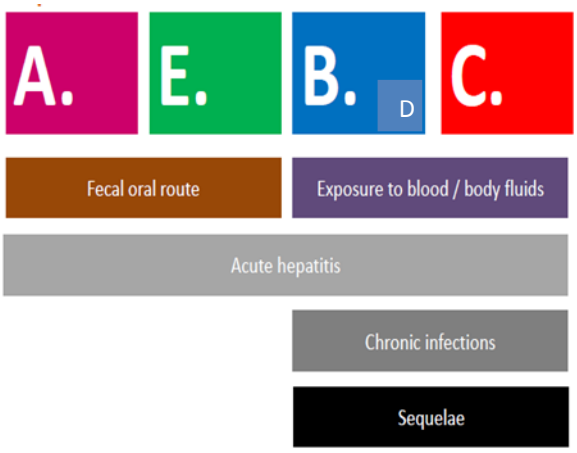
MINISTRY OF HEALTH

Implementation Framework & Clinical Guidance for Viral Hepatitis Prevention & Treatment

2019



Directorate of Public Health

Cover Page: Daliso Mumba

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Acronyms

Anti-HAV	Antibody against hepatitis A virus
Anti-HBc	Antibody against hepatitis B core antigen
Anti-HCV	Antibody against hepatitis C virus
Anti-HDV	Antibody against hepatitis D virus
Anti-HEV	Antibody against hepatitis E virus
APRI	AST to Platelet Ratio Index
CIDRZ	Centre for Infectious Disease Research in Zambia
DAA	Direct-acting antiviral
DNA	Deoxyribonucleic acid
EIA	Enzyme Immunoassay
FHF	Fulminant Heptatic Failure
GNC	General Nursing Council
HAV	Hepatitis A Virus
HBeAg	Hepatitis B e Antigen
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HDV	Hepatitis D Virus
HEV	Hepatitis E Virus
HepB_BD	Hepatitis B birth-dose vaccination in newborns
HIV	Human immunodeficiency virus
HPCZ	Health Professions Council of Zambia
ICT	Information and Communication Technology
IEC	Information, Education and Communication
Ig	Immunoglobulin
IPC	Infection Prevention and Control
LMTH	Levy Mwanawasa Teaching Hospital
M&E	Monitoring and Evaluation
MOH	Ministry of Health
NAT	Nucleic Acid Testing
NGO	Non-Governmental Organization
NSP	Needle and Syringe Programme
RNA	Ribonucleic acid
SVR	Sustained virological response
TB	Tuberculosis
UTH	University Teaching Hospital
WHD	World Hepatitis Day
WHO	World Health Organization

Foreword

The Government of the Republic of Zambia through the Ministry of Health is committed to ensuring that its people are healthy and productive, a prerequisite to making Zambia a middle income prosporous country by 2030. The high disease burden from both communicable and non-communicable diseases poses a threat to this aspiration. On the communicable diseases front, HIV and AIDS, Tuberculosis and malaria remain major public health concerns. However, going by the 2016, Zambia population based HIV impact assessment (ZAMPHIA), Viral hepatitis is one of the key infectious diseases we need to prioritize as a country on our journey to universal health coverage.

The Zambia Population Based HIV impact assessment of 2016, reported the prevalence of viral hepatitis in Zambia as ranging between 5.6% among adults aged 15 to 59% in the general population, and 7.1% among HIV infected individuals. It is estimated that the majority of persons with chronic hepatitis B and/ or hepatitis C are unware of their infection and do not benefit from promotive, preventive and curative services designed to reduce onward transmission.

Viral hepatitis is fully preventable and treatable: there are effective vaccines and treatments for hepatitis B virus and more than 90% of people with hepatitis C virus can be cured with treatment. Zambia introduced hepatitis B virus vaccine to the routine Under 5 vaccination schedule in 2005. Preliminary results from the ZAMPHIA indicate that hundreds of infections have been abated in children since then. However, its also clear that we continue to miss key opportunities to prevent transmission, diagnose and treat infections, prevent serious disease, and in many cases cure people. In addition, high risk groups inter alia health care workers still have limited access to the vaccine.

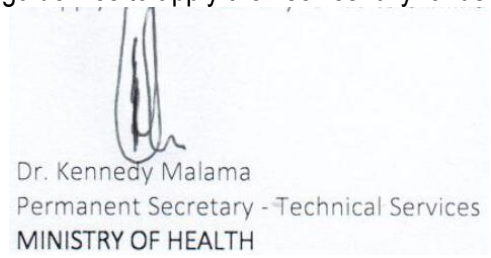
The development of this implementation framework and clinical guidance for viral hepatitis prevention and treatment has come has come at an opportune time when our transformation agenda as a sector is promised on universal health coverage across the continuum care. By providing steps for the implementation of preventive measures, as well as providing guidelines for treatment, it will now be possible to standardize preventive high impact interventions, as well as guide health care workers at different levels at different levels of care on viral hepatitis management.

I am therefore hopeful that the vision of eliminating viral hepatitis as a public health threat by 2030 in Zambia can be achievable. I urge all stakeholders to buy into this framework so that together we buid a strong coalition to improve access to integrated promotive, preventive and curative viral hepatitis services.

Acknowledgement

The development of the Implementation Framework & Clinical Guidance for Viral Hepatitis Prevention & Treatment involved the participation of various stakeholders. I wish to thank individuals and organisations from the Expanded Programme on Immunisation (EPI) Sub-committee who worked on the initial drafts. Special thanks go to members of the Viral Hepatitis Task Force who worked on the later drafts and ensured its finalisation. I also wish to thank the World Health Organization (WHO) and Centers for Infectious Research Diseases in Zambia (CIDRZ) for the technical and financial support.

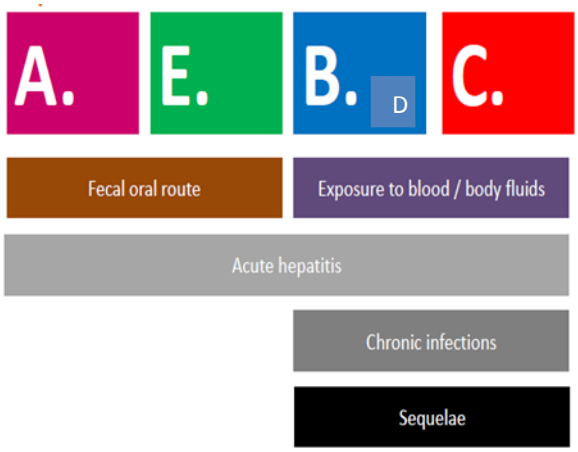
I therefore urge all those who will be using this implementation framework and clinical guidelines to apply themselves fully for us to eliminate viral hepatitis by 2030.



Chapter 1: Burden of Viral Hepatitis

Global Burden of Hepatitis

Every year it causes 1.34 million deaths (more deaths than are caused by HIV or malaria), making viral hepatitis the second biggest killer after tuberculosis. Every day, more than 3600 people die of viral hepatitis. Viral hepatitis is an inflammation of the liver, caused by five distinct hepatitis viruses (A, B, C, D, and E). While hepatitis A and E viruses are spread through the oral-faecal route, hepatitis B and C viruses are transmitted through exposure to blood, sexual intercourse, and from an infected pregnant mother to her unborn child. Although transmitted by blood, hepatitis D can cause infection only in individuals with active hepatitis B infection or in carriers. Hepatitis E is a cause of maternal and child deaths in settings with large diarrhoeal disease burdens. All five hepatitis viruses can cause acute disease, but the highest numbers of deaths result from liver cancer and cirrhosis of the liver which occur after decades of chronic hepatitis B or C infection. At least 60% of liver cancer deaths are due to late testing and treatment of viral hepatitis B and C.[1]



Although viral hepatitis B and C affect 325 million people globally, only 1 in 10 of those people have been tested, and only 1 in 5 have received appropriate treatment. Viral hepatitis is a highly endemic public health problem in the African Region, comparable to, even higher than other major communicable diseases, including HIV, tuberculosis and malaria.

An estimated 95% of people with hepatitis are unaware of their infection. This is mainly due to a lack of awareness and access to testing services. HIV-hepatitis coinfection is an important public health concern as it is a major cause of death in HIV-positive people and thus these patients have become key groups to identify and treat.

Burden of Viral Hepatitis In Zambia

The precise burden of viral hepatitis is actually unknown as no systematic studies have been undertaken to document this. However, various reports on individual hepatitis strains as well as data from the Zambia National Blood Transfusion Service (ZNBTS) provide insights into the national burden of the disease.

[1] https://www.who.int/who-campaigns/world-hepatitis-day/2018

The Zambia Population-Based HIV Impact Assessment (ZAMPHIA), a household-based national survey, conducted in 2016, indicated that the prevalence of infection with hepatitis B virus (HBV) among adults aged 15 to 59 years is higher among HIV-positive (7.1%) than HIV-negative (5.4%) individuals. Prevalence of HBV is especially high among HIV-positive males ages 15 to 59 years (10.2%).[2] Among children aged 0 to 14 years, HBV infection is more prevalent among those living with HIV (5.2%) than those living without HIV (1.3%). Surveillance data from ZNBTS on Hepatitis C Virus (HCV) antibody (serologies) since 2004 indicate that approximately 0.7-0.9% were HCV positive. In studies of HBV mono-infection and HIV-HBV co-infection in Zambia, Hepatitis D Virus (HDV) antibody was rare (2-3%). A study among people in Misisi compound in Lusaka observed high levels of Hepatitis E Virus (HEV) antibodies suggesting substantial transmission may be occurring. Other in-country studies among HIV infected patients in Lusaka identified HBsAg-positivity as a strong predictor of liver fibrosis and cirrhosis at the time of antiretroviral treatment (ART) initiation and this association increased with markers of HBV severity.[3] Further evidence of reduction in the liver stiffness in HBV patients on ART has been reported, reflecting a potentially missed opportunity given the wide availability of ART in this country.[4]

While little is known about other viral hepatitis infections (A,C, D & E) in Zambia, one report suggests that HEV is acquired throughout the first two decades of life and then the prevalence remains almost unchanged throughout the adult years.[5] This relatively small seroepidemiological study further reports that HIV was strongly associated with HEV infection. The lack of information on this clearly devastating public health problem is in many ways an important justification for this framework.

