

# Patient's preferences for health scenarios associated with hepatitis C and its treatment

Fabio Tinè

Unità di Gastroenterologia, Ospedali Riuniti Villa Sofia – Cervello, Palermo, Italy

**Background and aim:** Antiviral therapy with peg-interferon and ribavirin induces sustained virus eradication in 40%–80% of patients with chronic hepatitis C virus (HCV). We investigated patient views on their involvement in therapeutic decision making and on the desirability of disease and treatment-related outcomes.

**Methods:** The control preferences and visual analog scales were administered in a pencil and paper format to a series of 45 patients in order to assess their decisional role, preferences for scenarios of HCV disease and antiviral treatment, and estimates of success required to recommend treatment.

**Results:** The preferred decisional role of patients was passive in 26 (58%), collaborative in 12 (27%) and active in 7 (15%). Median preference scores ranged from 0.30 to 0.90 for scenarios of disease, from 0.05 to 0.80 for side effects and from 25% to 100% for estimates of benefit to recommend treatment.

**Conclusions:** Our patients prefer to defer to the doctor the final decision in starting therapy in a context of shared decision making. Reported preferences for HCV scenarios are in the range discussed in the literature. The wide variability in the values attributed to side effects by patients with chronic hepatitis C as well as in expected probabilities of successful treatment suggests a need for decision analysis tailored to the individual patient.

**Keywords:** hepatitis C, preferences, decision role, antiviral treatment

## Introduction

Hepatitis C virus (HCV) infection affects 170 million people worldwide (four million in USA and about five million in western Europe).<sup>1,2</sup> Although the majority of those with chronic hepatitis C infection are not going to develop complications, 15%–40% may develop cirrhosis, liver failure, or hepatocellular carcinoma (HCC).<sup>3</sup> Chronic hepatitis C is generally asymptomatic but has been associated with reduced health-related quality of life in the early stages.<sup>4</sup> Standard therapy is represented by combined use of pegylated interferon and ribavirin for 3–12 months. Such a regimen benefits 40%–80% of patients, depending on HCV genotype,<sup>5</sup> and has been shown to be cost-effective from a societal perspective.<sup>6</sup>

Perception of health by patients with HCV infection or harm from antiviral therapy strongly depends on the information given during the medical examination. It has been shown that the patient's treatment decisions are influenced by multiple factors besides the risks and benefits of antiviral therapy or the physician's recommendations. Social issues, some heuristics, particular conceptualizations of the illness, and considering therapy as a protected value are all factors which determine the patient's acceptance or refusal of therapy.<sup>7</sup>

Correspondence: Fabio Tinè  
Unità di Gastroenterologia, Ospedali Riuniti Villa Sofia – Cervello, Via Trabucco 180, 90100 Palermo, Italy  
Tel +39 9 1680 2937  
Fax +39 9 1688 5111  
Email fabiotinemd@virgilio.it

The patient's perspective is becoming more important in health care policy decisions worldwide. It is also becoming more and more common for patients to take an active role when medical decisions have to be made.<sup>8</sup> Research on cancer suggests that role preferences vary considerably and that whilst most patients prefer a collaborative role, a significant minority prefer a passive or active role.<sup>9</sup> To our knowledge no information exists regarding the common decision-making roles of patients with chronic hepatitis C in approaching a decision about treatment.

It is also well known that each individual patient provides different information about his/her own health state or disabilities, thus disclosing different preferences in drug therapy decisions with uncertain outcomes.<sup>10,11</sup> Utility measurement is a method of determining an individual's preference for a certain outcome represented by a quantitative score (utility). A systematic review of the available literature on health-state utilities for liver disease has been very recently published, producing estimates for major states of hepatitis C such as moderate disease, compensated cirrhosis, decompensated cirrhosis, and post-liver transplant.<sup>12</sup>

Both the desired/perceived decision-making role and the patient's views on desirability of disease and treatment-related outcomes are factors influencing the decision to start therapy and may be relevant for a perspective of shared decision making in chronic hepatitis C as in other clinical settings. To gain insight into these issues, we planned a pilot study to administer to a consecutive series of patients a questionnaire evaluating in a simple way their health status, the role they feel to play in decision making about antiviral therapy, and their preferences for some health scenarios related to chronic HCV and its treatment.

