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Health-related quality of life in patients with chronic hepatitis C and advanced fibrosis , †‡

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Abstract

Background/Aims—Although the antiviral and histological benefits of peginterferon/ribavirin therapy are well established, the effects on health-related quality of life (HRQOL) and sexual health

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are less certain. This study assessed HRQOL and sexual health in patients with advanced fibrosis or cirrhosis in the HALT-C Trial.

Methods—Subjects completed SF-36 and sexual health questionnaires prior to and after 24 weeks of peginterferon/ribavirin therapy ($n = 1144$). Three hundred and seventy-three (33%) subjects were HCV RNA negative at week 20 and continued therapy through week 48; 258 were seen at week 72. One hundred and eighty achieved sustained virological responses (SVR) and 78 relapsed.

Results—At baseline, patients had poorer scores for all eight SF-36 domains compared to healthy controls. Patients with cirrhosis had lower HRQOL scores than those with bridging fibrosis, as did patients with higher depression scores. SVR patients had significant improvements in seven domains, whereas relapsers had significant worsening in one domain. Sexual scores improved in SVR patients and decreased in relapsers ($p = 0.03$). In multivariate analyses, improvements in HRQOL and sexual scores were significantly associated with SVR but were less striking in patients with lower depression scores.

Conclusions—Achievement of SVR after peginterferon/ribavirin therapy improves HRQOL and sexual health in chronic hepatitis C patients with advanced fibrosis or cirrhosis.

Keywords

Cirrhosis; Fibrosis; Health-related quality of life; Hepatitis; Viral type C; Sexual functioning; Sustained virological response

1. Introduction

Chronic hepatitis C affects at least 3.2 million Americans and is the major cause of chronic liver disease, cirrhosis and liver cancer in the United States [1,2]. Chronic viral hepatitis is typically silent; symptoms and signs are present only in those with severe or advanced disease. Importantly, symptoms and poor health-related quality of life (HRQOL) are not reliable in separating patients with mild from those with moderate or advanced disease [3]. In some patients, symptoms do not develop until the onset of advanced cirrhosis or hepatocellular carcinoma. Other patients have marked fatigue and weakness, despite having histologically mild or early disease.

Chronic hepatitis C therapies are available and effective in approximately half of selected patients [4]. Because of its expense and many side effects, therapy is usually reserved for patients who have evidence of progressive disease [5,6]. The poor correlation of symptoms, signs, and liver test abnormalities with severity and stage of disease has led to the use of liver biopsy and staging of fibrosis as the major criterion for therapy. Furthermore, eradication of hepatitis C virus (HCV) and prevention of disease progression, rather than amelioration of symptoms or improvement in HRQOL, have been used as the major determinants of successful therapy. Indeed, in most trials of therapy of hepatitis C, symptoms and HRQOL are not mentioned as even secondary endpoints [7–10]. Nevertheless, a few prospective studies have shown that a sustained virological response (SVR) to therapy of chronic hepatitis C can be associated with significant improvements in HRQOL [11–15]. The role of contemporary therapy of chronic hepatitis C in ameliorating symptoms and improving HRQOL, especially in advanced liver disease, is not well defined [16–18].

We evaluated HRQOL and sexual health prospectively in a cohort of patients with advanced chronic hepatitis C who had failed to respond to a previous course of interferon- α (with or without ribavirin) enrolled in the lead-in phase of the Hepatitis C Antiviral Long-term Treatment against Cirrhosis (HALT-C) Trial. Patients were re-treated with a 24-week “lead-in” course of peginterferon α -2a and ribavirin [19,20]. Patients who responded continued

treatment for a full 48 weeks and were followed for another 24 weeks to assess whether they achieved SVR [19,20]. The aim of the current analysis was to identify correlates of impaired HRQOL at enrollment. Secondary aims included evaluation of changes in HRQOL and sexual health in the subset of patients who achieved an SVR and those who had a transient response (relapsers).

2. Patients and methods

2.1. Patients

HALT-C trial patients had chronic hepatitis C with detectable HCV RNA in serum and, within 12 months of enrollment, had undergone liver biopsy that demonstrated bridging fibrosis or cirrhosis (Ishak fibrosis scores of 3–6) [21]. Reasons for exclusion included evidence of hepatic decompensation, other co-existent liver disorder, serious medical disorders that would preclude treatment with interferon, interferon intolerance, active use of illicit drugs, active alcohol abuse, a suicide attempt or hospitalization for depression within the past 5 years, and history of a severe or uncontrolled psychiatric condition within the past 6 months.

After a thorough baseline evaluation, patients were re-treated with peginterferon α -2a (180 μ g per week: Pegasys™: Roche Pharmaceuticals) and ribavirin (1000–1200 mg per day: Copegus™: Roche). Patients who failed to clear serum HCV RNA by week 20 met the criterion for non-response and were randomized at week 24 to receive lower dose peginterferon α -2a (90 mcg weekly) or no therapy for 3½ years. Patients who were HCV RNA negative at week 20 continued higher dose peginterferon and ribavirin therapy for 48 weeks and then were followed for 24 weeks to assess whether an SVR occurred. This study was approved by all relevant local Institutional Review Boards and an external Data Safety Monitoring Board appointed by the National Institutes of Health. All patients gave written, informed consent.

