Liver International ISSN 1478-3223

CLINICAL STUDIES

Does cirrhosis affect quality of life in hepatitis C virus-infected patients?

Priscilla C. Hsu[1,2], Mel Krajden[1,2], Eric M. Yoshida[3], Frank H. Anderson[4], George A. Tomlinson[5] and Murray D. Krahn[6]

1 British Columbia Centre for Disease Control, Vancouver, BC, Canada
2 Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada
3 Division of Gastroenterology, University of British Columbia, Vancouver, BC, Canada
4 Liver and Intestinal Research Centre, Vancouver, BC, Canada
5 Toronto General Research Institute, and Department of Public Health Sciences, University of Toronto, Toronto, ON, Canada
6 Department of Medicine, Faculty of Pharmacy, and Toronto Health Economics and Technology Assessment Collaborative (THETA) University of Toronto, Toronto, ON, Canada

Keywords
cirrhosis – HCV – hepatitis C virus – quality of life – socioeconomic factors

Correspondence
Murray D. Krahn, MD, MSc, FRCPC, University Health Network, Toronto General Hospital, 200 Elizabeth St. 14EN-207, Toronto, ON, Canada M5G 2C4
Tel: 416 340 4155
Fax: 416 595 5826
e-mail: murray.krahn@theta.utoronto.ca

Received 28 February 2008
Accepted 8 July 2008

DOI:10.1111/j.1478-3231.2008.01865.x

Abstract

Background: Hepatitis C virus (HCV) infection is a major cause of chronic liver disease and is associated with impairments in health-related quality of life. *Aims:* To evaluate quality of life (QOL) in cirrhotic (compensated and decompensated) and non-cirrhotic patients with chronic HCV infection, using preference-based (utilities) and non-preference-based methods of evaluating QOL. *Methods:* In a tertiary care setting, 271 patients completed a self-administered time trade-off utility instrument, the Health Utility Index Mark 2 and Mark 3, and the Hepatitis Quality of Life Questionnaire Version 2. Mean QOL scores were compared across HCV disease stages and socio-demographical categories. We examined the association between QOL and disease stage using linear regression adjusting for age, education, marital status, log income and Charlson comorbidity scores. Mean utility scores were compared across disease stages using a propensity score method. *Results:* Mean utilities were lower than general population norms (0.81–0.92) and ranged from 0.62 to 0.82 in non-cirrhotic patients ($n = 197$), 0.56–0.84 in compensated cirrhotic patients ($n = 17$) and 0.55–0.76 for decompensated cirrhotic patients ($n = 57$). No significant association found was between disease stage and utility for current health status. Higher income, fewer comorbidities and living in a married or common-law relationship were significantly associated with higher utilities and better QOL. No significant difference in utilities was found between disease stages using propensity score matching. *Conclusions:* Our study confirms that changes in HCV disease stage explain only small changes in QOL and suggests that factors such as underlying comorbidities, income and marital status have a greater effect on QOL than disease stage.

More than 170 million people worldwide are chronically infected with the hepatitis C virus (HCV) (1, 2). Chronic infection with HCV may have serious consequences; 15–20% of those with chronic infection will develop cirrhosis after 20 years (1–3) and of these, 5–10% will develop hepatocellular carcinoma (3). HCV is now a major cause of chronic liver disease and is the leading indication for liver transplantation in developed countries (1, 2). In addition to its effects on progression of liver disease, HCV infection may also be associated with impairments in health-related quality of life (QOL) including fatigue, muscle and joint pain, depression, and other psychological disorders (2), even in the early stages of disease (4). To date, the majority of studies examining the effects of HCV on QOL utilize non-preference-based measurements such as the Short-Form 36 (SF-36) (5). Although these generic instruments are useful in describing health states and their effects on function and disability, they do not directly measure individual preferences for health outcomes.

Health utility is a preference-based measure of QOL that ascertains an individual's value or preference for a particular health state. Utilities are reported from a scale of 0 (dead) to 1 (full health) and can be obtained either (i) directly from individuals using time trade-off or standard gamble techniques or (ii) indirectly using questionnaires that incorporate weights representing the preferences of the community. Utilities are widely used in cost-effectiveness and decision analyses where costs and benefits associated with different treatments are compared. There is a need for patient-elicited utilities in the HCV literature because most of the cost-effectiveness studies rely on clinical opinion or expert panels to estimate utilities and these may differ substantially from patient-derived utilities (5). The purpose of this study was to compare QOL across stages of HCV disease; specifically, we sought to evaluate QOL in chronically infected non-cirrhotic patients and cirrhotic patients (both compensated and decompensated), using both preference-based (utilities) and non-preference based methods of evaluating health outcomes.

Methods

This analysis is part of a larger study that examined the QOL and economic burden of hepatitis C in a community-dwelling population. This study was approved by the Clinical Research Ethics Board at the University of British Columbia and the Ethics Review Office at the University of Toronto.

© 2009 The Authors. Journal compilation © 2009 Blackwell Publishing Ltd

Recruitment

This study was conducted in a tertiary care setting at five sites in the metropolitan area of Vancouver, BC: the BC Hepatitis Program at Vancouver General Hospital the Liver and Intestinal Research Centre, the BC Transplant Society Pre-Liver Transplant Assessment Clinic, the Solid Organ Transplant Clinic at Vancouver General Hospital, and the Gilwest Clinic at Richmond General Hospital. The BC Hepatitis Program (a partnership between the BC Centre for Disease Control and Division of Gastroenterology at the University of British Columbia) and the Liver and Intestinal Research Centre (a private practice clinic) are the two largest tertiary clinics in Vancouver offering specialized health care services for patients with chronic hepatitis and liver disease. The BC Transplant Society is a provincial health services agency that coordinates all liver transplants within BC and the Solid Organ Transplant Clinic provides posttransplant follow-up care. The Gilwest Clinic offers HIV- and HCV-related services to individuals living in Richmond, a municipality in the metropolitan area of Vancouver.

Between 1 January 2006 and 1 June 2007, a convenience sample was assembled using advertisements posted in the clinics, direct personal referrals and mailed recruitment letters from treating clinicians. Individuals were eligible if they had a prior HCV diagnosis and excluded if they were enrolled in a clinical drug trial, unable to effectively communicate in the English language or had a score of < 21 on the Telephone Interview for Cognitive Status (6–8). Patients were given the choice of completing a questionnaire package mailed to their home, over the telephone or in person at the clinic. Participants were given a stipend of $20 upon completion of the questionnaires.

