**Name of Journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 63009

**Manuscript Type:** REVIEW

**Progress and challenges in the comprehensive management of chronic viral hepatitis: Key ways to achieve the elimination**

Higuera-de la Tijera F *et al*. Viral hepatitis, achieving WHO's goals

Fátima Higuera-de la Tijera, Alfredo Servín-Caamaño, Luis Servín-Abad

**Fátima Higuera-de la Tijera,** Department of Gastroenterology and Hepatology, Hospital General de México, Mexico City 06726, Mexico

**Alfredo Servín-Caamaño,** Department of Internal Medicine, Hospital General de México, Mexico City 06726, Mexico

**Luis Servín-Abad,** Department of Gastroenterology, Saint Cloud Hospital, Saint Cloud, MN 56303, United States

**Author contributions:** Higuera-de la Tijera F designed the overall concept of the manuscript; Higuera-de la Tijera F and Servín-Caamaño A performed the literature review and wrote the manuscript; Servín-Abad L translated and edited the manuscript to its English version.

**Corresponding author: Fátima Higuera-de la Tijera, MD, MSc, PhD, Academic Research, Professor,** DepartmentofGastroenterology and Hepatology, Hospital General de México, Dr. Balmis 148 Col. Doctores, Del. Cuauhtémoc, Departamento de Gastroenterología 310-D., Mexico City 06726, Mexico. fatimahiguera@yahoo.com.mx

**Received:** January 22, 2021

**Revised:** March 4, 2021

**Accepted:** June 17, 2021

**Published online:**

**Abstract**

Chronic viral hepatitis is a significant health problem throughout the world, which already represents high annual mortality. By 2040, chronic viral hepatitis due to virus B and virus C and their complications cirrhosis and hepatocellular carcinoma will be more deadly than malaria, vitellogenesis-inhibiting hormone, and tuberculosis altogether. In this review, we analyze the global impact of chronic viral hepatitis with a focus on the most vulnerable groups, the goals set by the World Health Organization for the year 2030, and the key points to achieve them, such as timely access to antiviral treatment of direct-acting antiviral, which represents the key to achieving hepatitis C virus elimination. Likewise, we review the strategies to prevent transmission and achieve control of hepatitis B virus. Finally, we address the impact that the coronavirus disease 2019 pandemic has had on implementing elimination strategies and the advantages of implementing telemedicine programs.

**Key Words:** Hepatitis C; Hepatitis B; Vaccination; Elimination program; Telemedicine; Direct antiviral agents

Higuera-de la Tijera F, Servín-Caamaño A, Servín-Abad L. Progress and challenges in the comprehensive management of chronic viral hepatitis: Key ways to achieve the elimination. *World J Gastroenterol* 2021; In press

**Core Tip:** The World Health Organization proposes eliminating hepatitis infection as a threat to public health by 2030. Despite notable advances reached to achieve those goals, many challenges persist, such as guarantee access to complete vaccination schemes for hepatitis B virus and universal screening for all adults at least once in life to screen for hepatitis C virus. Those non-vaccinated against hepatitis B virus guarantee access to effective therapies programs to all patients who need it, emphasizing risk groups like prison inmates, sex workers, injecting drug users, and men who have sex with men, trying to reduce the high incidence of viral hepatitis in these groups. Telemedicine and telementoring approaches are valuable strategies to facilitate more patients access to healthcare systems and should be encouraged. Coronavirus disease 2019 pandemic affects all strategies significantly to eliminate viral hepatitis, particularly in low-income and middle-income countries. With available effective vaccines for anti-severe acute respiratory syndrome-coronavirus-2, strategies to immunize most people are crucial to restarting the viral hepatitis elimination programs throughout the world as soon as possible.

**INTRODUCTION**

More than 320 million people worldwide have chronic viral hepatitis. Around 248 million people are living with hepatitis B virus (HBV) chronic infection, which represents 3.2% of the global population[1-3]; and an estimated 71 to 80 million individuals (1.1%) are living with hepatitis C virus (HCV) chronic infection[3,4].

Chronic viral hepatitis and its related complications, cirrhosis and hepatocellular carcinoma (HCC), have been regarded as the leading causes of death for decades[1], causing globally more than 1 million deaths each year[5]. In fact, by 2040, deaths from chronic viral hepatitis are expected to exceed the related mortality as a whole from human immunodeficiency virus infection (HIV), tuberculosis, and malaria[5,6]. Liver disease due to viral hepatitis represents a substantial burden in the Asia-Pacific region. This region lives 1.8 billion people, which means around 25% of the world's population; a third of global deaths occur due to viral hepatitis, mainly driven by cirrhosis and HCC. Asia-Pacific represents 40% of the global burden of chronic hepatitis, where 115 million people in the Western Pacific are chronically infected with HBV and 14 million with HCV. Al least 58.6% of deaths due to cirrhosis and HCC in the Asia-Pacific region are related to HBV or HCV[7]. In 2013, China was the country that reported the most significant absolute number of deaths and disability-adjusted life-years attributable to viral hepatitis[1].

The North of Africa and the Middle East are also geographic regions extensively affected by viral hepatitis. They have a wide range of viral hepatitis causes, viremic prevalence, and diversity in HBV and HCV genotype distributions. Vaccination and treatment policies, socioeconomic conditions, and migration are responsible factors for the high prevalence of viral hepatitis in these particular regions. Here, elimination strategies might be challenging to implement because of a scarcity of reliable and profitable quality epidemiological data on hepatitis[8].

**Search methods**

It is a narrative review. We searched PubMed, EMBASE, MEDLINE, and Web of Science from January 2015 to January 2021 to identify all studies documenting achievements and challenges on vaccination, diagnosis, access to healthcare systems, therapy, and elimination programs on hepatitis B and hepatitis C viral infections. The following search terms alone or matched with the Boolean operators "AND" or "OR" were used: "Hepatitis C," "hepatitis B," "World Health Organization (WHO)'s goals," "vaccination," "detection," "access to diagnosis," "access to healthcare system," "direct antiviral agents," "sofosbuvir-velpatasvir (SOF-VEL)," "glecaprevir-pibrentasvir (G-P)," "entecavir (ETV)," "tenofovir disoproxil fumarate (TDF)," "tenofovir alafenamide (TAF)," "elimination program," "telemedicine," "coronavirus disease 2019 (COVID-19)". Using these terms, we found a total of 13497 articles; no study design or language restrictions were applied. We focused on full-text articles, but abstracts were considered if relevant. Finally, we selected the those with the most relevant content.

**WHO goals for 2030**

WHO goals are to achieve a 65% reduction in liver-related deaths, which means preventing more than 7 million related deaths by 2030, achieving a 90% reduction in viral hepatitis incidence, and reaching 90% of patients living with viral hepatitis diagnosed by 2030[9-12]. Specifically, in the case of HCV infection, the reduction in liver-related deaths is today achievable since the disponibility of direct-acting antivirals (DAAs), which have a high rate of sustained viral response (SVR). Nevertheless, an increase in harm reduction programs and treatment among populations at risk of transmission is undoubtedly still needed to reduce new infections[9].

For HBV infection, the WHO aims are divided into two main categories: First, prevention of new HBV cases through vaccination and blood safety; second, identification, linkage to care, and treatment of persons living with HBV who need it[10].

**The effective and safe cure for hepatitis C**

In the absence of an effective vaccine, the cornerstone to achieving HCV elimination worldwide is treatment with DAAs[2], which have excellent efficacy and good tolerability profiles, offering a unique opportunity[13,14].Currently, pan-genotypic regimens are available, which allows them to simplify decisions when initiating HCV therapy and ensuring universal access for these patients[15].

SOF-VEL is a pan-genotypic regimen that allows achieving the SVR in more than 95%. It can be prescribed even in decompensated cirrhosis because SOF-VEL is a protease inhibitor-free regimen proven effective and safe in this clinical scenario; HCV-infected liver posttransplant recipients are also effectively and safely treated with it SOF-VEL[16-29]. Several cohort studies also have validated the efficacy and safety of SOF-VEL in the real world[30-33]. Despite nearly 80% of SOF being renally excreted[4], the treatment with SOF-VEL is safe. It can be prescribed, achieving a SVR rate greater than 95% in patients with hepatitis C and end-stage renal disease, even in those requiring dialysis[34].

G-P, also a pan-genotypic regimen, is effective and safe in those without cirrhosis and with compensated cirrhosis[35-50] but is contraindicated in decompensated cirrhosis since glecaprevir is a protease inhibitor[4,15]. G-P is effective and safe in patients with end-stage renal disease[51-53]. The study MAGELLAN-2 validated that G-P is a safe and effective therapy to treat HCV infection in those patients who received a liver or kidney transplant[54].

Both pan-genotypic regimens, SOF-VEL, and G-P are also effective and safe in patients coinfected with HIV[55-57].

Around 5% of patients with chronic HCV infection treated with the first line DAAs do not achieve SVR; for this group of patients, sofosbuvir-velpatasvir-voxilaprevir (SOF-VEL-VOX) for 12 wk is the current option of rescue[4,15]. In a study including 137 patients who failed a previous combination of DAAs, a SVR of 95% was reached with SOF-VEL-VOX. Factors related to the reduced rate of SVR were genotype 3 and cirrhosis[58]. Even in those coinfected HIV-HCV patients who failed a previous combination of DAAs, the RESOLVE study demonstrated that 12 wk of SOF-VEL-VOX was safe and effective. The treatment response was not diminished by HIV coinfection[59].

Sixteen weeks of G-P treatment is an effective and safe option for those who failed NS5A or NS3-protease inhibitors[50,60,61]. In a randomized study including genotype 1 patients who failed previous treatment with SOF plus an NS5A inhibitor, retreatment with G-P achieved the SVR in greater than 90% of cases, including patients with compensated cirrhosis[60].

**DAAs and the liver transplant programs**

Since DAAs represent a highly effective and safe therapy, livers from HCV-infected donors can now be used to transplant, optimizing the transplant opportunity for more patients. After transplantation from an HCV-positive donor, the occurrence of HCV infection in HCV-negative recipients is practically universal, requiring post-transplant antiviral treatment[62].

Some interesting strategies are being studied to reduce HCV infection likelihood in organ recipients from HCV-infected donors. Feld *et al*[62] found that ezetimibe (10 mg; an HCV entry inhibitor) plus G-P (300 mg/120 mg) given previous and during 7 d after transplant avoided the occurrence of chronic hepatitis C in 30 (100%) recipients of different organs from HCV-positive donors.

