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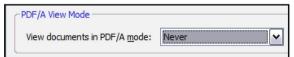
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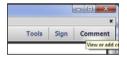


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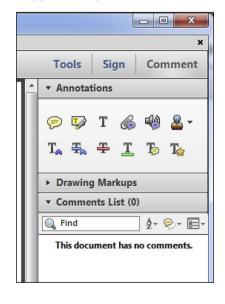
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Annals of Hepatology xxx (2025) 102134



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Original article

A multinational survey of physician knowledge about management of chronic hepatitis C

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ABSTRACT

Introduction and Objectives: Up-to-date knowledge of hepatitis C virus (HCV) management among healthcare providers is crucial for improving patient outcomes. This study evaluates physicians' awareness, attitudes, self-efficacy, perceptions, and barriers related to current HCV management guidelines and post-treatment follow-up.

Materials and Methods: We invited healthcare providers treating HCV patients to complete a 48-question survey regarding their practices, guideline familiarity, and related attitudes.

Results: The survey was completed by 183 physicians from 8 countries, including hepatologists (32 %), gastroenterologists (39 %), internal medicine specialists (12 %), and infectious disease specialists (16 %). The majority (95 %) were aware of at least one treatment guideline, with the EASL guideline cited by 84 % and the AASLD guideline by 72 %. Most (94 %) believed post-HCV treatment follow-up was effective for detecting complications, and 93 % recommended continued follow-up. Although 90 % felt well-informed about guidelines, 39 % reported encountering inconsistencies. Sixty-one percent recognized that HCV elimination reduces the rate of decompensation but does not abolish the risk of hepatocellular carcinoma (HCC). Overall, 86 % acknowledged the need for follow-up in patients who achieved sustained virological response (SVR), with the most commonly recommended intervals being six months for non-cirrhotic patients and three months for cirrhotic patients. Minimal barriers to follow-up were reported, with only 1.6 % to 4.4 % not discussing its benefits due to time or resource constraints.

Abbreviations: AASLD, American Association for the Study of Liver Diseases; APASL, Asian Pacific Association for the Study of the Liver; DAAs, direct-acting antiviral agents; EASL, European Association for the Study of the Liver; HCC, hepatocellular carcinoma; HCP, health care provider; HCV, hepatitis C virus; IFN, interferon; NASH, nonalcoholic steatohepatitis; SVR, sustained virologic response; UCHID, United Conference of Hepato-Gastroenterology and Infectious Diseases; UK, United Kingdom; USA, United States of America; WHO, World Health Organization

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> Conclusions: The surveyed physicians demonstrated a strong awareness of the current HCV guidelines but indicated potential gaps in knowledge and inconsistencies. Continuous education and support are essential to enhance adherence to HCV management protocols.

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1 1. Introduction

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M. El-Kassas, Y. Yilmaz, C.-J. Liu et al.

Hepatitis C virus (HCV) infection continues to be a global health crisis. According to the World Health Organization (WHO) estimates, in 2019, there were approximately 58 million individuals living with chronic HCV infection, and 400,000 deaths occurred annually [1]. Over the years, chronic HCV infection has been a leading cause of cirrhosis, HCC, and end-stage liver failure requiring liver transplantation [2]. Interferon (IFN)-based therapy was the sole treatment for HCV infection until 2011, but it had unsatisfactory outcomes and unfavorable side effects profile for many years.

Hepatitis C treatment has evolved rapidly, and several new directacting antivirals (DAAs) have been approved since WHO issued its first hepatitis C guidelines in 2014 [3]. These drugs have demonstrated high efficacy and safety profiles, enabling viral eradication even in patients with decompensated cirrhosis. As a result, a growing number of patients have achieved sustained virological response (SVR). Currently, a fixed dose of DAAs is accepted as the standard of care for HCV treatment for 8-12 weeks [4]. The SVR in non-cirrhotic patients exceeds 95% for all genotypes and 80-90% in cirrhotic patients [5]. For these reasons, eligibility criteria have become more liberal. Therefore, the WHO implemented a strategy in 2016 aimed at eradicating HCV infection as a public health threat by 2030. This strategy has been defined as achieving a 90 % reduction in number of new chronic infections and 65% reduction in mortality rates compared to 2015 levels [1,3]. Additionally, some countries have or are expanding their HCV treatment programs to treat all patients with HCV infection and 'eliminate' HCV in their populations.

Previous studies have shown that patients who achieve SVR tend to experience improvements in liver inflammation, fibrosis, and extrahepatic manifestations independent of the stage of the underlying liver disease [6,7]. However, in patients with advanced fibrosis or cirrhosis, long-term data show that HCV eradication does not eliminate the risk of HCC, warranting continued surveillance, especially when cofactors such as alcohol use, obesity, or type 2 diabetes are present [7–9]. Therefore, patients with advanced fibrosis (METAVIR score F3) and cirrhosis (F4) who achieve SVR should remain under surveillance for HCC every six months using liver ultrasound, and alpha-fetoprotein measurement. Additionally, surveillance for esophageal varices using endoscopy should be undertaken as recommended every 1-2 years [3,4,10]. To maximize the benefit of therapy, the risks of reinfection should be emphasized to patients at risk as well as positively reinforcing behavioral modifications.

Many hepatitis treatment guidelines are available, such as: the WHO guidelines for the screening, care, and treatment of patients with chronic HCV infection [1], the American Association for the Study of Liver Diseases (AASLD) HCV guidelines [10], the European Association for the Study of the Liver (EASL) recommendations on treatment of Hepatitis C [4] and the Asian Pacific Association for the Study of the Liver (APASL) that offer regionspecific guidance for HCV management [13,14]. In addition, national guidelines address specific demographic populations and offer tailored recommendations that help to optimize treatment decisions for different patient groups. The overall shared goals of these guidelines are to provide evidence-based treatment recommendations for using approved DAA therapy and to provide recommendations for the screening and follow-up care of patients with chronic HCV infection.

