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Health-related quality of life after sustained virological response to treatment for hepatitis C

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ABSTRACT

This study aimed to show the changes in health-related quality of life (HRQoL) after a sustained virological response (SVR) to hepatitis C treatment. A retrospective study was conducted among 1,546 patients with SVR to interferon-based (IFN-based) or direct-acting antiviral (DAA) anti hepatitis C virus treatments from January 1990 to March 2017 in five hospitals. The survey was conducted between November 2017 and October 2018. A questionnaire including the Japanese version of the EQ-5D-3L before and after SVR by IFN-based or DAA treatment was used to assess changes in HRQoL retrospectively. Of the 1,546 patients who achieved SVR, 580 achieved SVR with IFN-based treatment (SVR-IFN) and 966 achieved SVR with DAA treatment (SVR-DAA). Comparison of HRQoL before and after treatment revealed a significant increase in SVR-IFN (0.9078 vs. 0.9278, $p = 0.0406$). For SVR-IFN, patients in their 60s and 70s showed a significant increase in HRQoL after treatment. In contrast, changes in HRQoL in SVR-DAA were not statistically significant (0.9018 vs. 0.9063, $p = 0.3908$). For SVR-DAA, HRQoL significantly improved for patients in their 50s and 60s. The results of this study showed a trend toward improvement or unchanged HRQoL in patients who achieved SVR, despite advanced age. The results of this study can serve as a basis for follow-up after SVR and cost-effectiveness analyses.

Key words: *Hepatitis C*, *Interferons*, *Japan*, *Quality of Life*

INTRODUCTION

Globally, 71 million individuals are estimated to be persistently infected with the hepatitis C virus (HCV), and 399 000 deaths were recorded due to viral hepatitis C-related diseases[8)]. In Japan, 983,879–1,583,879 individuals are persistently infected with HCV, and 60% of liver cancer-related deaths are caused by HCV[15)]. Correspondingly, the World Health Organization (WHO) set a target for the elimination of viral hepatitis by 2030, and the governments of every country have established a health policy to achieve this goal[9)].

In recent years, the sustained virological response (SVR) rate to antiviral therapy for hepatitis C has dramatically improved with the approval of direct-acting antivirals (DAA). In the early 1990s, interferon (IFN) monotherapy for hepatitis C was approved; however, the SVR rate was only 20%–30%[14)]. In the early 2000s, ribavirin (RBV), a nonspecific oral antiviral agent against RNA viruses, was introduced[6)]. The combination of IFN and RBV significantly improved the SVR rates[4)]. In the 2010s, the antiviral drug DAA, which is specifically effective against HCV, was developed; the therapeutic

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effect was dramatically improved, and the side effects were reduced by using only DAA as an IFN-free therapy[18]. Although HCV elimination and side effects have improved, changes in carcinogenesis and health-related quality of life (HRQoL) remain unknown.

The Euro-QOL-5D (EQ-5D) questionnaire is one of the most widely used to measure HRQoL, with values of 1 for perfect health and 0 for death[1]. Many health technology assessment organizations also recommend the EQ-5D as a standard for assessing quality of life, such as National Institute for Health and Care Excellence (UK) and Haute Autorité de Santé (France). The EQ-5D has been published/translated in Japanese for the Euro-QOL questionnaire..

HRQoL is associated with age in the general population. In a nationwide random sampling study, HRQoL in individuals in their 30s was higher than in those in other age groups, and those aged ≥ 70 years had notably low HRQoL[16].

According to an open-ended self-administered questionnaire survey of 212 patients with hepatitis C during outpatient visits or hospitalizations at Hiroshima University Hospital in 2015, the HRQoL scores of patients with chronic hepatitis C and decompensated liver cirrhosis in Hiroshima Prefecture were 0.871 (n = 108) and 0.524 (n = 4), respectively[10].

