

Recommendations from primary care physicians, family, friends and work colleagues influence patients' decisions related to hepatitis screening, medical examinations and antiviral treatment

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Abstract. Identification and screening of patients with hepatitis B virus (HBV) or hepatitis C virus (HCV) is important to prevent liver cancer. Comprehensive antiviral treatments should follow three sequential steps: Hepatitis screening (step 1; examination of HB surface antigen and HCV antibody), medical examination (step 2; examination of HBV-DNA and/or HCV-RNA and performance of abdominal ultrasonography) and antiviral treatment (step 3). Patients who underwent these three steps were studied to determine effective information sources (factors) for raising awareness of comprehensive treatments. A total of 182 patients from 11 medical institutions were who were undergoing antiviral treatment were investigated. The number of patients who accessed each of the 18 information sources in each of the three steps and the percentage of these information sources that directly influenced the participants to make treatment-related decisions were calculated. 'Recommendation from a primary care physician' was the most common information source (64.3, 77.5, and 75.8% at steps 1, 2, and 3, respectively). 'Recommendation from a public health nurse (PHN),' 'recommendation from friends or family,' and 'recommendation from work colleagues' were the next most common human factors (3.3-19.8%). 'Recommendation from a primary care physician' had the greatest influence (76.9, 73.0, and 77.5% at

steps 1, 2, and 3, respectively). 'Recommendation from a PHN' (50.0, 26.3 and 64.3%), 'recommendations from friends and family' (58.3, 38.9 and 58.3%), and 'recommendations from work colleagues' (33.3, 33.3 and 42.9%) were highly influential factors. Media such as TV commercial messages and programs also had high recognition, but were not directly influential. The findings of the present study indicated that recommendations from primary care physicians, friends, family and work colleagues influenced patients' decision-making regarding hepatitis screening, examination and treatment.

Introduction

Chronic hepatitis B and C are caused by hepatitis B virus (HBV) and hepatitis C virus (HCV), respectively. Both cause liver cancer, but affected patients have few subjective symptoms (1-3). However, appropriate antiviral treatment can lower the risks associated with these conditions (4-6). Antiviral agents continue to improve, and a high percentage of patients with hepatitis C can achieve a sustained virological response with minimal adverse effects by using direct-acting antivirals (DAAs) (7-10). Additionally, in patients with hepatitis B, the levels of HB surface antigen (HBsAg) and HBV-DNA can be reduced using pegylated interferon or nucleotide analogues (11-14). Therefore, to prevent an increase in liver cancer, it is essential to improve the screening rates for viral hepatitis and administer appropriate antiviral treatment to patients with hepatitis. The following three steps are typically followed for comprehensive antiviral treatment: hepatitis screening, in which HBsAg and HCV antibody (HCVAb) are examined; medical examination for viral carriers, in which HBV-DNA and/or HCV-RNA are measured and imaging as abdominal ultrasonography is performed; and administration of individualized antiviral treatment or liver-supporting therapy (Fig. 1) (15).

As of 2011 in Saga prefecture, the rates of HBsAg and HCVAb positivity were 1.05 and 1.18%, respectively (16),

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which are higher than those of first blood donors from all of Japan (0.25-0.29% and 0.10-0.21%, respectively) (17). A rough estimate of the liver cancer rates in Saga prefecture for the 16-year period beginning in 1999 stands as the worst consecutive time period for liver cancer in all of Japan (18). Thus, reducing liver cancer mortality rates is one of the most important issues for Saga prefecture. Unfortunately, hepatitis screening rates remained low even in 2011: 26.3% for HBV and 47.0% for HCV. Additionally, 63.6% of viral carriers received a detailed examination, and 40.0% of both HBV and HCV carriers were accepted into antiviral treatment (16). In 2011, Saga prefecture established institutional protocols for the purpose of tracking a particular viral liver disease and established a Liver Center within Saga University Hospital in January 2012 (15). The Liver Center disseminates medical information to the public using various media. However, these enlightenment activities take time and are expensive. Therefore, it is essential to identify effective information sources (factors) that help patients to make better decisions.

Each of the three above-mentioned steps is expected to contribute to an increase in patients who reach the subsequent step and to expose which information sources may have led those patients to each step. The aim of our study was to determine which factors are effective in patients' decision-making processes from initial screening to receiving antiviral treatment.