Healthcare providers (HCPs) play a crucial role in HCV management, including screening, diagnosis, treatment, and post-treatment 60 follow-up. Therefore, HCPs must be aware and up to date with the 61 recent guidelines related to HCV management using DAA therapy, 62 particularly for specific high-risk groups of patients who are at high risk of developing complications, such as cirrhosis or HCC after DAA discontinuation. Moreover, HCPs should maintain a positive attitude 65 that motivates them to engage with patients, promoting better 66 adherence to medication, ensuring regular follow-up appointments, and raising patients' awareness about the screening program, time, and frequency essential to control disease stage progression and detect early complications. This is particularly important in countries like Egypt, which has implemented large-scale mass treatment program and treated more than a million patients [15]. The lack of a well-established post-treatment follow-up program for patients completing HCV treatment highlights the role of clear instructions that could be given to patients through the treating physician during treatment duration.

Annals of Henatology xxx (2025) 102134

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In this context, we internationally surveyed a group of physicians 77 involved in HCV management, aiming to assess their awareness, familiarity with the international guidelines, attitudes, self-efficacy, perceptions, and barriers related to HCV management and post-treatment follow-up practice.

2. Materials and methods

2.1. Study sample

While no formal sample size calculation was conducted, a mini- 84 mum of 180 responses was considered adequate for detecting moderate differences (Cohen's h = 0.4) between groups at 80% power with α =0.05. Physicians directly involved in HCV management, defined as those prescribing antiviral therapy or managing posttreatment follow-up, were eligible to complete a specifically designed 48-question survey. Survey domains were related to the 90 physicians' HCV practice, familiarity with guidelines, attitudes, perception, self-efficacy, and barriers they have in their practice. The survey was administered in English. Countries were included based on 93 existing collaborations within the Global NASH Council and the presence of investigators able to coordinate national dissemination. 95 Between June 2022 and April 2023, each national investigator disseminated the survey link to relevant specialists in their respective 97 countries through professional networks, institutional mailing lists, and national gastroenterology or hepatology societies. Participation was voluntary, anonymous, and open to all eligible providers.

2.2. The HCV provider survey

The survey was developed by the study team based on previously 102 validated frameworks [16], and subsequently reviewed by an international panel of HCV experts to ensure content validity and contextual relevance. Minor modifications were made following pilot 105 testing with five practicing HCV specialists. Survey authors did not 106 participate as respondents. Their role was limited to study design, 107 survey dissemination oversight, and manuscript preparation.

For this study, physicians' awareness of HCV treatment guidelines 109 was assessed through a list of questions about their familiarity with 110 and accessibility to the guidelines. In addition, attitudes regarding 111 the importance of post-HCV treatment follow-up were assessed 112

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M. El-Kassas, Y. Yilmaz, C.-J. Liu et al. Annals of Hepatology xxx (2025) 102134

through agreement with a series of statements related to outcome expectancy, perception of the guidelines (strength of evidence and conflicting guidelines), and self-efficacy (comfort while caring for HCV patients and ability to reduce post-treatment risks). Physician perceived external barriers to guidelines adherence were evaluated in the form of agreement with statements addressing time and resource barriers. The level of agreement with each statement was assessed using a 5-point Likert-type scale ranging from (1) strongly disagree to (5) strongly agree. Basic physician and practice characteristics such as specialty, career level, practice setting, and the number of HCV patients seen in each period of time, were also collected through the survey.

The survey was self-administered through an online survey platform and completed by participating HCPs using their own electronic devices. The online survey required a click to confirm participation that was displayed before any survey questions appeared so that respondents could read the informed consent form first and then click "Yes" to agree and begin the survey; an option to click "No" and close the page was also provided. The informed consent stated that the respondents could refrain from answering any question that they preferred not to answer either by selecting the "Decline to answer" option or by skipping the question. Respondents were grouped into 'hepatologists and gastroenterologists' and 'other specialties' for comparison, 'Other specialties' includes infectious disease and internal medicine physicians who were actively involved in HCV care. Working days per week were collected to explore if clinical time investment influenced adherence to guidelines.

140 2.3. Statistical analysis

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Only subjects completing the survey and pressing the "Submit" button were included in the study sample. However, the electronic data collection system did not require answering all the questions to submit the survey; in case of missing data, only observed data were used for analysis. The distributions of answers are summarized as number and frequencies (%) for categorical variables and as mean \pm SD for continuous variables. Comparison between groups were performed using chi-square for categorical parameters and Kruskal-Wallis for continuous parameters. All analyses were conducted in SAS version 9.4 (SAS Institute, Cary, NC, USA).

2.4. Ethical statement 151

This study was granted ethical approval by the Inova Health Care System Institutional Review Board, Falls Church, VA, USA. All participants consented prior to the beginning of the survey administration through the "click to consent" process. However, this survey was strictly anonymous. No personal identifiers were collected. This was a one-time questionnaire, and subjects were not re-contacted. All the answers were centrally stored in a secure electronic database and analyzed in the aggregate. The full survey instrument is provided as Supplementary File 1. Furthermore, all research was conducted in accordance with both the Declarations of Helsinki and Istanbul.

3. Results

3.1. Participant characteristics

A total of 183 HCPs from 8 countries completed the survey: 44% from Turkey, 28 % from Egypt, 21 % from Taiwan, 6 % from the USA, and <1 % from Cuba, Greece, Malaysia, and the UK. Because recruitment was via institutional and society mailing lists, the denominator of invited participants is unknown, and a response rate could not be calculated. About one-third (32%) of the participants were hepatologists, 39 % were gastroenterologists, 12 % were internal medicine, and $16\,\%$ were infectious disease specialists. Overall, $60\,\%$ of respondents

were hospital-based, with mean 18 ± 11 years of practice, managing 172 a median (IQR) of 50 (20–250) HCV patients per year (Table 1).

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The distribution of provider and practice characteristics was comparable between specialists (hepatologists and gastroenterologists) and other medical specialties, with no statistically significant differences (p > 0.05) (Table 1).

