

## Health-related quality of life (HRQoL) and health state utilities with chronic hepatitis-B (CHB): A population-based survey in Vietnam

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### Abstract

**Objective:** Hepatitis-B infection is a worldwide consideration despite of vaccination availability. Chronic Hepatitis-B (CHB) results in various complications and the impairment of health-related quality of life (HRQoL). Health state utilities and HRQoL are the fundamental input to decision models as well as economic evaluation analysis. Although the effect of CHB on the HRQoL and health state utilities is well-known, the results remain uncertain. The objective is to measure health state utilities and HRQoL among CHB patients at two provincial hospitals in southern Vietnam using both preference-based and non-preference-based tools.

**Methods:** A cross-sectional survey was conducted from August 2017 to July 2018 in Dongnai and Kiengiang General Hospitals (DNGH and KGGH). Patients with the ICD-10 code of B18 was enrolled using convenience sampling method. Each respondent was experienced a face-to-face interview with four health measurement instruments. SPSS 20.0 software was used for data analysis.

**Results:** The total research population included 546 patients at DNGH and 338 patients at KGGH, each of them was classified in to one of four stages of the disease. The majority were male, well-educated and alcohol-consumers. The average physical component score was highest in patients with compensated cirrhosis at KGGH ( $58.7 \pm 0.9$ ). The average mental component score was highest in patients with noncirrhotic CHB at DNGH ( $60.3 \pm 0.2$ ). In both hospitals, patients with noncirrhotic chronic Hepatitis B had the highest mean score of EuroQoL 5 dimensions questions; patients with decompensated cirrhosis had the lowest mean score of visual analogue scale.

**Conclusion:** This is the first study in Vietnam which used both preference-based and non-preference-based instrument to measure the HRQoL in HBV-infected patients. The results from different instruments were similar. These findings were promised to be a fundamental input for future cost-effectiveness analysis in the same field.

**Keywords:** Hepatitis B, HRQoL, health utility, Vietnam. (JPMA 69: S-80 (Suppl. 2); 2019)

### Introduction

The hepatitis B virus (HBV) is prevalent among more than 2 billion worldwide, with 400 million chronically infected once in their lifetime.<sup>1</sup> Though a vaccination process is in place, even the United State and Canada face the risk of this chronic infection.<sup>2-4</sup> There is an increased risk of liver failure and hepatocellular carcinoma (HC) among chronic hepatitis B (CHB) patients, which ultimately leads to death and liver disease-associated disorders and complications.<sup>5</sup> Compensated cirrhosis (CC) and decompensated cirrhosis (DC) are two fatal complications occurred when the host immune system was stimulated. HC, on the other hand, is a complication that may develop after a long duration of infection.

The use of health-related quality of life (HRQoL) measures

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has been increasing since the mid-1980s. Traditionally, health has been considered from a biomedical point of view. Although this approach is essential, it does not encompass all of the aspects that are important to health. In addition to physical functioning, the overall concept of HRQoL includes other aspects of health, called domains, such as psychological and social functioning, that are important to the patient. HRQoL instruments can be used to detect otherwise undiagnosed or undetected diseases such as depression. Health state utilities and HRQoL are the fundamental input to decision models as well as economic evaluation analysis. HRQoL and utility measurement instruments have been developed consecutively, including direct preference-based and non-preference-based tools.

Many patients are not well aware of the infection and do not consider the risk to the liver along with impaired life quality.<sup>6</sup> The limited impact of CHB has been reported in various research studies on life quality, and researchers have also utilized health state utilities in order to assess the cost-effective models of CHB treatment among patients.<sup>7,8</sup> Varying results have been reported about

HRQoL among CHB patients since 2007.<sup>9,10</sup> In these studies, the association of CHB with HRQoL was explored. Results, however, were different due to the variety of measurement and population. Although the effect of CHB on the HRQoL and health state utilities is well-known, the results remains uncertain.

