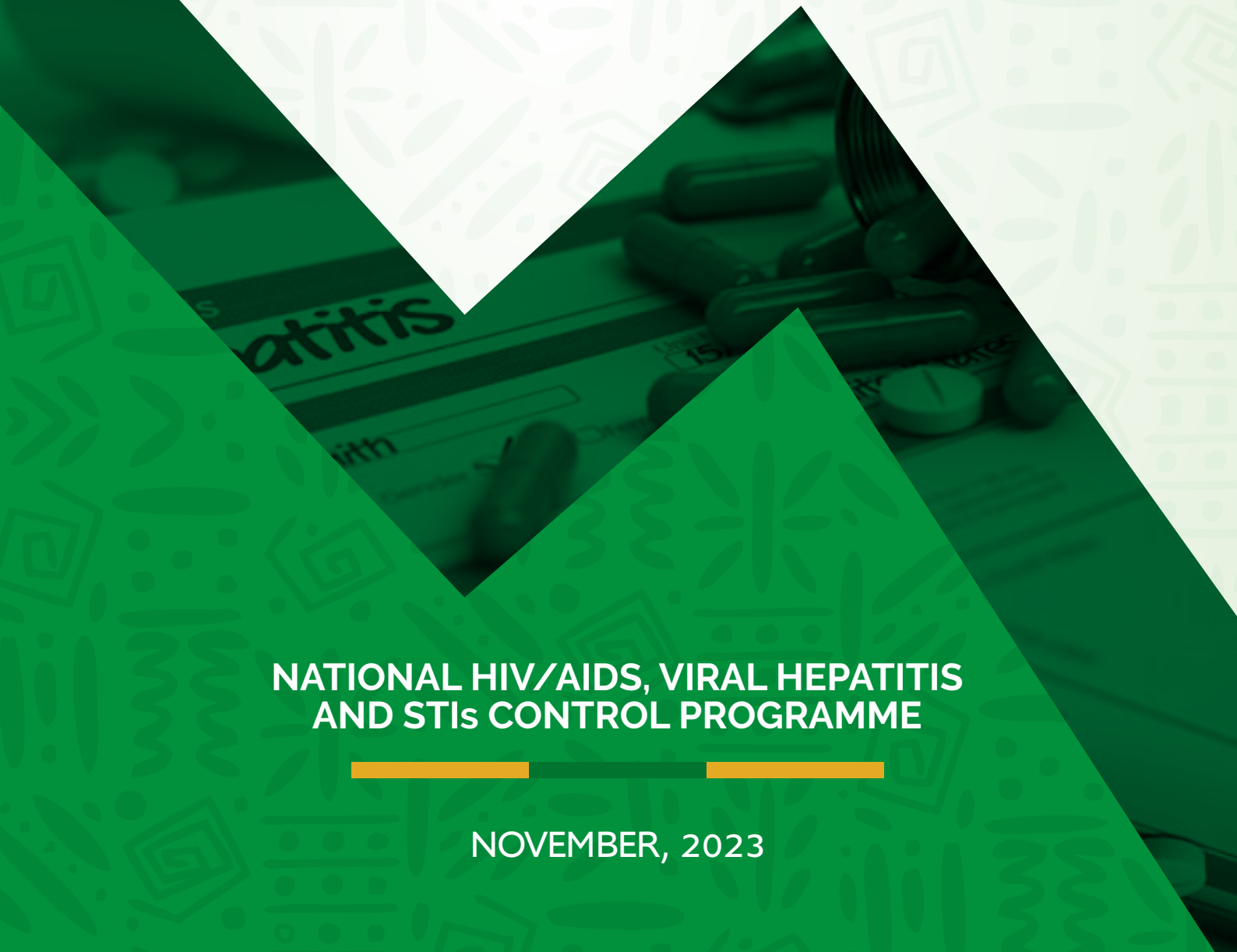
NATIONAL GUIDELINES FOR THE PREVENTION, TREATMENT, AND CARE OF VIRAL HEPATITIS



NATIONAL HIV/AIDS, VIRAL HEPATITIS AND STIs CONTROL PROGRAMME

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NATIONAL GUIDELINES FOR THE PREVENTION, TREATMENT AND CARE OF VIRAL HEPATITIS IN NIGERIA

National AIDS and STIs Control Programme

Federal Ministry of Health

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FEDERAL MINISTRY OF HEALTH, ABUJA

FOREWORD

Nigeria contributes significantly to the burden of chronic viral hepatitis infection globally with a prevalence of 8.1% and 1.1% for viral hepatitis B and C respectively according to the 2018 National HIV/AIDS Indicator and Impact Survey. This corresponds to above 20 million people living with viral hepatitis B and/or C in a population of over 177 million individuals, who are not aware and are at the risk of developing chronic complications of liver cirrhosis and primary liver cell cancers. The most worrisome is the continuous spread of the infections due to high-risk sexual and injection practices in the communities.

Following the expiration of the first edition of the National Guidelines for the Prevention, Treatment and Care of Viral Hepatitis in Nigeria in 2020, and in response to the World Health Assembly resolution for member nations to take action in the prevention, diagnosis, and treatment of viral hepatitis, the Federal Government of Nigeria embarked on this noble effort of revising the guidelines.

The revised National Guidelines for the Prevention, Treatment and Care of Viral Hepatitis was developed with the guiding principle of putting people at the centre of the response; addressing unique priorities for each population group and geographical area; taking a shared approach towards strengthening health and community systems and responding to a swiftly changing health and development context. The review also considered changes in health systems in the era of the COVID-19 pandemic.

This protocol provides guidance on treatment approaches and interventions on mother to child transmission of viral hepatitis; reaching children, adolescents, adults, and high-risk populations with viral hepatitis B vaccination; ensuring safety of blood transfusion services, organ donation and injection practices as well as use of new antiviral drugs for the treatment and cure of viral hepatitis B and C respectively. A simplified approach to providing diagnosis and treatment for persons infected with viral hepatitis B and C was also captured in this guideline as well as a minimum package for different levels of health care delivery in Nigeria.

It is expected that strict adherence to this guideline will assist with providing quality and efficient management of hepatitis B and C among infected children, adolescents and adults, as well as contribute significantly to achieving a reduction in the burden and impact of the disease in Nigeria, which are major ingredients toward reaching global elimination by 2030. I, therefore encourage all healthcare providers to avail themselves with a copy of this guideline in order to update their knowledge and skills for the purpose of providing appropriate care at service delivery points.

Prof. Muhammad Ali Pate.
Coordinating Minister of Health and Social Welfare

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On behalf of the Federal Ministry of Health, I wish to commend and appreciate the stakeholders and donor agencies who immensely contributed to the development of this document. This process would not have been successful without your technical guidance and financial support which have made the production of this document possible.

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Finally, we thank the staff of the National AIDS and STIs Control Programme (NASCP) for their perseverance and team spirit in coordinating the development of these guidelines and ensuring that the Federal Ministry of Health through NASCP delivers on its mandate in formulating policies and guidelines on the Viral Hepatitis Control Programme.

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ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Events
AEFI	Adverse Events Following Immunization
AIDS	Acquired Immunodeficiency Syndrome
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
ANC	Antenatal Care
APRI	Aspartate aminotransferase-to-Platelet Ratio Index
ART	Antiretroviral therapy
AST	Aspartate aminotransferase
BE	Blood Establishment
BMI	Body Mass Index
CBOs	Community Based Organizations
CHAI	Clinton Health Access Initiative
CHB	Chronic Hepatitis B
CHC	Chronic Hepatitis C
CHEW	Community Health Extension Workers
CHIPS	Community Health Influencers Promoters and Services
CHO	Community Health Officer
CLD	Chronic Liver Disease
CMS	Central Medical Store
CRRF	Combined Report Requisition Form
CSO	Civil Society Organizations
DAAs	Direct Acting Antivirals
DHIS	District Health Information System
EIA	Enzyme Immunoassay
EMR	Electronic Medical Record
EMTCT	Elimination of Mother to Child Transmission
ESLD	End-Stage Liver Disease
FIB-4	Fibrosis Index Based on 4 factors
FMOH	Federal Ministry of Health
GI	Gastrointestinal
HAV	Hepatitis A Virus
HBeAg	Hepatitis B e-antigen
HBIG	Hepatitis B Immunoglobulin
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma
HCVST	Hepatitis C Virus Self Testing
HCV	Hepatitis C Virus
HCWs	Health Care Workers
HDV	Hepatitis D Virus
HEV	Hepatitis E Virus
HIV	Human Immunodeficiency Virus

HTS	HIV Testing Services
ICSRs	Individual Case Safety Reports
IDP	Internally Displaced Persons
IEC	Information, Education and Communication
IFN	Interferon
INR	International Normalized Ratio
IPC	Infection, Prevention and Control
JHPIEGO	John Hopkins Program for International Education in Gynaecology and Obstetrics
KPa	Kilopascals
LGA	Local Government Area
LMICs	Low- and Middle-Income Countries
LMIS	Logistics Management Information System
M&E	Monitoring and Evaluation
MAH	Marketing Authorization Holder
MASLD	Metabolic Dysfunction Associated Steatotic Liver Disease
MAT	Medically Assisted Treatment
MNCH	Maternal Newborn and Child Health
MSF	Monthly Summary Form
MSM	Men who have Sex with Men
MTCT	Mother-To-Child Transmission
NAAT	Nucleic Acid Amplification Technique
NAFDAC	National Agency for Food and Drug Administration and Control
NAFLD	Non Alcoholic Fatty Liver Disease
NAs	Nucleos(t)ide Analogues
NASBA	Nucleic Acid Sequence-based Amplification
NASCP	National AIDS, Viral Hepatitis and STIs Control Programme
NAT	Nucleic acid testing
NBSC	National Blood Service Commission
NDR	National Data Repository
NGOs	Non-Governmental Organizations
NITs	Non-invasive tests
NPC	National Pharmacovigilance Centre
NPHCDA	National Primary Health Care Development Agency
NPI	National Programme on Immunization
NSP	Needle and Syringe Programme
OSS	One Stop Shop
PCR	Polymerase Chain Reaction
PEP	Post Exposure Prophylaxis
PHC	Primary Health Care
PMM	Patient Management and Monitoring
PMTCT	Prevention of Mother-To-Child Transmission
PPEs	Personal Protective Equipment
PRASCO	Pharmacovigilance Rapid Alert System for Consumer Reporting
PT	Prothrombin Time
PWID	People who inject drugs
RDTs	Rapid Diagnostic Tests

RNA	Ribonucleic Acid
RTKs	Rapid Test Kits
SDG	Sustainable Development Goals
SMOH	State Ministry of Health
SOGHIN	Society for Gastroenterology and Hepatology in Nigeria
STIs	Sexually Transmitted Infections
SVR	Sustained Virological Response
TAF	Tenofovir Alafenamide
TB	Tuberculosis
TDF	Tenofovir Diproxil Fumarate
TWG	Technical Working Group
UNODC	United Nations Office on Drugs and Crimes
VH	Viral Hepatitis
VOX	Voxilaprevir
WHO	World Health Organization

GLOSSARY OF TERMS

Acute HBV Infection	New-onset hepatitis B infection that may or may not be icteric or symptomatic. Diagnosis is based on the detection of hepatitis B Surface antigen (HBsAg) and IgM antibodies to hepatitis B core antigen (anti-HBc). Recovery is accompanied by clearance of HBsAg with seroconversion to anti-HBs (antibodies to hepatitis B surface antigen), usually within 6 months.
Adverse drug reaction/Adverse drug effect	Adverse drug reaction/effect is a broad term referring to unwanted, uncomfortable, or dangerous effects that a drug may have
Adverse events	An unexpected medical problem that happens during administration of vaccines which may not necessarily be related to the vaccine
Antenatal clinic testing	This approach means routine testing of pregnant women especially in settings where there is an intermediate or high sero-prevalence of viral hepatitis, to identify women in need of antiviral treatment for their own health and additional interventions to reduce mother-to-child transmission (MTCT)
Anti-HBc IgM	Subclass of anti-HBc. Detected in recent HBV infection but can be detected by sensitive assays in chronic HBV infection, however in very low titres
Anti-HCV antibodies	Antibodies to HCV, which can be detected in the blood usually within two or three months of HCV infection or exposure. Usually indicates history of exposure to HCV infection. The terms HCV antibodies and anti-HCV antibodies are equivalent, but in these guidelines, HCV antibodies is used throughout.
Community Health Influencers, Promoters and Services (CHIPS)	Any person who performs functions related to health-care delivery and has been trained to deliver services but has received no formal professional or paraprofessional certificate or tertiary education degree. They provide referrals, linkage to care etc.
Chronic HBV Infection	In addition to HBsAg persistence for at least six months, the presence of anti HBc IgG and absence

	of anti HBs is diagnostic of chronic HBV infection. However, in limited resource settings, HBsAg persistence in two specimens 6 months apart could be used for diagnosis of chronic HBV infection
Chronic HCV Infection	The presence of HCV RNA or HCVcAg in the blood six months or more after acquiring infection. Usually associated with positive serology for HCV antibody.
Cirrhosis	An advanced stage of liver disease characterized by extensive hepatic fibrosis, nodularity of the liver, alteration of liver architecture and disrupted hepatic circulation.
Community-based testing	Includes using outreach (mobile) approaches in general and key populations; home-based testing (or door-to-door outreach); testing in workplaces, places of worship, parks, bars, and other venues; in schools and other educational establishments; as well as through campaigns.
Decentralization	The process of delegating significant authority and resources to lower levels of the health system (state, local government, ward, and community)
Decompensated cirrhosis	Liver cirrhosis with the following clinical features: portal hypertension (ascites, variceal haemorrhage, and hepatic encephalopathy), coagulopathy, or liver insufficiency (jaundice). Other clinical features of advanced liver disease/cirrhosis may include hepatomegaly, splenomegaly, pruritus, fatigue, arthralgia, palmar erythema, and oedema.
Enzyme immunoassay (EIA)	Laboratory-based serological immunoassays that detect antibodies, antigens, or a combination of both
Facility-based testing	Includes testing in primary, secondary, and tertiary health care centres, both public and private, and their laboratories
General population testing	This approach refers to routine testing throughout the entire population without attempting to identify high-risk behaviours or characteristics. It means that

	all members of the population should have potential access to the testing programme.
Hepatitis B core antibody (anti-HBc)	Antibody to HBV core (capsid) protein. Anti-HBc antibodies are non-neutralizing antibodies and are detected in both acute and chronic infection
Hepatitis B core antigen (HBcAg)	HBV core protein. The core protein is coated with HBsAg and therefore not found free in serum
Hepatitis B envelope antigen (HBeAg)	Viral protein found in the high replicative phase of HBV. HBeAg is usually, a marker of high levels of replication with wild-type virus but is not essential for viral replication
Hepatitis B envelope antigen (HBeAg) seroconversion	Loss of HBeAg and seroconversion to anti-HBe
Hepatitis B surface antigen (HBsAg) reversion	Reappearance of HBeAg in a person who was previously HBeAg negative and usually associated with increased HBV replication
Hepatitis B envelope antigen (HBeAg) negative chronic hepatitis B (immune-escape phase)	HBeAg-negative but anti-HBe-positive disease with variable levels of HBV replication and liver injury. Also previously known as reactivation phase
Hepatitis B surface antibody (anti-HBs)	Antibody to HBsAg. Develops in response to hepatitis B vaccination and during recovery from hepatitis B, denoting past infection and immunity
Hepatitis B surface antigen (HBsAg)	HBV envelope protein often produced in excess and detectable in the blood and other body fluids in acute and chronic HBV infection
Hepatitis B surface antigen (HBsAg) seroconversion	Loss of HBsAg and development of anti-HBs
Hepatitis B Virus (HBV) DNA	HBV viral genome that can be detected and quantified in serum by nucleic acid testing (NAT). HBV DNA is also a marker for viral replication and infectivity
Hepatitis B virus envelope antibody (Anti-HBe)	Antibody to HBeAg. Detected in persons with lower levels of HBV replication but also in HBeAg-negative disease (i.e., HBV that does not express HBeAg)

Hepatitis B Virus treatment failure	May be primary or secondary. Primary antiviral treatment failure may be defined as failure of an antiviral drug to reduce HBV DNA levels by ≥1x $\log_{10}$ IU/mL within 3 months of initiating therapy. Secondary antiviral treatment failure may be defined as a rebound of HBV DNA levels of ≥1x $\log_{10}$ IU/mL from the nadir in persons with an initial antiviral treatment response (≥1 x $\log_{10}$ IU/mL decrease in serum HBV DNA).
Hepatitis C Virus core antigen (HCVcAg)	Nucleocapsid peptide 22 [p22] of HCV, which is released into plasma during viral assembly and can be detected from early on and throughout the course of infection
Hepatitis C Virus RNA	HCV viral genome that can be detected and quantified in serum by nucleic acid testing (NAT).
Hepatocellular carcinoma (HCC)	Primary cancer of the liver arising from the hepatocytes and may be a complication of chronic hepatitis B or C infection.
IgM anti-HBc	Subclass of anti-HBc. Detected in acute hepatitis B but can be detected in low titres by sensitive assays in active chronic HBV.
IgG anti-HBc	Subclass of anti-HBc detected in past or current infection
HBeAg positive Chronic Hepatitis B (Immune-active phase)	Phase of hepatitis B e antigen (HBeAg)-positive disease characterized by elevated aminotransferases, liver inflammation, and high HBV DNA concentrations. May result in seroconversion from HBeAg to anti-HBe (antibody to hepatitis B e antigen)
HBeAg positive Chronic Hepatitis B virus infection (Immune-tolerant phase)	High replicative phase of infection seen in the early stage of CHB among people infected at birth or in early childhood
HBeAg negative Chronic Hepatitis B virus infection (Inactive phase or immune-control phase)	Low replicative phase of chronic hepatitis B characterized by HBeAg negativity, anti-HBe positivity, normal alanine aminotransferase (ALT) and HBV DNA concentration below 2000 IU/mL
Hepatitis C Virus Self Testing (HCVST)	HCV self-testing (HCVST) is a process in which an individual collects their specimen (blood or oral

	fluid), performs a simple rapid diagnostic test (RDT) for the detection of HCV antibodies, and then interprets their result, often in a private setting, either alone or with someone they trust
Integration	The co-location and sharing of services and resources across different disease areas
Key populations	Groups of people who due to specific high-risk behaviours, are at increased risk for viral hepatitis irrespective of the epidemic type or local context. These guidelines refer to the following groups as key populations: men who have sex with men (MSM); people who inject drugs (PWID); people in prisons and other closed settings; sex workers (SW); and transgender (TG) people
Linkage to care	A process of actions and activities that connect persons who have been tested for HBV/HCV to engage with prevention, treatment, and care services as appropriate for their hepatitis B and C status.
Multiplex or multi-disease testing	Refers to testing using one specimen in the same test device (or reagent cartridge) that can detect other infections (e.g., HIV, syphilis, hepatitis C, hepatitis B).
Nucleic acid testing (NAT)	A molecular technology, for example, polymerase chain reaction (PCR)or nucleic acid sequence-based amplification (NASBA) that can detect very small quantities of viral nucleic acid (RNA or DNA), either qualitatively or quantitatively.
Occult HBV Infection	Ongoing, or current infection that is HBsAg negative but HBV DNA positive, although at very low levels (invariably <200 IU/mL). Most are also anti-HBc positive.
Pharmacovigilance	The science and activities relating to the detection, assessment, reporting, understanding and prevention of adverse effects or any other medicine/vaccine related problem
Positive Predictive Value (PPV)	The probability that when a person's test result is positive, they truly have the infection/disease.