3.2. Awareness and sources of knowledge

When asked to mention all the HCV treatment guidelines they 179 knew (95 % knew at least one), AASLD, EASL, APASL, and WHO guidelines were mentioned by 73 %, 85 %, 12 %, and 29 %, respectively. Nonspecialists mentioned national guidelines in addition to international ones more frequently than specialists (gastroenterologists and hepatologists): 42% vs. 26% (p = 0.04) (Table 2). The most common source of knowledge about the guidelines was the Internet (48%), followed by conferences (23%). The term 'Internet' includes official society websites (e.g., AASLD, EASL), open-access platforms, and online CME tools, but may also have also encompassed unvetted sources suggesting that greater scrutiny is needed to evaluate how source credibility impacts practice. The distribution of answers was similar across medical specialties, although specialists more commonly used medical journals compared to non-specialists (15 % vs. 4 %, p = 0.04) (Table 2). The most followed guideline was EASL (46%), followed by AASLD (23 %), with no significant differences across specialties (all p > 0.05) (Table 2). Of all survey completers, 50 % reported regularly attending workshops, conferences, or training courses about HCV treatment, most commonly those organized by AASLD, EASL, and the United Conference of Hepato-Gastroenterology and Infectious Diseases (UCHID) (10–12 % each). The distribution of answers was again similar across medical specialties (all p > 0.05) (Table 2). At least 70 % of HCPs applied all guidelines during their routine work, while 4–14% selected only specific sections (pretreatment assessment, treatment, or management of special populations) (Table 2).

3.3. Attitudes and self-efficacy

In the context of attitude, perception, and self-efficacy, 94 % of the 205 respondents believed that post-treatment follow-up is effective for early detection of HCC, cirrhosis, and other complications among 207 treated HCV patients, and 93 % recommended that their patients continue with post-treatment follow-up (Table 3). In addition, 91% of 209 respondents believed that guidelines for HCV treatment were based on sound evidence, but 39 % reported some inconsistencies (Table 3). Finally, 85% of respondents were confident in their ability to reduce the risk of HCC or cirrhosis in patients with HCV, and 90% reported feeling well-informed about guidelines for HCV treatment (Table 3). All these answers were similarly distributed between specialist and non-specialist providers (all p > 0.05) (Table 3).

3.4. Clinical practices and knowledge gaps

Regarding specific aspects of knowledge, 61% of respondents 218 were aware that in patients with advanced fibrosis and cirrhosis, 219 HCV elimination reduces the rate of decompensation but does not 220 abolish the risk of HCC. The difference between specialists and nonspecialists (65 % vs. 51 %) was not statistically significant (p = 0.09) 222 (Table 4). In addition, 81% believed that surveillance for HCC in 223 patients with advanced fibrosis and cirrhosis should be continued 224 forever (Table 4). Assessment of the liver fibrosis stage using non- 225 invasive tests (NITs) alone prior to treatment was reported by 79%, and 12% reported using both NITs and liver biopsy (Table 4). For 227 assessing the fibrosis stage, 85% of respondents believed that liver 228 biopsy should be reserved for cases where there is uncertainty or suspected additional etiologies of chronic liver disease (Table 4).

Description of the sample of healthcare providers who completed the survey.

Answer	Hepatologists and gastroenterologists	Other specialties	p	All providers
N	130	53		183
Country				
Cuba	1 (0.8 %)	0 (0.0 %)	0.52	1 (0.5 %)
Egypt	37 (28.5 %)	14 (26.4 %)	0.78	51 (27.9 %)
Greece	1 (0.8 %)	0 (0.0 %)	0.52	1 (0.5 %)
Malaysia	1 (0.8 %)	0 (0.0 %)	0.52	1 (0.5 %)
Taiwan	23 (17.7 %)	15 (28.3 %)	0.11	38 (20.8 %)
Turkey	58 (44.6 %)	22 (41.5 %)	0.70	80 (43.7 %)
UK	1 (0.8 %)	0 (0.0 %)	0.52	1 (0.5 %)
USA	8 (6.2 %)	2 (3.8 %)	0.52	10 (5.5 %)
Practice setting				
Hospital-based	73 (56.2 %)	37 (69.8 %)	0.09	110 (60.1 %)
Group practice	2 (1.5 %)	0 (0.0 %)	0.36	2 (1.1%)
Solo private practice	3 (2.3 %)	1 (1.9%)	0.86	4 (2.2 %)
Clinic-based	4 (3.1 %)	4 (7.5 %)	0.18	8 (4.4%)
Primary Practice	0 (0.0 %)	1 (1.9 %)	0.12	1 (0.5 %)
Hepatology	21 (16.2 %)	5 (9.4 %)	0.24	26 (14.2 %)
Gastroenterology	27 (20.8 %)	2 (3.8 %)	0.0043	29 (15.8 %)
Other	0 (0.0 %)	3 (5.7 %)	0.0062	3 (1.6%)
Career Level				
Resident	4 (3.1 %)	5 (9.4%)	0.07	9 (4.9 %)
Specialist	83 (63.8 %)	34 (64.2 %)	0.97	117 (63.9 %)
Consultant	35 (26.9 %)	7 (13.2 %)	0.0454	42 (23.0 %)
Advance Practice Provider (NP or PA)	3 (2.3 %)	1 (1.9 %)	0.86	4 (2.2 %)
Other	5 (3.8 %)	6 (11.3 %)	0.05	11 (6.0 %)
Specialty				
Internal medicine	0 (0.0 %)	22 (41.5 %)		22 (12.0 %)
Infectious diseases	0 (0.0%)	29 (54.7 %)		29 (15.8 %)
Hepatology	58 (44.6 %)	0 (0.0 %)		58 (31.7 %)
Gastroenterology	72 (55.4 %)	0 (0.0 %)		72 (39.3 %)
Other	0 (0.0%)	2 (3.8 %)		2 (1.1%)
Number of years in practice (mean \pm SD)	18.4 ± 11.2	16.5 ± 10.7	0.26	17.8 ± 11.1
Number of patients with HCV seen per year (median (IQR))	60 (20-200)	50 (20-250)	0.56	50 (20-250)
Working days in the center (number of working days/week)	4.53 ± 1.30	4.62 ± 1.42	0.81	4.56 ± 1.33

HCV, Hepatitis C Virus; IQR, inter-quantile range; NP, nurse practitioner; PA, physician assistant; SD, standard deviation; UK, United Kingdom: USA, United States of America.