[2] Ministry of Health; Zambia Population-Based HIV Impact Assessment; 2016; https://phia.icap.columbia.edu/countries/zambia/

[3] Vinikoor MJ, Mulenga L, Siyunda A, Musukuma K, Chilengi R, Moore CB, Chi BH, Davies MA, Egger M, and Wandeler G. Association between hepatitis B co-infection and elevated liver stiffness among HIV-infected adults in Lusaka, Zambia. *Trop Med Int Health* 2016;21(11): 1435-1441.

[4] Vinikoor MJ, Sinkala E, Chilengi R, Mulenga LB, Chi BH, Zyambo Z, Hoffmann CJ, Saag MS, Davies MA, Egger M, and Wandeler G. Impact of Antiretroviral Therapy on Liver Fibrosis Among Human Immunodeficiency virus infected Adults with without or without HBV Co-infection in Zambia. Clin Infect Dis 2017;64(10):1343-1349.

[5] Jacobs C, Chiluba C, Phiri C, Lusulo MM, Chomba M, Hill PC, Ijaz S, and Kelly P. Seroepidemiology of hepatitis E virus infection in an Urban population in Zambia: Strong Association with HIV and environmental enteropathy. J Infect Dis 2014;209(5):652-7.

Chapter 2: Situation of Health Sector Response to Viral Hepatitis

Leadership and Governance (2018)

Table 1: Leadership and Governance

Indicator	Description	National	PHO	DHO	Tertiary Hospitals	Secondary Hospitals	Primary Hospitals	Health Centres
Viral Hepatitis Focal Point	Availability of programme coordinator	✓	X	X	X	X	X	X
National Viral Hepatitis Task Force	Availability of coordinating mechanism to provide technical inputs related to viral hepatitis programmes. Includes Civil Society Involvement	✓	n/a	n/a	n/a	n/a	n/a	n/a
Zambia Immunisation Technical Advisory Group	The Zambia Immunisation Technical Advisory Group (ZITAG) is the principal advisory group to the immunisation programme and country for development of policy related to vaccines and immunisation	✓	n/a	n/a	n/a	n/a	n/a	n/a

Guidelines, Protocols, and Procedures (2018)

Table 2: Guidelines, Protocols, and Procedures

Indicator	Description	National	PHO	DHO	Tertiary Hospitals	Secondary Hospitals	Primary Hospitals	Health Centres
National Hepatitis Plan/Strategy	Integrated in the National Health Strategic Plan 2017-2021; and National AIDS Strategic Framework 2017-2021	✓	**n/a**	**n/a**	**n/a**	**n/a**	**n/a**	**n/a**
HBV Care and Treatment Guidelines	Guidelines for the care and treatment of persons diagnosed with chronic hepatitis B integrated in the Zambia Consolidated Guidelines for prevention and treatment of HIV infection. *No standalone national guidelines for the care and treatment of persons diagnosed with chronic hepatitis B & C virus infection*	✓	✓	✓	✓	✓	✓	✓
EPI Manual	EPI Manual available as a reference document for middle level managers to provide oversight; and health workers to conduct immunization activities	✓	✓	✓	✓	✓	✓	✓
Facility-level blood safety	Proportion of health facilities providing blood transfusion that meets requirements for sufficient and safe blood transfusion	**n/a**	**n/a**	**n/a**	✓	✓	✓	✓

Availability of Screening & Diagnostic Tests (2018)

Table 3: Availability of Screening & Diagnostic Tests

Test Type	Public Facilities					Private Facilities	
	Blood Banks	Tertiary Hospitals	Secondary Hospitals	Primary Hospitals	Health Centres	Private Hospitals	Private Laboratories
HBsAg	✓	✓	✓	✓	✓	✓	✓
Anti-HAV	✓	X	X	X	X	X	✓
Anti-HBc	✓	X	X	X	X	X	✓
HBV DNA	X	X	X	X	X	X	✓
HBeAg	✓	X	X	X	X	X	✓
ALT	X	✓	✓	✓	X	✓	✓
Anti-HCV	✓	X	X	X	X	✓	✓
HCV RNA	X	X	X	X	X	X	✓
Anti-HDV	X	X	X	X	X	X	✓
Anti-HEV	✓	X	X	X	X	X	✓
FibroScan	X	X	X	X	X	✓	X

Availability of Therapeutical Drugs (2018)

Table 4: Availability of Therapeutical Drugs

Type of Hepatitis	Drugs	Public Facilities				Private Facilities
		Tertiary Hospitals	Secondary Hospitals	Primary Hospitals	Health Centres	Private Hospitals
HBV	TDF	✓	✓	✓	✓	✓
	3TC	✓	✓	✓	✓	✓
	FTC	✓	✓	✓	✓	✓
	Entecavir	X	X	X	X	No data
HCV	Glecaprevir	X	X	X	X	No data
	Sofosbuvir	X	X	X	X	No data
	Ledipasvir	X	X	X	X	No data
	Ribavirin	X	X	X	X	No data
	Velpatasvir	X	X	X	X	No data
	Daclatasvir	X	X	X	X	No data
	Pibrentasvir	X	X	X	X	No data
HDV	Pegylated Interferon Alpha	X	X	X	X	No data

Service Provision for Primary Prevention of Viral Hepatitis Infection (2018)

Table 5: Service Provision for Primary Prevention of Viral Hepatitis Infection

Vaccination Type	Tertiary Hospitals	Secondary Hospitals	Primary Hospitals	Health Centres	Private Facilities
Provision of birth dose of hepatitis B vaccine (HepB_BD)	✓[6]	X	X	X	✓
Four doses, where a monovalent birth dose is followed by three (DPT-HepB-Hib) doses, usually given with other routine infant vaccines	✓[6]	X	X	X	✓
Three (DPT-HepB-Hib) doses given as pentavalent vaccines	✓	✓	✓	✓	✓
Hepatitis B vaccination among health-care workers	✓[7]	X	X	X	✓

Strategic Information (2018)

Table 6: Strategic Information

Indicator	National
HAV Prevalence Estimates	No data
WHO HBV Prevalence Estimates	541,337
Cumulated incidence of HBV infection in children 5 years of age	No data
Hepatitis coinfections among persons with HIV infection	72,831
Incidence of HCV infection	No data

[6] University Teaching Hospital (UTH) Pilot study
[7] UTH and Levy Mwanawasa Teaching Hospital (LMTH) (Program)

Indicator	National
Hepatitis B testing	241,300[8]
People living with HBV diagnosed	No data
Treatment coverage for hepatitis B patients	No data
Number of people on HBV treatment with viral suppression	No data
WHO HCV Prevalence Estimates	161,006
Hepatitis C testing	No data
People living with HCV diagnosed	No data
Treatment initiation for hepatitis C patients	No data
Number of people cured from HCV	No data
Proportion of cirrhosis deaths attributable to HCV and HBV	No data
Proportion of hepatocellular carcinoma deaths attributable to HCV and HBV	No data
Coverage of timely hepatitis B vaccine birth dose (within 24 hours) to prevent mother-to-child transmission of HBV	No data
Coverage of third dose of DPT-HepB-Hib vaccination	85.8%
Facility-level injection safety	No data
Blood screening coverage	100%
Hepatitis D coinfection among people living with chronic HBV infection	No data
National system for viral hepatitis surveillance	

[8] Medical Stores Limited (MSL) data on rapid surface antigen tests issued in 2018

Chapter 3: Priority Interventions and Actions

Vision, Goal and Guiding Principles

Vision

Transmission of viral hepatitis is halted and everyone living with viral hepatitis has access to safe, affordable and effective prevention, care and treatment services.

Goal

Eliminate viral hepatitis as a major public health threat by 2030.

Guiding Principles

- Country ownership to ensure that the national viral hepatitis response is coordinated.
- Effective partnerships for multisectoral cooperation involving all sectors of society.
- Universal Health Coverage as the overarching framework to ensure that all people obtain the viral hepatitis services.
- Integration of viral hepatitis services into health systems and strategies.
- A public health approach based on simplified and standardized interventions and services.
- Primary Health Care approach prioritizing prevention and early diagnosis over treatment and cure.

Information for Focused Action

Table 7: Information for Focused Action

Strategic Objective	Targets	Outputs	Timeframe												MOH Stakeholders
			2019				2020				2021				
			Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	
Increase knowledge of the general population and key populations on risks and protection from viral hepatitis	All Policy makers aware of National Strategic Plan for Viral Hepatitis Prevention, Control & Treatment 2017-2021	Highest level politicians, policymakers and international funders/stakeholders sensitized on viral hepatitis prevention & treatment			X	X	X	X	X	X	X	X	X	X	• Civil Society Groups • Non Governmental Organisations (NGOs) • Health Professions Council of Zambia (HPCZ) • General Nursing Council (GNC) • Training Institutions
		World Hepatitis Day commemorated annualy on 28 July			X				X				X		
		Community,Traditional and Church leaders oriented on viral hepatitis prevention & treatment	X	X	X	X	X	X	X	X	X	X	X	X	

Strategic Objective	Targets	Outputs	Timeframe												MOH Stakeholders
			2019				2020				2021				
			Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	
	80% of training schools know who is at risk, and how to protect from viral hepatitis	Training schools for doctors, laboratory, nursing and pharmacy orientated on viral hepatitis prevention & treatment		X	X	X	X	X	X	X	X	X	X	X	
Increase awareness of health-care providers in screening high risk populations	All primary level healthcare workers have received information on hepatitis	Guidelines for prevention, care and treatment of hepatitis adapted	X	X											• HPCZ • GNC • Civil Society Groups
		Service providers, clinicians, nurses, hospital administrators, laboratory biomeds, counselors for risk reduction; and Procurement and Supply Chain Management for essential drugs and Rapid Test kits oriented on viral hepatitis prevention & treatment		X	X	X	X	X	X	X	X	X	X	X	

Strategic Objective	Targets	Outputs	Timeframe												MOH Stakeholders
			2019				2020				2021				
			Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	
Estimate the national burden due to chronic hepatitis	Determine prevalence of chronic hepatitis B by 2021	National system for viral hepatitis surveillance established and functional	X	X	X	X	X	X	X	X	X	X	X	X	• Academia, • Civil Society • Zambia National Public Health Institute (ZNPHI) • NGOs • ZAMPHIA • ZNBTS • Zambia Demographic and Health Survey (ZDHS)
	Sentinel surveillance for cirrhosis in biggest five hospitals	Inventory of the existing sources of data on viral hepatitis (ZNBTS, Intergrated Disease, Surveillance and Response)	X	X	X	X	X	X	X	X	X	X	X	X	
		Estimates for number of hepatitis related cirrhosis, HCC, and deaths established	X	X	X	X	X	X	X	X	X	X	X	X	
		Sentinel surveillance on cases of cirrhosis or liver disease at UTH or other sentinel sites undertaken	X	X	X	X	X	X	X	X	X	X	X	X	
		Hepatitis surveillance tools (case investigating tools, reporting guides, outbreak response thresholds) developed and disseminated		X	X	X	X	X	X	X					

