

Absolute targets for HCV elimination and national health policy paradigms: Foreseeing future requirements

Loreta A. Kondili¹  | Antonio Craxi²  | Alessio Aghemo³ 

¹Center for Global Health, Istituto Superiore di Sanità, Rome, Italy

²Gastroenterology and Hepatology Unit, Department of Internal Medicine and Medical Specialties "PROMISE", University of Palermo, Palermo, Italy

³Humanitas University and Humanitas Clinical and Research Center IRCCS, Rozzano, Italy

Correspondence

Loreta A. Kondili, Center for Global Health, Istituto Superiore di Sanità, Rome, Italy.
Email: loreta.kondili@iss.it

Abstract

The World Health Organization (WHO) targets for eliminating HCV by 2030 may be overambitious for many high-income countries. Recent analyses (ie, data from 2017 to 2019) show that only 11 countries are on track for meeting WHO's elimination targets. For a country to be truly on track, it is important that the majority of infected individuals be identified and treated. There is still a need for country and population-specific evaluations within the different HCV screening and treatment strategies available, in order to assess their cost-effectiveness and sustainability and support an evidence-based policy for HCV elimination. Any health policy model is affected by the diversity and quality of the available data and by gaps in data. Given the differences among countries, comparing progress based on fixed global targets will not necessarily be suitable in the same measure for each country. In a recent document, the European Collaborators of Polaris Observatory provide insight into the limitations of the current WHO targets. The absolute targets identified by each country in accordance with the measures set by WHO would be essential in reaching the HCV elimination. All analytic models to assess the progress towards HCV elimination are based on projections to 2030 not including the impact of the COVID-19 pandemic on hepatitis-related services. With specific regard to the achievement of WHO hepatitis elimination goals, all measures that will be put in place during and after COVID-19 pandemic could be transferred in increasing diagnosis and linkage to care of people with hepatitis.

KEYWORDS

COVID-19, disease burden, HCV elimination, HCV screening, microelimination, WHO targets

"Essentially, all models are wrong, but some are useful"—George Edward Pelham Box, British statistician, 1919-2013

1 | STRIVING FOR ERADICATION

According to Louis Pasteur (1822-1895) 'It is within the power of man to eradicate infection from the Earth'. To date, humankind has eradicated

two infectious diseases, smallpox and rinderpest, and programmes are underway to eradicate poliomyelitis and guinea-worm disease. When deciding whether or not to invest in eradication, the given infection needs to meet certain criteria: it must cause a significant disease; humans must be the main host; effective vaccines or treatment must be available and there must be political and financial support for eradication efforts. It is important here to distinguish between eradication and elimination: elimination of an infection, and of the disease it causes, refers to efforts aimed at reducing the incidence of infection to almost zero in a defined geographic area. A disease

Abbreviations: DAA, Direct-Acting Antiviral; HCV, Hepatitis C virus; MSM, men who have sex with men; UI, uncertainty interval; WHO, World Health Organization.

can be eliminated from a specific region without being eradicated globally. Once an aetiological agent has been eliminated, actions to prevent the infection from being transmitted or from re-emerging, especially as a disease, are still necessary.^{1,2}

In his study on disease eradication, Walter R. Dowdle states: 'Elimination and eradication are the ultimate goals of public health. The only question is whether these goals are to be achieved in the present or by some future generation'.¹

With the introduction of direct-acting antivirals (DAA) against hepatitis C virus (HCV) and the possibility of eradicating the infection in almost all treated individuals, HCV become a major target for elimination worldwide by 2030.³ Although elimination of every infection might not be realistic, today, elimination of HCV infection absolutely is. In the absence of an effective vaccine, the elimination of HCV can only be achieved through treatment with DAAs combined with prevention practices, although one of the main limiting factors remains the ability to identify infected persons, who remain asymptomatic for long time following the infection.