231 3.5. Surveillance and follow-up

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After treatment, 65% of HCPs reported asking their non-cirrhotic patients with SVR-12 to repeat ALT and HCV RNA assessments at a later time. Additionally, 96% of HCPs explained the risk of reinfection to patients from high-risk populations, and 87% recommended annual HCV RNA testing to patients from those populations (Table 5). Furthermore, 91 % of HCPs advised their SVR patients to get HBV vaccination (Table 5). Overall, 86 % believed that there was a need for following up patients who achieved SVR, with the most commonly recommended follow up periods being 6 months for non-cirrhotic patients and three months for cirrhotic patients. However, hepatologists and gastroenterologists more commonly believed that there was no need to follow-up non-cirrhotic patients compared to other specialists (49 % vs. 28 %, respectively) (Table 5).

During follow-up, the majority of providers (88-96%) would order liver chemistry tests, alpha fetoprotein, and abdominal ultrasound; 70% would also do complete blood counts, while only 35% would double-check HCV RNA levels (Table 5).

3.6. Barriers to implementation 249

Regarding barriers, only 1.6 % to 4.4 % of respondents reported not informing their HCV patients about post-treatment follow-up or its potential benefits due to a lack of time or resources (Table 6).

253 4. Discussion

This international survey aimed to assess the knowledge, attitude, 254 self-efficacy, and barriers of HCPs related to HCV management and 255

post-treatment follow-up guidelines. While much of the data are 256 descriptive, our findings highlight subtle but meaningful discrepancies between guideline awareness and actual implementation, influenced by provider specialty and region. These insights may inform targeted educational interventions and support systems. To contextualize practice variability, it is important to note that Turkey and Egypt have implemented large-scale national HCV programs, whereas Taiwan has a more limited framework. This may contribute to differences in guideline use and perceptions.

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In this study, we demonstrated that the included HCPs exhibited a high level of awareness of HCV treatment guidelines. The strong influence of AASLD (73%) and EASL (85%) guidelines in HCV underscores their global recognition and trust, likely due to their broad dissemination and solid evidence base. In comparison, 269 APASL and WHO guidelines may be more regionally focused. Furthermore, our results indicate that EASL guidelines are followed 271 by 46% of respondents, while AASLD guidelines are followed by 272 23 % of respondents; this variation reflects differences in regional 273 influence and prominence, as most of the included respondents 274 were from countries more familiar with EASL guidelines. For 275 instance, the predominance of EASL use corresponds with the 276 large number of respondents from Turkey and Egypt, where these 277 guidelines are more familiar and accessible.

It is noted that the participants predominantly relied on two sources of knowledge related to HCV guidelines: the Internet (48%) and 280 conferences (23%). Specialists were more inclined to utilize medical 281 journals as additional sources of information. These results highlight 282 the important role of online resources as a primary and readily accessible source of up-to-date medical information. Additionally, conferences are another valuable source of updated knowledge, providing 285 M. El-Kassas, Y. Yilmaz, C.-I. Liu et al.

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Annals of Henatology xxx (2025) 102134

Table 2 Awareness about the HCV treatment guidelines among healthcare providers.

Question	Hepatologists and gastroenterologists	Other specialties	p	All providers
Are you aware of the current HCV treatment guidelines? "yes" [n (%)]	122 (93.8 %)	51 (96.2 %)	0.52	173 (94.5 %)
Mention all the guidelines you know				
AASLD	94 (72.3 %)	39 (73.6 %)	0.86	133 (72.7 %)
EASL	112 (86.2 %)	44 (83.0 %)	0.59	156 (85.2 %)
APASL	18 (13.8 %)	4 (7.5 %)	0.23	22 (12.0%)
WHO	34 (26.2 %)	19 (35.8 %)	0.19	53 (29.0 %)
NCCVH	5 (3.8 %)	0 (0.0 %)	0.15	5 (2.7 %)
CDC	3 (2.3 %)	1 (1.9%)	0.86	4 (2.2 %)
National (Egyptian, Turkish, Greek, unspecified)	34 (26.2 %)	22 (41.5%)	0.0409	56 (30.6 %)
How did you learn about HCV treatment guidelines?				
From internet	63 (52.1 %)	20 (39.2 %)	0.12	83 (48.3 %)
From conferences	24 (19.8 %)	16 (31.4%)	0.10	40 (23.3 %)
From supervisor	13 (10.7%)	11 (21.6%)	0.06	24 (14.0%)
From journals	18 (14.9%)	2 (3.9 %)	0.0407	20 (11.6%)
Other source	3 (2.5 %)	2 (3.9 %)	0.61	5 (2.9 %)
Which guideline do you follow when treating HCV patients in your center?				
NCCVH	24 (19.7 %)	7 (14.0 %)	0.38	31 (18.0%)
EASL	52 (42.6%)	27 (54.0%)	0.17	79 (45.9 %)
AASLD	29 (23.8 %)	10 (20.0%)	0.59	39 (22.7 %)
WHO	1 (0.8 %)	1 (2.0%)	0.51	2 (1.2 %)
Other	16 (13.1%)	5 (10.0%)	0.57	21 (12.2%)
Do you regularly attend any workshops, conferences or training courses about HCV treatment? "yes" $[n\ (\%)]$	64 (49.6 %)	27 (51.9%)	0.78	91 (50.3 %)
Mention the name of the conferences, workshops, or courses you regularly attend				
AASLD	15 (11.6%)	5 (9.6%)	0.70	20 (11.0%)
EASL	15 (11.6%)	7 (13.5 %)	0.73	22 (12.2 %)
APASL	7 (5.4%)	3 (5.8 %)	0.93	10 (5.5 %)
DDW	4(3.1%)	2 (3.8 %)	0.80	6 (3.3 %)
UCHID	15 (11.6%)	4 (7.7 %)	0.43	19 (10.5 %)
NCCVH	1 (0.8 %)	0 (0.0 %)	0.52	1 (0.6 %)
Which section of this guideline do you frequently apply during your routine work?	, ,	· · · · · /		/
Pretreatment assessment	8 (12.7%)	5 (18.5%)	0.47	13 (14.4%)
During treatment	7 (11.1 %)	3 (11.1 %)	1.00	10 (11.1%)
Special populations	2 (3.2 %)	2 (7.4%)	0.37	4 (4.4 %)
All of the above	46 (73.0 %)	17 (63.0%)	0.34	63 (70.0%)