	Predictive values are influenced by the prevalence of the disease in the population.
Negative Predictive Value (NPV)	The probability that when a person's test result is negative, they truly do not have the infection/disease.
Rapid diagnostic test (RDT)	Immunoassays that detect antibodies or antigens and can give a result in less than 30 minutes.
Rapid Virological Response	Undetectable HCV RNA in the blood at 4 weeks of treatment
Relapse	Undetectable HCV RNA in the blood at 12 weeks after treatment but detectable HCV RNA at 24 weeks of completing treatment
Sensitivity	The ability of a test to correctly identify those with the infection/disease (true positives/true positives + false negatives)
Serological assays	Assays that detect the presence of either antigens or antibodies, typically, in serum or plasma but also in capillary/venous whole blood and oral fluid.
Specificity	The ability of a test to correctly identify those without the infection/disease (true negatives/true negatives + false positives)
Sustained Virological Response (SVR)	Undetectable HCV RNA in the blood at defined time point after the end of treatment, usually at 12 or 24 weeks (SVR12 or 24). OR Undetectable HBV DNA in the blood at defined time point after the end of treatment with Pegylated Interferon, usually 6 months
Task-shifting/sharing	The rational redistribution of tasks from "higher-level" cadres of healthcare providers to other cadres
Testing algorithm	The combination and sequence of specific assays / steps used within hepatitis B and C testing strategies
Testing approach / Strategy	In the context of these guidelines, the testing approach describes both "who to test" i.e., different

	populations and “where to test” i.e., different settings. These can be delivered through either health-facility or community-based testing taking into consideration the presumed disease prevalence in the population being tested
True negative (TN)	When a person’s test is negative, and they truly do not have the infection or disease
True positive (TP)	When a person’s test is positive, and they truly have the infection or disease
False negative (FN)	When a person’s test is negative, but they do have the infection or disease. Such misclassifications are generally due to assay or test inaccuracy.
False positive (FP)	When a person’s test is positive, but they do not have the infection or disease. Such misclassifications are generally due to assay or test inaccuracy
***Viraemic infection* (HBV&HCV)**	Hepatitis B or C infection associated with the presence of virus in the blood (as measured by HBV DNA or HCV RNA), and often referred to as viraemia.
Vulnerable populations	Groups of people who are particularly vulnerable to HBV/HCV infection in certain situations or contexts. These guidelines refer to the following groups as vulnerable populations: migrant and mobile workers, Healthcare workers, Emergency workers (Road safety, fire service, and other uniformed personnel), IDPs, etc.

EXECUTIVE SUMMARY

In 2019, an estimated 296 million people were living with chronic hepatitis B (CHB) and 58 million people with chronic hepatitis C (CHC) worldwide. Nigeria has a high burden of viral hepatitis as an estimated 20 million of the population are infected with hepatitis B (HBV) and C (HCV) according to the report of the 2018 National AIDS Indicator and Impact Survey (NAIIS, 2018). In recognition of this public health challenge, the country has set a national target to eliminate viral hepatitis by 2030 through the implementation of effective prevention, diagnosis, treatment, and other health-related interventions at the community, health facility, state, and national levels as chronicled in this guideline.

The goal of this guideline is to provide evidence-based stepwise instructions for health care workers involved in the prevention, treatment, and care of viral hepatitis towards realizing the national hepatitis programme goals and Sustainable Development Goals (SDG). The principles of universal health coverage, public health approach, human rights, and equity informed the development of the guidelines and should guide its implementation. The protocol focuses on the prevention, diagnosis, and treatment of HBV and HCV infections which are of major public health importance in the country. The primary audience for this guideline includes policy makers and programme managers at the Ministry of Health and related health agencies and departments responsible for the national viral hepatitis response, healthcare providers including nurses, clinicians, pharmacists, laboratory personnel, disease control, and surveillance officers, public health experts working at all levels of the healthcare delivery system, research and academia staff, development and donor partners, non-governmental organizations (NGO), patient groups and community-based organizations (CBO).

The guidelines have been divided into nine (9) chapters. The first chapter provides context and background information on viral hepatitis. The second, third, fourth, fifth, and sixth chapters are structured along the continuum of care for Hepatitis B and C which include prevention, testing, treatment, and care. The third chapter specifically discusses approaches for the prevention of mother-to-child transmission (PMTCT) of HBV such as the administration of the HBV vaccine, concurrent administration of hepatitis B immunoglobulin (HBIG) to the baby if available, and the administration of oral nucleos(t)ide analogues to HBV-infected pregnant mothers in the 3rd trimester (28 weeks upwards) of pregnancy until delivery. The fourth and fifth chapters present information on the management of HBV and HCV respectively. These chapters clearly highlight the procedures for clinical and laboratory evaluation of viral hepatitis patients, with clear guidelines on who to test and treat for viral hepatitis, patient follow up, and management of co-infections and comorbidities.

The sixth chapter contains useful information on care and support including the provision of psychosocial support for people living with HBV and HCV, counselling, and disclosure to patients as key strategies in ensuring optimal patient-centered care both at facility and community levels, as well as Infection, Prevention, and Control (IPC) measures with special consideration for standard precaution by health care workers. The seventh chapter provides guidance on the management of adverse reactions and complications of anti-hepatitis medicines. The eighth chapter focuses on monitoring and evaluation of the viral

hepatitis programme while the ninth chapter provides an overview of programmatic management of viral hepatitis services with important information on leadership and governance, advocacy and resource mobilization, human resource for health, and the World Health Organization (WHO) service delivery models strategies of task sharing, integration and decentralization of health services to bring care nearer to the patients' community.

The ninth chapter also emphasizes the need for the minimum package for viral hepatitis services at all levels of care, capacity building of health care providers, and ensuring an effective and efficient supply chain management system for viral hepatitis control programme in Nigeria.

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National AIDS, Viral Hepatitis and STIs Control Programme (NASCP)

CHAPTER 1 – INTRODUCTION

1.0 Background

Nigeria has a high burden of viral hepatitis as an estimated 20 million of the population are infected with hepatitis B and C[1]. In recognition of this public health challenge, the country has planned to meet the national hepatitis elimination target by 2030 through the implementation of effective prevention, treatment, and support interventions at the national, state, health facility, and community levels as chronicled in the National Strategic Framework (2022- 2026)[2].

1.1 Epidemiology of Viral Hepatitis

Hepatitis is an inflammation of the liver and can be caused by infectious or non-infectious agents such as viruses, bacteria, toxins, drugs, alcohol, and metabolic syndrome (a major cause of Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD), formerly known as Non-Alcoholic Fatty Liver Disease (NAFLD)). Viral hepatitis is caused by one or more of the five main unrelated viruses that infect the liver (A, B, C, D, and E). In 2019, an estimated 296 million people were living with chronic hepatitis B (CHB) and 58 million people with chronic hepatitis C (CHC) worldwide. Despite an effective HBV vaccine and HCV treatment, 3 million people were estimated to be newly infected with HBV (1.5 million) and HCV (1.5 million) respectively. In 2019, an estimated 820,000 HBV-related deaths and 290,000 HCV-related deaths were documented mainly from chronic liver disease and liver cancer. Currently, Africa battles a substantial hepatitis burden, with 82 million and 9 million people living with chronic hepatitis B (CHB) and chronic hepatitis C (CHC) infections, respectively. These staggering figures are further exacerbated by the WHO report which states that only 0.1% of 2% diagnosed with CHB and 0% of 5% diagnosed with CHC received treatment in the year 2020. These figures sharply contrast with the notable progress made globally, with 10% and 25% of individuals diagnosed with CHB and CHC, respectively, receiving treatment. Despite a 70% - 90% risk of children acquiring HBV infection through mother-to-child transmission (especially in mothers who are HBeAg positive), only 14 out of 47 African countries have introduced routine hepatitis B birth dose (HepB-BD) vaccination, and merely 17% of newborns in Africa have received a timely HepB-BD vaccination. The greatest burden of HBV and HCV is concentrated by geography and population. People from poor regions, displaced people and migrants, and rural populations are more severely affected. Furthermore, injecting drug use is a major contributor to the hepatitis C epidemic globally. Other affected populations include health-care workers who are exposed to needle-stick injuries, people in correctional facilities and closed settings, and men who have sex with men (MSM)[3].

[1] FMOH. Nigeria HIV/AIDS Indicator and Impact Survey (NAIIS), 2018.
[2] FMOH. National Strategic Framework for Viral Hepatitis Control in Nigeria, 2022.
[3] WHO. Global Progress Report on HIV, Viral hepatitis and STIs, 2021.

Viral Hepatitis is endemic in Nigeria with a national HBV prevalence rate of 8.1% among adolescents and adults aged 15-64 years (10.3% in men and 5.8% in women), peaking at 10.2% for ages 35-39 years and lowest at 2.5% among ages 55-59 years respectively. HCV prevalence rate is 1.1% among adolescents and adults aged 15-64 years (1.3% in men and 1.0% in women), peaking at 3.3% for ages 50-54 years and lowest (0.4%) for ages 15-19 years.

Rural communities are affected more than urban areas with the Northern states having the highest burden of the disease. This is corroborated by systematic meta-analysis and state-specific studies that have shown that the Northern states, for example, Nasarawa, Taraba, Benue, Plateau, and FCT have shown evidence of double-digit prevalence rates. Majority of people infected with viral hepatitis are not aware, as knowledge of viral hepatitis remains limited amongst the policy makers, general population, key population, and even health-care providers[4]. These individuals are at greater risk for severe complications from the disease and the likelihood of spreading the infection.

Hepatitis A

Hepatitis A Virus (HAV) is transmitted through ingestion of contaminated food and water or direct contact with an infectious person. The disease occurs sporadically or in epidemics, with a tendency for cyclic recurrences in settings with poor sanitation and unsafe water. Generally, the infection causes mild disease, and most people recover fully with lifelong immunity. Children in regions of high prevalence are likely to have experienced an episode of HAV infection before the age of 10 years. Those infected in childhood do not experience any noticeable symptoms. Epidemics are uncommon because older children and adults are generally immune leading to herd immunity; a small proportion of people may develop fulminant hepatitis (acute liver failure) which is often fatal. Persons with pre-existing Chronic Liver Disease (CLD), including chronic HBV and HCV and elderly persons, are at an increased risk of serious complications from HAV infection. There is no specific treatment for HAV infection, but it can be prevented through improved sanitation, safe water supply, food safety, and vaccination.

Hepatitis B

The hepatitis B virus (HBV) is an enveloped DNA virus that infects the liver and causes injury through immune-mediated killing of infected liver cells. HBV is 50 to 100 times more infectious than HIV, 50 times more infectious than HCV, and can survive up to seven days on a surface (WHO, 2015). It is also a recognized oncogenic virus with a high risk of progressing to hepatocellular cancer (HCC). At least ten genotypes (A-J) have been identified worldwide, with varying geographical distribution. HBV genotypes determine virus activity, risk of progression of liver disease, and response to antiviral therapy. Higher rates of HCC have been found in persons infected with genotypes C and F compared with genotypes B or D. The predominant genotype in Nigeria and parts of the West African sub-region is E. HBV infection

[4] Ajuwon B.I., *et al., 2021* Hepatitis B virus infection in Nigeria: a systematic review and meta-analysis of data published between 2010 and 2019

can be either acute or chronic and may range from asymptomatic infection to mild, severe, or rarely fulminant hepatitis. Acute hepatitis B is usually a self-limiting disease while chronic hepatitis B (CHB) infection leads to a spectrum of diseases and is defined as persistent HBV infection (the presence of detectable hepatitis B surface antigen [HBsAg] in the blood or serum for longer than six months), with or without associated active viral replication and evidence of hepatocellular injury and inflammation[5].

The natural history and spectrum of disease of CHB in individuals differ. In some cases, it is inactive and does not lead to significant liver disease. In others, it may cause progressive liver fibrosis, leading to cirrhosis with end-stage liver disease, and a markedly increased risk of hepatocellular carcinoma (HCC), independent of the presence of cirrhosis. Co-infections with HIV, HCV, and hepatitis D virus (HDV) and co-factors such as alcohol use, may increase the rate of disease progression.

The age at which infection is acquired is also a major factor in the development of CHB. Over 90% of persons who get infected in adulthood clear it spontaneously. However, about 90% of neonates born to hepatitis B surface antigen (HBsAg) positive mothers and 20-60% of other children below five years develop CHB following acute infection. Complications such as liver cirrhosis and HCC are likely to emerge in the third and fourth decades after initial infection. Generally, an estimated 20-30% of persons with CHB will eventually develop cirrhosis, with approximately 2-7% annual risk of developing either end-stage liver disease (ESLD) or HCC[6].

In highly endemic areas such as Nigeria, transmission is commonly through vertical (i.e., mother to child during delivery) and horizontal means (i.e., through direct percutaneous or mucosal exposure to infected blood and other body fluids). Although infection through exposure to other body fluids such as saliva, sweat, and tears is unproven, transmission may still occur if contact occurs with broken skin. Also, transmission can be through transfusion of infected blood or blood products and exposure to unsafe injection equipment, medical procedures, dialysis, tattooing, scarification, shaving, manicures/pedicures, and circumcision. Sexual transmission of HBV is possible, particularly in susceptible men who have sex with men (MSM), people with multiple sexual partners, and individuals who have sexually transmitted infections (STIs). Another possible transmission route is in settings that involve close interpersonal contact over an extended period, such as household contacts or people in custodian centres and other closed settings. The HBV vaccine is protective against all HBV genotypes. Mother-to-child transmission is preventable with the use of maternal prophylaxis in addition to HBV vaccination. Life-long treatment with antiviral therapy is available and effective against all genotypes with the prospects of preventing the long-term sequelae of HBV infection.

[5] CDC. Hepatitis B FAQS for the public. 2015c. [February 7, 2016]. http://www.cdc.gov/hepatitis/hbv/bfaq.htm.
[6] WHO. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection, 2015.

Hepatitis C

Hepatitis C Virus (HCV) is an enveloped RNA virus that can be transmitted through exposure to contaminated blood, unsafe injection practices, inadequate sterilization of medical equipment, transfusion of unscreened blood and blood products as well as unsafe sexual practices. Mother-to-child transmission is rare but possible in pregnant women with HCV and HIV co-infection and those with very high serum HCV RNA levels. HCV infection can be acute or chronic, but the acute infection is hardly detected clinically. Incident infection is associated with early symptoms in about 20% of persons. About 15–45% of infected individuals (25% of adults) spontaneously clear the infection within six months of infection even in the absence of treatment. The remaining 55–85% 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. Initially, cirrhosis may be compensated, and decompensation may occur later, leading to variceal haemorrhages, ascites, or encephalopathy. HCV infection can lead to extrahepatic manifestations such as depression (25%), diabetes mellitus (15%), and chronic renal disease (10%) (WHO; guidelines for the treatment and care of persons diagnosed with chronic hepatitis C virus infection. July 2018). The prevalence of these extrahepatic manifestations is usually independent of the degree of liver fibrosis. Currently, there is no vaccine available to prevent HCV infection. However, there are, Direct Acting Antivirals (DAA) which are effective for the treatment of persons with HCV infection with a cure rate of over 95%[7].

Hepatitis D

Hepatitis D Virus (HDV) is an RNA virus that requires HBV for its replication and transmission (simultaneously or as a super-infection). The routes of transmission among the general population are like that of HBV. Infection can be acute (onset and resolution within six months) or chronic (prolonged for more than six months). HDV/HBV super-infection is considered the most severe form of chronic viral hepatitis due to very rapid progression to cirrhosis, HCC, and death. On the other hand, HDV/HBV simultaneous or co-infection leads to severe acute viral hepatitis, but recovery occurs where there is no progression to chronic conditions. Current antiviral medications do not seem to be very effective in treating HDV infection (pegylated interferon-α only have a modest therapeutic effect in chronic HDV), but it can be prevented with the HBV vaccine[8].

Hepatitis E

Hepatitis E Virus (HEV) is an RNA virus with 4 genotypes namely I, II, III, and IV. It is transmitted faeco-orally through the consumption of contaminated water or food hence a common cause of outbreaks in communities with poor sanitation and unsafe water. Other transmission routes have been identified, which include transfusion with infected blood products and perinatal transmission from mother to child. This form of transmission is mainly applicable to genotypes I and II. Genotypes III and IV commonly occur as zoonotic infection especially

[7] Younossi ZM, *et al*. Global epidemiology of non-alcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology, 2016.

[8] Farci P, Niro GA. Clinical features of hepatitis D. Seminars in Liver Disease vol.32, 2012.

among those exposed to wild animals such as warthog and deer. Outbreaks and sporadic cases of hepatitis E occur around the world. These outbreaks frequently occur in resource-limited countries. In recent years, some of these outbreaks have occurred in areas of conflict and humanitarian emergencies, such as war zones, and in camps for refugees or internally displaced persons (IDP). HEV infection is usually self-limiting. However, substantial morbidity or even mortality can occur in pregnant women. Acute HEV infection does not lead to chronic liver disease except in immunocompromised individuals (e.g., those living with HIV/AIDS). Such patients with chronic hepatitis E usually respond to treatment with ribavirin.

1.2 Goal

The goal of this guideline is to provide evidence-based stepwise instructions for health care workers involved in the prevention, treatment, and care of viral hepatitis toward realizing the national hepatitis goals and Sustainable Development Goals (SDG).

Specifically:

- **i.** Provide guidance on whom to screen for hepatitis B and hepatitis C infections, and which testing strategies and algorithms to use
- **ii.** Provide guidance on the care and treatment for those with acute hepatitis B and C and all persons living with chronic viral hepatitis B and C infections
- **iii.** Provide evidence-based guidance on prevention of mother-to-child transmission (PMTCT) of HBV
- **iv.** Provide guidance on general preventive strategies against viral hepatitis

1.3 Guiding Principles

The following principles informed the development and should guide the implementation of the recommendations which must be delivered within a public health and universal health coverage framework that promotes equity and respects human rights.

i. **Universal Health Coverage:** Affordable viral hepatitis services must be available at the different levels of the health care systems to ensure access for the populations most affected in a stigma-free and non-discriminatory environment. An enabling environment that removes barriers such as stigma, discrimination and, criminalization, and empowers the communities is important for increasing access to and uptake of viral hepatitis services.

ii. **Public Health Approach:** The guidelines are based on a public health approach that seeks to ensure the widest possible access to high-quality services at the population level, based on simplified and standardized approaches, and to strike a balance between implementing the best-proven standard of care and what is feasible on a large scale in resource-limited settings.

iii. **Human Rights and Equity:** Implementation of the guidelines should be informed by the Nigerian local context, including HBV and HCV epidemiology, prevalence of other comorbidities, available resources, and the capacity of the health system. This should be accompanied by efforts to promote and protect the human rights of people who need viral hepatitis services, including ensuring informed consent, preventing stigma and discrimination in the provision of services, and promoting gender equity.

iv. **Government Ownership:** Governments at the Federal, State, and Local levels should commit to ensuring the goal of health for all citizens through the provision of appropriate interventions for viral hepatitis infection.

v. **Partnerships:** Ensuring evidence-based interventions, services, and policies through inter-sectorial collaboration, service/programme integration, and involvement of affected people and communities.