Although patients with HCV infection had a higher risk of post-liver transplant (LT) graft failure and death in the pre-DAA era, this issue seems to be solved in the post-DAA era[63]. The burden of HCV-related LT waitlist and LT is declining in the DAA era, with improved post-transplant outcomes[64]. It probably reflects the impact of DAAs on bettering post-LT results in patients with hepatitis C and maybe also a better patient selection for a LT after 2014[63]. After the availability of DAAs, HCV as an indication for LT has reduced, patients exhibit a less severe disease at transplantation, and there is a trend towards better patient survival[65,66].

Overall listing rates for decompensated HCV cirrhosis have decreased in the DAA era. According to Bittermann and Reddy[67], waitlist recovery is more frequent for HCV patients post-DAAs [adjusted survival hazard ratio 1.78 *vs* pre-DAAs, 95% confidence interval (95%CI): 1.58-2.02; *P* <0.001], while improvements in waitlist mortality by era are similar to non-HCV candidates [adjusted survival hazard ratio 0.74 (95%CI: 0.7-0.78; *P* < 0.001) and 0.77 (95%CI: 0.74-0.8; *P* < 0.001), respectively][67].

**The strategies to control hepatitis B transmission and to control the burden of disease**

Universal vaccination is the essential strategy to prevent HBV transmission. Already in 1992, WHO recommended introducing universal childhood vaccination all around the world. Nowadays, at least 180 countries have adopted this recommendation[68]. The efficacy of universal vaccination programs has been demonstrated in several countries all around the world. In Taiwan, the prevalence of hepatitis B surface antigen (HBsAg) decreased notably from 14.3% in 1995 to 1.1% in 2009, and the seroprevalence of hepatitis B e-antigen (HBeAg) reduced from 5.9% in 1995 to 0.3% in 2009[69]. Furthermore, in Taiwan, the HCC incidence reduced from 0.57 to 0.17 *per* 100000 person-years following mass anti-HBV vaccination[70].

Before the HBV vaccination program, Korea was considered an area of high endemicity. Studies from the 1980s and 1990s revealed that chronic HBV carriage prevalence ranged from 8%-10% before introducing the anti-HBV vaccination in Korea. Since 1990, the percentage of vaccinated infants has surpassed 98.9%, and after 25 years of active vaccination, the HBsAg carrier rate in the general population decreased to 3.7% in 2007. Also, the administration of the anti-HBV vaccine reduced the risk of HCC among adults[71].

However, continuous efforts are needed to ensure timely access to be vaccinated with comprehensive schemes[72]. In spite of the success of vaccination and therapy, chronic hepatitis B (CHB) infection remains a major concern due to many patients ignoring their clinical status. The troubles in diagnosis and screening may be overcome by lifting awareness, favoring partnerships, and allocating resources[73]. In a meta-analysis of 26 studies, the prevalence of HBV infection in non-vaccinated and vaccinated cohorts went from 0.6% to 16.3% and from 0.3% to 8.5%, respectively. The relative prevalence, comparing vaccinated *vs* non-vaccinated, was 0.24 (95%CI: 0.16-0.35) for HBsAg and 0.23 (95%CI: 0.17-0.32) for antibody anti-hepatitis B core antigen. For populations with targeted vaccination, relative prevalence was 0.32 (95%CI: 0.24-0.43) and 0.33 (95%CI: 0.23-0.45), respectively. The residual burden of infection in cohorts offered vaccination suggests that longer-term evaluations of vaccination coverage, timeliness, and other program quality aspects are needed. As HBV-vaccinated infant cohorts reach adulthood, ongoing analysis of prevalence in adolescents and young adults will ensure that elimination efforts are on track[72].

Notwithstanding guidelines suggest screening in high-risk groups like immigrants, these recommendations have not been adopted everywhere[73]. Also, there is a need to improve the uptake of vaccination for household contacts of HBV carriers[74].

The second important strategy to avoid the transmission and control the disease's burden in people living with CHB infection is to guarantee access to medical care and treatment[75,76].However, most people with CHB live in resource-constrained countries where effective drugs are not always widely available[73]. First-choice drugs in patients with CHB, who meet the criteria for initiating treatment, include nucleoside analogs (ETV) and nucleotide analogs (TDF and TAF)[77-79].After 10 years of follow-up, TDF and ETV showed effective suppression of the HBV viral load, between 94% and 99%, both in HBeAg-positive and HBeAg-negative patients. HBeAg seroconversion in HBeAg-positive patients with TDF or ETV has been reported in 49%-53% of cases. Alanine aminotransferase normalization has been achieved between 77% and 83% of patients with CHB treated with any of these regimens. However, the annual frequency of HBsAg seroconversion is rare (< 1% annually)[80]. TAF is as effective as TDF but with a better bone and renal safety profile[81-84].However, some disparities in the opportunity to access hepatitis B therapy have been reported. Miquel *et al*[85]found that a minor proportion of non-immigrants with the indication of effectively receiving hepatitis B therapy got it, compared with non-immigrants (57.8 *vs* 83.2%, *P* <0.001)[85]. Similarly, other studies also have reported that immigrants are lost more frequently during the 1st year of follow-up[86]. Immigrants constitute a vulnerable group that would benefit from a more active approach to recognize timely HBV infection and access treatment programs[87].

**The efforts to construct micro and macro-elimination programs throughout the world**

The high chronic hepatitis prevalence groups should be recognized and prioritized for detection and linkage to healthcare to reduce the risk of transmitting these infectious diseases. The most vulnerable groups are prison inmates, homosexual men, intravenous drug users (IDU), and sex workers[88]. According to the study by Alonso *et al*[88], in Latin America and the Caribbean, the estimated pooled regional anti-HCV prevalence for IDU was 49% (95%CI: 22.6%-76.3 %); for homosexual men was 3% (95%CI: 1.7%-4.5%); for sex workers was 2% (95%CI: 1.0%-3.4%)[88].

In Canada, penitentiary test-and-treat programs could achieve the most significant decreases in incidence (48%; 95% crude incidence: 38%-57%) over 2018-2030 and prevent the newest first chronic infections (22%; 95% crude incidence: 16%-28%) within those who never exposed to HCV[89]. The project HIPPOCRATES is an example of a micro-elimination program conducted in prison inmates, a vulnerable population to receive treatment less frequently due to many obstacles in healthcare access. The onsite evaluation and treatment of HCV-infected prison inmates achieved an unprecedented effective success rate (SVR was 99%). This type of integral program should be replicated to favor hepatitis C elimination[90].

More attention should be paid to the risk group of homosexual men since HCV incidence in this high-risk group seems to be increasing. In France, a recently important change in HCV epidemiology was reported within HIV-infected patients since the higher rate of HCV transmission occurs in 2018 among homosexual men. From 2012 to 2018, the HCV prevalence among new HIV cases increased from 1.9% to 3.5% in homosexual men. Recently acquired HCV incidence increased from 0.36/100 person-years to 1.25/100 person-years in homosexual men. If well, the proportion of all viremic patients reduced from 67.0% to 8.9%, homosexual men became the first group of viremic patients in 2018 (37.9%), and recently acquired hepatitis represented 59.2% of viremic homosexual men in 2018. Global DAA treatment prescription went from 11.4% to 61.5%. More treatments were initiated in homosexual men in 2018 (41.2%). In homosexual men, treatment at the acute phase represented 30.0% of treatments in 2018[91]. In Spain, a very close to HCV elimination country, homosexual men also carry the highest HCV acquisition risk. The identified main risk factors contributing to new cases of HCV infection in Spain are history of sexually acquired infections [incidence rate ratio (IRR) = 18.2, 95%CI: 1.9-172.1; *P* = 0.01)], male gender (IRR = 8.3, 95%CI: 1.4-54.2; *P* = 0.03)] and sharing chem-sex drugs (IRR: 4.9, 95%CI: 1.2-20.8; *P* = 0.03)[92]. In the Netherlands, homosexual men also have the highest incidence and the highest HCV reinfection rate despite universal and unrestricted access to DAAs, stressing the need for additional preventive measures[93,94].

However, other risk factors should not be minimized either; for example, the unapparent parenteral transmission, through shared nail clippers, rakes, and manicure scissors can also be the primary source of viral infection[95]. Therefore, it is now recommended to perform universal one-time in-life routine HCV screening for all adults[15].

Likewise, the telemedicine programs and telementoring approaches are outstanding options that may help reduce urban-rural disparities, facilitate access to healthcare systems to receive timely therapy to all kinds of patients who need it, and save costs[96-104]. In Mexico, with the aid of a telemedicine approach, significant savings were achieved by minimizing costs since nearly half of the patients were outsiders. Coverage reached 86%, and treatment with DAAs achieved 99% of SVR[100] (see Table 1).

**How has the COVID-19 pandemic affected the WHO's goals to eliminate chronic viral hepatitis?**

Quarantine and social distancing for COVID-19 can drastically affect some parts of the HBV[105] and HCV elimination programs, such as diagnosis, treatment, and harm reduction programs. Therefore, the rate of diagnosis has decreased as voluntary activities such as the NoHep program have been reduced. Furthermore, the incidence of viral hepatitis may increase due to the closure of harm reduction centers[106]. According to the World Hepatitis Alliance global survey to evaluate the collateral damage of the pandemic on viral hepatitis elimination programs, civil society organizations are a vital contributor to the success of the elimination programs; of them, 123 of 131 (94%) reported that the effect of the COVID-19 pandemic altered their activities. A participant from the United States reported that collateral effects from the COVID-19 pandemic included the limitation or even the stop of presential interventions, also affecting community education and detection programs. As a negative outcome, fewer people living with viral hepatitis are expected to be diagnosed during 2020[107].The World Hepatitis Alliance survey data show that treatment access has been significantly deteriorated by COVID-19 in low-income and middle-income countries (LMICs), with 15 (52%) of 29 respondents from those countries described that the patients could not timely access treatments. However, in high-income countries, like the United Kingdom, the impact of COVID-19 on HCV treatment will be lesser, partly due to telemedicine and home delivery of medicines, conditions that are not very feasible in LMICs[108]. Sperring *et al*[109] explored the impact of the COVID-19 pandemic on screening HCV testing, finding a comprehensive hospital-wide HCV testing reduced by 49.6%, and new HCV+ patient identification reduced by 42.1%. In ambulatory clinics, testing reduced by 71.9%, and new HCV+ identification reduced by 63.3%[109].

