BMJ Open Assessing health-related quality of life and health utilities in patients with chronic hepatitis B-related diseases in China: a cross-sectional study

Meng Zhang ^{1,2}, Yaoguang Li,¹ Zihao Fan,³ Dongqi Shen,⁴ Xueying Huang,⁵ Qi Yu,⁶ Mei Liu,⁵ Feng Ren,³ Xiao Wang,^{2,7} Liping Dai,^{2,7} Peng Wang,^{1,2} Hua Ye,^{1,2} Jianxiang Shi,^{2,7} Xiaolang Yang,⁷ Shunxiang Zhang,^{1,7} Jianying Zhang^{1,7}

To cite: Zhang M, Li Y, Fan Z, *et al.* Assessing health-related quality of life and health utilities in patients with chronic hepatitis B-related diseases in China: a cross-sectional study. *BMJ Open* 2021;**11**:e047475. doi:10.1136/bmjopen-2020-047475

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2020-047475>).

Received 02 December 2020
Accepted 31 August 2021

© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to

Dr Jianying Zhang;
jianyingzhang@hotmail.com and
Dr Shunxiang Zhang;
zhangsx@szcdc.net

ABSTRACT

Objectives The health-related quality of life (HRQoL) and utilities of patients with chronic hepatitis B (CHB) virus infection, including compensated cirrhosis (CC), decompensated cirrhosis (DC) and different stages of hepatocellular carcinoma (HCC), have not been well described in China. This study aimed to evaluate HRQoL and utilities and provide parameters for the economic evaluation of CHB-related diseases.

Methods We conducted a multicentre cross-sectional and study to measure the HRQoL of patients with CHB, CC, DC and HCC using the Chinese short form (SF) 36 health survey V.2. The utilities were extracted based on the SF-six dimension scoring model. Multivariable regression analyses identified the effects on HRQoL.

Results A total of 1071 patients (639 with CHB, 125 with CC, 85 with DC and 222 with HCC) were invited to complete the questionnaire. Physical HRQoL was not impaired in the CHB stage, while mental HRQoL was significantly impaired. Physical composite summary scores have a more significant decrease than mental composite summary scores at the advanced stages (CC, DC and HCC). The utility scores of CHB only, CC, DC and HCC were 0.773, 0.750, 0.683 and 0.640, respectively. The utility scores in the early, middle and terminal stages of HCC were 0.656, 0.635 and 0.615, respectively.

Conclusion Slowing the progress of CHB-related diseases and providing psychological support early are the key points to improving the quality of life with the diseases. The utility values estimated in this study can provide a vital instrument for cost-effectiveness studies on CHB-related diseases.

INTRODUCTION

The high prevalence of chronic hepatitis B (CHB) calls for a significant global health concern. WHO member states have committed to global elimination with targets to reduce attributable deaths by 65% by the year 2030.^{1 2} Although new infectors with hepatitis B virus (HBV) have significantly declined among low age groups because of

Strengths and limitations of this study

- This multicentre cross-sectional survey aims to measure the health-related quality of life and health utility value of patients with hepatitis B-related diseases in China.
- Large-scale survey of 1071 patients with hepatitis B-related diseases, assessing the health-related quality of life and utility values of different sub-groups including different demographic sociological characteristics and, for the first time, the clinical stages of hepatocellular carcinoma.
- The adjustment has been made for confounders including the demographic sociological characteristics.
- All patients recruited from three tertiary hospitals may lead to selection bias.
- The health utility scores converted from short form (SF) 36 health survey V.2 based on the SF-six dimension scoring model for the Hong Kong Chinese population may differ from the mainland Chinese population.

hepatitis B vaccination campaigns in China, there is still a heavy burden in adults caused by CHB-related diseases, including compensated cirrhosis (CC), decompensated cirrhosis (DC) and different stages of hepatocellular carcinoma (HCC).^{3 4} It is not enough to draw increased attention to the social and health concerns of the diseases only through clinical indicators such as morbidity and mortality. The health-related quality of life (HRQoL) of CHB-related patients, which represent the patients' subjective feelings, should be accurately evaluated.⁵

Patients with CHB-related disease undergo decreased HRQoL, an essential patient-report outcome to evaluate any long-term therapeutic intervention and disease progression. Impaired HRQoL may be reflected in both psychological and physical aspects. To our knowledge, several

studies have shown the HRQoL of patients with CHB-related disease, but it is still uncertain whether the HRQoL of patients with CHB is similar to that of the normal population.^{6–11} Moreover, these studies only focused on Chinese patients with CHB and liver cirrhosis; few studies have focused on HCC or different stages of HCC.^{6,9} In addition, these studies were carried out almost 10 years ago, and HRQoL may change with societal development. Therefore, previous studies may not be able to explain the current HRQoL of patients with CHB-related diseases accurately.