## Materials and methods

The research protocol was approved by the local Ethical Committee. Participation in our study was proposed to a consecutive series of outpatients with biopsy proven chronic hepatitis C eligible for an Italian multicenter observational outcome study of pegylated interferon (alfa-2a or alfa-2b) and ribavirin.<sup>13</sup>

Eligibility criteria were: age 18–65 years; serum alanine aminotransferase ALT above the upper normal limit for at least six months; anti-HCV sero-positivity and detectable HCV viremia. Patients were treatment-naïve or previous relapsers or nonresponders and had clinical findings and laboratory parameters indicative of compensated liver disease. None had evidence of an ongoing cause of liver disease other than HCV.

Forty-five patients agreed to participate and provided written informed consent before entry into the study. A questionnaire was administered during the first visit after the diagnostic work-up, before starting treatment. In our clinical practice, it is during this visit that harm and benefit of antiviral therapy are thoroughly discussed with the patient in order to get informed consent to treatment. We formalized this approach and surveyed patients, using a pencil-and-paper format, by a questionnaire that consisted of five parts including:

1. Demographic data consisting of age, gender, level of education, employment and marital status;
2. A simple assessment of health status;
3. An assessment of decision-making role through the choice of one among five statements, according to the control preferences scale<sup>14</sup> (see Appendix 1);
4. An evaluation of patient's preferences (utilities) for six health scenarios with HCV, according to Cotler and colleagues.<sup>15</sup> Utilities were assessed by asking to each patient to indicate a judgment of relative desirability of each scenario by placing a mark on a visual analog scale (VAS) ranging from 0 (death) to 1 (health without hepatitis C). Scenarios described four possible disease outcomes (chronic hepatitis or cirrhosis without and with symptoms) and two treatment outcomes (adverse events, sustained response) that would be part of any discussion on benefit and harm of antiviral therapy for chronic hepatitis C. The study instrument published by Cotler and colleagues<sup>15</sup> was translated in Italian and slightly modified by excluding the health state 3 "hepatitis C with moderate symptoms, no cirrhosis", and by including a scenario representing sustained response (see Appendix 2 for descriptions).
5. Patient's judgment of what threshold of probability of treatment success they would consider minimally acceptable to start drug treatment. This judgment was indicated by placing a mark on a VAS representing probabilities of achieving sustained viral eradication ranging from 0% to 100%.

The content of the descriptions and response scales of the study instrument have been tested for clarity, comprehension, and relevance in physicians and patients from the United States.<sup>15</sup>

All analyses were carried out using StatsDirect statistical software (version 2.6.1, 19.1.2007; StatsDirect, Cheshire, UK) and STATA software (v. 8.0; Stata Corporation, College Station, TX, USA). Box plots were used to describe patient's preference values (utilities).

## Results

Patient demographic data and disease characteristics are summarized in Table 1. The majority of patients were naïve, infected with genotype 1, and highly viremic. Cirrhosis was present at histology in 14 patients (31%). Almost 70% of patients had a high school educational level and a full employment status. Accordingly, all patients completed the first three parts of the questionnaire. However, five patients (11%) refused to complete the assessment of utilities of clinical scenarios because of “tiredness and confusion” and

four (9%) were excluded because of illogical assessment (ie, value for cirrhosis higher than value for asymptomatic chronic hepatitis).

Assessment of health status was good to excellent in 90% of patients (Figure 1). Only a minority of patients (15%) preferred an active decisional role, that is they favored a personal decision about therapy fully independent from the doctor's opinion, and almost one third agreed for a shared decision (collaborative role). On the other hand, almost 60% of patients stated that the decision to start therapy is a matter of judgment for the health professional.

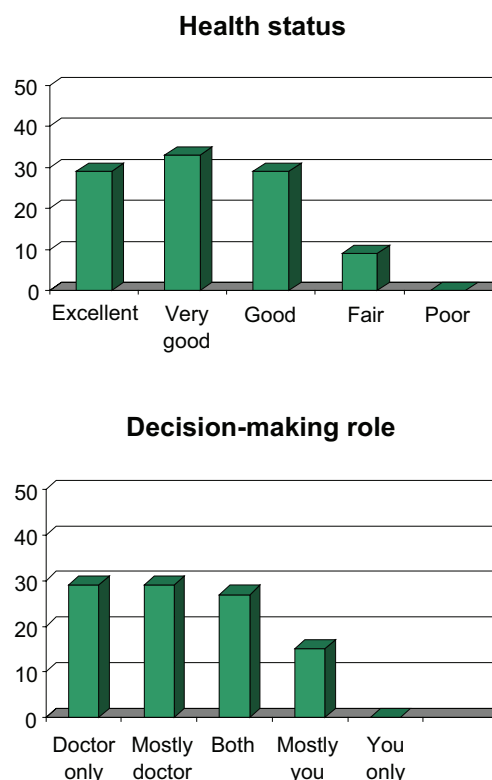
The descriptive statistics of preference values obtained from 36 patients is reported in Figures 2 and 3. As expected, median values decreased consistently between asymptomatic and symptomatic chronic hepatitis and cirrhosis. The distribution of median utility values, reported within the box plots, showed declining patient's estimates from the status scenario 1 (0.90) to the status scenario 4 (0.30). In other words patients assigned decrements of quality of life from 10% in asymptomatic chronic hepatitis to 70% in symptomatic cirrhosis. Looking at quartiles and range of estimates for each scenario, a large variability is evident in Figure 3 particularly for scenario describing side effects of treatment (range 0.05 to 0.80). The probability of treatment success that the patient considered

