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The case for simplifying and using absolute targets for viral hepatitis elimination goals

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ORIGINAL ARTICLE

The case for simplifying and using absolute targets for viral hepatitis elimination goals

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Abstract

The 69th World Health Assembly endorsed the Global Health Sector Strategy for Viral Hepatitis, embracing a goal to eliminate hepatitis infection as a public health threat by 2030. This was followed by the World Health Organization's (WHO) global targets for the care and management of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections. These announcements and targets were important in raising awareness and calling for action; however, tracking countries' progress towards these elimination goals has provided insights to the limitations of these targets. The existing targets compare a country's progress relative to its 2015 values, penalizing countries who started their programmes prior to 2015, countries with a young population, or countries with a low prevalence. We recommend that (1) WHO simplify the hepatitis elimination targets, (2) change to absolute targets and (3) allow countries to achieve these disease targets with their own service coverage initiatives that will have the maximum impact. The recommended targets are as follows: reduce HCV new chronic cases to ≤5 per 100 000, reduce HBV prevalence among 1-year-olds to ≤0.1%, reduce HBV and HCV mortality to ≤5 per 100 000, and demonstrate HBV and HCV year-to-year decrease in new HCV- and HBV-related HCC cases. The objective of our recommendations is not to lower expectations or diminish the hepatitis elimination standards, but to provide clearer targets that recognize the past and current elimination efforts by countries, help measure progress towards true elimination, and motivate other countries to follow suit.

1 | INTRODUCTION

In 2016, the 69th World Health Assembly endorsed the Global Health Sector Strategy for Viral Hepatitis, embracing a goal to eliminate hepatitis infection as a public health threat by 2030.[1] This was followed by the World Health Organization's (WHO) global targets for the care and management of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections.[2] These announcements and targets were important in raising awareness and calling for action. Since then, tracking countries' progress towards these elimination goals has provided insights to the limitations of these targets.[3] We recognize that the global COVID-19 pandemic has impacted priorities, but we

Abbreviations: PWID, people who inject drugs; HBsAg, HBV surface antigen; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HBV, hepatitis B virus; WHO, World Health Organization.

Polaris Observatory Collaborators are presented in Appendix 1

TABLE 1 WHO hepatitis elimination targets[2]

Target areas				Baseline 2015	2020 target	2030 target
Service coverage	Prevention	1. Three-dose hepatitis B vaccine for infants (coverage %)		82%	90%	90%
		2. Prevention of mother-to-child transmission of HBV: hepatitis B birth-dose vaccination or other approaches (coverage %)		38%	50%	90%
		3. Blood and injection safety (coverage %)	Blood safety: donations screened with quality assurance	89%	95%	100%
			Injection safety: use of engineered devices	5%	50%	90%
		4. Harm reduction (sterile syringe/needle set distributed per person per year for people who inject drugs [PWID])		20	200	300
	5. Treatment	5a. Diagnosis of HBV and HCV (coverage %)		<5%	30%	90%
		5b. Treatment of HBV and HCV (coverage %)		<1%	5 million (HBV)	80% eligible treated
Impact leading to elimination	Incidence of chronic HBV and HCV infections			6-10 million	30% reduction	90% reduction
	Mortality of chronic HBV and HCV infections			1.46 million	10% reduction	65% reduction

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus.