This particular research aimed to measure health state utilities and HRQoL among CHB patients at two provincial hospitals in southern Vietnam using four instruments which are both preference- and non-preference-based.

### Material/Subjects/Patients and Methods

This was a cross-sectional study from August 2017 to July 2018 at Dongnai General Hospital (DNGH) and Kiengiang General Hospital (KGGH) in southern Vietnam. Map of the study site in Kiengiang and Dongnai Province was presented in Figure-1. These two hospitals are provincial facilities with over one thousand beds for each.

The study protocol was approved by the Science Research Council in Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh City. All interviews were based on volunteer spirit with written consent. Participants might discontinued the interview whenever they felt unsatisfied. All collected information was entirely anonymous and used for science purposes only.

A convenient sampling technique was used to select the participants. All patients with a primary discharge diagnosis of CHB according to International Classification of Diseases Codes 10 version (ICD-10 code B18: chronic viral hepatitis disease) were invited to join a face-to-face interview. Patients at the age of 16 or older and fluently communicated in Vietnamese were enrolled. Those who refused to answer certain questions or discontinued the interview were eliminated.

A standardized interview was under three stages: i) greetings and introduction (the interviewer introduced his/herself and explained the purpose of the study); ii) collection of HRQoL using the study instruments; and iii) collection of demographical and clinical information. Information on drug usage and stage of disease was obtained from the patient's medical document. Each of them was classified into one of four stages: noncirrhotic CHB (NC), compensated cirrhosis (CC), decompensated cirrhosis (DC), and hepatocellular carcinoma (HC).

The questionnaire used in this study was combination of four HRQoL measurement instruments, including Short-Form 36 Health Survey second version (SF36v2), EuroQoL 5 dimensions 3 level (EQ-5D-3L), visual analogue scale (VAS), and standard gambling technique (SG).

The SF36v2 is a non-preference-based instrument divided into eight subgroups: physical functioning (PHF), social functioning (SOF), role limitations due to physical problems (ROP), role limitations due to emotional problems (REL), vitality (VIT), mental health (MEH), general health perception (GEH), and body pain (BOP). The eight subgroups are not presented in the questionnaire but in miscellaneous order from question 1 to question 36. From these eight subgroups, two summary scores were calculated: physical component score (PCS) and a mental component score (MCS).

The EQ-5D questionnaire, however, is a preference-based instrument divided into the EQ-5D descriptive system and the VAS. The EQ-5D-3L descriptive system comprises the following five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression with three levels for each: no problems, some problems, and extreme problems. A 1-digit number expresses the level selected for that dimension, and the combination for the five dimensions into a 5-digit number that describes the patient's health state (utilities). The VAS is vertical line with the left endpoint coded number 0 for the best imaginable health state and the number 1 at the other endpoint for the worst imaginable health state. The interviewees recorded their health state by self-rated on this scale.

In SG technique, the patient was offered the hypothetical choice: living his remaining life expectancy in present health state, or take an imaginable medication which leading to a full health or an immediate death. The probability of death in of the medication was consecutively changed until the respondent reached a point of indifference between the two options. This probability is considered as the utility for current health.

The Vietnamese version of these instruments was validated elsewhere.<sup>9,11-18</sup>

Statistical analysis was performed using IBM SPSS for Windows version 20.0 (IBM Corporation, Armonk, NY, US.). The participants' demographic and health data were analyzed using descriptive statistics, including frequency, percentage, mean, and standard deviation (SD). The present study used United State dollar (USD) for all mentioned costs based on the exchange rate for 2018 (1 USD=22,867 VND Dong).<sup>19</sup> 95% confidence interval (95% CI) was calculated by double bootstrapping technique with 1000 repeated times.

### Results

The study included 546 patients at DNGH and 338 patients at KGGH. Table-1 and Table-2 show the

Table-1: General characteristics of the patients with CHB.