Apart from being an index of patients' health and health utility, a preference indicator converted from HRQoL can be used in economic evaluation. The health utility value is a comprehensive indicator that integrates multiple dimensions and values full health as a score of one and death as a score of zero. The utility score is widely used to measure quality-adjusted life years in cost-effectiveness analyses. Owing to advances in early diagnosis by imaging and biomarkers, HCC can be detected at an early stage.¹² To improve the credibility of the cost-effectiveness analysis results, the health status in the Markov model is often divided according to the stages of HCC.^{13,14} When cost-effectiveness analysis focuses on antiviral treatment for patients with CHB-related disease, the utility scores of the patients with different characteristics are also required. The utility value is essential to the results of cost-effectiveness analyses, and a systematic review demonstrated that changes in utility should be used to test in sensitivity analysis.¹⁵ Few studies have described the health utility value of patients with HCC in various stages or with different characteristics in China.

The short form-36 V.2 (SF-36v2) health survey is widely used for HRQoL measures. The short form-six dimension (SF-6D) can be used to extract items from the SF-36 for preference-based valuation. Additionally, since differences in culture, economy and lifestyle are likely to impact HRQoL and health utility, studies of Chinese HRQoL and health utility should be converted based on Chinese population-based norms.^{6,9} The primary aim of this study was to evaluate the HRQoL of CHB-related diseases and the association between HRQoL and sociodemographic and clinical characteristics. The secondary aim was to extract the health utility score of patients with CHB-related disease, including CHB, CC, DC and stages of HCC. The results will allow us to understand the current health status of patients with CHB-related disease in China, and the health utility scores will play a vital role in measuring the cost-effectiveness of clinical and policy interventions for CHB-related diseases in China.

METHODS

Patient selection

This was a cross-sectional and multicentre study involving the clinical liver departments of three tertiary hospitals in China (two in Zhengzhou and one in Beijing). Consecutive CHB-related disease outpatients and HBV-related HCC inpatients were enrolled between July 2019 and January 2020. All patients had tested positive for hepatitis B surface antigen for more than 6 months.¹⁶ Patients with other chronic diseases (eg, chronic cardiovascular disease or diabetes) or infection with other viruses (eg, hepatitis C virus or HIV) were excluded. Patients younger than 18 years old or over 80 years old were also excluded.

Data collection

Each patient completed the Chinese SF-36v2 and provided his or her sociodemographic and disease characteristics data. The SF-36v2 is a widely used HRQoL questionnaire and has been proven to be suitable for the Chinese population. It contains 36 items that can measure eight scales of HRQoL: physical function (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE) and mental health (MH). The scores of the eight scales were aggregated into two summary scores based on the Standardisation of Chinese norms with a population mean of 50 and an SD of 10.¹⁷ The two summary scores are the physical composite summary (PCS) and mental composite summary (MCS). The utility scores were converted from SF-36v2 based on the SF-6D scoring model for the Hong Kong Chinese population established and validated by McGhee *et al*.^{18,19}

The CHB-related disease was characterised according to stages: CHB, CC, DC and HCC. Patients with CC or DC were diagnosed by Child-Pugh score.²⁰ Patients with HCC in early, middle or terminal stages were based on Barcelona clinic liver cancer (BCLC): BCLC (0/A), BCLC (B) and BCLC (C/D).²¹ Utility scores were also classified and calculated according to sociodemographic and disease characteristics.

Statistical analysis

For descriptive analysis of the study, categorical variables were described using proportions and continuous variables using the mean with SD and median with IQR. Comparisons among patients with CHB, CC, DC and HCC were carried out by the χ^2 test for categorical variables and the Wilcoxon rank-sum test for non-normally distributed continuous variables. In addition, multivariable regression analyses were conducted with PCS and MCS as dependent variables, adjusting for sociodemographic characteristics as possible confounders to investigate the effects of stage of disease and disease characteristics on HRQoL. All statistical analyses were performed using SPSS V.21.0 statistical software (IBM Corp.), and p values below 0.05 were considered statistically significant.

