

## Psychometrics of chronic liver disease questionnaire in Chinese chronic hepatitis B patients

Kai-Na Zhou, Min Zhang, Qian Wu, Zhen-Hao Ji, Xiao-Mei Zhang, Gui-Hua Zhuang

Kai-Na Zhou, Min Zhang, Qian Wu, Zhen-Hao Ji, Xiao-Mei Zhang, Gui-Hua Zhuang, Department of Epidemiology and Biostatistics, Xi'an Jiaotong University College of Medicine, Xi'an 710061, Shaanxi Province, China

**Author contributions:** All authors participated in the design of the study; Zhou KN, Zhang M, Ji ZH and Zhang XM collected data; Zhou KN, Zhang M and Zhuang GH were involved in data analysis and interpretation; Zhou KN and Zhuang GH drafted the manuscript; all authors have read and approved the final manuscript.

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**Correspondence to:** Gui-Hua Zhuang, PhD, Department of Epidemiology and Biostatistics, Xi'an Jiaotong University College of Medicine, No. 76 Yanta Western Road, Xi'an 710061, Shaanxi Province, China. [zhuanggh@mail.xjtu.edu.cn](mailto:zhuanggh@mail.xjtu.edu.cn)

Telephone: +86-29-82655108 Fax: +86-29-82655032

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### Abstract

**AIM:** To evaluate psychometrics of the Chinese (mainland) chronic liver disease questionnaire (CLDQ) in patients with chronic hepatitis B (CHB).

**METHODS:** A cross-sectional sample of 460 Chinese patients with CHB was selected from the Outpatient Department of the Eighth Hospital of Xi'an, including CHB (CHB without cirrhosis) ( $n = 323$ ) and CHB-related cirrhosis ( $n = 137$ ). The psychometrics includes reliability, validity and sensitivity. Internal consistency reliability was measured using Cronbach's  $\alpha$ . Convergent and discriminant validity was evaluated by item-scale correlation. Factorial validity was explored by principal component analysis with varimax rotation. Sensitivity was assessed using Cohen's effect size (ES), and independent sample  $t$  test between CHB and CHB-related cirrhosis groups and between alanine aminotransferase (ALT) normal and abnormal groups after stratifying the disease (CHB and CHB-related cirrhosis).

**RESULTS:** Internal consistency reliability of the CLDQ was 0.83 (range: 0.65-0.90). Most of the hypothesized item-scale correlations were 0.40 or over, and all of such hypothesized correlations were higher than the alternative ones, indicating satisfactory convergent and discriminant validity. Six factors were extracted after varimax rotation from the 29 items of CLDQ. The eligible Cohen's ES with statistically significant independent sample  $t$  test was found in the overall CLDQ and abdominal, systematic, activity scales (CHB vs CHB-related cirrhosis), and in the overall CLDQ and abdominal scale in the stratification of patients with CHB (ALT normal vs abnormal).

**CONCLUSION:** The CLDQ has acceptable reliability, validity and sensitivity in Chinese (mainland) patients with CHB.

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**Key words:** Chronic hepatitis B; Chronic liver disease questionnaire; Reliability; Validity; Sensitivity

**Core tip:** Chronic hepatitis B (CHB) is a common chronic liver disease in mainland China, and its adverse prognosis might impair the patients' health-related quality of life (HRQoL). The chronic liver disease questionnaire (CLDQ) is the first liver specific HRQoL instrument, however, few studies have examined psychometrics of the Chinese (mainland) CLDQ in CHB patients. This study tested psychometrics of the Chinese (mainland) CLDQ in patients with CHB (including CHB without cirrhosis and CHB-related cirrhosis). The findings will help find suitable disease-specific questionnaire in the management of CHB in mainland China and provide evidence for expanding the use of the CLDQ.

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## INTRODUCTION

Chronic hepatitis B (CHB), caused by persistent infection with hepatitis B virus (HBV), is a common chronic liver disease in mainland China. According to the latest national hepatitis B seroepidemiological survey<sup>[1]</sup>, the estimated current HBV carriers in mainland China run up to 93 million, including 20-30 million patients with CHB<sup>[2]</sup>. CHB patients suffer recurrent symptoms in the long disease natural history and are at a high risk of developing fatal complications of cirrhosis and hepatocellular carcinoma<sup>[3,4]</sup>. Therefore, CHB may result in a heavy disease burden not only in premature death but also in health impairment<sup>[5-8]</sup>.