Materials and methods

Study design and participants. During the 5-month period from March to August 2013, we recruited patients receiving antiviral treatment from one of the 11 medical institutions specializing in hepatitis treatment in Saga prefecture. Participants underwent face-to-face interviews by the hepatitis coordinator, who asked them about information sources that had affected their decision-making process, and filled in the unsigned questionnaire. Specifically, the questionnaire asked the participants which of 18 sources of information they had accessed (multiple choice answer) in each of the three steps mentioned above; which of the 18 information sources had been most influential (single answer) in each of the three steps; sex; age group; residential area; viral type; time of hepatitis screening; time of medical examination; and time of antiviral treatment. The hepatitis coordinators were paramedical staff members actively engaged in the field of liver disease, such as hospital nurses, public care nurses, pharmacists, and nutritionists.

In each of the three steps, we divided the number of participants who received all 18 information sources by the total number of participants to determine the participants' recognition of each information source. Then, to determine the influence of each information source (i.e., the direct influence that it provided each participant to reach the subsequent step), we divided the number of participants who answered, 'This information was most influential' by the number of participants who received each source of information.

The 18 sources of information that we investigated comprised 7 human factors, 10 public relations sources (social factors), and 1 other source. The seven human factors

Table I. Characteristics of patients who answered the questionnaire (n=182).

Variables	Number
Sex	
Male	93
Female	87
Unanswered	2
Age group	
20-29	5
30-39	16
40-49	24
50-59	49
60-69	61
70-79	23
80+	2
Unanswered	2
Residential area	
Middle	73
Eastern	2
Western	30
Southern	43
Northern	29
Other	5
Viral type	
HBV	24
HCV	153
Unanswered	5

HBV, hepatitis B virus; HCV, hepatitis C virus.

comprised recommendations from 'a primary care physician,' 'a hospital nurse,' 'a public health nurse (PHN),' 'a hepatitis coordinator,' 'a pharmacist,' 'friends or family,' and 'work colleagues.' The 10 social factors consisted of 'posters for enlightenment,' 'direct mail,' 'PR brochures from a city,' '3-minute TV programs for enlightenment,' 'a feature TV program about viral hepatitis and liver cancer,' 'a TV commercial message for enlightenment,' 'newspapers,' 'magazines,' 'websites about liver diseases,' and 'public lectures about liver diseases.' We defined 'hepatitis screening' as examinations that included tests for HBsAg and HCVAb, 'medical examination' as examinations that tested HBV-DNA or HCV-RNA and included imaging such as abdominal ultrasonography, and 'antiviral treatment' as a treatment plan that included pegylated interferon or nucleotide analogues for patients with HBV and pegylated interferon, ribavirin, and DAA for patients with HCV.

The present study was approved by the Institutional Review Board and Ethics Committee of Saga University Hospital (No. 2014-10-10) and conformed to the ethical guidelines of the 8th version of the Declaration of Helsinki (October 2013). We performed data extraction with consideration of the protection and privacy of our participants' personal information.