Strategic Objective	Targets	Outputs	Timeframe												MOH Stakeholders
			2019				2020				2021				
			Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	
		Hepatitis surveillance included in key public health documents (IDSR 3rd Edition)			X	X	X	X	X	X	X	X	X	X	
		National data repository for liver cancer (cancer registry) established & functional					X	X	X	X	X	X	X	X	
		Serosurveys in high-risk groups (correctional services, healthworkers, sex workers, etc) conducted			X	X	X	X	X	X	X	X	X	X	
		Analysis and annual reporting of national surveillance and research data on trends in chronic hepatitis conducted			X	X	X	X	X	X	X	X	X	X	

Interventions for Impact

Table 8: Interventions for Impact

Strategic Objective	Targets	Outputs	Timeframe												MOH Stakeholders
			2019				2020				2021				
			Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	
Reduce mother-to-child transmission of hepatitis B	<1% of under-5 prevalence of HBV infection	Antenatal care guidelines on hepatitis B testing of pregnant women developed				X	X	X	X	X					• Nurses' and midwives' associations, relevant • HPCZ • Medical Associations, • Civil society, Media
		Testing of pregnant women for hepatitis B and their partners					X	X	X	X	X	X	X	X	
		Screening of people who engage in high risk sexual practices for HBV					X	X	X	X	X	X	X	X	

Strategic Objective	Targets	Outputs	Timeframe												MOH Stakeholders
			2019				2020				2021				
			Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	
		Hepatitis B-positive pregnant women managed according to national guidelines					X	X	X	X	X	X	X	X	
		HBV and HCV testing of users of illicit substances					X	X	X	X	X	X	X	X	
		Infants born in health facilities vaccinated with hepatitis B birth dose in the first 24 hours of life	X	X	X	X	X	X	X	X	X	X	X	X	
Prevent health-care related transmission of hepatitis B and C	Zero healthcare related transmission of hepatitis B and C	Campaigns to reduce unnecessary injections conducted	X	X	X	X	X	X	X	X	X	X	X	X	• Professional associations, • Media • Professional associations

Strategic Objective	Targets	Outputs	Timeframe												MOH Stakeholders
			2019				2020				2021				
			Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	
		Campaigns to reduce transmission of hepatitis B in correctional settings conducted	X	X	X	X	X	X	X	X	X	X	X	X	• Professional associations • Media • Civil Society
		Health workers vaccinated against HBV	X	X	X	X	X	X	X	X	X	X	X	X	• Professional associations • HPCZ • GNC
		Staff working in Correctional Services, military personnel, commercial sex workers vaccinated against HBV	X	X	X	X	X	X	X	X	X	X	X	X	• Zambia Correctional Services • Ministry of Home Affairs

Strategic Objective	Targets	Outputs	Timeframe												MOH Stakeholders
			2019				2020				2021				
			Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	
		Students at nursing, laboratory, medical schools vaccinated against HBV	X	X	X	X	X	X	X	X	X	X	X	X	• Professional associations • HPCZ • GNC
		Key populations (such as HIV, cancer patients, prisoners) vaccinated against HBV					X	X	X	X	X	X	X	X	• HPCZ • GNC • Civil Society
		Partners and household mates of chronic HBV infected patients vaccinated against HBV					X	X	X	X	X	X	X	X	Civil Society
		Blood supply screened for HBV and HCV	X	X	X	X	X	X	X	X	X	X	X	X	ZNBTS

Strategic Objective	Targets	Outputs	Timeframe												MOH Stakeholders
			2019				2020				2021				
			Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	
		Infection prevention and control programmes in all public and private health-care facilities functional	X	X	X	X	X	X	X	X	X	X	X	X	
		Research on evaluation of effectiveness of infection prevention and control programmes undertaken	X	X	X	X	X	X	X	X	X	X	X	X	ZNPHI Research Institutes NGOs

Strategic Objective	Targets	Outputs	Timeframe												MOH Stakeholders
			2019				2020				2021				
			Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	
Reduce the number of susceptible people in the community	98% coverage among infants for 3rd dose of Pentavalent vaccine (which includes HBV)	Infants immunized with third (DPT-HepB-Hib) dose given as pentavalent vaccine	X	X	X	X	X	X	X	X	X	X	X	X	• National professional associations • Media, • Civil society
	Implement annual screening testing for food handlers	Food handlers periodically tested for HAV, HEV				X	X	X	X	X	X	X	X	X	Ministry of Local Government
Increase proportion of people who have chronic hepatitis who know their status	Increase number of patents with suspected liver disease who have diagnostic tests performed for hepatitis by 100%	Clinicians skilled up on management of acute and chronic hepatitis HBV infected individuals who qualify for antivirals initiated	X	X	X	X	X	X	X	X	X	X	X	X	• Professional societies, NGOs • HPCZ • GNC

Strategic Objective	Targets	Outputs	Timeframe												MOH Stakeholders
			2019				2020				2021				
			Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	
	Vaccinate >80% of non-immune health care workers for hepatitis B	Health care workers immunized against HBV				X	X	X	X	X	X	X	X	X	• Professional Bodies • NGOs • HPCZ • GNC
Ensure linkage to care and management of diagnosed people Eliminate hepatitis stigma	100% of people with chronic hepatitis are given appropriate counselling	People with chronic hepatitis provided with appropriate counselling messages	X	X	X	X	X	X	X	X	X	X	X	X	• Civil Society • Training Institutions • HPCZ • GNC • Civil Society
	90% of chronic hepatitis carriers linked to care	People diagnosed with chronic hepatitis linked to care and treatment	X	X	X	X	X	X	X	X	X	X	X	X	• Civil Society • Training Institutions • HPCZ • GNC • Civil Society

Strategic Objective	Targets	Outputs	Timeframe												MOH Stakeholders
			2019				2020				2021				
			Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	Q 1	Q 2	Q 3	Q4	
	50% of eligible people are started on treatment	People diagnosed with chronic hepatitis initiated on treatment	X	X	X	X	X	X	X	X	X	X	X	X	• HPCZ • GNC • Civil Society
		Antiviral drugs for treatment of viral hepatitis B & C included on the Essential Medicines List and available in the country	X	X	X	X	X	X	X	X	X	X	X	X	• HPCZ • GNC • Civil Society
Ensure mobilization of resources for care and management of viral hepatitis		Strategies and budget included in the national medium term expenditure framework	X	X	X	X	X	X	X	X	X	X	X	X	• MOH • ZNPHI • National immunization program • Blood transfusion safety • Antenatal, maternal and child health

Delivering for Equity

- Address critical underlying factors such as poor sanitation and poverty in order to make it safe for people to access hepatitis services.
- Involve communities in the planning and delivery of hepatitis services to improve their reach, quality and effectiveness.
- Train health care workers at all levels of care, in both public and private sectors about viral hepatitis risk and infection, and the package of essential hepatitis interventions.
- Core competencies related to viral hepatitis should be included in pre-service and in-service training for health workers.

Innovation for Acceleration

It is critical that local research is done to answer questions aimed at influencing national policy, and ultimately improve the well-being of those living with or at risk for viral hepatitis.

Table 9: Research Questions

Focus Area	Research Questions
Mother and Child Health	• What proportion of jaundice in pregnancy, maternal mortality, and neonatal deaths is attributed to hepatitis E virus? • What proportion of neonates are born from HbsAg positive mothers? • What proportion of under-five HBV cases are perinatal versus horizontally transmitted?
Clinical outcomes	• What are the viral and liver outcomes of HBV treatment, and the risk factors associated with poor outcomes? • What are the predictors of treatment outcome? • What are the causes of cirrhosis and liver-related mortality, particularly in young people? • How does HBV genotype and viral burden affect disease progression and treatment outcomes? • What are the causes of acute jaundice?

Focus Area	Research Questions
	• What proportion of chronic HBV carriers in the country meet criteria for antiviral therapy? • What are the characteristic causes of hepatocellular carcinoma, survival and outcomes?
Screening and diagnosis	• What is the 'real world' availability, affordability and performance (sensitivity, specificity, etc) of currently available rapid tests for hepatitis A, B, C, D and E? • What proportion of blood donors are HAV, HDV and HEV positive? • What is the probability of chronic HBV infection among partners and household contacts of chronic HBV carriers compared to the general population? • What are the barriers and facilitators to linking patients with HCV and HBV to care and treatment? • What percentage of patients with chronic HBV infection know their status and are appropriately managed? • What is the proportion of HCV Ab-positive blood donors have detectable HCV RNA? • What is the prevalence of HAV and HDV viruses in Zambia? • Evaluate point-of-care platforms for HBV DNA, ALT, AST, and platelets?
Prevention	• What are the HBV vaccine completion rates in groups targeted for prevention? • To determine the need for hepatitis A and E vaccination? • Characterize adult risk factors for acute HBV infection?
Key Populations	• What is the viral hepatitis epidemiology in correctional facilities and female sex workers? • What are the key populations for HCV in Zambia?
Other	• Explore stigma and disclosure issues among people with hepatitis in Zambia, including those taking ARVs for HBV. • What are the community beliefs and myths regarding hepatitis. • Perform situational analysis of hepatitis diagnosis, treatment, and prevention in the private sector in Zambia. • Develop and evaluate male-oriented approaches to HBV testing and linkage to care.

Governance and Leadership

The governance and leadership structure for service delivery for viral hepatitis prevention and treatment shall be in accordance with the existing Ministry of Health provisions.

The National Health Policy, anchored in the devolution of functions to the lower levels, sets out the guidelines for directing the implementation of national health strategies. The central level provides policy, strategic guidelines, overall coordination, and monitoring and evaluation (M&E). The provincial level is responsible for translating the policy and strategic guidelines to the district level for actual programme implementation. In addition, the Provincial Health Office (PHO) shall provide the necessary supervision as well. The lower level units are in turn expected to concentrate on programme implementation, supervised by the District Health Office (DHO).

In the same vein, the National Health Strategic Plan 2017 – 2021 focuses on attaining Universal Health Coverage using the primary health care (PHC) approach. Underpinning the approach is health system strengthening across the continuum of care and spanning promotive, preventive, curative, rehabilitative, and palliative health services. Through the PHC, the community is the platform for service delivery.

