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*REVIEW*

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

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## 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



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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.

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## 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 1$^{st}$ 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].

**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.

## 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.

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