Although the quality of life of patients who are persistently infected with hepatitis C has been shown to be lower than that of the general population[2,21], how much HRQoL improves after HCV-SVR and whether it is improved to the same level as that of the general population remains unclear. This study aimed to determine changes in HRQoL after SVR to HCV.

MATERIALS AND METHODS

Study participants

This retrospective study was conducted at five health facilities: Toranomon Hospital, Sapporo Kosei Hospital, Ogaki City Hospital, Hiroshima University Hospital, and Oita University Hospital.

We enrolled 1,785 patients who were undergoing anti-HCV treatment (IFN-based or DAA) between January 1990 and March 2017 and received health follow-ups in one of the five above-mentioned hospitals between November 2017 and October 2018. In addition to the information from the patients records, the participants were asked to complete a survey questionnaire to assess their basic information and HRQoL before and after anti-HCV treatment. After excluding unknown/non-SVR cases, 1,546 SVR cases were used to evaluate the HRQoL.

Questionnaire

The questionnaire included 14 items: five questions for the Japanese EQ-5D-3L (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) (Supplementary Table 1), nine questions for symptoms before and after treatment (malaise, taste, stomatitis, dermatitis, hair loss, anorexia, itching, leg cramps, and insomnia), and an additional five items (sex, age at response, anti-virus treatment because of which patients reached SVR, diagnosis at first visit, onset/not onset of Hepatocellular Carcinoma (HCC), and treatment period from first visit to SVR), which were obtained from medical records.

Statistical analysis

Based on responses to the EQ-5D-3L questionnaire, HRQoL was determined using a conversion table of Japanese HRQoL scores. The Wilcoxon signed-rank test was used to evaluate the changes in HRQoL scores before and after treatment according to sex, age group, HCC onset/non-onset, and disease state.

RESULTS

Patient Characteristics

During the study period, 1,546 patients were eligible for assessment of the change in HRQoL before and after successful anti-HCV treatment. Notably, 580 and 1,546 patients achieved SVR with IFN-based (SVR-IFN) and DAA treatment (SVR-DAA), respectively. The proportion of men in the SVR-IFN group was significantly higher than that in the SVR-DAA group (50.7% vs. 42.7%, $p = 0.0021$). The mean age was 67.6 ± 10.4 years and 69.9 ± 11.1 years old among the SVR-IFN and SVR-DAA groups, respectively. We reviewed the medical records of the patients to determine the duration from first diagnosis to SVR. The proportion of patient who took < 1 year was significantly higher in the SVR-IFN group than that in the SVR-DAA group (50.9% vs. 26.9%, $p < 0.0001$). The proportion of patients diagnosed with compensated cirrhosis at initial visit in the SVR-DAA group was significantly higher than in the SVR-IFN group (18.4% vs. 7.9%, $p < 0.0001$) (Table 1).

HRQoL before and after SVR

Among individuals who underwent SVR-IFN, HRQoL after treatment significantly increased compared to that before treatment (0.9078 vs. 0.9278, $p = 0.0406$). Whereas, in the SVR-DAA group, the HRQoL did not significantly change after treatment (0.9018 vs. 0.9063, $p = 0.3908$) (Fig. 1).

In terms of sex, no significant changes were observed in the HRQoL after treatment (Fig. 1).

In the age-specific analysis, HRQoL after treatment significantly increased in the age groups of 60–70 and 50–60 years in the SVR-IFN and SVR-DAA groups, respectively. Based on the diagnosis at initial visit, in the SVR-IFN group, the HRQoL improved after treatment in chronic hepatitis patients (0.9071 vs. 0.9297, $p = 0.0270$). Furthermore, HRQoL significantly improved in patients whose duration between initial diagnosis and achieving SVR was ≤ 5 years in the SVR-IFN group (Fig. 1).

In both the SVR-IFN and SVR-DAA groups, HRQoL decreased in patients who developed hepatocellular carcinoma (HCC) after HCV eradication. However, these changes were not statistically significant (Table 2).

