Training workshop on screening, diagnosis and treatment of hepatitis B and C



Session 1C

Viral hepatitis in the Western Pacific region



Learning objectives

At the end of this session, participants will be able

- to demonstrate improved knowledge of regional epidemiology of viral hepatitis
- to understand the regional response and strategies to combat hepatitis



Elimination of Viral Hepatitis in the Western Pacific Region

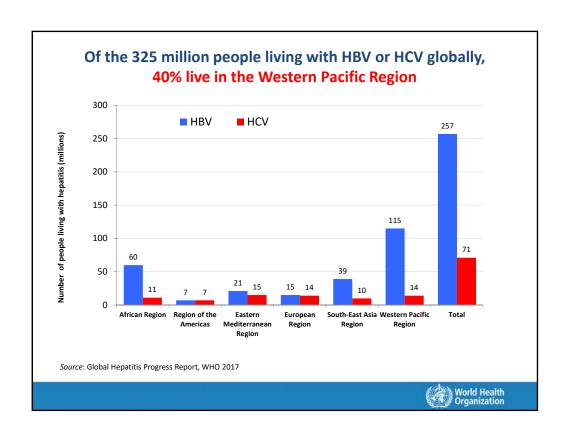
January 2020

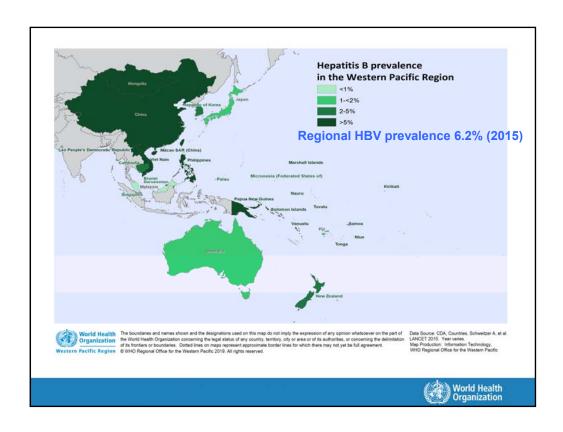


Outline

- Overview: current situation
- Implementing towards elimination: progress
- Future directions

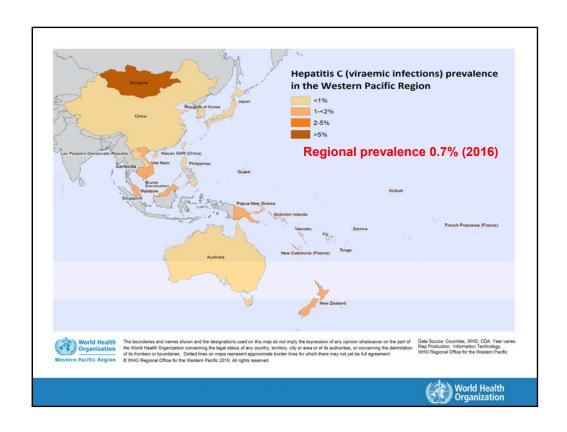




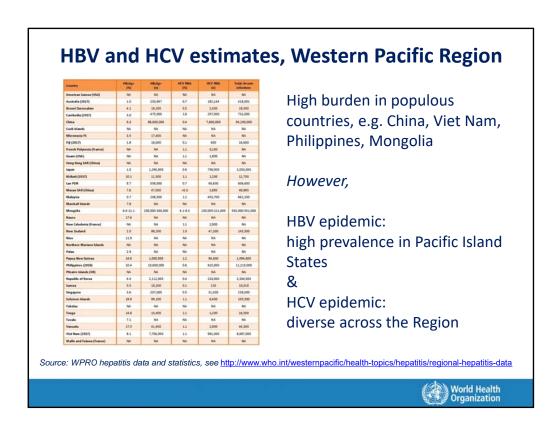


There is large diversity of the burden of hepatitis B in the Western Pacific Region.