1.4. Scope and Structure of the Guidelines

These guidelines focus on the prevention and treatment of hepatitis B and C infections which are of major public health importance in the country. These guidelines have been divided into nine chapters. The first chapter provides context and background information on viral hepatitis. The second, third, fourth, fifth, and sixth chapters are structured along the continuum of care for Hepatitis B and C which include prevention, testing, treatment, and care. The seventh chapter talks about the management of adverse reactions and complications of anti-hepatitis medicines. Chapters eight and nine provide an overview of the monitoring and evaluation, and programmatic management of viral hepatitis services respectively.

1.5 Target Audience:

The primary audience for this guideline includes policy makers and programme managers at the Ministry of Health and related health agencies and departments responsible for the national viral hepatitis response, clinicians, healthcare providers including nurses, pharmacists, laboratory personnel, disease control and surveillance officers, public health experts working at all levels of the healthcare delivery system, research and academia staff, development and donor partners, non-governmental organizations (NGO), patient groups and community-based organizations (CBO).

1.6 Guideline Development Process

In Nigeria, the National AIDS and STIs Control Programme (NASCP) coordinates the national viral hepatitis response. This role includes the provision of strategic guidance through policy formulation and implementation, guidelines, and tools development. The WHO guidance and recommendations on Viral Hepatitis B and C and learnings from the review of the National Guidelines for the Prevention, Care, and Treatment of Viral Hepatitis in Nigeria (2016-2020) formed the basis for the format and structure of this guideline.

The National Guideline was developed through a consultative process coordinated by NASCP and led by the National Viral Hepatitis Technical Working Group in collaboration with the National Drug Demand and Harm Reduction Programme of the Department of Hospital Services of the Federal Ministry of Health (FMOH), the National Blood Service Commission (NBSC), National Primary Health Care Development Agency (NPHCDA), World Health Organization (WHO), United Nations Office on Drugs and Crimes (UNODC), Clinton Health Access Initiative (CHAI), Jhpiego Nigeria, an affiliate of John Hopkins University, Society for Gastroenterology and Hepatology in Nigeria (SOGHIN), Patients Groups and Civil Society Organizations (CSO). A mixed method of desk-review, virtual consultations, stakeholders briefing, and physical workshops were used.

CHAPTER 2: PREVENTION OF VIRAL HEPATITIS

Prevention of viral hepatitis remains a critical component of control efforts. This section focuses on specific interventions around vaccination, injection and blood safety, and harm reduction. This cannot be achieved without public awareness and education.

2.1 General Preventive Measures

Health Education

i. Public awareness and education on HBV/HCV and their prevention (e.g., safe sexual and injection practices, etc.)
ii. Health education of health care workers (HCWs) on Infection, Prevention, and Control (IPC) such as standard precautions which include;
    - Use of Personal Protective Equipment (PPEs),
    - Proper disposal of all sharp instruments (needles, lancets, blades, etc.).
    - Non-recycling of disposable instruments used in medical procedures (needles, lancets, etc.)
    - Cleaning, disinfection, and sterilization of all instruments used by medical and alternative medical practitioners for invasive procedures e.g., circumcision, scarification, tattooing, ear piercing, etc.).
    - Hand hygiene
iii. Screening of all blood/organs and blood products before transfusion/transplantation.

2.2 Hepatitis B Vaccination

2.2.1 Hepatitis B Birth dose and Pentavalent vaccination for infants

The National Programme on Immunization (NPI) schedule for infants includes four doses of the HBV vaccine. The first dose is the monovalent HBV vaccine administered within the first 24 hours of life. Subsequent doses of the vaccine are given as a component of the pentavalent vaccine at 6, 10, and 14 weeks of age respectively. The pentavalent vaccine provides coverage for Diphtheria, Pertussis, Tetanus, Hepatitis B and Haemophilus influenza type B.

Table 2.1 Summary of HBV immunization schedule for infants

Age	HBV Vaccine	Dose	Route and vaccination site
At birth (within 24 hours)	Monovalent	10µg / 0.5 ml	Intramuscular, anterolateral aspect of the right thigh
6 weeks	Pentavalent	0.5 ml	Intramuscular, anterolateral aspect of the left thigh
10 weeks	Pentavalent	0.5 ml	Intramuscular, anterolateral aspect of the left thigh
14 weeks	Pentavalent	0.5 ml	Intramuscular, anterolateral aspect of the left thigh

2.2.2 Vaccination for older children, adolescents, and adults

It is recommended that all HBsAg negative individuals should be vaccinated. However, where the anti-HBs test is available and the titre is ≥10 mIU/mL, vaccination is not required.
The recommended vaccination schedule for unvaccinated persons is as follows:

- Children aged 1 – 11 years: Monovalent HBV vaccine at 0 (start dose), 4 weeks after start dose, and 6 months after start dose or 5 months after 2nd dose should be administered (dose – 10µg / 0.5ml, IM)
- Adolescents and adults: Monovalent HBV vaccine at 0 (start dose), 4 weeks after start dose, and 6 months after start dose or 5 months after 2nd dose should be administered (dose – 20µg / 1 ml, IM)

2.2.3 Vaccination in special circumstances

- Persons who do not respond to the first series of Hepatitis B vaccine should complete a second 3-dose vaccine series. The second vaccine series should be given on the usual 0, 1, and 6-month schedule. Polyvalent hepatitis B vaccine may be advisable in this setting.
- For persons living with HIV, haemodialysis, non-responders, and other immuno-compromised individuals, it is recommended that the vaccine dosage be doubled (dose 40µg / 2ml) and a fourth dose should be added, according to this schedule 0, 1, 2, and 6 months.

2.2.4 Accelerated (Rapid) Vaccination Schedule

Accelerated (rapid) vaccination is a short-term schedule for special circumstances. It is generally not recommended for individuals who do not need the vaccine within a certain

period. It is recommended for those travelling on short notice, at high risk of facing exposures (key populations, health care workers, etc.), and emergency responders in disaster areas.

The schedule is as follows:

- First shot – given at first contact
- Second shot – 7 days after the first shot
- Third shot – between 21 and 30 days after the first shot
- Fourth shot – 1 year after the first shot

2.2.5 Vaccination of Households and Sexual Contacts

- Household members and sexual partners of persons with chronic HBV are at an increased risk of HBV infection and should be vaccinated if they are negative for HBsAg, anti-HBs, and/or IgG anti-HBc tests.
- Dosing schedules depend on the type of vaccine, age at administration, need for rapid immunization, and previous response to HBV vaccination.

Recommendation:

Household members and sexual contacts of persons with chronic HBV should be vaccinated if vulnerable. The dose and schedule should be as mentioned above in *section 2.2.2*.

2.3 Post Exposure Prophylaxis (PEP)

2.3.1 Post-exposure prophylaxis following needle- stick injury, sexual exposure, mucosal or percutaneous (e.g., bite) HBV exposure

- Wounds should be washed with soap and water, and mucous membranes flushed with water
- The index case should be screened for HIV and HCV antibody
- HBsAg, anti-HBs, and IgG anti-HBc should be checked in the exposed individual, to determine whether the individual is infected, immune, or non-immune to HBV

****If the status of the index case is unknown, then HBIG (0.06 mL/kg or 500 IU) is given intramuscularly and active vaccination commenced (0, 1, and 6 months) if the exposed individual is non-immune. HBIG and vaccines should be given at different injection sites. HBIG is repeated at 1 month if the contact is HBeAg positive, has high HBV DNA levels, or if this information is not known.***

**** If the exposed individual is a known non-responder to HBV vaccination, then two doses of HBIG should be given 1 month apart. Anti-HBs titres should be measured 1–2 months after vaccination.***

2.4 Blood Safety

- Establishment of a national blood system with well-organized, coordinated blood transfusion services, evidence-based and ethical standards in line with national blood policies, legislation and regulation
- All blood/ blood products and organs should be screened for all types of viral hepatitis prior to transfusion/transplantation
- Rational use of blood and blood products to reduce unnecessary transfusions and minimize the risks associated with transfusion. However, the use of alternatives to blood transfusion where possible, is a safe and good clinical practice and should be encouraged
- Strengthening of donation systems through the collection of blood, plasma, and other blood components from low-risk, regular, voluntary unpaid donors and effective donor management, including care and counselling
- Blood group serology and testing for viral hepatitis B and C shall be carried out on a specimen collected at the time of donation, on every unit of whole blood or apheresis unit collected
- The test method to be used shall be chosen from the list of technologies indicated below:
    - **For HBV** - Minimum of Third Generation ELISA screening for HBsAg, Chemiluminescence, and HBV-DNA (Nucleic Acid Amplification Technique - NAAT)
    - **For HCV** - Minimum ELISA for Anti-HCV, Chemiluminescence and HCV RNA - Nucleic Acid Amplification Technique (NAAT)
- Only test kits approved by the appropriate regulatory authority should be used and the test system in which such is used shall be validated by the Blood Establishment (BE).
- The BE shall maintain algorithms for testing procedures and rejection in adherence to NBSC guidelines.
- Health facilities to establish hemovigilance processes

2.5 Injection Safety

2.5.1 Injection safety in health-care settings

Health care workers are required to use auto-disable syringes and needles for intravenous, intramuscular, intra-dermal, and subcutaneous injections and a sufficient supply of quality-assured syringes with matching quantities of safety boxes in health-care settings. Avoidable unsafe practices ultimately lead to large-scale transmission of blood-borne viruses among patients, health-care providers, and the community at large.

Unsafe practices include, but are not limited to the following prevalent and high-risk practices:

- Reuse of equipment to administer injections to more than one person, including reintroduction of injection equipment into multi-dose vials
- Recapping of used needles and unsafe handling of sharps may lead to accidental needle-stick injuries among health-care workers, which occur while giving an injection or after the injection
- The use of injections for health conditions where oral formulations are available and recommended as the first-line treatment
- Unsafe management of sharps waste includes incomplete incineration, disposal in open pits or dumping sites, leaving used injection equipment in the hospital laundry, and other practices that fail to secure infected sharps waste.
- Unsafe sharps waste management puts health-care workers, waste management workers, and the community at large at risk.

2.6 Harm Reduction

WHO (2019) defines harm reduction as an evidence-based public health response for Persons Who Inject Drugs (PWID) – which includes access to sterile injecting equipment through Needle and Syringe Programmes (NSP) and effective drug dependence treatment, such as Medically Assisted Treatment (MAT). The aim of a harm reduction approach is to reduce the negative consequences of risky behaviours, including the harmful effects of substance use[9].

Injecting drug use is the main route of transmission of HIV and hepatitis infections in PWIDs. Sexual transmission occurs through unprotected sex with their partners or clients. Stimulant use through injecting and non-injecting routes is often associated with risky sexual behaviours. Condom programming is thus an essential component of the comprehensive harm reduction package for PWIDs and their sexual partners.

Harm reduction package includes:

- Needle and Syringe Programme (NSP)
- Medically Assisted Treatment (MAT) and other evidence-based drug dependence treatments including naloxone
- Prevention, vaccination, diagnosis, and treatment of viral hepatitis
- Antiretroviral therapy (ART)
- Condom distribution programmes for PWIDs and their sexual partners
- Targeted information, education, and communication (IEC) for PWIDs and their sexual partners
- HIV Testing Services (HTS)
- Prevention and treatment of Sexually Transmitted Infections (STIs)
- Prevention, diagnosis, and treatment of Tuberculosis (TB)

[9] WHO. Policy Brief: Access to Hepatitis C Testing and Treatment for People Who Inject Drugs and People in Prisons — A Global Perspective, 2019.

- Mental health services

Needle and Syringe Programme (NSP) is useful in preventing HCV transmission among PWIDs. An effective NSP delivery should consider strategic collaboration and engagement between all stakeholders especially from the health sector, law enforcement, and civil society organizations. An enabling legal environment is very important for the smooth implementation of harm reduction programmes. Integrating the harm reduction programme into an already existing viral hepatitis programme is critical for sustainability.

Additional services for female PWIDs;

- Sexual and reproductive health services, including contraception
- Maternal and child health services
- PMTCT services
- Cervical cancer screening

CHAPTER 3: PREVENTION OF MOTHER TO CHILD TRANSMISSION OF VIRAL HEPATITIS B

The currently recommended practice to reduce mother-to-child (vertical) or horizontal transmission relies on the administration of the HBV vaccine and concurrent administration of hepatitis B immunoglobulin (HBIG) to the baby and the administration of oral nucleos(t)ide analogues to HBV-infected pregnant mothers in the 3rd trimester (28 weeks upwards) of pregnancy till delivery (see figure 3.1).

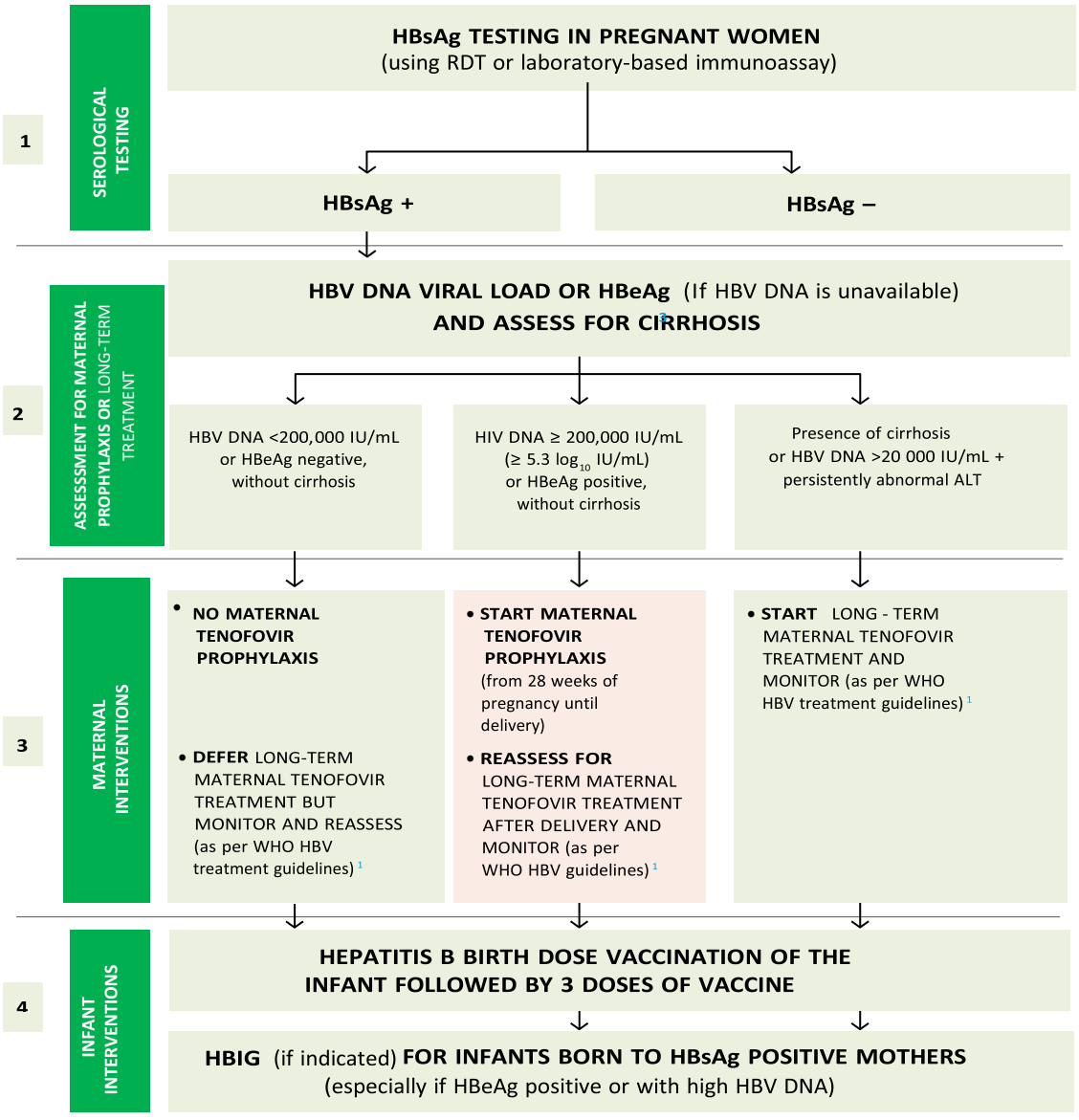


Figure 3.1 Algorithm on Prevention of Mother-to-Child Transmission of Hepatitis B Virus

Recommendation:

3.1 Hepatitis B testing among pregnant women

- **Counselling**: All pregnant women attending ANC should receive adequate information on Hepatitis B Virus infection, transmission, prevention, vaccination, and treatment options.
- **Screening**: Every pregnant woman should be screened for HBsAg, HCV, HIV, and syphilis at least once, as early as possible in the pregnancy. If the first presentation is during labour, it is recommended that the pregnant woman be screened for HBsAg. Screening should be carried out using rapid test or Enzyme Immunoassay (EIA) kits approved by regulatory authorities in Nigeria and/or WHO pre-qualified.
    - **Partner Notification**: All partners of HBsAg positive pregnant women should be offered HBsAg screening
- **Diagnostics**: All HBsAg positive mothers should be referred for HBV DNA testing. If not available, then perform HBeAg test. *(Refer to table 2.2 for HBV panel interpretation).*

3.2 Tenofovir prophylaxis

- **Treatment**: Every HBsAg-positive woman with HBV DNA ≥200,000 IU/ml should receive Tenofovir Disoproxil Fumarate (TDF) from the 28th week of gestation. Tenofovir Alafenamide Fumarate (TAF) is not recommended in pregnancy. Alternative to TDF is Telbivudine or Lamivudine. In place of HBV DNA, HBeAg positivity can be used as an indication to commence TDF therapy in areas without access to HBV viral load testing. A pregnant woman who does not meet the preceding criteria but has significant hepatic fibrosis or cirrhosis should be referred to a specialist for long-term HBV treatment for her health.

3.3 Vaccination for children born to mothers who are Hepatitis B positive

- **Vaccination**: All exposed babies (babies born to HBsAg positive mothers) should receive the HBV vaccine within 24 hours of birth and where indicated (e.g., birth trauma, obstructed labour, prenatal diagnostic procedures, assisted deliveries, etc.) hepatitis B immunoglobin (HBIG) may be given in addition. The sites of administration (intramuscular) for HBV vaccine and HBIG should be different (right and left upper arms).

3.4 WHO four-pronged PMTCT approach for Viral Hepatitis

Like PMTCT in the HIV programme, prevention of viral hepatitis can benefit from the four prongs of PMTCT as defined by the World Health Organization. The 4-pronged approach are as follows:

1. Primary prevention of viral hepatitis infection in women of reproductive age and their partners. Health education on risks and the mode of transmission for HBV infection

should be given to women of reproductive age. HBV sreening and vaccination should also be made available.