The health sector has diverse partners who provide financial, material, and technical support. The coordination challenges arising from such partnerships necessitate coordination mechanisms. Health systems leadership and governance deal with the interrelationships, roles, and activities of the various agencies in the production, distribution, and consumption of health services. The health services are delivered through Government institutions, NGOs, and the private sector. Services provided by the public sector are free or provided at a nominal charge in urban areas. Apart from provision of some drugs and other commodities free of charge, private health providers are not subsidised. The NGO health providers are dominated by churches, which are concentrated in rural areas, where access to services is difficult for the residents.

At the local level, village health and health facility committees provide an opportunity to capture views and sentiments from the community. However, any mechanisms to capture perceived or actual demand of services are not institutionalised. There are no effective tools for management to capture the views and experiences of communities. There is obvious need for improvement in this regard. A system for capturing this information and using it for management purposes is required.

Chapter 4: Clinical Guidance

Viral Hepatitis A

Transmission:

Hepatitis A (HAV) is a fecal-orally transmitted virus that causes acute hepatitis

Incubation Period:

- 15 to 45 days (average 4 weeks) between the time of exposure and onset of symptoms.
- The virus is excreted in stool during the first few weeks of infection, before the onset of symptoms.

Clinical Presentation:

- Outbreaks of HAV do occur.
- Patients may experience cholestatic hepatitis, marked by the development of an elevated alkaline phosphatase (ALP) level, in contrast to the classic picture of elevated aminotransferase levels.
- Others may experience several relapses during the course of a year.
- Less than 1% of cases result in fulminant hepatic failure (FHF).
- HAV infection does not persist and does not lead to chronic hepatitis.
- Acute Hepatitis A is more severe and has higher mortality in adults than in children with jaundice occurring in more than 70% of cases.
- Infected children under six years of age do not usually experience noticeable symptoms, and only 10% develop jaundice.
- Death is possible but rare and after infection, HAV antibodies develop.

Screening & Diagnosis:

Acute HAV infection is based on serologic testing for immunoglobulin M (IgM) antibody to HAV. Hepatitis A immunoglobulin G (IgG) cannot distinguish current from previous infection. Liver biopsy has a minimal role in the diagnosis of acute HAV infection.

Treatment:

Generally involves supportive care, avoidance of any hepatatoxic drugs, with specific complications treated as appropriate. Liver transplantation, in selected cases, is an option if the patient has fulminant hepatic failure.

Prevention:

Improved sanitation, food safety and immunization are the most effective ways to combat hepatitis A. The spread of hepatitis A can be reduced by:

- adequate supplies of safe drinking water;
- proper disposal of sewage within communities; and
- personal hygiene practices such as regular hand-washing with safe water.
- immunization when available. Nearly 100% of people develop protective levels of antibodies to the virus within one month after injection of a single dose of vaccine. Even after exposure to the virus, a single dose of the vaccine within two weeks of contact with the virus has protective effects. Still, manufacturers recommend two vaccine doses to ensure a longer-term protection of about five to eight years after vaccination.

Viral Hepatitis B

Hepatitis B infection is caused by the hepatitis B virus, an enveloped DNA virus that infects the liver, causing hepatocellular necrosis and inflammation.

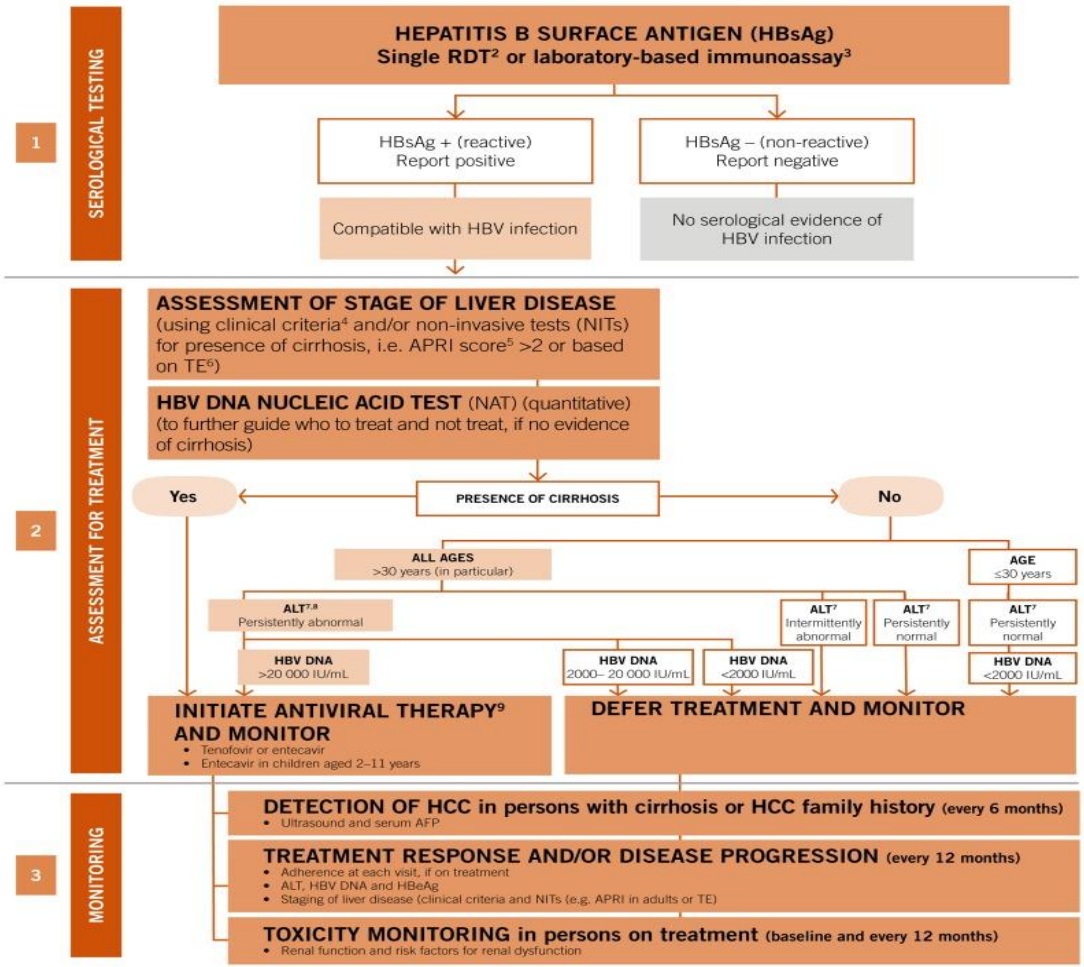
Transmission:

- Hepatitis B is a blood borne virus that can be transmitted sexually, as well as vertically from mother-to-child.
- The virus is highly contagious (100 times more than HIV) and is stable in the environment.

Incubation Period:

- The incubation period of Acute HBV is 40 to 150 days (average, approximately 12 weeks).

Figure 1: Summary algorithm for diagnosis, treatment and monitoring of chronic HBV infection



Clinical Presentation:

- HBV infection can be self-limited or chronic. It can cause acute hepatitis (like HAV) and chronic hepatitis B can quietly cause liver damage, liver failure, and hepatocellular carcinoma.
- Chronic HBV develops due to suboptimal host immune response and is common in infants (~90%) and HIV-infected individuals (~20 to 30%). But in adults with normal immune function only 5 to 10% will progress to the chronic form. The virus has a reservoir of infection in liver cells meaning that it cannot be completely eradicated from the body.
- The clinical illness associated with acute HBV infection may range from mild to severe disease (less than 1% of patients). After acute hepatitis resolves, 95% of adult patients and 5 to 10% of infected infants ultimately develop antibodies against hepatitis B surface antigen (HBsAg)—that is, anti-HBs to clear HBsAg (and HBV virions), an indication of full recovery.
- If the HBsAg persist for six months or more, then the infection becomes chronic. About 5% of adult patients and 90 to 95% of infected infants develop chronic infection.

Screening & Diagnosis:

- Laboratory diagnosis of hepatitis B infection focuses on the detection of the hepatitis B surface antigen.
- Acute HBV infection is characterized by the presence of HBsAg and immunoglobulin M antibody to the core antigen (Anti-HBc).
- Acute HBV is accompanied by acute onset of hepatitis symptoms. The window period for HBsAg is one month (meaning the test becomes positive by one month after infection).
- During the initial phase of infection, patients are also seropositive for hepatitis B envelope antigen (HBeAg). HBeAg is usually a marker of high levels of replication of the virus. The presence of HBeAg indicates that the blood and body fluids of the infected individual are highly infectious. Chronic infection is characterized by the persistence of HBsAg for at least 6 months (with or without concurrent HBeAg).
- Persistence of HBsAg is the principal marker of risk for developing chronic liver disease and hepatocellular carcinoma later in life. Although data from Africa are lacking, in Asia 25 to 40% of individuals with chronic HBV die prematurely as a result of cirrhosis or hepatocellular carcinoma.