General characteristic	Dongnai General Hospital (N=546)				Kiengiang General Hospital (N=338)			
	NC n=382	CC n=95	DC n=21	HC n=48	NC n=183	CC n=67	DC n=37	HC n=51
<b>Age (Mean±SD)</b>	45.9±1.2	53.2±1.8	55.7±4.4	54.3±2.5	49.2±2.7	54.8±3.5	58.3±7.1	52.3±3.6
<b>Male sex</b>	331 (86.6)	71 (74.7)	18 (85.7)	33 (68.8)	132 (72.1)	45 (67.2)	26 (70.3)	40 (78.4)
<b>Religion</b>								
None	273 (71.5)	65 (68.4)	17 (81)	34 (70.8)	154 (84.2)	54 (80.6)	29 (78.4)	41 (80.4)
Buddhism	42 (11.0)	18 (18.9)	3 (14.3)	9 (18.8)	15 (8.2)	6 (9.0)	3 (8.1)	10 (19.6)
Catholicism	31 (8.1)	4 (4.2)	1 (4.7)	5 (10.4)	6 (3.3)	3 (4.5)	2 (5.4)	-
Others	36 (9.4)	8 (8.5)	-	-	8 (4.3)	4 (5.9)	3 (8.1)	-
<b>Married</b>	312 (81.7)	72 (75.8)	16 (76.2)	37 (77.1)	142 (77.6)	62 (92.5)	28 (75.7)	45 (88.2)
<b>Full-time job</b>	297 (77.7)	79 (83.2)	17 (81)	44 (91.7)	171 (93.4)	65 (97)	36 (97.3)	49 (96.1)
<b>Education level</b>								
University/Postgraduate	306 (80.1)	64 (67.4)	8 (38.1)	18 (37.5)	160 (87.4)	34 (50.7)	21 (56.8)	45 (88.2)
High school/College	61 (16.0)	12 (12.6)	9 (42.9)	24 (50.0)	15 (8.2)	29 (43.3)	10 (27.0)	2 (3.9)
Under High school	15 (3.9)	19 (20.0)	4 (19.0)	6 (12.5)	8 (4.4)	4 (6.0)	6 (16.2)	4 (7.9)
<b>Annual income (USD)</b>								
<2,000	30 (7.9)	6 (6.3)	2 (9.5)	6 (12.5)	5 (2.7)	1 (1.5)	-	3 (5.9)
2,000 - <4,000	143 (37.4)	37 (38.9)	11 (52.4)	19 (39.6)	45 (24.6)	42 (62.7)	26 (70.3)	16 (31.4)
4,000 - <6,000	76 (19.9)	19 (20)	5 (23.8)	12 (25)	67 (36.6)	8 (11.9)	8 (21.6)	17 (33.3)
6,000 - <8,000	55 (14.4)	25 (26.3)	3 (14.3)	6 (12.5)	32 (17.5)	12 (17.9)	1 (2.7)	8 (15.7)
8,000 - <10,000	31 (8.1)	5 (5.3)	-	5 (10.4)	20 (10.9)	3 (4.5)	1 (2.7)	2 (3.9)
≥10,000	47 (12.3)	3 (3.2)	-	-	14 (7.7)	1 (1.5)	1 (2.7)	5 (9.8)
<b>Income satisfaction</b>	209 (54.7)	52 (54.7)	8 (38.1)	23 (47.9)	133 (72.7)	24 (35.8)	11 (29.7)	32 (62.7)

Abbreviations: NC: Noncirrhotic chronic Hepatitis B; CC: Compensated cirrhosis; DC: Decompensated cirrhosis; HC: Hepatocellular carcinoma; SD: Standard deviation; USD: United State Dollar.

Note: Data presented as n (%) unless otherwise indicated.

Table-2: Clinical characteristics of the patients with CHB.