2 | FORECASTING THE BURDEN OF HCV INFECTION AND THE IMPACT OF TREATMENT IN ACHIEVING HCV ELIMINATION BY 2030

Razavi and colleagues, in collaboration with experts from different countries worldwide, have developed the Polaris Observatory, a resource for epidemiological data and decision analytics based on a complex modelling approach to forecast the burden of viral hepatitis infection and disease progression at different geographic levels [global, country and regional (i.e., areas covering a number of countries)]. The modelling is calibrated and validated with each country's prevalence and treatment data and, when available, data from liver disease registries. The data from the country-level models are aggregated to create models for larger regions and for the entire world. The forecasts are based on scenarios in which the number of treated individuals and new diagnoses are considered to remain constant (with respect to current data) or to either decrease or increase over time, which depends on a given country's policies regarding HCV screening and who receives treatment.⁴ The peculiarity of this modelling is that the simulation scenarios allow for the production of estimates that can be modified as additional real-life information becomes available. National and regional models are updated once a year taking into account the latest available data. Using this unique approach, the current and future impact of the number of persons diagnosed and the number of persons treated can be quantified. Although the assumptions used in the Polaris Observatory modelling might be not perfect, considering the lack of precise epidemiological data, they are much more reliable than in the past. In fact, continuous updating of the Polaris model with new treatment data allows for better understanding of the disease burden and its estimates.⁴

The World Health Organization's (WHO) targets for eliminating HCV by 2030 (65% reduction in liver-related deaths, 90% reduction

Key points

- For a country to be truly on track for HCV elimination, it is important that the majority of infected individuals be identified and treated.
- To move from theory to practice, structured bottom-up process needs to be developed and funded sufficiently to complement top-down screening, treatment and harm reduction strategies.
- The initial costs of HCV elimination efforts are high, yet in the long-term these costs pay-off.
- There is a need to simplify the HCV elimination targets switching to absolute targets.
- Some innovative services used for the COVID-19 pandemic could be used efficiently for HCV diagnosis and treatment of submerged populations

in new infections and the diagnosis of 90% of infected individuals by 2030)³ have been considered ambitious by many high-income countries, which are at different points in their progress towards elimination. Back in 2017, the Polaris Observatory estimated that the global prevalence of HCV infection was 71.1 million (95% UI 62.5-79.4).⁵ At that time, of the 45 high-income countries whose progress in reaching the elimination goals, 9 were on track for meeting the goals by 2030 (Australia, France, Iceland, Italy, Japan, South Korea, Spain, Switzerland and the UK). While it was deemed that Austria, Germany and Malta could also reach the goals with expanded screening efforts, 30 countries were not projected to eliminate HCV before 2050. Reducing the incidence of infection by 90% was the most difficult target to achieve, followed by the 65% reduction in liver-related deaths.⁶

An updated analysis (i.e., data from 2017 to 2019) shows that only 11 countries (Australia, Canada, France, Germany, Iceland, Italy, Japan, Spain, Sweden, Switzerland and United Kingdom) are on track for meeting WHO's elimination targets by 2030; five others (Austria, Malta, Netherlands, New Zealand and South Korea) by 2040 and two (Saudi Arabia and Taiwan) by 2050. The remaining 27 countries, including the USA, are not expected to achieve elimination before 2050.⁷

3 | MOVING FROM THEORY TO PRACTICE: COUNTRY AND POPULATION-SPECIFIC EVALUATIONS AND ACTIONS

In some countries, the restriction criteria for treatment (i.e., only treating individuals with severe liver disease) were relaxed and universal treatment was adopted, with a consequent spike in the number of persons receiving treatment (i.e., a 'rebound effect'), leading to the impression that these countries were on track for reaching the elimination targets. However, for a country to be truly on track, it is important that the majority of infected individuals actually be

