Sustained Responders Have Better Quality of Life and Productivity Compared With Treatment Failures Long After Antiviral Therapy for Hepatitis C

Ava A. John-Baptiste, MHSc[1–3], George Tomlinson, PhD[1–4], Priscilla C. Hsu, MHA[5,6], Mel Krajden, MD, FRCPC[5,6], E. Jenny Heathcote, MD[1,2], Audrey Laporte, MA, PhD[1], Eric M. Yoshida, MD, MHSc, FRCPC[7], Frank H. Anderson, MD, FRCPC[8] and Murray D. Krahn, MD, MSc, FRCPC[1–3,9]

OBJECTIVES: **We sought to compare the health status of patients with a sustained response to antiviral therapy for hepatitis C virus (HCV) infection with that of treatment failures, using health-related quality of life and preference (utility) measures.**

METHODS: **Sustained responders had undetectable HCV viral levels 6 months after antiviral therapy. After antiviral therapy, participants completed, by mail or interview, the hepatitis-specific Medical Outcomes Study Short-Form 36-Item Health Survey (SF-36), the Health Utilities Index Mark 2/3 (HUI2/3), and time trade-off (TTO) for current health. The respondents provided information on demographics, history of substance abuse, comorbidities, and health history. Detailed clinical information was obtained by chart review. The respondents also indicated whether they missed work, volunteer opportunities, or household activities during the previous 3 months because of hepatitis C infection or its treatment.**

RESULTS: **A total of 235 patients (133 responders and 102 treatment failures) completed questionnaires at an average of 3.7 years after the end of treatment. Treatment failures had significantly lower scores on the eight SF-36 domains ($P<0.01$), lower scores on the hepatitis-specific domains ($P<0.0001$), and lower physical (42.5 vs. 49.2) and mental (40.5 vs. 46.1) component summary scores ($P<0.01$). HUI3 (0.57 vs. 0.70), HUI2 (0.74 vs. 0.80), SF-6D (0.65 vs. 0.71), and TTO (0.84 vs. 0.89) were lower for treatment failures ($P<0.05$). The regression-adjusted difference in HUI3, SF-6D, physical summary score, and mental summary score was 0.08 ($P=0.04$), 0.05 ($P=0.004$), 5.22 ($P=0.001$), and 5.73 ($P<0.0001$), respectively. Differences in the HUI2 and TTO scores were not significant after adjustment for demographic and clinical variables. Treatment failures were more likely to have missed work, volunteer opportunities, or household activities in the previous 3 months because of hepatitis C infection or its treatment (44 vs. 9%, $P<0.001$).**

CONCLUSIONS: **Patients with a sustained response to antiviral therapy for chronic HCV infection have better quality of life than treatment failures do. Our study validates the benefits associated with the sustained response to antiviral therapy in a real-world clinic population and shows that these benefits are maintained over the long term.**

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[1]Department of Health Policy, Management and Evaluation and Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada; [2]University Health Network, Toronto, Ontario, Canada; [3]Toronto Health Economics and Technology Assessment (THETA) Collaborative, Toronto, Ontario, Canada; [4]Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada; [5]British Columbia Centre for Disease Control, Vancouver, British Columbia, Canada; [6]Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, British Columbia, Canada; [7]Division of Gastroenterology, University of British Columbia, Vancouver, British Columbia, Canada; [8]Liver and Intestinal Research Centre, Vancouver, British Columbia, Canada; [9]Faculty of Pharmacy, University of Toronto, Toronto, Ontario, Canada. **Correspondence:** Ava A. John-Baptiste, MHSc, Department of Health Policy, Management and Evaluation and Faculty of Medicine, University of Toronto, Toronto General Hospital, EN13-239, 200 Elizabeth Street, Toronto, ON, Canada M5G 2C4. E-mail: a.john.baptiste@utoronto.ca
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INTRODUCTION

Chronic infection with hepatitis C virus (HCV) can result in cirrhosis, liver failure, and hepatocellular carcinoma. Individuals with chronic HCV infection also have impairments in quality of life, even in the absence of liver disease. HCV viremia is associated with fatigue (1), impaired cognition (2,3), stigmatization (4–6), emotional distress (7), and depression (8,9). However, the extent that HCV viremia itself contributes to lower health-related quality of life is unclear, given the high burden of psychiatric and medical comorbidities in patients with chronic HCV infection (6,10). Data collected alongside randomized controlled clinical trials, show a significant improvement in quality of life immediately after sustained response to therapy (11,12). However, patients enrolled in clinical trials represent highly selected populations, and it is not clear whether these results are generalizable. Our study focused on a clinic population and assessed whether differences in the quality of life between sustained responders and treatment failures persist over the long term. Using regression analysis to adjust for other factors related to the quality of life, we assessed whether or not differences were attributable to the clearance of HCV viremia. Differences in levels of fatigue and productivity between sustained responders and treatment failures were also assessed.