According to the mathematical model projection by Blach *et al*[110], a 1-year delay in viral hepatitis elimination programs will result in 44800 [95% uncertainty interval (UI): 43800-49300] excess HCC cases and 72300 (95%UI: 70600-79400) excess liver-related deaths, relative to the no-delay scenario globally, from 2020 to 2030. Most missed treatments would be in LMICs, whereas most excess HCC and liver-related deaths would be among high-income countries. Authorities should privilege hepatitis programs as soon as safe to attenuate the negative impact on elimination programs and reduce excess mortality from delayed treatment[110].

With the approval of a severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) vaccine, most of the possibility to reactivate elimination viral hepatitis programs throughout the world will rely on SARS-CoV-2 effective vaccination strategies that gradually allow restarting the function of viral hepatitis detection campaigns, safe-needle programs, and outpatient clinics to dispenser antiviral medication. According to mathematical modeling analyses, a vaccine with efficacy (VE) ≥ 70% can prevent the infection. A vaccine with VE < 70% may still control the infection transmission if it reduces infectiousness or infection duration among those vaccinated who acquire the infection if it is supplemented with a < 20% reduction in contact rate complemented with herd immunity. The probability of a significant outbreak is zero at VE ≥ 70% regardless of the number of virus introductions. However, an increase in the social contact rate among those vaccinated (behavior compensation) can undermine vaccine impact[111]. Existing reports of currently approved SARS-CoV-2 vaccines indicate their effectiveness at around 95%, making it very plausible to achieve collective herd-acquired immunity based on the mass implementation of vaccination programs against COVID-19 soon[112].

**CONCLUSION**

Chronic viral hepatitis and its complications, cirrhosis, and HCC affect many people worldwide. Without a plan of action, the projection to 2040 will exceed the related mortality as a whole from other significant infectious healthcare problems. Asia-Pacific, Middle East, and North Africa regions have the highest prevalence, representing a substantial burden of the disease. Hopefully, notable advances have been made to achieve WHO goals to 2030 regarding eliminating hepatitis infection better adaptable to actual reality. In that case, actions need to continue being implemented, which must include more harm limitation programs and timely therapy access for those at risk of transmission are certainly needed to reach an incidence decrease. Since universal vaccination is the essential strategy to prevent HBV transmission, continuous efforts are needed to ensure timely access to be vaccinated with comprehensive schemes. Strategies to find positive contacts ensuing a timely screening and diagnosis must be continuously promoted. To avoid viral hepatitis transmission and control the burden of the disease, guarantee access to medical care and effective therapies must include all people who need it, with more emphasis on including vulnerable groups with currently limited access like immigrants, prison inmates, and sex workers. More attention should be paid to the risk group of men who have sex with men since HCV incidence in this high-risk group seems to be increasing. Telemedicine and telementoring approaches facilitate access to healthcare systems and save costs; therefore, this kind of program should be implemented. Finally, the COVID-19 pandemic is currently a significant challenge to achieve viral hepatitis elimination; with the recent approval of a SARS-CoV-2 vaccine, most of the possibility to reactivate elimination viral hepatitis programs throughout the world will rely on SARS-CoV-2 effective vaccination strategies that gradually allows restarting the operativity of liver clinics and services.

**REFERENCES**

1 **The Lancet**. Towards elimination of viral hepatitis by 2030. *Lancet* 2016; **388**: 308 [PMID: 27477148 DOI: 10.1016/S0140-6736(16)31144-8]

2 **Lazarus JV**, Wiktor S, Colombo M, Thursz M; EASL International Liver Foundation. Micro-elimination - A path to global elimination of hepatitis C. *J Hepatol* 2017; **67**: 665-666 [PMID: 28760329 DOI: 10.1016/j.jhep.2017.06.033]

3 **Howell J**, Pedrana A, Cowie BC, Doyle J, Getahun A, Ward J, Gane E, Cunningham C, Wallace J, Lee A, Malani J, Thompson A, Hellard ME. Aiming for the elimination of viral hepatitis in Australia, New Zealand, and the Pacific Islands and Territories: Where are we now and barriers to meeting World Health Organization targets by 2030. *J Gastroenterol Hepatol* 2019; **34**: 40-48 [PMID: 30151932 DOI: 10.1111/jgh.14457]

4 **European Association for the Study of the Liver.** Clinical Practice Guidelines Panel: Chair:; EASL Governing Board representative:; Panel members:. EASL recommendations on treatment of hepatitis C: Final update of the series☆. *J Hepatol* 2020; **73**: 1170-1218 [PMID: 32956768 DOI: 10.1016/j.jhep.2020.08.018]

5 **Thomas DL**. Global Elimination of Chronic Hepatitis. *N Engl J Med* 2019; **380**: 2041-2050 [PMID: 31116920 DOI: 10.1056/NEJMra1810477]

6 **Foreman KJ**, Marquez N, Dolgert A, Fukutaki K, Fullman N, McGaughey M, Pletcher MA, Smith AE, Tang K, Yuan CW, Brown JC, Friedman J, He J, Heuton KR, Holmberg M, Patel DJ, Reidy P, Carter A, Cercy K, Chapin A, Douwes-Schultz D, Frank T, Goettsch F, Liu PY, Nandakumar V, Reitsma MB, Reuter V, Sadat N, Sorensen RJD, Srinivasan V, Updike RL, York H, Lopez AD, Lozano R, Lim SS, Mokdad AH, Vollset SE, Murray CJL. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016-40 for 195 countries and territories. *Lancet* 2018; **392**: 2052-2090 [PMID: 30340847 DOI: 10.1016/S0140-6736(18)31694-5]

7 **Kasai T**. Time to act to make elimination of viral hepatitis a reality. *Lancet Gastroenterol Hepatol* 2020; **5**: 102-103 [PMID: 31852633 DOI: 10.1016/S2468-1253(19)30303-6]

8 **Poortahmasebi V**, Baghi HB. Living in the shadows of hepatitis. *Lancet Infect Dis* 2019; **19**: 1171-1172 [PMID: 31657779 DOI: 10.1016/S1473-3099(19)30534-1]

9 **European Union HCV Collaborators**. Hepatitis C virus prevalence and level of intervention required to achieve the WHO targets for elimination in the European Union by 2030: a modelling study. *Lancet Gastroenterol Hepatol* 2017; **2**: 325-336 [PMID: 28397696 DOI: 10.1016/S2468-1253(17)30045-6]

10 **McMahon BJ**. Meeting the WHO and US Goals to Eliminate Hepatitis B Infection by 2030: Opportunities and Challenges. *Clin Liver Dis (Hoboken)* 2018; **12**: 29-32 [PMID: 30988906 DOI: 10.1002/cld.733]

11 **Ward JW**, Hinman AR. What Is Needed to Eliminate Hepatitis B Virus and Hepatitis C Virus as Global Health Threats. *Gastroenterology* 2019; **156**: 297-310 [PMID: 30391470 DOI: 10.1053/j.gastro.2018.10.048]

12 **Popping S**, El-Sayed M, Feld J, Hatzakis A, Hellard M, Lesi O, Ninburg M, Ward J, Boucher C. Report from the International Viral Hepatitis Elimination Meeting (IVHEM), 17-18 November 2017, Amsterdam, the Netherlands: gaps and challenges in the WHO 2030 hepatitis C elimination framework. *J Virus Erad* 2018; **4**: 193-195 [PMID: 30050685]

13 **Asselah T**, Marcellin P, Schinazi RF. Treatment of hepatitis C virus infection with direct-acting antiviral agents: 100% cure? *Liver Int* 2018; **38 Suppl 1**: 7-13 [PMID: 29427484 DOI: 10.1111/liv.13673]

14 **Asselah T**. A village without hepatitis C in Egypt: will micro-elimination lead to macro-elimination? *Lancet Gastroenterol Hepatol* 2018; **3**: 734-736 [PMID: 30030069 DOI: 10.1016/S2468-1253(18)30178-X]

15 **Ghany MG**, Morgan TR; AASLD-IDSA Hepatitis C Guidance Panel. Hepatitis C Guidance 2019 Update: American Association for the Study of Liver Diseases-Infectious Diseases Society of America Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. *Hepatology* 2020; **71**: 686-721 [PMID: 31816111 DOI: 10.1002/hep.31060]

16 **Feld JJ**, Jacobson IM, Hézode C, Asselah T, Ruane PJ, Gruener N, Abergel A, Mangia A, Lai CL, Chan HL, Mazzotta F, Moreno C, Yoshida E, Shafran SD, Towner WJ, Tran TT, McNally J, Osinusi A, Svarovskaia E, Zhu Y, Brainard DM, McHutchison JG, Agarwal K, Zeuzem S; ASTRAL-1 Investigators. Sofosbuvir and Velpatasvir for HCV Genotype 1, 2, 4, 5, and 6 Infection. *N Engl J Med* 2015; **373**: 2599-2607 [PMID: 26571066 DOI: 10.1056/NEJMoa1512610]

17 **Foster GR**, Afdhal N, Roberts SK, Bräu N, Gane EJ, Pianko S, Lawitz E, Thompson A, Shiffman ML, Cooper C, Towner WJ, Conway B, Ruane P, Bourlière M, Asselah T, Berg T, Zeuzem S, Rosenberg W, Agarwal K, Stedman CA, Mo H, Dvory-Sobol H, Han L, Wang J, McNally J, Osinusi A, Brainard DM, McHutchison JG, Mazzotta F, Tran TT, Gordon SC, Patel K, Reau N, Mangia A, Sulkowski M; ASTRAL-2 Investigators; ASTRAL-3 Investigators. Sofosbuvir and Velpatasvir for HCV Genotype 2 and 3 Infection. *N Engl J Med* 2015; **373**: 2608-2617 [PMID: 26575258 DOI: 10.1056/NEJMoa1512612]