HCV. Hepatitis C Virus: AASLD. American Association for the Study of Liver Diseases: FASL, European Association for the Study of Liver: APASL, Asian Pacific Association for the Study of the Liver; WHO, World Health Organization; NCCVH, National Committee for the Control of Viral Hepatitis; CDC, Centers for Disease Control and Prevention; DDW, Digestive Disease Week; UCHID, United Conference of Hepato-Gastroenterology and Infectious Diseases.

both direct interaction with experts and participation in scientific discussions.

We observed that approximately half of the respondents reported regular attendance at workshops, conferences, and training courses organized by international associations. This finding positively reflects that the HCPs are actively seeking regular education and training to stay up to date with advancements in HCV treatment. Interestingly, the distribution of workshop attendance was uniform across different medical specialties. This emphasizes the significance of interdisciplinary collaboration and knowledge sharing in managing HCV effectively.

Buller-Taylor et al. [17] conducted a study to evaluate pre-and post-test information gains about HCV management through a free, one-hour online course for physicians and patients. The study highlighted that the training courses enhanced the ability of physicians to educate and promote patients' involvement in HCV care. Furthermore, that short online course also enhanced filling knowledge gaps for both physicians and patients in various scenarios through easy and accessible tools. These results are consistent with our findings which emphasized the significant role of disseminating knowledge, mainly through specialized international organizations.

Another key finding in our study was that 70% of respondents reported applying all sections of the guidelines during their routine work. The majority of respondents (94%) expressed confidence in the effectiveness of post-treatment follow-up for early detection of complications such as cirrhosis and HCC. In addition, 93 % advised their patients to continue post-treatment follow-up. These findings indicate a strong adherence of included participants to the established

guidelines, ensuring comprehensive patient care and effective HCV 314 management.

Furthermore, the results highlighted the respondents' high level 316 of awareness of continuous monitoring to avoid long-term complications in HCV patients. This might be attributed to the high percentage of hepatologists and gastroenterologists who participated in this study, as these specialists are more experienced and continuously updated about guidelines. This is consistent with the findings of Doshi et al. [18], which demonstrated that HCV screening and treatment knowledge was higher among specialty physicians than among non-specialists. This high level of awareness includes detailed topics 324 such as pretreatment methods of fibrosis stage assessment, risk of 325 HCC development, surveillance for HCC in advanced fibrosis or cirrhotic patients, and post-treatment follow-up.

Our analysis showed that most participants trust evidence-based guidelines, as 91% of respondents declared. However, 39% of 329 respondents acknowledged encountering inconsistencies in some 330 HCV management guidelines, despite believing that they were based 331 on solid evidence. The contradiction between high trust and reported 332 inconsistencies may reflect regional variations in practice or divergent recommendations across societies (e.g., follow-up intervals, 334 reinfection screening). Furthermore, high self-efficacy may reflect 335 perceived rather than actual performance.

Furthermore, this survey demonstrated a high level of self-efficacy 337 among participants, with 85% expressing high confidence in their 338 ability to reduce the risk of HCC or cirrhosis complications in HCV patients. Moreover, 90 % of the respondents felt well-informed about 340 HCV treatment guidelines.

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Table 3Attitudes, perception, and self-efficacy regarding HCV treatment guidelines among healthcare providers.