Health-related quality of life (HRQoL) is defined as how the individual rates his/her life in terms of physical, psychological and social aspects<sup>[9]</sup>. In comparison with clinical parameters, HRQoL is a more holistic assessment of health status considering the individual's functional health and well-being, especially in chronic disease in which mortality is not an immediate concern<sup>[3]</sup>. Due to the complex natural history and phases of CHB<sup>[10]</sup>, it is particularly important to use HRQoL as the primary endpoint for evaluating health and treatment effects in patients with such disease.

Generally, HRQoL can be measured by generic and disease-specific instruments. Generic instruments are used to compare the HRQoL between groups of patients, but disease-specific questionnaires distinguish the impairment of a specific illness and are more sensitive to the change<sup>[11,12]</sup>. The 36-item short-form health survey version 2 (SF-36v2) performs well as a generic instrument in patients with CHB<sup>[13]</sup>. However, not every scale or summary component of the SF-36v2 has the required or eligible sensitivity<sup>[14]</sup>. Therefore, a disease-specific HRQoL instrument is recommended as a complement for clinical studies in CHB.

The chronic liver disease questionnaire (CLDQ) is the first liver specific instrument developed by Younossi *et al.*<sup>[15]</sup>. It has been translated into different languages for cross-cultural adaptation<sup>[16-23]</sup> and proved as a valid tool for HRQoL measurement and evaluation in patients with chronic liver disease<sup>[24,25]</sup>. The Chinese (Hong Kong, China) CLDQ has been validated in patients with CHB infection<sup>[14]</sup>. However, a dearth of study assessed psychometrics of the Chinese (mainland) CLDQ in mainland Chinese patients with CHB<sup>[26]</sup>.

The purpose of the study was to evaluate psychometrics including reliability, validity and sensitivity of the Chinese (mainland) CLDQ in CHB patients. The findings of this study will help find suitable disease-specific questionnaire in the management of CHB in mainland China and add to the body of evidence for expanding the use of the CLDQ.

## MATERIALS AND METHODS

### Patients and data collection

Participants were CHB outpatients from the Eighth Hospital of Xi'an, which is the only local infectious disease hospital in Xi'an, Shaanxi Province, China. Inclusion criteria were aged 18 years or over, Chinese-speaking, with diagnosis of CHB (CHB without cirrhosis) or CHB-related cirrhosis. The diagnosis was made following the standards in the Guideline of Prevention and Treatment for Chronic Hepatitis B (2005 version) issued by the Chinese Society of Hepatology and the Chinese Society of Infectious Diseases<sup>[27]</sup>. If the patients had other chronic diseases (including hypertension, diabetes, chronic obstructive pneumonia disease, cardiovascular disease, mental illness, arthritis, tuberculosis, or gallstone), non-hepatitis B related liver disease, malignancies of liver or other organs, liver transplantation, cognitive disorders, or co-infected with human immunodeficiency virus or other types of hepatitis virus (*e.g.*, hepatitis A virus, hepatitis C virus, hepatitis D virus or hepatitis E virus), or refused to give written informed consent, they would be excluded.

Data were collected from April to June 2010. An individual face-to-face interview was administered by the trained interviewers in a quiet and well-lit room. The patients answered questions of sociodemographics and the Chinese (mainland) CLDQ. In addition to this, a free alanine aminotransferase (ALT) test was provided for the patients immediately after the questionnaire survey. The test was conducted in the laboratory of the Eighth Hospital of Xi'an.

### Chinese (mainland) CLDQ

The Chinese (mainland) CLDQ was provided by the developers of the original CLDQ<sup>[15]</sup>. It consists of 29 items measuring six scales on abdominal symptoms (AB), fatigue (FA), systemic symptoms (SY), activity (AC), emotional function (EM) and worry (WO). Each item is rated on a 7-point Likert scale (1 = all of the time to 7 = none of the time). The six scale scores are calculated by the summated averages of corresponding endorsed item scores. The total score is calculated by the mean of all scale scores. Each scale and the total score ranged from 1 to 7, with a higher score indicating better HRQoL.

### Reliability and floor/ceiling effects

Cronbach's  $\alpha$  coefficient was used to assess the internal consistency reliability, with the value greater than 0.70 representing acceptable reliability<sup>[28]</sup>. Floor and ceiling effects were calculated as the number and percentage of CHB patients at the lowest and highest possible scores for each scale and the overall CLDQ. It should be less than 20% regarding both the floor and ceiling effect to ensure that the scales are capturing the full range of potential responses in the population and that changes over time can be detected<sup>[29]</sup>.