Table 1 Sociodemographic characteristics and clinical characteristics of study subjects

	HCC								
	CHB (n=639)	CC (n=125)	DC (n=85)	BCLC (0/A) (n=71)	BCLC (B) (n=60)	BCLC (C/D) (n=54)	BCLC (unknown) (n=37)	Overall (n=222)	Overall (n=1071)
Age n (%)	n*=597	n*=124							n*=1028
Mean (SD)	37.75 (9.62)	43.98 (10.31)	46.62 (10.66)	52.68 (9.69)	55.05 (9.76)	53.15 (10.629)	53.89 (11.56)	53.64 (10.26)	42.49 (11.85)
18–40	377 (63.2)	42 (33.9)	23 (27.1)	15 (21.1)	8 (13.3)	7 (13.0)	4 (10.8)	34 (15.3)	476 (44.4)
40–65	215 (36.0)	79 (63.7)	59 (69.4)	49 (69.0)	46 (76.7)	39 (72.2)	27 (73.0)	161 (72.5)	514 (38.1)
≥65	5 (0.8)	3 (2.4)	3 (3.5)	7 (9.9)	6 (10.0)	8 (14.8)	6 (16.2)	27 (12.2)	38 (3.5)
Gender n (%)									
Male	382 (59.8)	100 (80.0)	68 (80.0)	60 (84.5)	54 (90.0)	46 (85.2)	30 (81.1)	190 (85.6%)	740 (69.1)
Female	257 (40.2)	25 (20.0)	17 (20.0)	11 (15.5)	6 (10)	8 (14.9)	7 (18.9)	32 (14.4)	331 (30.9)
Marital status n (%)	n*=636							n*=221	n*=1066
Single	77 (12.1)	5 (4.0)	6 (7.1)	1 (1.4)	0 (0)	3 (5.6)	0 (0)	4 (1.8)	92 (8.6)
Married	550 (86.5)	117 (93.6)	74 (87.1)	66 (94.3)	59 (98.3)	48 (88.9)	36 (97.3)	209 (94.6)	950 (88.8)
Divorced	5 (0.8)	1 (0.8)	5 (5.9)	2 (2.9)	1 (1.7)	0 (0)	0 (0)	3 (1.4)	14 (1.7)
Widowed	4 (0.6)	1 (0.8)	0 (0)	1 (1.4)	0 (0)	3 (5.6)	1 (2.7)	5 (2.3)	10 (0.9)
Education level n (%)									
Primary or below	35 (5.4)	20 (16.0)	17 (20.0)	19 (26.8)	13 (21.7)	14 (25.9)	14 (37.8)	60(27)	132 (12.3)
High school	302 (47.3)	76 (60.8)	52 (60.8)	44 (62.0)	44 (73.3)	36 (66.7)	21 (56.8)	145 (65.3)	575 (53.7)
College or above	302 (47.3)	29 (23.2)	16 (23.2)	8 (11.2)	3 (5.0)	4 (7.4)	2 (5.4)	17 (7.7)	364 (34.0)
Occupation n (%)									
Farmer	34 (5.3)	18 (14.4)	16 (18.8)	19 (26.8)	14 (23.3)	16 (29.6)	17 (45.9)	66 (29.7)	134 (12.5)
Enterprise and institution staff	148 (23.2)	24 (19.2)	11 (12.9)	3 (4.2)	7 (11.7)	5 (9.3)	3 (8.1)	18 (8.1)	201 (18.8)
Commercial service provider	72 (11.3)	7 (5.6)	8 (9.4)	2 (2.8)	0 (0)	3 (5.6)	0 (0)	5 (2.3)	92 (8.6)
Professional and technical staff	67 (10.5)	7 (5.6)	4 (4.7)	3 (4.2)	0 (0)	1 (1.9)	1 (2.7)	5 (23.)	83 (7.7)
Manufacturing employees	92 (14.4)	32 (25.6)	28 (32.9)	28 (39.4)	30 (50.0)	21 (38.9)	9 (24.3)	89 (39.6)	240 (22.4)
Retired	27 (4.2)	7 (5.6)	5 (5.9)	6 (8.5)	4 (6.7)	4 (7.4)	4 (10.8)	18 (8.1)	57 (5.3)
Others	198 (31.0)	30 (24.0)	13 (15.3)	10 (14.1)	5 (8.3)	4 (7.4)	3 (8.1)	22 (9.9)	263 (24.6)
Receiving antiviral therapy n (%)					n*=59	n*=53			
Yes	485 (75.9)	113 (90.4)	71 (83.5)	40 (59.7)	34 (57.6)	29 (54.7)	27 (73.0)	130 (60.2)	799 (75.0)
No	154 (24.1)	12 (9.6)	14 (16.5)	27 (40.3)	25 (42.4)	24 (45.3)	10 (27.0)	86 (39.8)	266 (25.0)
Duration of infection with HBV n (%)					n*=53	n*=40		n*=190	n*=949
Less than 5 years	139 (24.9)	35 (29.7)	21 (25.3)	22 (36.7)	16 (30.2)	12((30.0)	12 (32.4)	62 (32.6)	257 (27.1)