18 **Curry MP**, O'Leary JG, Bzowej N, Muir AJ, Korenblat KM, Fenkel JM, Reddy KR, Lawitz E, Flamm SL, Schiano T, Teperman L, Fontana R, Schiff E, Fried M, Doehle B, An D, McNally J, Osinusi A, Brainard DM, McHutchison JG, Brown RS Jr, Charlton M; ASTRAL-4 Investigators. Sofosbuvir and Velpatasvir for HCV in Patients with Decompensated Cirrhosis. *N Engl J Med* 2015; **373**: 2618-2628 [PMID: 26569658 DOI: 10.1056/NEJMoa1512614]

19 **Grebely J**, Dalgard O, Conway B, Cunningham EB, Bruggmann P, Hajarizadeh B, Amin J, Bruneau J, Hellard M, Litwin AH, Marks P, Quiene S, Siriragavan S, Applegate TL, Swan T, Byrne J, Lacalamita M, Dunlop A, Matthews GV, Powis J, Shaw D, Thurnheer MC, Weltman M, Kronborg I, Cooper C, Feld JJ, Fraser C, Dillon JF, Read P, Gane E, Dore GJ; SIMPLIFY Study Group. Sofosbuvir and velpatasvir for hepatitis C virus infection in people with recent injection drug use (SIMPLIFY): an open-label, single-arm, phase 4, multicentre trial. *Lancet Gastroenterol Hepatol* 2018; **3**: 153-161 [PMID: 29310928 DOI: 10.1016/S2468-1253(17)30404-1]

20 **Isakov V**, Chulanov V, Abdurakhmanov D, Burnevich E, Nurmukhametova E, Kozhevnikova G, Gankina N, Zhuravel S, Romanova S, Hyland RH, Lu S, Svarovskaia ES, McNally J, Brainard DM, Ivashkin V, Morozov V, Bakulin I, Lagging M, Zhdanov K, Weiland O. Sofosbuvir/velpatasvir for the treatment of HCV: excellent results from a phase-3, open-label study in Russia and Sweden. *Infect Dis (Lond)* 2019; **51**: 131-139 [PMID: 30499360 DOI: 10.1080/23744235.2018.1535186]

21 **Guan WJ**, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS; China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020; **382**: 1708-1720 [PMID: 32109013 DOI: 10.1056/NEJMoa2002032]

22 **Agarwal K,** Castells L, Müllhaupt B, Rosenberg WMC, McNabb B, Arterburn S, Camus G, McNally J, Stamm LM, Brainard DM, Mani Subramanian G, Mariño Z, Dufour JF FX. Sofosbuvir / velpatasvir for 12 wk in genotype 1 – 4 HCV-infected liver transplant recipients. *J Hepatol* 2018; **69:** 603-607 [DOI: 10.1016/j.jhep.2018.05.039]

23 **Asselah T**, Shafran SD, Bourgeois S, Lai CL, Mathurin P, Willems B, Nguyen MH, Davis MN, Huang KC, Svarovskaia E, Osinusi A, McNally J, Brainard DM, Shaikh OS, Tran TT. Deferred treatment with a fixed-dose combination of sofosbuvir-velpatasvir for chronic hepatitis C virus genotype 1, 2, 4 and 6 infection. *J Viral Hepat* 2019; **26**: 1229-1232 [PMID: 31216086 DOI: 10.1111/jvh.13159]

24 **Sood A**, Duseja A, Kabrawala M, Amrose P, Goswami B, Chowdhury A, Sarin SK, Koshy A, Hyland RH, Lu S, Camus G, Stamm LM, Brainard DM, Subramanian GM, Prasad M, Bhatia S, Shah SR, Kapoor D, Shalimar, Saraswat V. Sofosbuvir-velpatasvir single-tablet regimen administered for 12 weeks in a phase 3 study with minimal monitoring in India. *Hepatol Int* 2019; **13**: 173-179 [PMID: 30790229 DOI: 10.1007/s12072-019-09927-6]

25 **Wei L**, Lim SG, Xie Q, Văn KN, Piratvisuth T, Huang Y, Wu S, Xu M, Tang H, Cheng J, Le Manh H, Gao Y, Mou Z, Sobhonslidsuk A, Dou X, Thongsawat S, Nan Y, Tan CK, Ning Q, Tee HP, Mao Y, Stamm LM, Lu S, Dvory-Sobol H, Mo H, Brainard DM, Yang YF, Dao L, Wang GQ, Tanwandee T, Hu P, Tangkijvanich P, Zhang L, Gao ZL, Lin F, Le TTP, Shang J, Gong G, Li J, Su M, Duan Z, Mohamed R, Hou JL, Jia J. Sofosbuvir-velpatasvir for treatment of chronic hepatitis C virus infection in Asia: a single-arm, open-label, phase 3 trial. *Lancet Gastroenterol Hepatol* 2019; **4**: 127-134 [PMID: 30555048 DOI: 10.1016/S2468-1253(18)30343-1]

26 **Takehara T**, Sakamoto N, Nishiguchi S, Ikeda F, Tatsumi T, Ueno Y, Yatsuhashi H, Takikawa Y, Kanda T, Sakamoto M, Tamori A, Mita E, Chayama K, Zhang G, De-Oertel S, Dvory-Sobol H, Matsuda T, Stamm LM, Brainard DM, Tanaka Y, Kurosaki M. Efficacy and safety of sofosbuvir-velpatasvir with or without ribavirin in HCV-infected Japanese patients with decompensated cirrhosis: an open-label phase 3 trial. *J Gastroenterol* 2019; **54**: 87-95 [PMID: 30203225 DOI: 10.1007/s00535-018-1503-x]

27 **Esteban R**, Pineda JA, Calleja JL, Casado M, Rodríguez M, Turnes J, Morano Amado LE, Morillas RM, Forns X, Pascasio Acevedo JM, Andrade RJ, Rivero A, Carrión JA, Lens S, Riveiro-Barciela M, McNabb B, Zhang G, Camus G, Stamm LM, Brainard DM, Subramanian GM, Buti M. Efficacy of Sofosbuvir and Velpatasvir, With and Without Ribavirin, in Patients With Hepatitis C Virus Genotype 3 Infection and Cirrhosis. *Gastroenterology* 2018; **155**: 1120-1127.e4 [PMID: 29958855 DOI: 10.1053/j.gastro.2018.06.042]

28 **Hezode C**, Reau N, Svarovskaia ES, Doehle BP, Shanmugam R, Dvory-Sobol H, Hedskog C, McNally J, Osinusi A, Brainard DM, Miller MD, Mo H, Roberts SK, O'Leary JG, Shafran SD, Zeuzem S. Resistance analysis in patients with genotype 1-6 HCV infection treated with sofosbuvir/velpatasvir in the phase III studies. *J Hepatol* 2018; **68**: 895-903 [PMID: 29221887 DOI: 10.1016/j.jhep.2017.11.032]

29 **Grebely J**, Dore GJ, Zeuzem S, Aspinall RJ, Fox R, Han L, McNally J, Osinusi A, Brainard DM, Subramanian GM, Natha M, Foster GR, Mangia A, Sulkowski M, Feld JJ. Efficacy and Safety of Sofosbuvir/Velpatasvir in Patients With Chronic Hepatitis C Virus Infection Receiving Opioid Substitution Therapy: Analysis of Phase 3 ASTRAL Trials. *Clin Infect Dis* 2016; **63**: 1479-1481 [PMID: 27553377 DOI: 10.1093/cid/ciw579]

30 **Mangia A**, Milligan S, Khalili M, Fagiuoli S, Shafran SD, Carrat F, Ouzan D, Papatheodoridis G, Ramji A, Borgia SM, Wedemeyer H, Losappio R, Pérez-Hernandez F, Wick N, Brown RS Jr, Lampertico P, Doucette K, Ntalla I, Ramroth H, Mertens M, Vanstraelen K, Turnes J. Global real-world evidence of sofosbuvir/velpatasvir as simple, effective HCV treatment: Analysis of 5552 patients from 12 cohorts. *Liver Int* 2020; **40**: 1841-1852 [PMID: 32449966 DOI: 10.1111/liv.14537]

31 **Mangia A**, Piazzolla V, Giannelli A, Visaggi E, Minerva N, Palmieri V, Carraturo I, Potenza D, Napoli N, Lauletta G, Tagarielli V, Santoro R, Piccigallo E, De Gioia S, Chimenti A, Cuccorese G, Metrangolo A, Mazzola M, Agostinacchio E, Mennea G, Sabbà C, Cela M, Copetti M, Losappio R. SVR12 rates higher than 99% after sofosbuvir/velpatasvir combination in HCV infected patients with F0-F1 fibrosis stage: A real world experience. *PLoS One* 2019; **14**: e0215783 [PMID: 31091254 DOI: 10.1371/journal.pone.0215783]

32 **von Felden J**, Vermehren J, Ingiliz P, Mauss S, Lutz T, Simon KG, Busch HW, Baumgarten A, Schewe K, Hueppe D, Boesecke C, Rockstroh JK, Daeumer M, Luebke N, Timm J, Schulze Zur Wiesch J, Sarrazin C, Christensen S. High efficacy of sofosbuvir/velpatasvir and impact of baseline resistance-associated substitutions in hepatitis C genotype 3 infection. *Aliment Pharmacol Ther* 2018; **47**: 1288-1295 [PMID: 29536554 DOI: 10.1111/apt.14592]

33 **Mangia A**, Cenderello G, Copetti M, Verucchi G, Piazzolla V, Lorusso C, Santoro R, Squillante MM, Orlandini A, Minisini R, Ciancio A. SVR12 Higher than 97% in GT3 Cirrhotic Patients with Evidence of Portal Hypertension Treated with SOF/VEL without Ribavirin: A Nation-Wide Cohort Study. *Cells* 2019; **8** [PMID: 30987413 DOI: 10.3390/cells8040313]

34 **Borgia SM**, Dearden J, Yoshida EM, Shafran SD, Brown A, Ben-Ari Z, Cramp ME, Cooper C, Foxton M, Rodriguez CF, Esteban R, Hyland R, Lu S, Kirby BJ, Meng A, Markova S, Dvory-Sobol H, Osinusi AO, Bruck R, Ampuero J, Ryder SD, Agarwal K, Fox R, Shaw D, Haider S, Willems B, Lurie Y, Calleja JL, Gane EJ. Sofosbuvir/velpatasvir for 12 weeks in hepatitis C virus-infected patients with end-stage renal disease undergoing dialysis. *J Hepatol* 2019; **71**: 660-665 [PMID: 31195062 DOI: 10.1016/j.jhep.2019.05.028]