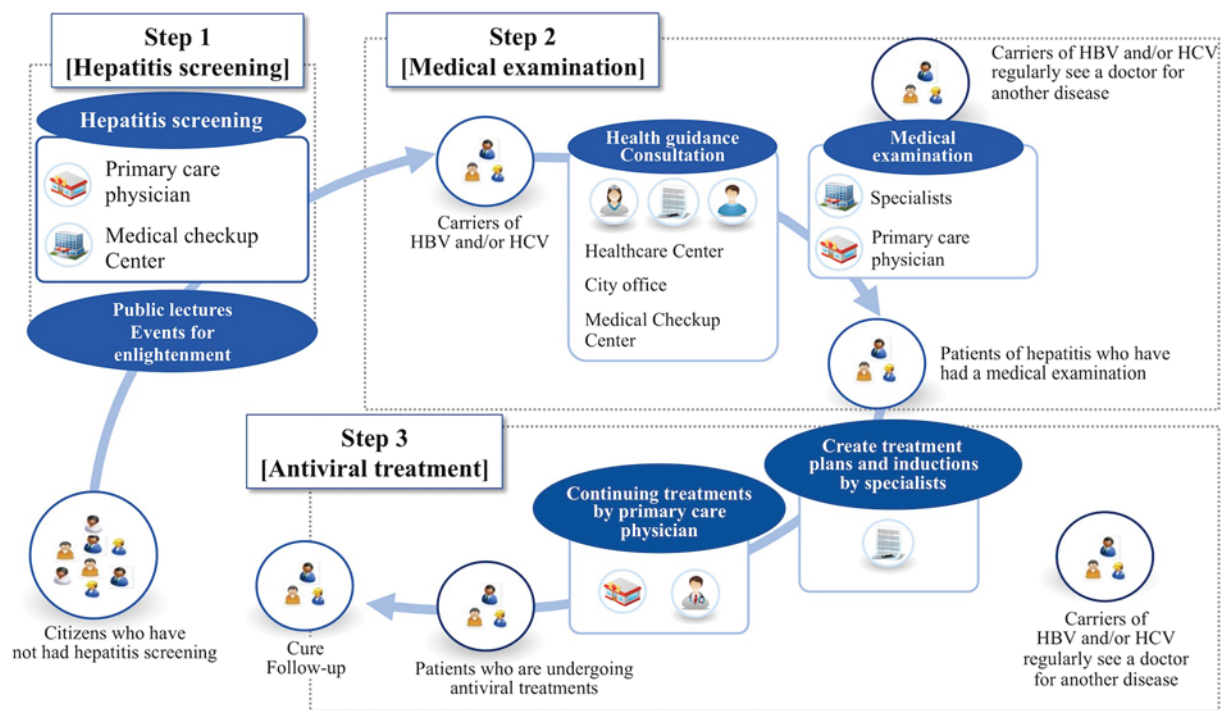


Figure 1. Examination and treatment process applied to individuals with chronic viral hepatitis. It is required that the patients pass through the three steps presented to receive appropriate antiviral treatment.

Statistical analysis. Microsoft Excel 2011 (Microsoft, Redmond, WA, USA) was used to aggregate the survey data and depict the scatter diagrams. Continuous variables are presented as mean (standard deviation) or median. Proportions and categorical variables were assessed using the χ^2 test or Fisher's exact test and residual analysis. $P < 0.05$ was considered to indicate a statistically significant difference. All analyses were carried out using IBM SPSS (v.21.0; SPSS, Tokyo, Japan).

Results

Background of participants. Table I shows the characteristics (including demographics) of the 182 participants who answered the questionnaire. They ranged in age from 20 to >80, and most were in their 60s. Of these participants, 93 (51.1%) were male and 153 (84.1%) were HCV carriers. We obtained questionnaire data from participants in all districts except the eastern district of the prefecture because there is no specialized medical institution in that region. Table II shows the time it took participants to progress from hepatitis screening through medical examination to antiviral treatment. Some participants could not answer this section because they forgot either the time at which they underwent hepatitis screening or the time at which they underwent medical examination. The median and mean periods of time between undergoing a hepatitis screening and undergoing a medical examination were 0.0 and 19.6 months, respectively, while the median and mean periods of time between undergoing a hepatitis screening and receiving an antiviral treatment were 8.0 and 56.2 months, respectively. Importantly, patients with HCV were classified into two groups: Those who had been receiving treatment for more than 10 years since their initial hepatitis screening, and those who had been treated for a short time since their initial

hepatitis screening. Data regarding the specific characteristics of these two groups are not shown.

Recognition and impact in the hepatitis screening step. Table III shows the number of participants who received information sources and who acted by direct influence of the information source at each of the three steps. Figs. 2-4 show the former and latter percentages in two dimensions for each of the three steps. In the first step (hepatitis screening), 117 (64.3%) participants received recommendations from their primary care physician, and 90 (76.9%) of these participants indicated that those recommendations were the most influential in their decision to undergo hepatitis screening (Fig. 2 and Table III). Another 13.2% of participants received recommendations from friends or family, and of those, 58.3% took the opportunity to act directly and get screened. From the information category of social factors, 13.7% of participants accessed a relevant TV commercial message; however, only 4.0% of this group took direct influence to undergo hepatitis screening.

Recognition and impact in the medical examination step. In the second step (medical examination), 77.5% of participants received recommendations from their primary care physician, of which 73.0% took direct action and underwent a medical examination (Fig. 3 and Table III). Recommendations from friends and family had a higher recognition rate than from PHC nurses (19.8% vs. 10.4%, respectively), but direct influence was not significant (38.9% vs. 26.3%, respectively; $P = 0.58$). In the information category of enlightenment activities, exposure to a TV commercial (20.3%) was higher than exposure to recommendations from humans except for those from primary care physicians; however, the relative

Table II. Time interval from hepatitis screening to antiviral treatment.