Many of the countries in the Pacific region (small island states) bear a high burden of hepatitis B (where prevalence of HBV is > 5%)



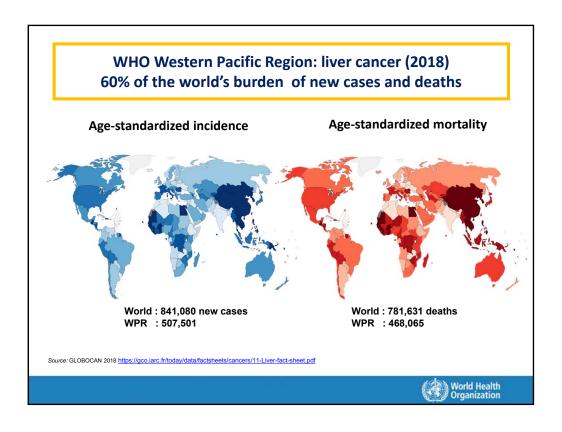
The Hepatitis C prevalence is variable across countries in the Region, and also within countries. The main drivers for hepatitis C are unsafe injections, injecting drugs use, and from unsafe blood (previously). Mother to child transmission is also a route of transmission but at low levels.



In the Western Pacific Region, HBV is endemic in several countries such as China, Papua New Guinea, Republic of Korea, Mongolia and Lao People's Democratic Republic.

HCV is endemic in Mongolia.

As compared to HCV, HBV is much more common in WPR countries.



Source: GLOBOCAN 2018. Link: https://gco.iarc.fr/today/data/factsheets/cancers/11-liver-fact-sheet.pdf (Accessed 14 January 2020)

WPR has the highest burden of liver cancer globally, accounting for 60.3% of new cases of liver cancer and 60% of liver cancer deaths worldwide.

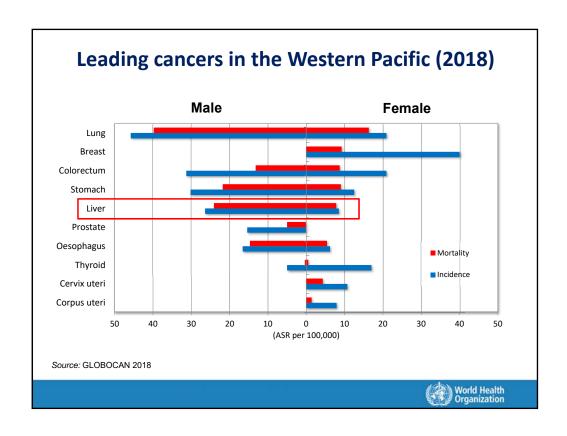
Most liver cancer is related to chronic hepatitis B or C.

	0-28 Days	1-59 Months	5-14 Years	15-29 Years	30-49 Years	50-59 Years	60-69 Years	70+ Years	Total
1	Preterm birth complications 55,245	Lower Respiratory infections 34,932	Drowning 13,554	Road Injuries 67,796	Road Injury 104,985	Stroke 196,098	Stroke 561,607	Stroke 1,636,563	Stroke 2,497,803
2	Birth asphyxia and Birth Trauma 39,787	Congenital heart anomalies 16,478	Road Injuries 8,814	Self-harm 26,238	Stroke 92,161	Ischemic Heart Disease 152,058	Ischemic Heart Disease 400,676	Ischemic Heart Disease 1,402,336	Ischemic Heart Disease 2,054,603
3	Congenital heart anomalies 14,700	Diarrheal Disease 14,909	Leukemia 4,883	Ischemic heart disease 10,905Leading	Ischemic Heart Disease 88,338	Trachea, bronchus, lung cancers 98,883	Chronic obstructive pulmonary Disease 195,097	Chronic obstructive pulmonary Disease 892,218	Chronic obstructive pulmonary Disease 1,141,932
4	Lower Respiratory Infections 10,824	Exposure to mechanical Forces 8,400	Lower Respiratory infections 4,506	Drowning 10,302	Liver Cancer 73,342 (70.55% due to hepatitis B and C)	Liver Cancer 96,723 (58.74% due to hepatitis B and C)	Trachea, bronchus, lung cancers 192,676	Trachea, bronchus, lung cancers 451,732	Trachea, bronchus, lung cancers 785,157
5	Neonatal Sepsis and Infections 10,406	Drowning 8,027	Congenital Heart anomalies 3,787	Interpersonal Violence 9,833	Self-Harm 49,945	Road Injuries 53,375	Liver Cancer 115,423 (52.86% due to hepatitis B and C)	Lower respiratory infections 378,841	Lower respiratory infections 518,171
6	Other congenital anomalies 9,886	Road Injury 8,009	Other Infectious Disease 3,221	Leukemia 9,265	Trachea, bronchus, lung cancers 39,979	Stomach Cancer 52,010	Stomach Cancer 103,241	Alzheimer disease and other dementias 353,850	Liver Cancer 488,245 (58.87% due to hepatitis B and C)
7	Other neonatal conditions 7,796	Other unintentional injuries 6,675	Other unintentional injuries 2,264	Stroke 8,728	Cirrhosis of the liver 33,068 (61.14% due to hepatitis B and C)	Cirrhosis of the liver 42,444 (62.43% due to hepatitis B and C)	Diabetes Mellitus 70,375	Stomach Cancer 232,486	Stomach Cancer 411,898
8	Neural tube defects 3,169	Childhood-cluster diseases 6,019	Falls 2,149	Other unintentional Injuries 8,727	HIV/AIDS 27,038	Chronic obstructive pulmonary Disease 38,704	Oesophagus Cancer 63,451	Hypertensive Heart Disease 229,328	Alzheimer disease and other dementias 396,757
9	Exposure to mechanical forces 2,525	Other congenital anomalies 4,904	Parasitic and vector diseases 1,869	Falls 6,616	Stomach Cancer 22,889	Self-harm 30,463	Cirrhosis of the Liver 63,281 (66.08% due to hepatitis B and C)	Liver Cancer 197,465 (57.38% due to hepatitis B and C)	Road Injuries 328,117
10	Other unintentional injuries 1,343	Preterm birth complications 4,523	Tuberculosis 1,762	Lower Respiratory infections 6,366	Kidney Diseases 22,164	Oesophagus Cancer 29,483	Hypertensive Heart Disease 59,695	Other circulatory diseases 169,432	Hypertensive Heart Disease 317,617
	urce: WHO Glob		nates, 2016, <u>ht</u>	tp://www.who	o.int/healthinfo/glo	bal_burden_diseas	e/estimates/en/in	dex1.html	