General characteristic	Dongnai General Hospital (N=546)				Kiengiang General Hospital (N=338)			
	NC n=382	CC n=95	DC n=21	HC n=48	NC n=183	CC n=67	DC n=37	HC n=51
<b>Alcohol Drinking</b>	368 (96.3)	79 (83.2)	19 (90.5)	41 (85.4)	165 (90.2)	66 (98.5)	34 (91.9)	45 (88.2)
<b>Treatment</b>								
No treatment	213 (55.8)	25 (26.3)	8 (38.1)	4 (8.3)	85 (46.4)	16 (23.9)	13 (35.1)	7 (13.7)
Lamivudine (LAM)	38 (9.9)	17 (17.9)	2 (9.5)	8 (16.7)	21 (11.5)	9 (13.4)	3 (8.1)	8 (15.7)
Adefovir (ADV)	14 (3.7)	3 (3.2)	1 (4.8)	3 (6.3)	11 (6.0)	5 (7.5)	5 (13.5)	5 (9.8)
Entecavir (ETV)	20 (5.2)	2 (2.1)	1 (4.8)	5 (10.4)	16 (8.7)	11 (16.2)	1 (2.7)	1 (2.0)
Telbivudine (LdT)	7 (1.8)	6 (6.3)	-	2 (4.2)	17 (9.3)	5 (7.5)	7 (18.9)	-
Tenofovir (TDF)	26 (6.8)	9 (9.5)	-	9 (18.8)	7 (3.8)	3 (4.5)	6 (16.2)	4 (7.8)
Interferon (IFN)	12 (3.1)	10 (10.5)	3 (14.3)	5 (10.4)	3 (1.6)	6 (9.0)	2 (5.4)	5 (9.8)
Peg IFN	8 (2.1)	6 (6.3)	2 (9.5)	5 (10.4)	8 (4.4)	3 (4.5)	-	4 (7.8)
LAM + ADV	13 (3.4)	8 (8.4)	1 (4.8)	7 (14.5)	5 (2.7)	5 (7.5)	-	8 (15.7)
LAM + TDF	18 (4.7)	3 (3.2)	2 (9.5)	-	9 (4.9)	4 (6.0)	-	3 (5.9)
ETV + TDF	13 (3.5)	6 (6.3)	1 (4.7)	-	1 (0.7)	-	-	6 (11.8)

Abbreviations: NC: Noncirrhotic chronic Hepatitis B; CC: Compensated cirrhosis; DC: Decompensated cirrhosis; HC: Hepatocellular carcinoma.

Note: Data presented as n (%).

demographical and clinical characteristics of the patients at each hospital. The majority were male, well-educated and alcohol-consumers. Table-3 illustrates the quality-of-life scores in eight subgroups of SF36v2 questionnaire. Data presented as mean score (SD). The average PCS was

highest in patients at CC stage at KGGH (58.7±0.9). The average MCS was highest in patients with NC Hepatitis-B at DNGH (60.3±0.2). Figure-2 presents the health utilities of CHB patients at different disease stage measured by preference-based instrument. The data presented as

Table-3: Non-preference-based quality of life in CHB patients.