Variables	Total		HBV infected patient		HCV infected patient	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Hepatitis screening to medical examination (months)						
0-3	76	73.8	12	92.3	63	70.8
4-6	5	4.9	1	7.7	4	4.5
7-12	6	5.8	0	0	6	6.7
12-36	4	3.9	0	0	4	4.5
36-120	6	5.8	0	0	6	6.7
>120	6	5.8	0	0	6	6.7
Median	0		0		0	
Mean (SD)	19.6 (53.2)		0.7 (1.2)		22.6 (56.6)	
Medical examination to antiviral treatment (months)						
0-3	68	59.1	5	71.4	61	57.5
4-6	13	11.3	0	0	13	12.3
7-12	6	5.2	0	0	6	5.7
12-36	12	10.4	2	28.6	10	9.4
36-120	4	3.5	0	0	4	3.8
>120	12	10.4	0	0	12	11.3
Median	0		0		0	
Mean (SD)	27.7 (67.6)		8.1 (11.7)		29.4 (70.1)	
Hepatitis screening to antiviral treatment (months)						
0-3	32	32	3	42.9	28	30.4
4-6	16	16	0	0	16	17.4
7-12	7	7	1	14.3	6	6.5
12-36	9	9	1	14.3	8	8.7
36-120	16	16	1	14.3	15	16.3
>120	20	20	1	14.3	19	20.7
Median	8		7		8	
Mean (SD)	56.2 (90.0)		70.9 (132.1)		56.3 (86.2)	

HBV, hepatitis B virus; HCV, hepatitis C virus; SD, standard deviation.

impact of a TV commercial (5.4%) was significantly lower. Exposure to other social factors comprised public lectures (3.3% received, of which 16.7% took action), PR brochures (7.7% received, of which 14.3% took action), and websites (4.9% received, of which 11.1% took action); these sources might have served as direct opportunities for participants to some extent.

Recognition and impact in the antiviral treatment step. In the third step (antiviral treatment), more participants (75.8%) obtained recommendations from their primary care physician than from any other information source; this source also had the strongest impact (77.5%) of any information source (Fig. 4 and Table III). Although recommendations from PHNs (7.7%), friends and family (13.2%), and work colleagues (3.8%) represented a small proportion of participants' exposure to information, these sources had a high impact (64.3, 58.3, and 42.9%, respectively) on participants' decisions to accept antiviral treatment. In the category of social factors, despite wide

exposure, no source except PR brochures (7.1% received, of which 15.4% took action) evidenced an impact that led patients to accept antiviral treatment.

Recognition and impact after February 2013. Table IV shows the recognition and impact of participants who first accessed each step after February 2013, when the Liver Center began conducting enlightenment activities. In this period, recommendations from their primary care physician had a high impact in each of the three steps (100, 90.0, and 76.7%, respectively). Although relatively few participants received other sources of information, the recommendations that they received from friends and family also showed a high impact in each of the three steps (100, 100, and 50%, respectively). Recognition of a TV commercial in this period was significantly higher than that during the whole study period for step 3 (28.6% vs. 10.4%); however, no more than 10.0% of this group took direct influence to receive antiviral treatment.

Table III. Numbers of participants who received information sources and who acted in direct opportunity to the information source at each of the three steps.

Source of information	Step 1 hepatitis screening		Step 2 medical examination		Step 3 antiviral treatment	
	Participants who received information (%) ^a	Direct influence (%) ^b	Participants who received information (%) ^a	Direct influence (%) ^b	Participants who received information (%) ^a	Direct influence (%) ^b
Recommendations from human						
Recommendation from a primary care physician	117 (64.3)	90 (76.9 ^c)	141 (77.5)	103 (73.0 ^c)	138 (75.8)	107 (77.5 ^c)
Recommendation from a hospital nurse	19 (10.4)	2 (10.5)	36 (19.8)	6 (16.7)	25 (13.7)	4 (16.0)
Recommendation from a public health nurse	12 (6.6)	6 (50.0)	19 (10.4)	5 (26.3)	14 (7.7)	9 (64.3)
Recommendation from a hepatitis coordinator	19 (10.4)	2 (10.5)	31 (17.0)	3 (9.7 ^c)	24 (13.2)	2 (8.3 ^c)
Recommendation from a pharmacist	3 (1.6)	0	9 (4.9)	0	5 (2.7)	0
Recommendation from friends or family	24 (13.2)	14 (58.3)	36 (19.8)	14 (38.9)	24 (13.2)	14 (58.3)
Recommendation from work colleagues	9 (4.9)	3 (33.3)	6 (3.3)	2 (33.3)	7 (3.8)	3 (42.9)
Information provided passively						
Posters for enlightenment	15 (8.2)	1 (6.7)	20 (11.0)	0	11 (6.0)	0
Direct Mail	3 (1.6)	0	2 (1.1)	0	3 (1.6)	0
PR brochures from a city	12 (6.6)	1 (8.3)	14 (7.7)	2 (14.3)	13 (7.1)	2 (15.4)
3-minute TV programs for enlightenment	18 (9.9)	0	31 (17.0)	0	10 (5.5)	0
Feature TV program about viral hepatitis and hepatocellular carcinoma	17 (9.3)	0	19 (10.4)	0	20 (11.0)	0
TV commercial message for enlightenment	25 (13.7)	1 (4.0 ^c)	37 (20.3)	2 (5.4 ^c)	19 (10.4)	0
Newspapers	17 (9.3)	0	26 (14.3)	1 (3.8 ^c)	14 (7.7)	0
Magazines	6 (3.3)	0	10 (5.5)	0	5 (2.7)	0
Information obtained actively						
Websites about liver diseases	4 (2.2)	1 (25.0)	9 (4.9)	1 (11.1)	6 (3.3)	0
Public lectures about liver diseases	2 (1.1)	0	6 (3.3)	1 (16.7)	1 (0.5)	0
Others	15 (8.2)	4 (26.7)	15 (8.2)	1 (6.7)	9 (4.9)	3 (33.3)