Standard demographic, clinical, medication, laboratory, and radiological data were obtained at ten clinical centers. Self-administered HRQOL forms and the Beck Depression Inventory II (BDI) [22,23] were completed. Data were entered into a central database maintained by the Data Coordinating Center (New England Research Institutes, Watertown, MA). Although the HALT-C Trial is not a blinded study, study design rules preclude analysis of group data on patients in the randomized phase of the study until the randomization phase is completed.

2.2. Health questionnaires

HRQOL was assessed with the 36-item Short Form Health Survey (SF-36) [24], a 36-item self-administered questionnaire encompassing eight physical and mental health domains and two physical and mental summary scales [25]. The SF-36 has demonstrated consistently high reliability and validity in a variety of patient populations [24,26–29]. SF-36 scales have been used to evaluate change in health-status over time in several studies [30–33], including therapeutic trials of chronic hepatitis C [7,12,13,15,17,18,34–39].

Three additional questions (see Appendix A) that addressed self-reported sexual functioning, desire, and satisfaction were hypothesized to measure sexual effects of chronic hepatitis C and its treatment. Correlation of this Sexual Summary Scale score with the Beck Depression Inventory II item “Loss of Interest in Sex” was high (Pearson correlation coefficient = -0.603 , $p < 0.0001$) [22,23].

A semi-quantitative estimate of lifetime alcohol consumption was obtained using an adaptation of the Skinner survey [40–42]. Three neuropsychiatrists reviewed the composition of all concomitant prescription medications used by study patients and, from the drugs used, inferred indications for their use.

2.3. Data analysis

Data were analyzed using SAS (Statistical Analysis Software, version 8.2, SAS Institute, Cary, NC, USA). When data were missing on an SF-36 item, a patient-specific mean scale score was substituted if at least 50% of the items in the scale were completed [24]. The Sexual Summary Scale was calculated as the mean of all completed items in the scale. Change in HRQOL was calculated by subtracting the patient's baseline score for each scale from the week 72 score. The results of HALT-C SF-36 scores were compared to a general population sample of 750 healthy controls [43]. This Well-Norm group was selected by excluding those who reported such chronic diseases as congestive heart failure, diabetes mellitus, recent myocardial infarction, angina, cancer, chronic allergies, arthritis, chronic back problems, and chronic lung disease. The average age (\pm SD) of the Well-Norm group was 40.2 ± 15.3 years; 53.5% were female [11].

Univariate *t*-tests were used to identify variables that were significantly different between the groups. Paired *t*-tests were used to compare changes in HRQOL scores from baseline to week 72. Linear multivariate regression models were constructed to identify factors that independently and significantly predicted summary physical, mental, and sexual scores at baseline and improvements in these scores following therapy.

3. Results

3.1. Baseline characteristics of cohort

As shown in Fig. 1, among the 1145 patients enrolled in the lead-in phase of the HALT-C Trial, 1144 completed the baseline HRQOL questionnaire. Selected demographic and clinical features of the patients are provided in Table 1. Average age was 50 years, 28% were women, approximately three-quarters were non-Hispanic whites, and 15% were blacks. According to self-reports, 17% of patients had diabetes mellitus, 14% had heart disease, and 8% had depression. One-third of patients (31%) were taking antidepressant or anxiolytic medications at baseline. Although most patients had previously used alcohol (84%), the majority (81%) reported no longer drinking at baseline.

Table 1 presents comparison of patients with baseline physical and mental summary scores above and below the 50 point mark, which represents the average summary score in the US population [25]. A majority of the cohort (57%) had baseline physical summary scores ≤ 50 . These patients were significantly more likely to be women, unmarried, non-college graduates, black, current smokers, and current abstainers from alcohol; to have a history of diabetes, heart disease, and/or depression; and to have cirrhosis and lower ALT levels than those with baseline physical summary scores >50 points. One-third of the cohort (37%) had baseline mental summary scores ≤ 50 . These patients were significantly more likely to be women, unmarried, non-college graduates, Hispanic, current smokers, and current abstainers from alcohol; to have a history of depression and injection drug use; and to have cirrhosis than those with baseline mental summary scores >50 points.

Comparison of HRQOL scores for the eight SF-36 domains among patients with cirrhosis ($n = 432$) and those with bridging fibrosis ($n = 712$) is shown in Fig. 2. Patients with cirrhosis had statistically significantly lower scores for seven of eight HRQOL domains. Mean scores for all eight HRQOL domains were consistently lower in HALT-C patients than in the Well-Norm cohort, although strict comparability between these cohorts could not be assured. HALT-C patients also had significantly lower mean scores on four of eight HRQOL domains (physical functioning, role physical, general health, and vitality) when compared to age-matched general US population norms (data not shown).

Factors that correlated with lower baseline HRQOL in the cohort of patients with hepatitis C enrolled in the lead-in phase of the HALT-C trial were evaluated using univariate and multivariate linear regression analysis of the three HRQOL summary scores: physical, mental, and sexual. We analyzed models that included and excluded BDI scores. We present the model that includes BDI, which assesses the effect of the other variables on mental summary, holding depression constant. Results of models excluding BDI were similar (data not shown).