Subgroup	Dongnai General Hospital (N=546)				Kiengiang General Hospital (N=338)			
	NC n=382	CC n=95	DC n=21	HC n=48	NC n=183	CC n=67	DC n=37	HC n=51
PHF	57.8 (0.5)	50.7 (1.1)	38.3 (7.7)	52.4 (1.8)	46.9 (0.9)	59.1 (1.4)	40.4 (4.7)	53.3 (2.2)
ROP	52.6 (0.3)	52.3 (1.5)	44.7 (6.3)	47.9 (2.6)	47.2 (0.3)	54.5 (1.2)	36.8 (4.2)	47.6 (2.0)
BOP	59.6 (0.4)	57.8 (1.2)	43.9 (5.8)	48.2 (2.4)	53.8 (0.5)	55.1 (1.4)	39.3 (4.2)	53.4 (3.3)
GEH	60.1 (0.2)	58.4 (1.3)	42.8 (5.9)	51.5 (2.3)	49.4 (0.7)	56.7 (0.9)	36.7 (5.9)	47.9 (2.8)
VIT	54.5 (0.7)	53.7 (1.3)	32.8 (5.5)	46.5 (1.7)	52.6 (0.8)	52.1 (1.4)	40.3 (4.6)	55.5 (2.1)
SOF	54.6 (0.6)	49.3 (1.1)	39.8 (5.6)	48.6 (2.4)	60.2 (0.9)	55.3 (1.1)	38.1 (5.1)	54.3 (3.2)
REL	58.7 (0.2)	59.7 (1.4)	42.4 (6.5)	46.3 (2.3)	48.3 (0.6)	52.1 (1.3)	39.7 (4.6)	52.3 (2.6)
MEH	58.9 (0.3)	54.4 (1.4)	37.2 (6.5)	54.9 (2.1)	57.8 (0.9)	56.8 (1.4)	40.2 (5.3)	48.3 (2.3)
PCS	54.5 (0.6)	51.1 (1.3)	40.2 (5.7)	50.4 (2.0)	47.8 (0.5)	58.7 (0.9)	37.1 (5.7)	49.5 (3.1)
MCS	60.3 (0.2)	59.1 (1.5)	40.9 (6.9)	52.1 (1.9)	57.3 (0.7)	52.6 (1.4)	37.3 (6.1)	56.9 (3.1)

Abbreviations: PHF: Physical functioning; ROP: role limitations due to physical problems; BOP: Bodily pain perception; GEH: General health perception; VIT: Energy/Vitality; SOF: Social Functioning; REL: role limitations due to emotional problems; MEH: Mental health; PCS: Physical Component Score; MCS: Mental Component Score; NC: Noncirrhotic chronic Hepatitis B; CC: Compensated cirrhosis; DC: Decompensated cirrhosis; HC: Hepatocellular carcinoma. Note: Data presented as mean score (standard deviation).