Table 1 Background of the study subjects

Characteristics	SVR-IFN (N = 580)	SVR-DAA (N = 966)	*P*-value
Gender: Male	294 (50.7%)	412 (42.7%)	0.0021
Age (mean)	67.6 ± 10.4	69.9 ± 11.1	< 0.0001
Duration between initial diagnose to SVR			
Less than 1 year	270 (50.9%)	243 (26.9%)	< 0.0001
1–5 years	149 (28.1%)	226 (25.0%)	
6–10 years	70 (13.2%)	206 (22.3%)	
10 and over years	41 (7.7%)	230 (25.4%)	
Diagnose at initial visit			
Chronic hepatitis	534 (92.1%)	788 (81.6%)	< 0.0001
Compensated cirrhosis	46 (7.9%)	178 (18.4%)	
HRQoL mean score before treatment [range]	0.908 [–0.063, 1.000]	0.902 [0.026, 1.000]	0.3295

Abbreviation: SVR, sustained virological response; SVR-IFR, achieved sustained virological response by interferon-based treatment; SVR-DAA, achieved sustained virological response by direct acting antiviral; HRQoL, health related quality of life.

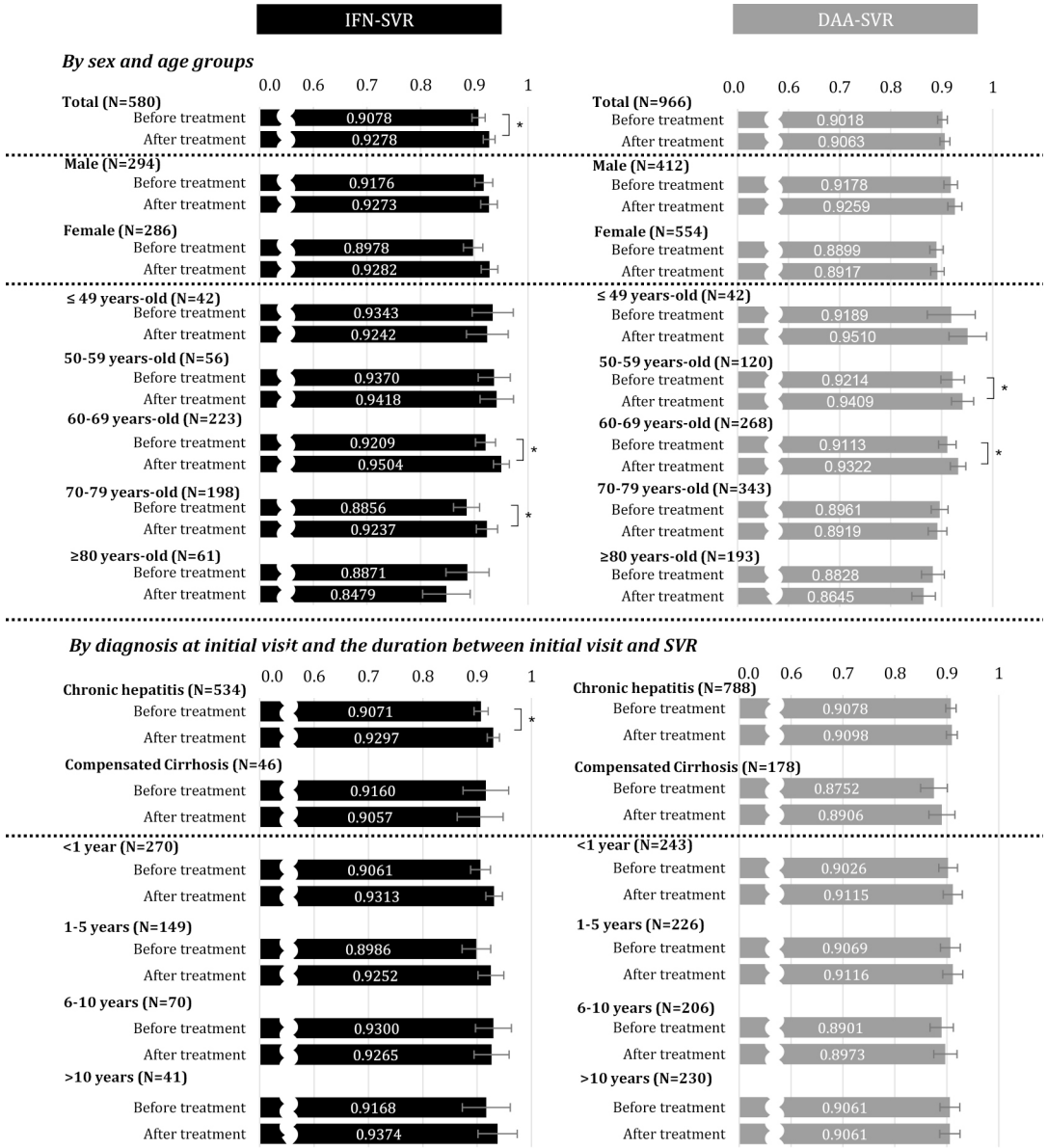

Fig. 1 This figure illustrates the changes in HRQoL, ranging from 0 (death) to 1 (perfect health), before and after anti-HCV treatment. The results are separately presented in two main sections, SVR-IFN and SVR-DAA, based on total number of participants, sex, age group, diagnosis at initial visit, and the duration from initial diagnosis to achieving SVR. HRQoL, Health Related Quality of Life; IFN, Interferon; DAA, direct acting antiviral; SVR, sustained virological response; SVR-IFN, achieved sustained virological response by interferon-based treatment; SVR-DAA, achieved sustained virological response by direct acting antiviral.

Table 2 HRQoL before and after SVR by treatment group

Group		Frequency	HRQoL mean score	SD	*P*-value
DAA treatment					
No HCC after SVR	Before treatment	498	0.898	0.143	0.5031
	After treatment	498	0.903	0.143	
HCC after SVR	Before treatment	17	0.942	0.112	0.25000
