



Hepatitis C Virus Infection: What Are We Currently Doing in Latin America About WHO's Proposals for 2030?

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Hepatitis C virus (HCV) infection is a serious health problem worldwide. It has been estimated that it affects 1% of the global population, and most of these individuals are unaware until the development of advanced liver disease. Currently, 400,000 people die each year of causes related to HCV infection. It is projected that by 2040 there will be 840,000 deaths per year from cirrhosis and hepatocellular carcinoma (HCC) associated to HCV.¹ The introduction of short-term, pangenotypic direct-acting antiviral (DAA) regimens, with nearly 100% effectiveness in real life, has been a tremendous medical advance that allowed us to think that the elimination

of HCV infection could be possible.² Furthermore, treatment at the early stages of the disease has proved to be cost-effective by reducing the risk for cirrhosis, HCC, liver transplantation, and mortality. This is even more evident when the indirect costs in the economy resulting from the reduction in the workforce caused by HCV infection are also considered.³ The effectiveness and benefits of DAAs prompted the World Health Organization (WHO) in 2016 to approve the global strategy for eliminating HCV infection. The ambitious goals set for 2030 were to achieve a 90% HCV diagnosis rate, a 90% reduction in the incidence, and a 65% decrease in mortality

Abbreviations: DAA, direct-acting antiviral; DCV, daclatasvir; EBV/GZR, elbasvir/grazoprevir; GLE/PIB, glecaprevir/pibrentasvir; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HIV, human immunodeficiency virus; LDV, ledipasvir; ND, no data available; SOF, sofosbuvir; VEL, velpatasvir; VOX, voxilaprevir; WHO, World Health Organization.

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Potential conflict of interest: Nothing to report.

Received September 13, 2020; accepted December 4, 2020.

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TABLE 1. CURRENT SITUATION IN LATIN AMERICA AND PROJECTIONS ON THE WHO PROPOSALS FOR 2030

Country	Number (%) of Population With HCV Infection	Diagnosed 2019	Diagnosed Accumulated	Treated 2019	Accumulated Treated	Goal 90% Diagnosis	Goal Treat 80%	Goal Decrease 65% Mortality	Goal Decrease 90% Incidence
Argentina	326,000 (0.8%)	9%	3%	1%	3%	>2051	>2051	>2051	2048
Brazil	1,787,000 (0.9%)	8%	31%	2%	25%	2035	2029	2034	2038
Chile	56,500 (0.3%)	10%	19%	<1%	1%	>2051	>2051	>2051	>2051
Colombia	409,000 (0.8%)	9%	13%	<1%	1%	>2051	>2051	>2051	>2051
Cuba	35,000 (0.3%)	56%	ND	<1%	1%	2028	>2051	>2051	>2051
Dominican Republic	68,200 (0.6%)	12%	14%	1%	4%	>2051	>2051	>2051	>2051
El Salvador	32,300 (0.5%)	3%	9%	ND	ND	>2051	>2051	>2051	>2051
Mexico	532,000 (0.4%)	49%	53%	<1%	2%	2037	>2051	>2051	>2051
Peru	167,000 (0.5%)	11%	15%	1%	5%	>2051	>2051	>2051	>2051
Venezuela	118,000 (0.4%)	25%	ND	ND	2%	>2051	>2051	>2051	>2051

compared with 2015.⁴ However, progress toward these goals has been slow globally and arduous, especially in low- and middle-income countries. A study that modeled the impact of DAA treatment on HCV infection course showed that achieving the WHO 2030 targets would require a 7% net cure per year starting from 2016. Net cure considers the number of cures, HCV-related deaths, and new infections.⁵ Projections made with data from countries with detailed electronic records suggest that the net annual regression of the epidemic is currently only 0.4% worldwide.⁴ Currently, only five countries in the world could achieve the proposed objectives.⁶

WHERE DO WE STAND IN LATIN AMERICA?