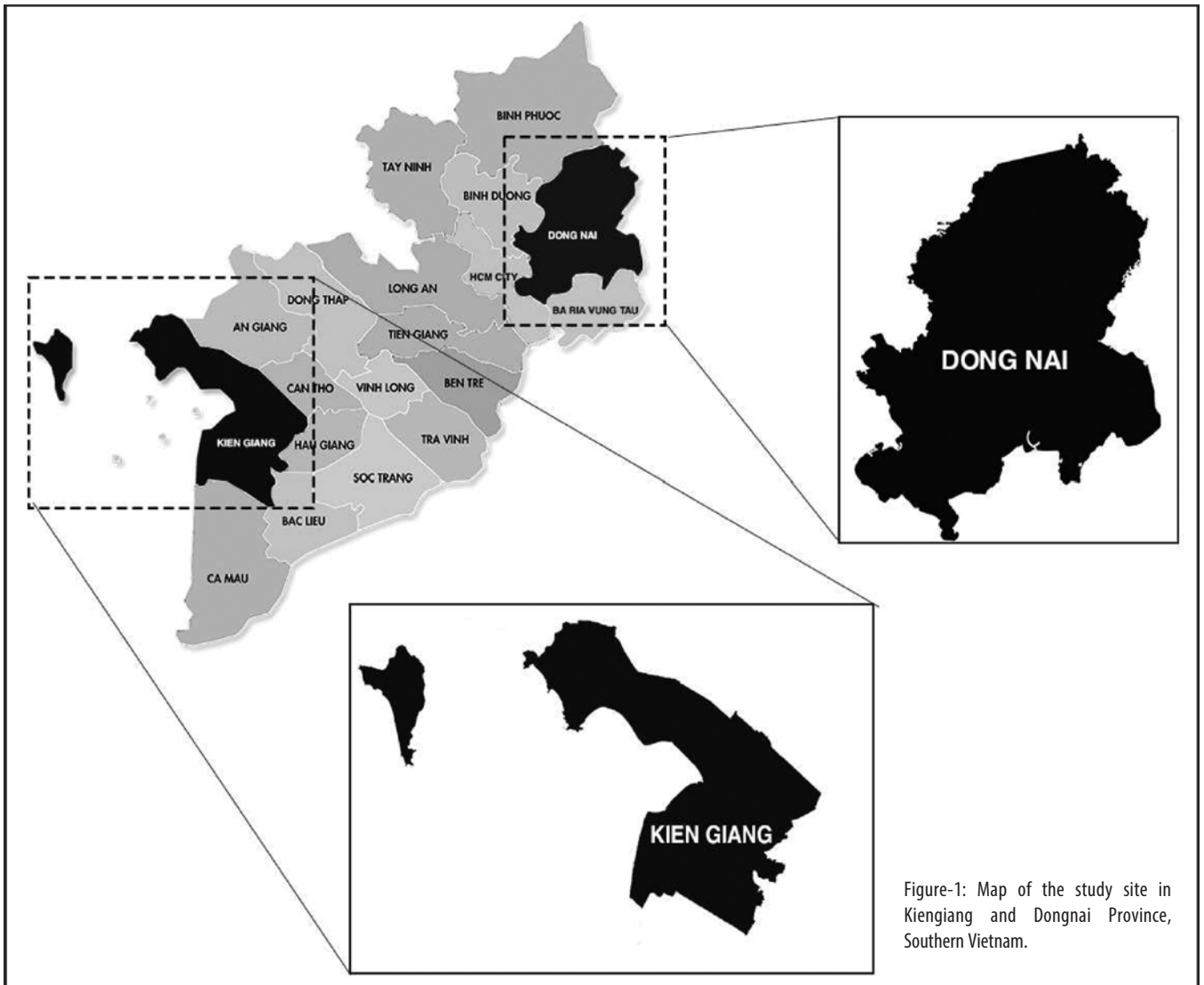


Figure-1: Map of the study site in Kiengiang and Dongnai Province, Southern Vietnam.