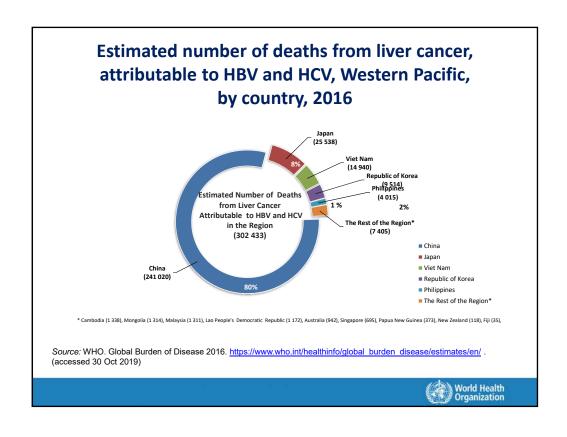
Let's look further in the impact of chronic hepatitis infection to health in the Region:

- We see that cirrhosis and liver cancer is already an issue from ages 30 years and above
- We know that the risk of cancer increases with age and this is evident as liver cancer is within the top 10 leading causes of death in the region
- Overall in WPR, liver cancer is the 6th top cause of deaths

These deaths, including related morbidity, is preventable. Earlier Treatment can prevent liver cancer

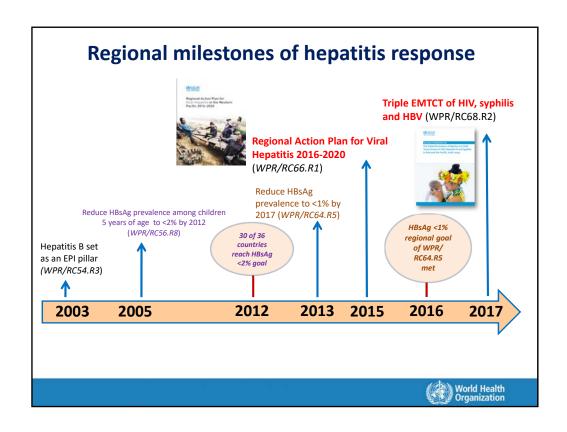


- Liver cancer is the 6th most common cancer worldwide; 5th in the Western Pacific region
- Liver cancer in the Western Pacific Region countries are mostly due to chronic hepatitis B or C infection, and can be prevented by treatment of those infected with hepatitis.
- Hepatitis C can be cured with effective direct acting antiviral combinations, while Hepatitis B can be effective treated with use of highly effective antivirals drugs.