The majority of studies measure quality of life using psychometric instruments, such as the Medical Outcomes Study Short-Form-36 (SF-36). Although psychometric measures describe the health status of individuals with chronic HCV infection, they do not provide information on what value either the individual or society places on the health status nor do they provide a single, summary measure of global health status. Utility measures rate quality of life on a scale from 0 to 1, which indicates the strength of preference for a health state and provides a single measure of global health status. Utility measures are also essential inputs in cost-effectiveness analyses, as they are used to weight life expectancy in estimating quality-adjusted life expectancy gains associated with new treatments. Such analyses can inform health-care policy on treatment of chronic HCV infection, weighing potential health gains against the costs of treatment.

METHODS

This analysis is part of a larger study examining the quality of life and economic burden of HCV in a community-dwelling population (13). The study design included a cross-sectional administration of questionnaires along with a retrospective review of medical records. A convenience sample of patients with chronic HCV infection was recruited between 1 January 2006 and 1 March 2008 through five health-care settings in the metropolitan area of Vancouver, British Columbia, including the BC Hepatitis Program at the Vancouver General Hospital, the Solid Organ Transplant Clinic at the Vancouver General Hospital, the BC Transplant Society Pre-Liver Transplant Assessment Clinic, the Liver and Intestinal Research Centre, and the Gilwest Clinic at the Richmond General Hospital. Recruitment was carried out through advertisements posted in clinics, personal referrals, and letters from clinicians. Participants had the choice to complete questionnaires by mail (self-administered), phone (interviewer administered), or in person at the clinic (self-administered or interviewer administered).

Individuals were included in the current analysis if they had a previous diagnosis of chronic HCV infection on the basis of a history of positive HCV RNA and if they had received previous HCV antiviral therapy. Patients were treated with contemporary conventional therapies, including interferon α-2b, alone or in combination with ribavirin, pegylated interferon α-2b in combination with ribavirin, (Intron A, Rebetron and Pegetron, Schering Plough, Kenilworth, NJ), and interferon α-2a and peginterferon α-2a, alone or in combination with ribavirin (Roferon A, Pegasys and Copegus, Hoffmann–La Roche, Basel, Switzerland). The response status was classified in the following manner. Sustained responders were defined as those with undetectable HCV viral levels 24 weeks after antiviral therapy. HCV RNA assays were carried out at the virology laboratory of the BC Centre for Disease Control, Vancouver, British Columbia (Cobas Amplicor HCV Test V2.0, limit of detection 50 IU/ml, Roche Diagnostic Systems, Mississauga, ON, Canada). Treatment failures were defined as those with detectable HCV viremia after antiviral therapy or those with an end-of-treatment response who relapsed. Individuals were excluded from the study if they were enrolled in a clinical drug trial, had limited English proficiency or limited cognitive status as measured by a score of <21 on the Telephone Interview for Cognitive Status (14,15), or had advanced liver disease at the time of questionnaire completion (decompensated cirrhosis, hepatocellular carcinoma, liver transplant). Patients with advanced disease were excluded from this analysis on the basis of research showing that health status and quality of life are substantially lower in these patients when compared with other patients with chronic HCV infection (16).

Data collection

Participants provided information on ethnicity, marital status, education level, and monthly income from all sources, including employment, retirement, and social assistance (disability, employment insurance, family bonus, child tax, or native health benefits). Participants answered questions about their medical history, including comorbidities, physical impairments, risk factors for HCV infection, and current and past substance use. A history of problematic substance abuse was determined by asking participants if they had ever injected or snorted drugs regularly for 4 weeks. A history of alcohol dependency was determined by asking participants if they had ever become dependent on alcohol. A history of mental health problems was determined by self-report of ever having sought clinical help, been hospitalized, or treated with prescription medicine for depression, anxiety, or mood disorders. Participants were also asked if they currently injected or snorted drugs.