Latin America is constituted by 20 countries, with a total population of 626 million inhabitants. It is a heterogeneous region, with low- and middle-resource economies and deep socioeconomic inequalities between and within the countries. One of the main problems in achieving the WHO’s objectives throughout Latin America is the fragile sustainability of health care systems and scarce resources destined to preventive medicine. Moreover, the health system is segmented and fragmented, with poor health infrastructure and organization, which ultimately implies very limited access to diagnostics and medications for most of the population.⁷

Less than half of the Latin American countries have HCV prevalence studies, and most of them have a poor quality design. When we extrapolate the data from countries with registries, the estimated HCV prevalence rate in Latin America is less than 1%.⁶ According to epidemiological data from the Polaris Observatory online database, in 2019, several countries were able to diagnose a significant percentage of the population with HCV infection. Still, only Brazil was able to treat the necessary number of patients to achieve an annual cure net greater than 1% of those infected (Table 1).⁶ As described in Table 2, some countries have not yet developed clinical guidelines for the diagnosis and treatment of HCV. Furthermore, some countries still have the challenge of creating a national viral hepatitis program coordinated by their Ministry of Health to estimate HCV disease burden, coordinate screening policies, and fund DAA therapies ultimately. Screening strategies still focus on populations with risk factors, and universal screening is being carried out in a minority of countries in the region. Although several DAAs regimens are available in most Latin American countries, drug costs continue to

TABLE 2. NATIONAL PROGRAMS, AVAILABILITY, AND FINANCING OF DAAS IN LATIN AMERICAN COUNTRIES

Country	Government Financial Coverage	National Clinical Guidelines (Latest Version)	Screening	National Registry Patients Treated	DAAs Available	Generic DAAs
Argentina	Yes	Yes (2020)	Universal	Yes	SOF, LDV, VEL, VOX, EBV/GZR, GLE/PIB	Yes
Brazil	Yes	Yes (2019)	Universal	Yes	SOF, LDV, VEL, EBV/GZR, GLE/PIB	Yes
Chile	Yes	Yes (2019)	Risk populations	Yes	SOF, LDV, VEL, EBV/GZR	No
Colombia	Yes	Yes (2019)	Risk populations	Yes	SOF, LDV, VEL, VOX, EBV/GZR, GLE/PIB	No
Dominican Republic	Yes	Yes	Risk populations	No	SOF, LDV, VEL, VOX	No
Ecuador	No	No	Risk populations	No	SOF	No
Mexico	Yes	Yes (2018)	Risk populations	Yes	SOF, VEL, GLE/PIB	No
Peru	No	Yes (2018)	Risk populations	No	SOF, VEL, EBV/GZR	No
Uruguay	No	No	Risk populations	No	SOF, LDV, VEL, GLE/PIB	No

be a significant barrier, and only Argentina and Brazil have DAA generic options.

WHAT IS LACKING IN LATIN AMERICA TO ACHIEVE THE WHO'S GOALS?

First, it is essential to perform well-designed prevalence studies and reliable registries to better understand the problem of HCV in every Latin American country. These efforts need the participation and leadership of policy-makers, scientific societies, patient associations, and general society. Second, HCV screening should be universal and not only directed to the population with well-known risk factors. Different studies from countries with low HCV prevalence have reported that single universal screening for HCV infection in adults 18 years and older is cost-effective.⁸ In Latin America, most of the patients who have been treated had acquired HCV infection through blood products transfusions or unsafe medical procedures. Over the last few years, HCV prevalence among injecting drug users has been increasing. Also, sexual transmission has increased considerably, especially in men who have sex with men, prisoners, and people who are living with human immunodeficiency virus (HIV).^{9,10} Third, the high cost of DAAs is a complex problem affecting Latin American countries. To improve access to care, Pharma companies should allow low- and middle-income countries to have access to new treatments through appropriate transfer technology (generic) policies. There are multiple proposed strategies; however, to find real solutions, it is necessary that policy-makers and the World Trade Organization evaluate this inequity and find appropriate solutions.^{7,11} Finally, it is necessary to establish educational and prevention programs and carry out periodic screening in high-risk populations in which the prevalence of infection is increasing in the region, especially in men who have sex with men, people with HIV, and injecting drug users.