Who to Test for Chronic HBV Infection

Table 10: Who to test for Chronic HBV Infection

Specific Populations	Who to Test	Routine Testing	Focused testing in most affected populations & Blood donors
Pregnant Women	Preferably at the start of prenatal care	✓	
Children	Neonates born to mothers infected with Hepatitis at 6 weeks		✓
	Clinical suspicion of chronic viral hepatitis		✓
Adolescents	Contacts of those with HBV infection: sexual partners, children, other family members, and close household members		✓
	Clinical suspicion of chronic viral hepatitis		✓
Adults	Healthcare workers: HBsAg serological testing should be offered and hepatitis B vaccination given to all healthcare workers who have not been vaccinated previously HIV-infected populations		✓
	Populations who are consider for PrEP (HIV pre-exposure prophylaxis)		✓
	Partners and close family members of a known HBsAg-positive person		✓
	Clinical suspicion of chronic viral hepatitis		✓

Monitoring Disease Progression and Treatment Response

Table 11: Monitoring Disease Progression and Treatment Response

Test Type	Recommendations	Baseline	Third Month	Sixth Month	Twelveth Month	Every Three Months	Every Six Months	Annually
HBsAg	Confirms HBV diagnosis and guides when to stop antiviral therapy	✓		✓[a]				✓
HBV DNA	More frequent monitoring in persons who do not yet meet the criteria for antiviral therapy; or persons on treatment or following treatment discontinuation	✓		✓	✓			✓
ALT	More frequent monitoring in persons who do not yet meet the criteria for antiviral therapy; or persons on treatment or following treatment discontinuation	✓	✓	✓	✓	✓[b]		✓
HBeAg	Provides information on disease stage	✓						✓
APRI Score (AST and platelets)	Non-invasive test for cirrhosis	✓						
FibroScan	Non-invasive test for cirrhosis	✓						
Renal Function Test	To ensure safety of tenofovir when initiating antiviral therapy	✓						
	Persons on long-term Tenofovir or Entecavir therapy	✓					✓	
Abdominal	• Persons with cirrhosis, regardless	✓		✓	✓		✓	

Ultrasound	of age or other risk factors							
Alpha-fetoprotein	• Persons with a family history of Hepatocellular Carcinoma • Persons aged >40 years, APRI score ≤2, HBV DNA level >2000 IU/mL	✓		✓	✓		✓	
HIV test	Annually and at the time of initiation of antiviral therapy	✓						✓
[a] If acute infection was clinically suspected, recheck HBsAg at 6 months. [b] More frequent monitoring in persons who do not yet meet the criteria for antiviral therapy; or persons on treatment or following treatment discontinuation								

Treatment:

- The primary treatment goals for patients with HBV infection are to prevent progression of the disease, particulary to cirrhosis, liver failure, and hepatocellular carcinoma.
- The risk factors for progression of chronic HBV include the following: Persistently elevated levels of HBV DNA and, in some patients, alanine aminotransferase (ALT), as well as the presence of core and precore mutations seen most commonly in HBV genotype C and D infections; male sex; older age; family history of HCC; alcohol use; elevated alpha-fetoprotein (AFP); and coinfection with HDV, HCV, or HIV. A synergistic approach of suppressing viral load and boosting the patient's immune response with immunotherapeutic interventions is needed for the best prognosis. Treatment is supportive as there is no specific therapy that is available for acute hepatitis B.

Recommendations for Initiating Treatment of Chronic Viral Hepatitis B Disease

Table 12: Recommendations for Initiating Treatment of Chronic HBV Disease

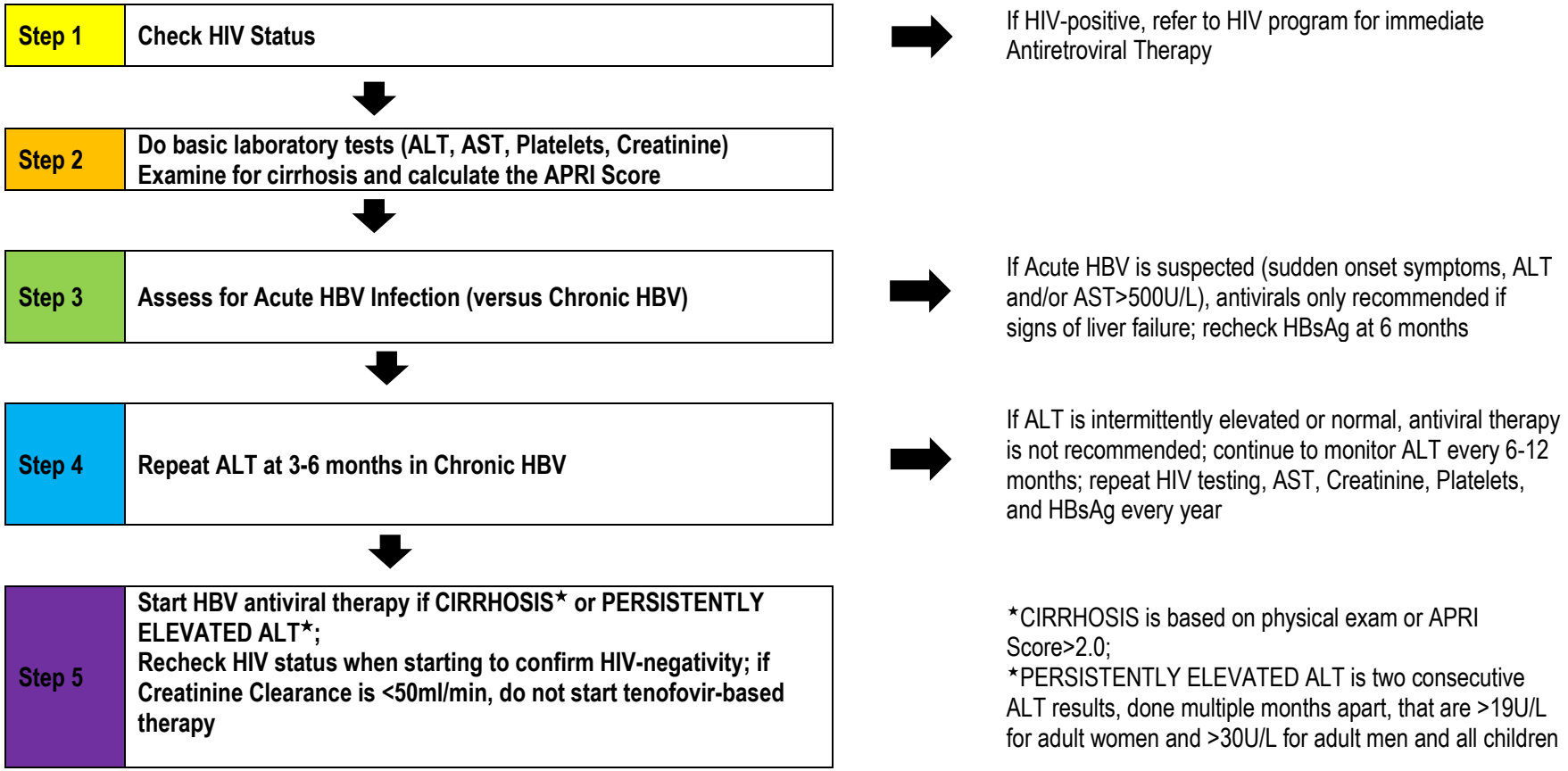
Specific Populations	HIV Status	Severity of Liver Disease & Level of Viral Replication						First-Line Antiviral Therapies	Second-Line Antiviral Therapies
		Clinical cirrhosis	APRI Score	ALT levels (U/L)	HBV DNA (IU/ml)	HBeAg	Age (years)		
Pregnant Women	**HBV/HIV-Coinfected**	N/A	N/A	N/A	N/A	N/A	N/A	TDF + 3TC containing cART	TDF + AZT + 3TC + LPV-r (or ATV-r)
	HBV Monoinfected	Yes	N/A	N/A	N/A	N/A	N/A	TDF + 3TC	Refer to Specialist
		No	>2.0	N/A	N/A	N/A	N/A		
		No	≤2.0	Elevated ALT level (>19)	>20,000	N/A	>30		
		No	≤2.0	Persistently abnormal ALT levels (>19)	HBV DNA testing not available	N/A	N/A		
		No	≤2.0	N/A	HBV DNA testing not available	HBeAg-positive	N/A		
		No	N/A	N/A	>200,000	N/A	N/A		
Children less than 2 years old	**HBV/HIV-Coinfected**	N/A	N/A	N/A	N/A	N/A	N/A	XTC containing cART	Refer to Specialist
	HBV Monoinfected	Yes	N/A	N/A	N/A	N/A	N/A	Lamivudine	Refer to Specialist
		No	N/A	Persistently abnormal ALT levels (greater than twice upper limit of normal)	>2,000	HBeAg-positive	N/A		
		No	N/A	Persistently abnormal ALT levels (greater	>20,000	HBeAg-negative	N/A	Lamivudine	Refer to Specialist

Specific Populations	HIV Status	Severity of Liver Disease & Level of Viral Replication						First-Line Antiviral Therapies	Second-Line Antiviral Therapies
		Clinical cirrhosis	APRI Score	ALT levels (U/L)	HBV DNA (IU/ml)	HBeAg	Age (years)		
				than twice upper limit of normal)					
Children aged 2 to 11 years old	**HBV/HIV-Coinfected**	N/A	N/A	N/A	N/A	N/A	N/A	Age 2-5 (<25kg): XTC containing cART + Entecavir Age 6-11 and (>25kg): TAF + FTC + DTG	Refer to Specialist; consider TAF + FTC + DTG + PI-r in children >6 years and >25 kgs
	HBV Monoinfected	Yes	N/A	N/A	N/A	N/A	N/A	Lamivudine or Entecavir	Refer to Specialist
		No	N/A	Persistently abnormal ALT levels (greater than twice the upper limit of normal)	>2,000	HBeAg-positive	N/A		
		No	N/A	Persistently abnormal ALT levels (greater than twice the upper limit of normal)	>20,000	HBeAg-negative	N/A	Lamivudine or Entecavir	Refer to Specialist
Adolescents (at least 12 years)	**HBV/HIV-Coinfected**	N/A	N/A	N/A	N/A	N/A	N/A	TDF + XTC containing cART or TAF + FTC + DTG	TDF + AZT + 3TC + LPV-r (or ATV-r)
	HBV Monoinfected	Yes	N/A	N/A	N/A	N/A	N/A	TDF + XTC	Refer to Specialist
		No	>2.0	N/A	N/A	N/A	N/A		
		No	≤2.0	Persistently abnormal ALT levels (greater than twice the upper limit of normal)	HBV DNA testing not available	N/A	N/A		
Adults	**HBV/HIV-**	N/A	N/A	N/A	N/A	N/A	N/A	TDF + XTC containing	TDF + AZT + 3TC +

Specific Populations	HIV Status	Severity of Liver Disease & Level of Viral Replication						First-Line Antiviral Therapies	Second-Line Antiviral Therapies
		Clinical cirrhosis	APRI Score	ALT levels (U/L)	HBV DNA (IU/ml)	HBeAg	Age (years)		
	Coinfected							cART or TAF + FTC + DTG	LPV-r (or ATV-r)
	HBV Monoinfected	Yes	N/A	N/A	N/A	N/A	N/A	TDF + XTC	Refer to specialist
		No	>2.0	N/A	N/A	N/A	N/A		
		No	≤2.0	Elevated ALT level (>19 women, >30 men)	>20,000	N/A	>30		
		No	≤2.0	Persistently abnormal ALT levels (>19 women, >30 men)	HBV DNA testing not available	N/A	N/A		
N/A = not applicable; APRI = AST-to-platelet ratio index; HBeAg, hepatitis B 'e' antigen; ALT elevation is >19 U/L in adult women, >30 U/L in adult men, and >30 U/L in children and adolescents									

- For HBsAg positive patients with renal insufficiency (CrCl <50mL/min), consult or refer to next level
- Persistent means at least two elevated ALT levels over 6-12 months and newer HBV guidelines now define 'ALT elevation' as ALT >19 U/L for women and ALT>30 U/L for men.
- Special attention must be given to patients on liver transplantation lists.
- For HBsAg positive patients with renal insufficiency (CrCl <50mL/min), consult or refer to next level
- Persistent means at least two elevated ALT levels over 6-12 months and newer HBV guidelines now define 'ALT elevation' as ALT >19 U/L for women and ALT>30 U/L for men.
- Special attention must be given to patients on liver transplantation lists.