Medical records of participants who consented to chart review were accessed at the clinics in which patients received care for HCV. Pathology records (liver biopsy results), blood tests (HCV Ab, HCV RNA, alanine aminotransferase), imaging reports, and clinic notes were abstracted and used to classify the disease stage at the time of questionnaire completion. Medical records were reviewed by a trained research assistant knowledgeable in the field of HCV infection.

Comorbidity scores

The Charlson comorbidity score (17) is a weighted index of the number of comorbid diseases, commonly used to adjust for comorbidity in studies of hospitalization, mortality, and resource use. The Index of Coexistent Disease (ICED), another comorbidity index, has two subscales measuring the severity of disease and physical impairment level, which are condensed into a single composite index with 4 levels ranging from 0 (no comorbidities and no physical impairment) to 3 (severe comorbidities and severe physical impairment) (18). The Charlson score and the ICED were calculated using information obtained from both the medical records and the patient questionnaires. For example, congestive heart failure was considered a comorbid condition if the patient reported a history of a single episode of congestive heart failure or if physician notes indicated a history of congestive heart failure. Some index items were removed from the scores based on the rationale that they were the primary condition being considered rather than a comorbid condition (liver disease), or because they may be affected by HCV viremia (items related to mental health status).

Quality-of-life measures

The SF-36 version 2 (SF-36 V2) measures health-related quality of life in eight domains (physical functioning, role physical, bodily pain, general health perception, energy/vitality, social functioning, role emotional, and mental health) along with a physical summary score (PCS) and mental summary score (MCS). Each of the 8 domains and the summary scores are scored out of 100, with higher scores indicating better quality of life (19). The HQLQ (Hepatitis Quality of Life Questionnaire) is a version of the SF-36 developed to better capture the aspects of quality of life affected by hepatitis infection. The HQLQ has four additional domains (also scored from 0 to 100) represented by 15 additional questionnaire items, measuring generic health distress, positive well-being, hepatitis-specific limitations and hepatitis-specific health distress (20,21).

The Health Utilities Index Mark 2/3 (HUI2/3) is a preference-based utility instrument that measures health status (symptoms and functional status) using a 15-item questionnaire (22). The HUI3 classifies individuals into levels of functioning on eight attributes, namely vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain. The HUI2 classifies individuals using seven attributes, such as sensation, mobility, cognition, self-care, emotion, pain, and fertility. Using preference weights obtained from members of the general public, an overall utility score is calculated. HUI2 scores range from -0.03 to 1 and HUI3 scores from -0.36 to 1.00. Higher scores indicate better quality of life and negative scores represent states considered worse than death.

The SF-6D is a preference-based utility instrument that classifies respondents into six dimensions of health (physical functioning, role limitation, social functioning, bodily pain, mental health, and vitality), using 11 items from the SF-36 questionnaire. Using preference weights obtained from members of the general public in the United Kingdom, a utility weight ranging from 0.3 to 1 is calculated, with higher scores indicating better quality of life (23,24).

The time trade-off (TTO) is a preference-based direct utility measure in which an individual's own preference for a health state is shown by the individual's willingness to live a shorter but healthier life (25). The questionnaire prompted respondents to imagine that they have a 20-year life expectancy, and to indicate on a scale of 0–20, the number of years of perfect health that are equivalent to 20 years of life in their current health state. A utility score from 0 to 1 is calculated by dividing the number of years of perfect health by 20. Higher scores indicate better quality of life.

Productivity measures

Participants were asked whether they missed work, were unable to do volunteer work, household chores, or participate in leisure activities during the past 3 months because of hepatitis C or its treatment. The participants also indicated the amount of time for each category in hours or days. They were asked whether they had difficulty in working and provided an estimate of the percentage reduction in working capacity. Estimates of lost productivity, given in days, were translated to lost hours by multiplying by 7. The participants were also asked whether they experienced symptoms of fatigue during the past 4 weeks.

Statistical analyses

Descriptive statistics were used to characterize the patients, including means and s.d. for continuous variables and proportions for categorical variables. We compared continuous variables between responders and treatment failures using the independent samples Student's *t*-test. We compared categorical variables using Pearson's χ^2-test and Fisher's exact test, when the expected cell counts were <5. Quality-of-life measures were compared with normative population data, adjusting for age and sex. The HUI3 norms were obtained from the 3,505 Canadian respondents of the Joint Canada/United States Survey of Health (26). The SF-36 norms were collected from a survey of 9,423 randomly selected Canadians (27). Normative data for the SF-6D were obtained from the National Health Measurement Survey, a survey of 3,844 non-institutionalized adults living in the United States (28).