This shows the number of death from liver cancer, attributable to HBV and HCV in the Western Pacific Region, 2016, by country

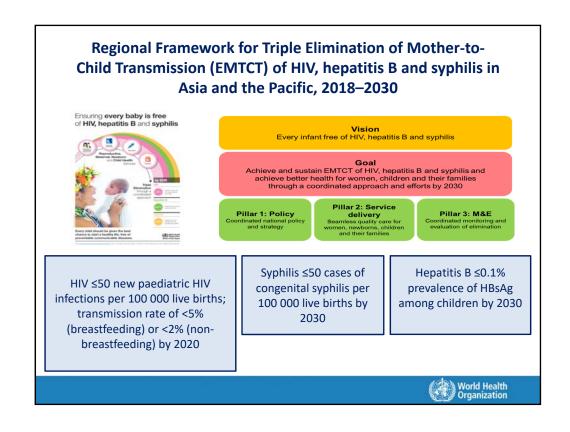
In term of numbers, China has the largest numbers because of the large population size.



The Western Pacific Region has led the combat on hepatitis since the start with immunisation, moving EPI targets to achieve, and in 2015 — countries endorsed a comprehensive approach to elimination of hepatitis as public health threats, including prevention care and treatment.

In 2017, building on the progress achieved in the region, the framework for triple elimination of mother to child transmission of HIV, hepatitis B and syphilis was endorsed

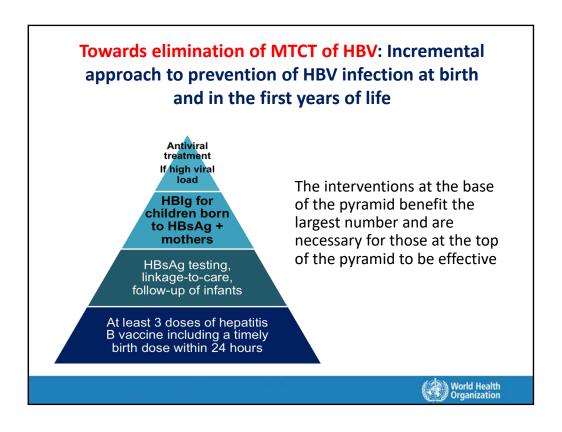
Note: immunization targets are for reduction of HBsAg prevalence among children 5 years of age



The triple elimination framework has a clear vision, goals and targets to be achieved.

This framework piggybacks on the existing dual elimination, with HBV elimination added on.

The ultimate target for HBV is 0.1% prevalence among children by 2030.



Taking the incremental approach, and building from the foundation of the immunization programme, working upwards through improving access to testing, linkage to care and follow up, and antiviral drug use for some women who have high viral load — so as to work towards an "almost zero infection".

Targets	Interventions	Global 2020 target (Regional targets in parenthesis)	Global 2030 target	Western Pacific Region 2019 status
Impact	Incidence	-30% (1% HBsAg in children)	-90% 0.1% HBsAg in children	HBV prevalence in children: 0.93% (2016) HCV incidence: 6 per 100,000 (2015)
	Mortality	-10%	-65%	24.1 deaths per 100,000 (2015)
Service coverage	3 dose hepatitis B vaccination	90% (95% by 2017)	90%	90% (2018)
	Birth dose hepatitis B vaccination	50% (95% by 2017)	90%	83% (2018)
	Blood safety	95 % screened donations	100 % screened donations	98% screened (2015)
	Safe injections	100%	100%	98.8% safe injections (2019)
	Harm reduction	200 injection sets / PWID	300 injection sets / PWID	57 injection sets/PWID (2015)
	Testing	30% diagnosed	90% diagnosed	HBV: 17% (2016) HCV: 21% (2016)
	Treatment	5M and 3M treated for HBV and HCV	80% eligible treated	HBV: 4 million (2016) HCV: 257,000 (2016)

Shown here are the Global Health Sector Strategy for Viral Hepatitis (GHSS) 2016-2021 service and impact targets. Targets for 2020 include getting 3 dose hep B vaccine coverage to 90% and hep B birth dose coverage to 50%. Also, GHSS looks to reduce the incidence to 1% in children by 2020 and to 0.1% by 2030.

The Western Pacific Region has met the prevention targets for the region and for global level. However, the main gap is in harm reduction, testing and treatment.

Note:

Mortality rate: highest in the WPRO region (24.1 deaths per 100,000) followed by SEAR region (21.2 per 100,000).