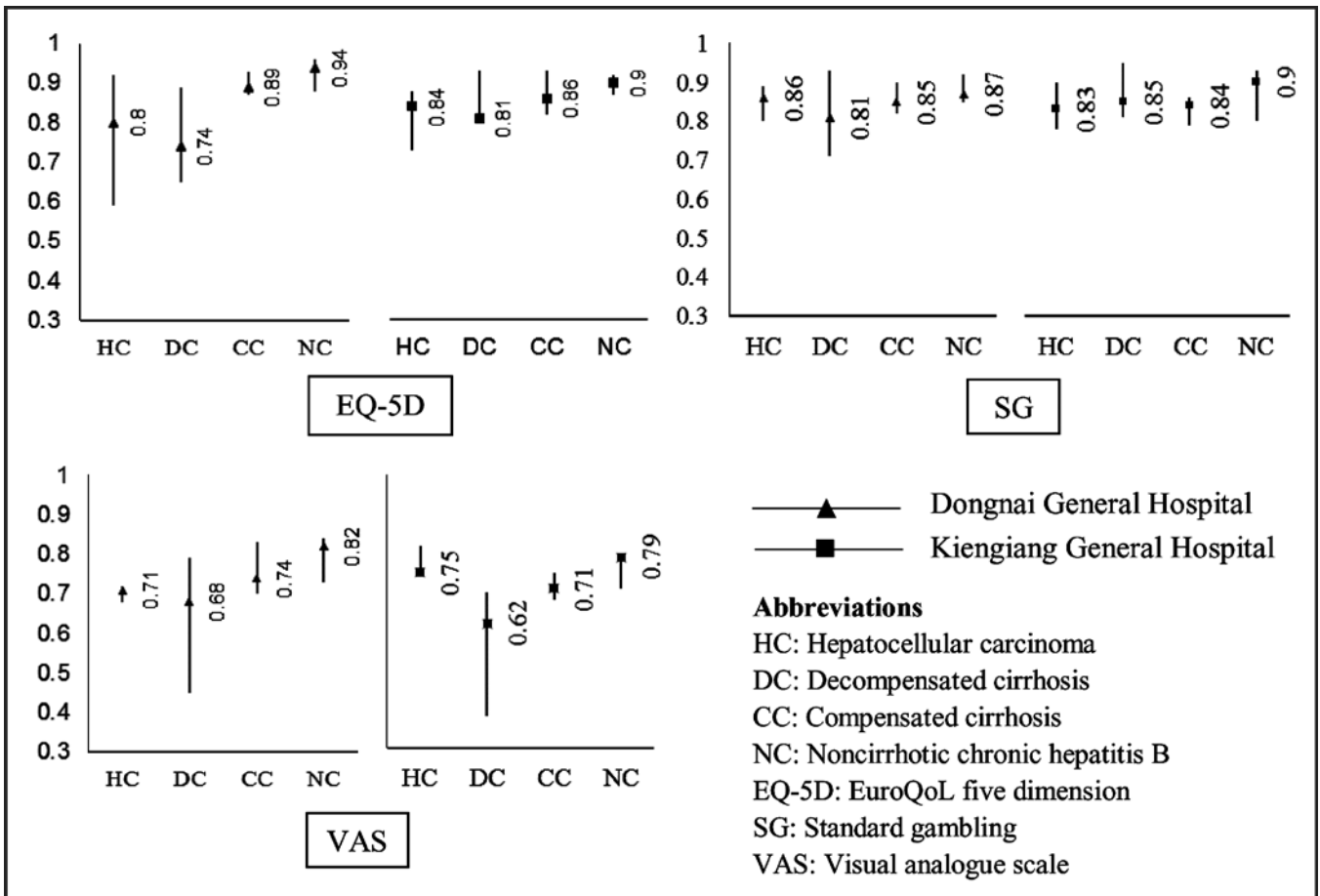


Figure-2: Utilities of CHB patients at different disease stages measured by different instruments.

mean utility (95% CI). In both hospitals, patients with NC Hepatitis-B had the highest mean score of EQ-5D questions; patients at DC stage had the lowest mean score of VAS. CC patients in KGGH and DC patients in DNGH supposed the lowest score in SG.

**Discussion**

In this study, among patients who were infected by HBV, HRQoL impairment was reported in the patients with late-stage liver disease. Due to no use of any statistical tests in this work, the impairment was not proved to be associated with the disease stage. However, the association between the HRQoL reduction and the development of liver disease were reported over a decade.<sup>6,17,20,21</sup> Most of the studies, including this study, enrolled only CHB patients in different stages, which resulted in under-evaluated utilities due to no fundamental comparison. On the other hand, Levy (2008) conducted a multinational study which included two categories of respondents, HBV-infected and uninfected people. Collecting data from six countries, this was the

largest study ever. As predicted, they observed that uninfected respondents had higher mean utilities than infected respondents for most of the health states.<sup>22</sup>

Beyond the patients with HC, most of the CHB patients with or without cirrhosis received no oral anti-viral medication. In treated population, lamivudine as well as its combination to adefovir or tenofovir were the common therapies, which agreed with Woo G (2012).<sup>21</sup> This might be explained that the early stage of CHB need less medication treatment than those in the late-stage. Surprisingly, the patients receive interferon or PEG-interferon was higher than what we predicted, while Woo G (2012) observed no cases treated with interferon.<sup>21</sup> This was good news because interferon as well as the PEG-interferon were the latest anti-viral interventions. The application of this modern therapy on liver disease patients, especially in provincial facilities, proved that Vietnamese healthcare system had updated the development of medical innovation globally. Nevertheless, previous study in 2012 found no associated

between anti-HBV administering and HRQoL among patients.<sup>21</sup> However, that was neither a prospective study nor longitudinal study, which the result may be affected by adverse drug reactions. Therefore, there were no affirmation that drug treatment reduce or improve the HRQoL in CHB patients.