As shown in Table 2, baseline factors associated with lower physical summary scores in a multivariate model were female gender, greater body mass index (BMI = weight in kilograms/height in meters squared), older age, current cigarette smoking, a higher BDI score, and use of antidepressant or anxiolytic medications at baseline. Factors that were less strongly but still significantly associated with lower physical summary scores included evidence of cirrhosis (palpable spleen), being not married or living as married, and abstinence from alcohol during the preceding six months. Notably, race or ethnicity, presence of diabetes or heart disease, serum alanine aminotransferase (ALT) levels, viral genotypes, or HCV RNA levels were not significant predictors.

Factors associated with lower baseline mental summary scores in a multivariate model included three elements also associated with lower physical summary scores: use of antidepressant or anxiolytic medications at baseline, higher BDI score, lower BMI, and in addition, lifetime number of alcoholic drinks. Age, current smoking, gender, marital status, and recent alcohol abstinence were not significant predictors.

Factors associated with lower baseline sexual summary scores in a multivariate model were similar to the factors that were associated with lower physical summary scores. Factors that were also significantly associated with lower sexual summary scores were higher Ishak fibrosis score and history of cholesterol medication use. A history of diabetes or heart disease and higher ALT and HCV RNA levels (among several other variables from Table 1) were not significant predictors of sexual summary score.

3.2. Changes in HRQOL in patients with sustained virological response

Three hundred and seventy-three (32.6%) subjects were HCV RNA negative at week 20 and continued therapy through week 48 (Fig. 1). At week 72, 258 patients were seen and were aware of their week 60 HCV RNA status when completing the HRQOL questionnaires. Changes from baseline in 178 patients who achieved SVR compared to 76 patients who tested HCV RNA positive prior to week 72 (relapsers) are shown in Fig. 3. Among patients with SVR, HRQOL scores were statistically significantly improved in four of eight HRQOL domains: role physical, general health, vitality, and role emotional. In contrast, relapser patients had significant worsening only on the physical functioning domain.

The changes in the physical, mental and sexual summary scales between the SVR and relapser patients are shown in Fig. 4. Patients with SVR had statistically significant improvements in physical and mental scores compared to baseline. In comparison to patients who responded and then relapsed, patients with SVR had statistically significant improvements in physical and sexual scores. These improvements occurred in men and women and patients with cirrhosis and with fibrosis only (data not shown).

3.3. Factors associated with changes in quality of life scores

Multivariate linear regression analyses were performed to assess factors associated with changes in summary scores, controlling for baseline summary score (Table 3). The major predictor of improvement in physical summary scores was achievement of SVR ($p = 0.0003$). Patients without diabetes mellitus were more likely to have improvements in physical summary

scores ($p = 0.0007$). A lack of improvement in physical summary scores was weakly associated with lower baseline BDI score and BMI, male gender, and persons who never drank alcohol (p values 0.02–0.05). Importantly, age, presence of cirrhosis, fibrosis scores, race and ethnicity, and baseline ALT and HCV RNA levels were not associated with changes in physical summary scores.

Baseline factors associated in a multivariate model with lack of improvement in mental summary scores were a history of heart disease, lower baseline ALT, lower baseline BDI score and BMI, and use of antidepressant or anxiolytic medications. Overall, however, mental summary scores tended to be lower at week 72.

Improvements in sexual summary score were associated with SVR ($p = 0.03$) and lower baseline BDI score ($p = 0.007$) in a multivariate model. There was no additional influence of presence of cirrhosis, Ishak fibrosis score, alcohol use, or history of diabetes or heart disease at baseline.

Two patients who were complete virological responders during lead-in therapy and who relapsed late in the post-treatment follow-up phase are of special interest. At the time that they completed the HRQOL questionnaires at week 72, they believed that they were sustained responders. However, their week 72 (and confirmatory) HCV RNA levels were positive (6.18 \log_{10} and 6.90 \log_{10} IU/mL) and their serum ALT levels were elevated at week 72 (69 and 221 U/L). Their HRQOL and sexual functioning scores were low, similar to those of early relapsers, rather than of patients with SVR.

4. Discussion

Despite the availability and efficacy of peginterferon and ribavirin, therapy of chronic hepatitis C remains problematic. Shortcomings of current therapy include the protracted and complicated nature of treatment and unpleasant side effects. In addition, SVR rates are only 50–60% in published clinical trials and are appreciably lower in community practice [44,45]. Therapy is usually recommended only for patients with evidence of fibrosis or substantial necroinflammatory disease on liver biopsy [5,6]. Because the majority of treated patients are asymptomatic or minimally symptomatic, improvements in symptoms or HRQOL have not been considered reasons for recommending therapy.

As in many chronic diseases, HRQOL in chronic hepatitis C is of substantial importance to patients. Fearing a reduction in HRQOL associated with the adverse effects of treatment, some patients decline antiviral therapy [37,46]. Others request therapy in hopes that their physical, mental, and sexual functioning will improve. Previous studies in patients with less advanced hepatitis C have shown that HRQOL is measurably reduced and that successful therapy can lead to clinically meaningful improvements in several HRQOL domains [7,12,34,37].