Data collection

Participants completed three QOL instruments in their questionnaire package: the Hepatitis Quality of Life Questionnaire Version 2 (HQLQv2), the Health Utility Index Mark 2 (HUI2) and Mark 3 (HUI3), and a self-administered, paper-based time trade-off (TTO) utility instrument. In addition to the QOL measurements, participants answered questions regarding their personal and medical history including comorbidities, physical impairments, risk factors for HCV, and alcohol and drug use. Individuals were considered to have abused alcohol if they had answered in the affirmative to the question, 'Thinking back to the phase of your life when you were drinking regularly, did you ever become dependent on alcohol?' The criteria for problematic substance use included a history of injecting or snorting drugs on a daily basis for at least 4 weeks. Sociodemographic data included date of birth, sex, ethnicity, marital status, income and education level. A retrospective chart review was conducted for individuals who consented to have their clinical information reviewed by the researchers. Clinical information was garnered from liver biopsies, blood test results and radiology reports. Physician notes were used to estimate an HCV diagnosis date and confirm any signs or symptoms of liver decompensation such as ascites, variceal bleeding, hepatic encephalopathy and jaundice. All charts were reviewed by a single research assistant who was trained and knowledgeable in the field of HCV infection.

Measures of quality of life

The HQLQ is a non-preference-based measurement of health-related QOL in patients with HCV infection (9, 10). It consists of the SF-36 Health Survey Version 2 (SF-36v2), a 36-item self-administered questionnaire assessing an individual's general health within a 4-week recall period on eight domains: physical functioning (limitation in physical activities because of health problems), role physical (limitations in usual role activities because of physical health problems), bodily pain, general health, vitality (energy and fatigue), role emotional (limitations in usual role activities because of emotional problems), social functioning (limitations in social activities because of physical or emotional problems) and mental health. Two summary measures, a Physical Component Summary and a Mental Component Summary, are constructed from scores on the eight domains. In addition to the SF-36v2, a supplement of 15 items assesses the impact of hepatitis on patient health including general health distress, positive well-being, hepatitis-specific distress and limitation in functional status.

The HUI2/HUI3 is a preference-scored indirect utility instrument that measures health status, reports on health-related QOL and produces utility scores (11, 12). This 15-item self-administered questionnaire asks patients to evaluate various aspects of their heath within a 1-week recall period. Item-level data are used to generate seven single-attribute levels (for HUI2): sensation, mobility, cognition, self-care, emotion, pain and fertility. The eight attribute levels of the HUI3 are vision, hearing, speech, emotion, pain, ambulation, dexterity and cognition. A utility score is calculated by using a function of the seven attribute levels for the HUI2 (eight levels for HUI3) and by incorporating community derived utility weights, producing an overall utility score on the scale 0 (dead) to 1 (perfect health).

The TTO instrument is a self-administered, preference-based direct utility measurement that assesses the individual's willingness to live a shorter but healthier life (13, 14). It asks individuals to imagine that they only have 20 years left to live and to indicate on a scale of 0–20, the number of years of perfect health they think is of equal value to 20 years in their current health. A utility score is calculated by dividing the number of years of perfect health at the equivalence point by 20.

The SF-6D, derived from the SF-36v2, is a preference-scored indirect utility measure of health status (15). It uses 11 of the 36 questions from the SF-36v2 to produce six domains: physical functioning, role limitation, social functioning, pain, vitality, and mental health. A single utility score is computed by using an algorithm incorporating the six domains, producing a score ranging from 0.3 to 1.0, with 1.0 indicating full health.

The HQLQ, HUI2, TTO and SF-6D have been used in several other studies to assess the QOL and utilities of individuals with HCV infection and chronic liver disease (4, 5, 14–19).

Measures of comorbidities

Two methods of calculating patient comorbidities were utilized: the Charlson Index and the Index of Coexistent Disease (ICED). The Charlson Index is a weighted index that accounts for a person's age and the number of comorbid diseases (20). It is the most widely used comorbidity index for predicting mortality (21) and has been used to assess comorbidity in various infectious disease populations such as hepatitis B and C virus-infected patients (4, 22) and HIV/AIDS patients (23, 24). The ICED consists of two subscales measuring disease severity and disability level (25). The two subscales are condensed into a single composite index with four levels from 1 (no comorbidities) to 4 (severe comorbidities). The ICED has been used to evaluate comorbid diseases in numerous populations such as

© 2009 The Authors. Journal compilation © 2009 Blackwell Publishing Ltd

the elderly (26, 27), people with arthritis (28, 29) and individuals undergoing dialysis (30–32).

Comparison groups

Patients were categorized into three disease stage groups: non-cirrhosis, compensated cirrhosis and decompensated cirrhosis. Individuals were classified as non-cirrhotic ($n = 197$) if they were chronically infected with HCV and had no evidence of cirrhosis or decompensated liver disease including ascites, variceal bleeding, hepatic encephalopathy, jaundice or thrombocytopenia. Patients with documented cirrhosis on liver biopsy or radiological evidence of cirrhosis (ultrasound, computed tomography scan), but no evidence of decompensated liver disease were assigned to the compensated cirrhosis group ($n = 17$). The decompensated cirrhosis group ($n = 57$) included patients with a history of any one of ascites, variceal bleeding, hepatic encephalopathy, or jaundice in the presence or absence of cirrhosis, or thrombocytopenia in the presence of cirrhosis.

Statistical analysis

Continuous variables were summarized as means and SDs and proportions were calculated for categorical variables. One-way analysis of variance was used to compare the means of continuous variables and *P*-values < 0.05 were considered to be statistically significant. We explored the association between QOL and disease stage by performing a series of linear regressions with utility scores as the dependent variables. After reviewing all of the sociodemographical variables, this study team selected the variables age, education, marital status, log income and comorbidity score (Charlson Index) as predictors in the linear regression model. This *ex ante* method of selecting predictors has been shown to be less biased than methods based on evaluation of individual predictors in univariate or stepwise regression (33, 34). Method of response to questionnaire (i.e. at home, over the phone, in person) was also included as a variable in the regression model to ensure the results were independent of response method. The assumptions of linear regression were checked by examining normal quantile plots of residuals and plots of residuals vs predicted values. The analysis was repeated on the logit transformation of the utilities as one check on the robustness of the findings. As a second check, we used bootstrap on the linear regression model for the utilities to obtain *P*-values and confidence intervals for estimates that were not dependent on parametric assumptions. The qualitative results were consistent across these approaches.

We also estimated differences in QOL attributable to disease stage using the propensity score method to adjust for differences in covariates between patients in different stages (35). This method uses either logistic regression or discriminant analysis to collapse the collection of confounding study covariates into a single score, called the propensity score, which is used as if it were the only confounding covariate in the study (36). The propensity score is calculated for each subject, and subjects from different groups are matched according to the proximity of their propensity scores. Propensity score adjustment is an effective method of controlling for confounding (37–40) and has been employed in numerous research studies (41–43) including patients with hepatitis B and C viruses (44, 45), HIV/AIDS (46–48) and liver disease (49).

Two pair-wise comparisons were constructed from the three disease stage groups: (i) the compensated cirrhosis group vs the non-cirrhosis group and (ii) the decompensated cirrhosis group vs the non-cirrhosis group. We used a multivariable logistic regression model to estimate propensity scores for each of these two comparisons, using the following variables as predictors: age, education, marital status, log income and Charlson Index. After stratifying patients by quintile of propensity score, we checked for adequate overlap in propensity scores and balance of covariates for each pair-wise comparison within every quintile of propensity score (50). We compared the mean utility scores of every propensity score quintile for each pair-wise comparison. Differences in propensity-adjusted mean utility scores and 95% confidence intervals were calculated for each pair-wise comparison. All analyses were performed by using SPSS, version 13.0, for Windows.