TABLE 2 Simplified hepatitis elimination targets using absolute targets

Primary objective	Reduce incidence		Reduce mortality	
2030 Target	Reduce HCV new chronic cases to ≤5 per 100 000 (excluding the new cases from immigration)	Reduce HBsAg prevalence among 1-y-olds to ≤0.1%	Reduce HBV & HCV mortality to ≤5 per 100 000	Demonstrate HBV & HCV year-to-year decrease in new HCV- and HBV-related HCC cases
Measure Options	Conduct two national surveys (minimum 1 y apart) and estimate incidence between the two by age group.	Conduct HBsAg surveys in 1-y-olds in multiple regions in the country and maintain prophylaxis measures.	Establish/use national registry for HCC, decompensated cirrhosis linked to patient and death registries, attributed cause, & adjust for under reporting.	Establish/use national registry for HCC, decompensated cirrhosis linked to patient and death registries, attributed cause, & adjust for under reporting.
	Conduct two surveys (minimum 1 y apart) in high-risk groups accounting for >80% of new infections and estimate incidence rate.	Conduct HBsAg surveys among 1-y-olds in high prevalence regions/ populations and maintain prophylaxis measures.	Establish/use national HCC registry. Estimate annual decompensated cirrhosis to HCC incident ratio in ≥1 major centre. Use HCC and cirrhosis survival studies to estimate overall mortality by year.	Establish/use national HCC registry. Estimate annual decompensated cirrhosis to HCC incident ratio in ≥1 major centre. Use HCC and cirrhosis survival studies to estimate overall mortality by year.
	Use modelling to estimate incidence.	Use modelling that considers the impact of prophylaxis to estimate incidence and maintain prophylaxis measures.	Use modelling to estimate HBV- and HCV-related HCC and cirrhosis mortality.	Use modelling to estimate HBV- and HCV-related HCC and cirrhosis mortality over time.

Abbreviations: HBsAg, HBV surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus.

TABLE 3 Countries/regions reaching the existing WHO elimination targets by 2030

HBV 90% reduction in incidence	HBV <=0.1% prevalence among 5-year-olds		HBV 65% reduction mortality	Countries/ regions meeting all HBV targets	HCV 90% reduction in incidence	HCV 65% reduction in mortality	Countries/ regions meeting all HCV targets
Italy	Albania	Korea, Republic of	None	None	Egypt	Austria	Egypt
Japan	Algeria	Kosovo			France	Canada	France
UK	Argentina	Kuwait			Iceland	Egypt	Iceland
	Armenia	Latvia			Korea, Republic of	France	Spain
	Australia	Lebanon			Spain	Georgia	
	Austria	Lithuania				Iceland	
	Belgium	Macedonia				Italy	
	Brazil	Malaysia				Japan	
	Bulgaria	Mexico				**Mongolia**	
	Canada	Morocco				Netherlands	
	Chile	Netherlands				Spain	
	China	New Zealand				Sweden	
	Colombia	Nicaragua				Switzerland	
	Costa Rica	Norway				**Taiwan**	
	Croatia	Oman				United States	
	Cuba	Panama					
	Czechia	Peru					
	Dominican Republic	Poland					
	Ecuador	Portugal					
	Egypt	Qatar					
	El Salvador	Russia					
	Finland	Saudi Arabia					
	France	Serbia					
	Gambia	Singapore					
	Germany	Slovakia					
	Greece	Spain					
	Guatemala	Sweden					
	Hong Kong	Switzerland					
	Hungary	Taiwan					
	Iceland	Thailand					
	Iran	Tunisia					
	Ireland	Turkey					
	Israel	UAE					
	Italy	UK					
	Japan	United States					
	Jordan	Uruguay					
	Kazakhstan	Uzbekistan					
	Kenya						

Note: Blue countries/regions—those not achieving the absolute targets for a similar category in Table 4; only countries/ regions analysed by Polaris Observatory are listed; UAE: United Arab Emirates, UK: United Kingdom.

recommend that these targets be updated to better reflect the original goals—clear, measurable targets that better signpost progress towards true viral hepatitis elimination.