	After treatment	17	0.880	0.185	
IFN based treatment					
No HCC after SVR	Before treatment	286	0.904	0.152	0.8555
	After treatment	286	0.916	0.137	
HCC after SVR	Before treatment	33	0.926	0.142	0.7599
	After treatment	33	0.921	0.174	

n = 871 (excluding liver cancer cases or unknown before SVR)
Abbreviation: SVR, sustained virological response; SVR-IFR, achieved sustained virological response by interferon-based treatment; HRQoL, health related quality of life; HCC; hepatocellular carcinoma; SD, standard deviation.

Table 3 HRQoL before and after achieved SVR by symptoms improvement

	Subjects whose symptoms were improved				Subjects whose symptoms were not improved			
		HRQoL mean score				HRQoL mean score		
Symptom	N	Before treatment	After treatment	*P*-value	N	Before treatment	After treatment	*P*-value
Malaise	123	0.857	0.919	**< 0.0001**	23	0.787	0.813	0.1533
Taste	24	0.788	0.898	**0.0096**	7	0.826	0.835	0.4907
Stomatitis	39	0.813	0.869	0.0943	12	0.766	0.793	0.4463
Dermatitis	29	0.773	0.900	**0.0040**	14	0.914	0.906	0.3356
Hair loss	31	0.797	0.878	**0.0173**	7	0.878	0.873	0.1744
Anorexia	45	0.812	0.900	**0.0013**	13	0.755	0.804	0.3247
Itch	60	0.827	0.900	**0.0024**	22	0.898	0.905	0.7551
Leg cramps	63	0.850	0.898	**0.0148**	39	0.897	0.905	0.7124
Insomnia	17	0.819	0.928	0.0522	29	0.850	0.853	0.9371

Association between improvement of symptoms and HRQoL change

HRQoL significantly increased among participants with improved symptoms of malaise, taste, dermatitis, hair loss, anorexia, itching, and leg cramps after treatment. Stomatitis and insomnia also improved after treatment; however, the HRQoL of these patients did not significantly change. As expected, the patients whose symptoms did not improve after treatment did not show significant changes in HRQoL (Table 3).