35 **Wei L**, Wang G, Alami NN, Xie W, Heo J, Xie Q, Zhang M, Kim YJ, Lim SG, Fredrick LM, Lu W, Liu W, Kalluri HV, Krishnan P, Tripathi R, Mobashery N, Burroughs M, Asatryan A, Jia J, Hou J. Glecaprevir-pibrentasvir to treat chronic hepatitis C virus infection in Asia: two multicentre, phase 3 studies- a randomised, double-blind study (VOYAGE-1) and an open-label, single-arm study (VOYAGE-2). *Lancet Gastroenterol Hepatol* 2020; **5**: 839-849 [PMID: 32682494 DOI: 10.1016/S2468-1253(20)30086-8]

36 **Toyoda H**, Atsukawa M, Watanabe T, Nakamuta M, Uojima H, Nozaki A, Takaguchi K, Fujioka S, Iio E, Shima T, Akahane T, Fukunishi S, Asano T, Michitaka K, Tsuji K, Abe H, Mikami S, Okubo H, Okubo T, Shimada N, Ishikawa T, Moriya A, Tani J, Morishita A, Ogawa C, Tachi Y, Ikeda H, Yamashita N, Yasuda S, Chuma M, Tsutsui A, Hiraoka A, Ikegami T, Genda T, Tsubota A, Masaki T, Tanaka Y, Iwakiri K, Kumada T. Real-world experience of 12-week direct-acting antiviral regimen of glecaprevir and pibrentasvir in patients with chronic hepatitis C virus infection. *J Gastroenterol Hepatol* 2020; **35**: 855-861 [PMID: 31609495 DOI: 10.1111/jgh.14874]

37 **Gane E**, Poordad F, Zadeikis N, Valdes J, Lin CW, Liu W, Asatryan A, Wang S, Stedman C, Greenbloom S, Nguyen T, Elkhashab M, Wörns MA, Tran A, Mulkay JP, Setze C, Yu Y, Pilot-Matias T, Porcalla A, Mensa FJ. Safety and Pharmacokinetics of Glecaprevir/Pibrentasvir in Adults With Chronic Genotype 1-6 Hepatitis C Virus Infections and Compensated Liver Disease. *Clin Infect Dis* 2019; **69**: 1657-1664 [PMID: 30923816 DOI: 10.1093/cid/ciz022]

38 **Foster GR**, Asselah T, Kopecky-Bromberg S, Lei Y, Asatryan A, Trinh R, Zadeikis N, Mensa FJ. Safety and efficacy of glecaprevir/pibrentasvir for the treatment of chronic hepatitis C in patients aged 65 years or older. *PLoS One* 2019; **14**: e0208506 [PMID: 30601818 DOI: 10.1371/journal.pone.0208506]

39 **Flamm S**, Mutimer D, Asatryan A, Wang S, Rockstroh J, Horsmans Y, Kwo PY, Weiland O, Villa E, Heo J, Gane E, Ryder SD, Welzel TM, Ruane PJ, Agarwal K, Ng TI, Xue Z, Lovell SS, Krishnan P, Kopecky-Bromberg S, Trinh R, Mensa FJ, Wyles DL. Glecaprevir/Pibrentasvir in patients with chronic HCV genotype 3 infection: An integrated phase 2/3 analysis. *J Viral Hepat* 2019; **26**: 337-349 [PMID: 30421537 DOI: 10.1111/jvh.13038]

40 **Asselah T**, Lee SS, Yao BB, Nguyen T, Wong F, Mahomed A, Lim SG, Abergel A, Sasadeusz J, Gane E, Zadeikis N, Schnell G, Zhang Z, Porcalla A, Mensa FJ, Nguyen K. Efficacy and safety of glecaprevir/pibrentasvir in patients with chronic hepatitis C virus genotype 5 or 6 infection (ENDURANCE-5,6): an open-label, multicentre, phase 3b trial. *Lancet Gastroenterol Hepatol* 2019; **4**: 45-51 [PMID: 30393106 DOI: 10.1016/S2468-1253(18)30341-8]

41 **Krishnan P**, Pilot-Matias T, Schnell G, Tripathi R, Ng TI, Reisch T, Beyer J, Dekhtyar T, Irvin M, Xie W, Larsen L, Mensa FJ, Collins C. Pooled Resistance Analysis in Patients with Hepatitis C Virus Genotype 1 to 6 Infection Treated with Glecaprevir-Pibrentasvir in Phase 2 and 3 Clinical Trials. *Antimicrob Agents Chemother* 2018; **62** [PMID: 30061289 DOI: 10.1128/AAC.01249-18]

42 **Puoti M**, Foster GR, Wang S, Mutimer D, Gane E, Moreno C, Chang TT, Lee SS, Marinho R, Dufour JF, Pol S, Hezode C, Gordon SC, Strasser SI, Thuluvath PJ, Zhang Z, Lovell S, Pilot-Matias T, Mensa FJ. High SVR12 with 8-week and 12-week glecaprevir/pibrentasvir therapy: An integrated analysis of HCV genotype 1-6 patients without cirrhosis. *J Hepatol* 2018; **69**: 293-300 [PMID: 29551706 DOI: 10.1016/j.jhep.2018.03.007]

43 **Zeuzem S**, Foster GR, Wang S, Asatryan A, Gane E, Feld JJ, Asselah T, Bourlière M, Ruane PJ, Wedemeyer H, Pol S, Flisiak R, Poordad F, Chuang WL, Stedman CA, Flamm S, Kwo P, Dore GJ, Sepulveda-Arzola G, Roberts SK, Soto-Malave R, Kaita K, Puoti M, Vierling J, Tam E, Vargas HE, Bruck R, Fuster F, Paik SW, Felizarta F, Kort J, Fu B, Liu R, Ng TI, Pilot-Matias T, Lin CW, Trinh R, Mensa FJ. Glecaprevir-Pibrentasvir for 8 or 12 Weeks in HCV Genotype 1 or 3 Infection. *N Engl J Med* 2018; **378**: 354-369 [PMID: 29365309 DOI: 10.1056/NEJMoa1702417]

44 **Asselah T**, Kowdley KV, Zadeikis N, Wang S, Hassanein T, Horsmans Y, Colombo M, Calinas F, Aguilar H, de Ledinghen V, Mantry PS, Hezode C, Marinho RT, Agarwal K, Nevens F, Elkhashab M, Kort J, Liu R, Ng TI, Krishnan P, Lin CW, Mensa FJ. Efficacy of Glecaprevir/Pibrentasvir for 8 or 12 Weeks in Patients With Hepatitis C Virus Genotype 2, 4, 5, or 6 Infection Without Cirrhosis. *Clin Gastroenterol Hepatol* 2018; **16**: 417-426 [PMID: 28951228 DOI: 10.1016/j.cgh.2017.09.027]

45 **Chayama K**, Suzuki F, Karino Y, Kawakami Y, Sato K, Atarashi T, Naganuma A, Watanabe T, Eguchi Y, Yoshiji H, Seike M, Takei Y, Kato K, Alves K, Burroughs M, Redman R, Pugatch DL, Pilot-Matias TJ, Krishnan P, Oberoi RK, Xie W, Kumada H. Efficacy and safety of glecaprevir/pibrentasvir in Japanese patients with chronic genotype 1 hepatitis C virus infection with and without cirrhosis. *J Gastroenterol* 2018; **53**: 557-565 [PMID: 28948366 DOI: 10.1007/s00535-017-1391-5]

46 **Wyles D**, Poordad F, Wang S, Alric L, Felizarta F, Kwo PY, Maliakkal B, Agarwal K, Hassanein T, Weilert F, Lee SS, Kort J, Lovell SS, Liu R, Lin CW, Pilot-Matias T, Krishnan P, Mensa FJ. Glecaprevir/pibrentasvir for hepatitis C virus genotype 3 patients with cirrhosis and/or prior treatment experience: A partially randomized phase 3 clinical trial. *Hepatology* 2018; **67**: 514-523 [PMID: 28926120 DOI: 10.1002/hep.29541]

47 **Toyoda H**, Chayama K, Suzuki F, Sato K, Atarashi T, Watanabe T, Atsukawa M, Naganuma A, Notsumata K, Osaki Y, Nakamuta M, Takaguchi K, Saito S, Kato K, Pugatch D, Burroughs M, Redman R, Alves K, Pilot-Matias TJ, Oberoi RK, Fu B, Kumada H. Efficacy and safety of glecaprevir/pibrentasvir in Japanese patients with chronic genotype 2 hepatitis C virus infection. *Hepatology* 2018; **67**: 505-513 [PMID: 28865152 DOI: 10.1002/hep.29510]

48 **Forns X**, Lee SS, Valdes J, Lens S, Ghalib R, Aguilar H, Felizarta F, Hassanein T, Hinrichsen H, Rincon D, Morillas R, Zeuzem S, Horsmans Y, Nelson DR, Yu Y, Krishnan P, Lin CW, Kort JJ, Mensa FJ. Glecaprevir plus pibrentasvir for chronic hepatitis C virus genotype 1, 2, 4, 5, or 6 infection in adults with compensated cirrhosis (EXPEDITION-1): a single-arm, open-label, multicentre phase 3 trial. *Lancet Infect Dis* 2017; **17**: 1062-1068 [PMID: 28818546 DOI: 10.1016/S1473-3099(17)30496-6]

49 **Kwo PY**, Poordad F, Asatryan A, Wang S, Wyles DL, Hassanein T, Felizarta F, Sulkowski MS, Gane E, Maliakkal B, Overcash JS, Gordon SC, Muir AJ, Aguilar H, Agarwal K, Dore GJ, Lin CW, Liu R, Lovell SS, Ng TI, Kort J, Mensa FJ. Glecaprevir and pibrentasvir yield high response rates in patients with HCV genotype 1-6 without cirrhosis. *J Hepatol* 2017; **67**: 263-271 [PMID: 28412293 DOI: 10.1016/j.jhep.2017.03.039]

50 **Poordad F**, Felizarta F, Asatryan A, Sulkowski MS, Reindollar RW, Landis CS, Gordon SC, Flamm SL, Fried MW, Bernstein DE, Lin CW, Liu R, Lovell SS, Ng TI, Kort J, Mensa FJ. Glecaprevir and pibrentasvir for 12 weeks for hepatitis C virus genotype 1 infection and prior direct-acting antiviral treatment. *Hepatology* 2017; **66**: 389-397 [PMID: 28128852 DOI: 10.1002/hep.29081]