**Table 1** Social-demographic characteristics *n* (%)

Items	Total ( <i>n</i> = 460)	CHB ( <i>n</i> = 323)	CHB-related cirrhosis ( <i>n</i> = 137)
Age (yr)			
18-35	240 (52.2)	216 (90.0)	24 (10.0)
36-50	152 (33.0)	87 (57.2)	65 (42.8)
51-65	64 (13.9)	20 (31.3)	44 (68.8)
66-76	4 (0.9)	0 (0.0)	4 (100.0)
mean $\pm$ SD	35.75 $\pm$ 12.82	31.53 $\pm$ 10.94	45.71 $\pm$ 11.36
Gender			
Male	305 (66.3)	212 (69.5)	93 (30.5)
Female	155 (33.7)	111 (71.6)	44 (28.4)
Marital status			
Single	125 (27.2)	119 (95.2)	6 (4.8)
Married	328 (71.3)	200 (61.0)	128 (39.0)
Others	7 (1.5)	4 (57.1)	3 (42.9)
Education level			
No schooling and primary	63 (13.7)	31 (49.2)	32 (50.8)
Secondary	311 (67.6)	217 (69.8)	94 (30.2)
Tertiary	86 (18.7)	75 (87.2)	11 (12.8)
Occupation			
Peasants	153 (33.3)	73 (47.7)	80 (52.3)
Non-peasants	307 (66.7)	250 (81.4)	57 (18.6)
Annual per capita household incomes (RMB)			
< 5000	236 (51.3)	147 (62.3)	89 (37.7)
5000-9999	111 (24.1)	88 (79.3)	23 (20.7)
$\geq$ 10000	113 (24.6)	88 (77.9)	25 (22.1)
Received ALT test			
Yes	375 (81.5)	311 (82.9)	64 (17.1)
No	85 (18.5)	12 (14.1)	73 (85.9)

CHB: Chronic hepatitis B; ALT: Alanine aminotransferase.

### Validity

The hypothesized item-scale correlation ( $\gamma$  coefficient)  $\geq$  0.40 was considered as satisfactory convergent validity<sup>[30]</sup>. Discriminant validity was supported whenever the hypothesized item-scale correlation was significantly higher than the correlation of the item with other scales<sup>[31]</sup>. Factorial validity of the CLDQ was explored using the principal component analysis with varimax rotation. The predictive items with factor loading coefficient (FLC)  $\geq$  0.45<sup>[32]</sup> and the extracted factors with an eigenvalue  $\geq$  1.0<sup>[33]</sup> were considered to be relevant.

### Sensitivity

Sensitivity was evaluated by Cohen's effect size (ES), and independent sample *t* test between CHB and CHB-related cirrhosis groups and between ALT normal and abnormal groups after stratifying the disease (CHB and CHB-related cirrhosis). The ES value was calculated as the difference between group mean scores divided by overall standard deviation. According to Cohen, the ES of 0.2-0.5 is small, of 0.5-0.8 moderate, and those of 0.8 or above large<sup>[31]</sup>. Besides, multiple linear regression analysis was used to further prove sensitivity of the CLDQ under the influence of ALT (normal *vs* abnormal). The six scales and overall CLDQ scores were dependent variables, respectively, while the controlled independent variables were age, gender, marital status, education level,

**Table 2** Internal consistency reliability, floor and ceiling effects of the chronic liver disease questionnaire (*n* = 460) *n* (%)

Items	Cronbach's $\alpha$	Floor and ceiling effects <sup>1</sup>	
		Floor effects	Ceiling effects
Abdominal symptoms	0.80	1 (0.2)	50 (10.9)
Fatigue	0.82	1 (0.2)	1 (0.2)
Systemic symptoms	0.65	2 (0.4)	16 (3.5)
Activity	0.66	1 (0.2)	36 (7.8)
Emotional function	0.90	1 (0.2)	5 (1.1)
Worry	0.85	1 (0.2)	17 (3.7)
Overall	0.83	1 (0.2)	1 (0.2)

<sup>1</sup>Floor and ceiling effect: The number and percentage of the chronic hepatitis B patients at the lowest and highest possible scores.

occupation, annual per capita household incomes and the disease (CHB and CHB-related cirrhosis).

### Ethics statement

The study protocol was reviewed and approved by the Human Research Ethics Committee of Xi'an Jiaotong University. The written informed consent was obtained from each recruited patient before the questionnaire survey.

### Statistical analysis

A database was built using the software EpiData 3.1 and the data were double-entered by two different persons to capture data entry errors. All analyses were performed with SPSS version 13.0 (SPSS Inc., Chicago, IL, United States).