Question	Hepatologists and gastroenterologists	Other specialties	p	All providers
Post-treatment follow-up is effecti	ve for early detection of HCC	and other cirrhosis related o	complications amo	ong HCV-treated patients
Strongly disagree	5 (3.8 %)	1 (1.9 %)	0.50	6 (3.3 %)
Disagree	1 (0.8 %)	0 (0.0 %)		1 (0.5 %)
Neither agree nor disagree	3 (2.3 %)	1 (1.9 %)		4 (2.2 %)
Agree	22 (16.9 %)	10 (18.9 %)		32 (17.5 %)
Strongly agree	99 (76.2 %)	41 (77.4%)		140 (76.5 %)
I am recommending my patient to	continue with post-treatmen	t follow-up		
Strongly disagree	4 (3.1 %)	0 (0.0 %)	0.20	4 (2.2 %)
Disagree	0 (0.0 %)	0 (0.0 %)		0 (0.0 %)
Neither agree nor disagree	5 (3.8 %)	3 (5.7 %)		8 (4.4 %)
Agree	31 (23.8 %)	10 (18.9 %)		41 (22.4%)
Strongly agree	90 (69.2 %)	40 (75.5 %)		130 (71.0 %)
I am comfortable discussing the be	enefits of adherence to post-tr	eatment follow-up with my	patients and thei	ir families
Strongly disagree	2 (1.5 %)	0 (0.0 %)	0.36	2 (1.1 %)
Disagree	2 (1.5 %)	0 (0.0 %)		2 (1.1 %)
Neither agree nor disagree	2 (1.5 %)	1 (1.9 %)		3 (1.6%)
Agree	45 (34.6%)	18 (34.0%)		63 (34.4%)
Strongly agree	79 (60.8 %)	34 (64.2 %)		113 (61.7 %)
Guidelines for liver disease treatm	ent for HCV patients are base	d on sound evidence		` ′
Strongly disagree	2 (1.5 %)	2 (3.8 %)	0.35	4 (2.2 %)
Disagree	3 (2.3 %)	2 (3.8 %)		5 (2.7 %)
Neither agree nor disagree	5 (3.8 %)	3 (5.7 %)		8 (4.4 %)
Agree	61 (46.9%)	26 (49.1 %)		87 (47.5 %)
Strongly agree	59 (45.4%)	20 (37.7 %)		79 (43.2 %)
There are inconsistent guidelines i	, ,	,		
Strongly disagree	7 (5.4 %)	3 (5.7 %)	0.37	10 (5.5 %)
Disagree	39 (30.0 %)	16 (30.2 %)		55 (30.1 %)
Neither agree nor disagree	31 (23.8 %)	16 (30.2 %)		47 (25.7 %)
Agree	48 (36.9 %)	13 (24.5 %)		61 (33.3 %)
Strongly agree	5 (3.8 %)	5 (9.4%)		10 (5.5 %)
I am confident in my ability to red				10 (515 %)
Strongly disagree	3 (2.3 %)	0 (0.0%)	0.26	3 (1.6 %)
Disagree	2 (1.6 %)	1 (1.9 %)	0.20	3 (1.6 %)
Neither agree nor disagree	11 (8.5 %)	10 (18.9%)		21 (11.5 %)
Agree	63 (48.8 %)	29 (54.7 %)		92 (50.5 %)
Strongly agree	50 (38.8 %)	13 (24.5 %)		63 (34.6%)
I feel well-informed regarding guid		.5 (2 1.5 %)		33 (3 1.0 %)
Strongly disagree	2 (1.5 %)	0 (0.0 %)	0.0385	2 (1.1 %)
Disagree	3 (2.3 %)	2 (3.8 %)	0.0303	5 (2.7 %)
Neither agree nor disagree	7 (5.4%)	4 (7.5 %)		11 (6.0%)
Agree	64 (49.2 %)	35 (66.0%)		99 (54.1 %)
Strongly agree	54 (41.5 %)	12 (22.6%)		66 (36.1 %)

HCV, Hepatitis C Virus; HCC, Hepatocellular Carcinoma.

The incidence of HCC in patients with cirrhosis and ongoing HCV infection ranges between 1% - 7% annually [19]. Ioannou and his colleagues [20] reported that patients with advanced fibrosis remain at high risk of developing HCC even after SVR achievement. This risk may persist up to 10 years after successful treatment in cirrhotic patients or patients with a high FIB-4 score (>3.25) before treatment. Thus, it is universally accepted that HCC incidence in patients with cirrhosis prior to treatment and SVR achievement is sufficiently high to justify surveillance following HCV eradication [21]. In this context, EASL guidelines recommend that patients with advanced fibrosis and cirrhosis should be included in HCC screening programs [4]. In this study, strong support for post-treatment follow-up was observed considerably, as it was advocated by 86% of the respondents. Nevertheless, specialists (hepatologists and gastroenterologists) more commonly believed post-treatment follow-up in non-cirrhotic patients was unnecessary. Observed differences in knowledge and attitudes between specialists and non-specialists may reflect variations in formal training, exposure to liver-specific CME, or institutional expectations. Future studies with larger samples may clarify these relationships.

Moreover, we observed that most respondents (88%–96%) reported ordering liver-related blood investigations combined with abdominal ultrasounds during post-treatment follow-up. This may reflect their commitment to follow the guidelines and use the

available standardized tools to monitor liver health in HCV patients after treatment. In this context, our findings align with the study by 367 Dormanesh et al. [22], which evaluated how well patients with HCV 368 adhered to their physicians' recommendations and established 369 guidelines for HCV management and follow-up care. This previous 370 research underscored the critical role of effective communication 371 between patients and healthcare providers regarding follow-up care 372 guidelines, which is essential for monitoring serious complications 373 such as HCC.

The results of this survey also confirmed that a high level of knowledge and adherence from HCPs to different international HCV area management guidelines and recommendations are prerequisites for the implementation of HCV screening and elimination. Accordingly, in line with WHO recommendations, several countries have implemented ambitious campaigns aiming at eradicating HCV infection as a public health problem by 2030. These efforts will yield the desired aresults if they are conducted by well-educated HCPs. Egypt has been a global leader in HCV elimination efforts. A mass screening and treatment program was launched in 2018, aiming to screen >60 million individuals and treat millions infected with HCV [23–25]. Georgia also launched its first national campaign aimed at HCV area dication in 2015. In 2022, 2.6 million people have been screened for HCV antibodies, and 80,000 persons with HCV RNA detected were treated [26,27]. Therefore, we emphasize that the lessons from Egypt 389

Table 4Knowledge of management guidelines for fibrosis and cirrhosis in HCV among healthcare providers.