51 **Atsukawa M**, Tsubota A, Toyoda H, Takaguchi K, Nakamuta M, Watanabe T, Michitaka K, Ikegami T, Nozaki A, Uojima H, Fukunishi S, Genda T, Abe H, Hotta N, Tsuji K, Ogawa C, Tachi Y, Shima T, Shimada N, Kondo C, Akahane T, Aizawa Y, Tanaka Y, Kumada T, Iwakiri K. The efficacy and safety of glecaprevir plus pibrentasvir in 141 patients with severe renal impairment: a prospective, multicenter study. *Aliment Pharmacol Ther* 2019; **49**: 1230-1241 [PMID: 30873651 DOI: 10.1111/apt.15218]

52 **Kumada H**, Watanabe T, Suzuki F, Ikeda K, Sato K, Toyoda H, Atsukawa M, Ido A, Takaki A, Enomoto N, Kato K, Alves K, Burroughs M, Redman R, Pugatch D, Pilot-Matias TJ, Krishnan P, Oberoi RK, Xie W, Chayama K. Efficacy and safety of glecaprevir/pibrentasvir in HCV-infected Japanese patients with prior DAA experience, severe renal impairment, or genotype 3 infection. *J Gastroenterol* 2018; **53**: 566-575 [PMID: 29052790 DOI: 10.1007/s00535-017-1396-0]

53 **Gane E**, Lawitz E, Pugatch D, Papatheodoridis G, Bräu N, Brown A, Pol S, Leroy V, Persico M, Moreno C, Colombo M, Yoshida EM, Nelson DR, Collins C, Lei Y, Kosloski M, Mensa FJ. Glecaprevir and Pibrentasvir in Patients with HCV and Severe Renal Impairment. *N Engl J Med* 2017; **377**: 1448-1455 [PMID: 29020583 DOI: 10.1056/NEJMoa1704053]

54 **Reau N**, Kwo PY, Rhee S, Brown RS Jr, Agarwal K, Angus P, Gane E, Kao JH, Mantry PS, Mutimer D, Reddy KR, Tran TT, Hu YB, Gulati A, Krishnan P, Dumas EO, Porcalla A, Shulman NS, Liu W, Samanta S, Trinh R, Forns X. Glecaprevir/Pibrentasvir Treatment in Liver or Kidney Transplant Patients With Hepatitis C Virus Infection. *Hepatology* 2018; **68**: 1298-1307 [PMID: 29672891 DOI: 10.1002/hep.30046]

55 **Younossi ZM**, Stepanova M, Sulkowski M, Wyles D, Kottilil S, Hunt S. Patient-reported outcomes in patients co-infected with hepatitis C virus and human immunodeficiency virus treated with sofosbuvir and velpatasvir: The ASTRAL-5 study. *Liver Int* 2017; **37**: 1796-1804 [PMID: 28470938 DOI: 10.1111/liv.13462]

56 **Wyles D**, Bräu N, Kottilil S, Daar ES, Ruane P, Workowski K, Luetkemeyer A, Adeyemi O, Kim AY, Doehle B, Huang KC, Mogalian E, Osinusi A, McNally J, Brainard DM, McHutchison JG, Naggie S, Sulkowski M; ASTRAL-5 Investigators. Sofosbuvir and Velpatasvir for the Treatment of Hepatitis C Virus in Patients Coinfected With Human Immunodeficiency Virus Type 1: An Open-Label, Phase 3 Study. *Clin Infect Dis* 2017; **65**: 6-12 [PMID: 28369210 DOI: 10.1093/cid/cix260]

57 **Rockstroh JK**, Lacombe K, Viani RM, Orkin C, Wyles D, Luetkemeyer AF, Soto-Malave R, Flisiak R, Bhagani S, Sherman KE, Shimonova T, Ruane P, Sasadeusz J, Slim J, Zhang Z, Samanta S, Ng TI, Gulati A, Kosloski MP, Shulman NS, Trinh R, Sulkowski M. Efficacy and Safety of Glecaprevir/Pibrentasvir in Patients Coinfected With Hepatitis C Virus and Human Immunodeficiency Virus Type 1: The EXPEDITION-2 Study. *Clin Infect Dis* 2018; **67**: 1010-1017 [PMID: 29566246 DOI: 10.1093/cid/ciy220]

58 **Llaneras J**, Riveiro-Barciela M, Lens S, Diago M, Cachero A, García-Samaniego J, Conde I, Arencibia A, Arenas J, Gea F, Torras X, Luis Calleja J, Antonio Carrión J, Fernández I, María Morillas R, Rosales JM, Carmona I, Fernández-Rodríguez C, Hernández-Guerra M, Llerena S, Bernal V, Turnes J, González-Santiago JM, Montoliu S, Figueruela B, Badia E, Delgado M, Fernández-Bermejo M, Iñarrairaegui M, Pascasio JM, Esteban R, Mariño Z, Buti M. Effectiveness and safety of sofosbuvir/velpatasvir/voxilaprevir in patients with chronic hepatitis C previously treated with DAAs. *J Hepatol* 2019; **71**: 666-672 [PMID: 31203153 DOI: 10.1016/j.jhep.2019.06.002]

59 **Wilson E**, Covert E, Hoffmann J, Comstock E, Emmanuel B, Tang L, Husson J, Chua J, Price A, Mathur P, Rosenthal E, Kattakuzhy S, Masur H, Kottilil S. A pilot study of safety and efficacy of HCV retreatment with sofosbuvir/velpatasvir/voxilaprevir in patients with or without HIV (RESOLVE STUDY). *J Hepatol* 2019; **71**: 498-504 [PMID: 31173815 DOI: 10.1016/j.jhep.2019.05.021]

60 **Lok AS**, Sulkowski MS, Kort JJ, Willner I, Reddy KR, Shiffman ML, Hassan MA, Pearlman BL, Hinestrosa F, Jacobson IM, Morelli G, Peter JA, Vainorius M, Michael LC, Fried MW, Wang GP, Lu W, Larsen L, Nelson DR. Efficacy of Glecaprevir and Pibrentasvir in Patients With Genotype 1 Hepatitis C Virus Infection With Treatment Failure After NS5A Inhibitor Plus Sofosbuvir Therapy. *Gastroenterology* 2019; **157**: 1506-1517.e1 [PMID: 31401140 DOI: 10.1053/j.gastro.2019.08.008]

61 **Poordad F**, Pol S, Asatryan A, Buti M, Shaw D, Hézode C, Felizarta F, Reindollar RW, Gordon SC, Pianko S, Fried MW, Bernstein DE, Gallant J, Lin CW, Lei Y, Ng TI, Krishnan P, Kopecky-Bromberg S, Kort J, Mensa FJ. Glecaprevir/Pibrentasvir in patients with hepatitis C virus genotype 1 or 4 and past direct-acting antiviral treatment failure. *Hepatology* 2018; **67**: 1253-1260 [PMID: 29152781 DOI: 10.1002/hep.29671]

62 **Feld JJ**, Cypel M, Kumar D, Dahari H, Pinto Ribeiro RV, Marks N, Kamkar N, Bahinskaya I, Onofrio FQ, Zahoor MA, Cerrochi O, Tinckam K, Kim SJ, Schiff J, Reichman TW, McDonald M, Alba C, Waddell TK, Sapisochin G, Selzner M, Keshavjee S, Janssen HLA, Hansen BE, Singer LG, Humar A. Short-course, direct-acting antivirals and ezetimibe to prevent HCV infection in recipients of organs from HCV-infected donors: a phase 3, single-centre, open-label study. *Lancet Gastroenterol Hepatol* 2020; **5**: 649-657 [PMID: 32389183 DOI: 10.1016/S2468-1253(20)30081-9]

63 **Young K**, Liu B, Bhuket T, Wong RJ. Lower Likelihood of Post-transplant Graft Failure, Death, and Retransplantation in the Era of Direct-Acting Antivirals. *J Clin Exp Hepatol* 2020; **10**: 581-589 [PMID: 33311895 DOI: 10.1016/j.jceh.2020.02.003]

64 **Arora SS**, Axley P, Ahmed Z, Satapathy SK, Wong R, Kuo YF, Singal AK. Decreasing frequency and improved outcomes of hepatitis C-related liver transplantation in the era of direct-acting antivirals - a retrospective cohort study. *Transpl Int* 2019; **32**: 854-864 [PMID: 30866110 DOI: 10.1111/tri.13424]

65 **Choudhary NS**, Saraf N, Saigal S, Rastogi A, Bhangui P, Thiagrajan S, Soin AS. Outcome of hepatitis C-related liver transplantation in direct-acting antiviral era. *Indian J Gastroenterol* 2020; **39**: 539-543 [PMID: 33230754 DOI: 10.1007/s12664-020-01105-z]

66 **Young K**, Liu B, Bhuket T, Gish RG, Wong RJ. Improved liver transplant waitlist mortality and lower risk of disease progression among chronic hepatitis C patients awaiting liver transplantation after the introduction of direct-acting antiviral therapies in the United States. *J Viral Hepat* 2019; **26**: 350-361 [PMID: 30412318 DOI: 10.1111/jvh.13039]

67 **Bittermann T**, Reddy KR. In the Era of Direct-Acting Antivirals, Liver Transplant Delisting Due to Clinical Improvement for Hepatitis C Remains Infrequent. *Clin Gastroenterol Hepatol* 2020 [PMID: 32971230 DOI: 10.1016/j.cgh.2020.09.033]

68 **Gerlich WH**. Prophylactic vaccination against hepatitis B: achievements, challenges and perspectives. *Med Microbiol Immunol* 2015; **204**: 39-55 [PMID: 25523195 DOI: 10.1007/s00430-014-0373-y]

69 **Chen SM**, Kung CM, Yang WJ, Wang HL. Efficacy of the nationwide hepatitis B infant vaccination program in Taiwan. *J Clin Virol* 2011; **52**: 11-16 [PMID: 21767983 DOI: 10.1016/j.jcv.2011.06.012]

