

HEADING TOWARD THE ELIMINATION OF HEPATITIS C VIRUS

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ABSTRACT

Chronic hepatitis C is often asymptomatic and may progress over the years to cirrhosis and hepatocellular carcinoma. Although the prevalence and incident cases are decreasing, the peak mortality of hepatitis C virus (HCV)-related complications is ahead of us in most countries. The economic impact of this burden is enormous. Scaling up the identification of new opportunities to facilitate the road toward HCV elimination includes increasing screening, awareness, and the number of prescribing physicians. Screening should occur within the context of linkage-to-care and patient retention across the care continuum. Awareness and access to treatment in different countries are not systematic as countries have diverse healthcare organizations so that treatment eligibility and availability criteria vary significantly. The simplicity of oral regimens with direct-acting antiviral drugs that are effective across HCV genotypes expands the number of physicians who can prescribe them with accessible treatment models. The ultimate aim is the elimination of HCV by 2030.

Key words: Hepatitis C. Chronic hepatitis. Direct Antiviral Agents. Continuum of care.

INTRODUCTION

In November 2017, Sao Paulo, Brazil, hosted the World Hepatitis Summit (WHS), under the initiative of the World Health Organization (WHO) and the World Hepatitis Alliance, a global biennial event to advance the viral hepatitis agenda with the ultimate goal toward the elimination of hepatitis C virus (HCV) by 2030. An astonishing aim, considering that the discovery of HCV occurred in 1989, identified as an RNA virus, family flaviviridae, and composed of 9600 - nucleotide genome - single poly-protein¹. Early recognition of the non-structural proteins involved in its replication soon made them targets of therapy, inaugurating the curative era of hepatitis C, with the

introduction of direct-acting oral antiviral drugs (DAAs) that eliminate the virus in 98–100% of treated patients.

The pipeline of new DAAs is streaming, and new regimens should improve treatment adherence. Pangenotypic drugs have added benefit to the hepatitis C medicines portfolio. These drugs can be used for most patients, simplifying the diagnosis and treatment algorithms^{2,3}.

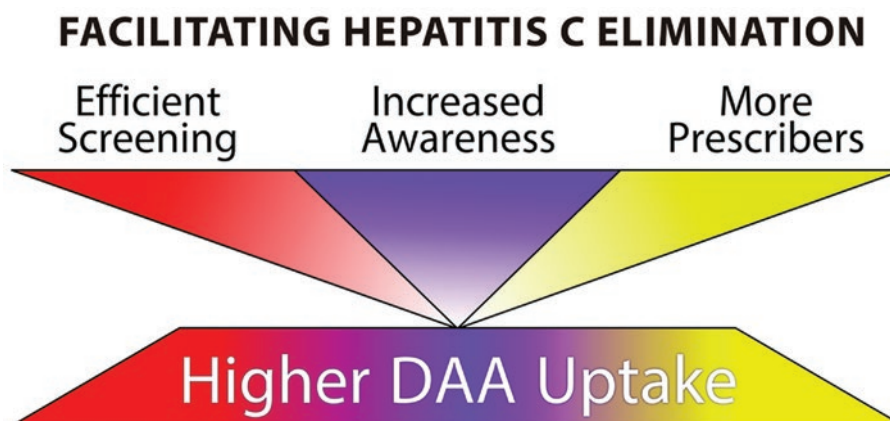
Affordability of DAAs has improved significantly through strategies such as price negotiation, compulsory licensing, or generic competition. The WHS 2017 was an excellent opportunity to widen the spectrum for countries to access treatment. Exploring financial

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Figure 1. Identification of feasible strategies that would assist in the process to eliminate hepatitis C.



means by governments, insurance companies, or patients is a strategic issue.

Identification of new opportunities to facilitate the road toward elimination of HCV includes the increase in screening, awareness, and the number of prescribers. The purpose of linkage-to-care and uptake of DAAs is essential (Fig. 1).

SCREENING

Worldwide, the number of people that are aware of the diagnosis of hepatitis C is low. The coverage of those with a confirmed positive test that have been treated is modest. In 2015, the WHO estimated that of the 71 million persons living with HCV infection globally, only 20% (14 million) knew of their diagnosis. Of those diagnosed, 7.4% (1.1 million) were started on treatment in 2015. In 2016, additionally, 1.76 million people received treatment, bringing the global coverage of hepatitis C curative treatment to 13%⁴.