^a100%=182. ^b100%=number of participants who received each source of information. ^cstatistically significant by χ^2 test ($P<0.05$).

Table IV. Number of participants who received information sources and who acted in direct opportunity to the information source at each of the three steps (after February 2013).

Source of information	Step 1 hepatitis screening		Step 2 medical examination		Step 3 antiviral treatment	
	Participants who received information (%) ^a	Direct influence (%) ^d	Participants who received information (%) ^b	Direct influence (%) ^d	Participants who received information (%) ^c	Direct influence (%) ^d
Recommendations from human						
Recommendation from a primary care physician	2 (28.6)	2 (100)	10 (71.4)	9 (90.0)	30 (85.7)	23 (76.7)
Recommendation from a hospital nurse	1 (14.3)	0	3 (21.4)	0	5 (14.3)	0
Recommendation from a public health nurse	0		0		1 (2.9)	0
Recommendation from a hepatitis coordinator	1 (14.3)	0	3 (21.4)	0	10 (28.6)	0
Recommendation from a pharmacist	0		1 (7.1)	0	0	
Recommendation from friends or family	3 (42.9)	3 (100)	2 (14.3)	2 (100)	10 (28.6)	5 (50.0)
Recommendation from work colleagues	1 (14.3)	0	0		2 (5.7)	1 (50.0)
Information provided passively						
Posters for enlightenment	1 (14.3)	0	4 (28.6)	0	9 (25.7)	0
Direct Mail	0		0		0	
PR brochures from a city	0		1 (7.1)	1 (100)	2 (5.7)	0
3-minute TV programs for enlightenment	1 (14.3)	0	2 (14.3)		8 (22.9)	0
Feature TV program about viral hepatitis and hepatocellular carcinoma	1 (14.3)	0	2 (14.3)	0	3 (8.6)	0
TV commercial message for enlightenment	0		4 (28.6)	0	10 (28.6)	1 (10.0)
Newspapers	0		1 (7.1)	0	6 (17.1)	1 (16.7)
Magazines	0		0		1 (2.9)	0
Information obtained actively						
Websites about liver diseases	0		0	0	1 (2.9)	0
Public lectures about liver diseases	0		0	0	0	
Others	2 (28.6)	2 (100)	2 (14.3)	2 (100)	1 (2.9)	1 (100)

^a100%=7. ^b100%=14. ^c100%=35. ^d100%=number of participants who received each source of information.