As previously mentioned, a great advantage of the new pangenotypic DAA regimens is that treatment has been simplified in such a way that primary care providers can treat patients with mild-to-moderate liver disease. Evaluation with laboratory tests before starting therapy is becoming easier, and follow-up during treatment can be avoided in these cases. Nevertheless, difficult-to-manage patients, such as patients with previously unsuccessful DAA regimens, patients with hepatitis B virus or HIV coinfection, patients with severe renal failure, and people with cirrhosis, should be monitored and treated by liver

REVIEW

specialists.¹¹ New HCV models of care addressing the challenge of providing treatment in underserved populations should also be promoted to improve linkage to care. In this sense, the ECHO project (Extension for Community Healthcare Outcome) has been replicated in many Latin American countries.¹²

CONCLUSION

Latin America needs to lay the foundation for HCV elimination with a strong political commitment based on high levels of screening and diagnosis, unrestricted access to DAA therapies, and a diverse range of care models. Nevertheless, applying all these initiatives in resource-limited settings requires a continuous effort to overcome practical and political challenges. In conclusion, a greater effort is needed from the scientific community, society, and regional governments, as well as the conviction and the will to achieve HCV elimination.

Acknowledgment: The authors acknowledge Martin Tagle, M.D., Nelia Hernandez, M.D., Roberta Chavez, M.D., Aldo Torre, M.D., Juan Suarez, M.D., Fernando Contreras, M.D., Virginia Garcia, M.D., and Juan Restrepo, M.D.

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REFERENCES

- 1) Foreman KJ, Marquez N, Dolgert A, et al. 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.

Hepatitis C Virus Infection in Latin America *Roblero et al.*

- 2) Kapadia SN, Marks KM. Hepatitis C management simplification from test to cure: a framework for primary care providers. *Clin Ther* 2018;40:1234-1245.
- 3) Scott N, Kuschel C, Pedrana A, et al. A model of the economic benefits of global hepatitis C elimination: an investment case. *Lancet Gastroenterol Hepatol* 2020;5:P940-P947.
- 4) World Health Organization. Assembly WHOS-NWH. Global health sector strategy on viral hepatitis 2016–2021 [WHO reference number: WHO/HIV/2016.06]. Available at: <https://www.who.int/hepatitis/strategy2016-2021/ghss-hep/en/>. Published June 2016.
- 5) Hill A, Nath S, Simmons B. The road to elimination of hepatitis C: analysis of cures versus new infections in 91 countries. *J Virus Erad* 2017;3:117-123.
- 6) CDA Foundation's Polaris Observatory; 2020. Available at: <https://cdafound.org/polaris/>. Published April 17, 2020. Accessed July 2020.
- 7) Pedrana A, Howell J, Scott N, et al. Global hepatitis C elimination: an investment framework. *Lancet Gastroenterol Hepatol* 2020;5:927-939.
- 8) FitzSimons D, Hendrickx G, Hallauer J, et al. Innovative sources for funding of viral hepatitis prevention and treatment in low- and middle-income countries: a roundtable meeting report. *Med Policy* 2016;1:16.
- 9) Viola L, Marciano S, Colombato L, et al. HEPLA: a multicenter study on demographic and disease characteristics of patients with hepatitis C in Latin America. *Ann Hepatol* 2020;19:161-165.
- 10) Alonso M, Gutzman A, Mazin R, et al. Hepatitis C in key populations in Latin America and the Caribbean: systematic review and meta-analysis. *Int J Public Health* 2015;60:789-798.
- 11) Dieterich D, Ahn J, Bacon B, et al. A simplified algorithm for the management of hepatitis C infection. *Gastroenterol Hepatol* 2019;15:S3.
- 12) Mendizabal M, Ridruejo E, Ceballos S, et al. The ECHO Model proved to be a useful tool to increase clinicians' self-effectiveness for care of patients with hepatitis C in Argentina. *J Viral Hep* 2019;26:1284-1292.