Continued

	CHB (n=639)	CC (n=125)	DC (n=85)	HCC					Overall (n=1071)
				BCLC (0/A) (n=71)	BCLC (B) (n=60)	BCLC (C/D) (n=54)	BCLC (unknown) (n=37)	Overall (n=222)	
More than 5 years	419 (75.1)	83 (70.3)	62 (74.7)	38 (63.3)	37 (69.8)	28 (70.0)	25 (67.6)	128 (67.4)	692 (72.9)
Surgery treatment n (%)									
No	–	–	–	20 (28.2)	12 (20.0)	12 (22.2)	14 (37.8)	58 (26.1)	–
Within 6 months	–	–	–	36 (50.7)	33 (55.0)	31 (57.4)	9 (24.3)	109 (49.1)	–
More than 6 months	–	–	–	15 (21.1)	15 (25.0)	11 (20.4)	14 (37.8)	55 (24.8)	–

BCLC, Barcelona clinic liver cancer; CC, compensated cirrhosis; CHB, chronic hepatitis B; DC, decompensated cirrhosis; HBV, hepatitis B virus; HCC, hepatocellular carcinoma.

The univariate regression analysis results reflect the associations between each summary score and

Table 2 Mean short form-36 (SF-36) scores and health utility scores (SD) for each group of patients

SF-36 v2	CHB (n=639)	CC (n=125)	DC (n=85)	HCC			
				BCLC (0/A) (n=71)	BCLC (B) (n=60)	BCLC (C/D) (n=54)	Overall (n=222)
PF	53.97 (6.00)	49.17 (10.92)*	46.21 (11.14)*†	42.31 (13.22)	37.48 (16.20)	39.93 (14.72)	40.42 (14.57)*†‡
RP	51.48 (9.90)	47.31 (13.02)*	39.39 (15.31)*†	35.73 (17.04)	34.68 (17.33)	28.94 (16.34)	34.54 (16.95)*†‡
BP	50.61 (9.17)	49.59 (11.49)	43.51 (12.68)*†	39.86 (13.83)	38.21 (14.74)	36.84 (15.51)	39.06 (14.70)*†‡
GH	44.69 (10.75)	40.87 (10.79)*	36.54 (12.74)*†	38.13 (11.85)	37.49 (11.12)	37.67 (11.39)	37.56 (11.16)*†
VT	46.18 (10.45)	42.00 (11.42)*	38.05 (13.03)*†	41.00 (14.38)	40.99 (12.85)	37.45 (14.10)	39.50 (13.71)*
SF	50.03 (10.44)	47.63 (12.70)	42.91 (13.61)*†	39.92 (15.09)	37.02 (14.23)	37.08 (15.65)	38.49 (15.44)*†‡
RE	48.82 (12.22)	48.62 (13.31)	42.40 (15.05)*†	38.33 (17.74)	36.64 (18.42)	33.01 (19.65)	37.34 (18.29)*†‡
MH	45.02 (10.56)	43.27 (12.35)	42.97 (12.10)	40.19 (15.36)	41.33 (13.74)	39.44 (15.42)	40.49 (14.61)*
PCS	52.86 (6.848)	48.56 (10.03)*	42.63 (11.48)*†	40.26 (11.05)	36.93 (11.17)	36.82 (11.80)	38.63 (11.42)*†‡
MCS	44.99 (11.30)	43.76 (11.93)	41.30 (12.30)*	39.61 (14.93)	39.92 (13.19)	37.17 (16.70)	39.23 (14.85)*†
Utility	0.773 (0.131)	0.750 (0.146)	0.683 (0.128)*†	0.656 (0.145)	0.635 (0.132)	0.615 (0.128)	0.640 (0.133)*†‡

*Significant different with chronic hepatitis B (CHB) ($p<0.05$).

†Significant different with compensated cirrhosis (CC) ($p<0.05$).

‡Significant different with decompensated cirrhosis (DC) ($p<0.05$).

BCLC, Barcelona clinic liver cancer; BP, bodily pain; GH, general health; HCC, hepatocellular carcinoma; MCS, mental components summary; MH, mental health; PCS, physical component summary; PF, physical functioning; RE, role emotional; RP, role physical; SF, social functioning; VT, vitality.

sociodemographic and disease characteristics (table 4). Male sex, older age, lower education, occupation as a farmer and advanced stages of disease were significantly associated with worse summary scores.