identified and treated. It is instead easy to predict that, as countries that have been successful in treating all diagnosed cases run out of patients without increasing the diagnosis rate through screening, their progress towards elimination will slow down substantially.⁸ A real-life example from a country with a high prevalence of chronic HCV infection comes from Italy. This country had been on track for 2 years (until 2019), yet following the implementation of universal treatment, Italy fell out of track as a result of the decrease in the number of patients treated in 2019 (i.e., once the country began running out of diagnosed patients to treat).⁹ However, beginning in 2021, a nationwide corrective action will be implemented, consisting of the performance of screening tests among key populations and specific birth cohorts estimated to have a high prevalence of undiagnosed individuals (1969-1989).¹⁰ Nonetheless, screening is only the first step: sufficient healthcare needs to be provided, and efforts must be made to reach otherwise neglected individuals. Regarding mortality, Italy is on track for achieving the 65% reduction by 2023-2025. This is because the epidemic wave occurred much earlier than in other countries and many more infected individuals have developed progressive liver disease, so that the effects of treatment on mortality are evident much earlier.⁸

For countries whose most impactful epidemic wave can be attributed to intravenous drug use, given that HCV infection is usually asymptomatic for decades, universal treatment will have a relatively modest impact on deaths by 2030, but it will significantly influence the incidence and the overall prevalence of infection. There are also projections of the impact of treatment on transmission among injecting drug users in Europe. According to these projections, the year 2017 treatment rates may result in meaningful reductions in the prevalence of chronic HCV carriers (38%-63%) within 10 years in several European countries, but doubling treatment rates could reduce prevalence in other areas only by 12%-24%. Reducing HCV infection to minimal levels throughout Europe will require scaling-up both HCV treatment and other interventions that reduce the risk of acquiring HCV through injection.¹¹ A further challenge to elimination is posed by the continuing HCV epidemic among men who have sex with men (MSM) who have been diagnosed with HIV, as shown by epidemiological data and suggested in various countries by modelling estimates. For MSM, high treatment rates and behavioural interventions for harm reduction appear to be only moderately effective, indicating there is a need to develop effective interventions to address high-risk behaviours associated with injecting and other drug use among MSM.¹²

Elimination by 2030 is even less likely in most low-income and middle-income countries. The Georgia model of elimination¹³ is not applicable in countries where the epidemiology of infection differs from that in Georgia, with larger populations affected, such as Italy, where more than one epidemic wave affecting different birth cohorts has occurred, first as a result of nosocomial transmission and later because of intravenous drug use.⁸

Given these considerations, the Polaris Observatory data should not be used merely to construct a *Formula 1*-like grid of countries in the race towards HCV elimination.

According to the Polaris Observatory estimate, reaching the WHO targets in Europe will require 180,000 new diagnoses annually.¹⁴ However, because availability of and access to treatment vary in each country, the number of newly diagnosed cases might not be sufficient as an outcome measurement of the effectiveness of elimination strategies. The number of HCV infections would remain high relative to the WHO target unless additional screening was implemented. Moreover, even considering a successful screening strategy, the elimination targets are based on the prevalence rate in 2015, which has not always been accurate. Inaccuracy could make the elimination standards inadequate for measuring the effectiveness of elimination strategies, and thus the recommended screening strategies, based on cost-effectiveness at a country level, would be scarcely relevant.¹⁵ There is still a need for country and population-specific evaluations within the different HCV screening and treatment strategies available, in order to assess their cost-effectiveness and sustainability and fully support an evidence-based policy for HCV elimination. To move from theory to practice, a structured bottom-up process needs to be developed and sufficiently funded to complement top-down screening strategies. The field should now concentrate on designing implementable national screening frameworks, learning from available examples to understand the pitfalls that need to be avoided.¹⁶

4 | PRIORITIES IN HCV ELIMINATION PROGRAMS FOR THE NEXT DECADE

The three components of national health programmes (i.e., surveillance, prevention and healthcare) should be addressed using a comprehensive, holistic approach, targeting the population as a whole but also including individual interventions that focus on prevention and early diagnosis and treatment. HCV infection is transmitted through blood transfusion, injecting drug use or procedures performed with inadequately sterilised equipment, which still account for a great burden of HCV worldwide. Suitable diagnostics and cost-saving measures for diagnosis and cure should be conducted in synergy to combat this iatrogenic silent epidemic and make elimination feasible.¹⁷ In addition to treatment costs, additional challenges consist of the cost of scaling-up testing to find the non-identified infected individuals and implementing effective models of care for diverse populations. In this regard, a wide array of policies has been implemented in different countries.^{18,19}