DISCUSSION

In this study, using the EQ-5D-3L, we evaluated the HRQoL before and after anti-HCV treatment in 1,546 patients who achieved SVR after undergoing IFN-based or DAA treatment (580 SVR-IFN and 966 SVR-DAA). Overall, the comparison of HRQoL before and after treatment showed a significant improvement in the SVR-IFN group. The change in HRQoL in the SVR-DAA group was not statistically significant, despite the advanced age of participants in the group. The differences in the HRQoL between the two treatment groups could be explained by several factors. Age is negatively correlated with HRQoL. We observed that the proportion of older people (≥ 70 years old) was smaller in the SVR-IFN group than in the SVR-DAA group (44.66% vs 55.49%), and the general mean age was younger in the SVR-IFN group than that in the SVR-DAA group (67.6 ± 10.4 vs 69.9 ± 11.1). Moreover, patients who received IFN-based regimens experienced longer treatment durations and more severe adverse effects than patients receiving DAA regimens. The duration of IFN-based treatment usually ranges from 24 to 48 weeks depending on the viral genotype and can be prolonged to 72 weeks for slow-response patients[3]. However, the duration of DAA treatment was 8–24 weeks depending on the stage of liver disease[17]. During IFN-based treatment, the physical and mental health-related quality of life deteriorates. However, once treatment is completed, most people feel physically and mentally better than before starting treatment[3,12,17,19–21]. Therefore, a significant improvement in the HRQoL was observed in the SVR-IFN group. Our results, which found no significant difference between HRQoL before and after DAA treatment, are consistent with previous findings[11,13], which could be due to the age effect (older people in the SVR-DAA group than in the SVR-IFN group) and disease status at initial visit (more compensated cirrhosis patients in the SVR-DAA group than in the SVR-IFN group).

In the SVR-IFN group, a significant improvement in HRQoL was observed among patients in their 60s and

70s. In the SVR-DAA group, improvement in HRQoL was observed in patients in their 50s and 60s. However, no significant differences were observed in the HRQoL of patients aged ≤ 49 years in either treatment group. Patients in younger age groups seemed to be exposed to HCV for shorter duration, and the side effects of anti-HCV treatment was possibly lower in them. This suggests the possibility of age-related effects[7]. Therefore, no significant changes were observed in HRQoL among young patients, even after achieving SVR.

In patients aged > 80 years, HRQoL scores tended to decrease after treatment in both treatment groups, although the difference was not significant, suggesting that the decline in HRQoL in the study populationmay be due to aging. Therefore, patient background must be carefully considered when initiating treatment in older patients. However, in this study, HRQoL after treatment in patients in their 80s was higher than the standard HRQoL scores of the general population in the same age group for both treatments[16].

The HRQoL did not significantly change in patients diagnosed with compensated cirrhosis at initial visit in either treatment group. With improvements in anti-HCV drugs, we expect an improvement in HRQoL after treatment. The current guidelines of the Japanese Society of Hepatology recommend aggressive IFN-free DAA treatment for compensated cirrhosis type C[5].

The longer a patient is infected with hepatitis C, the more it impairs their quality of life[2,21]. However, considering the duration from initial diagnosis to achieving SVR, HRQoL after treatment tended to be higher across all time periods; however, it was significantly higher in patients who had received SVR-IFN for ≤ 5 years.

Our study had some limitations. First, the questionnaire was distributed after achieving SVR; therefore, information on HRQoL before treatment might have been affected by recall bias. Furthermore, the survey was conducted only among patients who achieved SVR and were likely to report their post-treatment HRQoL. Future studies are needed to compare the changes in HRQoL before and after treatment and examine the factors associated with HRQoL using the EQ-5D-3L after adjusting for age, sex, and psychological factors.

