>[8]</sup>, whereas the other tools consist of  $36^{[14-16]}$  or  $45^{[11]}$  questions. The number of questions affects study compliance, especially in the elderly<sup>[37]</sup>. If possible, the number of questions should be minimized.

The last concern is about gaining permission to use such questionnaires for health utility assessments. It takes great effort to develop a questionnaire. However, health utility assessments need to be repeated continuously. In certain human health emergencies, the use of some vaccines has been allowed without patent royalties having to be paid<sup>[38]</sup>. Commercial companies that own the rights to health assessments should reconsider their policies regarding their use.

#### **CONCLUSION**

Health assessments that allow free registration would be useful for evaluating health utility in patients with liver disease. <u>Alternatively, a portable QOL tracker could be used to perform QOL evaluations of any patient-reported outcome, and we are currently developing such a tracker.</u>

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