70 **Chang MH**, You SL, Chen CJ, Liu CJ, Lee CM, Lin SM, Chu HC, Wu TC, Yang SS, Kuo HS, Chen DS; Taiwan Hepatoma Study Group. Decreased incidence of hepatocellular carcinoma in hepatitis B vaccinees: a 20-year follow-up study. *J Natl Cancer Inst* 2009; **101**: 1348-1355 [PMID: 19759364 DOI: 10.1093/jnci/djp288]

71 **Park NH**, Chung YH, Lee HS. Impacts of vaccination on hepatitis B viral infections in Korea over a 25-year period. *Intervirology* 2010; **53**: 20-28 [PMID: 20068337 DOI: 10.1159/000252780]

72 **Whitford K**, Liu B, Micallef J, Yin JK, Macartney K, Van Damme P, Kaldor JM. Long-term impact of infant immunization on hepatitis B prevalence: a systematic review and meta-analysis. *Bull World Health Organ* 2018; **96**: 484-497 [PMID: 29962551 DOI: 10.2471/BLT.17.205153]

73 **Niederau C**. Chronic hepatitis B in 2014: great therapeutic progress, large diagnostic deficit. *World J Gastroenterol* 2014; **20**: 11595-11617 [PMID: 25206267 DOI: 10.3748/wjg.v20.i33.11595]

74 **Scognamiglio P**, Girardi E, Fusco M, Piselli P, Spena SR, Maione C, Pisanti FA, Serraino D; Collaborating Study Group. Lack of implementation of Hepatitis B Virus (HBV) vaccination policy in household contacts of HBV carriers in Italy. *BMC Infect Dis* 2009; **9**: 86 [PMID: 19500412 DOI: 10.1186/1471-2334-9-86]

75 **Wallace J**, Hajarizadeh B, Richmond J, McNally S. Challenges in managing patients in Australia with chronic hepatitis B: the General Practitioners' perspective. *Aust N Z J Public Health* 2013; **37**: 405-410 [PMID: 24090321 DOI: 10.1111/1753-6405.12127]

76 **Sievert K**, Liddle R, Tan A, Arachchi N, Valaydon Z, Allard N. Promoting hospital and primary care collaboration for timely and effective care for chronic hepatitis B in western Melbourne. *Aust Health Rev* 2020; **44**: 521-526 [PMID: 32718420 DOI: 10.1071/AH19135]

77 **Terrault NA**, Lok ASF, McMahon BJ, Chang KM, Hwang JP, Jonas MM, Brown RS Jr, Bzowej NH, Wong JB. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology* 2018; **67**: 1560-1599 [PMID: 29405329 DOI: 10.1002/hep.29800]

78 **European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu.**; European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. *J Hepatol* 2017; **67**: 370-398 [PMID: 28427875 DOI: 10.1016/j.jhep.2017.03.021]

79 **Yim HJ**, Kim JH, Park JY, Yoon EL, Park H, Kwon JH, Sinn DH, Lee SH, Lee JH, Lee HW. Comparison of clinical practice guidelines for the management of chronic hepatitis B: When to start, when to change, and when to stop. *Clin Mol Hepatol* 2020; **26**: 411-429 [PMID: 32854458 DOI: 10.3350/cmh.2020.0049]

80 **Tenney DJ**, Rose RE, Baldick CJ, Pokornowski KA, Eggers BJ, Fang J, Wichroski MJ, Xu D, Yang J, Wilber RB, Colonno RJ. Long-term monitoring shows hepatitis B virus resistance to entecavir in nucleoside-naïve patients is rare through 5 years of therapy. *Hepatology* 2009; **49**: 1503-1514 [PMID: 19280622 DOI: 10.1002/hep.22841]

81 **Zhang Y**, Xu W, Zhu X, Li X, Li J, Shu X, Lai J, Xie J, Xie C, Peng L. The 48-week safety and therapeutic effects of tenofovir alafenamide in hbv-related acute-on-chronic liver failure: A prospective cohort study. *J Viral Hepat* 2021; **28**: 592-600 [PMID: 33423348 DOI: 10.1111/jvh.13468]

82 **Kaneko S**, Kurosaki M, Tamaki N, Itakura J, Hayashi T, Kirino S, Osawa L, Watakabe K, Okada M, Wang W, Shimizu T, Higuchi M, Takaura K, Yasui Y, Tsuchiya K, Nakanishi H, Takahashi Y, Watanabe M, Izumi N. Tenofovir alafenamide for hepatitis B virus infection including switching therapy from tenofovir disoproxil fumarate. *J Gastroenterol Hepatol* 2019; **34**: 2004-2010 [PMID: 31017689 DOI: 10.1111/jgh.14686]

83 **Seto WK**, Asahina Y, Brown TT, Peng CY, Stanciu C, Abdurakhmanov D, Tabak F, Nguyen TT, Chuang WL, Inokuma T, Ikeda F, Santantonio TA, Habersetzer F, Ramji A, Lau AH, Suri V, Flaherty JF, Wang H, Gaggar A, Subramanian GM, Mukewar S, Brunetto MR, Fung S, Chan HL. Improved Bone Safety of Tenofovir Alafenamide Compared to Tenofovir Disoproxil Fumarate Over 2 Years in Patients With Chronic HBV Infection. *Clin Gastroenterol Hepatol* 2018 [PMID: 29933096 DOI: 10.1016/j.cgh.2018.06.023]

84 **Agarwal K**, Brunetto M, Seto WK, Lim YS, Fung S, Marcellin P, Ahn SH, Izumi N, Chuang WL, Bae H, Sharma M, Janssen HLA, Pan CQ, Çelen MK, Furusyo N, Shalimar D, Yoon KT, Trinh H, Flaherty JF, Gaggar A, Lau AH, Cathcart AL, Lin L, Bhardwaj N, Suri V, Mani Subramanian G, Gane EJ, Buti M, Chan HLY; GS-US-320-0110; GS-US-320-0108 Investigators. 96 weeks treatment of tenofovir alafenamide vs. tenofovir disoproxil fumarate for hepatitis B virus infection. *J Hepatol* 2018; **68**: 672-681 [PMID: 29756595 DOI: 10.1016/j.jhep.2017.11.039]

85 **Miquel M**, Pardo A, Forné M, Martínez-Alpin G, Rodríguez-Castellano A, Casas M, Rosinach M, Roget M, Dalmau B, Temiño R, Quer JC, Sanchez-Delgado J, Ortiz J, Vergara M. Current trends in access to treatment for hepatitis B in immigrants vs non-immigrants. *Gastroenterol Rep (Oxf)* 2020; **8**: 362-366 [PMID: 33163191 DOI: 10.1093/gastro/goaa010]

86 **Voulgaris T**, Vlachogiannakos J, Ioannidou P, Papageorgiou MV, Zampeli E, Karagiannakis D, Georgiou A, Papazoglou A, Karamanolis G, Papatheodoridis GV. Adherence to follow-up and treatment recommendations in Greek and immigrant patients with chronic hepatitis B in Greece. *Eur J Gastroenterol Hepatol* 2017; **29**: 264-270 [PMID: 27922484 DOI: 10.1097/MEG.0000000000000788]

87 **Contini C**, Badia L, Cultrera R, Grilli A, De Togni A. Epidemiological, clinical and laboratory features of chronic hepatitis B infection in a cohort of immigrant and Italian patients from Ferrara, Italy. *Ann Hepatol* 2012; **11**: 862-869 [PMID: 23109449]

88 **Alonso M**, Gutzman A, Mazin R, Pinzon CE, Reveiz L, Ghidinelli M. Hepatitis C in key populations in Latin America and the Caribbean: systematic review and meta-analysis. *Int J Public Health* 2015; **60**: 789-798 [PMID: 26298439 DOI: 10.1007/s00038-015-0708-5]

89 **Godin A,** Kronfli N, Cox J, Alary M, Maheu-Giroux M. The role of prison-based interventions for hepatitis C virus (HCV) micro-elimination among people who inject drugs in Montréal, Canada. *Int J Drug Policy* 2020; 102738 [DOI: 10.1016/j.drugpo.2020.102738]

90 **Gaspar R**, Liberal R, Tavares J, Morgado R, Macedo G. HIPPOCRATES® project: A proof of concept of a collaborative program for hepatitis C virus micro-elimination in a prison setting. *World J Hepatol* 2020; **12**: 1314-1325 [PMID: 33442457 DOI: 10.4254/wjh.v12.i12.1314]

91 **Cotte L**, Hocqueloux L, Lefebvre M, Pradat P, Bani-Sadr F, Huleux T, Poizot-Martin I, Pugliese P, Rey D, Cabié A; Dat’AIDS study group. Microelimination or not? The changing epidemiology of HIV-HCV coinfection in France 2012-2018. *Clin Infect Dis* 2021 [PMID: 33400777 DOI: 10.1093/cid/ciaa1940]

92 **Gonzalez-Serna A**, Macias J, Palacios R, Gómez-Ayerbe C, Tellez F, Rivero-Juárez A, Fernandez M, Santos J, Real LM, Gonzalez-Domenech CM, Gomez-Mateos J, Pineda JA; HEPAVIR study group. Incidence of recently acquired hepatitis C virus infection among HIV-infected patients in southern Spain. *HIV Med* 2021; **22**: 379-386 [PMID: 33369104 DOI: 10.1111/hiv.13039]

93 **Smit C**, Boyd A, Rijnders BJA, van de Laar TJW, Leyten EM, Bierman WF, Brinkman K, Claassen MAA, den Hollander J, Boerekamps A, Newsum AM, Schinkel J, Prins M, Arends JE, Op de Coul ELM, van der Valk M, Reiss P; ATHENA observational cohort. HCV micro-elimination in individuals with HIV in the Netherlands 4 years after universal access to direct-acting antivirals: a retrospective cohort study. *Lancet HIV* 2021; **8**: e96-e105 [PMID: 33357835 DOI: 10.1016/S2352-3018(20)30301-5]

94 **Koopsen J**, Parker E, Han AX, van de Laar T, Russell C, Hoornenborg E, Prins M, van der Valk M, Schinkel J. HCV transmission among MSM in Amsterdam: external introductions may complicate micro-elimination efforts. *Clin Infect Dis* 2020 [PMID: 33289036 DOI: 10.1093/cid/ciaa1830]

95 **Stasi C**, Silvestri C, Voller F. Update on Hepatitis C Epidemiology: Unaware and Untreated Infected Population Could Be the Key to Elimination. *SN Compr Clin Med* 2020: 1-8 [PMID: 33103061 DOI: 10.1007/s42399-020-00588-3]