Table 13: Locally-Adapted Approach to Assess Persons with Hepatitis B Infection for Antiviral Therapy in Zambia (When HBV DNA and HBeAg are not available)



Note on Persistent ALT elevation

It is important to note that in HBV management, more sensitive ALT thresholds are recommended by WHO (greater than 19 for adult women and greater than 30 for adult men and for children), because previous studies have indicated that even with slight elevation of ALT, cirrhosis and cancer can develop. Access to the full package of HBV diagnostic tools listed above may not be available at all centers, but using just a small core set of routine tests (HBsAg, ALT, AST, platelets, creatinine), virtually all health centers and hospitals in Zambia can manage and safely and effectively treat chronic HBV. As mentioned above, it is the chronic persistent damage to the liver from HBV infection that leads to cirrhosis and liver cancer. Thus, if an HBV-infected patient has chronic ALT elevation, this is evidence of risk to develop these complications. The suggested interval of at least two ALT tests 6 to12 months apart is arbitrary and based on expert opinion. In Zambia, repeating an ALT after 1 to 3 months may be more practical and may improve retention of patients. ALT is neither a highly specific nor highly sensitive test. Although sensitive, ALT greater than 19 (women) or greater than 30 (men and children) in an HBV-infected individual may be due to other causes such as heavy alcohol use, other medications (such as for TB), and fatty liver disease. It is important as part of the history to assess these.

Who Not to Treat but Continue to Monitor

As mentioned above, half or more of chronic HBV-infected patients may never develop an indication for antiviral therapy (meaning they remain at low risk of HBV complications). Regarless of whether a patient is on antiviral therapy, long-term monitoring is needed.

Table 14: Who Not to Treat but Continue to Monitor

	APRI score	ALT levels	HBV DNA Replication	HBeAg	Age
1.	≤2 in adults	Persistently normal ALT levels	<2000 IU/mL (low levels)	Not applicable	Not applicable
2.	≤2 in adults	Persistently normal ALT levels	HBV DNA testing not available	Positive	30 years or less
3.	≤2 in adults	Persistently normal ALT levels	>20 000 IU/mL	Not applicable	30 years or less
4.	≤2 in adults	Intermittently abnormal ALT levels	Fluctuate between 2000 and 20 000 IU/mL	Negative	30 years or less
5.	≤2 in adults	Persistently normal ALT levels	HBV DNA testing not available	Not applicable	30 years or less

When to Stop Treatment:

- If cirrhosis is present, based on physical exam, imaging, or APRI score greater than two, lifelong treatment is needed. In patients with cirrhosis, stopping antiviral therapy can trigger a lethal episode of hepatitis flare.
- In patients without cirrhosis, antiviral therapy can be stopped confidently when there is HBeAg seroconversion (from HBeAg positive to negative) or when there is HBsAg clearance (developing a negative test).
- Also, in pregnant women who are started on antivirals solely to prevent transmission to baby, if there is no indication (cirrhosis, persistently high ALT) to continue long-term, therapy can be stopped at six weeks post-partum.
- If therapy is stopped in other scenarios, most patients, over a period of months or possibly years, will develop an indication to re-start therapy. Thus, it is not currently advised to stop if the above criteria are not met.

After stopping period monitoring of the ALT (every 1-3 months) is recommended to see if there is a flare.

Table 15: When to Stop Treatment

	APRI score	HBsAg	Anti-HBe	ALT	HBV DNA Replication	HBeAg	Treatment Duration
Discontinuation	≤2 in adults (Can be followed carefully long term for reactivation)	-	Seroconversion to anti-HBe (in persons who were HBeAg positive when they started)	Persistently normal ALT levels	Persistently undetectable HBV DNA levels	Evidence of loss	Completion of at least one additional year of treatment
	-	Evidence of persistent HBsAg loss	-	Persistently normal ALT levels	HBV DNA testing not available	Not applicable	Completion of at least one additional

	APRI score	HBsAg	Anti-HBe	ALT	HBV DNA Replication	HBeAg	Treatment Duration
							year of treatment
Retreatment	-	Positive	-	ALT levels increase	HBV DNA becomes detectable again	Positive	-

HIV Pre-exposure Prophylaxis

TDF+XTC recommended for HIV pre-exposure prophylaxis (PrEP) is also recommended for HBV treatment. In HBsAg positive patients referred for PrEP, baseline assessment of ALT and for cirrhosis (with APRI, physical exam, etc,) are recommended. If there is an indication for treatment of chronic HBV, the person should receive long-term antiviral therapy. If not, the drugs can be taken short-term for PrEP until the period of high HIV risk is over. The combination of TDF+XTC requires close monitoring in those infected with Hepatitis B due to the concern for rebound viraemia. If PrEP is stopped, consideration should be given to continuing another active HBV treatment (if indicated) to avoid the risk of virological and clinical hepatitis flares.

Primary Prevention of Viral Hepatitis B Infection

Table 16: Primary Prevention of Viral Hepatitis B Infection

Specific Populations	Recommendation
Pregnant Women	Prevention of mother-to-child HBV transmission using antiviral therapy in HBV-monoinfected pregnant women
	Prevention of mother-to-child HBV transmission using HBV-active antiretroviral therapy in HIV-infected pregnant and breastfeeding women (including pregnant women in the first trimester of pregnancy and women of childbearing age)
Children	First dose of hepatitis B vaccine as soon as possible after birth, preferably within 24 hours, followed by followed by three additional (DPT-HepB-Hib) doses given during routine infant immunisation. The complete vaccine series induces protective antibody levels in more than 95% of infants, children and young adults. Protection lasts at least 20 years and is probably lifelong. Thus, WHO does not recommend booster vaccination for persons who have completed the 3 dose vaccination schedule.
Adolescents **Adults**	High-risk groups who may need to be vaccinated include: • people who frequently require blood or blood products, dialysis patients, recipients of solid organ transplantations; • sexual partners of HBsAg-positive individuals • persons who inject drugs; • persons who engage in high risk sexual activity • healthcare workers and others who may be exposed to blood and blood products through their work.

Viral Hepatitis C

Transmission:

Through blood, exposure to needles, and rarely can be sexually transmitted (particularly if the immune system is compromised).

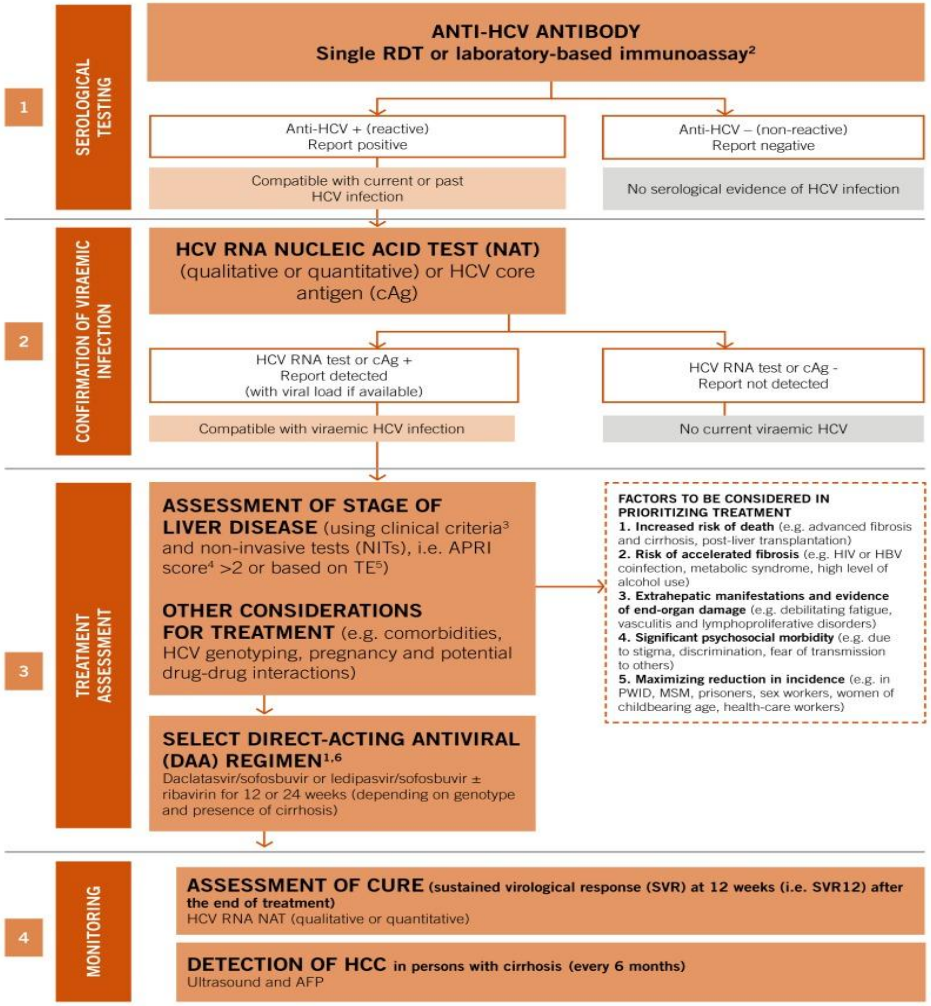
Incubation:

Hepatitis C virus (HCV) has a viral incubation period of approximately eight weeks.

Clinical Presentation:

- Most cases of acute HCV infection are asymptomatic. Even when it is symptomatic, acute HCV infection tends to follow a mild course.
- It does not have a reservoir so once treated it gets cured.
- HCV infection causes both acute and chronic hepatitis. It can rarely cause acute hepatitis and is usually a chronic form that ends in liver damage, liver failure, and liver cancer.
- Spontaneous clearance occurs within six months of infection in 15 to 45% of infected individuals in the

Table 16: Algorithm for diagnosis, treatment & monitoring of chronic HCV infection



absence of treatment. The remaining 55 to 85% develop chronic infection, which can lead to progressive fibrosis and cirrhosis.