2. Prevention of unintended pregnancies among women of reproductive age using family planning
3. Prevention of viral hepatitis transmission from infected mothers to their infants (HBV prophylaxis and birth dose vaccination for infants)
4. Provision of appropriate treatment, care, and support to viral hepatitis-infected mothers, their infants, and family members
    - Breastfeeding is not contraindicated for HBV infected mothers
    - Refer HBV infected mothers for specialist care post-delivery
    - Commencement of treatment

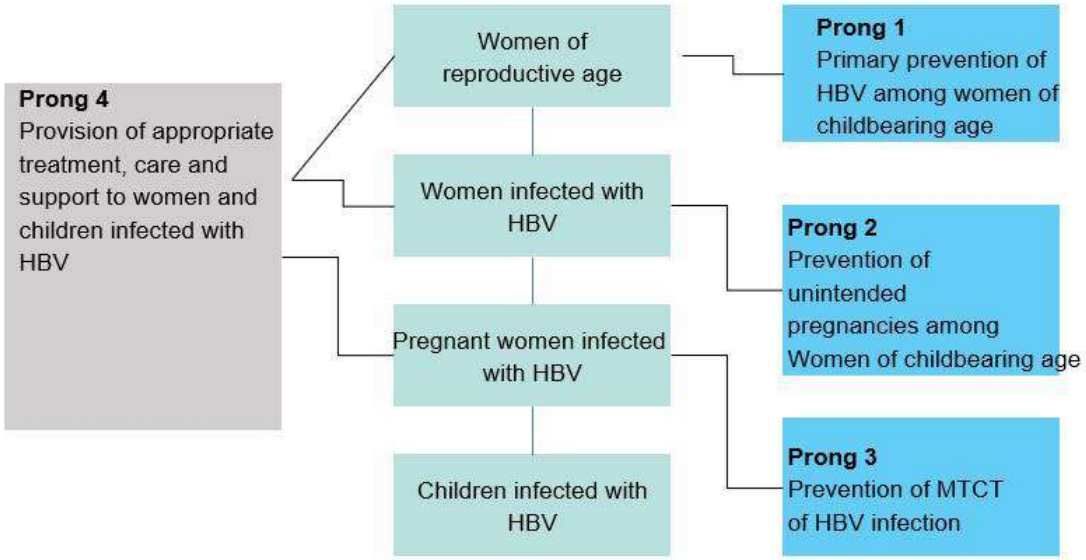


Figure 3.2 Four prongs to eliminate Mother-to-Child transmission of viral hepatitis infection

3.5 Implementation Strategies

3.5.1 Service Integration

- The integration of viral hepatitis services into the existing MNCH/PMTCT-HIV programmes should be encouraged to ensure that every pregnant woman that attends ANC is screened for viral hepatitis and their babies receive the birth dose HBV vaccine.
- Dual test kits for HIV/Syphilis have been incorporated in the 2020 National Guidelines on HIV Prevention, Treatment, and Care. With the recent WHO Global Health Sector Strategy (GHSS) which recommends triple elimination of HIV, viral hepatitis, and

Syphilis, it has become necessary to ensure that all pregnant women are screened for these three diseases.

Elimination of Mother to Child Transmission (EMTCT) of HIV, Syphilis, and HBV

WHO triple elimination initiative encourages countries to simultaneously commit to the elimination of mother-to-child transmission (EMTCT) of HIV, syphilis, and HBV.

Essential triple EMTCT services include:

1. Testing for HIV, syphilis, and HBV in antenatal Care clinics;
2. Prompt and efficacious interventions to treat women who test positive, and to prevent transmission of the infection(s) to their children;
3. Counselling for women and their partners to reduce transmission risk and ensure appropriate treatment;
4. Skilled birth attendant and safe delivery
5. Appropriate follow-up of exposed infants, including HBV birth dose vaccine, optimal infant feeding; and
6. Appropriate treatment and care for mothers living with HIV, or eligible for treatment for HBV or syphilis.

CHAPTER 4: MANAGEMENT OF HEPATITIS B VIRUS INFECTION

Hepatitis B virus infection which occurs early in life is likely to become chronic (>90%) while in adulthood more than 90% clear the virus. In those with persistent infection, there is progression to CLD (Cirrhosis and HCC) in about 25% to 40% of patients. The likelihood of developing cirrhosis and HCC is related to high viral load and ongoing liver inflammation. Thus, those with persistently high viral load and raised liver enzymes are at greater risk of developing liver cirrhosis and HCC and should be considered in urgent need of treatment.

4.1 WHO TO TEST FOR VIRAL HEPATITIS B

It is recommended that everyone is aware of their status through routine screening and the following categories of people should be targeted for screening:

- Those with clinical evidence of chronic liver disease or abnormal liver enzyme tests
- Pregnant women at ANC
- Infants born to HBV positive mothers
- Persons who inject drugs
- Persons with a history of blood or blood products transfusion or organ transplant/history of haemodialysis
- Health care workers especially those exposed to needle sticks/sharps, blood, and blood products
- Contacts of HBV infected persons
- Persons with sexually transmitted diseases
- Survivors of sexual assault and gender-based violence (GBV)
- Law enforcement and emergency personnel, e.g., Federal Road Safety Officers and National Emergency Management Agency (NEMA) who evacuate road traffic accident and disaster victims
- Other occupational groups who handle knives and sharps as part of their job, e.g., butchers

4.2 CLINICAL AND LABORATORY EVALUATION FOR HEPATITIS B

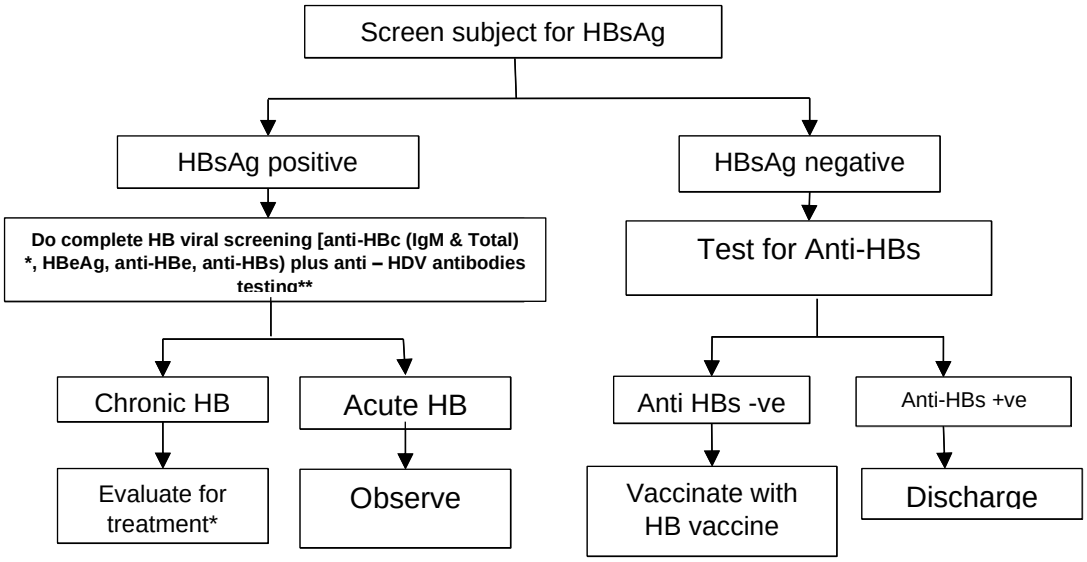
4.2.1 Screening test for Viral Hepatitis B

Rapid Diagnostic Tests

Rapid Diagnostic Tests (RDTs) are single-use disposable assays that are provided in simple-to-use formats that generally require no additional reagents except those supplied in the test kit. They are read visually and can give a simple qualitative result in 30 minutes. Due to their simplicity, low cost, and rapid turnaround time, they can be performed by trained community volunteers or health-care workers, without the need for venepuncture for specimen

collection. Quality-assured RDTs are therefore particularly useful in settings where conventional laboratory-based testing services are not available or accessible. They can also be used as a point of care (POC) testing in outreach programmes (e.g., prison services, prevention and treatment services for key populations). Most RDTs can be performed with capillary whole blood collected by a finger prick procedure using a lancet, but many have also been developed for use with venous whole blood, serum, or plasma. For HBV, test kits that detect HBsAg are used. HBsAg positive blood specimens should also be screened for anti-HDV antibodies followed by a Nucleic Acid Test (NAT) for detecting HDV RNA and active (viraemic) infection among people who are anti-HDV positive.

Following the identification of an HBsAg positive person using the RDT kits, the algorithm below should be used for the evaluation of the patient.



**Evaluate for treatment using viral load, liver enzymes, and evidence of CLD*

*** For those positive for anti-HDV antibodies, see section 4.5*

Figure 4.1: Screening and Evaluation for Hepatitis B virus infection

Table 4.1: HBV serological marker and Interpretation

Test	Results	Interpretation
HBsAg	Negative	Susceptible, not previously infected
Anti-HBc (total)	Negative	
Anti-HBs	Negative	
HBsAg	Negative	Immune due to vaccination

Anti-HBc (total)	Negative	
Anti-HBs	Positive with >10mIU/mL*	
HBsAg	Negative	Immune due to recovery from previous infection
Anti-HBc (total)	Positive	
Anti-HBs	Positive	
HBsAg	Positive	Acutely infected
Anti-HBc (total)	Positive	
IgM anti-HBc	Positive	
Anti-HBs	Negative	
HBsAg	Positive	Chronically infected
Anti-HBc (total)	Positive	
IgM anti-HBc	Negative	
Anti-HBs	Negative	
HBsAg	Negative	***Four possible interpretations**
Anti-HBc (total)	Positive	
Anti HBs	Negative	

***Four possible interpretations**

1. May be recovering from an acute HBV infection
2. May be distantly immune and the test is not sensitive enough to detect a very low level of anti-HBs in the serum
3. May be susceptible with a false positive anti-HBc
4. May be chronically infected and have an undetectable level of HBsAg present in the serum (Occult HBV infection)

In areas where the complete HBV serology panel is inaccessible, a repeat HBsAg test is required in 6 months. Where positive, chronic Hepatitis B is confirmed.

Chronic Hepatitis B (CHB) is defined as the persistence of HBsAg for more than 6 months or the presence of chronic liver disease attributable to HBV infection. HBeAg positivity in persons with CHB usually indicates the presence of active HBV replication and high infectivity. However, in cases of infection by mutant HBV variants, HBeAg may be negative whereas the serum HBV DNA could be very high; such cases are also highly infectious.

4.2.2. Clinical Evaluation of Chronic Hepatitis B infection

A detailed history and physical examination of patients are required. Alcohol, drugs (including herbal remedies), and history of other risk factors should be taken. Physical examination should be conducted to evaluate for features of chronic liver disease such as jaundice, hepatomegaly, splenomegaly, and gastrointestinal (GI) bleeding. There is a need to exclude MASLD caused by obesity, type II diabetes mellitus, dyslipidaemia and gastric by-pass surgery. In this case, anthropometric measurements such as Body Mass Index (BMI), waist-hip ratio, weight-for-age, and weight-for-height Z score for children can be carried out. The presence of ascites is highly suggestive of decompensated liver cirrhosis. These patients should be considered for treatment prioritization and referred for specialized care.

Assessment of Hepatic injury/severity:

Liver injury and the severity can be assessed using the following tests: Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), bilirubin, albumin, prothrombin time (PT), and ultrasonography. Where MASLD is suspected, additional investigations such as fasting lipid profile, fasting blood sugar, and glycated haemoglobin (HbA1c) should be carried out.

Liver enzymes

Aminotransferase levels may fluctuate with time, and single measurements of ALT and AST do not indicate disease stage. Usually, the ALT concentrations are higher than those of AST, but with disease progression to cirrhosis, the AST/ALT ratio may be reversed. Tests of liver synthetic function and/or portal hypertension include serum albumin, bilirubin, platelet count, and prothrombin time. A progressive decline in serum albumin concentrations, rise in bilirubin, and prolongation of the prothrombin time are characteristically observed as decompensated cirrhosis develops.

Haematological tests

Full blood count (including platelets). Platelet count may be reduced in cases of significant liver fibrosis and patients with decompensated liver cirrhosis especially if there is splenomegaly.

Imaging

Ultrasound scan: This should be the first imaging technique to be used in evaluating patients with chronic hepatitis B as it may demonstrate evidence of advanced liver disease or comorbidity.

CT scan: Applicable where ultrasound result is non-specific.

Non-invasive tests (NITs)

Non-invasive methods for assessing the stage of liver disease are supplanting liver biopsy and have been validated in adults with CHB. Non-invasive tests of liver fibrosis such as aspartate aminotransferase (AST)-to-Platelet Ratio Index (APRI) and fibrosis index based on 4 factors (FIB-4), as well as commercial markers such as Fibro Test, can be estimated, or transient elastography (Fibro Scan) performed to rule out advanced fibrosis.

Liver Fibrosis Assessment by Non–Invasive Tests

Aspartate aminotransferase (AST)-to-Platelet Ratio Index (APRI) is a simple index for estimating hepatic fibrosis based on a formula derived from AST and platelet concentrations. For the purpose of early initiation of patients on therapy, the cut-off of 2.0 should be considered. Below is the formula to be used to calculate the APRI Score.

$$\text{APRI} = \frac{\frac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelets Count } (10^9)/\text{L}} \times 100$$

NB: In this formula the platelet count is expressed in 1000 of platelets per microliter. If the patient has 137,000 platelets per microlitre, then you use 137 as the denominator in the formula.

An online calculator can be found at: http://www.hepatitisc.uwedu/page/clinical-calculators/apri

Table 4.2: Interpretation of APRI Score

APRI Value	Interpretation	Action
≥1	High Probability (94%) of Cirrhosis (F4) or Risk of Advanced Fibrosis	Prioritize for treatment
0.5-1	Risk of Advanced Fibrosis	Consider for treatment
<0.5	Less risk of significant Fibrosis	Monitor and/or delay treatment

Fibrosis Index Based on 4 factors (FIB-4) is a simple index for estimating hepatic fibrosis based on a formula utilizing 4 factors: age, AST level, platelet count, and ALT level. The formula for calculating this index is shown below:

$$\text{FIB-4} = \frac{\text{Age (yrs.)} \times \text{AST level (IU/L)}}{\text{Platelets Count } (10^9/\text{L}) \times \sqrt{\text{ALT(IU/L)}}}$$

Table 4.3: Interpretation of FIB-4 index

FIB-4 Value	Interpretation	Action
< 1.3	Advanced fibrosis excluded	Monitor. Check other parameters
1.3 – 3.24	Possible fibrosis	Consider for treatment
≥ 3.25	Advanced fibrosis present (F3, F4)	Prioritize for treatment

Fibro Scan: An ultrasound device that uses transient elastography to assess liver shear wave velocity. This is converted to equivalent liver stiffness measured in kilopascals (KPa) and this correlates with the liver fibrosis stage. A fibro scan value of ≥ 12.5Kpa is diagnostic of cirrhosis (F4).

Liver biopsy:

Liver biopsy has been used to ascertain the degree of necroinflammation and fibrosis and to help guide the decision to treat. There are several established methods of scoring histology and measuring activity (grading of necroinflammation) separately from staging (fibrosis). However, limitations of biopsy include sampling error, subjectivity in reporting, high costs, the risks of complications, discomfort to the patient, and the need for training and infrastructure in Low- and Middle-Income Countries (LMICs). The pathological features of CHB on liver biopsy depend upon the stage of the disease, host immune response, and degree of virus replication.

Liver biopsy findings should be categorized into mild, moderate, or severe chronic necroinflammation or, better still, semi-quantitatively scored by a scoring system like the Knodell Histological Activity Index (HAI). Comments about the degree of fibrosis should also be included using the METAVIR system.

Recommendation:

To be done by a Specialist.

4.2.3 Evaluation for Antiviral Therapy in HBV infection

Who to treat

Recommendation:

- As a priority, all adults, adolescents, and children with CHB and clinical evidence of compensated or decompensated cirrhosis (or cirrhosis based on **APRI score ≥1, or FIB-4 index ≥ 3.25** in adults) should be treated, regardless of ALT levels, HBeAg status or HBV DNA levels.
- Treatment is recommended for adults with CHB who do not have clinical evidence of cirrhosis (or based on **APRI score < 1, or FIB-4 index ≥ 3.25** in adults), but are aged more than 20 years, and have persistently abnormal ALT levels and have evidence of high-level HBV replication (HBV DNA >20,000 IU/mL), in HBeAg positive patients.
- Treatment is recommended for HBeAg negative patients with serum HBV DNA ≥ 2,000IU/ml

- Treatment should be considered based on persistently abnormal ALT levels alone, regardless of HBeAg status, in the absence of other known causes of elevated ALT.
- HBsAg positive patients with a positive family history of liver cancer should be treated irrespective of other parameters.

Who not to treat but continue to monitor

Recommendation:

- Antiviral therapy is not recommended and can be deferred in persons without clinical evidence of significant fibrosis (or based on **APRI score <1, or FIB-4 index < 1.3** in adults), or fibro scan score <11Kpa where available and with persistently normal ALT level and low levels of HBV replication (HBV DNA <2000 IU/mL), regardless of HBeAg status provided the person does not have family history of liver cancer.
- Treatment can be deferred in HBeAg positive persons aged 20 years or less and persistently normal ALT levels except in healthcare workers who are in contact with patients.
- Continued monitoring is necessary for all persons with CHB, but in particular, those who do not currently meet the above-recommended criteria for who to treat or not to treat, to determine if antiviral therapy may be indicated in the future to prevent progressive liver disease. These include persons without cirrhosis aged 20 years or below, with HBV DNA levels >2000 IU/ mL but persistently normal ALT.

4.3 TREATMENT OF CHRONIC HEPATITIS B VIRUS INFECTION

4.3.1 Goals of Treatment

Short term goals

- To achieve undetectable HBV DNA levels
- To achieve HBeAg seroconversion and development of anti-HBe

Medium term goals

- To normalize serum ALT
- To achieve HBsAg loss and development of anti-HBs

Long term goals

- To prevent liver disease progression to cirrhosis, liver failure, and liver cancer
- To prevent mortality and reduce the need for transplant
- To improve quality of life

4.3.2 Pre-treatment Counselling

To improve adherence, it is important that patients or their caregivers are fully informed in simple terms about the following:

1. The health implications of chronic HBV infection – liver failure, cirrhosis (hardening /scarring of the liver), liver cancer
    a. The chronic nature of the disease – monitoring and treatment may be lifelong.
    b. The possibility that the spouse(s), children, and close relatives may be infected as well as the need to screen and protect them if uninfected.
    c. The need to avoid further health risks such as alcohol, herbal concoctions, aflatoxins (mouldy foods), multiple sexual partners, tattooing, and scarification marks (to avoid the risk of co-infections).
2. The financial implications of treatment options in relation to the desired goals of treatment.
3. Potential side effects of the treatment options should be discussed.
4. The objectives and likely outcomes of treatment should be discussed in terms of virological response, normalization of liver functions, and prevention of further liver damage.

Refer to section 6.2 on the 5 Cs of viral hepatitis management.