Results

Of the 2067 patients we attempted to contact, 375 (18%) were unreachable through mail because of outdated addresses and 888 (43%) failed to respond. Of the 804 who responded, 149 (19%) refused to participate, 10 (1%) were ineligible because they were unable to speak English or had a score of < 21 on the Telephone Interview for Cognitive Status, 645 (80%) were eligible and agreed to participate, and 489 returned completed questionnaires. For the purposes of this analysis, we analysed only the data of chronically infected HCV patients with no cirrhosis, compensated cirrhosis or decompensated cirrhosis ($n = 271$). The 218 responding patients excluded from the analysis consisted of patients currently receiving antiviral therapy, transplant recipients and patients with hepatocellular carcinoma.

Sociodemographical characteristics

The mean age of the study population was 50 years and 62% were males. The majority of participants were Caucasian (90%), and 51% of individuals were married or in common-law relationships. Eighty per cent of the total sample graduated from high school, and 24% had graduated from college or university. Approximately one-third of respondents reported a monthly income of $<$ \$1000 CDN, but one-third also reported a monthly income of $>$ \$4000/month. Forty-six percent of participants admitted to either injection drug or alcohol abuse at some point in their lives. Table 1 compares the sociodemographical characteristics between the three disease stage groups. Decompensated cirrhotic patients were the oldest group and non-cirrhotic chronically infected HCV individuals were the youngest. The decompensated group had the highest mean Charlson comorbidity score, most probably because these patients were older.

Short Form-36 scores

The mean scores for each of the eight SF-36 domains (Table 2) for all groups were below 50, the normalized mean score for the US general population (mean = 50, standard deviation = 10) (51). In comparison with normative data for the general Canadian population (52), the SF-36 scores of the three disease stage groups were statistically significantly lower for all SF-36 domains (Table 3). Non-cirrhotic patients scored the lowest in the domains of general health and social functioning (Table 2). For the compensated cirrhosis group, scores were the lowest in psychological domains, including role emotional and the Mental Component Summary while the lowest scores for the decompensated cirrhosis group were in the role physical and general health domains. In general, scores for the non-cirrhosis

© 2009 The Authors. Journal compilation © 2009 Blackwell Publishing Ltd

Table 1. Sociodemographical characteristics of study population

	Total ($n = 271$)	Non-Cirrhosis ($n = 197$)	Compensated ($n = 17$)	Decompensated ($n = 57$)
Age, mean (SD)	49.7 (8.6)	48.9 (9.2)	50.6 (5.3)	52.3 (6.8)
Gender (%)				
Male	169 (62.4)	123 (62.4)	7 (41.2)	39 (68.4)
Female	102 (37.6)	74 (37.6)	10 (58.8)	18 (31.6)
Ethnicity (%)				
White	243 (89.7)	176 (89.3)	14 (82.4)	53 (93.0)
Native/aboriginal	13 (4.8)	10 (5.1)	1 (5.9)	2 (3.5)
Asian	9 (3.3)	6 (3.0)	1 (5.9)	2 (3.5)
Other	6 (2.2)	5 (2.5)	1 (5.9)	0
Marital status (%)				
Married or common-law	139 (51.3)	96 (48.7)	9 (52.9)	34 (59.6)
Divorced	41 (15.1)	27 (13.7)	3 (17.6)	11 (19.3)
Separated	15 (5.5)	13 (6.6)	3 (17.6)	2 (3.5)
Single	64 (23.6)	55 (27.9)	2 (11.8)	6 (10.5)
Widowed	12 (4.4)	6 (3.0)	1 (6.7)	4 (7.0)
Highest education (%)				
< High school	55 (20.3)	42 (21.3)	2 (11.8)	11 (19.3)
High school	48 (17.7)	34 (17.3)	6 (35.3)	8 (14.0)
Incomplete trade/college/university	68 (25.1)	52 (26.4)	3 (17.6)	13 (22.8)
Completed trade	35 (12.9)	25 (12.7)	2 (11.8)	8 (14.0)
Completed college/university	65 (24.0)	44 (22.3)	4 (23.5)	17 (29.8)
Monthly income				
$0–999	88 (32.5)	63 (32.0)	8 (47.1)	17 (29.8)
$1000–3999	107 (39.5)	73 (37.1)	8 (47.1)	26 (45.6)
$4000+	76 (28.0)	61 (31.0)	1 (5.9)	14 (24.6)
Problematic substance use* (%)				
None	145 (53.5)	106 (53.8)	9 (52.9)	30 (52.6)
Injection drugs	42 (15.5)	32 (16.2)	2 (11.8)	8 (14.0)
Alcohol	34 (12.5)	21 (10.7)	4 (23.5)	9 (15.8)
Both	48 (17.7)	37 (18.8)	2 (11.8)	9 (15.8)
Comorbidities, mean (SD)				
Charlson†	1.4 (1.2)	1.3 (1.2)	1.6 (0.8)	1.8 (1.5)
Index of coexistent disease†	2.0 (1.1)	1.9 (1.2)	2.6 (0.8)	2.0 (1.2)

*Excluding non-response, total ($N = 269$), non-cirrhosis ($N = 196$), decompensated ($N = 56$).
†Total ($N = 263$), non-cirrhosis ($N = 190$), compensated ($N = 16$).

group were higher when compared with both cirrhosis groups, with both cirrhosis groups scoring similar to each other. More specifically, scores for general health and the Physical Component Summary were significantly higher for the non-cirrhosis group when compared with both cirrhosis groups, with the decompensated cirrhosis group scoring the lowest ($P < 0.005$). Physical functioning and role physical of the non-cirrhosis group was much better than both cirrhosis groups ($P < 0.005$). Role emotional in the non-cirrhosis group was much higher than both cirrhosis groups, with the compensated cirrhosis group scoring the lowest ($P < 0.025$).

Hepatitis-specific questions

In general, the non-cirrhosis group scored higher than both cirrhosis groups when it came to the hepatitis-specific questions (Table 2). Non-cirrhotic patients scored the lowest in positive well-being while individuals with compensated cirrhosis scored the lowest in hepatitis-specific health distress; the lowest score for the decompensated cirrhosis group was in the general health distress domain. Only hepatitis-specific health distress was found to be significantly different between the three groups with the non-cirrhosis group reporting much less distress than both cirrhosis groups ($P < 0.025$).

Utilities

The HUI2 and HUI3 scores were consistently lower than the TTO scores; the SF-6D scores were in between the HUI2 and HUI3 scores (Table 2). The HUI2, HUI3 and SF-6D scores were the highest in the non-cirrhosis group when compared with both cirrhosis groups, with the compensated cirrhosis group scoring similar to the decompensated cirrhosis group. The TTO scores for the non-cirrhosis group were comparable to the compensated group while the decompensated group scoring the lowest. However, none of these differences were found to be statistically significant.