We are now 10 years away from the 2030 Sustainable Development Goal finish line. The health sector continues to expand faster than the economy. Between 2000 and 2017, global health spending in real terms grew by 3.9% a year while the economy grew 3.0% a year.²⁰ However, the extent of this increase will depend on how successful policies are at containing healthcare costs over time. HCV elimination goals require nationwide hepatitis-specific action plans including holistic approaches to disease awareness, prevention and integrated care, combining willingness and resources in a joined response.³ We should fight

the wrong belief that in the long run prevention may cost more than treatment, the fact that many people would prefer to relieve the suffering of an identified individual than to fund an intervention which does not address current ill health.²¹ The savings related to preventing and treating HCV may exceed the cost of elimination. The resources spent on HCV provide good value for the money, given that high initial annual spending will give way to a decrease in cost in the medium term.²² HCV elimination averts a significant toll in terms of deaths and societal and economic costs. In light of this, controlling a disease can be more expensive because of the continued burden the disease poses on a health-care system and the lost productivity of a sick population. The initial costs of elimination efforts are high, yet in the long term these costs pay-off. Expenditure on prevention remains low in many countries compared with the sums spent on curative care. In a recent study conducted in several European countries and in which the cost profile of liver disease was evaluated, a significant cost saving of antiviral therapy has been reported in the four European countries, varying from 45.00 million Euro to 275.00 million Euro per 1,000 patients treated with DAA over a 20-year period. The return on investment for HCV antiviral therapy was estimated to range from 4 to 10 years, with the most favourable profile for countries where the restrictions for DAA treatment have been lifted.²³

5 | WHO ELIMINATION GOALS VS ABSOLUTE AND TAILORED ELIMINATION TARGETS

Any health policy model is affected by the diversity and quality of the available data and by gaps in data among countries of a given region in Europe or worldwide. To achieve WHO's elimination targets, a country needs to perform large-scale serological surveys. The lack of available national epidemiological data and the financial and regulatory hurdles for publicly funded screening programmes are the bottleneck of elimination strategies in almost all countries.¹⁸ Mathematical modelling estimates of epidemiological data have been used as tools to measure the burden of infection and disease, as well as the progress made towards achieving the elimination targets. Considering these surrogate estimates, the first question regards the validity of the WHO elimination targets derived by the modelling approach. The model itself needs to reflect that which is occurring in the real world, given that good predictions cannot be based on false assumptions. Only a modelling approach that relies on validated assumptions, that have been tested and refined and are continuously updated is considered to have the potential to inform future policy making.

Striving for elimination and eradication is an admirable endeavour, yet it entails a great responsibility. A resolution by the World Health Assembly is a vital booster to the success of any eradication programme. Careful and deliberate evaluation is a prerequisite for any eradication/elimination programme,¹ but first the targets should

be reliable. As it has been previously indicated, targets should be feasible and developed based on country realities, the best possible data, trends and responses, and monitored by a set of standard and measurable indicators.²⁴ Given the differences in epidemiology and disease burden,²⁵ WHO asks every country to identify its most affected populations and tailor its response accordingly.³ The WHO organization's strategy document directs countries to 'develop as soon as practicable ambitious national goals and targets for 2020 and beyond'.³ To meet WHO's elimination goals for viral hepatitis, the diagnosis coverage worldwide should be increased from 9% to 20% in 2015 to 90% in 2030, and treatment coverage should increase from 7% to 8% in 2015 to 80% in 2030. For HCV infection, 80% of high-income countries are not on track to meet elimination targets by 2030, and 67% will not achieve elimination even if given an additional 20 years to do so.^{6,19} The reality is that progress towards the elimination of HCV could not occur with the same rate in all locations and all populations. Knowledge about transmission routes of infection contains several uncertainties and the parameters for monitoring the infection and disease burdens differ significantly among different countries.