The current analyses from the HALT-C Trial confirm the reduction in HRQOL among patients with chronic hepatitis C. In addition, they indicate that HRQOL scores are lower in patients with cirrhosis than in those with advanced fibrosis. ALT levels, viral titers, or other features of hepatic histology did not correlate with lower HRQOL or sexual scores, suggesting that disease stage is the major determinant of the effect of chronic hepatitis on HRQOL. Not surprisingly, other important determinants of lower HRQOL scores included the use of antidepressant or anxiolytic medications, cigarette smoking, and higher BDI scores. Thus, the common co-morbidities found in patients with chronic hepatitis C, such as depression, diabetes, heart disease and obesity, are likely to contribute to the overall poor quality of life.

Of perhaps the greatest importance were the findings that (1) successful antiviral therapy led to improvement in many physical and sexual health scores and (2) that these effects occurred

even in patients with advanced fibrosis and cirrhosis. In contrast, mental health scores showed less improvement. These observations suggest that HCV infection *per se* has a minimal effect on emotional states. Although many patients with chronic hepatitis C describe difficulty in thinking, concentrating, and memory, such symptoms may result from underlying conditions, such as anxiety, depression, or use of psychotropic medications, rather than from HCV infection [16]. Separate analyses of a subset of patients in the HALT-C Trial have led to similar conclusions regarding impairments in cognitive function in chronic hepatitis [18].

For most people, a satisfying personal sexual life is an important dimension of good quality of life [47]. In this study, three sexual health questions focused on desire, performance, and satisfaction domains. The current analysis suggests that sexual health is diminished among patients with chronic hepatitis C and that a component of the reduction in sexual functioning and satisfaction is associated with the degree of hepatic fibrosis or cirrhosis. Lower sexual summary scores were highly associated as well with female gender, older age, higher BDI score, history of cholesterol medication use, and concomitant use of antidepressant or anxiolytic medications. Overall, our findings suggest that diminished sexual health in patients with chronic hepatitis C can be improved, at least in part, by successful antiviral therapy. Patients who achieve an SVR may feel less stigmatized and concerned about potential transmission of HCV to their sexual partners, which has been a factor associated with lower HRQOL [48–50].

A potential confounder in most longitudinal studies of HRQOL in chronic hepatitis C, including this one, is that patients have known whether they responded to treatment or not when they completed post-treatment HRQOL instruments. Perhaps their emotional, physical, and sexual well-being are affected by knowledge of response status. Because of the design of this Study (and those of most previous studies in this field), this confounder cannot be avoided. Our Study was designed nearly a decade ago; in retrospect, it would have been preferable for the post-treatment HRQOL assessment to have been performed before patients learned their post-treatment HCV RNA status. However, because this assessment was performed at 72 weeks by design, results of post-treatment serum ALT or HCV RNA tests could not be withheld from patients. Although it is possible that a temporary reduction in viral load brings about an improvement in quality of life, it should be noted that the reductions in HRQOL among responders who relapsed were statistically significant in only one domain. It is also worth keeping in mind that these patients were followed for at least 1½ years. In people of mean age 50 years, the passage of time itself is associated with decrements in health-related quality of life.

In summary, our analyses indicate that HRQOL is decreased significantly in patients with chronic hepatitis C who have advanced fibrosis and cirrhosis. It is well known that side effects of current therapy result in further decrements in HRQOL and are major impediments to initiation and successful completion of therapy. Successful antiviral therapy is associated with clinically meaningful, significant improvements in HRQOL. Thus, the rationale for antiviral therapy of chronic hepatitis C should include a reduction in liver disease progression and hepatocellular carcinoma development and an improvement in health-related and sexual quality of life.

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Appendix A. Sexual Summary Scale Items

Mean score on the following three questions if answered 1–5 (transformed to a 0–100 scale):
How much of the time during the last four weeks, have you ...

- Felt your health interfered with your enjoyment of sex?
- Lacked interest in sex?
- Felt your health interfered with your sexual performance?

Answer possibilities

Not at all	A little bit	Moderately	Quite a bit	Extremely	Does not apply
1	2	3	4	5	–1

Abbreviations

HRQOL	health-related quality of life
HALT-C	Hepatitis C Antiviral Long-term Treatment against Cirrhosis Trial
SF-36	Short-Form-36 Health Survey
SVR	sustained virological response
HCV	hepatitis C virus
BDI	Beck Depression Inventory II
PF	physical functioning
RP	role physical
BP	bodily pain
VT	vitality
GH	general health

SF	social functioning
RE	role emotional
MH	mental health
BMI	body mass index
ALT	alanine aminotransferase