To meet the task of eliminating hepatitis C, it is necessary to innovate in the screening process, uncovering previously unidentified cases and those in the greatest need of treatment or at a high risk of transmitting the infection.

Point-of-care testing for hepatitis C has advanced significantly, allowing for screening outside the clinical laboratory, and performed where the patient is receiving care. Rapid diagnostic tests are single-use disposable assays supplied in test kits performed without the need of

venipuncture; most are done in capillary blood collected by a finger stick procedure or in oral fluid specimens, and results are available usually in 30–90 min. Newly developed nucleic acid technologies (NATs) are simpler and more robust and may avoid laboratory-based NAT technologies, simplifying the screening strategies⁵.

The WHO published, in 2017, global guidelines for testing hepatitis B and C and defined three main possible testing approaches for HCV infections:

- a. Focused or targeted testing of specific high-risk groups
- b. Birth cohort testing
- c. General population screening.

Targeted testing involves screening high-risk groups such as persons who inject drugs, persons in prisons, and other closed settings, men who have sex with men, sex workers, HIV-infected individuals, partners or family members of infected persons, health-care workers, alcoholics, persons with abnormal liver function tests or ultrasound scan, and patients with fatty liver disease or diabetes mellitus.

Birth cohort testing is recommended in some countries for people born during 1945–1965.

The WHO guidelines consider general population screening only in areas where the prevalence of HCV is > 2%.

Screening should occur in the context of linkage-to-care and patient retention across the care continuum. A review of 26 studies of cost-effectiveness of different testing approaches in Europe, the United States,

and Egypt found that testing high-risk groups were cost-effective in all settings⁶.

AWARENESS

Chronic hepatitis C is often asymptomatic and may progress over the years to cirrhosis and hepatocellular carcinoma. Although prevalence and incident cases are decreasing, the peak mortality of HCV-related complications is ahead of us in most countries. The economic impact of this burden is enormous. Scaling up the number of patients treated annually will result in larger savings over the next 20 years, particularly in underdeveloped countries where a large undiagnosed and untreated population exists⁷.

Access to treatment in different countries is not systematic as they organize their health care in diverse ways so that eligibility and availability criteria vary significantly. Furthermore, specific guidance about healthcare entitlement in many countries is either not available, unclear or not known to medical professionals involved in treating viral hepatitis C.

There is a sliver of hope as newer and innovative strategies are emerging. Implementation of interdisciplinary models, providing trained personnel and equipment for diagnosis, assessment of disease stage, treatment initiation, and monitoring in the same location, should help in the access, utilization, and adherence to treatment. Focusing on case management, where patients are asked about their concerns and what is preventing them from treatment, is being created in real time. Soon, we visualize universal access to the new DAA regimens. The number of networks of diverse advocacy organizations is increasingly providing opportunities to facilitate treatment access.

PRESCRIBERS

Up to 2010, the treatment of hepatitis C depended on the administration of pegylated interferon and ribavirin, achieving a sustained viral response in approximately 50%. Treatment was frequently as aggressive as a storm. Its duration varied between 6 and 12 months, and side effects were very common. Patients and physicians zigzagged using hematopoietic growth factors, resulting in many cases in a daunting and depressing experience. Treatment was time-consuming and stressful. When a patient failed, frustration became a

significant part of the patient-physician relation. Liver specialists, gastroenterologists, and infectious diseases specialists historically delivered the HCV treatment.

This treatment saga dramatically changed with the arrival of DDA-based treatments that are safe, tolerable, and with higher success rates. The simplicity of oral regimens that are effective across HCV genotypes expands the number of physicians that can prescribe DAAs with scalable treatment models. Novel new systems of prescribing are being developed whereby internists and general practitioners may be eligible to prescribe DAAs in consultation with one of the aforementioned specialists.

There are, however, caveats to this approach. Most practitioners refer persons with HCV to subspecialty care, and a great proportion does not feel sufficiently knowledgeable about HCV treatment. This knowledge gap can be addressed through training. Primary care physicians have treatment outcomes similar to those of subspecialists.

CONCLUSION

The long-lasting failure to diagnose a hepatitis infection hampers the current management of hepatitis C. There is a need to increase awareness of the diagnosis of hepatitis C. Understanding the care cascade is vital for eliminating the virus. Reducing the HCV burden requires educational effort and scale-up of DAA therapies.

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