For the multivariable regression analyses, sociodemographic characteristics were accounted for, and a stepwise regression model evaluated disease characteristics. Only variate disease status was selected for the three summary scores. Patients with CC had 3.603 points worse PCS (95% CI -5.395 to -1.811) and 1.679 points worse MCS (95% CI -4.182 to 0.823) compared with patients with CHB. Patients with DC had 9.110 points worse PCS (95% CI -11.244 to -6.976) and 4.130 points worse MCS (95% CI -7.112 to -1.148) compared with patients with CHB. Patients with HCC had 12.772 points worse PCS (95% CI -14.535 to -11.009) and 6.951 points worse MCS (95% CI -9.414 to -4.488) compared with patients with CHB.

DISCUSSION

HRQoL subjectively reported by the patient is a significant outcome in evaluating any intervention, mainly in patients with chronic or poorly curable diseases and is more relevant than the length of life, which is more of a concern for patients than longevity.^{22 23} CHB-related disease is still the chronic liver disease with the heaviest disease burden in China; more than 50% of liver-related deaths were caused by HBV infection in 2015.²⁴ Therefore, a comprehensive evaluation of HRQoL for CHB-related diseases is valuable for identifying patients' needs and benefits of treatment and improvement of care and treatment services, that fit with the global hepatitis

elimination targets set by WHO.^{1 2} This study is a multi-centre and systematic study to measure HRQoL and utility scores of patients at all stages of CHB-related diseases in China. We found that the impairment of HRQoL in patients with CHB is mainly manifested in the psychological aspect, while physical HRQoL is similar to that of the general population, which is similar to the findings of Xi'an.⁶ The mental HRQoL impairment of patients with CHB has not been found in the USA, Hong Kong or Canada.^{7 8 10} Patients in CC had worse HRQoL than those in CHB, and more profound impairment was presented in advanced stages (DC and HCC). The results illustrate that the progress of the disease can cause the gradual impairment of HRQoL in patients with CHB-related disease. In addition, the mental HRQoL impairment in patients with CHB suggested that psychological support therapy should be strengthened, rather than just focusing on the normality of clinical indicators.

There is an increasing demand for the use of health utility in economic evaluations of health policy.^{25 26} Assessments of utility values for various health states in CHB disease are essential to estimate the cost-effectiveness of the management of CHB disease. This study is also the first to evaluate the HRQoL and utility value of patients in early, middle and terminal HCC stages in China. We also calculated the utility value of different groups by reclassifying them according to age, gender, whether they had received antiviral treatment and the time of the last operation. The utility value of patients with DC receiving antiviral therapy is significantly lower than that of patients not receiving antiviral therapy. The reasons may be as follows. First,

Status of disease	Age			Gender		Antiviral therapy*		Surgery treatment†	
	18–40	40–65	≥65	Male	Female	Yes	No	No	>6 months
CHB	0.765 (0.134)	0.872 (0.126)	0.845 (0.093)	0.770 (0.131)	0.778 (0.131)	0.772 (0.131)	0.777 (0.129)	–	–
CC	0.751 (0.137)	0.744 (0.152)	0.896 (0.037)	0.751 (0.149)	0.744 (0.138)	0.718 (0.175)	0.753 (0.143)	–	–
DC	0.702 (0.134)	0.670 (0.123)	0.780 (0.200)	0.676 (0.133)	0.711 (0.106)	0.665 (0.123)	0.771 (0.125)	–	–
HCC	0.626 (0.100)	0.645 (0.138)	0.625 (0.144)	0.642 (0.135)	0.627 (0.125)	0.640 (0.135)	0.640 (0.134)	0.688 (0.138)	0.613 (0.123)

The difference between the two groups in bold is statistically significant.

*Significant differences were found in the patients with decompensated cirrhosis (DC) between received antiviral therapy group and not received antiviral therapy group ($p < 0.05$).

†Significant differences were found in the patients with hepatocellular carcinoma (HCC) between not undergone surgery group and less than 6 months from the last surgery group ($p < 0.05$). CC, compensated cirrhosis; CHB, chronic hepatitis B.

whether to receive antiviral treatment is generally based on the patient's condition, and patients with more serious conditions are more likely to receive antiviral treatment. Second, since the price of antiviral drugs in China has fallen sharply in recent years, it is unlikely that the antiviral treatment that should be accepted is unacceptable for reasons of drug prices. Significant difference was also observed between the not undergone surgery group and the less than 6 months from the last surgery group. This may be because the surgical trauma is severe, and the HRQoL of patients who have just undergone liver cancer surgery may decrease significantly. The results can also provide parameters for the cost-effectiveness analyses of HCC early screening, treatment methods and drugs applicable to different stages of HCC, the utility parameter, which is an important instrument, generally came from data from other countries, which may affect the reliability of the research results to a certain extent. Nevertheless, the results of this study can provide reliable instrument support for the cost-effectiveness analysis related to HCC in China.