A multivariable linear regression analysis was carried out to adjust for factors identified *a priori* as potential confounders of the relationship between response status and quality of life.

The factors included age, sex, ethnicity, marital status, education level, Charlson comorbidity, and ICED score. Employment status and income were not included in the regression analysis based on the rationale that they may partially mediate the effect of HCV viremia on quality of life. Variables believed to be in the causal pathway between the independent and dependent variables should not be adjusted for in regression analyses because of the potential for over fitting.

The primary quality-of-life outcome for the linear regression analysis was the HUI3. Regressions using the HUI2, SF6-D, MCS, PCS, and TTO as outcomes were carried out in secondary analyses. Regression analyses were also repeated with a log transformation and logit transformation of the dependent variable to assess the robustness of results.

Ethics

The research protocol was approved by the University of British Columbia and the University Health Network research ethics boards. Participants provided written informed consent.

RESULTS

Of a total of 657 participants in the overall study of HCV in a community-dwelling population, 321 had undergone antiviral therapy at the time of completion of the questionnaires. Of these, 86 participants were excluded because they had advanced liver disease at the time of questionnaire completion—63 had decompensated cirrhosis, 7 had hepatocellular carcinoma, and 16 had received a liver transplant. A total of 235 patients met the inclusion criteria for the analysis; 102 treatment failures and 133 responders. At the time of questionnaire completion, the average time that had elapsed since the end of antiviral therapy for sustained responders and treatment failures was 3.9 and 3.5 years, respectively. Treatment failures were more likely to be men, infected (or previously infected) with genotype 1, 4, or 6 and had significantly higher levels of the alanine aminotransferase enzyme recorded in the most recent laboratory test report. The number of patients with a biopsy was 155 (66%). Five of the treatment failures and six of the sustained responders had compensated cirrhosis at the time of questionnaire completion. Only three patients were infected with HIV (human immunodeficiency virus) (two treatment failures and one sustained responder). The distribution of the Charlson comorbidity score and ICED scores did not differ between treatment failures and responders. Sustained responders and treatment failures also had similar proportions with a history of injection drug use, history of dependence on alcohol, and a history of mental health problems. (**Table 1**) Four respondents indicated active substance abuse (three responders and one treatment failure).

Treatment failures and sustained responders had similar levels of total monthly income, with some variation in the source of income. (**Table 2**) Treatment failures were significantly less likely to be employed (51 vs. 67%), and a greater proportion of them received income from social assistance (36 vs. 26%), but this difference did not reach statistical significance ($P=0.1$). They had lower productivity at work, volunteering, and household activities. (**Table 2**) Treatment failures were significantly more likely to have missed work, volunteer opportunities, or chores because of hepatitis C infection or its treatment in the 3 months before completing the questionnaires (44 vs. 9%) and were significantly more likely to have experienced difficulty in working (22 vs. 11%). Among those who missed work, volunteer opportunities, or chores because of hepatitis C infection or its treatment, the mean number of hours missed was 154 for sustained responders and 177 for treatment failures. Treatment failure, who had difficulty with work and leisure, reported a significantly greater percentage reduction in work and leisure capacity compared with sustained responders who reported difficulty with work and leisure. (**Table 2**) The proportion of sustained responders who reported experiencing any fatigue during the 4 weeks before completing the questionnaire was 69% compared with 81% of treatment failures ($P=0.05$).

Treatment failures had lower scores on each domain of the SF-36 (including generic and disease-specific domains) and on all utility measures when compared with sustained responders. (**Table 3**) All of the differences between sustained responders and treatment failures were statistically significant with the exception of the positive well-being scale ($P=0.06$). Treatment failures had significantly lower quality of life and utility scores than population norms. Sustained responders had similar bodily pain and physical component summary scores when compared with population norms, but scored significantly lower on all other measures.

After adjustment for age, sex, ethnicity, marital status, education, Charlson comorbidity, and ICED scores using multivariable linear regression, sustained responders had significantly higher HUI3 and SF-6D scores, PCS, and MCS compared with treatment failures (**Table 4**). When income and employment were added to the linear regression model, the differences between sustained responders and treatment failures were no longer significant for the HUI3, but remained significant for the SF-6D score, PCS, and MCS (data not shown). Performing log and logit transformations of the dependent variables produced results that were qualitatively similar (data not shown). All analyses were carried out using R, version 2.3.0. (R Foundation for Statistical Computing, Vienna, Austria, 2005).