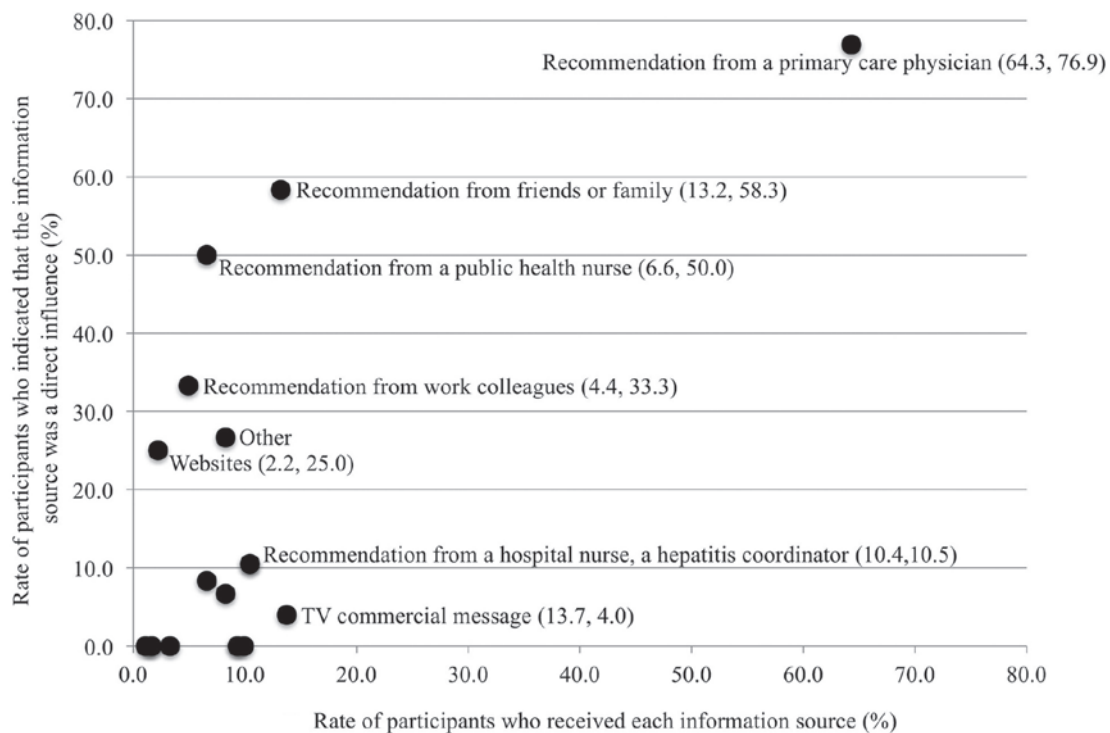


Figure 2. Scatter diagram of participants' awareness of information sources and their relative impact at step 1 (hepatitis screening). The horizontal axis indicates the rate of participants who received each information source during hepatitis screening (n=182). The vertical axis presents the rate of participants who indicated that the information source was a direct influence (100%=number of participants who received each information source).

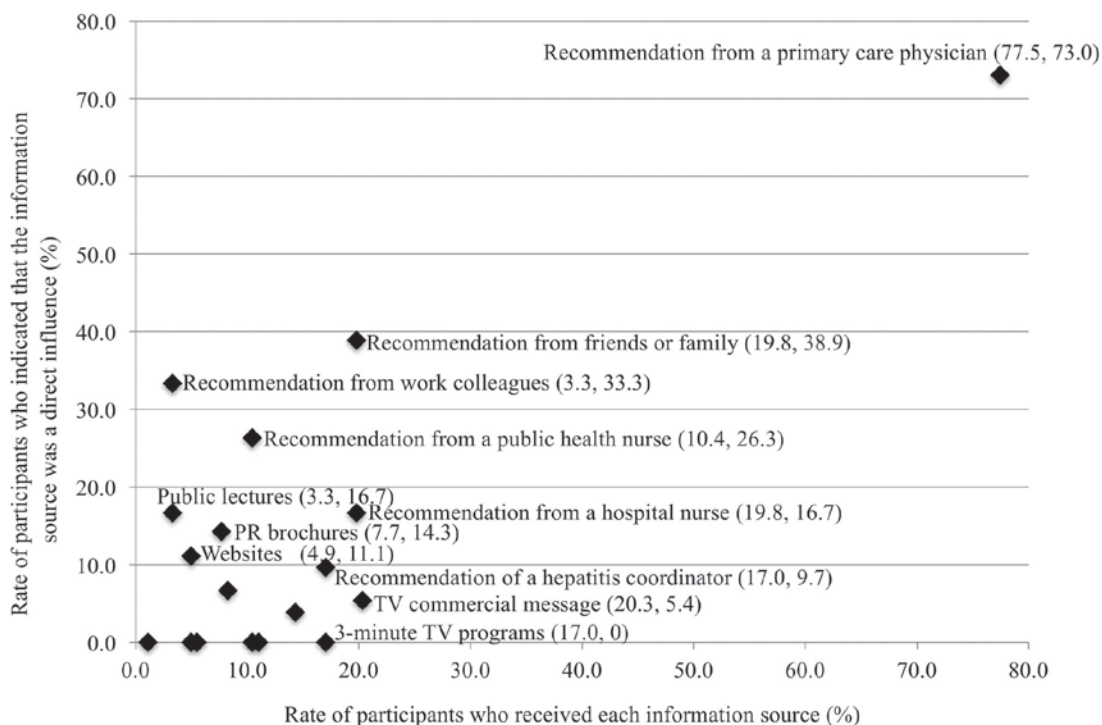


Figure 3. Scatter diagram of participants' awareness of information sources and their relative impact at step 2 (medical examination). The horizontal axis presents the rate of participants who received each information source during medical examination (n=182). The vertical axis presents the rate of participants who indicated that the information source was a direct influence (100%=number of participants who received each information source).