Given the differences among countries, comparing progress based on fixed global targets will not necessarily be suitable in the same measure for each country. Relaxing treatment criteria has been documented as cost effective in any epidemiological context, but it was soon realized that this was only the beginning. The cost of HCV elimination includes surveillance, the evaluation of National Action Plans, awareness and communication campaigns, prevention programmes such as blood and injection safety, prevention of transmission in persons who practice injecting, and testing and treatment programmes.³

World Health Organisation guidance is important in helping to define progress towards true elimination. However, absolute targets identified by each country in accordance with the measures set by WHO would be essential in achieving the HCV elimination. In a recent document, the European Collaborators of Polaris Observatory provided insight into the limitations of the current WHO targets. The existing targets compare a country's progress relative to its 2015 values, penalizing countries that started their programmes before 2015, countries with a young population and countries with a low HCV prevalence. The recommendations of Polaris Observatory collaborators to WHO were (a) to simplify the hepatitis elimination targets, (b) to switch to absolute targets and (c) to allow countries to achieve these disease targets with their own service coverage initiatives in order to reach the maximum impact.²⁶ (Figure 1).

6 | HOW ABOUT THE IMPACT OF COVID 19 PANDEMIC IN REACHING THE ELIMINATION GOALS?

One further issue to consider is COVID-19. All analytic models to assess the progress towards HCV elimination are based on historical treatment and screening data up to 2019, with projections to 2030