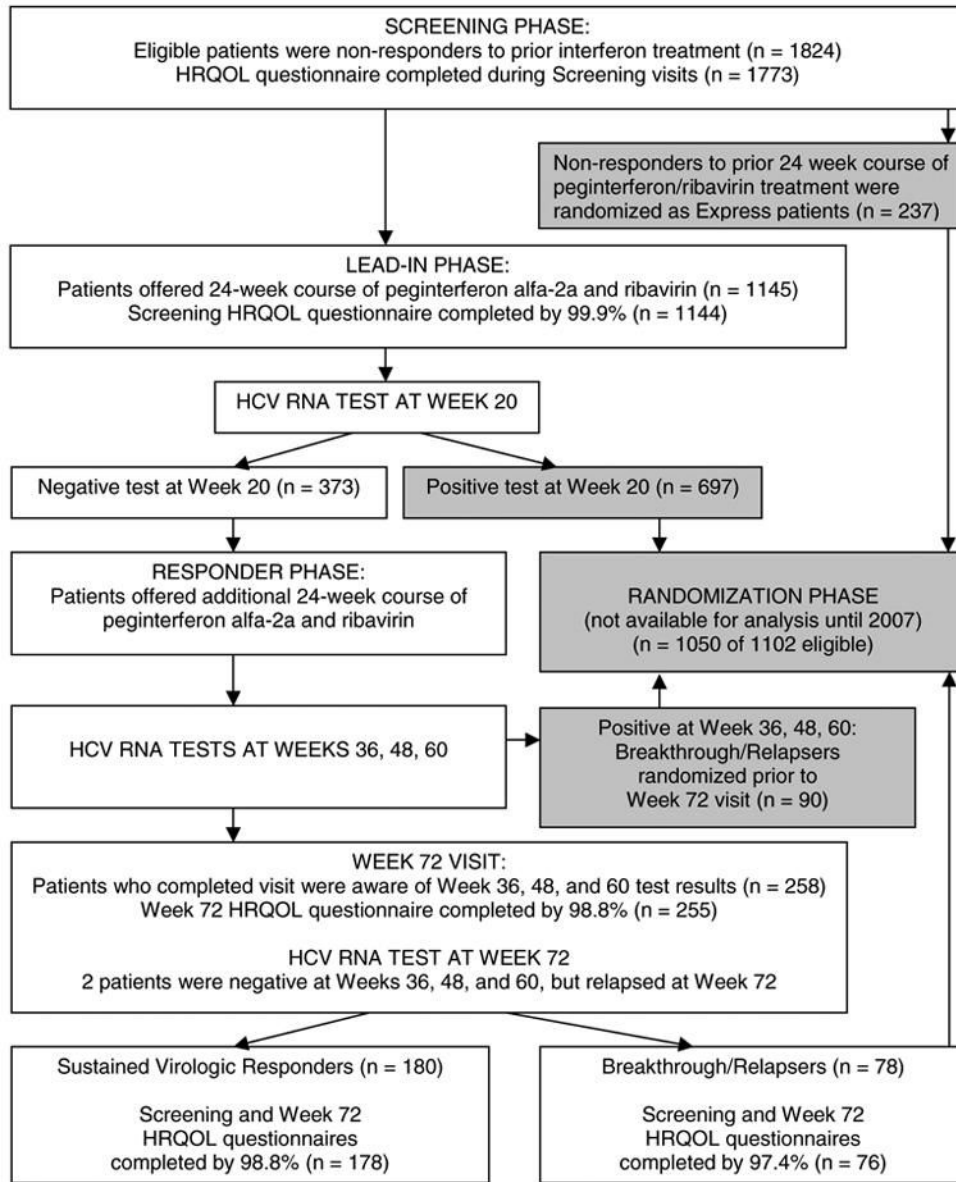
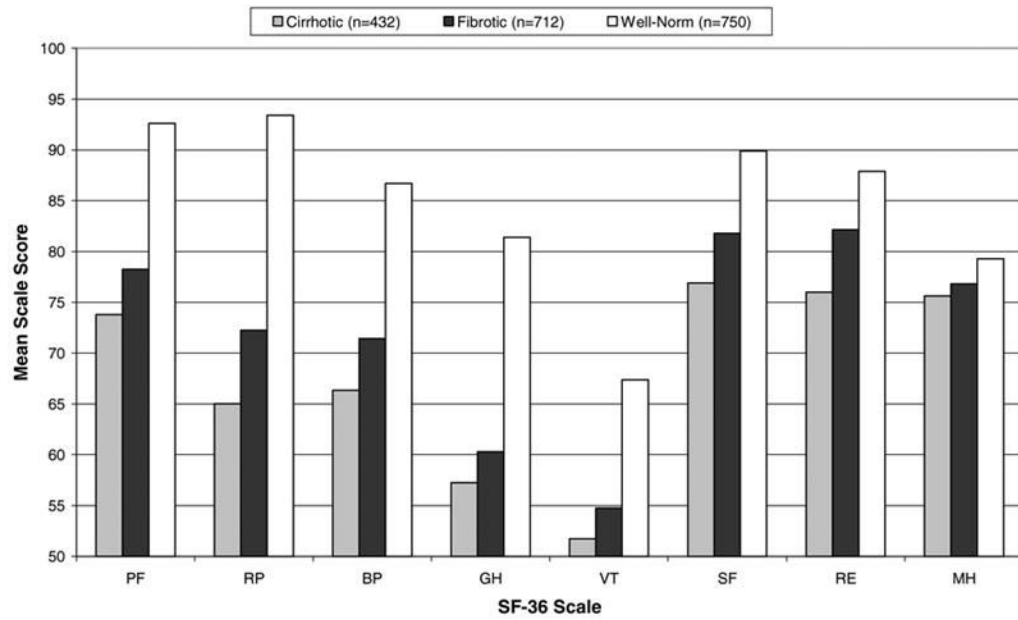
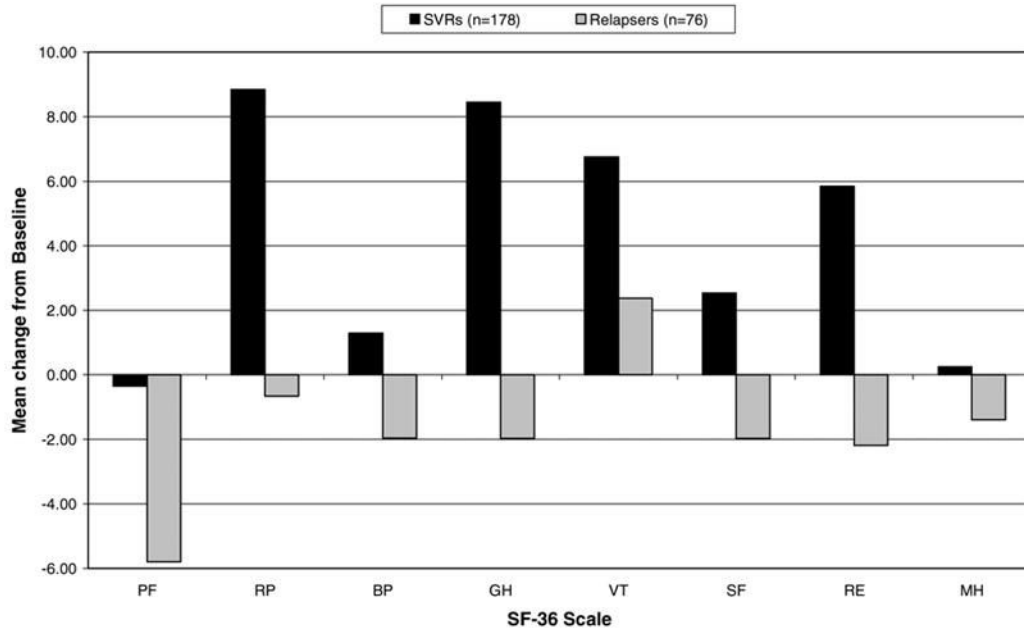