Question	Hepatologists and gastroenterologists	Other specialties	p	All providers
In patients with advanced fibrosis and cirrhosis, HCV eradication	n:			
A. Reduces the rate of decompensation	15 (11.5 %)	7 (13.2 %)	0.09	22 (12.0 %)
B. Does not abolish the risk of HCC	9 (6.9 %)	7 (13.2 %)		16 (8.7 %)
C. Abolishes the risk of HCC	1 (0.8 %)	1 (1.9%)		2 (1.1 %)
D. A and B	84 (64.6 %)	27 (50.9 %)		111 (60.7 %)
E. A and C	21 (16.2 %)	11 (20.8 %)		32 (17.5 %)
In patients with advanced fibrosis and cirrhosis, surveillance fo	r HCC should be continu	ied for:		
3 months	10 (7.7 %)	4 (7.5 %)	0.06	14 (7.7 %)
6 months	13 (10.0 %)	1 (1.9%)		14 (7.7 %)
12 months	3 (2.3 %)	3 (5.7 %)		6 (3.3 %)
Forever	104 (80.0 %)	45 (84.9 %)		149 (81.4%)
How do you assess the fibrosis stage before treatment?				
Non-invasive methods (ultrasound, biomarkers, FibroScan)	102 (78.5 %)	42 (79.2 %)	0.91	144 (78.7 %)
Invasive method (biopsy)	5 (3.8 %)	2 (3.8 %)		7 (3.8 %)
Both non-invasive and invasive methods	15 (11.5 %)	7 (13.2 %)		22 (12.0 %)
I do not assess fibrosis	8 (6.2 %)	2 (3.8 %)		10 (5.5 %)
For assessing the fibrosis stage, liver biopsy is reserved for case	s where there is:			
Confirmed aetiology	3 (2.3 %)	2 (3.8 %)	0.08	5 (2.7 %)
Uncertainty or potential additional aetiologies	107 (82.3 %)	49 (92.5 %)		156 (85.2 %)
None of the above	20 (15.4%)	2 (3.8 %)		22 (12.0 %)
Why is identifying patients with cirrhosis of particular importa	nce?			
A. Their treatment must be adapted	4 (3.1 %)	1 (1.9 %)	0.65	5 (2.7 %)
B. Their post-treatment surveillance must be adapted	7 (5.4 %)	4 (7.5 %)		11 (6.0 %)
C. A and B	117 (90.0 %)	48 (90.6 %)		165 (90.2 %)
D. None of the above	2 (1.5 %)	0 (0.0%)		2 (1.1 %)

HCV, Hepatitis C Virus; HCC, Hepatocellular Carcinoma.

Table 5Knowledge of post-SVR HCV management guidelines among healthcare providers.

	Hepatologists and gastroenterologists	Other specialties	p	All providers
What is the suitable time for non-cirrhotic HCV patients who achieved SVR to be reteste	d for HCV RNA?			
12 weeks post-treatment	68 (53.1 %)	35 (66.0 %)	0.06	103 (56.9 %)
24 weeks post-treatment	39 (30.5 %)	9 (17.0%)		48 (26.5 %)
48 weeks post-treatment	21 (16.4%)	9 (17.0%)		30 (16.6%)
If HCV RNA is still not detected, the infection can be considered as:				
Definitely cured	82 (63.6 %)	27 (51.9%)	0.15	109 (60.2 %)
Not definitely cured	15 (11.6%)	11 (21.2 %)		26 (14.4%)
HCV RNA does not need to be retested	32 (24.8 %)	14 (26.9 %)		46 (25.4%)
Definitely, SVR should be assessed at:				
12 or 24 weeks post-treatment	105 (80.8 %)	40 (75.5 %)	0.42	145 (79.2 %)
24 and 48 weeks post-treatment	15 (11.5 %)	5 (9.4%)		20 (10.9%)
12 and 24 months post-treatment	10 (7.7 %)	8 (15.1 %)		18 (9.8 %)
Do you ask your non-cirrhotic patients who achieved SVR 12 to repeat ALT and PCR after SVR visit? "Yes" [n (%)]	81 (62.3 %)	38 (71.7 %)	0.23	119 (65.0 %)
Do you explain the risk of reinfection to high-risk population (e.g., PWID, MSM, hemo- dialysis patients etc.)? "Yes" [n (%)]	123 (94.6%)	52 (98.1 %)	0.29	175 (95.6 %)
Do you ask high-risk population (e.g., PWID, MSM, hemodialysis patients etc.) to repeat	112 (86.2 %)	48 (90.6 %)	0.41	160 (87.4 %)
HCV RNA annually? "Yes" [n (%)]	112 (80.2 %)	40 (30.0%)	0.41	100 (87.4%)
Do you advise patients with SVR to get vaccination for HBV? "Yes" [n (%)]	119 (91.5 %)	47 (88.7 %)	0.55	166 (90.7 %)
Is there a need to follow up patients who achieved SVR? "Yes" [n (%)]	104 (83.9%)	44 (89.8 %)	0.32	148 (85.5 %)
What is the interval of following up non-cirrhotic patients?	104 (85.5%)	44 (03.0 %)	0.52	140 (05.5 %)
3 months	1 (0.8 %)	2 (3.8 %)	0.0270	3 (1.6 %)
6 months	65 (50.0 %)	36 (67.9 %)	0.0270	101 (55.2 %)
No need for follow up	64 (49.2 %)	15 (28.3 %)		79 (43.2 %)
What is the follow-up interval of cirrhotic patients?	01 (13.270)	13 (20.3 %)		75 (15.270)
3 months	64 (49.2 %)	38 (71.7 %)	0.0055	102 (55.7 %)
6 months	65 (50.0 %)	14 (26.4%)	0.0055	79 (43.2 %)
9 months	1 (0.8 %)	1 (1.9%)		2 (1.1 %)
Which investigations do you order during the follow-up? (Check all that apply)	1 (0.0 %)	1 (1.5 %)		2 (1.1 %)
Liver chemistry tests	115 (88.5 %)	46 (86.8 %)	0.75	161 (88.0%)
Complete blood count	86 (66.2 %)	42 (79.2 %)	0.08	128 (69.9 %)
Alpha fetoprotein	125 (96.2 %)	50 (94.3 %)	0.59	175 (95.6 %)
Abdominal ultrasound	125 (96.2 %)	47 (88.7 %)	0.05	172 (94.0 %)
HCV RNA	40 (30.8 %)	24 (45.3 %)	0.06	64 (35.0%)

HCV, Hepatitis C Virus; HCV RNA, Hepatitis C Virus Ribonucleic Acid; SVR, Sustained Virologic Response; PWID, People Who Inject Drugs; MSM, Men who have Sex with Men; HBV, Hepatitis B Virus.