Differences in sex, age group, and viral type. We found no significant differences in the results in any of the three steps according to sex, age group, or viral type. We also found no

significant differences in the results between the two groups of patients with HCV classified by the time from hepatitis screening to antiviral treatment.

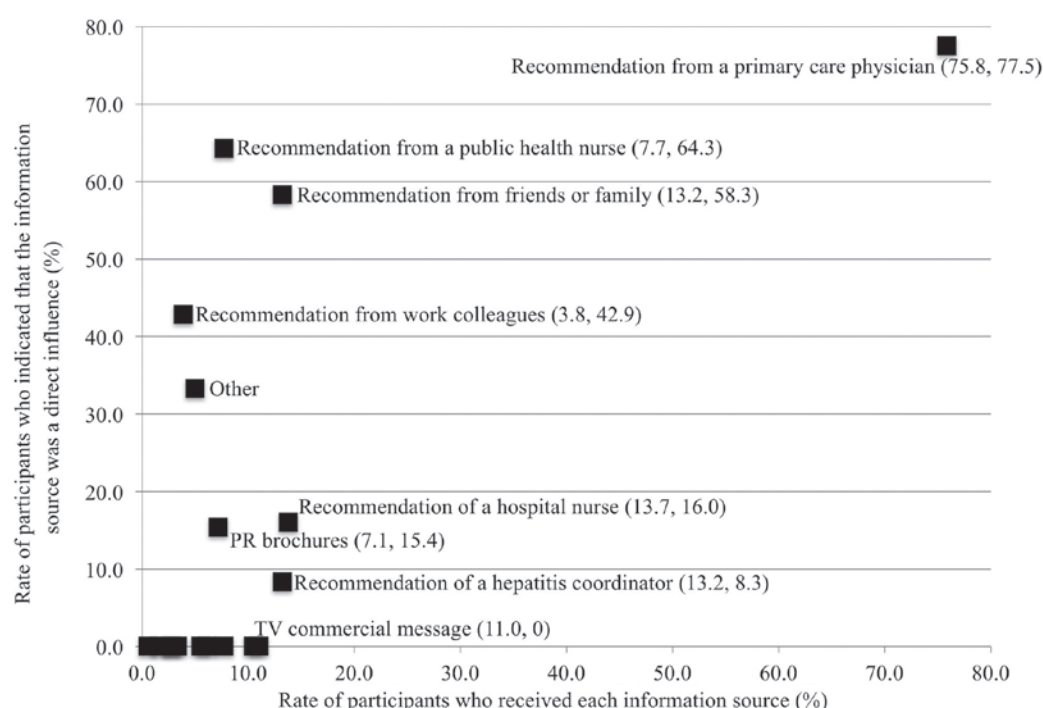


Figure 4. Scatter diagram of participants' awareness of information sources and their relative impact at step 3 (antiviral treatment). The horizontal axis presents the rate of participants who received each information source during antiviral treatment ($n=182$). The vertical axis presents the rate of participants who indicated that the information source was a direct influence (100%=number of participants who received each information source).

Discussion

The present study is the first to assess factors that influence citizens' recognition and decisions about receiving antiviral treatment for viral liver disease in Japan. Most patients in this study received recommendations from a primary care physician and were strongly influenced by this factor in their decisions. Therefore, we believe that primary care physicians who promote appropriate antiviral therapy can be an important factor in the prevention and management of liver cancer. Furthermore, recommendations from friends, family, or work colleagues appear to have as much power as those from a PHN to move patients toward a decision. Within each of the three steps, hospital nurses had many opportunities for contact with patients, but PHNs were more effective in taking advantage of opportunities to persuade the patient directly. With respect to educational activities, the majority of participants were most aware of TV commercials. However, public lectures, PR brochures, and websites might also have persuasive power with patients.

With respect to the influence a primary care physician can have on patient decision-making, a previous study showed that primary care physicians' encouragement of patients to undergo cancer screening did not increase the number of examinees (19). In contrast, another study showed that the primary reason patients with arthritis chose not to use disease-modifying anti-rheumatic drugs was 'because the doctor did not recommend it' (20). One study regarding the influence of others on patient decision-making revealed that family and friends were involved in the decision-making process around active surveillance (i.e., actively awaiting treatment) in patients with prostate cancer (21). However, these findings do not specify their impact.