The results of multiple linear regression analyses suggest that the advanced stages of disease have a negative impact on physical HRQoL, and lower education and advanced stages of disease have a negative impact on mental HRQoL. Hepatitis B infection may cause more anxiety and tension among patients with low education than among highly educated patients because of their lower awareness of the disease. Therefore, more attention should be paid to the psychology of patients with low education. Doctors should inform patients of disease-related knowledge when treating them to minimise patients' fear and anxiety, encouraging better HRQoL. This study did not observe significant differences in HRQoL between patients receiving antiviral therapy and those who did not receive antiviral therapy, regardless of the stage of disease, which is different from the study in Xiamen.²⁷ We found that antiviral therapy was not associated with worse or better HRQoL. However, this study is a cross-sectional study, and the study in Xiamen was a follow-up study that may be better able to distinguish differences in HRQoL before and after antiviral treatment.

Our study has some limitations. All patients were recruited from three tertiary hospitals in two cities, in which the patients might have worse HRQoL. There is no strict tiered medical treatment system in China; most patients in tertiary hospitals can receive reasonable treatment in community hospitals. Therefore, it is unlikely that selection bias was caused by the patient source. This study is not a follow-up study, so it cannot be absolutely judged that the patient's life treatment will become worse as the disease progresses. Nevertheless, this cross-sectional study can suggest the above result. The utility scores were converted from SF-36v2 based on the SF-6D scoring model for the Hong Kong

Table 4 Univariate analysis and multivariate analysis of physical composite summary, mental composite summary and utility scores for patients with chronic hepatitis B (CHB)-related disease

Variable	Physical component summary		Mental component summary	
	Univariate analysis coefficient (95% CI)	Multivariate analysis coefficient (95% CI)	Univariate analysis coefficient (95% CI)	Multivariate analysis coefficient (95% CI)
Age	-0.319 (-0.371 to -0.268)	-0.048 (-0.114 to 0.018)	-0.007 (-0.073 to 0.058)	0.178 (0.086 to 0.270)
Sex				
Female	Reference	Reference	Reference	Reference
Male	-2.961 (-4.318 to -1.604)	-0.388 (-1.642 to 0.865)	-0.880 (-2.498 to 0.739)	0.207 (-1.544 to 1.958)
Marital status				
Single	Reference	Reference	Reference	Reference
Married	-4.679 (-6.857 to -2.501)	-1.302 (-3.358 to 0.755)	0.182 (-2.430 to 2.795)	-0.043 (-2.917 to 2.831)
Divorced	-12.568 (-18.410 to -6.726)	-7.764 (-13.160 to -2.269)	-1.262 (-8.269 to 5.745)	-1.211 (-8.750 to 6.327)
Widowed	-10.475 (-17.261 to -3.688)	-3.666 (-9.614 to 2.282)	-0.105 (-8.269 to 5.745)	0.419 (-7.891 to 8.729)
Education level				
Primary or below	Reference	Reference	Reference	Reference
High school	4.600 (2.670 to 6.530)	-1.302 (-3.358 to 0.755)	3.904 (1.557 to 6.252)	3.091 (0.587 to 5.595)
College or above	8.648 (6.617 to 10.680)	-7.764 (-13.160 to -2.369)	4.956 (2.485 to 7.427)	3.521 (0.364 to 6.679)
Occupation				
Farmer	Reference	Reference	Reference	Reference
Enterprise and institution staff	7.668 (5.466 to 9.870)	1.083 (-0.710 to 2.875)	3.725 (1.011 to 6.439)	1.380 (-1.838 to 4.597)
Commercial service provider	8.160 (5.485 to 10.863)	1.541 (-0.719 to 3.801)	4.109 (0.812 to 7.406)	1.408 (-2.165 to 4.597)
Professional and technical staff	6.657 (3.897 to 9.417)	0.525 (-1.778 to 2.828)	3.488 (0.086 to 6.890)	0.921 (-3.084 to 4.927)
Manufacturing employees	1.936 (-0.193 to 4.065)	1.153 (-1.405 to 3.710)	1.578 (-1.045 to 4.202)	1.081 (-1.599 to 3.762)
Retired	2.690 (-0.436 to 5.815)	0.850 (-2.203 to 3.903)	4.476 (0.623 to 8.328)	-0.488 (-4.754 to 3.777)
Others	7.947 (5.852 to 10.042)	0.654 (-1.452 to 2.760)	3.621 (1.038 to 6.203)	2.004 (-0.939 to 4.946)
Status of disease				
CHB	Reference	Reference	Reference	Reference
CC	-4.304 (-5.989 to -2.618)	-3.603 (-5.395 to -1.811)	-1.229 (-3.583 to 1.126)	-1.679 (-4.182 to 0.823)
DC	-10.229 (-12.218 to -8.239)	-9.110 (-11.244 to -6.976)	-3.687 (-6.467 to -0.907)	-4.130 (-7.112 to -1.148)
HCC	-14.227 (-15.569 to -12.884)	-12.772 (-14.535 to -11.009)	-5.760 (-7.636 to -3.885)	-6.951 (-9.414 to -4.488)
Receiving antiviral therapy				
No	Reference	Reference	Reference	Reference
Yes	1.186 (-0.273 to 2.645)		-0.650 (-2.384 to 1.084)	
Duration of infection with HBV				