4.3.3 HBV Treatment Recommendations

- In all adults, adolescents, and children aged 12 years and above, in whom antiviral therapy is indicated, the nucleos(t)ide analogues (NAs) which have a high barrier to drug resistance are recommended.
- The preferred drug of choice is Tenofovir with Entecavir as an alternative. Both Tenofovir Diproxil Fumarate (TDF) and Tenofovir Alafenamide (TAF) are recommended for use in adults and children ≥12 years.
- In patients with renal impairment, TDF should be avoided. TAF is the preferred choice.
- Entecavir is only recommended in children aged 2-11 years or those who cannot tolerate Tenofovir.
- **Pegylated interferon therapy is not recommended for first-line treatment.** However, it can be used in patients for finite treatment who have the following parameters:
    - Viraemia of HBV DNA < 10^7 IU/ml
    - Elevated serum ALT (> 1x upper limit of normal)
    - Young patients aged ≤ 35 years (it is also approved for use in children aged ≥ 2 years)
- Pegylated interferon is contraindicated in decompensated cirrhosis
- Nucleos(t)ide analogues (NAs) with a low genetic barrier to resistance (lamivudine, adefovir & Telbivudine) can lead to drug resistance and are not recommended.
- ***Conventional interferon is no longer recommended*.**

TABLE 4.4 Profile of HBV treatment options

Treatment Option	Resistance Barrier	Dose	Duration	Route	Indication	Remarks
Tenofovir Diproxil Fumarate (TDF)	Low risk of resistance	300mg daily	Life-long, or until loss of HBsAg/HBeAg positivity	Per oral	High viral load	Watch out for nephrotoxicity
Tenofovir Alafenamide (TAF)	Low risk of resistance	25mg daily	Life-long, or until loss of HBsAg/HBeAg positivity	Per oral	High viral load	Low risk of nephrotoxicity and bone toxicity
Entecavir	Low risk of resistance	0.5mg daily Lamivudine naïve 1mg daily Lamivudine experienced Patients >16kg should use the adult dose >30kg: 0.45mg >20kg: 0.30mg >10kg: 0.15mg	Life-long, or until loss of HBsAg/HBeAg positivity	Per oral	High viral load	May be used in place of TDF
Pegylated Interferon alpha-2a	Low risk of resistance	180 µg weekly	48 weeks	**SC	Medium viral load High ALT	High incidence of side effects, Higher HBsAg loss

****TAF = Tenofovir Alafenamide. TAF has a longer plasma half-life and greater stability than TDF. It has comparable HBV DNA suppression and efficacy to TDF. It has much less nephrotoxicity and is safer in chronic kidney disease (CKD) patients. Also, decreased bone mineral density sometimes seen with TDF therapy does not usually occur with TAF.***

****SC = Sub-cutaneous***

4. 4 MONITORING AND FOLLOW-UP

The success of therapy is dependent on appropriate baseline investigations and patient monitoring for desirable clinical outcomes and reduced risk of harm to the patient.

In addition to investigations for evaluation, the baseline investigations to initiate therapy for CHB should include:

- Serum Electrolytes, Urea, and Creatinine for all patients
- HIV screening
- Exclusion of non-viral causes of liver disease if suspected (e.g., liver scan)

- Pregnancy test
- Psychiatric assessment (especially for pegylated interferon therapy)
- HDV test (if available)

The monitoring tests and the frequency for patients on nucleos(t)ide analogue and interferon therapy can be found in tables 4.5 and 4.6 respectively.

Table 4.5 Treatment monitoring for CHB (Nueclos(t)ide analogue therapy)

BASELINE	4 WEEKS	12 WEEKS	24 WEEKS	48 WEEKS	ANNUALLY	REMARKS
HBV viral load		+			+	Monitor annually subsequently (if available)
ALT	+	+	+			Every 6 months
Serum Urea, Creatinine & electrolytes	+	+	+			Every 6 months
HBsAg test					+	Annual monitoring until HBsAg loss
HBeAg test			+			Annual monitoring

Table 4.6 Treatment monitoring for CHB (Peg-interferon Therapy)

BASELINE	4 WEEKS	8 WEEKS	12 WEEKS	24 WEEKS	48 WEEKS	18 MONTHS	REMARKS
HBV viral load			+	+	+	+	(End of monitoring for Interferon)
ALT	+	+	+				Treatment completed
Psychiatric assessment							As the need arises
WBC & Platelet count	+	+	+	+	+	+	Treatment completed
Thyroid function				+	+		Treatment completed
HBsAg test				+	+	+	Check annually
HBeAg							Baseline & post-treatment

ALT = alanine aminotransferase *WBC = white blood count*

Table 4.7 Treatment endpoints/indices of CHB (Nucleos(t)ide analogue / Peg-interferon Therapy)

AGENTS	DURATION OF TREATMENT	
	HBeAg positive	HBeAg negative
Nucleos(t)ide Analogues	6-12 months after HBeAg seroconversion, undetectable serum HBV DNA and appearance of anti-HBe	Until HBsAg loss and the development of Anti-HBs
Pegylated Interferon	Sustained immunological control, HBeAg seroconversion. Stop treatment at 48 weeks, if no response, consider Nucleos(t)ide Analogues	Stop treatment at 48 weeks, sustained immunological control, and loss of HBsAg

4.5 MANAGEMENT OF COINFECTIONS / COMORBIDITIES

HBV, HIV, and HDV share similar transmission routes. In general, concurrent, or sequential infection with these viruses usually results in more severe and progressive liver disease, and a higher incidence of cirrhosis, HCC, and mortality.

HBV-HIV Co-infection

HIV coinfection has a profound impact on almost every aspect of the natural history of HBV infection based on available data. The consequences include higher rates of chronicity after acute HBV infection, higher levels of HBV replication and rates of reactivation, less spontaneous clearance, higher rates of occult HBV (i.e., detectable HBV DNA positivity in the absence of HBsAg seropositivity), more rapid progression to cirrhosis and HCC, higher liver-related mortality, and decreased treatment response compared with persons without HIV coinfection. Also, liver disease has been found to be a leading cause of death in HIV-infected persons coinfected with either hepatitis B or C, as mortality due to other HIV-related conditions has declined following the introduction of antiretroviral therapy (ART). Coinfection with HBV also can lead to increased progression to AIDS-related outcomes and all-cause mortality.

Therapy: Simultaneous treatment for both diseases; treatment should include drugs effective for both conditions and these include tenofovir+emtricitabine, in combination with non-nucleoside reverse transcriptase inhibitor or protease inhibitor.

HBV-HDV Co-infection

Patients who are anti-HDV antibody positive should undergo a Nucleic Acid Test (NAT) for detecting HDV RNA and active (viraemic) infection. Severe or fulminant hepatitis is more frequently observed in HBV/HDV coinfection compared to HBV mono-infection. Two major types of HDV infection are seen. In acute coinfection, persons are infected simultaneously

with both HBV and HDV, leading to mild-to-severe or even fulminant hepatitis. Recovery is usually complete and chronic infection is rare (around 2%). In superinfection, there may be HDV superinfection of a person who already has CHB, leading to a more severe disease course and accelerated progression to cirrhosis in all ages including children, with occurrence of complications almost a decade earlier. However, all cases of HBV-HDV coinfection should be referred for specialist care.

Therapy: Treatment is with Pegylated Interferon for 48 weeks

HBV-Tuberculosis Co-infection

Groups at increased risk of infection with HBV are also at risk of infection with TB, largely because they live in regions of the world that are endemic for both infections. This can pose a particular challenge for clinical management and warrants extra clinical vigilance. PWID and inmates have a high risk of acquiring HBV and HCV and are also at increased risk of coinfection with TB. In the absence of a cough, weight loss, fever, and night sweats, active TB can be confidently ruled out. Otherwise, further investigations for TB and other disease would be recommended. Drug-induced liver injury with elevation of aminotransferases is three to six-fold higher in persons co-infected with HBV, HCV, or HIV who are receiving anti-TB drugs, due to hepatotoxicity with isoniazid, rifampicin, and pyrazinamide. Patients co-infected with TB should have anti-TB therapy first before commencing anti-viral therapy for CHB.

HBV-HCV Co-infection

In HBV-infected persons, HCV coinfection accelerates the progression of liver disease and increases the risk of HCC. In persons with low or undetected levels of HBV DNA where HCV is responsible for the activity of chronic hepatitis in most persons, they should generally receive initial treatment for HCV infection. If there is no access to HCV and HBV viral load measurements, it may be difficult to determine which virus is responsible for abnormal aminotransferases, and treatment of both infections may be required. However, HBV DNA monitoring is necessary as there is a potential risk of HBV reactivation during treatment or after clearance of HCV, which can be treated with NAs.

Therapy: HBV and HCV co-infection may result in an accelerated disease course. In this instance, HCV is considered to be the main driver of the disease. Persons co-infected with HBV and HCV can be treated with antiviral therapy for HCV. SVR rates are similar to those of HCV mono-infected persons. After HCV clearance, there is a risk for HBV reactivation and this may require treatment with anti-HBV antiviral therapy.

HBV and Anti-Cancer Chemotherapy

Patients with HBV infections who receive anti-cancer chemotherapy are at risk of HBV reactivation during and after the completion of chemotherapy. The consequences of HBV reactivation range from self-limited conditions to fulminant hepatic failure and death. HBV reactivation also leads to premature termination of chemotherapy or delay in treatment

schedules. Pre-emptive antiviral therapy for HBsAg-positive patients undergoing chemotherapy is recommended, irrespective of their baseline viral load. Screening for occult/past infections in HBsAg-negative patients is also strongly recommended, especially among lymphoma patients who receive rituximab-based chemotherapy or patients undergoing intensive immunosuppression.

Before commencing chemotherapy or steroids, every patient should be screened for HBsAg/anti-HBc as HBV infection may flare on starting treatment. HBsAg positive patients should be started on oral nucleos(t)ide analogues one week before commencement of chemotherapy and continued for 6 months after stopping chemotherapy.

CHAPTER 5 - MANAGEMENT OF HEPATITIS C VIRUS INFECTION

The majority (80%) of HCV infections progress to Chronic Liver Disease (CLD). Outcomes vary widely from subclinical infection to End Stage Liver Disease (ESLD). Those patients with HCV-related ESLD developed liver cancer at the rate of 2-4% per year. The more advanced the liver fibrosis, the more severe the disease outcomes. Management of HCV infection requires a comprehensive strategy to prevent and control HCV infection and related chronic liver disease.

5.1 GOALS OF MANAGEMENT

The general goals of management include the following:

- To achieve a sustained virologic response (SVR) or cure where possible
- To prevent liver disease progression to cirrhosis, liver failure, and hepatocellular carcinoma (HCC)
- To prevent transmission of HCV infections
- To improve quality of life

5.2 DIAGNOSIS OF HCV INFECTION

5.2.1 Screening

Detection of HCV antibodies is the first step to diagnosis. Screening is conducted on whole blood, serum, plasma, or oral fluid specimen, using rapid test or Enzyme Immunoassay (EIA) kits that are approved by NAFDAC and other stringent regulatory authorities (FDA, WHO).

Who to screen:

- Persons with a history of blood or blood products transfusion or organ transplant
- Persons Who Inject Drugs (PWID)
- People in custodial centres (PICC), other closed settings, and persons with a history of incarceration
- Persons with a history of haemodialysis
- Infants born to HCV positive mothers
- Contacts of HCV infected persons
- Health care workers especially those with known history of needle sticks/sharps exposure
- Clinical evidence of chronic liver disease or abnormal liver enzyme tests
- Persons living with HIV (PLHIV)
- Persons positive for HBV
- Persons with sexually transmitted diseases
- Pregnant women at ANC
- Patients with tattoos, scarification marks, or other local surgical procedures
- Men who have Sex with Men (MSM), Sex Workers (SWs)

- Survivors of sexual assault and Gender Based Violence (GBV)
- Law enforcement and Emergency personnel, e.g., Federal Road Safety and NEMA Officers who evacuate road traffic accident and disaster victims
- Other occupational groups who handle knives and sharps as part of their job, e.g., butchers

Rapid Diagnostic Tests

Refer to chapter 4, section 4.2.1 for details related to Rapid Diagnostic Tests (RDTs). However, apart from the use of blood, serum, or plasma, there is now a new RDT that makes use of oral fluid specimen for self-testing known as HCV Self Testing (HCVST).

HCV Self Testing (HCVST)

HCV self-testing (HCVST) refers to a testing approach where individuals can test themselves for hepatitis C virus (HCV) antibodies using oral or blood samples. HCVST is an additional approach to HCV testing services designed to increase testing uptake and improve access to care and treatment for HCV, especially among populations that may face barriers to accessing traditional testing services. HCVST has been found to be acceptable, feasible, and cost-effective among key populations in various settings. HCVST offers several advantages over facility-based testing approaches including increased privacy, convenience, and ease of use, and studies have shown that it is acceptable, feasible, and cost-effective among key populations. HCVST has the potential to improve testing rates and access to care and treatment for HCV, however community engagement is crucial to ensure the effectiveness and sustainability of HCVST programmes.

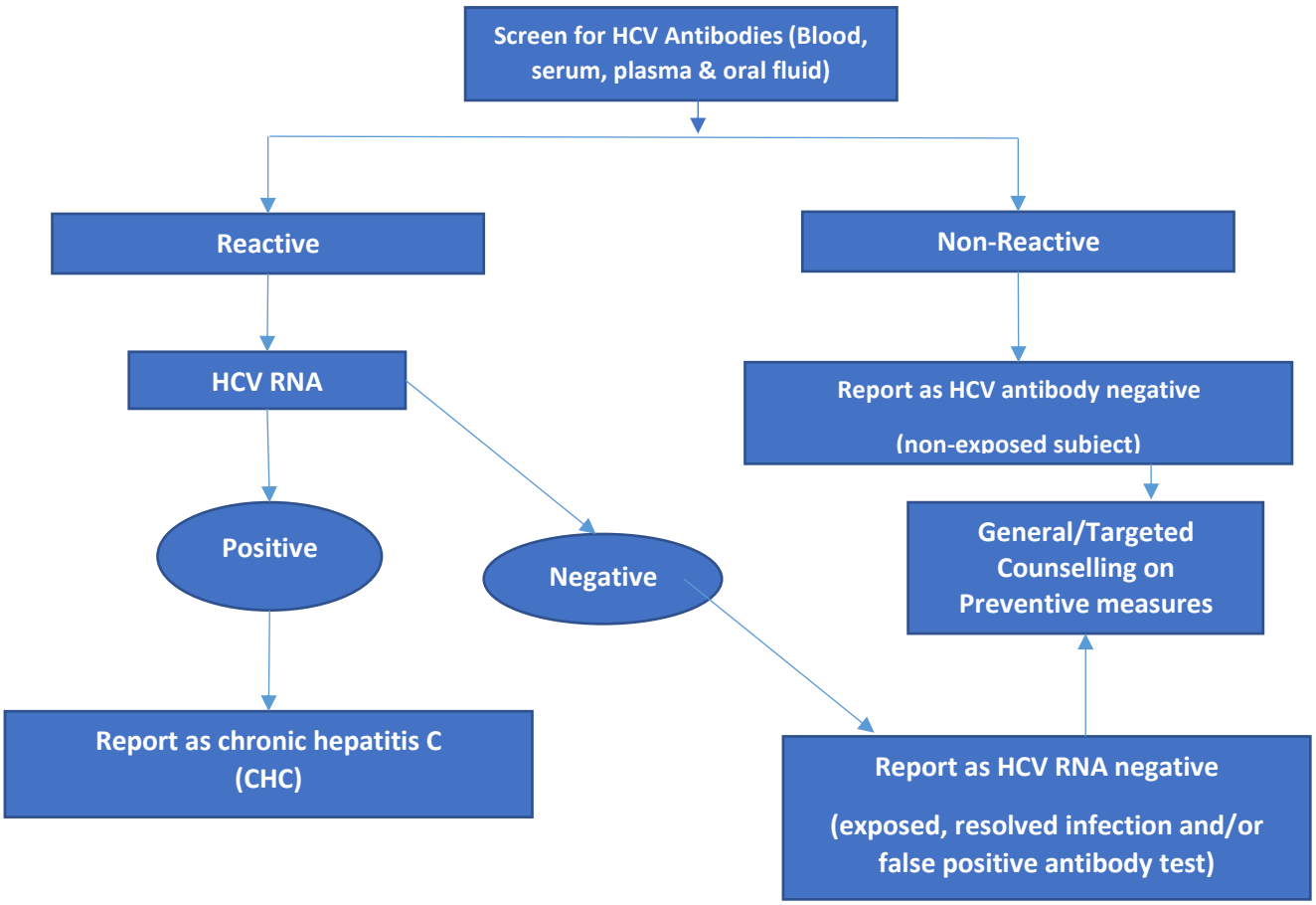


Figure 5.1: Algorithm for the screening and diagnosis of HCV Infection

5.2.2 CONFIRMATION OF HCV INFECTION (VIROLOGIC EVALUATION OF HCV INFECTION)

Approximately 15–45% of persons who are infected with HCV will spontaneously clear the infection and not develop a chronic infection. These persons are HCVAb seropositive but no longer infected with HCV. A nucleic acid test (NAT) for HCV RNA, which detects the presence of the virus, is needed to distinguish persons with chronic HCV infection from those who have cleared the infection. NAT for HCV RNA is important prior to commencing and after treatment to assess treatment response. NAT can include RNA quantitative or qualitative testing for the detection of HCV RNA and should be performed directly following a positive HCV serological test to establish the diagnosis of chronic HCV infection.

HCV RNA Genotyping

There are six HCV genotypes (Genotypes 1-6). HCV RNA genotyping is no longer compulsory for confirmed HCV positive patients before starting treatment. However, in cases of resistance requiring retreatment, genotyping should be done.

5.3 ASSESSMENT OF LIVER DISEASE

5.3.1 Clinical Evaluation

Detailed history and physical examination of patients are required. Alcohol, drugs (including herbal remedies), and history of other risk factors are evaluated. Physical examination is conducted to evaluate for features of decompensated liver disease such as jaundice, hepatomegaly, splenomegaly, and GI bleeding. There is a need to exclude MASLD caused by obesity, type II diabetes mellitus, dyslipidaemia, and gastric by-pass surgery. In this case, anthropometric measurements such as Body Mass Index (BMI), waist-hip ratio, weight-for-age, and weight-for-height Z score for children can be carried out. The presence of ascites is highly suggestive of decompensated liver cirrhosis. These patients should be considered for treatment prioritization and referred for specialized care.

5.3.2 Assessment of hepatic injury/severity

1. Liver enzymes and other tests of liver function:

Liver enzymes to be evaluated include aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP). Other tests of liver synthetic function and/or portal hypertension include serum albumin, bilirubin, platelet count, and prothrombin time. A progressive decline in serum albumin concentrations, rise in bilirubin, ALT, AST, ALP, and prolongation of the prothrombin time are characteristically observed as decompensated cirrhosis develops. Where MASLD is suspected, additional investigations such as fasting lipid profile, fasting blood sugar, and glycated haemoglobin (HbA1c) should be carried out.

2. Haematological test:

Full blood count (including platelets count) and test of coagulation such as Prothrombin Time and International Normalized Ratio (INR) are useful to evaluate liver disease

3. Liver Imaging:

This is to evaluate hepatic parenchyma, and adnexa to detect possible intra-hepatic masses.

- **Ultrasound scan**: This should be the first imaging technique to be used in evaluating patients with chronic hepatitis C as it may demonstrate evidence of advanced liver disease or comorbidity (e.g. fatty liver disease).
- **CT scan**: Applicable where ultrasound result is non-specific

4. Non-invasive tests (NITs) for Liver Fibrosis Assessment

Non-invasive methods for assessing the stage of liver disease are supplanting liver biopsy and have been validated in adults with chronic HCV. Non-invasive tests of liver fibrosis such as APRI and FIB-4, as well as commercial markers such as Fibro Test can be determined, or transient elastography (Fibro Scan) is performed to rule out advanced fibrosis.

APRI Score:

Aspartate aminotransferase(AST)-to-Platelet Ratio Index (APRI) is a simple index for

estimating hepatic fibrosis based on a formula derived from AST and platelet concentrations. For the purpose of early initiation of patients on therapy, the cut-off of 1.0 should be considered. APRI and FIB-4 scores are easily calculated using standard clinical labs. Below is the formula to be used for APRI Score:

$$APRI = \frac{\frac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelets Count } (10^9)/L} \times 100$$

NB: In this formula, the Platelets Count is expressed in thousands of platelets per microliter.