Covariates

Mean utilities and SF-36 component summary scores for our study groups, stratified by sociodemographical characteristic are reported in Table 4. Individuals in a married or common-law relationship or with higher monthly income scored significantly better on all measurements of utility and health-related QOL. Patients with higher comorbidity reported significantly reduced health utility and QOL. Individuals who were older, female or reported a history of problematic substance use scored significantly worse in the Mental Component Summary of the SF-36.

© 2009 The Authors. Journal compilation © 2009 Blackwell Publishing Ltd

Table 2. Mean quality of life and utility scores by hepatitis C virus disease stages

	Non-cirrhosis ($n = 197$)	Compensated ($n = 17$)	Decompensated ($n = 57$)
SF-36 component of HQLQ			
Physical functioning	**46.2 (11.8)**	**40.1 (12.5)**	**40.3 (11.4)**
Role physical	**42.8 (13.1)**	**37.0 (15.0)**	**36.6 (13.5)**
Bodily pain	45.4 (12.3)	42.1 (11.9)	42.8 (10.6)
General health	**41.3 (13.3)***	**37.6 (12.1)**	**34.8 (11.2)**
Vitality	43.6 (12.5)*	40.3 (11.1)	41.0 (12.4)
Social functioning	40.5 (13.7)	37.0 (15.9)	38.0 (12.9)
Role emotional	**42.0 (13.8)**	**32.8 (17.9)**	**38.7 (15.3)**
Mental health	43.3 (12.3)*	38.9 (15.4)	43.2 (12.6)
Physical Component Summary (PCS)	**45.1 (12.0)***	**41.2 (10.6)**	**38.6 (10.3)**
Mental Component Summary (MCS)	41.6 (13.5)*	36.2 (17.1)	41.3 (13.0)
Hepatitis-specific component of HQLQ			
Generic health distress	62.6 (30.7)	51.2 (31.0)	53.2 (29.5)
Positive Well-being	54.4 (27.2)	53.8 (28.4)	53.9 (26.0)
Hepatitis-specific limitations	69.5 (33.1)	58.8 (36.8)	59.6 (33.5)
Hepatitis-specific health distress	**65.5 (32.0)**	**46.8 (35.9)**	**53.9 (35.6)**
Utilities			
Time Trade-Off (TTO)	0.82 (0.25)†	0.84 (0.20)	0.76 (0.28)‡
Health Utility Index Mark 2 (HUI2)	0.76 (0.20)§	0.71 (0.21)	0.72 (0.21)
Health Utility Index Mark 3 (HUI3)	0.62 (0.32)§	0.56 (0.34)	0.55 (0.33)
SF-6D	0.67 (0.15)	0.61 (0.14)	0.63 (0.11)

Numbers in parentheses are SDs and bolded numbers represent $P < 0.05$.

*$N = 196$.

†$N = 192$.

‡$N = 56$.

§$N = 194$.

HQLQ, Hepatitis Quality of Life Questionnaire; SF-6D, Short-Form 6D; SF-36, Short-Form 36.

Table 3. Comparison of Canadian general population SF-36 scores (using 0–100 scoring) to HCV patients at different disease stages*,†

SF-36 domains	Canadian population‡	Non-cirrhosis ($n = 197$)	Compensated ($n = 17$)	Decompensated ($n = 57$)
Physical functioning	85.8 (20.0)	74.2 (27.9)	59.7 (29.6)	60.3 (27.0)
Role physical	82.1 (33.2)	64.1 (33.4)	49.3 (38.2)	48.3 (34.4)
Bodily pain	75.6 (23.0)	60.5 (29.1)	52.7 (28.1)	54.3 (25.0)
General health	77.0 (17.7)	52.5 (27.9)§	44.8 (25.4)	38.9 (23.4)
Vitality	65.8 (18.0)	45.4 (24.9)§	39.0 (22.2)	40.4 (24.8)
Social functioning	86.2 (19.8)	62.6 (31.4)	54.4 (36.4)	56.8 (29.6)
Role emotional	84.0 (31.7)	70.3 (29.6)	50.5 (38.5)	63.2 (32.8)
Mental health	77.5 (15.3)	63.1 (21.8)§	55.2 (27.3)	63.0 (22.3)

*Numbers in parentheses are SDs.

†$P < 0.005$ for all comparisons to Canadian population norms on every domain.

‡$9367 < N < 9411$ for Canadian population norms.

§$N = 196$.

SF-36, Short-Form 36.

Association between disease stage and health utility

Disease stage was not shown to be significantly associated with health utility in our regression analysis for most of the pair-wise comparisons (Table 5). Only the SF-6D was found to be significantly associated with disease stage when comparing the non-cirrhosis and decompensated cirrhosis groups. After propensity score matching, differences in utilities ranged from -0.03 to 0.09 between the non-cirrhosis and compensated cirrhosis groups while differences in utilities between the non-cirrhosis and decompensated cirrhosis groups ranged from -0.06 to -0.11 (Fig. 1). However, none of these estimated differences across disease stage was found to be statistically significant. On the other hand, covariates that consistently showed to be significantly associated with utility included marital status and income. Although comorbidity was found to be significantly associated with utility in our initial regression analysis, this finding is weaker using the logit and bootstrap transformation analyses.

Discussion

Global quality of life is lower in hepatitis C patients

Using both preference- and non-preference-based measurements of QOL, we found that global QOL for individuals

© 2009 The Authors. Journal compilation © 2009 Blackwell Publishing Ltd

Table 4. Mean utilities and SF-36 summaries by sociodemographical characteristic*