## RESULTS

### Sociodemographics

A total of 460 patients were recruited. In the face-to-face interview, they understood the questions of the CLDQ well, and finished the questionnaire completely. The patients aged 35.75  $\pm$  12.82 years (range: 18-76 years), with 305 (66.3%) males and 155 (33.7%) females. Three hundred and twenty-eight (71.3%) patients were married. Education levels of the patients were no schooling and primary (*n* = 63, 13.7%), secondary (*n* = 311, 67.6%) and tertiary (*n* = 86, 18.7%); 153 (33.3%) were peasants and the others were non-peasants. Annual per capita household incomes (RMB) of the patients were < 5000 (*n* = 236, 51.3%), 5000-9999 (*n* = 111, 24.1%) or  $\geq$  10000 (*n* = 113, 24.6%). With respect to the disease, the CHB and CHB-related cirrhosis patients accounted for 70.2% (*n* = 323) and 29.8% (*n* = 137) respectively. Three hundred and seventy five (81.5%) patients received ALT test immediately after the questionnaire survey, 311 (82.9%) with CHB and 64 (17.1%) with CHB-related cirrhosis. The detailed information of patients with CHB or CHB-related cirrhosis is shown in Table 1.

### Reliability and floor/ceiling effects

Cronbach's  $\alpha$  of the total CLDQ was 0.83, with the

**Table 3** Convergent validity and discriminant validity of the chronic liver disease questionnaire (*n* = 460)

Items	Item-scale correlation (Spearman $\gamma$ )					
	AB	FA	SY	AC	EM	WO
Abdominal symptoms						
1. Abdominal bloating	0.82 <sup>1</sup>	0.40	0.42	0.38	0.33	0.22
5. Abdominal pain	0.79 <sup>1</sup>	0.41	0.56	0.39	0.35	0.30
17. Abdominal discomfort	0.91 <sup>1</sup>	0.52	0.57	0.47	0.46	0.33
Fatigue						
2. Tiredness or fatigue	0.46	0.78 <sup>1</sup>	0.48	0.42	0.53	0.37
4. Feel sleepy during the day	0.23	0.61 <sup>1</sup>	0.30	0.27	0.30	0.23
8. Decreased strength	0.45	0.79 <sup>1</sup>	0.50	0.64	0.52	0.41
11. Decreased energy	0.46	0.79 <sup>1</sup>	0.50	0.62	0.65	0.42
13. Drowsiness	0.37	0.76 <sup>1</sup>	0.43	0.42	0.50	0.31
Systemic symptoms						
3. Bodily pain	0.61	0.47	0.71 <sup>1</sup>	0.40	0.46	0.33
6. Shortness of breath	0.46	0.50	0.66 <sup>1</sup>	0.49	0.42	0.30
21. Muscle cramps	0.35	0.31	0.59 <sup>1</sup>	0.36	0.28	0.21
23. Dry mouth	0.32	0.35	0.64 <sup>1</sup>	0.26	0.38	0.31
27. Itching	0.35	0.31	0.65 <sup>1</sup>	0.29	0.28	0.23
Activity						
7. Not able to eat as much as you would like	0.37	0.49	0.35	0.78 <sup>1</sup>	0.41	0.28
9. Trouble in lifting or carrying heavy objects	0.41	0.54	0.49	0.84 <sup>1</sup>	0.38	0.28
14. Bothered by a limitation of the diet	0.45	0.53	0.43	0.73 <sup>1</sup>	0.44	0.28
Emotional function						
10. Anxiety	0.36	0.57	0.46	0.43	0.81 <sup>1</sup>	0.53
12. Unhappiness	0.34	0.50	0.36	0.39	0.80 <sup>1</sup>	0.44
15. Irritability	0.33	0.53	0.42	0.41	0.78 <sup>1</sup>	0.43
16. Difficulty in sleeping at night	0.30	0.44	0.39	0.32	0.70 <sup>1</sup>	0.33
19. Mood swings	0.36	0.51	0.42	0.35	0.77 <sup>1</sup>	0.54
20. Difficulty in falling asleep at night	0.33	0.38	0.40	0.35	0.67 <sup>1</sup>	0.35
24. Depression	0.39	0.58	0.48	0.43	0.80 <sup>1</sup>	0.58
26. Problems with concentration	0.36	0.54	0.43	0.36	0.73 <sup>1</sup>	0.48
Worry						
18. Worries about the impact of the liver disease	0.19	0.32	0.30	0.24	0.47	0.78 <sup>1</sup>
22. Worries that symptoms will develop into major problem	0.33	0.45	0.38	0.31	0.53	0.89 <sup>1</sup>
25. Worries that the condition is getting worse	0.33	0.41	0.38	0.31	0.53	0.88 <sup>1</sup>
28. Worries about never feeling any better	0.31	0.39	0.34	0.30	0.50	0.83 <sup>1</sup>
29. Availability of a liver for transplant	0.19	0.15	0.24	0.18	0.22	0.35 <sup>2</sup>

Convergent validity: <sup>1</sup>The hypothesized item-scale correlations  $\geq 0.40$ ; <sup>2</sup>correlations  $< 0.40$ . Discriminant validity: The hypothesized item-scale correlations are higher than the alternative ones. AB: Abdominal symptoms; FA: Fatigue; SY: Systemic symptoms; AC: Activity; EM: Emotional function; WO: Worry.

range from 0.65 to 0.90 in the six scales. Both floor and ceiling effect percentages of the six scales and total score of the CLDQ were less than 20% (Table 2).