The results of the current study showed a trend toward improvement or unchanged HRQoL in patients who achieved SVR, despite their advanced age. The results of this study can serve as a basis for follow-up after SVR and cost-effectiveness analyses.

List of abbreviation

HCV, hepatitis C virus; WHO, World Health Organization; SVR, sustained virological response; DAA, direct-acting antivirals; IFR, interferon; RBV, ribavirin; HRQoL, health-related quality of life; EQ-5D, EuroQOL-5D; SVR-IFN, achieved SVR by IFN-based treatment; SVR-DAA, achieved SVR through DAA-based treatment; HCC, hepatocellular carcinoma.

DECLARATIONS

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and the study protocol was approved by the Epidemiology Ethics Review Committee of Hiroshima University (E-873). The objectives of the survey were explained to each participant, and informed consent was obtained after confirming that the participants understood the study objectives thoroughly.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed in the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors Contribution

Study concept and design: Junko Tanaka, Kazuaki Chayama; Conducting the study: Junko Tanaka, Tomokazu Kawaoka, Michio Imamura, Hiroshi Aikata, Kazuaki Chayama, Masataka Seike, Norio Akuta, Takashi Kumada, Yoshiyasu Karino; Data analysis: Tomoyuki Akita, Akemi Kurisu, Fumi Masumoto, Aya Sugiyama; Data Interpretation: Junko Tanaka, Tomoyuki Akita, Tomokazu Kawaoka, Michio Imamura, Hiroshi Aikata, Kazuaki Chayama; Manuscript development: Junko Tanaka, Tomoyuki Akita, Fumi Masumoto, Bunthen E; Critical revision for important intellectual content: Junko Tanaka, Kazuaki Chayama.

All authors have read and approved the final version of the manuscript.

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REFERENCES

1. Balestroni, G. and Bertolotti, G. 2012. EuroQol-5D (EQ-5D): an instrument for measuring quality of life. Monaldi. Arch. Chest Dis. 78(3): 155–159.
2. Barboza, K.C., Salinas, L.M., Sahebjam, F., Jesudian,