**Table 1** Baseline characteristics of 45 enrolled patients

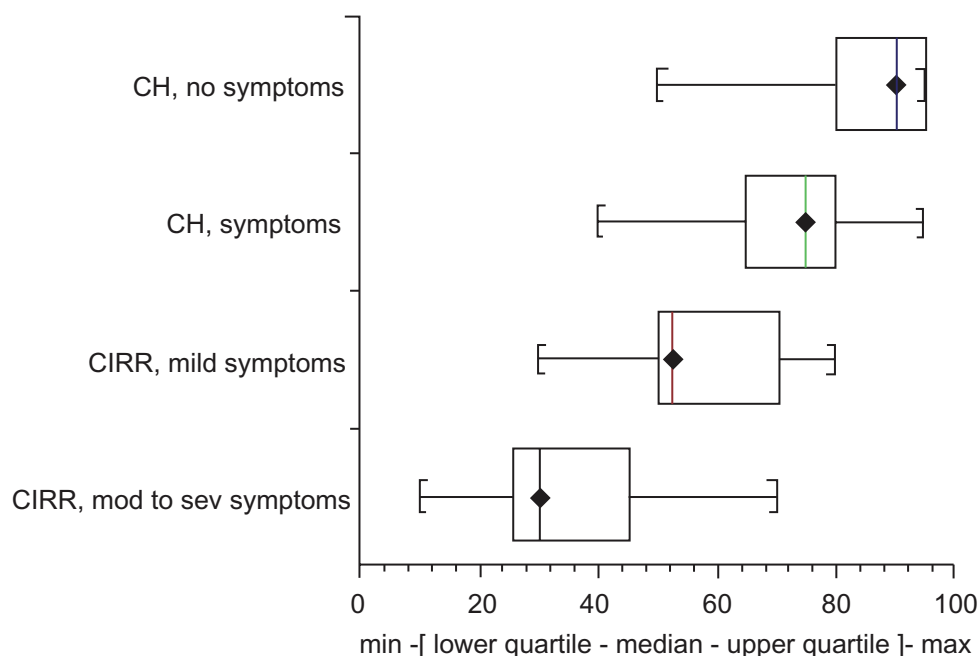
Age	52 ± 12
Sex male	30 (67%)
<b>Risk factors</b>	
– Transfusion	5 (11%)
– IDU	0
– Unknown	40 (89%)
<b>Education level</b>	
– Elementary school	17 (37%)
– High school	17 (37%)
– University or college	7 (15%)
– Professional/graduate	4 (9%)
<b>Employment status</b>	
– Full time	29 (64%)
– Part-time	9 (20%)
– Not employed	6 (13%)
– Retired	1 (2%)
<b>Co-morbidity</b>	
– Diabetes	10 (22%)
– Hypertension	10 (22%)
– Hypothyroidism	2 (4%)
– Other	4 (9%)
Naïve	33 (74%)
Previous treatment	12 (26%)
<b>Histology</b>	
– Cirrhosis	14 (31%)
<b>Biochemical/virological parameters</b>	
– Hb	15 (1.2)
– WBC	6,300 (1,682)
– PLT	194,911 (58,032)
– ALT × UNL	2.5 (1.8)
<b>Virological parameters</b>	
– HCV viremia (UI/ml)*	586790 (19,110–6,534,500)
– Genotype 1–4	37 (82%)
– Genotype 2–3	8 (18%)

**Note:** \*Bayer (median and range).

**Abbreviations:** ALT, alanine aminotransferase; IDU, intrauterine device; HCV, hepatitis C virus; PLT, platelet; UNL, upper normal limit; WBC, white blood cells.