	N	TTO	HUI2	SF-6D	PCS	MCS
Age						
< 40	27	0.84 (0.04)	0.76 (0.05)	0.71 (0.03)	47.2 (2.5)	**44.7 (2.6)**
40–49	111	0.80 (0.02)	0.74 (0.02)	0.64 (0.01)	43.2 (1.1)	**38.3 (1.4)**
50–59	99	0.83 (0.02)	0.77 (0.02)	0.66 (0.01)	43.6 (1.2)	**42.1 (1.3)**
60+	25	0.76 (0.06)	0.75 (0.04)	0.69 (0.03)	43.6 (2.4)	**45.2 (2.4)**
Gender						
Male	159	0.81 (0.02)	0.76 (0.02)	0.67 (0.01)	43.7 (0.9)	**42.3 (1.1)**
Female	91	0.80 (0.03)	0.75 (0.02)	0.65 (0.01)	43.8 (1.3)	**38.9 (1.4)**
Ethnicity						
White	235	0.82 (0.02)	0.75 (0.01)	0.66 (0.01)	44.1 (0.8)	41.1 (0.9)
Native/aboriginal	12	0.69 (0.08)	0.68 (0.06)	0.61 (0.04)	41.7 (3.6)	35.2 (3.9)
Other	15	0.79 (0.07)	0.77 (0.04)	0.67 (0.03)	41.4 (3.0)	44.8 (2.5)
Marital status						
Married or common-law	127	**0.85 (0.02)**	**0.80 (0.01)**	**0.70 (0.01)**	**46.1 (0.9)**	**44.4 (1.1)**
Other	135	**0.77 (0.02)**	**0.70 (0.02)**	**0.63 (0.01)**	**41.4 (1.1)**	**37.5 (1.2)**
Highest education						
< High school	49	0.77 (0.04)	0.75 (0.03)	0.63 (0.02)	43.3 (1.7)	39.3 (2.1)
High school	41	0.78 (0.04)	0.77 (0.03)	0.66 (0.02)	43.3 (2.0)	40.0 (2.2)
Incomplete trade/college/university	66	0.79 (0.03)	0.73 (0.02)	0.67 (0.02)	42.5 (1.5)	41.7 (1.7)
Completed trade	34	0.89 (0.03)	0.76 (0.04)	0.68 (0.03)	45.0 (1.9)	40.9 (2.4)
Completed college/university	60	0.82 (0.03)	0.76 (0.02)	0.68 (0.02)	45.0 (1.5)	42.6 (1.6)
Monthly income						
$0–999	82	**0.71 (0.03)**	**0.69 (0.02)**	**0.61 (0.01)**	**38.7 (1.1)**	**37.3 (1.4)**
$1000–3999	104	**0.82 (0.02)**	**0.72 (0.02)**	**0.65 (0.01)**	**42.8 (1.3)**	**38.8 (1.4)**
$4000+	76	**0.91 (0.02)**	**0.86 (0.01)**	**0.74 (0.01)**	**50.7 (1.0)**	**48.2 (1.2)**
Problematic substance use						
None	140	0.83 (0.02)	0.76 (0.02)	**0.68 (0.01)**	44.5 (1.0)	**43.6 (1.1)**
Injection drugs	41	0.83 (0.03)	0.76 (0.03)	**0.65 (0.02)**	44.9 (1.6)	**40.0 (2.3)**
Alcohol	33	0.75 (0.05)	0.71 (0.04)	**0.62 (0.02)**	41.1 (2.0)	**37.8 (2.3)**
Both	46	0.80 (0.04)	0.75 (0.03)	**0.64 (0.02)**	43.7 (1.7)	**37.2 (2.1)**
Charlson						
0	59	**0.81 (0.03)**	0.75 (0.03)	0.67 (0.02)	**47.1 (1.5)**	39.9 (2.0)
1	97	**0.86 (0.02)**	0.78 (0.02)	0.67 (0.01)	**45.2 (1.1)**	41.3 (1.3)
2	55	**0.84 (0.03)**	0.76 (0.03)	0.64 (0.02)	**43.0 (1.6)**	40.6 (1.8)
3+	43	**0.68 (0.05)**	0.70 (0.03)	0.64 (0.02)	**37.0 (1.8)**	42.7 (2.1)
Index of coexistent disease						
0	50	**0.90 (0.03)**	**0.85 (0.02)**	**0.75 (0.02)**	**51.9 (1.2)**	**44.6 (2.0)**
1	27	**0.91 (0.04)**	**0.88 (0.02)**	**0.75 (0.02)**	**52.7 (1.7)**	**46.6 (2.6)**
2	68	**0.82 (0.03)**	**0.76 (0.02)**	**0.64 (0.01)**	**44.0 (1.2)**	**39.2 (1.5)**
3	109	**0.74 (0.03)**	**0.67 (0.02)**	**0.61 (0.01)**	**37.8 (1.1)**	**39.2 (1.3)**

*Numbers in parentheses are SDs and bolded numbers represent $P < 0.05$.

HUI2, Health Utility Index Mark 2; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-6D, Short-Form 6D; TTO, time trade-off.

with HCV that met the study inclusion criteria was lower than that of the general populations of US and Canada. Specifically, our TTO scores (range of mean scores, by group: 0.76–0.84) for the three disease stages were lower than the TTO score of 0.92 for the general US population between the ages of 45–54 years as determined by the Beaver Dam Health Outcomes Study (53). Our scores for HUI2 (0.71–0.76) and HUI3 (0.55–0.62) were much lower than general US population norms with a mean age of 45 years (HUI2 = 0.86, HUI3 = 0.81) (54). The Canadian National Population Health Survey found the HUI3 score for the general Canadian population with a mean age of 44 years to be 0.90, which is much higher than the HUI3 scores in our study (55). Our SF-6D scores (0.61–0.67) were lower than the SF-6D score of 0.80 for the general US population between the ages of 45–54 years as reported by the National Health Measurement study (56). In fact, non-cirrhotic and compensated cirrhotic individuals had utilities similar to those suffering from arthritis (0.82–0.84) or hypertension (0.83) (53, 55, 57). The utilities for decompensated cirrhotic individuals were comparable to patients with Type II diabetes (0.76) and emphysema (0.75) (53). Furthermore, the SF-36 summary scores for the decompensated group were similar to the scores of a longitudinal study of the QOL in patients with asthma (Physical Component Summary = 37.4, Mental Component Summary = 42.5) (58). Studies have shown that QOL in patients with chronic liver disease is similar to those suffering from stroke, COPD and congestive heart failure (16, 59).

Our SF-36 and utility data are consistent with those reported in other studies looking at QOL in HCV patients (4, 14, 16, 18, 19, 60, 61). It is generally believed that a 3–5-point difference on any SF-36 scale score represents a clinically important difference (62, 63). It also has been suggested that a 7–15-point difference observed between individuals with compensated

© 2009 The Authors. Journal compilation © 2009 Blackwell Publishing Ltd

Table 5. Results from regression models

	Compensated cirrhosis vs non-cirrhosis						Decompensated cirrhosis vs non-cirrhosis					
	HUI2		TTO		SF-6D		HUI2		TTO		SF-6D	
Variable	*B**	95% CI	*B**	95% CI	*B**	95% CI	*B**	95% CI	*B**	95% CI	*B**	95% CI
Disease Stage	−0.01	−0.11, 0.09	0.07	−0.05, 0.19	−0.04	−0.12, 0.04	−0.04	−0.10, 0.02	−0.05	−0.13, 0.03	−0.05	−0.09, −0.01
Age†	0.02	0.00, 0.04	0.01	−0.03, 0.05	0.01	−0.01, 0.03	0.02	0.00, 0.04	0.01	−0.01, 0.03	0.01	−0.01, 0.03
Education‡	−0.01	−0.07, 0.05	0.06	0.00, 0.12	0.02	−0.02, 0.06	−0.02	−0.08, 0.04	0.04	−0.02, 0.10	0.02	−0.02, 0.06
Marital status§	0.10	0.04, 0.16	0.08	0.02, 0.14	0.07	0.03, 0.11	0.10	0.04, 0.16	0.08	0.02, 0.14	0.07	0.03, 0.11
Log_{10} income	0.04	0.02, 0.06	0.05	0.01, 0.09	0.02	0.00, 0.04	0.03	0.01, 0.05	0.05	0.01, 0.09	0.02	0.00, 0.04
Charlson¶	−0.04	−0.08, 0.00	−0.03	−0.07, 0.01	−0.02	−0.04, 0.00	−0.02	−0.04, 0.00	−0.04	−0.08, 0.00	−0.01	−0.03, 0.01

*Unstandardized coefficient.

†This was recorded as age at beginning of disease stage. Results are difference in utility per 5 years of age.