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Question	Hepatologists and gastroenterologists	Other specialties	p	All providers			
I do not tell my patient about required investigations for post-treatment follow up							
Strongly disagree	85 (65.4 %)	30 (56.6 %)	0.26	115 (62.8 %)			
Disagree	34 (26.2 %)	19 (35.8 %)		53 (29.0 %)			
Neither agree nor disagree	6 (4.6 %)	1 (1.9%)		7 (3.8 %)			
Agree	4 (3.1 %)	2 (3.8 %)		6 (3.3 %)			
Strongly agree	1 (0.8 %)	1 (1.9%)		2 (1.1 %)			
I do not describe the benefits o	f post-treatment follow	low up to my patients due to the lack of time					
Strongly disagree	75 (57.7 %)	23 (43.4%)	0.08	98 (53.6 %)			
Disagree	39 (30.0 %)	27 (50.9 %)		66 (36.1 %)			
Neither agree nor disagree	11 (8.5 %)	1 (1.9%)		12 (6.6 %)			
Agree	3 (2.3 %)	1 (1.9%)		4 (2.2 %)			
Strongly agree	2 (1.5 %)	1 (1.9%)		3 (1.6%)			
I do not describe the benefits of post-treatment follow up to my patients due to the lack of resources							
Strongly disagree	80 (61.5 %)	20 (37.7 %)	0.0194	100 (54.6 %)			
Disagree	40 (30.8 %)	26 (49.1 %)		66 (36.1 %)			
Neither agree nor disagree	9 (6.9 %)	5 (9.4%)		14 (7.7 %)			
Agree	1 (0.8 %)	1 (1.9%)		2 (1.1%)			
Strongly agree	0 (0.0 %)	1 (1.9%)		1 (0.5 %)			

and Georgia regarding HCV management can be replicated in other countries. Consequently, continuous education for HCPs on HCV management is crucial for enhancing the quality of care for HCV patients and contributing to the global target of HCV eradication by 2030.

Finally, the current study identified minimal barriers to posttreatment follow-up. A minority of respondents (<5%) reported that they were not informing their patients about follow-up due to time and/or resource restrictions. This finding highlights a widespread acknowledgment of the importance of follow-up by the respondents, even in the presence of possible practical obstacles such as time and resources.

The strengths of this study include the inclusion of a diverse sample of physicians from various countries, which enhances the generalizability of the findings across different healthcare systems and cultural contexts. Additionally, the incorporation of healthcare providers from various specialties and practice settings, including hospital-based environments, offers a comprehensive perspective on knowledge and practices related to HCV management. Furthermore, this study assessed the adherence of HCPs to different specific aspects of HCV management guidelines, offering valuable insights into the extent to which physicians follow established recommendations. This focus is crucial for identifying gaps and areas that need improvement in clinical practice.

However, the study had some limitations worth noting. While the participant pool was diverse, it may not fully capture the experiences of all healthcare providers managing HCV worldwide, especially lowresource community-based practitioners who might have been out of reach for our study sites. The geographic distribution of respondents—heavily concentrated in three countries—introduces a potential source of bias that may limit the broader generalizability of the study's findings. Additionally, the study relied on self-reported data from healthcare providers, which could introduce recall bias or occasional overestimations of guideline adherence. Despite these limitations, the insights gained from this study remain valuable and can inform future research and clinical practice in HCV management.

5. Conclusions 426

In conclusion, our study's key findings indicate that the participating HCPs demonstrated a strong level of knowledge regarding HCV management, effectively applying this knowledge while also adhering to established guidelines. The study also highlighted the positive attitudes, self-efficacy, and perceptions of these providers, with few

barriers reported in HCV management and post-treatment follow-up. 432 Moreover, the survey results reflect the commitment of participating HCPs to continue educating themselves and monitoring their patients after therapy. There are opportunities for improvement, particularly in addressing perceived inconsistencies in guidelines and establishing uniform procedures across different specialties. Overall, these results provide valuable insights into how knowledgeable and engaged HCPs can positively influence the outcomes for patients with HCV infection.

Author contributions

Mohamed El-Kassas – study design, study oversight, data acquisition, data interpretation, manuscript writing and critical editing of final manuscript; Yusuf Yilmaz – study oversight, data acquisition, data interpretation, manuscript writing and critical editing of final manuscript; Chun-Jen Liu – study oversight, data acquisition, data interpretation, manuscript writing and critical editing of final manuscript; Marlen I. Castellanos Fernández – study oversight, data acquisition, data interpretation, manuscript writing and critical editing of final manuscript; Yuichiro Eguchi - critical editing of final manuscript; Khalid Al-Naamani – study oversight, data acquisition, data interpretation, manuscript writing and critical editing of final manuscript; Doaa Abdeltawab – study oversight, data acquisition, data interpretation, manuscript writing and critical editing of final manuscript; Mohammed A. Medhat – study oversight, data acquisition, data interpretation, manuscript writing and critical editing of final manuscript; Wah-Kheong Chan – study oversight, data acquisition, data interpretation, manuscript writing and critical editing of final manuscript; Stuart Gordon – study oversight, data acquisition, data interpretation, manuscript writing and critical editing of final manuscript; Vasily Isakov – study oversight, data acquisition, data interpretation, manuscript writing and critical editing of final manuscript; Ming Lung Yu – study oversight, data acquisition, data interpretation, manuscript writing and critical editing of final manuscript; Maria Buti - study oversight, data acquisition, data interpretation, manuscript writing and critical editing of final manuscript; George V. Papatheodoridis – study oversight, data acquisition, data interpretation, 467 manuscript writing and critical editing of final manuscript; Fatema 468 Nader – project oversight and review of manuscript; Andrei Racila – database administration and review of manuscript; Linda Henry – critical review and editing of final manuscript; Maria Stepanova statistical analysis, data interpretation, manuscript writing and criti- 472 cal review and editing of final manuscript; Zobair M. Younossi -

M. El-Kassas, Y. Yilmaz, C.-J. Liu et al. Annals of Hepatology xxx (2025) 102134

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