Continued

Variable	Physical component summary		Mental component summary	
	Univariate analysis coefficient (95% CI)	Multivariate analysis coefficient (95% CI)	Univariate analysis coefficient (95% CI)	Multivariate analysis coefficient (95% CI)
	Reference		Reference	
Less than 5 years				
More than 5 years	1.357 (0.036 to 2.677)		-0.532 (-2.096 to 1.033)	

CC, compensated cirrhosis; DC, decompensated cirrhosis; HBV, hepatitis B virus; HCC, hepatocellular carcinoma (HCC).

Chinese population, which might be different from the mainland Chinese population. However, the population of the Hong Kong model is the closest available to the mainland Chinese population. This also reminds us that the establishment of a model for the mainland Chinese population is urgently needed.

CONCLUSION

In summary, our study shows that the impairment of HRQoL is mainly reflected in the psychological aspect in the stage of CHB. The overall HRQoL will decrease as the disease progresses. Therefore, slowing the progress of CHB-related diseases can help patients maintain a better HRQoL. We not only focused on the normality of clinical indicators but also provided psychological support in the early stage of the disease, which is a key point to improve the disease-related quality of life. The utility results estimated in this study can provide an essential instrument for cost-effectiveness studies on CHB-related disease.

Author affiliations

¹Department of Epidemiology and Health Statistics & Henan Key Laboratory for Tumor Epidemiology, College of Public Health, Zhengzhou University, Zhengzhou, Henan, People's Republic of China

²State Key Laboratory of Esophageal Cancer Prevention & Treatment, Zhengzhou University, Zhengzhou, Henan, People's Republic of China

³Beijing Institute of Hepatology, Beijing Youan Hospital, Capital Medical University, Beijing, People's Republic of China

⁴Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, People's Republic of China

⁵Department of Oncology, Beijing Youan Hospital, Capital Medical University, Beijing, People's Republic of China

⁶Department of Interventional Radiology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, People's Republic of China

⁷Henan Academy of Medical and Pharmaceutical Sciences & BGI College, Zhengzhou University, Zhengzhou, Henan, People's Republic of China

Contributors MZ, JZ and SZ were responsible for study concept and design. MZ, YL, ZF, DS, XH, QY, ML and FR contributed to data acquisition and interpretation. MZ and YL performed all statistical analyses. MZ had main responsibility for writing the article. XW, LD, PW, HY, JS, XY, SZ, JZ provided comments on the manuscript. All authors read and approved the final manuscript.

Funding The study was funded by the Major Project of Science and Technology in Henan Province (161100311400).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was approved by the ethics committee of Zhengzhou University (ZZURIB2019-001) and all participants of the cross-sectional study provided written informed consent.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. No data are available.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Meng Zhang <http://orcid.org/0000-0003-2971-5109>