‡Education is a binary variable with 0 = completed high school or less, 1 = started or completed trade/college/university.

§Marital status is a binary variable with 0 = not married or common-law, 1 = married or common-law.

¶A measurement of comorbidity, where a higher score reflects more serious comorbidity (17).

HUI2, Health Utility Index Mark 2; SF-6D, Short-Form 6D; TTO, time trade-off.

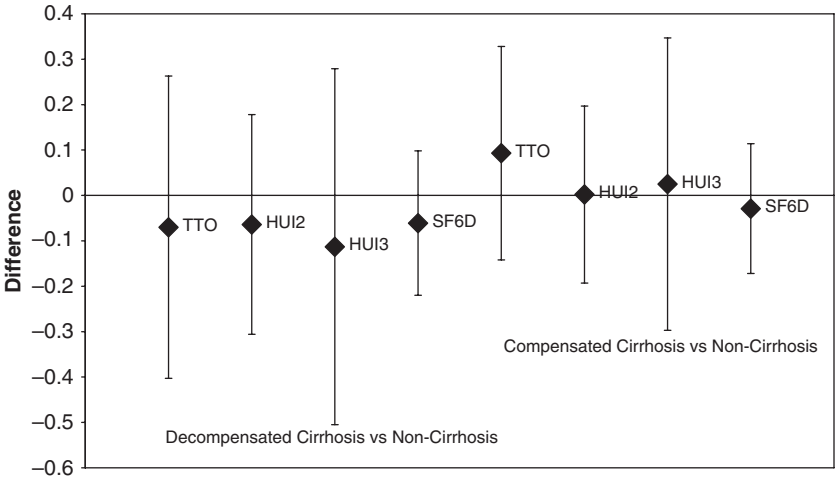

Fig. 1. Mean differences in utilities between disease stages and 95% confidence intervals after propensity score matching.

cirrhosis and healthy controls represent a clinically important difference across all SF-36 scales (64). We found the SF-36 scores for our HCV patients were 11.6–38.1 points lower than the general population (Table 3). Furthermore, the SF-36 vitality domain has been characterized as the most relevant domain in patients with HCV and a 4.2-point difference in vitality score has been suggested to be the minimal clinically important difference (64). The vitality scores for our HCV patients were 20.4–26.8 points lower than the general population (Table 3). Our findings, therefore, are consistent with the literature – individuals with HCV experience noticeable impairments in QOL compared with the general population.

Small differences in global quality of life between disease stages

Using preference measurements of QOL, we found small differences in global QOL between disease stages. Even after propensity score matching, the largest absolute difference in utilities between disease stages was 0.11 but the 95% confidence intervals were very wide. Chong *et al*. also described smaller than expected utility differences across disease stages (4). Chong *et al*. determined utilities for individuals without cirrhosis, compensated and decompensated cirrhosis to be 0.64–0.83, 0.66–0.83 and 0.52–0.85 respectively (4). In addition, Sherman (14) *et al*. reported no significant association between patient-derived health utilities and clinical measures of HCV. According to these authors, HCV utilities were 0.81–0.89 for the non-cirrhotics, 0.72–0.93 for patients with compensated cirrhosis and 0.60–0.84 for individuals with decompensated cirrhosis. Estimating utilities from published SF-36 scores for the HCV population, Thein *et al*. (5) found utilities for individuals without cirrhosis, compensated and decompensated cirrhosis to be 0.70–0.86, 0.67–0.84 and 0.63–0.80 respectively. In contrast, Younossi *et al*. (16) showed that measures of liver disease severity using the Child–Pugh score (a cirrhosis severity scoring method) were associated with poorer QOL in populations with viral, cholestatic and autoimmune liver diseases. According to these authors, utilities were 0.82 for patients without cirrhosis, 0.83 for those with Child's A cirrhosis, 0.67 for Child's B and 0.56 for Child's C. However, in another study that used the Child–Pugh classification, Hauser *et al*. (65) found that QOL in chronic HCV infection was not determined by the severity of the liver disease.

© 2009 The Authors. Journal compilation © 2009 Blackwell Publishing Ltd

Although global QOL remained relatively constant between disease stages, we did find significant differences across groups in select domains of the SF-36, specifically physical functioning, role physical, general health, role emotional and the physical component summary. Clearly there are differences across groups in SF-36 domains, but these differences in attributes fail to translate into significant differences in global QOL measured by utility instruments. This discrepancy between preference- and non-preference-based measurements of QOL may have several explanations. First, differences in the individual dimensions of the SF-36 may not have a large influence on global health status. The true difference in overall health status may be very small or negligible. Alternatively, the observed discrepancy may be attributable to the measurement properties of utility instruments. The larger amount of random error (noise) associated with measuring utilities may limit the ability to detect small differences in global QOL between groups. We suspect that both factors may play a role. There do appear to be consistent differences in mean scores across all utility instruments between decompensated cirrhotics and patients with chronic disease, but differences are small, and associated with large confidence intervals. A larger sample size may be required to exclude the possibility of small differences in mean utility scores between these stages of hepatitis C-related liver disease.

Income, marital status and comorbidities have large effect on global quality of life

Variables other than liver disease stage have greater effect on global QOL in HCV patients, namely marital status, income and to a lesser degree comorbidities. We found that individuals in married or common-law relationships experienced significantly better QOL than their single counterparts. Higher income and fewer comorbidities also seemed to lead to better QOL. Studies have shown that lower income and increasing number of comorbid conditions is associated with lower utility scores (66–68). Chong *et al.* (4) reported that higher income and less comorbidity predicted better utilities and SF-36 scores in HCV patients. In addition, Braitstein *et al.* (69) found that poorer quality of life in HIV/HCV coinfected patients was primarily related to sociodemographical factors such as poverty rather than HCV infection by itself. Both Thein *et al.* (5) and Hauser *et al.* (65) suggested that psychiatric and medical comorbidities had the strongest correlation with QOL in chronic HCV patients instead of the severity of the liver disease. Our findings, therefore, are consistent with what other investigators have reported – QOL in HCV patients is affected by medical and non-medical comorbid conditions that are largely extra-hepatic in nature.

Limitations and conclusions

Because we utilized a convenience sampling method of recruiting individuals from a tertiary care setting, our sample might not accurately reflect the general HCV population due to potential sampling bias. Our participants may have been more educated and affluent than the general HCV population with underrepresentation of socially marginalized individuals. As injection drug use is currently the most common risk factor for contracting HCV, it would be useful to determine the QOL experienced by individuals from these marginalized populations who are more likely to be homeless, have lower socioeconomic status and poorer access to tertiary care centres. It is possible that the results derived from this sample might be different than if they had been taken from a random selection of all eligible participants in the general HCV population. Although our sample size was relatively small, particularly for the compensated cirrhosis group, we feel that it was representative of patients from each of the three clinical categories of HCV disease (i.e. non-cirrhosis, compensated cirrhosis and decompensated cirrhosis).