The global average death rate is 18.3 per 100,000.

Source:

HBV vaccination: WHO Global and regional immunization profile (data as of 01 Dec 2019) Link:

https://www.who.int/immunization/monitoring surveillance/data/gs wprprofile.pdf?ua=1

Blood safety:

WHO. Global Status Report on Blood Safety and Availability, 2016

Safe injections:

Safe injections as defined as "use of an unopen syringe or needle". Unsafe injections per person per year in WPRO =0.019

Hayashi T et al. Injection practices in 2911-2015L a review using data from the demographic and health surveys (DHS). BMC Health Services Research (2019)19:600

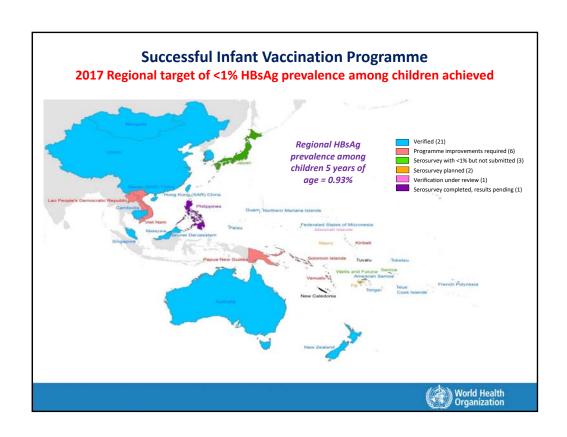
Harm reduction among people who inject drugs: https://aidsinfo.unaids.org/

Indicator: Number of needles per person who inject drugs

Note – in 2018, there was no data estimated for the region, but data is available in several countries:

Testing and Treatment: Modelling estimates 2016 from WHO/CDA Foundation



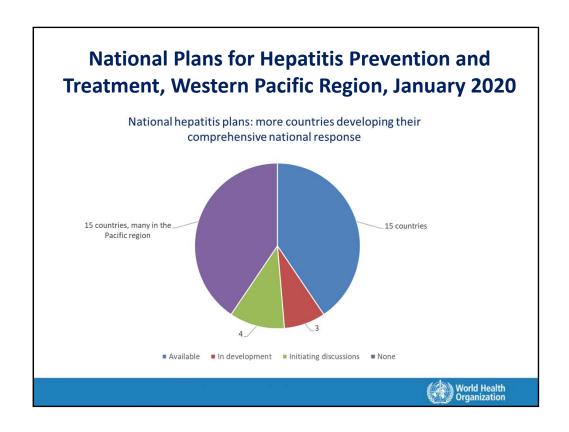


			Interv	entions for infants				
	Antenatal testing			Antiviral prophylaxi	for prevention of MTCT of H	IBV	Immediately after birth During the first 12 months a	
Countries	HBsAg	HBeAg	HBV DNA	eligibility	timing	drug	HBIG for exposed infants	Post-vaccination serologic t
Australia	Yes	Yes	Yes	HBV DNA >200,000 IU/mL	30–32 weeks to 6 weeks postpartum	TDF	All HBV-exposed infants <12 hours ideally <4 hours	Anti-HBs and HBsAg 3-12 months after completing vaccine series
Brunei Darussalam	Yes	Yes	Yes if referred to gastroenterologist	HBV DNA >10 ⁶ IU/ml hepatology clinics in tertiary hospitals	28-32 weeks to 4 weeks postpartum	TDF, 3TC	YES, all HBV-exposed infants	Yes, 9-12 months. Infants refe paediatric clinic
Cambodia	TA PROHM pilot	Yes	No	HBeAg in pilot study	24 weeks of gestation until delivery	TDF	No	Yes at 6 months
China 2018	Yes	No Partially	No	≥2,000,000 (2×10 ⁶) IU/mI	24-28 weeks of gestation	TDF or TBV	YES, all HBV-exposed infants	7-9 months Pilot only
Cook Islands	Yes							
Fiji	Yes	No	No	Roll-out planned in coming weeks to months		TDF	YES, all HBV-exposed infants	Not done
Hong Kong (China SAR)	Yes	No (under study)	No (under study)	Under study	Under study	Under study	YES, all HBV-exposed infants	Under study
Japan	Yes	Yes	Not official policy	NA NA	NA		Yes	Yes
Kiribati	Yes	Yes (at VIDRL)	Yes (at VIDRL)	-	-	-	No	No, planned
Lao PDR	Yes Trial in 9 hospitals	Yes	No	HBeAg+ pregnant women	28 weeks to 2 months postpartum	TDF	No	Yes at 6 months by HBV DNA PCR
Macao (China SAR)	Yes	No	No	HBV DNA >200,000 IU/mL	24-28 weeks until delivery or 3 months postpartum	TDF or TBV	Yes, all HBV-exposed infants	Yes, 9-15 months
Malaysia	Yes	Yes	Yes	HBV DNA >200,000 IU/mL or HBeAg+	28-32 weeks to 2 or 3 months postpartum	TDF	Yes, all HBV-exposed infants	Yes, 9 months
Mongolia	Yes	Yes	Yes	HBeAg+ pregnant women with HBV DNA >200,000 IU/mL	28 weeks to 12 weeks postpartum	TDF or TBV	Infants of HBeAg+ mothers only <12 hours	HBsAg, anti-HBs and anti- 2 months after completio vaccination
New Zealand	Yes	Yes	Yes	HBV DNA >200,000 IU/mL	30–32 weeks to 6 weeks postpartum	TDF	All HBV-exposed infants <12 hours ideally <4 hours	Anti-HBs and HBsAg 3-12 months after completing vaccine series
Niue	Yes							
Papua New Guinea	No	No	No	-	-	TDF (HIV treatment only)	No	No
Philippines	Yes	No	No	-		-	-	-
Republic of Korea	Yes			NA NA	NA		Yes	Yes (free)
Samoa	Yes							
Singapore	Yes	Yes	Yes, if necessary	Recommended (HBV DNA >200,000 IU/mL)	28-32 weeks to 4 weeks postpartum	TDF	Yes, all HBV-exposed infants	Yes, 3 months after complet vaccination
Solomon Islands	Yes	No	No	-	-	-	No	No
Tonga	Yes							
Viet Nam	Yes	Yes	Yes	Current guidelines - No Being updated	Being updated to 24-28 weeks	TDF	Yes, infants of HBeAg+ mothers	No

As more countries achieve the target of <1% HBsAg among children under 5 years of age, there is new interventions to further reduce the risk of mother to child transmission particularly among infants born to HBV-infected pregnant women. The Framework for triple elimination of HIV, syphilis and hepatitis B calls for coordinated delivery of integrated services for preventing mother to child transmission. Interventions consists of antenatal testing for HBV, antiviral prophylaxis for prevention of MTCT of hepatitis B among pregnant women who need it. The WHO guidelines for use of antiviral drugs among pregnant women infected with hepatitis B and the criteria to start is under development, and will be released in 2020.

Among HBV exposed infants, providing the timely birth dose of HBV vaccines within 24 hours is essential. HBIG use is recommended as part of current standard guidelines, but may not be available or affordable in many low and income countries.

The table provides an overview of national guidelines or interventions delivered for HBV EMTCT in WPRO, as of December 2019



Beyond vaccination for hepatitis B as the prevention, to get towards hepatitis elimination by 2030, it is important to have national comprehensive strategic or action plans, which include both prevention and treatment. National Plans articulate the vision, goals and set targets to be achieved and funded for the country.

In the Western Pacific Region, which consists of 37 countries and territories, more and more countries are development their national plans for prevention and treatment

WHO recommends tenofovir or entecavir to treat hepatitis B (2015)

Both tenofovir and entecavir are off-patent

Tenofovir US\$ 30 per person-year (median price)



Entecavir

US\$ 36 per person-year (minimum estimated price)

Source of entecavir figure: https://medicalxpress.com/news/2015-04-global-hepatitis-epidemic-person-year.html. Hill et al. Analysis of minimum target prices for production of entecavir to treat hepatitis B in high- and low-income countries. J Virus Erad. 2015 Apr; 1(2): 102-110.



Hepatitis B medicines (tenofovir and entecavir) are available in all countries, in generic and originator options.

Tenofovir and entecavir are off-patent

The median prices for tenofovir globally is US\$ 30 per person-year

For entecavir: this is estimated at US\$ 36 per person year

The prices of both medicines are approaching similar prices as countries list both into their essential medicines list, and promote generic options for both.