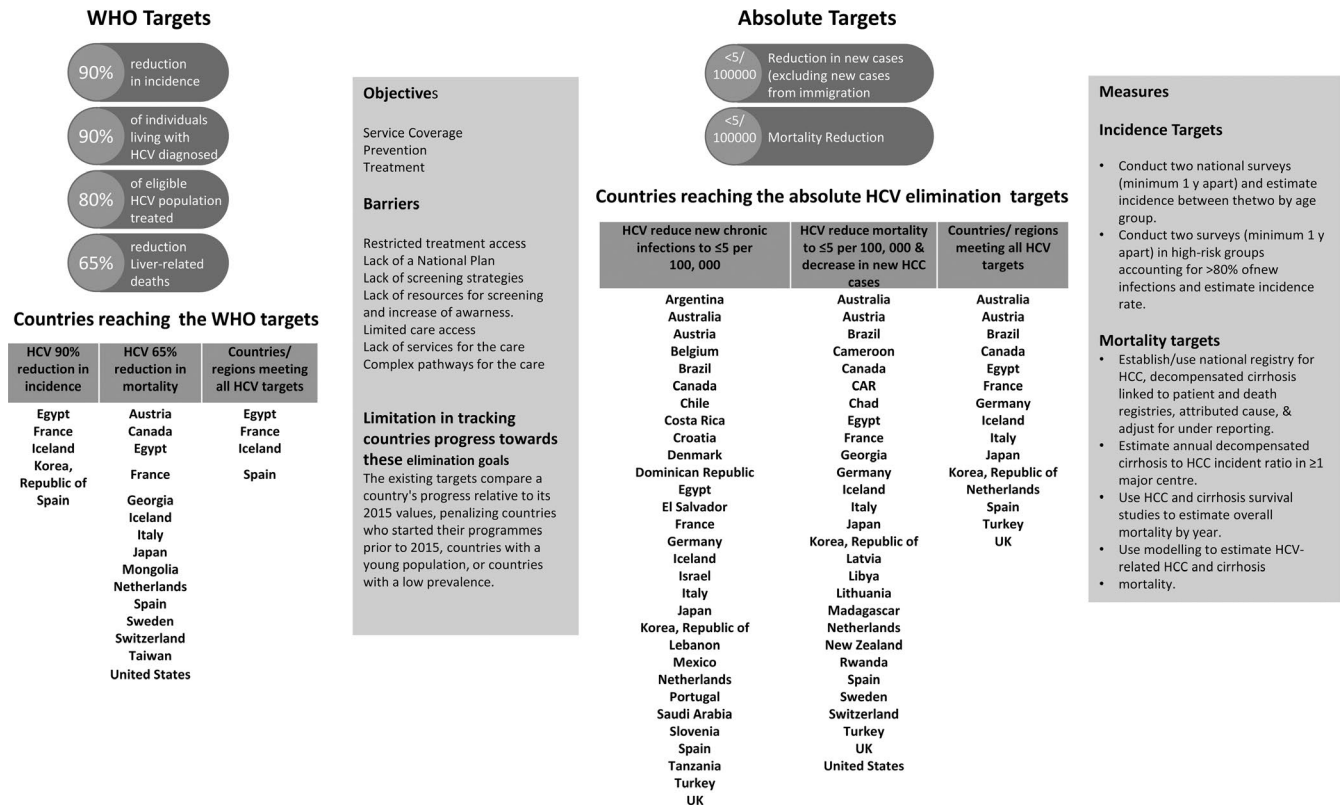


FIGURE 1 Absolute vs WHO elimination targets: Efforts towards moving in the right direction

not including the impact of the COVID-19 pandemic on hepatitis-related services.²⁷ At the time of this writing, the COVID-19 pandemic is ongoing, with millions of cases reported worldwide, with major implications for communities and economies. The number of deaths continues to increase, and the impact of the pandemic is grave. As the coronavirus pandemic focuses medical attention on treating affected patients and protecting others from infection, how do we best care for people with non-COVID disease? 'One of the yet-to-be-told stories of the Covid-19 pandemic is the recognition that the (necessary) prescriptions on the performance of less urgent cases have led to collateral damage to so many patients with medical conditions that truly couldn't wait'.²⁸ In a recent assessment performed using the Polaris Observatory model adapted to the reduction in treatment uptake caused by the pandemic, it was estimated that the '1-year delay' scenario resulted in 44,800 (95% uncertainty interval [UI]: 43,800-49,300) excess hepatocellular carcinoma cases and 72,300 (95% UI: 70,600-79,400) excess liver-related deaths, relative to the 'no-delay' scenario globally, from 2020 to 2030.²⁷ Most missed treatments would be in lower-middle-income countries, whereas most excess hepatocellular carcinoma and liver-related deaths would be among high-income countries. We are aware of and sensitive to the global health crisis caused by COVID-19, which has undoubtedly made the fight against other diseases more challenging. However, this current crisis should not impede progress in other diseases care, especially one such as HCV, which can be eliminated. If we accept as

unavoidable the need to decrease temporarily the efforts made towards HCV elimination as a result of the COVID-19 pandemic, we should at least preserve the availability of immediate treatment for patients with advanced fibrosis or cirrhosis. Although this could reduce severe disease outcomes, it would only be partially effective since: (a) patients with less severe stages of fibrosis may proceed further, if treatment is delayed and (b) undiagnosed HCV patients with severe fibrosis would not be diagnosed and treated in time. In all countries worldwide, when pursuing the exit strategy from strict lockdown measures for COVID-19, HCV screening and the prescription of DAAs should continue to be a high priority, in order to continue to follow the HCV elimination strategy and to reach the WHO goal.^{23,29} (Figure 2).

The COVID-19 pandemic will change the delivery of care forever and adjust our approaches to this pandemic, and to other future health demand accordingly. Its experience has highlighted the need for greater focus and greater operational capacity together with a need for refocusing and increased global funding.³⁰ The possibility to eliminate an infection requires health systems to place greater focus on shifting from reactive to proactive care. In the field of hepatitis, this includes the capacity to provide greater operational support where this is needed. With specific regard to the achievement of WHO hepatitis elimination goals, all measures and innovations around virtual health, outpatient services and actions targeting 'hard to reach' populations that are going to be put in place and work in practice against COVID-19 pandemic could be transferred and could efficiently be