So, if a patient has 137,000 platelets/µl, we would use 137 as the denominator of the formula.

ALT - alanine aminotransferase IU - international unit

AST - aspartate aminotransferase ULN - upper limit of normal

An online calculator can be found at: http://wwwhepatitisc.uw.edu/page/clinical- calculator/APRI

Table 5.1: APRI Score Interpretation

APRI Value	Interpretation	Action
>2	High Probability (94%) of F4 Cirrhosis	Place on liver cancer surveillance after treatment*
1 – 2	Risk of Advanced Fibrosis	
0.6 - <1	Reduced Risk of Advanced Fibrosis	Treat. Liver cancer surveillance not required
≤0.5	*Less risk of significant Fibrosis*	

**Monitor with Alpha feto protein and ultrasound every 6 months*

Fibrosis Index Based on 4 factors (FIB-4): is a simple index for estimating hepatic fibrosis based on a formula utilizing 4 factors: age, AST level, platelet count, and ALT level. The formula for calculating this index is shown below:

$$FIB\text{-}4 = \frac{\text{Age (yrs.) x AST level}}{\text{Platelets Count x } \sqrt{\text{ALT}}}$$

Table 5.2: Interpretation of FIB-4 index

FIB-4 Value	Interpretation	Action
< 1.3	*Advanced fibrosis excluded*	*Treat. Liver cancer surveillance not required*
1.3 – 3.24	*Possible fibrosis*	
≥ 3.25	*Advanced fibrosis present (F3, F4)*	*Place on liver cancer surveillance after treatment**

**Monitor with Alpha feto protein and ultrasound every 6 months*

Table 5.3. Low and High cut-off values for the detection of significant fibrosis and cirrhosis

	APRI (low-cut off)	APRI (high cut-off)	FIB4 (low cut-off)	FIB4 (high cut-off)	Transient elastography (Fibroscan)
Significant fibrosis (METAVIR ≥ F2)	*0.5*	*1.5*	*1.45*	*3.25*	*7-8.5kPa*
Cirrhosis (METAVIR F4)	*1.0*	*2.0*	*-*	*-*	*11-14kPa*

kPa- ***Kilopascal, APRI- Aminotransferase platelet ratio index***

APRI ***>1.5 has been associated with advanced fibrosis (METAVIR F3);***

APRI ***>2.0 has been associated with cirrhosis (METAVIR F4) in the setting of chronic HCV infection.***

FIB-4 >3.25 has been associated with advanced fibrosis (METAVIR F3-F4) in the setting of chronic HCV infection.

5. Liver biopsy

Liver biopsy has been used to ascertain the degree of necroinflammation and fibrosis and to help guide the decision to treat. There are several established methods of scoring histology and measuring activity (grading of necroinflammation) separately from staging (fibrosis).

Limitations of biopsy include sampling error, subjectivity in reporting, high costs, the risks of complications, discomfort to the patient, and the need for training and infrastructure in LMICs. Liver biopsy findings should be categorized into mild, moderate, or severe chronic necroinflammation.

Using the METAVIR group scoring system:
Fibrosis is staged on a scale of F0 to F4, as follows:
F0 = no fibrosis.
F1 = portal fibrosis without septa.
F2 = few septa (moderate fibrosis).
F3 = numerous septa without cirrhosis (advanced fibrosis).
F4 = cirrhosis.

Significant fibrosis is defined by the presence of F2, F3, and cirrhosis by F4.

5.4 ANTIVIRAL THERAPY

Antiviral therapy is the cornerstone for the treatment of chronic HCV infection. The arrival of new antiviral therapies has led to a high rate of Sustained Virologic Response (SVR) in almost all patients.

5.4.1 Goal of Antiviral Therapy

The goal of antiviral therapy in patients with chronic HCV is the eradication of HCV RNA, which is predicted by the attainment of SVR. SVR is defined as aviraemia 12 or 24 weeks after completion of antiviral therapy. An SVR confers a 97% to 100% chance of remaining HCV RNA negative during long-term follow-up and can therefore be considered a virologic cure for HCV infection. SVR has been associated with a decrease in all-cause mortality, liver-related death, need for liver transplantation, hepatocellular carcinoma, and liver-related complications even among those patients with advanced liver fibrosis.

5.4.2 Evaluation for Antiviral Therapy in HCV Infection

All patients with HCV infection (confirmed with HCV RNA) should be treated.

Pre-treatment Counselling

To improve adherence, HCV counselling before the commencement of HCV treatment should include:

1. The health implications of chronic HCV infection (liver failure, cirrhosis, liver cancer)
2. The chronic nature of the disease – monitoring may be lifelong
3. The possibility that spouse(s), children, and close relatives may be infected and the need to screen and provide health education on how to protect themselves if uninfected
4. The need to avoid further health risks such as alcohol, herbal concoctions, aflatoxins (mouldy foods), multiple sexual partners, tattooing, and scarification procedures (to avoid the risk of co-infections and possibly re-infection)
5. The financial implications of treatment options in relation to the desired goal of treatment
6. The potential side effects of treatment options
7. The objectives and likely outcomes of treatment regarding virologic response, normalization of liver function, prevention/reduction in the risk of further liver damage and liver cancer
8. The potential drug-drug or drug-food interactions (see Chapter 7)

Refer to section 6.2 on the 5 Cs of viral hepatitis management.

5.4.3 Treatment Options

Direct Acting Antivirals (DAAs) have revolutionized HCV treatment and improved treatment outcomes. However, antiviral resistance may occur in rare instances. Pan-genotypic DAA regimens are widely recommended as they provide high efficacy across all genotypes, have excellent safety profiles, and are administered orally.

Because of their virological efficacy, ease of use, safety and tolerability, interferon (IFN)-free, ribavirin-free properties, pan-genotypic DAA-based regimens – sofosbuvir/daclatasvir (SOF/DCV), sofosbuvir/velpatasvir (SOF/VEL), glecaprevir/pibrentasvir (GP) or sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX) – are the recommended options in HCV-infected patients without cirrhosis and in those with compensated (Child-Pugh A) cirrhosis, including "treatment-naïve" patients (defined as patients who have never been treated for their HCV infections) and "treatment-experienced" patients (defined as patients who were previously treated with anti-HCV medications but did not achieve SVR).

The following oral pangenotypic regimens are recommended for the treatment of patients infected with HCV:

1. A combination of sofosbuvir and velpatasvir, administered once daily
2. A combination of sofosbuvir and daclatasvir, administered once daily
3. A combination of glecaprevir and pibrentasvir, administered once daily with food
4. A combination of sofosbuvir, velpatasvir, and voxilaprevir, in a single tablet administered once daily with food

The only information needed to start treatment with either sofosbuvir/velpatasvir or glecaprevir/pibrentasvir in patients without cirrhosis or with compensated (Child-Pugh A) cirrhosis, including treatment-naïve or treatment-experienced patients (as defined above), is the presence of HCV viraemia (as assessed by HCV RNA or HCV core antigen testing).

Interferon-based regimens are no longer recommended as their usage is characterized by significant adverse events (flu-like syndrome, anaemia, pancytopenia, etc.), long treatment duration and lower efficacy rates.

Table 5.4: Existing HCV Medicines and Dosage

Product	Presentation	Dosage
Sofosbuvir (SOF)	400mg tablets	One tablet daily (morning)
Ledipasvir (LDV)	90mg tablets	One tablet daily (morning)
Velpatasvir (VEL)	100mg tablets	One tablet daily (morning)
Glecaprevir (G)	100mg tablets	Three tablets taken daily
Pibrentasvir (P)	40mg tablets	Three tablets taken daily
Voxilaprevir (VOX)	100 mg tablets	One tablet daily (morning)
Daclatasvir (DCV)	30 or 60mg tablets	One tablet daily (morning)

The choice of HCV treatment regimen should be individualized based on the efficacy of treatment and response. However, for a public health approach, a simplified regimen with

limited side effects, good efficacy, and an oral route of administration is recommended. Tables 5.5 to 5.7 provide guidance on the treatment regimens and doses recommended for children, adolescents, and adults.

Table 5.5. Preferred regimens for the Treatment of Hepatitis C

Regimen	Features	Major Contraindications
Sofosbuvir (400mg) / Velpatasvir (100mg)	Highly efficacious (97%) across all genotypes Available as singles or fixed-dose combination	No clinically significant contraindication
Sofosbuvir (400mg)/ Daclatasvir(60mg)	Highly efficacious (95%) across all genotypes, and lower costs Available as singles or fixed-dose combination	No clinically significant contraindication
Sofosbuvir (400mg)/ Ledipasvir (90mg)	Highly efficacious across most genotypes except genotype 3. Available as singles or fixed-dose combination	No clinically significant contraindication
Glecaprevir (100mg) / Pibrentasvir (40mg)	Highly efficacious across all genotypes, well tolerated, short duration of 8-12 weeks, minimum SEs, limited drug interactions Administered in 2 fixed-dose combination tablets containing 300mg of glecaprevir and 120mg of pibrentasvir, administered once daily with food	It is not approved for use in patients with decompensated cirrhosis
Sofosbuvir (400 mg)/ Velpatasvir (100mg)/and Voxilaprevir (100 mg)	*Found effective for retreatment in treatment-experienced patients who did not achieve SVR* *Available as singles or fixed-dose combination*	*No clinically significant contraindication*

Table 5.6 Dosing and duration of DAA regimen in adolescents and adults

Age group	Regimen	Stage	Duration	Dose
Adolescents and adults (12 years & above)	*SOF/DCV	Noncirrhotic	12 weeks	400mg/60mg
		Cirrhotic	24 weeks	400mg/60mg
	SOF/VEL	Noncirrhotic/cirrhotic	12 weeks	400mg/100mg
	SOF/LDV	Noncirrhotic/cirrhotic	12 weeks	400mg/90mg
	G/P	Noncirrhotic/cirrhotic	8 weeks	300mg/120mg

* SOF = Sofosbuvir, DCV = Daclatasvir, VEL = Velpatasvir, LDV = Ledipasvir, G= Glecaprevir, P = Pibrentasvir

Table 5.7 Dosing and duration of DAA regimen in children 3 – <12 years of age

Regimen	Weight band	Stage	Duration	Dose
*SOF/DCV	≥26kg	Noncirrhotic	12 weeks	400mg/60mg
		Cirrhotic	24 weeks	400mg/60mg
	14-25kg	Noncirrhotic	12 weeks	200mg/30mg
		Cirrhotic	24 weeks	200mg/30mg
SOF/VEL	≥30kg	Noncirrhotic/cirrhotic	12 weeks	400mg/100mg
	17-29kg			200mg/50mg
	<17kg			150mg/37.5mg
SOF/LDV	≥ 35kg	Noncirrhotic/cirrhotic	12 weeks	400mg/90mg
	17-35kg			200mg/45mg
	<17kg			100mg/33.75mg
G/P	≥45kg	Noncirrhotic/cirrhotic	8 weeks	300mg/120mg
	30-45kg			250mg/100mg
	20-30kg			200mg/80mg
	<20kg			150mg/60mg

* SOF = Sofosbuvir, DCV = Daclatasvir, VEL = Velpatasvir, LDV = Ledipasvir, G= Glecaprevir, P = Pibrentasvir

Retreatment

Several real-world studies assessing the efficacy of the triple combination of sofosbuvir, velpatasvir, and voxilaprevir in the retreatment of DAA-containing regimen failures confirmed the high SVR rates achieved with this regimen, regardless of patient gender, body mass index, HCV genotype, and baseline HCV RNA[10]. The only pre-treatment parameter associated with a slightly lower SVR rate was cirrhosis. Thus, the triple combination of sofosbuvir, velpatasvir, and voxilaprevir appears as the treatment of choice for retreatment of patients who failed to achieve SVR after an IFN-free, DAA-based treatment course. Refer non-responders to Specialists.

5.5 MONITORING AND FOLLOW-UP

5.5.1 Treatment Monitoring

Direct Acting Antivirals

Monitoring is not generally required because DAA regimens are much better tolerated by

[10] Stefan Z, M.D, *et al*. Glecaprevir–Pibrentasvir for 8 or 12 Weeks in HCV Genotype 1 or 3 Infection, 2018.

patients, as they have fewer adverse events and are less likely to be discontinued early.

Recommendations:
Laboratory treatment monitoring is not generally required when using all-oral regimen, except in renal impaired patients who should be in specialist care where they can be provided specialized monitoring such as estimated Glomerular Filtration Rate (eGFR).

5.5.2 Confirmation of Efficacy

Confirmation of SVR can be done with qualitative or quantitative nucleic acid test (NAT) post-treatment to evaluate virologic response to therapy.

DAA Regimens: Testing at 12 weeks post-treatment (SVR12) or 24 weeks post-treatment (SVR24).

Patients who do not achieve SVR should be referred to a Specialist and evaluated for re-treatment. After achieving cure, there remains a possibility of re-infection. Patients must be counselled on risk reduction to prevent re-infection.

5.5.3 Post-treatment HCC Surveillance

Surveillance to detect evidence of HCC is an essential part of the care of persons with HCV-related significant hepatic fibrosis (F2, F3) or cirrhosis. Compensated cirrhosis may progress over time to decompensated cirrhosis associated with ascites, oesophageal and gastric varices, and eventually to liver failure, renal failure, and sepsis, all of which are life-threatening. The diagnosis of decompensated liver disease is based on both laboratory and clinical assessment, and therefore a careful medical examination of patients must be made before starting treatment. Persons with cirrhosis (including those who have achieved SVR) should be screened for HCC with a six-monthly ultrasound examination and α-fetoprotein estimation and should have endoscopy every 1-2 years to exclude oesophageal varices.

Fig 5.2: Programmatic Approach to HCV Management

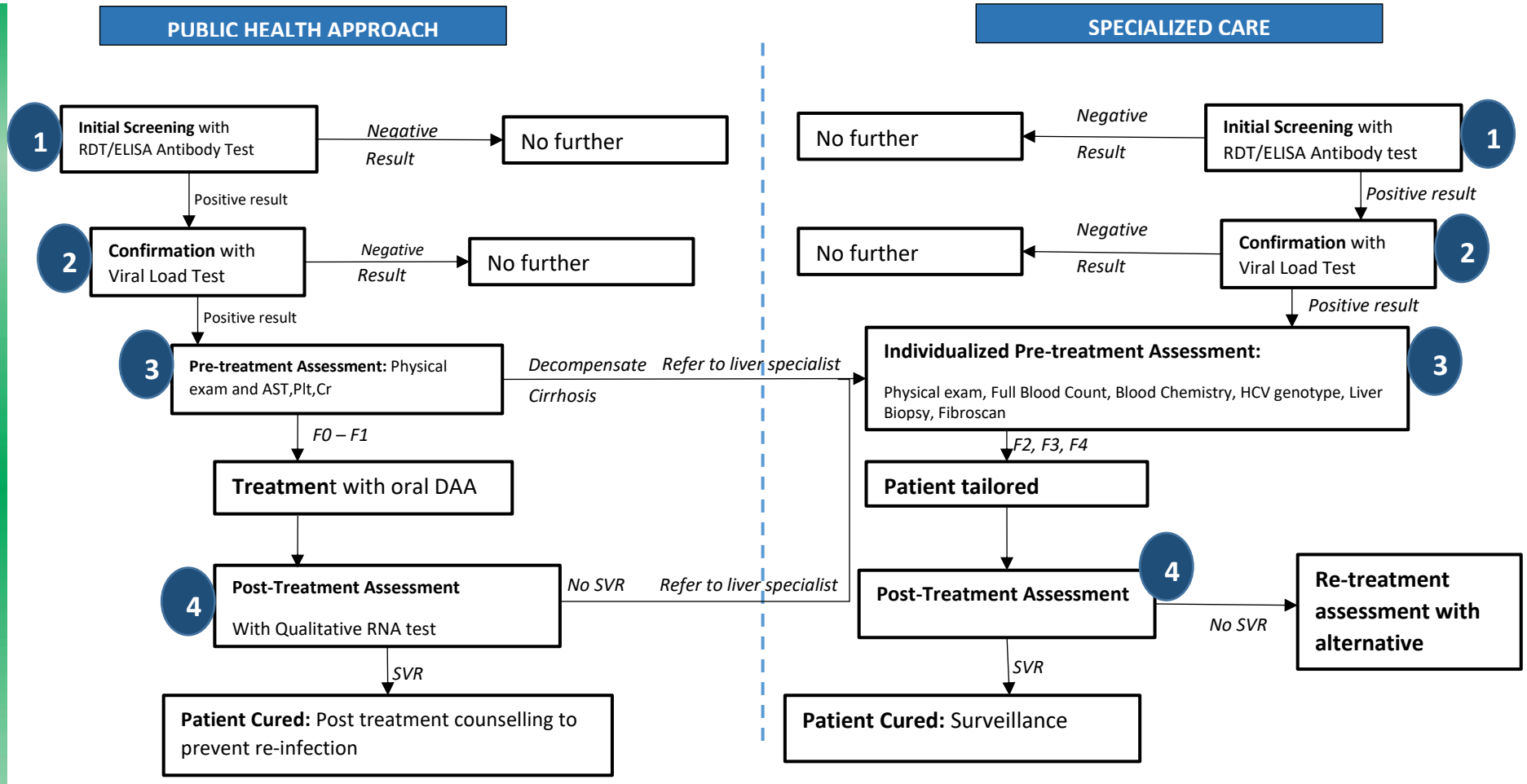


Table 5.8. Implementing the public health approach to HCV therapy

Item	Protocol Section	Specialized Standard of Care Lab Description	Included in public health approach (Yes/No)	Implementation modalities
1	Pre-treatment Screening	Hepatitis C antibody (Serum, oral fluid HCV Ab)	Yes	The HCV Ab test can be performed using an ELISA assay or rapid test. A number of rapid tests are available with differing performance characteristics, such as sensitivity and specificity, which should be considered during the selection of screening tests.
2	Pre-treatment Assessment	Qualitative /quantitative HCV RNA	Yes	Confirmation of chronic HCV infection is required secondary to false positives during initial screening as well as clearance of previous HCV infection. As with screening tests, NAT performance characteristics should be considered in the selection of confirmatory testing platforms.
3	Pre-treatment Assessment	Physical Examination: Pulse, blood pressure, heart rate, cardiac, respiratory, abdominal, and neurological examination	Yes	Physical examination allows for evaluation of advanced liver disease (decompensated cirrhosis) manifested by evidence of bleeding from varices in the stomach or oesophagus, jaundice, ascites (fluid in abdomen), oedema of the lower extremities, and mental changes. Individuals with evidence of decompensated cirrhosis will be referred to a liver specialist for management.
4	Pre-treatment Assessment	HCV Genotype and subtype	No	A pan-genotypic treatment regimen should be adopted.
5	Pre-treatment Assessment	Platelet count	Yes- AST, Platelet Yes- Albumin, Bilirubin, Alkaline Phosphatase, ALT	AST and Platelet allows for calculation of APRI score (AST to Platelet ratio index). Referral to specialists is not required for patients with APRI<1 and no signs of decompensation. However, where there are indications for liver cancer screening for advanced liver disease (ascites, encephalopathy, GI bleeding), referral to specialists is recommended.
6	Post-treatment Assessment at week 24 (End of Treatment + 12 Weeks)	At Week 24 (12 weeks after ending treatment): Qualitative HCV RNA	Yes	Measurement of sustained virological response (SVR) is recommended at 12 weeks post treatment. If there is no HCV detected in the blood 12 weeks after finishing treatment, the patient has achieved SVR 12 and is considered cured.