### Validity

The hypothesized item-scale correlation of the six scales (range) were AB (0.79-0.91), FA (0.61-0.79), SY (0.59-0.71), AC (0.73-0.84), EM (0.67-0.81) and WO (0.35-0.89), all were higher than the range of the corresponding items with other scales, indicating better convergent and discriminant validity (Table 3).

Six factors were extracted from the 29 items of CLDQ, which explained 61.69% of the total variance. Factor loadings of the 29 items were not entirely consistent with the six scales. The items of EM scale loaded on factor 1, except for “difficulty in sleeping at night” (item 16) and “difficulty in falling asleep at night” (item 20), which loaded on factor 6. Factor 2 covered WO scale. The items of FA and AC scales loaded on factor 3, except for “tiredness or fatigue” (item 2), “feel sleepy during the day” (item 4) and “drowsiness” (item 13) loaded on fac-

tor 5. Both of AB scale and item 3 (bodily pain) loaded on factor 4 (Table 4).

### Sensitivity

Regarding the between-group comparison in CHB and CHB-related cirrhosis patients, the eligible ES was found in AC (0.71), SY (0.52), AB (0.33) scales and the overall CLDQ (0.37). After controlling the influences of the disease (CHB and CHB-related cirrhosis), the ES in AB (0.30) scale and the overall CLDQ (0.23) were satisfactory by comparison between the normal and abnormal ALT groups in the stratification of patients with CHB. Meanwhile, the corresponding between-group independent sample *t* test was statistically significant ( $P < 0.05$ ) (Tables 5 and 6). Other eligible ES was also found in patients with normal or abnormal ALT after stratification, including SY (0.22) scale (CHB), and AB (0.27), FA (0.23), AC (0.23) scales and the overall CLDQ (0.21) (CHB-related cirrhosis). However, the corresponding between-group *t* test was not statistically significant ( $P > 0.05$ ) (Table 6).

Based on controlling the influences of sociodemo-



**Table 4** Factor analysis of the chronic liver disease questionnaire (*n* = 460)

Items	F 1 (EM)	F 2 (WO)	F 3 (AC + FA)	F 4 (AB + SY)	F 5 (FA)	F 6 (sleep)
Abdominal symptoms						
1. Abdominal bloating				0.68		
5. Abdominal pain				0.82		
17. Abdominal discomfort				0.75		
Fatigue						
2. Tiredness or fatigue					0.52	
4. Feel sleepy during the day					0.75	
8. Decreased strength			0.66			
11. Decreased energy			0.63			
13. Drowsiness					0.72	
Systemic symptoms						
3. Bodily pain				0.68		
6. Shortness of breath				(0.32)		
21. Muscle cramps				(0.35)		
23. Dry mouth				(0.32)		
27. Itching				(0.28)		
Activity						
7. Not able to eat as much as you would like			0.76			
9. Trouble in lifting or carrying heavy objects			0.64			
14. Bothered by a limitation of the diet			0.65			
Emotional function						
10. Anxiety	0.73					
12. Unhappiness	0.78					
15. Irritability	0.77					
16. Difficulty in sleeping at night						0.79
19. Mood swings	0.66					
20. Difficulty in falling asleep at night						0.75
24. Depression	0.65					
26. Problems with concentration	0.55					
Worry						
18. Worries about the impact of the liver disease		0.69				
22. Worries that symptoms will develop into major problem		0.82				
25. Worries that the condition is getting worse		0.81				
28. Worries about never feeling any better		0.75				
29. Availability of a liver for transplantation		0.51				
Eigenvalue	36.14%	7.94%	5.44%	4.57%	4.01%	3.59%
Cumulative	36.14%	44.08%	49.52%	54.09%	58.10%	61.69%

Kaiser-Meyer-Olkin measure of sampling adequacy: 0.929. Bartlett's test of sphericity:  $P < 0.001$ . The items with factor (F) loading coefficient less than 0.45 are written in bracket. EM: Emotional function; WO: Worry; AC: Activity; FA: Fatigue; AB: Abdominal symptoms; SY: Systemic symptoms.