As an example, China's prices are US\$ 10 per person-year for both tenofovir and entecavir, using generically manufactured medicines, and central procurement

Medicines	Countries where the medicine is registered by the national regulatory authority			
Hepatitis C direct acting				
antivirals (DAA)				
Sofosbuvir	AUS, CHN, HOK, JPN, KHM, KOR, LAO, MNG, MYS, NZL, PHL, PYF, SGP, VNM			
Ledipasvir + sofosbuvir	AUS, CHN, HOK, JPN, KHM, KOR, LAO, MNG, MYS, NZL, PHL, PYF, SGP, VNM			
Simeprevir	CHN, JPN, PYF, SGP			
Daclatasvir	AUS, CHN, HOK, JPN, KHM, KOR, LAO, NZL, PHL, PYF, SGP, VNM			
Dasabuvir/ombitasvir + paritaprevir + ritonavir	AUS, BRN, CHN, HOK, JPN, KOR, MYS, NZL, PYF, SGP			
Ribavirin	AUS, BRN, CHN, HOK, JPN, KHM, KOR, LAO, MNG, MYS, NZL, PHL, PRC, PYF, SGP, VNM			
Velpatasvir + sofosbuvir	AUS, CHN, KHM, HOK, LAO, MNG, MYS, NZL, PYF, SGP			
Elbasvir + grazoprevir	AUS, CHN, HOK, JPN, NZL, PYF, KOR, SGP, VNM			
Glecaprevir + pibrentasvir*	AUS, CHN, HOK, JPN, NZL, KOR, SGP			
Sofosbuvir + velpatasvir + voxilaprevir*	AUS, CHN, NZL, SGP			
HBV and HCV				
Pegylated interferon alfa (2a or 2b) WPRO: data from countries, 2019	AUS, BRN, CHN, HOK, JPN, KHM, KOR, LAO, MNG, MYS, NZL, PHL, PYF, SGP, VNM			

Hepatitis C direct acting antiviral drugs (DAAs) are increasingly being registered in countries.

New pangenotypic combination DAAs such as glecaprevir/pibrentasvir & sofosbuvir/velpatasvir/voxilaprevir is being registered in some countries but mainly high income.

Sofobuvir/daclastavir is registered in most countries, and is the most widely used pangenotypic regimen currently (as of Jan 2020).

Country	HBV	HCV-DAA	Country	HBV	HCV-DAA
Australia	Financed	Financed	Malaysia	Financed	Financed
Brunei Darussalam	Financed	Financed*	Mongolia	Financed	Financed
Cambodia	ООР	ООР	New Zealand	Financed	Financed
China	Financed	Financed**	Papua New Guinea	OOP*	ООР
Hong Kong (China)	Financed	Financed	Philippines	OOP*	OOP*
Japan	Financed	Financed	Republic of Korea	Financed	Financed
Lao PDR	ООР	ООР	Singapore	Financed	Financed
Macao (China)	Financed	Financed	Viet Nam	Financed	Financed
* Brunei: using PEG-INF. DAA planned ** China: DAA under health reimburse			Papua New Guinea: pilot employer * Philippines: pilots for HBV and HC financing		

Access to medicines for HBV and HCV has seen improvements.

In general, most countries have drugs for hepatitis B registered, and most countries do have registration of DAA completed or in progress.

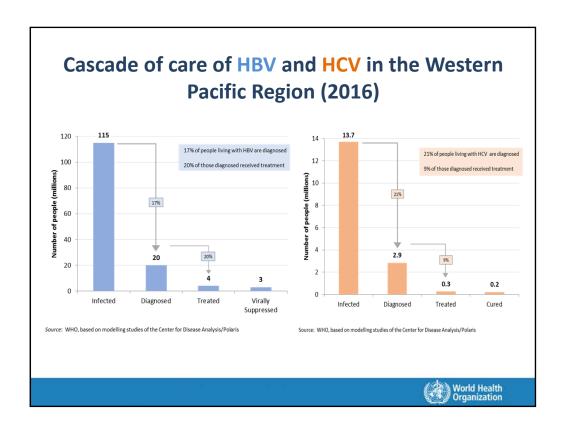
However, registration of drugs does not mean access to most of the people who need it.

In several countries, hepatitis C drugs are now under universal health coverage (taken here as being financed under health insurance and thus, accessible to most of the population).

High costs for HCV DAAs remain challenging in the region even among countries which have the drug registered, and/or covered through health insurance Affordability of tests and treatment remains an issue in many countries. Thus more work is needed for price reductions of tests and medicines.