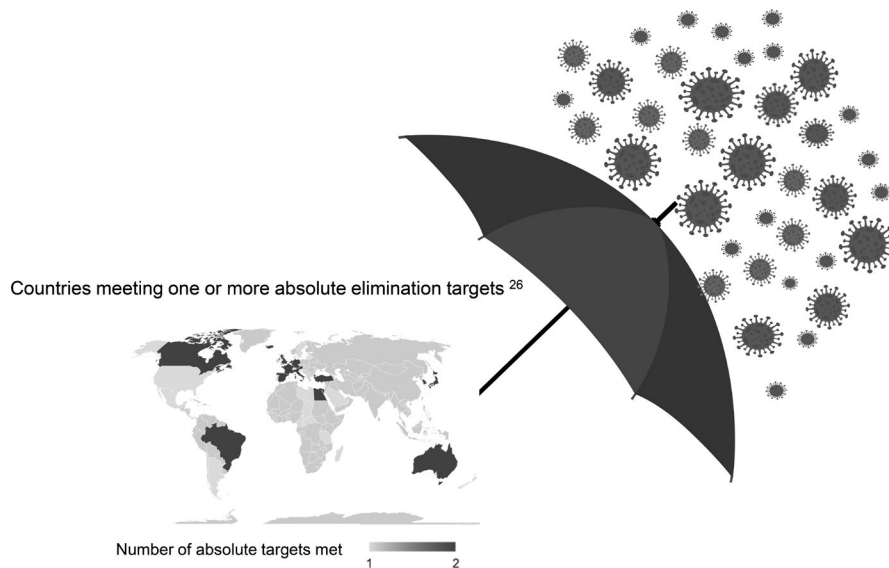


FIGURE 2 Meeting one or more Absolut HCV Target by 2030 on risk caused by COVID-19 pandemic. Countries showed with dark grey colour could meet one or more Absolut HCV Target for HCV elimination by 2030

used for HCV diagnosis and treatment of submerged populations with the objective of halting this 'silent pandemic' by 2030.

CONFLICT OF INTEREST

All authors declare no conflict of interest related to the subject matter of this study.