2 | PROBLEMS

First, the current impact targets for reduction in mortality and incidence are relative to a 2015 baseline (Table 1) when hepatitis epidemiology data were not being systematically collected in most countries. The 2015 relative targets also penalize countries that had a low starting point in 2015. Countries with young HCV-infected populations (eg, Australia and United Kingdom [UK]) will have a difficult time achieving the current mortality targets, even with robust national elimination programmes, since their 2015 mortality was already low. Similarly, countries with a low incidence in 2015 (eg, the Netherlands for HCV; much of Western Europe and the Americas for HBV) will have difficulty reaching an additional 90% incidence reduction by 2030. Second, the current guidelines are ambiguous. A 90% reduction in incidence of chronic HBV infections (compared to 2015 baseline) is inconsistent with a 0.1% prevalence of HBV infection in children five years of age in 2030 as suggested by WHO.[4] The former favours

TABLE 4 Countries/regions reaching the absolute HBV and HCV elimination targets by 2030

HBV ≤0.1% HBsAg prevalence among 1-year-olds		HBV reduce mortality to ≤5 per 100,000 & decrease in new HCC cases	Countries/ regions meeting all HBV targets	HCV reduce new chronic infections to ≤5 per 100,000	HCV reduce mortality to ≤5 per 100,000 & decrease in new HCC cases	Countries/ regions meeting all HCV targets
Albania	Kosovo	**Finland**	**Finland**	**Argentina**	**Australia**	**Australia**
Algeria	Kuwait	**Japan**	**Japan**	**Australia**	Austria	**Austria**
Argentina	**Kyrgyzstan**			**Austria**	**Brazil**	**Brazil**
Armenia	Latvia			**Belgium**	**Cameroon**	**Canada**
Australia	Lebanon			**Brazil**	Canada	Egypt
Austria	**Libya**			**Canada**	**CAR**	France
Azerbaijan	Lithuania			**Chile**	**Chad**	**Germany**
Bangladesh	Macedonia			**Costa Rica**	Egypt	Iceland
Belarus	Malaysia			**Croatia**	France	**Italy**
Belgium	Mexico			**Denmark**	Georgia	**Japan**
Brazil	**Moldova**			**Dominican Republic**	**Germany**	**Korea, Republic of**
Bulgaria	**Mongolia**			Egypt	Iceland	**Netherlands**
Cambodia	Morocco			**El Salvador**	Italy	Spain
Canada	**Nepal**			France	Japan	**Turkey**
Chile	Netherlands			**Germany**	**Korea, Republic of**	**UK**
China	New Zealand			Iceland	**Latvia**	
Colombia	Nicaragua			**Israel**	**Libya**	
Costa Rica	Norway			**Italy**	**Lithuania**	
Croatia	Oman			**Japan**	**Madagascar**	
Cuba	Panama			Korea, Republic of	Netherlands	
Czechia	Peru			**Lebanon**	**New Zealand**	
DPR Korea	Poland			**Mexico**	**Rwanda**	
Denmark	Portugal			**Netherlands**	Spain	
Dominican Republic	Qatar			**Portugal**	Sweden	
Ecuador	**Romania**			**Saudi Arabia**	Switzerland	
Egypt	Russia			**Slovenia**	**Turkey**	
El Salvador	Saudi Arabia			Spain	**UK**	
Finland	Serbia			**Tanzania**	United States	
France	Singapore			**Turkey**		
Gambia	Slovakia			**UK**		
Georgia	**Slovenia**					
Germany	Spain					
Greece	Sweden					
Guatemala	Switzerland					
Hong Kong	Taiwan					
Hungary	**Tajikistan**					
Iceland	Thailand					
India	Tunisia					
Iran	Turkey					
Ireland	**Turkmenistan**					
Israel	**Ukraine**					
Italy	UAE					
Jamaica	UK					
Japan	United States					
Jordan	Uruguay					
Kazakhstan	Uzbekistan					
Kenya	**Venezuela**					
Korea, Republic of						

Note: Blue countries/regions—those not achieving the current targets for a similar category in Table 3, only countries/regions analysed by Polaris Observatory are listed; CAR: Central African Republic, DPR Korea: Democratic People's Republic of Korea, UAE: United Arab Emirates, UK: United Kingdom.

countries that began universal vaccination between 2015-2020 (eg, Japan and UK), while the latter favours countries/regions that have had long-standing vaccination programmes prior to 2015 (eg, China & Taiwan). Finally, the service coverage targets are confusing since they do not include all options available to countries (eg, antiviral treatment of pregnant women, use of hepatitis B immune globulin).