**Table 5** Sensitivity of the chronic liver disease questionnaire: scores (mean  $\pm$  SD) and effect size

Scales	Total ( <i>n</i> = 460)	CHB ( <i>n</i> = 323)	CHB-related cirrhosis ( <i>n</i> = 137)	ES
AB	5.48 $\pm$ 1.11	5.59 $\pm$ 1.07	5.22 $\pm$ 1.16	0.33 <sup>1,b</sup>
FA	4.76 $\pm$ 1.11	4.82 $\pm$ 1.08	4.61 $\pm$ 1.17	0.19
SY	5.41 $\pm$ 0.86	5.54 $\pm$ 0.82	5.09 $\pm$ 0.87	0.52 <sup>1,b</sup>
AC	5.45 $\pm$ 1.13	5.69 $\pm$ 1.03	4.89 $\pm$ 1.15	0.71 <sup>1,b</sup>
EM	4.85 $\pm$ 1.10	4.87 $\pm$ 1.13	4.80 $\pm$ 1.01	0.06
WO	5.06 $\pm$ 1.19	5.03 $\pm$ 1.23	5.11 $\pm$ 1.08	-0.07
Overall	5.17 $\pm$ 0.83	5.26 $\pm$ 0.83	4.95 $\pm$ 0.78	0.37 <sup>1,b</sup>

<sup>1</sup>The effect size (ES)  $\geq 0.20$ . Effect size is calculated as the difference between chronic hepatitis B (CHB) and CHB-related cirrhosis groups mean score divided by the overall standard deviation. Significant difference between CHB and CHB-related cirrhosis groups by independent sample *t* test: <sup>b</sup> $P < 0.01$ . AB: Abdominal symptoms; FA: Fatigue; SY: Systemic symptoms; AC: Activity; EM: Emotional function; WO: Worry.

graphics and the disease (CHB and CHB-related cirrhosis), multiple linear regression analysis detected differenc-

es (unstandardized coefficient, 95%CI) in AB scale [-0.39, (-0.63, -0.15),  $P = 0.001$ ], SY scale [-0.23, (-0.41, -0.06),  $P = 0.009$ ] and the overall CLDQ [-0.22, (-0.40, -0.04),  $P = 0.018$ ] with statistical significance under the influence of ALT (normal *vs* abnormal) (Table 7).

## DISCUSSION

The CLDQ is a non-generic, disease-specific instrument for assessing HRQoL in patients with chronic liver disease. We used the Chinese (mainland) CLDQ in patients with CHB and proved that this instrument has acceptable reliability, validity and sensitivity.

Internal consistency reliability of AB, FA, EM, WO scales and the overall CLDQ were satisfactory, with Cronbach's  $\alpha$  coefficient greater than 0.70. It was consistent with the reports from similar studies using the original and other different language versions of CLDQ<sup>[15,16,19,34]</sup>. However, Cronbach's  $\alpha$  of SY (0.65) and AC (0.66) scales were less than the recommended value of 0.70. This is probably due to heterogeneous manifestations of system-

**Table 6 Sensitivity of the chronic liver disease questionnaire in different alanine aminotransferase results after stratifying the disease**

Scales	CHB with ALT test ( <i>n</i> = 311)				CHB-related cirrhosis with ALT test ( <i>n</i> = 64)			
	Total score	Normal ( <i>n</i> = 170)	Abnormal ( <i>n</i> = 141)	ES	Total score	Normal ( <i>n</i> = 29)	Abnormal ( <i>n</i> = 35)	ES
Abdominal symptoms	5.59 ± 1.08	5.73 ± 1.04	5.41 ± 1.11	0.30 <sup>1,b</sup>	5.34 ± 1.16	5.51 ± 1.17	5.20 ± 1.14	0.27 <sup>1</sup>
Fatigue	4.81 ± 1.08	4.88 ± 1.09	4.72 ± 1.08	0.15	4.61 ± 1.13	4.75 ± 1.21	4.49 ± 1.06	0.23 <sup>1</sup>
Systemic symptoms	5.54 ± 0.83	5.62 ± 0.82	5.44 ± 0.84	0.22 <sup>1</sup>	5.17 ± 0.83	5.24 ± 0.83	5.11 ± 0.84	0.16
Activity	5.70 ± 1.03	5.76 ± 1.00	5.62 ± 1.06	0.14	4.94 ± 1.21	5.09 ± 1.30	4.81 ± 1.14	0.23 <sup>1</sup>
Emotional function	4.85 ± 1.13	4.94 ± 1.16	4.75 ± 1.09	0.17	4.77 ± 1.06	4.85 ± 1.14	4.71 ± 1.00	0.13
Worry	5.02 ± 1.23	5.10 ± 1.23	4.93 ± 1.23	0.14	4.98 ± 1.20	4.94 ± 1.31	5.01 ± 1.12	-0.06
Overall	5.25 ± 0.84	5.34 ± 0.83	5.15 ± 0.84	0.23 <sup>1,a</sup>	4.97 ± 0.81	5.06 ± 0.88	4.89 ± 0.74	0.21 <sup>1</sup>