5.6 MANAGEMENT OF HCV CO-INFECTIONS

HIV and HCV co-infection

Assessment of potential drug-drug interactions is of critical significance in HIV-infected persons who are about to start HCV treatment. Careful consideration of such interactions is important to avoid toxicity and to ensure efficacy of the regimens used to treat both HIV and HCV hence preventing the development of ARV resistance and increase the likelihood of achieving SVR. Preliminary guidance on interactions can be found in Chapter 7 of this Guideline. However, interactions are updated regularly and therefore consultation with a frequently updated database is strongly recommended.

Special Considerations for ART patients:

- Increase daclatasvir dosage to 90mg per day when co-administered with Efavirenz
- Decrease daclatasvir dosage to 30mg per day when co-administered with Atazanavir/Ritonavir
- Decrease daclatasvir dosage to 30 mg per day with the antibiotics - clarithromycin, telithromycin, erythromycin, and the antifungals – ketoconazole, itraconazole, posaconazole, and voriconazole.

HBV and HCV co-infection

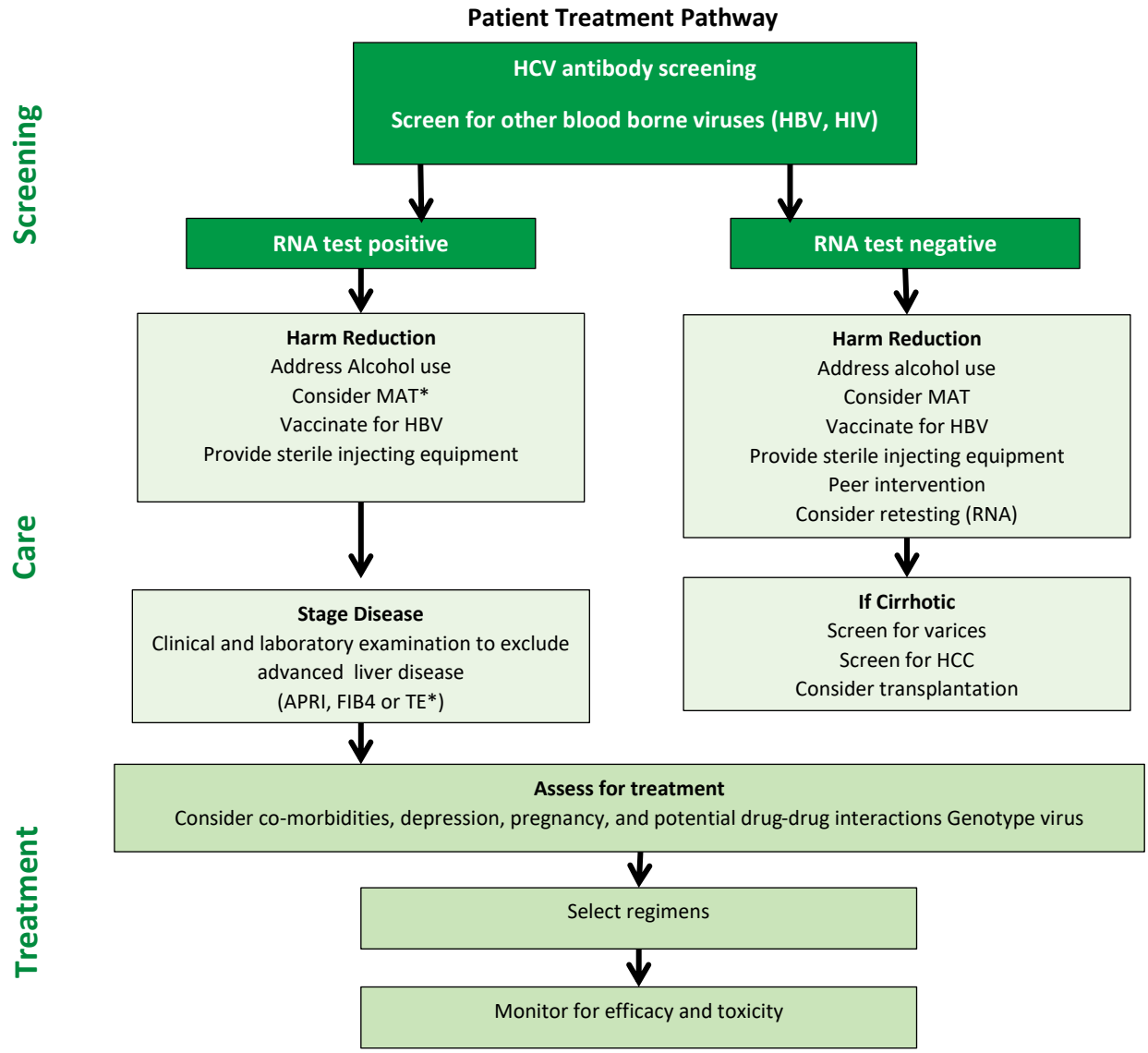
HBV and HCV co-infection may result in an accelerated disease course. In this instance, HCV is considered to be the main driver of the disease. Persons co-infected with HBV and HCV can be treated with antiviral therapy for HCV. Sustained Virological Response (SVR) rates are similar to those of HCV mono-infected persons. After HCV clearance, there is a risk for HBV reactivation, and this may require treatment with anti-HBV antiviral therapy.

TB and HCV co-infection

Severe concurrent infections such as TB should generally be treated before commencing therapy for HCV. ART should be initiated with persons with HIV-associated TB as soon as possible, regardless of CD4 count. There is limited reported data on the co-management of persons co-infected with HCV, HIV, and TB but such cases should be referred for multidisciplinary specialist care as they need specialized clinical judgment in order to reduce the additive side effects, pill burden, and drug-drug interactions.

Persons Who Inject Drugs (PWID)

Persons Who Inject Drugs (PWID) who are at risk for HCV infection should be managed using the treatment pathway below (Figure 5.3).



MAT= Medically Assisted Therapy, TE= Transient Elastography

Figure 5.3: Patient Treatment Pathway for PWID

Persons with renal impairment

All oral DAAs are recommended in this group. However, Glecaprevir/Pibrentasvir is the preferred option.

CHAPTER 6: CARE AND SUPPORT

6.1 Introduction

Care and Support means providing for the socioeconomic and psychosocial needs of people living with viral hepatitis B and C and giving appropriate support to them, their families, and caregivers. Care and Support is a component of the holistic facility-based, multidisciplinary, and patient-centred care for the infected and affected. Adequate counselling and appropriate disclosure to patients are key to achieving optimal patient-centred care. This should be provided both at the facility and community levels. In providing treatment, care and support for clients with viral hepatitis there is a need to adopt the 5 C's approach as listed below:

A. **Consent**: People receiving viral hepatitis screening services should give informed consent to be tested and counselled (verbal consent is sufficient). They should be informed of the process for testing and counselling and of their right to decline testing.

B. **Confidentiality**: Screening for viral hepatitis should be confidential, meaning that what the viral hepatitis screening test provider and the client discuss will not be disclosed to anyone else without the expressed consent of the person being tested. Confidentiality should be respected, but it should not be allowed to reinforce secrecy, stigma, or shame. Counsellors should discuss, among other issues, whom the person may wish to inform and how they would like this to be done. Shared confidentiality with a partner or family members – trusted others – and health-care providers is often highly beneficial.

C. **Counselling**:
Pre-test information may be provided in a group setting, but all people should have the opportunity to ask questions in a private setting. All screening for viral hepatitis must be accompanied by appropriate and high-quality post-test counselling, based on the outcome of the test result.

D. **Correct Test Results**:
Providers of viral hepatitis testing services should strive to provide high-quality testing services using recommended laboratory tests to ensure accurate diagnosis.

E. **Connection with Prevention, Treatment, Care, and Support services**: Linkage to prevention, treatment, and care services should include effective and appropriate follow-up, including long-term prevention and treatment support.

6.2 Components of Care and Support for Viral Hepatitis

6.2.1 Counselling

a. Pre and Post Testing Counselling:

Pre-testing counselling is aimed at ensuring that a client makes a well-informed decision to have

HBV and/or HCV tests conducted or not and prepares the client to accept the possible outcome of the test results. Once the test has been done, the client will receive post-testing counselling.

Post-test counselling is a component of viral hepatitis care that involves educating the client on accepting the test results and adopting a positive lifestyle. During the post-test counselling, the client is also provided with information on the next level of care.

People living with viral hepatitis may experience some mental health challenges, e.g., anxiety and depression, and might benefit from mental health counselling and referral. For adherence counselling see section 6.8 below.

b. Disclosure of Hepatitis Status to Children and Caregivers

Disclosing hepatitis infection status to children is a sensitive issue, which must consider the needs, feelings, age, beliefs, and understanding of the child and caregiver. It must however be done to improve outcomes in the treatment and care of children. The importance of disclosure to children includes:

- Reduction of developing myths about their infection
- Improvement of access to care and support services
- Enhancement of adherence to treatment and coping strategies
- Reduction of the negative psychosocial impact
- Reduction of the risk of transmission

Counselling for disclosure in children

This involves counselling the caregivers to support age-appropriate hepatitis infection status disclosure to the child with minimal negative impact. Parents who decline or fail to disclose to their children should be counselled on the importance of the child knowing his/her status and assisted to do so.

Steps for Counselling hepatitis infected Children and their Families

- Evaluate the child and family for readiness-including the child's age and maturity.
- Ascertain a child's and caregiver's understanding of hepatitis infection
- Explain the benefits of early awareness of hepatitis infection to the child and caregiver/family
- Provide continuous psychosocial support.

6.3 Community sensitization and awareness

Communities should be sensitized on the prevention and control of viral hepatitis. Information, Education, and Communication (IEC) materials should be made available in the communities and appropriate messaging should be adapted from national resource documents.

6.4 Hygiene and Nutritional Support

6.4.1 Proper environmental and personal hygiene should be maintained to prevent opportunistic infections

People with viral hepatitis thrive best on a balanced diet in addition to the recommended therapy and therefore need nutritional support to achieve this. Patients living with viral hepatitis B and C should be counselled on the following:

- The need for adequate intake of energy and protein-rich foods, fruits, and vegetables for micronutrient supplementation
- These micronutrients may enhance the immune status of the patients. They may be found in dark green leafy vegetables, yellow and orange fruits, sweet potatoes, pumpkins, carrots, avocado and tomatoes
- Patients should be counselled against using herbal medicines as the specific treatment for viral hepatitis and other medical conditions
- In a situation where chronic Hepatitis B and/or C has been established, iron supplementation should be discouraged
- Fatty food should be discouraged
- Obesity should be discouraged as steatosis (fatty liver) may worsen the effect of HBV and HCV infections

It is recommended that family members should continually watch over the client and provide a safe and secure environment while encouraging socio-economic activities for the client.

6.4.2 Social Support

Facilities can provide disadvantaged clients with needed support while the client is in the facility and can also help to identify and refer the client to other welfare groups outside the health facility that can help the clients with both material and financial support, including linking them to a Hepatitis Patient Care-group.

6.5 Immunization

Immunization is an effective way of preventing diseases. Immunization should be given according to the national immunization schedule. Adults with HCV infection should have the standard three doses of Hepatitis B vaccine to prevent coinfection with HBV (refer to Chapter 2, table 2.1).

Human Immunoglobulin (HBIG) as a passive immunization should be made available to those exposed to the virus, and who are hepatitis B virus negative.

6.6 Standard Precautions

For details on Standard Precautions to be observed by health workers, refer to Chapter 2, section 2.1. This section deals with its operationalization.

Materials should be provided for the universal precautions. The minimum materials/equipment to be provided include:

- Liquid soap from a dispenser or container
- Running water or a bucket with a tap kept full of clean water or a ladle for dripping, if running water is not available
- Single-use towels (paper towels, or cloth towels that will be used once and laundered). If not available, hands should be air-dried
- SOPs and Job aids to educate personnel on susceptibility to hepatitis virus infection and means of prevention

Medical Waste Management

- This is the collection, processing, recycling, disposal, monitoring, and transport of waste materials. Waste should be properly segregated, well packaged, labelled, disposed, and incinerated through complete burning using higher temperatures (>1000°F). It is mandatory that all waste should be managed properly to prevent viral hepatitis infection.

6.7 Linkages, Networks, and Referral services

Referral is the process by which client needs for treatment, care, and support services are assessed and prioritized, and clients are provided with assistance in accessing such services. Referral should also include proactive actions necessary to facilitate initial contact with treatment, care, and support service providers. Patients who are screened in primary health centres should have access to treatment and more advanced services in secondary and tertiary level facilities.

In a two-way referral system, there ought to be effective communication between healthcare providers at the same or different levels of the health care system. It is obligatory for the referring healthcare providers to refer a patient promptly, in a manner that guarantees efficient, cost-effective, optimal, and quality care for the patient. It also requires the healthcare providers in the receiving hospital/health care facility to refer the patient back after treatment, to the health care facility or physician that initiated the referral in the first instance, with clear feedback on the observed findings, investigations conducted and the treatment given to the patient.

6.7.1 Reasons for referral

Clinical services

These include clinical evaluation and management, monitoring the progression of liver disease, more advanced investigation and monitoring of treatment, and development of Hepatocellular Carcinoma (HCC).

Social/Legal support services

Clients who test positive may require legal and/or social services for counselling on how to prevent or deal with discrimination in school, employment, housing, and public accommodation.

6.8 Adherence

6.8.1 Definition

Medication Adherence can simply be described as drug compliance. It measures the closeness of patient's behaviour taking prescribed drugs compared to the recommendations made by the health care provider. This involves taking the right drug(s), the right dose, the right frequency, and at the right time.

Medication Adherence is a primary determinant of treatment outcome. Non-adherence to therapy is a serious problem which can affect the patient and the health care system. Medication non-adherence in viral hepatitis patients leads to substantial worsening of disease condition, death, and increased health care costs. Other components of adherence in viral hepatitis include:

Adherence to non-pharmacological methods of preventing hepatitis: Adherence to safe sex practices, harm reduction, lifestyle modification, and vaccination of partners and new-borns are effective non-pharmacological methods of preventing viral hepatitis.

Adherence to clinic appointments: This is total compliance with clinic appointments. Adherence to clinic appointments is important in monitoring progression in the treatment/management of the disease, drug efficacy, and adverse drug reactions.

6.8.2 Adherence preparation for antiviral therapy

The success of any adherence strategy depends on patient education before treatment initiation, an assessment of their understanding of and readiness for treatment. Adherence counselling includes giving basic information on Hepatitis B and C infections and their manifestations, and the benefits and side effects of antiviral medications. It also includes how the medications should be taken and the importance of not missing any dose, what to do if doses are missed and steps to be taken to restart therapy if doses are missed. Information and education materials can be particularly useful in this process. Consideration should be given to the patient's lifestyle when possible and may involve relatives, friends and/or community

members as agreed with the patient.

Adherence treatment Support

Families of people living with viral hepatitis should be sensitized on the need to support their infected family members to adhere with viral hepatitis care services.

Partner support for discordant couples

Uninfected partners should be educated on viral hepatitis to enable them to provide appropriate support to their infected partners. Partner support can reduce stigma, encourage healthy living, and prevent further infection.

6.8.3 Ongoing adherence for clients on antiviral therapy

It is essential to continue with adherence counselling. This should involve adherence assessments during every visit and repost treatment follow up.

6.8.3.1 Measurement of Adherence

Virologic cure for HCV and functional cure for HBV are strongly dependent on adherence to taking the prescribed medications. Adherence in many studies is measured by expressing the number of doses taken as a percentage of the number of doses prescribed. Measurement methods include patient self-report, pharmacy drug pick-up, pill count, questionnaire, and electronic drug monitoring methods.

6.8.3.2 Factors known to improve adherence

The following factors have been associated with high adherence rates:

- Increased access to antiviral therapy
- Individual patients, family, peers and friends, community members, or treatment-supporter engagement in adherence education
- Family-based care if more than one family member is infected
- Continuous and effective adherence counselling, including knowledge and understanding of hepatitis B and C infections, course of treatment, expected adverse reactions, and management of such reactions.
- Drug regimen simplicity, e.g., Fixed Drug Combination (low pill burden)
- Shorter duration of therapy
- When possible, use drugs with fewer adverse effects.

6.8.3.3 Factors Associated with Poor Adherence

- Poor patient-caregiver relationship
- Forgetfulness
- Depression
- Lack of patient education

- Drug toxicity
- Severe illness
- Pregnancy related conditions
- Incarceration
- Long duration of treatment
- Lack of social support
- Substance abuse
- Cost of drugs and monitoring tests
- Use of alternative or unconventional medicine.
- Self-medication
- Drug regimen factors; dose frequency and regimen complexity
- Lifestyle factors; alcoholism, attitude, sociocultural factors, religious beliefs, nature of work

6.8.3.4 Strategies for Improving Adherence

- Adherence counselling for patient and treatment partner
- Routine assessment and reinforcement of adherence during follow up
- Fixed dose combination
- Reminders and patient engagement tools (e.g., drug calendars, pill boxes, a reminder call/ SMS, alarm clock)
- Positive feedback on health improvements

CHAPTER 7: MANAGEMENT OF ADVERSE REACTIONS AND COMPLICATIONS OF ANTI-HEPATITIS MEDICINES

The fundamental guiding principle in the use of medicines is that their therapeutic benefits should always outweigh the risks. While the safety profiles for medicinal products have been established, adverse events are not uncommon in the course of prevention and patient management. Adverse Events (AEs) are identified and managed on time through effective Pharmacovigilance.

7.1 Pharmacovigilance, Adverse Drug Reaction (ADR) And Adverse Events Following Immunization (AEFI)

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding, response, and prevention of adverse drug reactions (ADRs) and other potential medicine-related problems including Adverse Events Following Immunization (AEFIs). A pharmacovigilance system is designed to monitor the safety of authorised medicinal products and detect any change in their risk-benefit ratio. A pharmacovigilance system like any system is characterised by its structures, processes, and outcomes (refer to Good Vigilance Practice). The pharmacovigilance system should be in such a way that public health emergencies and preparedness plans are developed as appropriate.

Adverse Event (AE) is any untoward medical occurrence in a patient or clinical trial participant administered a medicinal product and which does not necessarily have a causal relationship with the treatment.

An adverse event can therefore be any unfavourable and unintended sign (e.g., an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether considered related to the medicinal product or not. An Adverse Drug Reaction (ADR) is defined as a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of a disease, or for the modification of physiological function.

Adverse Event Following Immunization (AEFI) is any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. If not rapidly and effectively dealt with, can undermine confidence in a vaccine and ultimately have dramatic consequences for immunization coverage and disease incidence.

Reporting of ADR and AEFI requires structures and processes for the collection, recording, and transmission of reports of suspected adverse reactions associated with medicinal products for human use to the National Pharmacovigilance Centre. These can be achieved by ensuring all stakeholders adhere to their roles and responsibilities as shown in Table 7.1 below.