DISCUSSION

Our study shows that sustained responders to antiviral therapy for chronic HCV infection have significantly better quality of life compared with treatment failures, as estimated by both psychometric and utility measures. The observed differences remain significant after adjustment for factors known to be associated with the quality of life—age, sex, ethnicity, marital status, comorbidity, and the severity of physical impairments—for the HUI3 (our primary outcome), SF-6D, PCS, and MCS, but not the HUI2 and TTO, suggesting that viral factors contribute to quality of life independent of host factors. Our results show that a sustained response to antiviral therapy is also associated with improved productivity and

Table 1. Demographic and clinical variables

	Treatment failures (*n*=103)		Sustained responders (*n*=133)		
	n	%	*n*	%	*P* value
Age in years (mean, s.d.)	53	9	52	10	0.44
Male	69	68	62	47	*P*<0.0001
Married/common-law	60	59	74	56	0.72
White ethnicity	87	86	108	82	0.56
Education					
Attended high school	15	15	14	11	
Completed high school	19	19	24	18	
Attended college, university, or trade school	32	31	33	25	
Completed trade school/apprenticeship	13	13	16	12	
Completed college or university	23	23	45	34	0.37
History of injection drug use	56	55	72	55	0.95
History of dependence on alcohol	33	37	33	31	0.51
History of mental health problems	63	62	76	58	0.59
Time since end of therapy (years) (mean, s.d.)	3.5	3	3.9	2	0.34
Infected (or previously infected) with genotype 1 or 4	69	77	60	53	*P*<0.0001
Alanine aminotransferase level (ALT) (mean, s.d.)	86.8	67	35.5	42	*P*<0.0001
Liver biopsy	71	70	84	63	0.37
Fibrosis score					
0	2		1		
1	11		15		
2	36		45		
3	17		17		
4	5		6		
Index of Coexistent Disease (ICED) score[a]					
0	24	24	26	20	
1	16	16	39	30	
2	21	21	21	16	
3	40	40	45	34	0.1
Charlson score category[b]					
0	58	57	86	65	
1	23	23	32	24	
2	21	21	15	11	0.14

[a]The ICED consists of two subscales: coexistent disease and physical impairment. The coexistent disease subscale identifies and scores the severity of the following conditions: ischemic heart disease/cardiomyopathy, non-ischemic heart disease/cardiomyopathy, primary arrhythmias and conduction problems, congestive heart failure, hypertension, cerebral vascular accident, peripheral vascular disease, diabetes mellitus, respiratory problems, malignancies/neoplasm/cancer, hepatobiliary disease, renal disease, arthritis, gastrointestinal disease, and infectious disease. It classifies severity into the following five levels (0–4) 0: absence of coexistent disease; 1: a comorbid condition that is asymptomatic or mildly symptomatic; 2: a mild-to-moderate condition that is generally symptomatic and requires medical intervention; 3: an uncontrolled condition that causes moderate-to-severe disease manifestations during medical care; and 4: an uncontrolled condition that causes severe manifestations during medical care. The physical impairment subscale assesses functional impairment in the following categories: circulation, respiration, neurological, mental status, urinary, fecal, feeding, ambulation, transfer, vision, hearing, and speech. There are 3 levels of impairment (0–2), where 0 indicates no significant impairment/normal function, 1 indicates mild or moderate impairment, and 2 indicates serious/severe impairment. The ICED score is based on the highest disease severity level and the highest physical impairment level. Scores range from 0 to 3, where 0 is absence of coexistent disease and no significant impairment, and 3 is serious/severe physical impairment combined with any level of disease severity. As noted in the Methods section, the ICED score was modified for our study by assigning a weight of zero to hepatobiliary disease (coexistent disease subscale) and to mental status (physical impairment subscale).

[b]The Charlson score assigns the following weights for each condition that a patient has: 1 for myocardial infarct, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, mild liver disease, diabetes; 2 for hemiplegia, moderate or severe renal disease, diabetes with end-organ damage, any tumor, leukemia, lymphoma; 3 for moderate or severe liver disease; 6 for metastatic solid tumor or acquired immunodeficiency syndrome. Diabetes with end organ damage, metastatic solid tumor, and moderate or severe renal disease override diabetes, any tumor, and mild liver disease, respectively. Thus, only the higher weight is assigned. The sum of the weights equals the score. As noted in the Methods section, liver disease was not counted as a comorbidity and was assigned a weight of zero for this analysis.