Our study provides direct patient-elicited utilities for the HCV population, specifically for individuals without cirrhosis, compensated cirrhosis and decompensated cirrhosis. Indeed while our patients with HCV experience poorer QOL compared with the general population, our results confirm that changes in HCV disease stage do not appear to be the key factor related to changes in QOL. We determined that concomitant factors such as comorbidity, income and marital status have a greater effect on QOL than disease stage. To our knowledge, our study is the first to utilize the propensity score methodology to examine differences in QOL between HCV disease stages. The utility scores provided by our study will contribute towards the precision of future quality-adjusted life year estimates used in cost-effectiveness analyses of prevention and treatment interventions in hepatitis C infection.

Acknowledgements

The authors would like to thank the subjects who participated in this study, Andrew Tu for his assistance with statistical analysis, Doug Ford for his programming expertise and Carole Federico for her thorough chart reviews. We greatly appreciate the support of Dr Erb, Dr Steinbrecher, Dr Weiss, and the staff at BC Hepatitis Services, BC Hepatitis Program, Liver and Intestinal Research Centre, BC Transplant Society, Solid Organ Transplant Clinic and Gilwest Clinic. We would also like to thank the Canadian Institutes of Health Research for providing operating funds for this study.

References

1. Burak KW, Lee SS. Treatment options in patients with chronic hepatitis C. *Can J Public Health* 2000; **91**(Suppl. 1): S22-6–S24-8.
2. Teo M, Hayes P. Management of hepatitis C. *Br Med Bull* 2004; **70**: 51–69.
3. Fischer B, Haydon E, Rehm J, *et al.* Injection drug use and the hepatitis C virus: considerations for a targeted treatment approach – the case study of Canada. *J Urban Health* 2004; **81**: 428–47.
4. Chong CA, Gulamhussein A, Heathcote EJ, *et al.* Health-state utilities and quality of life in hepatitis C patients. *Am J Gastroenterol* 2003; **98**: 630–8.
5. Thein HH, Krahn M, Kaldor JM, Dore GJ. Estimation of utilities for chronic hepatitis C from SF-36 scores. *Am J Gastroenterol* 2005; **100**: 643–51.
6. Brandt J, Spencer M, Folstein M. The telephone interview for cognitive status. *Neuropsychiat Neuropsychol Behav Neurol* 1998; **1**: 111–7.
7. Barber M, Stott DJ. Validity of the telephone interview for cognitive status (TICS) in post-stroke subjects. *Int J Geriatr Psychiatry* 2004; **19**: 75–9.
8. Debling D, Amelang M, Hasselbach P, Sturmer T. Assessment of cognitive status in the elderly using telephone interviews. *Z Gerontol Geriatr* 2005; **38**: 360–7.
9. Bayliss MS, Gandek B, Bungay KM, *et al.* A questionnaire to assess the generic and disease-specific health outcomes of patients with chronic hepatitis C. *Qual Life Res* 1998; **7**: 39–55.

© 2009 The Authors. Journal compilation © 2009 Blackwell Publishing Ltd

10. Gutteling JJ, de Man RA, Busschbach JJ, Darlington AS. Overview of research on health-related quality of life in patients with chronic liver disease. *Neth J Med* 2007; **65**: 227–34.
11. Furlong WJ, Feeny DH, Torrance GW, Barr RD. The health utilities index (HUI) system for assessing health-related quality of life in clinical studies. *Ann Med* 2001; **33**: 375–84.
12. Torrance GW, Furlong W, Feeny D, Boyle M. Multi-attribute preference functions. Health utilities index. *Pharmacoeconomics* 1995; **7**: 503–20.
13. Torrance GW. Utility approach to measuring health-related quality of life. *J Chronic Dis* 1987; **40**: 593–603.
14. Sherman KE, Sherman SN, Chenier T, Tsevat J. Health values of patients with chronic hepatitis C infection. *Arch Intern Med* 2004; **164**: 2377–82.
15. 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.
16. Younossi ZM, Boparai N, McCormick M, *et al.* Assessment of utilities and health-related quality of life in patients with chronic liver disease. *Am J Gastroenterol* 2001; **96**: 579–83.
17. Bryce CL, Angus DC, Switala J, *et al.* Health status versus utilities of patients with end-stage liver disease. *Qual Life Res* 2004; **13**: 773–82.
18. Dan AA, Kallman JB, Srivastava R, *et al.* Impact of chronic liver disease and cirrhosis on health utilities using SF-6D and the health utility index. *Liver Transpl* 2008; **14**: 321–6.
19. Longworth L, Bryan S. An empirical comparison of EQ-5D and SF-6D in liver transplant patients. *Health Econ* 2003; **12**: 1061–7.
20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373–83.
21. de Groot V, Beckerman H, Lankhorst GJ, Bouter LM. How to measure comorbidity. A critical review of available methods. *J Clin Epidemiol* 2003; **56**: 221–9.
22. Ulcickas YM, Quesenberry CP Jr, Guo D, *et al.* Incidence of non-Hodgkin's lymphoma among individuals with chronic hepatitis B virus infection. *Hepatology* 2007; **46**: 107–12.
23. Skiest DJ, Rubinstien E, Carley N, Gioiella L, Lyons R. The importance of comorbidity in HIV-infected patients over 55: a retrospective case-control study. *Am J Med* 1996; **101**: 605–11.
24. Zavascki AP, Fuchs SC. The need for reappraisal of AIDS score weight of Charlson comorbidity index. *J Clin Epidemiol* 2007; **60**: 867–8. Epub 2007, 23 March.
25. Greenfield S, Apolone G, McNeil BJ, Cleary PD. The importance of co-existent disease in the occurrence of postoperative complications and one-year recovery in patients undergoing total hip replacement. Comorbidity and outcomes after hip replacement. *Med Care* 1993; **31**: 141–54.
26. Cocci C, Bianchi G, Nativio V, *et al.* Perception of health-related quality of life and psychological status in oldest hospitalized patients without cognitive impairment. *Arch Gerontol Geriatr* 2004; (Suppl.)**9**: 75–84.
27. Harboun M, Ankri J. Comorbidity indexes: review of the literature and application to studies of elderly population. *Rev Epidemiol Sante Publique* 2001; **49**: 287–98.
28. Gabriel SE, Crowson CS, O'Fallon WM. Comorbidity in arthritis. *J Rheumatol* 1999; **26**: 2475–9.
29. Gabriel SE, Crowson CS, O'Fallon WM. A comparison of two comorbidity instruments in arthritis. *J Clin Epidemiol* 1999; **52**: 1137–42.
30. Stojanovic M, Ilic S, Stefanovic V. Influence of co-morbidity on health-related quality of life in patients treated with hemodialysis. *Int J Artif Organ* 2006; **29**: 1053–61.
31. Miskulin DC, Martin AA, Brown R, *et al.* Inc. Predicting 1 year mortality in an outpatient haemodialysis population: a comparison of comorbidity instruments. *Nephrol Dial Transplant* 2004; **19**: 413–20.
32. Miskulin DC, Meyer KB, Martin AA, *et al.* Comorbidity and its change predict survival in incident dialysis patients. *Am J Kidney Dis* 2003; **41**: 149–61.
33. Judd CM, McClelland GH. *Data Analysis: A Model Comparison Approach.* New York: Harcourt Brace Jovanovich, 1989; 204.
34. Henderson HV, Velleman PF. Building multiple regression models interactively. *Biometrics* 1981; **37**: 391–411.
35. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika* 1983; **70**: 41–55.
36. Rubin DB. Estimating causal effect from large data sets using propensity scores. *Ann Intern Med* 1997; **127**: 757–63.
37. Fitzmaurice G. Confounding: propensity score adjustment. *Nutrition* 2006; **22**: 1214–6.
38. Hill J, Reiter JP. Interval estimation for treatment effects using propensity score matching. *Stat Med* 2006; **25**: 2230–56.
39. Sturmer T, Schneeweiss S, Rothman KJ, *et al.* Performance of propensity score calibration – a simulation study. *Am J Epidemiol* 2007; **165**: 1110–8.
40. Perkins SM, Tu W, Underhill MG, *et al.* The use of propensity scores in pharmacoepidemiologic research. *Pharmacoepidemiol Drug Saf* 2000; **9**: 93–101.
41. Glynn RJ, Schneeweiss S, Sturmer T. Indications for propensity scores and review of their use in pharmacoepidemiology. *Basic Clin Pharmacol Toxicol* 2006; **98**: 253–9.
42. Shah BR, Laupacis A, Hux JE, Austin PC. Propensity score methods gave similar results to traditional regression modeling in observational studies: a systematic review. *J Clin Epidemiol* 2005; **58**: 550–9. Epub, 19 April 2005.
43. Weitzen S, Lapane KL, Toledano AY, *et al.* Principles for modeling propensity scores in medical research: a systematic literature review. *Pharmacoepidemiol Drug Saf* 2004; **13**: 841–53.
44. Hagan H, Thiede H. Changes in injection risk behavior associated with participation in the Seattle needle-exchange program. *J Urban Health* 2000; **77**: 369–82.
45. Cologne JB, Shibata Y. Optimal case–control matching in practice. *Epidemiology* 1995; **6**: 271–5.
46. Nosyk B, Sun H, Li X, *et al.* Highly active antiretroviral therapy and hospital readmission: comparison of a matched cohort. *BMC Infect Dis* 2006; **6**: 146.
47. Liu C, Weber K, Robison E, *et al.* Assessing the effect of HAART on change in quality of life among HIV-infected women. *AIDS Res Ther* 2006; **3**: 6.
48. Merito M, Pezzotti PICONA Study Group. Comparing costs and effectiveness of different starting points for highly active antiretroviral therapy in HIV-positive patients. Evidence from the ICONA cohort. *Eur J Health Econ* 2006; **7**: 30–6.
49. Price LA, Thombs B, Chen CL, Milner SM. Liver disease in burn injury: evidence from a national sample of 31,338 adult patients. *J Burns Wounds* 2007; **7**: e1.
50. Baser O. Too Much ado about propensity score models? Comparing methods of propensity score matching. *Value Health* 2006; **9**: 377–85.
51. Saris-Baglama RN, Dewey CJ, Chisholm GB, *et al. SF Health Outcomes Scoring Software User's Guide.* Lincoln, RI: QualityMetric Incorporated, 2004.
52. Hopman WM, Towheed T, Anastassiades T, *et al.* Canadian normative data for the SF-36 health survey. *Can Med Assoc J* 2000; **163**: 265–71.