Fig 1. Overview of HALT-C Trial: HRQOL assessments at baseline and week 72.



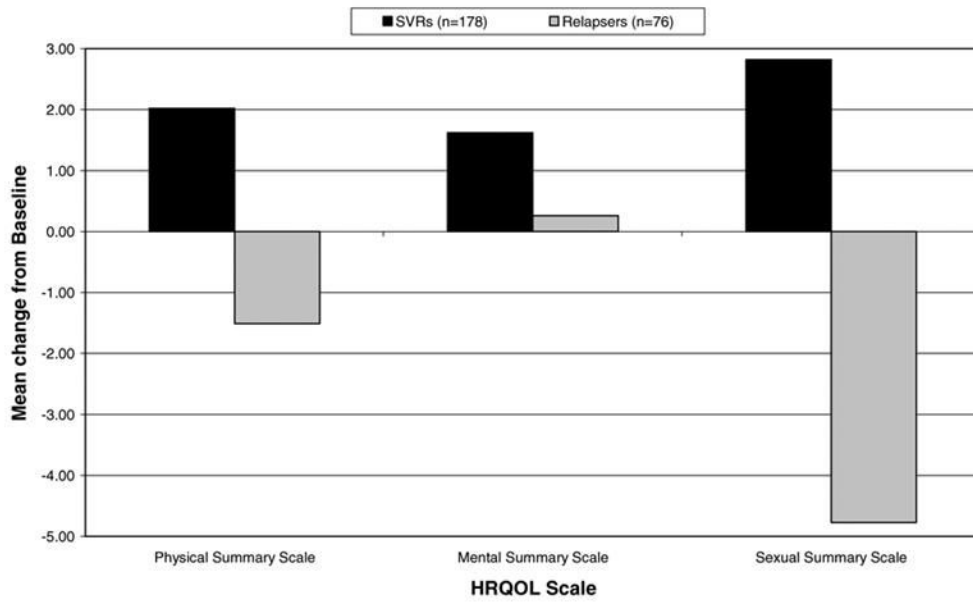
<i>Comparing pts. with fibrosis and pts. with cirrhosis:</i>								
t-test	2.84	2.95	3.29	2.25	2.06	3.33	2.88	1.20
p-value	0.005	0.003	0.001	0.03	0.04	<0.001	0.004	0.23
<i>Comparing pts. with fibrosis and Well-Norm patients:</i>								
t-test	6.56	6.35	7.02	11.01	6.03	3.95	1.98	1.76
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.05	0.08

Fig 2. HRQOL scores at baseline of the eight scales of the SF-36 Health Survey ($n = 1144$). Higher scores indicate better HRQOL. Abbreviations: BP, bodily pain; GH, general health; MH, mental health; PF, physical functioning; pts., patients; RE, role emotional; RP, role physical; SF, social functioning; VT, vitality.