ORCID

Loreta A. Kondili  <https://orcid.org/0000-0003-2656-224X>

Antonio Craxi  <https://orcid.org/0000-0002-4480-9544>

Alessio Aghemo  <https://orcid.org/0000-0003-0941-3226>

REFERENCES

1. Dowdle WR. The principles of disease elimination and eradication. *Bull World Health Organ.* 1998;76:22-25.
2. Roser M, Ochmann S, Behrens H, Ritchie H, Dadonaite B. Eradication of Diseases. 2014. <https://ourworldindata.org/eradication-of-diseases> Accessed October 1, 2020.
3. World Health Organization. Global health sector strategy on viral hepatitis, 2016–2021: towards ending viral hepatitis. 2016. <http://apps.who.int/iris/bitstream/10665/246177/1/WHO-HIV-2016.06-eng.pdf>
4. Razavi H, Waked I, Sarrazin C, et al. The present and future disease burden of hepatitis C virus (HCV) infection with today's treatment paradigm. *J Viral Hepat.* 2014;21:34-59.
5. The Polaris Observatory HCV collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. *Lancet Gastroenterol Hepatol.* 2017;2:161-167.
6. Razavi H, Gonzalez YS, Yuen C, Cornberg M. Global timing of hepatitis C virus elimination in high-income countries. *Liver Int.* 2020;40:522-529.
7. Gamkrelidze I, Pawlotsky J-M, Lazarus JV, et al. Progress towards hepatitis C virus elimination in high income countries: an updated analysis. *Liver Int.* 2021. in press. <https://doi.org/10.1111/liv.14779>.
8. Kondili LA, Robbins S, Blach S, et al. Forecasting Hepatitis C liver disease burden on real-life data. Does the hidden iceberg matter to reach the elimination goals? *Liver Int.* 2018;38:2190-2198.
9. Kondili LA, Blach S, Razavi H, Craxi A. Tailored screening and dedicated funding for direct acting antiviral drugs: how to keep Italy on the road to hepatitis C virus elimination? *Ann Ist Super Sanita.* 2020;56:325-329.
10. Kondili LA, Gamkrelidze I, Blach S, et al. Optimization of hepatitis C virus screening strategies by birth cohort in Italy. *Liver Int.* 2020;40:1545-1555.
11. Fraser H, Martin NK, Brummer-Korvenkontio H, Korvenkontio HB et al. Model projections on the impact of HCV treatment in the prevention of HCV transmission among people who inject drugs in Europe. *J Hep.* 2018;68:402-411.
12. Martin NK, Thornton A, Hickman M, et al. Can Hepatitis C Virus (HCV) Direct-Acting Antiviral treatment as prevention reverse the HCV epidemic among men who have sex with men in the United Kingdom? Epidemiological and Modeling Insights. *Clin Infect Dis.* 2016;1:1072-1080.
13. Averbhoff F, Shadaker S, Gamkrelidze A, et al. Progress and challenges of a pioneering hepatitis C elimination program in the country of Georgia. *J Hepatol.* 2020;72:680-687.
14. 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.
15. Cortesi PA, Barca R, Giudicatti G, et al. Systematic review: economic evaluations of HCV screening in the direct-acting antivirals era. *Aliment Pharmacol Ther.* 2019;49:1126-1133.
16. Parigi TL, Aghemo A. HCV screening: moving from theory to practice. *Liver International.* 2020;40:1538-1540.
17. Lazarus JV, Fenton KA. Hepatitis—a devastating epidemic in Europe. *BMC Infect Dis.* 2014;14:S1.
18. Hatzakis A, Lazarus JV, Cholongitas E, et al. Securing sustainable funding for viral hepatitis elimination plans. *Liver Int.* 2020;40:260-270.
19. Cox AL, El-Sayed MH, Kao J-H, et al. Progress towards elimination goals for viral hepatitis. *Nature Reviews Gastroenterol Hepatol.* 2020;17:533-542.
20. Health Expenditure World Health Organization. Global Spending on Health: A World in Transition. Global report 2019. https://www.who.int/health_financing/documents/health-expenditure-report-2019.pdf?ua=1. Accessed October 1, 2020.
21. Richardson AK. Investing in public health: barriers and possible solutions. *Journal of Public Health.* 2012;34:322-327.
22. Younossi ZM, Bireddinc A, Henry L. Hepatitis C infection: a multifaceted systemic disease with clinical, patient reported and economic consequences. *J Hepatol.* 2016;65:109-119.

23. Mennini FS, Marcellusi A, Robbins Scott S, et al. The Impact of Direct Acting Antivirals on Hepatitis C Virus Disease Burden and Associated Costs in Four European Countries. *Liv Int*. 2021; In press.
24. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on a National Strategy for the Elimination of Hepatitis B and C. *A national strategy for the elimination of hepatitis B and C: phase two report*. In: Strom BL, Buckley GJ, eds. Washington (DC): National Academies Press (US); 2017.
25. Deuffic-Burban S, Deltenre P, Buti M, et al. Predicted effects of treatment for HCV infection vary among European countries. *Gastroenterology*. 2012;143:974-985.
26. Polaris Observatory Collaborators. The case for simplifying and using absolute targets for viral hepatitis elimination goals. *J Viral Hepat*. 2021;28:4-11.
27. Blach S, Kondili LA, Aghemo A, et al. Impact of COVID-19 on global HCV elimination efforts. *J Hepatol*. 2021;74:31-36.
28. Rosenbaum L. The Untold Toll—The pandemic's effects on patients without COVID-19. *New Engl J Med*. 2020;382:2368-2371.
29. Kondili LA, Marcellusi A, Ryder S, Craxi A. Will the COVID-19 pandemic affect HCV burden? *Correspondence Dig Liv Dis*. 2020;52:947-949.
30. Wingrove C, Ferrier L, James C, Wang S. The impact of COVID-19 on hepatitis elimination. *Lancet Gastroenterol Hepatology*. 2020;5:792-794.

How to cite this article: Kondili LA, Craxi A, Aghemo A. Absolute targets for HCV elimination and national health policy paradigms: Foreseeing future requirements. *Liver Int*. 2021;00:1-7. <https://doi.org/10.1111/liv.14796>