Table 2. Work and productivity variables

	Treatment failures (n=103)		Sustained responders (n=133)		
	n	%	*n*	%	*P* value
Monthly income from all sources (mean, s.d.)	2,470	2,419	3,174	6,583	0.26
Monthly income category					
$0	14	14	20	15	
Less than $1,000	18	18	23	17	
$1,000–$1,999	20	20	20	15	
$2,000–$3,999	25	25	35	26	
$4,000–$5,999	18	18	22	17	
$6,000 or more	7	7	13	10	0.92
Employed	52	51	89	67	0.02
Receiving social assistance income	37	36	34	26	0.1
As a result of hepatitis C or treatment					
Missed work	14	14	4	3	$P<0.001$
Missed volunteer opportunities	3	3	2	2	0.65
Missed chores	32	31	10	8	$P<0.001$
Missed work, volunteer opportunities, and/or chores	45	44	12	9	$P<0.001$
Total hours of missed work, volunteer opportunities, and/or chores in the previous 3 months (mean, s.d.)	154	200	177	239	0.76
Difficulty working	15	15	5	4	$P<0.001$
Difficulty with leisure	22	22	11	8	$P<0.001$
Percent reduction in work capacity (mean, s.d.)	5.8	18	1.1	6	0.01
Percent reduction in leisure capacity (mean, s.d.)	10.7	24	3.3	13	0.01
Fatigue	82	81	90	69	0.05

increased employment rates. The key implication of this work is that the quality-of-life improvement shown in randomized clinical trials translates to a real-world clinic population, and that quality-of-life improvements are maintained long after the 24-week follow-up of the clinical trials (11,12,29).

In a study of Swiss clinic patients, significant differences were observed between sustained responders to therapy and treatment failures in the physical component summary score of the SF-36 (30). Multivariable regression analysis indicated that total household income rather than viral factors were significantly associated with quality of life. Adjustment for comorbid illnesses in this study was not as extensive as our study—diabetes was the only comorbid illness adjusted for—and this may explain the divergent results. In addition, adjusting for income may have attenuated the association between HCV viremia and quality of life if sustained responders had higher income. A systematic review of the literature in which SF-36 data were translated into utilities estimated that the benefit associated with sustained response to antiviral therapy for chronic HCV infection was 0.03–0.04 units (31). A randomized controlled trial involving 69 patients undergoing antiviral therapy obtained longitudinal measures of utility using the EQ-5D (European Quality of Life 5 dimension) instrument (32). After therapy, sustained responders (n=24) had larger change scores than treatment failures (n=45) (0.02 vs. 0), but likely because of small sample size the difference was not statistically significant.

The results of our study related to work and productivity are corroborated by other studies. Research shows that individuals with chronic HCV infection perceive a decrease in functioning in aspects of daily life, such as work, household functioning, sexual functioning, and leisure (33,34). In a longitudinal study conducted alongside a randomized clinical trial, 20% of sustained responders showed an improvement in the need to work shorter hours and the proportion of missed work days compared with treatment failures (35).

Our study has several limitations. Awareness of viremia status has been associated with decreased quality of life (4). Although we did not have data on the respondents' awareness, 93% of sustained responders completed questionnaires more than 90 days after the assessment of response to antiviral therapy and 98% of treatment failures completed questionnaires 90 days after the end of therapy. The majority of patients were likely to be aware of their HCV viremia status. Although sustained responders had higher quality-of-life scores than treatment

Table 3. Comparison of mean quality-of-life scores among treatment failures, sustained responders, and age- and sex-adjusted population norms