**Figure 1** Assessments of health status and decision-making role.



**Figure 2** Box plots of preference values for HCV disease outcomes assessed by visual analog score.

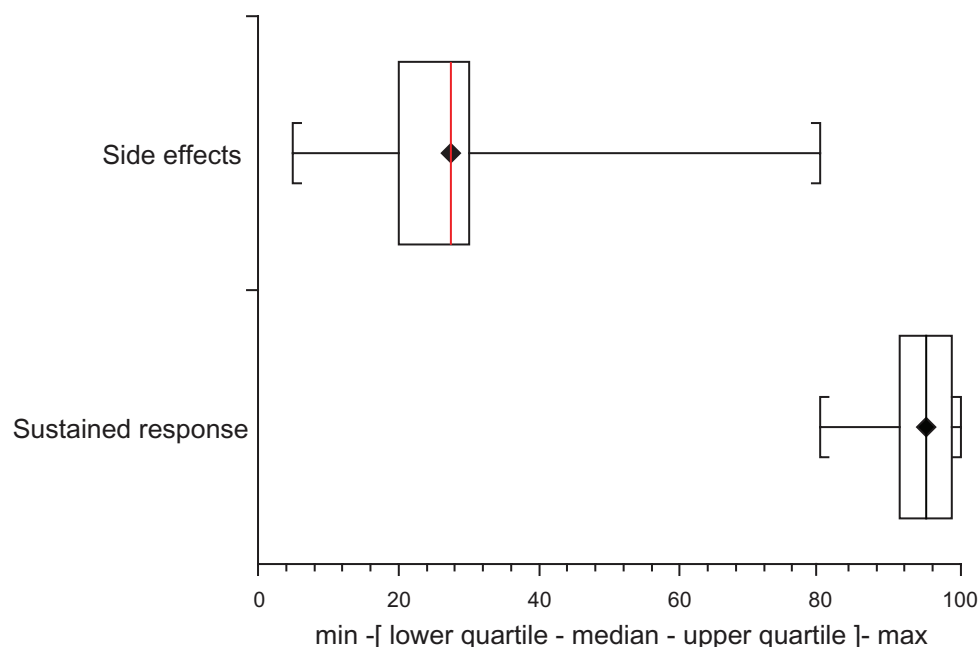
**Abbreviation:** CH, chronic hepatitis; CIRR, cirrhosis; HCV, hepatitis C virus.

to recommend treatment that showed wide estimates ranging from 25% to 100% (Figure 4).

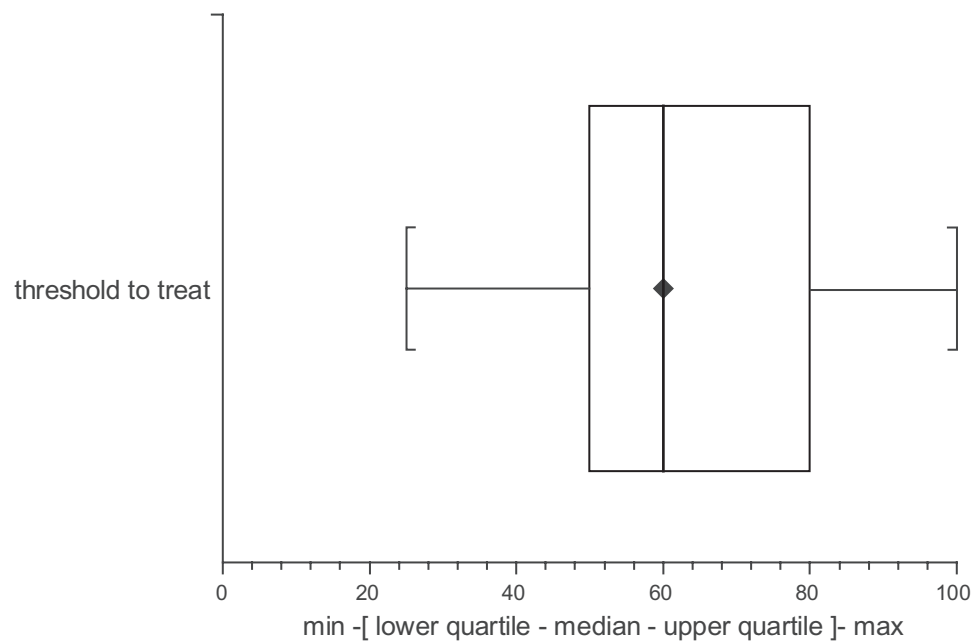
## Discussion

Current health care policy advocates patient participation in treatment decision making. In this pilot study we explored

the preferred level of involvement in treatment decisions of a small series of patients from Italy with chronic hepatitis C, and used utility-based methods to measure how they valued the health states or disabilities that result from such disease and its treatment. Chronic hepatitis C is a long-term condition in which self-management and participation in