<sup>1</sup>The effect size (ES) ≥ 0.20. Effect size was calculated as the difference between alanine aminotransferase (ALT) normal and abnormal group mean scores divided by standard deviation of the total score. Significant difference by independent sample *t*-test between ALT normal and abnormal groups: <sup>a</sup>*P* < 0.05, <sup>b</sup>*P* < 0.01.

**Table 7 Multiple linear regression analysis (*n* = 460)**

Dependent variable	<i>B</i>	<i>SE</i>	<i>t</i>	<i>P</i>	95%CI
Abdominal symptoms	-0.39	0.12	-3.22	0.001	-0.63, -0.15
Systemic symptoms	-0.23	0.09	-2.63	0.009	-0.41, -0.06
Overall CLDQ	-0.22	0.09	-2.37	0.018	-0.40, -0.04

Independent variable: alanine aminotransferase (normal *vs* abnormal). The other controlled independent variables were age, gender, marital status, education level, occupation, annual per capita household incomes and the disease [chronic hepatitis B (CHB) and CHB-related cirrhosis]. CLDQ: Chronic liver disease questionnaire.

atic symptoms severity and activity limitations in patients with CHB or CHB-related cirrhosis and, consequently, influences the corresponding scoring. Percentages of the floor and ceiling effects regarding the six scales and total score of the CLDQ were less than 20%, indicating that this instrument can capture the full range of potential responses and detect small changes in CHB patients during treatment process.

The convergent and discriminant validity of the CLDQ was satisfactory, proving that the items of each scale can reflect the major characteristics consistently. Lam *et al*<sup>[14]</sup> and Mahmoudi *et al*<sup>[35]</sup> reported similar results in their studies. However, “availability of a liver for transplant” (item 29) in the present study did not better correlate to WO scale ( $\gamma = 0.35$ ), possibly due to few patients confronted with the problem of liver transplantation. Therefore, this item was less correlated to WO scale than the other four items within the same dimension.

The factor structure of the Chinese (mainland) CLDQ conform to the six scale structure of the original US version, with a new scale of “sleep” (factor 6) covering the item “difficulty in sleeping at night” (item 16) and “difficulty in falling asleep at night” (item 20) being the only major difference. Such new factor was also found in the Spanish, Italian and German population<sup>[19,20,34]</sup>. It was reasonable to believe that sleeping habits vary among cultures (napping habits and bedtimes), so it may not be surprising that these items clustered differently. For patients with CHB or CHB-related cirrhosis, they may have sleep difficulties due to various reasons other than emotional

problems, including pain or other disease-related factors. Except for the two items of “sleeping difficulty”, all other items of the EM scale loaded on factor 1 consistently.

The items of WO, AC and AB scales loaded on factor 2, 3 and 4. However, AC and AB scales also combined with other items. The finding showed that “decreased strength” (item 8) and “decreased energy” (item 11) of FA scale loaded on factor 3 (AC scale), whereas “bodily pain” (item 3) of SY scale loaded on factor 4 (AB scale), which demonstrated that decreased strength and energy highly correlate to activity<sup>[14]</sup>, and bodily pain may be better related to AB, especially abdominal pain in CHB patients. “Tiredness or fatigue” (item 2), “feel sleepy during the day” (item 4) and “drowsiness” (item 13) were found loading on factor 5 as measuring fatigue symptoms. However, the FLC of “shortness of breath” (item 6) (0.32), “muscle cramps” (item 21) (0.35), “dry mouth” (item 23) (0.32) and “itching” (item 27) (0.28) were less than the recommended value of 0.45. It was probably because that most of the patients were in CHB stage and did not have distinct clinical manifestations as the items reflected.

By comparison between CHB and CHB-related cirrhosis groups, the CLDQ was sensitive in detecting differences in the overall and AB, SY and AC scale scores. It suggests that, based on measuring the physical and psychological health, the CLDQ could further detect the difference of hepatitis-related physical symptoms in CHB patients with or without cirrhosis. After controlling for influences of the disease (CHB and CHB-related cirrhosis), the CLDQ was very good in measuring differences in the overall and AB and SY scale scores between normal and abnormal ALT groups in CHB patients without cirrhosis. Multiple linear regression analysis also confirmed this result through further controlling other confounding factors such as sociodemographics.