- The risk of cirrhosis ranges from 15% to 30% after 20 years of infection with HCV. Initially, cirrhosis may be compensated. Decompensation may occur later, leading to variceal haemorrhages, ascites or encephalopathy. The risk of progression to cirrhosis and HCC varies according to the person's characteristics and behaviours. Alcohol use, HBV or HIV coinfection and immunosuppression due to any cause increases the risk of developing cirrhosis or HCC.
- Among HCV-infected persons, the three most common comorbidities are depression (24%), diabetes mellitus (15%) and chronic renal disease (10%). A proportion of these morbidities is directly attributable to HCV and is therefore referred to as extrahepatic manifestations. Coinfected persons, particularly those with advanced immunodeficiency (CD4 count less than 200 cells/mm3), have significantly accelerated progression to cirrhosis, decompensated cirrhosis and HCC compared to HCV-monoinfected persons. It is unclear whether HCV infection accelerates HIV disease progression, but after initiation of antiretroviral therapy, CD4 recovery is impaired in HIV/HCV-coinfected persons when compared to those with HIV mono-infection.

Screening & Diagnosis

Diagnosis of hepatitis C requires two steps: HCV Antibody-positive and confirmation with a HCV RNA (viral load) test; in settings with low HCV prevalence, HCV Antibody-positives are likely to be false positives. Only patients with HCV RNA-confirmed infection should be treated.

Who to Test for Chronic HCV Infection

Table 17: Who to Test for Chronic HCV Infection

Specific Populations	Focused testing in most-affected populations
Pregnant Women	Routine testing of pregnant women for HCV infection is currently not recommended
Children	Presence of clinical suspicion of chronic viral hepatitis
Adolescents	Presence of clinical suspicion of chronic viral hepatitis
	History of exposure and/or high-risk behaviours for HCV infection
Adults	Presence of clinical suspicion of chronic viral hepatitis
	History of exposure and/or high-risk behaviours for HCV infection

Testing for Chronic HCV Infection and Monitoring Treatment Response

Table 18: Testing for Chronic HCV Infection and Monitoring Treatment Response

Test Type	Recommendations	Baseline	Three Months	Six Months	Twelve Months	Every Six Months	Annually
Anti-HCV Antibodies	Serological evidence of past or present infection in adults, adolescents and children (>18 months of age)	✓					✓
HCV RNA	To diagnose viraemic infection	✓					✓
	Test of cure at 12 or 24 weeks (i.e. sustained virological response (SVR12 or SVR24)) after completion of antiviral treatment.						
HCV core (p22) antigen	Alternative to NAT to diagnose viraemic infection	✓					✓
Liver biopsy		✓					

Test Type	Recommendations	Baseline	Three Months	Six Months	Twelve Months	Every Six Months	Annually
APRI Score		✓					
Genotype of the hepatitis C strain	To assess the genotype of the hepatitis C strain. There are 6 genotypes of the HCV and they respond differently to treatment. Furthermore, it is possible for a person to be infected with more than 1 genotype.	✓					
HIV	HIV -1/2 antibody test	✓					
HBV	Hepatitis B surface antigen test	✓					

Recommendations for Initiating Treatment of Chronic Viral Hepatitis C Disease

Because HCV is uncommon in Zambia and some of the assays have suboptimal accuracy, many positive HCV antibody tests in Zambia are false positives. Positive HCV antibody tests must be confirmed with HCV RNA (viral load) or core antigen or there must be strong clinical suspicion of HCV-induced liver disease before treatment can be initiated. Treatment of chronic HCV infection has two goals. The first is to achieve sustained eradication of HCV (sustained virological response), which is defined as the persistent absence of HCV RNA in serum 12 weeks after completing antiviral treatment. The second goal is to prevent progression to cirrhosis, hepatocellular carcinoma (HCC), and decompensated liver disease requiring liver transplantation.

Table 19: Recommendations for Initiating Treatment of Chronic HCV Disease

Specific Populations	HCV RNA Detection	Cirrhosis	HCV Genotype						DAA Regimens	Duration of DAA
			1	2	3	4	5	6		
Pregnant Women									Not Recommended	
Children less than 12 years old									Defer treatment until 12 years of age	
Adolescents (12–17 years old or Weighing ≥ 35 kg)	✓	Without Cirrhosis or with only Compensated Cirrhosis	✓			✓	✓	✓	Sofosbuvir/ Ledipasvir	12 weeks
				✓					Sofosbuvir/ Ribavirin	12 weeks
					✓				Sofosbuvir/ Ribavirin	24 weeks
	✓	Treatment experienced and with Compensated cirrhosis	✓			✓	✓	✓	Sofosbuvir/ Ledipasvir	24 weeks
Adults & Adolescents ≥18 years of age	✓	Without Cirrhosis	N/A	N/A	N/A	N/A	N/A	N/A	Glecaprevir/ Pibrentasvir	8 weeks[1]
			N/A	N/A	N/A	N/A	N/A	N/A	Sofosbuvir/ Daclatasvir	12 weeks
			N/A	N/A	N/A	N/A	N/A	N/A	Sofosbuvir/ Velpatasvir	12 weeks
	✓	With Compensated Cirrhosis	N/A	N/A	N/A	N/A	N/A	N/A	Glecaprevir/ Pibrentasvir	12 weeks[1]
			N/A	N/A	N/A	N/A	N/A	N/A	Sofosbuvir/ Daclatasvir	24 weeks
			N/A	N/A	N/A	N/A	N/A	N/A	Sofosbuvir/ Velpatasvir	12 weeks

N/A = not applicable; DAA = Direct-Acting Antiviral Agents Regimens

[1] Persons with HCV genotype 3 infection who have received interferon and/or ribavirin in the past should be treated for 16 weeks.

- The use of pangenotypic regimens obviates the need for genotyping before treatment initiation
- Treatment for HCV infection needs to consider drug–drug interactions with antiretroviral medications.
- Persons with HIV/HCV coinfection are at a higher risk for progression of fibrosis and are included in the list of persons prioritized for treatment
- Persons with HBV/HCV coinfection are at risk for HBV reactivation during and following HCV treatment.
- Persons with cirrhosis, including those who have achieved SVR, may be regularly screened for hepatocellular carcinoma (HCC).

General Clinical Considerations

Table 20: General Clinical Considerations

Condition	
HIV/HCV Co-infection	Persons with HIV/HCV coinfection are at a higher risk for progression of fibrosis and were included in the list of persons prioritized for treatment since the 2014 WHO treatment guidelines. Treatment for HCV infection needs to consider drug–drug interactions with antiretroviral medications.
HBV/HCV Co-infection	Persons with HBV/HCV coinfection are at risk for HBV reactivation during and following HCV treatment. An assessment for HBV treatment eligibility with initiation of HBV treatment for those eligible may prevent HBV reactivation during HCV treatment.
Cirrhosis	Persons with cirrhosis, including those who have achieved SVR, may be regularly screened for hepatocellular carcinoma (HCC).
Chronic Kidney Disease	Data are insufficient on the safety and efficacy of sofosbuvir-based regimens in persons with severe renal impairment. Glecaprevir/pibrentasvir is effective against infection with all six major genotypes in persons with chronic kidney disease.
TB/HCV Co-infection	In persons with TB/HCV coinfection, treatment for active TB is considered before treatment of HCV infection. TB/HCV-coinfected persons treated for TB are at an increased risk of hepatotoxicity
Retreatment after DAA Treatment Failure	• Currently, only one pangenotypic DAA regimen, sofosbuvir/velpatasvir/ voxilaprevir, is approved by a stringent regulatory authority for the retreatment of persons who have previously failed DAA treatment. • Investigations of a failure to achieve SVR with DAA therapy includes re-examination of adherence and of potential drug–drug interactions.

Prevention

There is no vaccine for hepatitis C, therefore prevention of HCV infection depends upon reducing the risk of exposure:

- hand hygiene: including surgical hand preparation, hand washing and use of gloves;
- safe and appropriate use of health care injections;
- safe handling and disposal of sharps and waste;
- provision of comprehensive harm-reduction services to people who inject drugs including sterile injecting equipment;
- testing of donated blood for hepatitis B and C (as well as HIV and syphilis);
- training of health personnel; and promotion of correct and consistent use of condoms.

Viral Hepatitis D

Hepatitis D is a rare virus that only HBV carriers can acquire. It requires coexisting HBV infection and uses the viral machinery of HBV to replicate itself. Therefore, only patients with chronic HBV infection would have this. Prevention of HBV would result in prevention of HDV.

Clinical Presentation:

- When HBV and HDV are co-infecting, there is very rapid liver disease progression. Acute hepatitis: simultaneous infection with HBV and HDV can lead to a mild-to-severe or even fulminant hepatitis, but recovery is usually complete and development of chronic hepatitis D is rare (less than 5% of acute hepatitis).
- Superinfection: HDV can infect a person already chronically infected with HBV. The superinfection of HDV on chronic hepatitis B accelerates progression to a more severe disease in all ages and in 70–90% of persons. HDV superinfection accelerates progression to cirrhosis almost a decade earlier than HBV monoinfected persons, although HDV suppresses HBV replication. The mechanism in which HDV causes more severe hepatitis and a faster progression of fibrosis than HBV alone remains unclear.

Screening & Diagnosis

HDV infection is diagnosed by high titres of Immunoglobulin G and Immunoglobulin M anti-HDV, and confirmed by detection of HDV RNA in serum. However, HDV diagnostics are not widely available and there is no standardization for HDV RNA assays, which are used for monitoring response to antiviral therapy.

Treatment

- There is no specific treatment for acute or chronic HDV infection. Persistent HDV replication is the most important predictor of mortality and the need for antiviral therapy.
- Pegylated interferon alpha is the only drug effective against HDV; antiviral nucleotide analogues for HBV have no or limited effect on HDV replication. The optimal duration of therapy is not well defined, nor how long patients need to be HDV RNA negative after the end of therapy

to achieve a sustained virological response. More than 1 year of therapy may be necessary. The overall rate of sustained virological response remains low, including in children, and most patients relapse after discontinuation of therapy. Liver transplantation may be considered for cases of fulminant hepatitis and end-stage liver disease.

Prevention:

Prevention and control of HDV infection requires prevention of HBV transmission through hepatitis B immunization, blood safety, injection safety, and harm reduction services.

Viral Hepatitis E

Transmission:

Hepatitis E is another fecal-orally transmitted virus that causes acute hepatitis.