<i>Change from baseline in patients who achieved SVR:</i>								
t-test	-0.23	2.99	0.77	6.10	4.14	1.59	2.22	0.19
p-value	0.82	0.003	0.44	<0.0001	<0.0001	0.11	0.03	0.85
<i>Change from baseline in patients who relapsed after Week 20:</i>								
t-test	-2.66	-0.18	-0.82	-0.98	1.01	-0.82	-0.60	-0.71
p-value	0.01	0.86	0.42	0.33	0.31	0.41	0.55	0.48
<i>Comparing patients who achieved SVR and pts. who relapsed after Week 20:</i>								
t-test	1.99	1.83	1.07	4.14	1.49	1.54	1.70	0.68
p-value	0.05	0.07	0.29	<0.0001	0.14	0.12	0.09	0.50

Fig 3. Change from baseline to week 72 in SF-36 scores by virologic response status ($n = 254$). Positive values indicate improvements; negative values indicate worsening. Abbreviations are as in the legend to Fig. 2. (SVRs, sustained virological responders.)



<i>Change from baseline in patients who achieved SVR:</i>			
t-test	3.06	2.46	1.28
p-value	0.003	0.01	0.20
<i>Change from baseline in patients who relapsed after Week 20:</i>			
t-test	-1.60	0.25	-1.74
p-value	0.11	0.80	0.09
<i>Comparing patients who achieved SVR and pts. who relapsed after Week 20:</i>			
t-test	3.47	1.35	2.23
p-value	0.001	0.18	0.03

Fig 4. Change from baseline to week 72 in HRQOL summary scales by virologic response status ($n = 254$). Positive values indicate improvements; negative values indicate worsening. (SVRs, sustained virological responders.)

Table 1

Selected demographic and historical features of patients studied

	All patients (n = 1144)	Patients with baseline physical summary score >50 points (n = 490)	≤50 points (n = 654)	p value ^a
<i>Demographics</i>				
Age (y), mean (±SD)	49.9 (±7.30)	49.4 (±7.07)	50.3 (±7.46)	0.06
Gender (% female)	28%	17%	36%	<0.0001
Marital status (% married or living as married)	71%	78%	65%	<0.0001
Education level (% college graduate)	26%	34%	21%	<0.0001
Race and ethnicity (%)				
White	74%	78%	71%	0.01
Black	15%	11%	18%	0.0009
Hispanic	8%	8%	9%	0.65
Other race/ethnicity	3%	3%	2%	0.24
Body mass index (kg/m ²), mean (±SD)	29.7 (±5.42)	28.4 (±4.36)	30.7 (±5.91)	<0.0001
<i>Medical disorders (self-reported)</i>				
History of diabetes mellitus (% yes)	17%	12%	20%	0.0001
History of serious or other heart disease (% yes)	14%	11%	16%	0.008
History of cholesterol medication use (% yes)	3%	2%	4%	0.30
History of major depression (% yes)	8%	3%	11%	<0.0001
Anxiolytic/antidepressant use at baseline (% yes)	31%	16%	42%	<0.0001
Beck Depression Inventory score (range 0–63)	7.43 (±7.43)	3.61 (±4.20)	10.28 (±8.02)	<0.0001
<i>Hepatitis factors</i>				
HCV genotype 1 (%)	89%	90%	88%	0.48
Ever received a transfusion (% yes)	39%	36%	42%	0.08
Ever experienced a needle stick (% yes)	19%	18%	19%	0.68
Ever used needles to inject recreational drugs (% yes)	47%	46%	47%	0.73
Ever exposed to blood at work (% yes)	24%	21%	25%	0.11
No exposures reported (%)	14%	17%	13%	0.04
Platelet count (×10 ³ /mm ³), mean (±SD)	169 (±64.8)	171 (±60.4)	168 (±68.0)	0.39
Palpable spleen on baseline exam (% yes)	11%	10%	12%	0.26
Baseline biopsy Ishak fibrosis score, mean (±SD)	4.0 (±1.3)	3.8 (±1.2)	4.2 (±1.3)	<0.0001
Cirrhosis on biopsy [Ishak score 5 or 6] (%)	38%	31%	43%	<0.0001
HCV RNA level at baseline (log ₁₀ IU/ml), mean (±SD)	6.42 (±0.53)	6.43 (±0.54)	6.41 (±0.52)	0.62
ALT level at baseline (U/L), mean (±SD)	115 (±82.2)	125 (±86.8)	108 (±78.0)	0.0007
<i>Smoking and alcohol use</i>				
Ever drank alcohol regularly? (% yes)	84%	87%	82%	0.04
Number of alcoholic drinks over lifetime (±SD)	18,390 (±30,721)	15,281 (±26,109)	20,721 (±33,601)	0.003
Regular alcohol use at baseline (% yes)	19%	22%	16%	0.006
Ever smoked cigarettes? (% yes)	76%	75%	78%	0.26
Current smoking at baseline (% yes)	30%	24%	34%	0.0002
Patients with baseline mental summary score				
	>50 points (n = 718)	≤50 points (n = 426)		
<i>Demographics</i>				
Age (y), mean (±SD)	50.0 (±7.56)	49.7 (±6.85)		0.52
Gender (% female)	25%	31%		0.03
Marital status (% married or living as married)	75%	64%		<0.0001
Education level (% college graduate)	30%	19%		<0.0001
Race and ethnicity (%)				
White	74%	73%		0.79
Black	16%	14%		0.22
Hispanic	7%	11%		0.02
Hispanic	3%	2%		0.65
Body mass index (kg/m ²), mean (±SD)	29.6 (±5.28)	29.9 (±5.65)		0.49
<i>Medical disorders (self-reported)</i>				