UHC: covered by health insurance and/or government financed

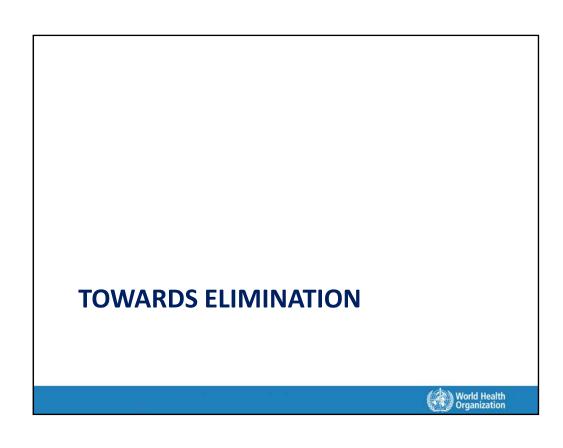
OOP: out of pocket

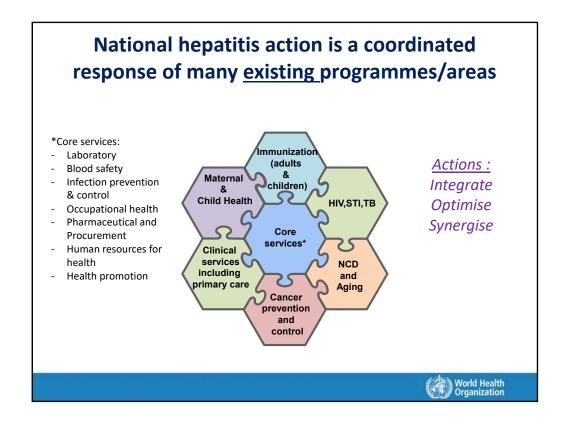


However, there is a large gap in care. Of those who are infected, only a minority know their status and are accessing treatment.

HBV cascade: not all people infected with HBV need treatment according to their disease staging.

Thus, much more needs to be done to scale up service delivery





The learning from countries is that national comprehensive action is a coordinated response of many programmes and technical areas and is country-specific to the health systems, financing systems, current health reforms, approaches to access medicines, civil society, delivery systems etc.

All these programs/areas already exists.

The actions are to deliver integrated services, optimizing delivery of services, and synergizing common outcomes that programmes share:

Example 1: for the hepatitis B prevention of mother to child transmission – this requires at minimum the roles of immunization programmes, maternal child health to deliver prevention of mother to child transmission interventions and clinical services (physicians) to care for mother and child

Example 2: Treating chronic hepatitis B and C will reduce the risk of developing liver cancer. Thus, treating hepatitis early prevents liver cancer, and more can be done to advocate and communicate to the public in this area. Linking reporting of viral hepatitis and the cancer registry will help improve information

Eliminating Viral Hepatitis in Western Pacific Region by 2030

We have achieved,

- √ Successful hepatitis B vaccination programme
- √ National action plans / guidelines developed
- ✓ Increased availability and affordability of hepatitis medicine

Challenges remain,

- X Lack of political commitment and resources
- X Lack of data at national/subnational levels
- X Low coverage of harm reduction
- **X** Limited access to testing and treatment

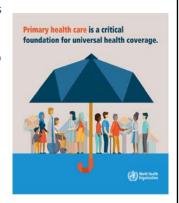


In the journey to elimination of hepatitis,

Delivering at scale

using the public health approach to hepatitis elimination

- ✓ Scale-up and decentralize testing and treatment services to primary health care
- ✓ Accelerate HBV elimination of mother to child transmission through integrated antenatal and follow-up services
- ✓ Enhance integrated service delivery and task-sharing delivered by non-specialists and non-physicians
- ✓ Integrate hepatitis reporting and monitoring into existing surveillance and health information systems
- ✓ Sustain hepatitis services as part of universal health coverage
- ✓ Engage community and peer support to promote access and linkages





Summary

- Hepatitis is a major public health burden
- Prevention needs to be scaled up and sustained
- Chronic hepatitis B and C cause substantial health and related costs (economic burden, human suffering...)
 - Highly effective drugs available and high price still barrier in some countries
 - Treatment prevents progression of disease, lowers risk of developing liver cancer
 - HCV treatment (with new DAAs): CURE
- Countries are overcoming barriers much progress, but more needs to be done