Incubation Period:

- Ranges from 2 to 10 weeks, with an average of 5 to 6 weeks.
- The infected persons are believed to excrete the virus beginning a few days before to around 3-4 weeks after the onset of disease

Clinical Presentation:

- Outbreaks of HEV do occur.
- One notable detail is that the infection disproportionately affects pregnant women and neonates.
- In areas with high disease endemicity, symptomatic infection is most common in young adults aged 15–40 years. In these areas, although infection does occur in children, they often have either no symptoms or only a mild illness without jaundice that goes undiagnosed.
- In rare cases, acute hepatitis E can be severe, and results in fulminant hepatitis; these patients are at risk of death.
- Fulminant hepatitis occurs more frequently when hepatitis E occurs during pregnancy.
- Pregnant women with hepatitis E, particularly those in the second or third trimester, are at an increased risk of acute liver failure, fetal loss and mortality.
- Case fatality rates as high as 20–25% have been reported among pregnant women in their third trimester.
- Cases of chronic hepatitis E infection have been reported in immunosuppressed people, particularly organ transplant recipients on immunosuppressive drugs, with genotype 3 or 4 HEV infection.

Screening & Diagnosis

Definitive diagnosis of hepatitis E infection is usually based on the detection of specific IgM antibodies to the virus in a person's blood; this is usually adequate in areas where disease is common. Additional tests include reverse transcriptase polymerase chain reaction (RT-PCR) to detect the hepatitis E virus RNA in blood and/or stool; this assay requires specialised laboratory facilities.

Treatment

There is no specific treatment capable of altering the course of acute hepatitis E. Hospitalization is required for people with fulminant hepatitis, however, and should also be considered for symptomatic pregnant women. Immunosuppressed people with chronic hepatitis E benefit from specific treatment using ribavirin, an antiviral drug. In some specific situations, interferon has also been used successfully.

Prevention

Prevention is the most effective approach against the disease and can be reduced by:

- maintaining quality standards for public water supplies;
- establishing proper disposal systems for human feces.
- maintaining hygienic practices such as hand-washing with safe water, particularly before handling food;
- avoiding consumption of water and/or ice of unknown purity

Chapter 5: Surveillance

The full epidmeiological information on burdern of hepatits in the Zambian population is unkown. To date the blood transfusion services have provided the most consistent information on the hepattis burden amoung donors and more recently the ZAMPHIA study. Blood donor data are not likely to be representative of the general population. The high prevalence assocsited with HIV, a high burden priority disese in Zambia warrants a better understanding of the true burden of hepatitis countrywide. Like other priority disese trends in estimates from weekly facility case based reporting or senntinal surveillnce , hepatitis surveillnce shall be conducted through the existing Inegrated Disease Surveillnce & Response System (IDSR).

Successful introduction of hepatitis surveillnce will be determined by a number of factors. Hepatitis often has multiple outcomes from the acute and asymptomtic forms to secondry manfestions that can all be indictors for monitoring the disease indidence. In both the acute and chronic forms symptom presentation of the 5 serotypes are similar making them cinicIly indeistriguishble form one another. The asyptomatic nature of both new and chronic infection often result in poor health seeking behavior and modes of transmsssion vary. Due to the combination of these mutifcitded presentions ,no single surveillnce method will provide a complete description of the country's epidemiological profile.

Varitions between between population groups and geographical areas means the three tired surveillnce system should be developed that to estimate the burden of hepatitis in the general population. The order of implemention will be determined by the TWG in accordnce with the buren, need, availibity of resources and laboratory / case msnagement capacity.

The strategic objectives for viral hepatitis surveillance are:

- To detect outbeaks, monitor trends in incidence and identify risk fctors for new incident infections (acute hepatitis)
- Estimate the prevalence of chronic hepatitis B virus and hepatitis C virus infections, and monitor trends in sentinel groups(Chronic Infections)
- Estimate the burden of sequel and mortality from the sequelae, including cirrhosis and hepatocellular carcinoma (Cirrhosis & HCC)
- To measure indicators that track progress towards hepatitis elimination

Surveillance of Hepatitis Viruses

Table 21: Surveillance of Hepatitis Viruses

	Acute Hepatitis	Chronic Infections	Cirrhosis & HCC
Surveillance approach	Detect outbreaks, monitor trends in incidence and identify risk factors for new, incident infections hepatitis and identify risk factors	Estimate the prevalence of chronic infections and monitor trends in sentinel groups	Estimate the incidence of HCC and cirrhosis
Intervention outcome	Prevention of new infections	Management of chronic hepatitis	Mortality reduction
Population under Surveillance	• Syndromic surveillance in the general population using indictor based surveillance • Enhanced case reporting (with in vitro diagnosis and collection of information on risk factors), countrywide or in sentinel sites	• Case reporting from laboratories or health-care facilities • Regular surveys	Combination of data from: • Cancer registries • Death certificates • Testing of cirrhosis and HCC patients for HBV and HCV infection
Population under surveillance	Persons presenting with acute hepatitis in health-care facilities (discrete onset of symptoms)	• Persons without acute symptoms tested in health-care facilities/ laboratories • Persons without acute symptoms tested during population surveys	Persons diagnosed with cirrhosis and HCC
Condition to look for	Unspecified acute hepatitis Type-specific acute hepatitis	Biomarker evidence of past or present infection Chronic infection, irrespective of symptoms	Cases of HCC or cirrhosis with chronic HBV or HCV infection
Analysis and reporting	Weekly notifications of acute hepatitis new infections	Burden of chronic, prevalent infections	Burden of sequelae

Chapter 6: Programme Monitoring

Monitoring and evaluation of services pertaining to the implementation of the Framework & Clinical Guidance for Viral Hepatitis Prevention & Treatment will be done through mechanisms that are already in place in the Ministry of Health, as well as through mechanisms that might be agreed upon with partners from time to time.

Monitoring

The Ministry of Health will be responsible for monitoring of the implementation of this Framework, using mechanisms that are already in place within MOH. Periodically, surveys and other processes will be embarked on whenever need arises. The M&E systems that will be applied will include the HMIS, established routine management reporting, routine Performance Assessments, and Joint Annual Reviews (JARs). JARs will be planned and conducted jointly with the sector partners, including relevant line ministries and government departments, private sector, civil society, and CPs. The information obtained, through the various monitoring instruments, will be used for policy and management decision making, particularly in the programming and management of viral hepatitis services.

Evaluation

Implementation of this Framework will be evaluated routinely, as well as as part of the NHSP 2017 – 2021, as stated in the NHSP. This is considered necessary for purposes of harmonisation of M&E activities, and reduction of evaluation costs. From time to time, need might arise in which evaluation of the Framework might be necessary whereby it would be done through approval by MOH.

The following indicators are a set of mechanisms to generate information for provision of evidence for programme decisions.

Table 22: Programme Indicators

Indicator	Numerator	Denominator
Prevalence of chronic HBV infection	Number of persons with chronic HBV infection defined by HBsAg-positive serological status for over 6 months	Number of persons (total population)
Prevalence of chronic HCV infection	Number of persons with chronic HCV infection defined as positive for HCV RNA or positive for HCV Ag	Number of persons (total population)
Infrastructure for HBV and HCV testing	Number of facilities with capacity to test for chronic hepatitis	Number of facilities (Total Number)
Coverage of timely hepatitis B vaccine birth dose (within 24 hours)	Number of newborns receiving timely birth dose of hepatitis vaccine within 24 hours (HepB_BD)	Number of live births
Coverage of third dose of DPT-HepB-Hib vaccination	Number of infants (<12 months of age) who received third dose of DPT-HepB-Hib vaccination	Number of infants (<12 months of age in a year) surviving to age 1 year
People living with HBV diagnosed	Number of persons with chronic HBV infection who have been diagnosed	Estimated number of persons with chronic HBV infection
People living with HCV diagnosed	Number of persons with chronic HCV infection who have been diagnosed	Estimated number of persons with chronic HCV infection
Treatment coverage for hepatitis B patients	Number of persons with chronic HBV infection (defined by HBsAg-positive serological status for over 6 months) who are currently receiving treatment	Number of persons with chronic HBV infection
Treatment initiation for hepatitis C	Number of persons already diagnosed with chronic HCV infection (defined as positive	Number of persons already diagnosed with chronic HCV infection (defined as positive for

Indicator	Numerator	Denominator
	for HCV RNA or positive for HCV Ag) who initiated treatment during a specified time frame (e.g. 12 months)	HCV RNA or positive for HCV Ag) for the specified time period (12 months)
Viral suppression for chronic hepatitis B patients treated	Number of patients with chronic HBV infection on treatment who have a suppressed VL (HBV DNA not detectable), based on VL measurement in the past 12 months	Number of patients with chronic HBV infection on treatment and assessed for VL in the past 12 months
Cure for chronic hepatitis C patients treated	Number of patients who completed hepatitis C treatment and had a sustained virological response (SVR) based on VL measurement 12–24 weeks after the end of treatment (in the past 12 months)	Number of patients who completed hepatitis C treatment and were assessed for SVR 12–24 weeks after the end of treatment (in the past 12 months)
Cumulated incidence of HBV infection in children 5 years of age	Number of survey children 5 years of age living with biomarkers of past or present infection and/or chronic infection	Number of children aged 5 years of age in surveys
Incidence of HCV infection	Total number of new infections with HCV defined as anti-HCV positive per year	Total population minus people living with hepatitis C
Proportion of cirrhosis deaths attributable to HCV and HBV	Number of cirrhosis deaths multiplied by the proportion of cirrhosis with chronic HVB and HCV infections	n/a
Proportion of hepatocellular carcinoma deaths attributable to HCV and HBV	Number of hepatocellular carcinoma deaths multiplied by the proportion of HCC with chronic HBV and HCV infections	n/a
HBV coinfections among persons with HIV infection	Number of people living with hepatitis B (HBsAg positive) coinfected with HIV	Number of people living with hepatitis B (HBsAg positive)

Indicator	Numerator	Denominator
Hepatitis B testing	Number of persons who were tested for hepatitis B during the reporting period using HBsAg testing	Population size
Hepatitis C testing	Number of persons who were tested for hepatitis C during the reporting period using HCV RNA testing/ using anti-HCV testing	Population size
Blood Transfusion HBV screening	Number of persons who were tested for hepatitis B during Blood screening	
Blood Transfusion HCV screening	Number of persons who were tested for hepatitis C during Blood screening	

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