History of diabetes mellitus (% yes)	15%	19%	0.11
History of serious or other heart disease (% yes)	14%	13%	0.65
History of cholesterol medication use (% yes)	3%	3%	0.73
History of major depression (% yes)	5%	13%	<0.0001
Anxiolytic/antidepressant use at baseline (% yes)	23%	45%	<0.0001
Beck Depression Inventory score (range 0–63)	4.22 (±4.09)	12.82 (±8.59)	<0.0001
<i>Hepatitis factors</i>			
HCV genotype 1 (%)	90%	87%	0.14
Ever received a transfusion (% yes)	40%	39%	0.72
Ever experienced a needle stick (% yes)	19%	18%	0.51
Ever used needles to inject recreational drugs (% yes)	44%	52%	0.01
Ever exposed to blood at work (% yes)	23%	24%	0.64
No exposures reported (%)	16%	12%	0.03
Platelet count ($\times 10^{-3}/\text{mm}^3$), mean (±SD)	172 (±65.6)	165 (±63.3)	0.07
Palpable spleen on baseline exam (% yes)	10%	13%	0.16
Baseline biopsy Ishak fibrosis score, mean (±SD)	3.9 (±1.3)	4.2 (±1.3)	0.002
Cirrhosis on biopsy [Ishak score 5 or 6] (%)	35%	42%	0.02
HCV RNA level at baseline (log ₁₀ of IU/ml), mean (±SD)	6.44 (±0.54)	6.39 (±0.52)	0.17
ALT level at baseline (U/L), mean (±SD)	115 (±80.4)	115 (±85.3)	0.99
<i>Smoking and alcohol use</i>			
Ever drank alcohol regularly? (% yes)	83%	86%	0.23
Number of alcoholic drinks over lifetime (±SD)	15,892 (±29,630)	22,619 (±32,081)	0.0003

Table 2

Factors associated with HRQOL summary scores at baseline

Baseline factors	Physical summary score ($n = 1093$)			Mental summary score ($n = 1093$)			Sexual summary score ($n = 1085$)		
	b	Standard error	p value	b	Standard error	p value	b	Standard error	p value
BDI score (+1 unit)	-0.69	0.04	<0.0001	-0.76	0.029	<0.0001	-1.95	0.11	<0.0001
Taking anxiolytic/ antidepressant	-3.81	0.65	<0.0001	-1.86	0.46	<0.0001	-6.39	1.81	0.0004
Body mass index (+1 unit)	-0.33	0.051	<0.0001	+0.085	0.036	0.02	-5.1	1.1	<0.0001
Age (+10 yr.)	-1.33	0.39	0.001				5.07	1.77	0.004
Male gender	2.20	0.65	0.0007				4.31	1.99	0.03
Alcohol use in past 6 months	1.65	0.72	0.02						
No palpable spleen on physical exam	2.12	0.89	0.02						
Married or living as married	1.35	0.63	0.03						
No current cigarette smoking	1.94	0.63	0.002	0.017	0.0065	0.008			
Number of alcoholic drinks over lifetime (+1000 drinks)							18.83	4.47	<0.0001
No history of cholesterol medication use							-1.48	0.61	0.02
Ishak fibrosis score (+1 unit)									

All of the variables listed in Table 1 were tested in models using backwards multivariate linear regression (SAS 8.2). All variables remaining in each model are significant at the 0.05 level or less (b = change in HRQOL score per unit of baseline factor, holding all other variables in the model constant). The R^2 values for these best-fit models are as follows: physical summary score, $R^2 = 0.38$; mental summary score, $R^2 = 0.46$; sexual summary score, $R^2 = 0.32$.

Table 3
Factors associated with improvements in HRQOL summary scores from baseline to week 72

Baseline factors	Physical summary score ($n = 245$)			Mental summary score ($n = 245$)			Sexual summary score ($n = 246$)		
	b	Standard error	p value	b	Standard error	p value	b	Standard error	p value
BDI score (+1 unit)	-0.17	0.074	0.02	-0.18	0.087	0.04	-0.61	0.22	0.007
Body mass index (+1 unit)	-0.14	0.10	0.15	-0.29	0.096	0.003			
No history of diabetes mellitus	5.18	1.50	0.0007						
Ever drank alcohol regularly in past	3.17	1.46	0.03						
Male gender	2.45	1.23	0.05	3.59	1.18	0.003			
Not taking anxiolytic/antidepressant				4.10	1.48	0.006			
No history of heart disease				-0.012	0.0053	0.02			
Serum ALT (+1 unit)	4.00	1.09	0.0003				7.49	3.37	0.03
Achieved sustained virological response									

The “achieved sustained virological response” variable and all of the variables listed in Table 1 were tested in models using backwards multivariate linear regression (SAS 8.2). All variables remaining in each model are significant at the 0.05 level or less, after adjustment by baseline summary score (b = change in HRQOL score per unit of baseline factor, holding all other variables in the model constant). The R^2 values for these best-fit models are as follows: physical summary score, $R^2 = 0.26$; mental summary score, $R^2 = 0.33$; sexual summary score, $R^2 = 0.25$.