	Treatment failures		Sustained responders		Population norms[a]		*P* value for the comparison between groups		
	Mean	s.d.	Mean	s.d.	Mean	s.d.	TF vs. SR	TF vs. norms	SR vs. norms
SF-36 scales[b]									
Physical functioning	68	29.1	80.7	22.7	85.8	20	$P<0.001$	$P<0.0001$	$P<0.05$
Role—physical	58.3	34.9	75.6	28	82.1	33.2	$P<0.001$	$P<0.0001$	$P<0.05$
Bodily pain	56.9	27.4	72	25.8	75.6	23	$P<0.0001$	$P<0.0001$	0.1
General health	45.5	26.9	64.7	24.5	77	17.7	$P<0.0001$	$P<0.0001$	$P<0.0001$
Vitality	42.3	24.8	55	22.7	65.8	18	$P<0.001$	$P<0.0001$	$P<0.0001$
Social functioning	60.5	30.4	74.4	26.2	86.2	19.8	$P<0.001$	$P<0.0001$	$P<0.0001$
Role—emotional	63.6	31.6	77.5	26.2	84	31.7	$P<0.001$	$P<0.0001$	$P<0.01$
Mental health	62.3	21.6	71.6	19.7	77.5	15.3	$P<0.001$	$P<0.0001$	$P<0.0001$
Physical component summary score	42.5	11.6	49.2	9.9	50.5	9	$P<0.0001$	$P<0.0001$	0.21
Mental component summary score	40.5	13	46.1	12.6	51.7	9.1	$P<0.01$	$P<0.0001$	$P<0.0001$
Additional general scales									
Generic health distress	57.6	30.6	75.8	25.4	NA	NA	$P<0.0001$	NA	NA
Positive well-being	55.1	25.9	61.2	22.7	NA	NA	0.06	NA	NA
Hepatitis-specific scales									
Hepatitis-specific limitations	61.3	34.4	85	25.3	NA	NA	$P<0.0001$	NA	NA
Hepatitis-specific health distress	59.3	34	82.8	24.8	NA	NA	$P<0.0001$	NA	NA
Utilities[c]									
Health Utilities Index Mark 3	0.58	0.34	0.7	0.28	0.87	0.21	$P<0.01$	$P<0.0001$	$P<0.0001$
Health Utilities Index Mark 2	0.74	0.2	0.8	0.16	NA	NA	$P<0.05$	NA	NA
Short Form 6D	0.65	0.14	0.71	0.14	0.77	0.14	$P<0.001$	$P<0.0001$	$P<0.0001$
Time trade-off	0.84	0.24	0.89	0.18	NA	NA	$P<0.05$	NA	NA

HQLQ, Hepatitis Quality of Life Questionnaire; HUI3, Health Utilities Index Mark 3; MCS, mental component summary score; PCS, physical component summary score; SF-36, Medical Outcomes Study Short-Form-36; SF-6D, Short Form 6D; SR, sustained responder; TF, treatment failures; TTO, time trade-off.

[a]Canadian norms for the SF-36 were obtained from Hopman *et al.* (27), Canadian norms for the HUI3 were obtained from the Joint Canada/United States Survey of Health (26), normative data for the SF-6D were obtained from the National Health Measurement Survey (28).

[b]The SF-36 version 2 measures health-related quality of life in 8 domains (physical functioning, role—physical, bodily pain, general-health perception, energy/vitality, social functioning, role—emotional, and mental health) along with a PCS and MCS. Each of the 8 domains and the summary scores are scored out of 100, with higher scores indicating better quality of life (19). The additional domains of the HQLQ—generic health distress, positive well-being, hepatitis-specific limitations, and hepatitis-specific health distress—are also scored from 0 to 100 with higher scores indicating better quality of life (20,21).

[c]The HUI3 scores can range from −0.36 to 1.00. The HUI2 scores can range from −0.03 to 1.00. Higher scores indicate better quality of life and negative scores represent states considered worse than death (22). The SF-6D utility scores can range from 0.3 to 1 (23,24) and the TTO utility scores can range from 0 to 1. Higher scores indicate better quality of life.

failures, we cannot rule out the possibility that the quality of life before antiviral therapy was higher in this group, as quality-of-life measures were obtained at a single time point. However, although our quality-of-life measure is cross-sectional, the timing of the measurement is relevant and informative. Our cohort of more than 200 patients was assessed at an average of 3.7 years after antiviral therapy, indicating that the short-term benefit of successful therapy shown in clinical trials is maintained over the long term. Respondents provided information on productivity for the previous 90 days, and it is unclear whether improvement in work productivity applies to the entire follow-up period.

Although treatment with antiviral therapy can result in viral clearance for more than 50% of patients, the uptake of antiviral therapy among HCV-infected patients is low (36,37). In our population, sustained responders to antiviral therapy had improved quality of life, higher employment rates, and better productivity at work, leisure, household activities, and volunteering compared with treatment failures. These benefits should be considered by patients and providers as they make decisions about antiviral therapy. The results should also inform health-care policy makers' decisions about strategies to reduce the morbidity and economic impact of HCV infection.