REFERENCES

- 1 World Health Organisation. Combating hepatitis B and C to reach elimination by 2030. Advocacy brief, 2016. Available: <https://www.who.int/publications/i/item/combating-hepatitis-b-and-c-to-reach-elimination-by-2030>
- 2 World Health Organisation. Global health sector strategy on viral hepatitis, 2016–2021: towards ending viral hepatitis, 2016. Available: <https://www.who.int/publications/i/item/WHO-HIV-2016.06>
- 3 Cui F, Shen L, Li L, *et al.* Prevention of chronic hepatitis B after 3 decades of escalating vaccination policy, China. *Emerg Infect Dis* 2017;23:765–72.
- 4 Wang H, Men P, Xiao Y, *et al.* Hepatitis B infection in the general population of China: a systematic review and meta-analysis. *BMC Infect Dis* 2019;19:811.
- 5 Cella D, Stone AA. Health-Related quality of life measurement in oncology: advances and opportunities. *Am Psychol* 2015;70:175–85.
- 6 Zhuang G, Zhang M, Liu Y, *et al.* Significant impairment of health-related quality of life in mainland Chinese patients with chronic hepatitis B: a cross-sectional survey with pair-matched healthy controls. *Health Qual Life Outcomes* 2014;12:101.
- 7 Bondini S, Kallman J, Dan A, *et al.* Health-related quality of life in patients with chronic hepatitis B. *Liver Int* 2007;27:1119–25.
- 8 Lam ETP, Lam CLK, Lai CL, *et al.* Health-related quality of life of southern Chinese with chronic hepatitis B infection. *Health Qual Life Outcomes* 2009;7:52.
- 9 Gao R, Gao F, Li G, *et al.* Health-Related quality of life in Chinese patients with chronic liver disease. *Gastroenterol Res Pract* 2012;2012:1–7.
- 10 Younossi ZM, Stepanova M, Younossi I, *et al.* Patient-reported outcomes in patients chronic viral hepatitis without cirrhosis: the impact of hepatitis B and C viral replication. *Liver Int* 2019;39:1837–44.
- 11 Evon DM, Lin H-HS, Khalili M, *et al.* Patient-reported outcomes in a large North American cohort living with chronic hepatitis B virus: a cross-sectional analysis. *Aliment Pharmacol Ther* 2020;51:457–68.
- 12 Wang K, Li M, Qin J, *et al.* Serological biomarkers for early detection of hepatocellular carcinoma: a focus on autoantibodies against tumor-associated antigens encoded by cancer driver genes. *Cancers* 2020;12:e127.
- 13 Kim SY, An J, Lim Y-S, *et al.* MRI with liver-specific contrast for surveillance of patients with cirrhosis at high risk of hepatocellular carcinoma. *JAMA Oncol* 2017;3:456–63.
- 14 Lima PH, Fan B, Bérubé J. Cost-Utility analysis of imaging for surveillance and diagnosis of hepatocellular carcinoma. *AJR Am J Roentgenol* 2019;17:1–9.
- 15 Schackman BR, Gold HT, Stone PW, *et al.* How often do sensitivity analyses for economic parameters change cost-utility analysis conclusions? *Pharmacoeconomics* 2004;22:293–300.
- 16 European Association For The Study Of The Liver. EASL clinical practice guidelines: management of chronic hepatitis B. *J Hepatol* 2009;50:227–42.
- 17 Wang HM. *The influence of common chronic diseases on patients' quality of life in Chinese and German communities*. 1st ed. Zhejiang, China: Zhejiang University Press, 2015: 207–8.
- 18 Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. *J Health Econ* 2002;21:271–92.
- 19 Lam CLK, Brazier J, McGhee SM. Valuation of the SF-6D health states is feasible, acceptable, reliable, and valid in a Chinese population. *Value Health* 2008;11:295–303.
- 20 Chinese Society of Infectious Diseases, Chinese Medical Association, Chinese Society of Hepatology, Chinese Medical Association. [The guidelines of prevention and treatment for chronic hepatitis B (2019 version)]. *Zhonghua Gan Zang Bing Za Zhi* 2019;27:938–61.
- 21 Bruix J, Sherman M, Practice Guidelines Committee, American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma. *Hepatology* 2005;42:1208–36.
- 22 Gandhi S, Khubchandani S, Iyer R, *et al.* Quality of life and hepatocellular carcinoma. *J Gastrointest Oncol* 2014;5:296–317.
- 23 Qiao C-X, Zhai X-F, Ling C-Q, *et al.* Health-Related quality of life evaluated by tumor node metastasis staging system in patients with hepatocellular carcinoma. *World J Gastroenterol* 2012;18:2689–94.
- 24 Sarin SK, Kumar M, Eslam M, *et al.* Liver diseases in the Asia-Pacific region: a Lancet Gastroenterology & Hepatology Commission. *Lancet Gastroenterol Hepatol* 2020;5:167–228.
- 25 Higgins AM, Harris AH. Health economic methods: cost-minimization, cost-effectiveness, cost-utility, and cost-benefit evaluations. *Crit Care Clin* 2012;28:11–24.
- 26 Angevine PD, Berven S. Health economic studies: an introduction to cost-benefit, cost-effectiveness, and cost-utility analyses. *Spine* 2014;39:S9–15.
- 27 Xue X, Cai S, Ou H, *et al.* Health-related quality of life in patients with chronic hepatitis B during antiviral treatment and off-treatment. *Patient Prefer Adherence* 2017;11:85–93.