3 | RECOMMENDATION

We recommend that (1) WHO simplify the hepatitis elimination targets, (2) change to absolute targets shown in Table 2 and (3) allow countries to achieve these disease targets with their own service coverage initiatives that will have the maximum impact. The recommended targets roughly correspond to the WHO targets but are translated to absolute numbers. Table 2 also shows different levels of recommended measures to track progress towards these goals. The reduction in mortality must be coupled with a decrease in new HBV/HCV-related hepatocellular carcinoma (HCC) cases: a measurable surrogate for overall liver-related mortality. Countries with a low viral hepatitis prevalence may meet the mortality target and still have an increasing incident number of HBV/HCV-related HCC cases. This combination will ensure that steps are taken to reduce HBV/HCV mortality and disease burden.

Using models developed by Polaris Observatory, the projected countries that will achieve the existing 2030 WHO elimination targets and the recommended absolute targets are shown in Table 3. The analyses are based on historical treatment and screening data up to 2019 with projections to 2030, not including the impact of the COVID-19 pandemic. There has been a negative impact on hepatitis-related services; however, the full impact of COVID-19 is difficult to incorporate at the time of this analysis.

Using existing criteria, only three countries are expected to achieve the 90% reduction in HBV incidence. None will achieve a 65% reduction in mortality relative to 2015, and no country will achieve all of the current HBV elimination targets. Similarly, only four countries are expected to achieve all of the current HCV elimination targets.

Hepatitis B virus surface antigen (HBsAg) prevalence among 5-year-olds reflects the impact of prophylaxis programmes instituted 5 years earlier. Table 4 shows that changing the target for prevalence among children from 5-year-olds to 1-year-olds would allow another 20 countries to achieve the absolute target of ≤0.1% by 2030. This reflects the benefits of their vaccination programmes over the additional 4 years. This measure also correlates well with a low incidence (≤5 per 100 000) among the total population. Thus, a separate (relative) target is not needed.

An estimated 76 countries will meet an HBV mortality rate of 5 per 100 000, but only two will also have a year-on-year reduction of HCC cases (Finland and Japan). This highlights the need for further debate, beyond the scope of this editorial, regarding the current international and national HBV treatment guidelines that are too narrow and restrictive to sufficiently result in a year-to-year decrease in HBV-related HCC cases.

Table 4 also shows that moving from a relative reduction in HCV incidence to an absolute cut-off of ≤5 per 100 000 allows 25 additional countries with low HCV prevalence to meet the new targets. It makes little sense to expect a country with a low HCV prevalence and incidence to spend resources to further reduce incidence if HCV is not considered a large public health problem. Similarly, moving to an absolute target of ≤5 per 100 000 for HCV mortality allows all countries that started with a low mortality rate in 2015 to achieve the new targets (15 countries). Overall, an additional 11 countries are expected to achieve all new targets relative to the existing WHO elimination targets.

The objective of our recommendations is not to lower expectations or diminish the hepatitis elimination standards, but to provide clearer targets that recognize the past and current elimination efforts by countries, help measure progress towards true elimination, and motivate other countries to follow suit. We also believe that countries are in the best position to select the mix of service coverages that will allow them to meet these revised global targets. This is particularly important during the COVID-19 pandemic that may have led to diversion of resources from the hepatitis programmes. After 5 years of progress and assessment, we strongly recommend that WHO reconsiders and refines the existing elimination targets in 2020.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

H. Razavi, S. Blach and D. Razavi-Shearer contributed to the conception, design and the initial drafting of the manuscript. All authors contributed to the interpretation of results, revision of the manuscript, approved the final version, and agreed to be accountable for the manuscript.

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APPENDIX 1

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