Table 4. Results from regression models

	HUI3		HUI2		SF6D		TTO		PCS		MCS	
	B[a]	95% CI	B[a]	95% CI	B[a]	95% CI	B[a]	95% CI	B[a]	95% CI	B[a]	95% CI
SVR	0.08	(0.01, 0.15)	0.03	(−0.01, 0.07)	0.05	(0.02, 0.08)	0.05	(−0.01, 0.11)	5.73	(3.24, 8.22)	5.22	(2.07, 8.37)
Age[b]	−0.0008	(−0.02, 0.02)	0.002	(−0.01, 0.01)	−0.004	(−0.01, 0.005)	−0.01	(−0.03, 0.002)	−1.18	(−1.82, −0.54)	0.71	(−0.1, 1.53)
Male sex	−0.05	(−0.12, 0.02)	−0.04	(−0.09, 0)	−0.003	(−0.04, 0.03)	0.01	(−0.05, 0.07)	0.76	(−1.71, 3.23)	0.23	(−2.9, 3.36)
White ethnicity	−0.05	(−0.15, 0.04)	−0.04	(−0.1, 0.01)	−0.003	(−0.05, 0.04)	0.03	(−0.04, 0.11)	0.47	(−2.82, 3.75)	−0.77	(−4.93, 3.4)
Marital status[c]	0.07	(−0.002, 0.14)	0.04	(0, 0.08)	0.04	(0.01, 0.07)	0.02	(−0.04, 0.07)	0.51	(−1.93, 2.94)	6.04	(2.95, 9.13)
Education[d]	−0.04	(−0.12, 0.04)	−0.01	(−0.06, 0.03)	0.01	(−0.03, 0.04)	−0.01	(−0.07, 0.05)	−0.55	(−3.17, 2.08)	−0.29	(−3.62, 3.04)
Charlson score[e]												
1	−0.07	(−0.16, 0.02)	−0.04	(−0.1, 0.01)	−0.03	(−0.08, 0.01)	−0.04	(−0.12, 0.03)	−3.02	(−6.14, 0.1)	−2.58	(−6.53, 1.38)
2	−0.14	(−0.25, −0.03)	−0.09	(−0.15, −0.02)	−0.04	(−0.09, 0.01)	−0.09	(−0.18, −0.01)	−4.84	(−8.61, −1.06)	−0.09	(−4.87, 4.69)
ICED score[f]												
1	0.1	(−0.02, 0.22)	0.03	(−0.04, 0.1)	0.02	(−0.03, 0.08)	0.06	(−0.04, 0.15)	1.65	(−2.52, 5.82)	2.08	(−3.21, 7.36)
2	−0.19	(−0.29, −0.08)	−0.11	(−0.18, −0.05)	−0.1	(−0.15, −0.05)	−0.04	(−0.13, 0.04)	−3.85	(−7.48, −0.22)	−9.2	(−13.8, −4.61)
3	−0.26	(−0.37, −0.16)	−0.15	(−0.22, −0.09)	−0.12	(−0.17, −0.07)	−0.03	(−0.11, 0.05)	−8.79	(−12.45, −5.12)	−8.01	(−12.65, −3.36)

CI, confidence interval; HUI2, Health Utilities Index 2; HUI3, Health Utilities Index 3; ICED, Index of Coexistent Disease; MCS, mental component summary score; PCS, physical component summary score; SF-6D, Short Form 6D; SVR, sustained virological response; TTO, time trade-off.

[a]Unstandardized coefficient. [b]Results are difference in utility per 5 years of age. [c]Marital status is a binary variable with 0=not married or common-law, 1=married or common-law. [d]Education is a binary variable with 0=completed high school or less, 1=started or completed trade/college/university. [e]The reference category is Charlson score=0. [f]The reference category is ICED score=0.

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CONFLICT OF INTEREST

Guarantor of the article: Ava A. John-Baptiste, MHSc.

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Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Patients with chronic hepatitis C virus (HCV) infection have poor quality of life.
- ✓ Because of a high burden of comorbid illness in these patients, the effect of HCV viremia on quality of life is unclear.

WHAT IS NEW HERE

- ✓ Sustained responders had better quality of life and productivity than treatment failures long after antiviral therapy.
- ✓ Differences remained after adjustment for comorbidity and demographics.
- ✓ Eliminating HCV viremia is associated with improved quality of life, even with comorbid illnesses.

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