**Figure 3** Box plots of preference values for HCV treatment outcomes assessed by visual analog score.



**Figure 4** Box plots of patient' estimates of benefit to recommend antiviral treatment.

treatment decision making must be encouraged. Because the communication skills of professionals are central to facilitating patient participation we used a simple approach by selecting well known user-friendly instruments. We underline that many respondents in this study identified communication as an area requiring improvement, and many would have liked to be more involved in treatment decision making.

Our findings confirm the results of previous studies<sup>8,9,16,17</sup> showing that respondents had identifiable preferences, from active through to passive, regarding their level of participation in treatment decision making. In general, patients wish to be more involved in decisions regarding a minor illness more than a major illness,<sup>18</sup> and women tend to desire more involvement than do men in clinical decisions.<sup>19</sup> In our study, most patients felt they had little or no role in treatment decisions. Near 60% of them most preferred one of the passive decisional roles from the control preference scale. However, the most passive option was least preferred by more than half of respondents and almost 30% of respondents

chose the D option which involves some, if limited, patient involvement, rather than the E option where the patient entirely defers decision making to health professionals. Thus, most respondents preferred some input into decision making. Typically, this extended to individuals feeling included in the decision and having their views respected.

Overall, while most patients were happy to defer overall control of treatment decision making to doctors, our data supports the notion of partnership. Our results are close with those of a study evaluating patients with hemato-oncological diseases showing that 60% among 117 interviewed patients desired more a passive than an active role.<sup>20</sup> Moreover, in a telephone survey of elderly patients with chronic heart failure 21% of patients preferred an active role versus 31% favoring a collaborative role and 48% a passive role in decision making.<sup>21</sup>

According to a previous study<sup>15</sup> we used utility analysis to evaluate patient's perceptions of hepatitis C-related health states and patient's threshold to recommend treatment. Although the rating scale method does not have its roots in expected utility theory, ie, it is not strictly utility, we believe it is similar to and has measurement advantages over true utilities.<sup>14</sup> We found that the majority of patients understood descriptions of health states and were able to provide an utility assessment of the scenarios using a VAS. The validity of the health state construct was supported by the significant decline of utilities assigned with increasing health state severity (from chronic hepatitis to cirrhosis). Although derived from

**Table 2** Assessment of decision-making role by CPS

Patient alone	0
Patient primarily	7 (15%)
Shared equally	12 (27%)
Doctor primarily	13 (29%)
Doctor alone	13 (29%)

**Abbreviation:** CPS, control preferences scale.

**Table 3** Patient's utilities of health states with HCV by rating scale method

	Cotler and colleagues <sup>15</sup>	Chong and colleagues <sup>23</sup>	Sherman and colleagues <sup>24</sup>
HCV infection, no symptoms	0.89 (0.79–0.94) <sup>^</sup>	0.68 (0.60–0.77) <sup>§</sup>	
Chronic hepatitis, mild symptoms	0.71 (0.54–0.83) <sup>^</sup>	0.70 (0.63–0.76)	0.67 ± 0.03 <sup>°</sup>
Cirrhosis, mild symptoms (compensated)	0.44 (0.30–0.60) <sup>^</sup>	0.65 (0.56–0.73)	0.65 ± 0.04
Cirrhosis, decompensated	0.27 (0.16–0.46) <sup>^</sup>	0.57 (0.40–0.73)	
SVR	ne	0.74 (0.68–0.81)	

**Notes:** <sup>^</sup>Median and range; <sup>§</sup>Mean and 95% CI; <sup>°</sup>Mean ± SE.

**Abbreviations:** CI, confidence interval; HCV, hepatitis C virus; SE, standard error; SVR, sustained virological response.

a small sample our estimates are similar to those reported in previous studies which have directly assessed utilities from patients by using the rating scale method as well as other methods (Table 3).