Another study showed that nurses affect the decision-making of patients with breast cancer (22). Our study is the first to examine factors that influence the treatment-related decisions of patients with viral liver disease.

In agreement with previous research, our findings indicate that primary care physicians are a strong force in patients' health-related decision-making processes and can thus improve the likelihood of a patient receiving detailed examinations and antiviral therapy for viral liver disease. Furthermore, this study shows that it is possible to quantify that influence on participants. Importantly, although recommendations from family, friends, and work colleagues affected a high percentage of the decision-making process of patients with viral liver disease, we do not consider them to be strong factors because very few participants accessed them. PHNs might have more influence on patients than hospital nurses; a difference in job descriptions was considered one of the reasons. That is, a PHN's focus is the prevention of disease progression, while a hospital nurse's main work is caring for patients. Of all social factors that we investigated, websites and public lectures were the factors that participants searched and visited independently. Thus, it is understandable that these two sources became influential factors in interested participants' decision-making process. In contrast, other factors were observed regardless of a participant's intentions.

Because the primary care physician has a strong influence on the decision-making of the patient, an increase in the number of both liver disease specialists and primary care physicians with an interest in liver disease is important for the prevention and management of liver cancer. Few participants received a recommendation from family, friends, or work colleagues; however, because those particular sources have considerable influence

in moving patients toward healthy decisions, increasing the opportunities for patients to access those factors could be an effective strategy. Finally, although participants were not moved directly to make decisions about liver screening or therapy based on information gleaned from the media, their awareness of this source was high. Given that the provision of appropriate information is assumed to improve the right knowledge of citizens, it might also improve the right knowledge of other persons involved in the patient's life, and then their recommendations would influence the patients. We suggest that synergy of human and media sources may contribute to effective management of viral hepatitis and liver cancer.

Our study of patients with HCV involved two groups: Patients who had been receiving treatment for more than 10 years since their initial hepatitis screening and those who had been treated for a short time since their hepatitis screening. There were no significant differences in the characteristics of the two groups, such as sex, age group, residential area, or information sources. Further investigation into the former group might contribute to the identification of different factors that urge HCV-positive persons to undergo antiviral treatment.

We assessed the recognition of aggressive enlightenment activities and their impact on participants during the period when these activities were conducted. During this period, human factors might have influenced the decision-making process of the patient. Recognition of TV commercials increased, and the results showed that TV commercials were watched. However, it was difficult for commercials to directly influence the decision making of the patient. The benefit of media is the ability to send information to people who are not interested and allow them to recognize information regarding diseases. However, a very large amount of information is presented by the media; people recognize information regarding diseases, but they receive it as only one aspect of a very large amount of information. This is why it may be difficult for the media to influence patients' decision making. In addition, use of the media is associated with certain costs, and we did not examine outcomes and cost-effectiveness in the present analysis.

One limitation of this study was the small sample size. Furthermore, the etiology of liver disease among the enrolled patients included both HBV and HCV because there were fewer patients with HBV than HCV. In fact, these etiologies differ, and patients with HBV and HCV should ideally be analyzed separately. Moreover, sex- and age-related differences might be revealed in a larger sample of patients. Another limitation was the data collection method. The hepatitis coordinators collected the data retrospectively. Thus, information bias and selection bias may have been present. Furthermore, the hepatitis coordinators comprised paramedical staff members, so human factors were duplicated. We might not have obtained accurate results. It should also be noted that this study was conducted during a time when interferon-based treatment was mainstream; had DAA treatment been mainstream, different results may have been obtained. Finally, we did not analyze sex- or age-related differences in the participants' decisions to take subsequent steps. The older citizens become, the more they may go to the hospital, and they tend to receive recommendations from their primary care physician more often as they become older.

Practically, clinical doctors have the right of final decisions regarding examinations. Additional analysis of such factors could lead to better insights into more effective strategies in patients' decision-making process.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contribution

MO, NK and YE designed the present study. MO, SO, SI, YK and KM acquired, analyzed and interpreted the data, and drafted the manuscript. SK, YT and JF performed statistical analysis. HT and KA developed the study protocol, generated the original database and supervised the current study. KA and YE gave final approval of the version to be published. MO and NK analyzed data using various software applications. SO, SI and YE assessed data integrity and the accuracy of data analysis. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Institutional Review Board and Ethics Committee of Saga University Hospital (approval no. 2014-10-10) and conformed to the ethical guidelines of the 8th version of the Declaration of Helsinki (October 2013). An opt-out approach was used to obtain informed consent from the patients and personal information was protected during data collection.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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