96 **Mohsen W**, Chan P, Whelan M, Glass A, Mouton M, Young E, Tran Q, Arora S, Davison S, Lama T, Cobrador C, Levy M. Hepatitis C treatment for difficult to access populations: can telementoring (as distinct from telemedicine) help? *Intern Med J* 2019; **49**: 351-357 [PMID: 30091164 DOI: 10.1111/imj.14072]

97 **Morey S**, Hamoodi A, Jones D, Young T, Thompson C, Dhuny J, Buchanan E, Miller C, Hewett M, Valappil M, Hunter E, McPherson S. Increased diagnosis and treatment of hepatitis C in prison by universal offer of testing and use of telemedicine. *J Viral Hepat* 2019; **26**: 101-108 [PMID: 30315691 DOI: 10.1111/jvh.13017]

98 **Sterling RK**, Cherian R, Lewis S, Genther K, Driscoll C, Martin K, Goode MB, Matherly S, Siddiqui MS, Luketic VA, Stravitz RT, Puri P, Lee H, Smith P, Patel V, Sanyal AJ. Treatment of HCV in the Department of Corrections in the Era of Oral Medications. *J Correct Health Care* 2018; **24**: 127-136 [PMID: 29566611 DOI: 10.1177/1078345818762591]

99 **Talal AH**, Andrews P, Mcleod A, Chen Y, Sylvester C, Markatou M, Brown LS. Integrated, Co-located, Telemedicine-based Treatment Approaches for Hepatitis C Virus Management in Opioid Use Disorder Patients on Methadone. *Clin Infect Dis* 2019; **69**: 323-331 [PMID: 30329042 DOI: 10.1093/cid/ciy899]

100 **Perez Hernandez JL,** Lehmann Mendoza R, Luna Martinez J, Torres Roldan JF, Chaidez Rosales PA, Martinez Arredondo HA, Rebollar Gonzalez V, De la Cruz Silva L, Santana-Vargas D, Higuera de la Tijera MF ASC. Chronic Viral Hepatitis C Micro-Elimination Program Using Telemedicine. the Mexican Experience. *Rev Española Enfermedades Dig* 2020 [DOI: 10.17235/reed.2020.7425/2020]

101 **Du P**, Wang X, Kong L, Jung J. Can Telementoring Reduce Urban-Rural Disparities in Utilization of Direct-Acting Antiviral Agents? *Telemed J E Health* 2021; **27**: 488-494 [PMID: 32882154 DOI: 10.1089/tmj.2020.0090]

102 **Cuadrado A**, Cobo C, Mateo M, Blasco AJ, Cabezas J, Llerena S, Fortea JI, Lázaro P, Crespo J. Telemedicine efficiently improves access to hepatitis C management to achieve HCV elimination in the penitentiary setting. *Int J Drug Policy* 2021; **88**: 103031 [PMID: 33221615 DOI: 10.1016/j.drugpo.2020.103031]

103 **Jiménez Galán G**, Alia Alia C, Vegue González M, García Berriguete RMª, Fernández González F, Fernández Rodríguez CM, González Fernández M, Gutiérrez García ML, Losa JE, Velasco M, Moreno L, Hervás R, Delgado-Iribarren A, Palacios García-Cervigón G. The contribution of telemedicine to hepatitis C elimination in a correctional facility. *Rev Esp Enferm Dig* 2019; **111**: 550-555 [PMID: 31215210 DOI: 10.17235/reed.2019.6152/2018]

104 **Haridy J**, Iyngkaran G, Nicoll A, Hebbard G, Tse E, Fazio T. eHealth Technologies for Screening, Diagnosis, and Management of Viral Hepatitis: A Systematic Review. *Clin Gastroenterol Hepatol* 2021; **19**: 1139-1150.e30 [PMID: 32896632 DOI: 10.1016/j.cgh.2020.09.011]

105 **Pley CM**, McNaughton AL, Matthews PC, Lourenço J. The global impact of the COVID-19 pandemic on the prevention, diagnosis and treatment of hepatitis B virus (HBV) infection. *BMJ Glob Health* 2021; **6** [PMID: 33402334 DOI: 10.1136/bmjgh-2020-004275]

106 **Karimi-Sari H**, Rezaee-Zavareh MS. COVID-19 and viral hepatitis elimination programs: Are we stepping backward? *Liver Int* 2020; **40**: 2042 [PMID: 32319207 DOI: 10.1111/liv.14486]

107 **Wingrove C**, Ferrier L, James C, Wang S. The impact of COVID-19 on hepatitis elimination. *Lancet Gastroenterol Hepatol* 2020; **5**: 792-794 [PMID: 32730783 DOI: 10.1016/S2468-1253(20)30238-7]

108 **The Lancet Gastroenterology Hepatology**. Eliminating viral hepatitis in the COVID-19 era: weighing challenge and opportunity. *Lancet Gastroenterol Hepatol* 2020; **5**: 789 [PMID: 32730787 DOI: 10.1016/S2468-1253(20)30237-5]

109 **Sperring H**, Ruiz-Mercado G, Schechter-Perkins EM. Impact of the 2020 COVID-19 Pandemic on Ambulatory Hepatitis C Testing. *J Prim Care Community Health* 2020; **11**: 2150132720969554 [PMID: 33225792 DOI: 10.1177/2150132720969554]

110 **Blach S**, Kondili LA, Aghemo A, Cai Z, Dugan E, Estes C, Gamkrelidze I, Ma S, Pawlotsky JM, Razavi-Shearer D, Razavi H, Waked I, Zeuzem S, Craxi A. Impact of COVID-19 on global HCV elimination efforts. *J Hepatol* 2021; **74**: 31-36 [PMID: 32777322 DOI: 10.1016/j.jhep.2020.07.042]

111 **Makhoul M**, Ayoub HH, Chemaitelly H, Seedat S, Mumtaz GR, Al-Omari S, Abu-Raddad LJ. Epidemiological Impact of SARS-CoV-2 Vaccination: Mathematical Modeling Analyses. *Vaccines (Basel)* 2020; **8** [PMID: 33182403 DOI: 10.3390/vaccines8040668]

112 **Feleszko W**, Lewulis P, Czarnecki A, Waszkiewicz P. Flattening the Curve of COVID-19 Vaccine Rejection-An International Overview. *Vaccines (Basel)* 2021; **9** [PMID: 33451104 DOI: 10.3390/vaccines9010044]

**Footnotes**

**Conflict-of-interest statement:** Fátima Higuera-de-la-Tijera is speaker for Gilead Sciences Inc. Alfredo Servín-Caamaño and Luis Servín-Abad have not conflict of interests.

**Open-Access:** This article is an open-access article selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed by the Creative Commons Attribution-NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, and the use is non-commercial. See: http://creativecommons.org/Licenses/by-nc/4.0/

**Manuscript source:** Invited manuscript

**Corresponding Author's Membership in Professional Societies:** Asociación Mexicana de Gastroenterología; and Asociación Mexicana de Hepatología.

**Peer-review started:** January 22, 2021

**First decision:** February 28, 2021

**Article in press:**

**Specialty type:** Gastroenterology and hepatology

**Country/Territory of origin:** Mexico

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B, B

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Kumar R, Martin Mateos RM **S-Editor:** Fan JR **L-Editor:** Filipodia **P-Editor:**

**Table 1 World Health Organization's goals to achieve viral hepatitis elimination and strategies to make it**

|  |  |  |  |
| --- | --- | --- | --- |
| **Goal to 2030** | **Existing resources** | **Barriers** | **Strategies that should be improved** |
| **Hepatitis C** | | | |
| 90% reduction of new viral hepatitis infections | Harm reduction programs: Safe-sex, safe-needles, and safe-syringes | If well, programs exist in the real-life world are not always sufficiently implemented | Target high-risk population such as MSM, prison inmates, sexual workers, patients with HIV, IDU, immigrants, children born from an HCV+ mother |
| To reach 90% of patients with viral hepatitis infections being diagnosed | Tests with high sensitivity | If well, detection campaigns exist, it is not enough to reach all people in a real-life setting | Once in life, universal screening for all adults. Also target high-risk population such as immigrants, MSM, prison inmates, sexual workers, patients with HIV, IDU, children born from an HCV+ mother |
| 65% reduction in liver-related deaths | DAAs. Telemedicine and telementoring programs | Still, there is limited access to therapy. More restrained access in LMICs. Vulnerable groups with high prevalence and incidence of viral hepatitis have restricted access to therapy | Flexible policies that guarantee timely access to treatment to all who need it, including vulnerable groups such as immigrants, prison inmates, sexual workers, patients with HIV, IDU, children born from an HCV+ mother when appropriate. Consider including those without healthcare insurance to cover their medication. Encourage telemedicine programs to access communities of difficult access |
| **Hepatitis B** | | | |
| Prevention of new HBV infections through vaccination and blood safety | Effective and safe vaccine | In the real-life world they are not always available or schemes are applied incompletely | Programs that effectively ensure universal and complete schemes of vaccination at birth for infants and later for those who did not receive the vaccination in childhood. Coverage should be extended and also prioritized for vulnerable groups |
| Identification, linkage to care, and treatment of persons with chronic HBV | Serologic HBV panels. Nucleos(t)ide analogs with a highly effective and high barrier to resistance  Telemedicine and telementoring programs | Serologic HBV panels for diagnosis sometimes are restricted to specialists. Still, there is limited access to therapy, more restrained in LMICs. Vulnerable groups with high prevalence and incidence of viral hepatitis have restricted access to therapy | Basic diagnostic tests (HBsAg and anti-HBc) should be available at primary healthcare. More flexible policies that guarantee timely access to treatment to all who need it, including vulnerable groups such as immigrants, prison inmates, sexual workers, IDU, children born from an HCV+ mother when appropriate. Consider including those without healthcare insurance to cover their medication. Encourage telemedicine programs to access communities of difficult access |

anti-HBc: Antibody against hepatitis B core antigen; DAAs: Direct antiviral agents; HBsAg: Hepatitis B surface antigen; HBV: Hepatitis B virus; HCV+: Positive to hepatitis C virus; HIV: Human immunodeficiency virus; IDU: Injecting drug users; LMICs: Low and middle-income countries; MSM: Men who have sex with men.