© 2009 The Authors. Journal compilation © 2009 Blackwell Publishing Ltd

53. Fryback DG, Dasbach EJ, Klein R, *et al*. The Beaver Dam Health Outcomes Study: initial catalog of health-state quality factors. *Med Decis Making* 1993; **13**: 89–102.
54. Luo N, Johnson JA, Shaw JW, *et al*. Self-reported health status of the general adult U.S. population as assessed by the EQ-5D and Health Utilities Index. *Med Care* 2005; **43**: 1078–86.
55. Maddigan SL, Feeny DH, Johnson JA. Health-related quality of life deficits associated with diabetes and comorbidities in a Canadian National Population Health Survey. *Qual Life Res* 2005; **14**: 1311–20.
56. Fryback DG, Dunham NC, Palta M, *et al*. US norms for six generic health-related quality-of-life indexes from the National Health Measurement study. *Med Care* 2007; **45**: 1162–70.
57. Lawrence WF, Fryback DG, Martin PA, *et al*. Health status and hypertension: a population-based study. *J Clin Epidemiol* 1996; **49**: 1239–45.
58. Mancuso CA, Peterson MG. Different methods to assess quality of life from multiple follow-ups in a longitudinal asthma study. *J Clin Epidemiol* 2004; **57**: 45–54.
59. Younossi ZM, Boparai N, Price LL, *et al*. Health-related quality of life in chronic liver disease: the impact of type and severity of disease. *Am J Gastroenterol* 2001; **96**: 2199–205.
60. Ware JE, Bayliss JS, Mannocchia M, *et al*. Health-related quality of life in chronic hepatitis C: impact of disease and treatment response. *Hepatology* 1999; **30**: 550–5.
61. Niederau C, Bemba G, Kautz A. Changes in socio-economics, quality of life and knowledge of patients with chronic hepatitis C during the Hepatitis Competence Net Project. *Z Gastroenterol* 2008; **46**: 22–33.
62. Stewart AL, Greenfield S, Hays RD, *et al*. Functional status and well-being of patients with chronic conditions. Results from the medical outcomes study. *JAMA* 1989; **262**: 907–13. Erratum in: *JAMA* 1989; 262:2542.
63. Samsa G, Edelman D, Rothman ML, *et al*. Determining clinically important differences in health status measures: a general approach with illustration to the Health Utilties Index Mark II. *Pharmacoeconomics* 1999; **15**: 141–55.
64. Spiegel BM, Younossi ZM, Hays RD, *et al*. Impact of hepatitis C on health related quality of life: a systematic review and quantitative assessment. *Hepatology* 2005; **41**: 790–800.
65. Hauser W, Zimmer C, Schiedermaier P, Grandt D. Biopsychosocial predictors of health-related quality of life in patients with chronic Hepatitis C. *Psychosom Med* 2004; **66**: 954–8.
66. Mittmann N, Trakas K, Risebrough N, Liu BA. Utility scores for chronic conditions in a community-dwelling population. *Pharmacoeconomics* 1999; **15**: 369–76.
67. Roberge R, Berthelot JM, Wolfson M. The health utility index: measuring health differences in Ontario by socioeconomic status. *Health Rep* 1995; **7**: 25–32 (Eng); 29–37.
68. Rizzo JA, Pashko S, Friedkin R, *et al*. Linking the health utilities index to National medical expenditure survey data. *Pharmacoeconomics* 1998; **13**(Part 1): 531–41.
69. Braitstein P, Montessori V, Chan K, *et al*. Quality of life, depression and fatigue among persons co-infected with HIV and hepatitis C: outcomes from a population-based cohort. *AIDS Care* 2005; **17**: 505–15.

Liver International (2009)
© 2009 The Authors. Journal compilation © 2009 Blackwell Publishing Ltd