Potential factors causing variability of utility estimates could be due to both the tool used (VAS generates the lowest estimates of all the methods, with standard gamble and time trade-off having much higher estimates), the type of respondent (patients, nondiseased subjects, health professionals), and geographical and cultural differences. We recruited individuals from a tertiary care setting representing a population of European HCV-infected patients with no known risk factors eligible for antiviral treatment. The results derived from this convenience sample might be different from those that could have been derived should have the sample been randomly drawn from all eligible participants in the general population with chronic HCV infection.

It is of interest that the median rating for life with side effects of antiviral therapy was 0.25, suggesting a perceived 75% reduction from good health during time on therapy. Thus, patients viewed side effects unfavorably at least in the proposed scenario. Moreover, the large range of patient ratings is striking and indicate that patient views about the impact of side effects on health status varies substantially. We don't know the difference in disutility of each patient among different adverse events, ie, flu-like versus depression or alopecia, or the value patients could assign to possible life-threatening adverse event such as a severe infection. This information is lacking in the literature but it is very important for the generation of recommendations for treatment.<sup>25</sup> As the ratings of adverse events overlap with the ratings of future disease scenarios (without or with symptoms) and as patients' estimates of benefit in recommended treatment are also largely variable, it seems that decision analysis could be of help in decision making.

The strength of our study include the novelty of assessing hepatitis C patient views on their role in therapeutic decision

making by means of established scales. In fact, to our knowledge, this was not assessed previously in a population of liver patients. However, our study suffers from some methodological limitations such as a unique geographical location and a limited sample size, so that characteristics of small subgroups could not be investigated. Evidence of the association of factors such as age, gender, level of education, marital status, socioeconomic status, and health status with preferences for involvement in treatment decision making or with health utilities of patients with chronic hepatitis C remain inconclusive and should be assessed in future studies.

In conclusion, our patients prefer to defer to the doctor the final decision in starting therapy in a context of shared decision making. Preferences for HCV scenarios are in the range reported in the literature. The wide variability in the values attributed by patients with chronic hepatitis C to both scenarios of health with HCV and health with antiviral treatment as well as in expected probabilities of cure suggests a need for decision analysis tailored to the individual patient. Further research is needed to identify predictors of preferences for active or passive patient roles and further utility analysis is needed to generate data on the values patients assign to single side effects from antiviral therapy.

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## Disclosures

The authors report no conflicts of interest in this work.

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# Appendix

## Appendix 1 Decision-making role by control preferences scale

Which of the following is closest to your feeling about the role you feel you should have in your medical decision about treatment of chronic hepatitis C?

- A. I would prefer to make the final decision about which treatment I will receive on the basis of the facts I learn from my physician's opinion
- B. I would prefer to make the final decision about my treatment after considering my physician's opinion
- C. I would prefer that my physician and I share responsibility for deciding which treatment is best for me
- D. I would prefer that my physician make the final decision about which treatment will be used but he or she seriously consider my opinion
- E. I would prefer to leave all decisions regarding treatment to my physician

## Appendix 2 Description of six scenarios of health with HCV (Cotler, modified)

### 1. Asymptomatic chronic hepatitis, no cirrhosis

Absence of symptoms  
Transmission to sexual partner possible  
May progress to cirrhosis

### 2. Symptomatic chronic hepatitis, no cirrhosis

Sometimes do not feel rested  
Tire more easily than usual  
Limitation of physical activity possible  
Transmission to sexual partner possible  
May progress to cirrhosis

### 3. Chronic hepatitis with cirrhosis, mild symptoms

Sometimes do not feel rested  
Tire more easily than usual  
Limitation of physical activity possible  
Transmission to sexual partner possible  
Have cirrhosis  
May get liver cancer  
May get liver failure

### 4. Cirrhosis, moderate to severe symptoms

Usually feel tired  
Tire more easily than usual  
Limitation of physical activity possible  
Little interest in sex  
Have cirrhosis  
May get liver cancer  
May get liver failure  
May need liver transplantation

### 5. Side effects from pegylated interferon and ribavirin

Needle stick one time a week  
Pills twice daily  
Flu-like symptoms (fever, chills, nausea, headache, poor appetite) that tend to improve after 2 weeks  
Tiredness, difficulty in sleeping, irritability, difficulty in concentrating  
Chance of other non life-threatening problems that go away after treatment is completed, such as low blood count, hair loss and depression

### 6. Sustained response to treatment

Absence of symptoms  
Transmission to sexual partner unlikely  
Progression to cirrhosis very likely reduced

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