A.B., Weisberg, I.L. and Sigal, S.H. 2016. Impact of depressive symptoms and hepatic encephalopathy on health-related quality of life in cirrhotic hepatitis C patients. Metab. Brain. Dis. 31(4): 869–880.
3. Chayama, K., Hayes, C.N., Yoshioka, K., Moriwaki, H., Okanoue, T., Sakisaka, S., et al. 2011. Factors predictive of sustained virological response following 72 weeks of combination therapy for genotype 1b hepatitis C. J. Gastroenterol. 46(4): 545–555.
4. Conteduca, V., Sansonno, D., Russi, S., Pavone, F. and Dammacco, F. 2014. Therapy of chronic hepatitis C virus infection in the era of direct-acting and host-targeting antiviral agents. J. Infect. 68(1): 1–20.
5. Drafting Committee for Hepatitis Management Guidelines tJSoH. Japan Society of Hepatology guidelines for the management of hepatitis C virus infection: 2019 update. 2020. Hepatol. Res. 50(7): 791–816.
6. Drug Approval Package: U.S. Food and Drug Administration; Available from: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2002/21-511_Copegus.cfm.
7. EPAR-Public assessment report: European Medicines Agency; 2014. Available from: https://www.ema.europa.eu/en/documents/assessment-report/olysio-epar-public-assessment-report_en.pdf.
8. Fact sheets/Hepatitis C: World Health Organization; updated 27 July 2020. Available from: https://www.who.int/news-room/fact-sheets/detail/hepatitis-c
9. Global hepatitis report, 2017: World Health Organization; Available from: https://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/.
10. Kaishima, T., Akita, T., Ohisa, M., Sakamune, K., Kurisu, A., Sugiyama, A., et al. 2018. Cost-effectiveness analyses of anti-hepatitis C virus treatments using quality of life scoring among patients with chronic liver disease in Hiroshima prefecture, Japan. Hepatol. Res. 48(7): 509–520.
11. Kierepa, A., Witkowska, A., Kaczmarek, M., Książek, K., Mikuła-Pietrasik, J., Żeromski, J., et al. 2020. Impact of chronic HCV treatment on quality of life of patients with metabolic disorders in context of immunological disturbances. Sci. Rep. 10(1): 10388.
12. Marcellin, P., Chousterman, M., Fontanges, T., Ouzan, D., Rotily, M., Varastet, M., et al. 2011. Adherence to treatment and quality of life during hepatitis C therapy: A prospective, real-life, observational study. Liver Int. 31(4): 516–524.
13. Miyasaka, A., Yoshida, Y., Suzuki, A. and Takikawa, Y. 2021. Health-related quality of life in patients with chronic hepatitis C treated with sofosbuvir-based treatment at 1-year post-sustained virological response. Qual. Life Res. 30: 3501–3509.
14. Sibley, A., Han, K.H., Abourached, A., Lesmana, L.A., Makara, M., Jafri, W., et al. 2015. The present and future disease burden of hepatitis C virus infections with today's treatment paradigm—volume 3. J. Viral. Hepat. 22 Suppl 4: 21–41.
15. Tanaka, J., Akita, T., Ohisa, M., Sakamune, K., Ko, K., Uchida, S., et al. 2018. Trends in the total numbers of HBV and HCV carriers in Japan from 2000 to 2011. J. Viral. Hepat. 25(4): 363–372.
16. Tanaka, J. 2018. Report on the Awareness and Course of Action after Hepatitis Virus Testing. Japan: MHLW Scientific Research Subsidy, Research Project for Emergency Measures to Conquer Hepatitis, Japan: Ministry of Health, Labour and Welfare of Japan.
17. WHO Guidelines Approved by the Guidelines Review Committee. 2018. Guidelines for the Care and Treatment of Persons Diagnosed with Chronic Hepatitis C Virus Infection. Geneva: World Health Organization © World Health Organization 2018.
18. Xie, Q., Xuan, J.W., Tang, H., Ye, X.G., Xu, P., Lee, I.H., et al. 2019. Hepatitis C virus cure with direct acting antivirals: Clinical, economic, societal and patient value for China. World J. Hepatol. 11(5): 421–441.
19. Younossi, Z., Kallman, J. and Kincaid, J. 2007. The effects of HCV infection and management on health-related quality of life. Hepatology. 45(3): 806–816.
20. Younossi, Z. and Henry, L. 2015. Systematic review: Patient-reported outcomes in chronic hepatitis C—the impact of liver disease and new treatment regimens. Aliment Pharmacol. Ther. 41(6): 497–520.
21. Younossi, Z., Park, H., Henry, L., Adeyemi, A. and Stepanova, M. 2016. Extrahepatic manifestations of Hepatitis C: A meta-analysis of prevalence, quality of life, and economic burden. Gastroenterology. 150(7): 1599–1608.

SUPPLEMENTARY MATERIALS

Supplementary Table 1 EQ-5D-3L Questionnaire

Categories	Choice
MOBILITY	I have no problems in walking about
	I have some problems in walking about
	I am confined to bed
SELF-CARE	I have no problems with self-care
	I have some problems washing or dressing myself
	I am unable to wash or dress myself
USUAL ACTIVITIES*	I have no problems with performing my usual activities
	I have some problems with performing my usual activities
	I am unable to perform my usual activities
PAIN / DISCOMFORT	I have no pain or discomfort
	I have moderate pain or discomfort
	I have extreme pain or discomfort
ANXIETY / DEPRESSION	I am not anxious or depressed
	I am moderately anxious or depressed
	I am extremity anxious or depression

*(e.g. work, study, housework, family or leisure activities)