However, due to close scores, FA, EM and WO scales did not show significant difference in CHB patients with or without considering ALT test results and controlling for influences of the disease (CHB and CHB-related cirrhosis). Specifically, the difference of between-group comparison in AC scale changed from significant to not significant after stratification, indicating the confounding role of the disease (CHB and CHB-related cirrhosis).

Unlike such finding, Lam *et al.*<sup>[14]</sup> used the Chinese (Hong Kong, China) CLDQ in patients with CHB infection and reported significant differences in FA, AC, EM and WO scales between uncomplicated and complicated CHB patients. Such discrepancy might be the result that CHB-related complications have impact on the patients' health regardless of the disease (CHB and CHB-related cirrhosis) and, subsequently, influence the scoring of the corresponding scales. Therefore, the sensitivity of FA, AC, EM and WO scales of the CLDQ in patients with CHB or CHB-related cirrhosis need further examination.

In patients with CHB-related cirrhosis, the ES values of AB (0.27), FA (0.23), AC (0.23) scales and the overall CLDQ (0.21) were greater than 0.20, confirming the major impact of ALT on the hepatitis-related physical health. Other scales including SY (0.16), EM (0.13) and WO (-0.06) did not have the required ES value, indicating the similar conditions of hepatitis-related symptoms and mental health under the influence of ALT (normal *vs* abnormal) in cirrhotic patients. However, no statistical significance of independent sample *t* test was found in any scales and the overall CLDQ in the present study. The probable explanation for this might be the small sample size ( $n = 64$ ). Different from such result, Lam *et al.*<sup>[13]</sup> found significant differences in SY scale and the overall CLDQ between impaired liver function and cirrhosis groups in CHB patients. Accordingly, more attention should be paid to proving the sensitivity of the CLDQ in CHB-related cirrhosis patients under the influence of normal and abnormal ALT.

There were some limitations in the present study. First, the Chinese (mainland) CLDQ was administered using a face-to-face interview, the performance of the instrument by self-completion will need to be confirmed by future work. Second, the responsiveness of the Chinese (mainland) CLDQ in detecting changes with disease progression or ALT status will also need to be determined. Third, this study was conducted in the single-site of the Eighth Hospital of Xi'an. Therefore, it was limited to generalize the results to all of Chinese mainland CHB patients.

The Chinese (mainland) CLDQ has been proved as a valid tool for assessing HRQoL in patients with CHB. Both reliability and validity were demonstrated to be strongly satisfactory, and better sensitivity was confirmed in detecting the difference of AB, SY and AC scales and the overall CLDQ, especially the differences in AB scale and the overall CLDQ under the influence of ALT status. The Chinese (mainland) CLDQ can be a suitable disease-specific questionnaire for evaluating the change of HRQoL and treatment effects of CHB in clinical practice. Future work in a larger cohort of patients is needed to further prove the responsiveness of the Chinese (mainland) CLDQ.

The patients are at high risk of developing fatal complications of cirrhosis and hepatocellular carcinoma, which consequently lead to the impairments of the patients' health-related quality of life (HRQoL).

### Research frontiers

HRQoL should be used as the primary endpoint in the evaluation of treatment effectiveness for patients with CHB, since it is a more holistic assessment of health status considering the individual's functional health and well-being.

### Innovations and breakthroughs

The chronic liver disease questionnaire (CLDQ) has been translated into many different languages for cross-cultural adaptation and proved as a valid tool for HRQoL measurement and evaluation in patients with chronic liver disease. However, a dearth of study assessed psychometrics of the Chinese (mainland) CLDQ in mainland Chinese patients with CHB. This study determined that the Chinese (mainland) CLDQ has acceptable reliability, validity and sensitivity in patients with CHB. It can be applied to mainland Chinese CHB patients to evaluate their HRQoL.

### Applications

The Chinese (mainland) CLDQ can be used as a suitable disease-specific questionnaire for evaluating the change of HRQoL and treatment effects of CHB in clinical practice. The CLDQ can be used as a cross-cultural HRQoL measure in international studies that include mainland Chinese.

### Terminology

Reliability concerns the random variability associated with measurements. Validity refers to the extent to which a test measures what it is intended to measure. Sensitivity is the ability of measurements to detect differences between patients or groups of patients.

### Peer review

The authors tested psychometrics of the Chinese (mainland) CLDQ and proved that this questionnaire was reliable, valid and sensitive for Chinese mainland patients with CHB. The study was well done and used appropriate methodology to validate and test the questionnaire.

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## COMMENTS

### Background

Chronic hepatitis B (CHB) is a common chronic liver disease in mainland China.

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