The feature of this study was reporting alcohol-consumption in CHB patients, which did not mention in previous studies. The preference of self-reported alcohol intake in this study was extremely high (over 80% in all four stages). Especially, 98.5% patients with CC in KGGH stated to be alcohol drinkers. Although there were clinical evidences in the development of liver disease as the result from alcohol-intake, there were no prove in the impairment of HRQoL in CHB patients. In 2006, Strauss E<sup>23</sup> found the responsibility of alcoholism or a history of alcoholism for the reduction of the QoL in HCV-infected patients. However, the association between HRQoL in CHB patients and the alcohol consumption remain under-explored.

The mean PCS and MCS measured by SF36v2 in this study was varied, partly agreed with those reported in previous studies. There were only two studies included patients with different stages of disease,<sup>6,21</sup> which observed the same decrease of mean PCS and MCS from NC to CC and then DC patients. However, there was a point out of the line. Ong (2008)<sup>6</sup> found the higher MCS in CC patients (48.48) compared to 44.81 in NC patients. This study also found the higher PCS in CC patients (58.7) compared to 47.8 in NC patients in KGGH. However, this was a comparison based on the absolute value, which might not be statistical significance that should be tested further.

Beside the SF36v2, the two studies by Woo (2012)<sup>21</sup> and Ong (2008)<sup>6</sup> also reported health utilities measured by EQ5D and VAS. The mean score of EQ-5D in CHB patients in this study was slightly higher than Canadian norm [0.81 (0.80-0.82)], explored by Johnson (2000).<sup>24</sup> This finding was similar to those from Woo (2012)<sup>21</sup>, ranging 0.73 to 0.92, and Ong (2008),<sup>6</sup> ranging 0.83 to 1.0. DC patients found to had the lowest utilities in Woo's study, while HC patients hold the lowest score in Ong's study. Despite of the difference in EQ-5D questions, these two studies agreed with us in VAS, reflecting the impairment in VAS mean score from early to late-stage of CHB. Furthermore, unlike EQ-5D, VAS mean score in this three studies were significantly lower than Canadian norm 0.86 (0.85-0.87).<sup>24</sup>

In term of SG technique, the mean probability of death reported in this study was slightly higher than those from Woo (2012),<sup>21</sup> ranging 0.82 to 0.89, but much higher than those in Levy (2008),<sup>25</sup> ranging 0.35 to 0.69. This gap was

proved to be significant difference, however, could be explained by the difference in the study subjects. Levy (2008),<sup>25</sup> as stated above, included both HBV-infected patients and control group, leading to lower mean score due to the uninfected people. Healthy individuals usually offered lower probability of death in SG technique because they did not experience the disease state.

Out study had limitations. First, the recruitment of study subject was undertaken at two provincial hospitals, so the patients included in this study may not be representative of the whole country population. Second, as the largest consideration, statistical analysis was not applied in this study due to time restriction. This could make this study under-valuable and under-applicable. Third, SG technique had itself disadvantages that the respondents could not gamble the probability of death if their current health state was considered worst than death. Last but not least, our survey based on face-to-face interview which could have several biases. The respondents tended to give the answers to please the interviewers. However, compared with either paper-based or computer-based methods, interview-administered measurement proved its dominant strengths. Beyond the above limitations, this study was the first study in Vietnam using a different measurement instrument to give the comprehensive reflection of CHB on HRQoL. These findings formed a baseline input for cost-effectiveness analysis related to CHB in the future.

## Conclusion

This study used both preference-based and non-preference-based instruments to measure the HRQoL in HBV-infected patients. The patients at DC stage had the lowest health utility by most of the measurements. The results from different instruments were similar. These findings were promised to be a fundamental input for future cost-effectiveness analysis in the same field.

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**Conflict of Interest:** None to declare.

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