Table 7.1: Roles and responsibilities of stakeholders in the Pharmacovigilance system for viral hepatitis

STAKEHOLDER	RESPONSIBILITIES
FMOH, SMOH, NPHCDA, SPHCDA, State NAFDAC Offices and NAFDAC Headquarters	• Strengthen facility-based pharmacovigilance units to ensure that the collected reports are authentic, legible, accurate, consistent, verifiable, and as complete as possible for clinical assessment (FMOH, NAFDAC). • Ensure consumers and Healthcare professionals have requisite knowledge to enable them report suspected AR and where necessary immediate investigation should be carried out to ascertain the authenticity of the information (SMOH, SPHCDA, NAFDAC) • Establish and disseminate policies that drive pharmacovigilance activities (FMOH, NAFDAC) • Establish systems to ensure counselling of all caregivers on AEFIs and pharmacovigilance (SMOH, SPHCDA) • AEFI Investigation backed with laboratory analysis and documentation (SMOH, SPHCDA, NAFDAC) • ADR Investigation backed with laboratory analysis and documentation (FMOH, SMOH, NAFDAC)
Marketing Authorization Holder (MAH)	• Establish mechanisms enabling the traceability of products and systems for the collection and reporting of ADRs/AEFIs, including follow-up of reports while complying with data protection principles. • Ensure that all ADR/AEFI information regarding medicinal products marketed by the MAH, within or outside Nigeria are reported to NAFDAC (refer to MAH guideline and propriety vendor (PV) policy).
Healthcare providers	• Assess patients for AE at every encounter and report all suspected adverse events using the ADR/AEFI reporting form.

	• Monitor and document outcomes of intervention
Community/Individuals/CSOs/NGOs and patient groups	• Identify and report all AEs through designated channels (Health facilities, NAFDAC, SMOH, FMOH, SPHCDA, NPHCDA) • Support patients with AEs to cope with the condition
NAFDAC	• Receive, investigate, assess, provide feedback, and archive information on ADR/AEFIs in compliance with the data protection requirements. • Establish systems for capacity building and knowledge dissemination on PV. Increase PV awareness and ensure the availability of "Yellow Forms" across the healthcare system. • Causality assessment and safety communication. • Post-market surveillance of all registered anti-hepatitis drugs and vaccines to ensure quality, safety, and efficacy.

7.2 Classification of Adverse Drug Reactions

The World Health Organization classifies ADRs into four categories based on the severity grades. Severity is a subjective assessment made by the healthcare provider and/or the patient. Despite being subjective, it is useful in identifying adverse reactions that may affect adherence or that needs prompt intervention. The following guide can be used to estimate the severity grade of ADRs:

Table 7.2: WHO Severity Grading of ADR

Grade 1 – mild ADR	Transient or mild discomfort (<48 hours) No limitation of activity No medical intervention or therapy required
Grade 2 – moderate ADR	Mild to moderate limitation of activity Some assistance may be needed No or minimal medical intervention required

Grade 3 – severe ADR	Marked limitation of activity. Some assistance usually required. Medical intervention or therapy required Hospitalization possible
Grade 4 – life threatening ADR	Extreme limitation of activity Significant assistance required Significant medical intervention or therapy required Hospitalization or hospice care probable

Vaccine reactions (AEFI) can be classified into two types:

1. Common, usually minor and self-limiting
2. Rare and serious

An AEFI is considered serious if it results:

- In death or life-threatening,
- In-patient hospitalization or prolongation of existing hospitalization,
- Persistent or significant disability/incapacitation,
- Congenital anomaly/birth defect
- Requires intervention to prevent permanent impairment or damage.

Table 7.3. Common adverse events associated with hepatitis vaccinations

Hepatitis B vaccine	Nausea, vomiting, redness of the face, neck, arms, and occasionally, upper chest, drowsiness, sleeplessness, fatigue, pain and tenderness at injection site, pruritus, fever, dizziness, headache, vertigo, swelling at injection site, induration at injection site, erythema, ecchymoses, joint pain, skin rash or welts (may occur days or weeks after receiving the vaccine), blurred or other vision changes, confusion, difficulty in breathing or swallowing, dizziness, faintness or light headedness when getting up suddenly from a lying or sitting position, itching especially of the feet or hands, muscle weakness, numbness or tingling of the arms and legs, reddening of the skin, especially around the ears, sweating, swelling of the eyes, face, or inside of the nose, unusual redness or weakness (sudden and severe), Hard lump, unusual tiredness or weakness, muscle pain, agitation, back pain or stiffness in neck or shoulder, chills, constipation, diarrhoea, difficulty with moving, feeling of warmth, general feeling of discomfort or illness, sore throat, runny nose, lack/decreased appetite, stomach cramps or pain, sudden redness of skin, swelling of glands in the armpit or neck, trouble with sleeping, unable to sleep, weight loss.
Hepatitis A vaccine	Tiredness, headache, loss of appetite, nausea, slightly raised temperature (normal temperature is 36-36.8ºC), swelling and induration at injection site.

Table 7.4: Adverse Drug Reaction associated with medicines for management of viral hepatitis

Tenofovir (TDF)	Tubular renal dysfunction, Fanconi syndrome [Risk factors: Underlying renal disease; Older age; BMI <18.5 (or body weight<50 kg); Untreated diabetes mellitus; Untreated hypertension; Concomitant use of nephrotoxic drugs or a boosted PI], Decreases in bone mineral Density [Risk factors: History of osteomalacia and pathological fracture; risk factors for osteoporosis or bone loss], Lactic acidosis or severe, hepatomegaly with, steatosis, [Risk factors: Prolonged exposure to nucleoside analogues; Obesity], Exacerbation of hepatitis B (hepatic flares) [Risk factors: Discontinuation of TDF due to toxicity] **Central Nervous system:** Insomnia, headache, dizziness, depression, Fatigue, anxiety, peripheral neuropathy **Dermatologic:** Skin rash (includes maculopapular, pustular, or vesiculo-bullous rash); pruritus; or urticaria, pruritus, diaphoresis

	Endocrine & metabolic: Hypercholesterolaemia, increased serum triglycerides, Weight loss, glycosuria, hyperglycaemia, lipodystrophy **Gastrointestinal:** Abdominal pain, nausea, diarrhoea, vomiting, Increased serum amylase, anorexia, dyspepsia, flatulence **Neuromuscular & skeletal:** Decreases in bone mineral density [Risk factors: History of osteomalacia and pathological fracture; risk factors for osteoporosis or bone loss], increased creatinine phosphokinase, weakness, Back pain, arthralgia, myalgia **Miscellaneous:** Fever **Cardiovascular:** Chest pain **Genitourinary:** Haematuria **Hematologic & oncologic:** Neutropenia **Hepatic:** Increased serum ALT, increased serum AST, increased serum transaminases, increased serum alkaline phosphatase **Renal:** Increased serum creatinine, renal failure **Respiratory:** Sinusitis, upper respiratory tract infection, nasopharyngitis, pneumonia Post marketing and/or case reports: Angioedema, exacerbation of hepatitis B (following discontinuation), Fanconi syndrome, hepatitis, hypersensitivity reaction, hypokalaemia, hypophosphatemia, immune reconstitution syndrome, increased gamma-glutamyl transferase, interstitial nephritis, lactic acidosis, myopathy, nephrogenic diabetes insipidus, nephrotoxicity, osteomalacia, pancreatitis, polyuria, proteinuria, proximal tubular nephropathy, renal insufficiency, renal tubular necrosis, rhabdomyolysis, severe hepatomegaly with steatosis
Entecavir	**Hepatic:** Elevated ALT, post-treatment exacerbation of hepatitis/ALT flare, deaths due to liver-related causes (e.g., hepatic failure, hepatic encephalopathy, hepato-renal syndrome, upper gastrointestinal haemorrhage; hepatic encephalopathy. On-treatment exacerbation of hepatitis/ALT flares, Elevated AST, lactic acidosis, and severe hepatomegaly with steatosis (including fatal cases), severe acute exacerbations of hepatitis B (after discontinuation of therapy). Post-treatment exacerbations of hepatitis or ALT flare other such as hepatic failure, hepatic encephalopathy, hepato-renal syndrome, and upper gastrointestinal haemorrhage. **Haematologic:** Decreased albumin (less than 2.5 g/dL), platelets (less than 50,000/mm3) with hepatic decompensation.

	Gastrointestinal: Elevated lipase, Diarrhoea, dyspepsia, nausea, vomiting, elevated amylase, abdominal pain, upper gastrointestinal haemorrhage, peripheral oedema, ascites, pyrexia/fever, fatigue, ascites, and pyrexia were reported in patients with hepatic decompensation **Oncologic:** Hepatocellular carcinoma, Malignant neoplasms, **Renal:** Creatinine increase of at least 0.5 mg/dL, increase serum creatinine of 0.5 mg/dL and renal failure were reported in patients with hepatic decompensation. Increased serum creatinine, Renal failure **Respiratory:** Upper respiratory infection, cough, nasopharyngitis, rhinitis **Metabolic:** Fasting hyperglycaemia, decreased blood bicarbonate, Elevated alkaline phosphatase, lactic acidosis. **Genitourinary:** Haematuria, glycosuria, dysuria. **Nervous system:** Headache, dizziness, somnolence, insomnia **Dermatologic:** Erythema, photosensitivity with lethargy **Musculoskeletal:** Arthralgia, myalgia, back pain
Ribavirin	**Respiratory:** Dyspnoea, cough, pharyngitis, rhinitis, and sinusitis, pulmonary infiltrates, pneumonitis, pulmonary hypertension, pneumonia, sarcoidosis, and exacerbation of sarcoidosis. Mechanically ventilated patients may be predisposed to respiratory deterioration. **Immunologic:** Hypersensitivity reactions (urticaria, angioedema, bronchoconstriction, and anaphylaxis.) **Dermatologic:** Severe skin reactions including vesiculo-bullous eruptions, Stevens-Johnson syndrome, erythema multiforme, and exfoliative dermatitis/erythroderma) skin irritation from prolonged drug contact. Alopecia, pruritus dermatitis, dry skin, increased sweating, eczema, lichenoid eruptions, and maculopapular rashes. Rash has been reported in patients treated with and health care workers exposed to aerosolized ribavirin. Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported during post-marketing. **Cardiovascular:** Angina, arrhythmia, and fatal and nonfatal myocardial infarctions, cardiac arrest, hypotension, bradycardia, bigeminy, tachycardia, hypertension, digitalis toxicity and congenital heart disease. **Hematologic:** Anaemia, lymphopenia, neutropenia, thrombocytopenia, and leukopenia. Aplastic anaemia and thrombotic thrombocytopenic purpura, pancytopenia (marked decreases in red blood cells, neutrophils, and platelets)

	Ocular: blurred vision, corneal ulcer, conjunctivitis, eye irritation, lacrimation, damage to contact lenses. **Gastrointestinal:** Nausea and vomiting, diarrhoea, vomiting, abdominal pain, dry mouth, dyspepsia, constipation, peptic ulcer, gastrointestinal bleeding, pancreatitis, and colitis. **Musculoskeletal:** Myalgia, arthralgia, musculoskeletal pain, and back pain, Myositis. **Nervous system:** Headache, dizziness (excluding vertigo), memory impairment, peripheral neuropathy, coma, cerebral haemorrhage, taste perversion, hearing impairment, hearing loss. **Metabolic:** Anorexia, weight decrease, diabetes mellitus, dehydration, falsely low haemoglobin A1c levels. **Psychiatric:** Irritability/anxiety/nervousness/emotional lability, insomnia, depression, concentration impairment, mood alteration, and agitation. Suicide, suicidal ideation, psychosis, aggression, anxiety, drug abuse/overdose, psychotic disorder, and hallucination **Endocrine:** Hypothyroidism **General:** Pyrexia, myalgia, headache, and rigors, fatigue/asthenia, pyrexia, rigors, chills, influenza-like illness, unspecified pain, right upper quadrant pain, pain, chest pain, malaise, hyperuricaemia in association with haemolysis and flushing. **Hepatic:** Hepatic dysfunction, fatty liver, cholangitis, hyperbilirubinaemia, hepatomegaly, and ALT. **Immunologic:** Sepsis, osteomyelitis, endocarditis, pyelonephritis, pneumonia, sarcoidosis, systemic lupus erythematosus, rheumatoid arthritis, resistance mechanism disorders, including viral infection, fungal infection. **Genitourinary:** Menstrual disorder.
Pegylated Interferon	**Nervous system:** Dizziness, headache, concentration impairment, Vertigo, syncope, migraine, memory impairment, weakness, hypoesthesia, hyperesthesia, paraesthesia, tremor, taste disturbance, somnolence, tinnitus, Influenza-like signs/symptoms, fatigue/asthenia, pyrexia, fatigue, rigors, asthenia, pain, overall resistance mechanism disorders, Fever, chills, chest pain, influenza-like illness, malaise, lethargy, shivering, hot flushes, thirst, infections (fungal, viral, bacterial), peripheral oedema, flushing, earache.

	Musculoskeletal: Back pains have been reported in CHC patients. Myalgia, arthralgia, arthritis, muscle weakness, neck pain, musculoskeletal pain, and muscle cramps **Haematologic:** Neutropenia, anaemia, lymphopenia, lymphadenopathy, and thrombocytopenia **Gastrointestinal:** Nausea/vomiting, diarrhoea, abdominal pain, dry mouth, dyspepsia, upper abdominal pain, dysphagia, mouth ulceration, gingival bleeding, glossitis, stomatitis, flatulence, gastritis, gingivitis, cheilitis, constipation, and oral candidiasis **Psychiatric:** Insomnia, irritability/anxiety/nervousness, irritability, depression, anxiety, concentration impairment, mood alteration, nightmares, aggression, emotional disorders, nervousness, decreased libido, affect lability, apathy, sexual satisfaction affected (potentially) and sexual dysfunction **Dermatologic:** *Common*: Increased sweating, eczema, psoriasis, urticaria, skin disorder, photosensitivity reaction, night sweats, herpes simplex, lipodystrophy, Injection site reactions, and cutaneous necrosis. *Others*: Alopecia, pruritus, dermatitis, dry skin, increased sweating, rash and eczema combination therapy, **Hepatic:** Elevated ALT **Metabolic:** Anorexia, weight decrease, decreased appetite and Hyperlacticaemia/lactic acidosis **Respiratory:** Dyspnoea, cough and exertional dyspnoea **Immunologic:** Autoimmune phenomena include hypothyroidism, sarcoidosis, systemic lupus erythematosus, rheumatoid arthritis, immune thrombocytopenic purpura, thyroiditis, psoriasis. **Cardiovascular:** Tachycardia, palpitations, **Ocular:** Blurred vision, eye pain, eye inflammation, xerophthalmia Post marketing reports: Serous retinal detachment **Endocrine:** Hypothyroidism, abnormal thyroid laboratory values **Genitourinary:** Chromaturia, impotence, hypersensitivity (Anaphylaxis, Anaphylactic shock)
Sofosbuvir	**General:** Fatigue, asthenia, pyrexia, chills, influenza-like illness, pain, Chest pain

	Nervous system: Headache, dizziness, disturbance in attention, migraine, memory impairment. **Gastrointestinal:** Increased lipase, nausea, diarrhoea, vomiting, Increased lipase, abdominal discomfort, constipation, dyspepsia, dry mouth, gastroesophageal reflux. **Dermatologic**: Pruritus, rash, alopecia, dry skin. **Psychiatric**: Insomnia, irritability, depression, anxiety, agitation. Severe depression was reported, particularly in patients with history of psychiatric illness. **Haematologic:** Decreased haemoglobin, anaemia, neutropenia, decreased lymphocyte count, decreased platelet count and pancytopenia. **Cardiovascular**: Bradycardia (including cases requiring pacemaker intervention), decreased weight **Musculoskeletal**: Myalgia, arthralgia, increased creatinine kinase, back pain, muscle spasms **Respiratory:** Dyspnoea, cough, nasopharyngitis, exertional dyspnoea **Hepatic**: Increase serum bilirubin (greater than 1.5 times ULN).
Daclatasvir	**General:** Fatigue, asthenia, influenza-like illness, pyrexia, hot flush, pain, decreased weight. **Nervous system:** Headache, dizziness, migraine **Dermatologic:** Pruritus, rash, dry skin, alopecia **Psychiatric:** Insomnia, irritability, depression, anxiety **Haematologic:** Anaemia, neutropenia, thrombocytopenia, decreased haemoglobin, eosinophilia **Respiratory:** Cough, nasopharyngitis, dyspnoea, exertional dyspnoea, nasal congestion, upper respiratory tract infection **Gastrointestinal:** Diarrhoea, nausea, upper abdominal pain, constipation, flatulence, gastroesophageal reflux disease, dry mouth, vomiting, elevated lipase **Musculoskeletal:** Myalgia, arthralgia, common: back pain **Metabolic:** Decreased appetite **Cardiovascular:** Bradycardia heart block, cardiac arrhythmias **Hepatic**: Increased ALT, increased AST, increased total bilirubin

	Genitourinary: Urinary tract infection **Ocular:** Common: Dry eye
Ledispavir	Applies to ledipasvir / sofosbuvir: oral tablet **General**: Fatigue **Nervous system:** Headache **Gastrointestinal:** Nausea, diarrhoea, increased lipase. Lipase elevation was transient and asymptomatic. **Psychiatric:** Insomnia **Hepatic:** Increased bilirubin **Cardiovascular:** Bradycardia, fatal cardiac arrest, cases requiring pacemaker intervention **Musculoskeletal:** Increased creatinine kinase

7.3 Drug Toxicity

Drug toxicity is the unwanted effect of drugs resulting from administration of more than the required therapeutic dose, or accumulation of the drug in the body due to excessive absorption and inefficient distribution, metabolism, or excretion. Drug toxicity can be detected clinically (history and clinical examination) and/or through laboratory testing.

In the event of drug toxicity, the offending drug(s) must be discontinued and changed to another drug from an appropriate class. In adverse drug reactions, the patient should be managed based on the classification of the ADR.

7.3.1 Laboratory Toxicity Monitoring

Laboratory monitoring of patients receiving Pegylated interferon-based regimens for hepatitis treatment is very important for early detection and prevention of some ADRs. The abnormal laboratory values (laboratory test abnormalities) may be early warning signals preceding the clinical manifestations of some ADRs in patients receiving anti-hepatitis medicines. The laboratory tests in Table 7.5 are desirable for laboratory toxicity monitoring of patients receiving medicines for treatment or prophylaxis.

The severity grading of laboratory test abnormalities may guide prompt intervention and prevent the negative consequences of ADR. The following guide (Table 7.5) can be used to estimate the severity grade of laboratory adverse events;

Table 7.5: Severity Grading of Laboratory Adverse Events in Adults and Adolescents

LABORATORY TEST ABNORMALITIES					
Item	**Reference Range**	**Grade 1 Toxicity**	**Grade II Toxicity**	**Grade III Toxicity**	**Grade IV Toxicity**
HAEMATOLOGY					
Haemoglobin	10.5 - 18.0g/dl	8.0 – 9.4 g/dl	7.0 - 7.9 g/dl	6.5 - 6.9 g/dl	< 6.5 g/dl
Absolute neutrophil count or Granulocyte count	2.0 –7.5 x10^9/L	1-1.5x10^9/L	0.75 – 0.99x10^9/L	0.5 - 0.749 x10^9/L	<0.5 x 10^9 /L
Platelet count	100–450 x 10^9/L	70–99x 10^9/L	50 – 69 x 10^9/L	30 – 49 x10^9/L	< 29 x 10^9/L
Total WBC	4.0 – 11.0x10^9/L	2.03.9x10^9/ l	1.0 – 1.9 x 10^9/L	< 1.0 x 10^9/L	-
CHEMISTRY					
ALT	5.0 – 38U/L	1.25 - 2.5 x ULN	>2.5 - 5xULN	>5.0 -10 x ULN	>10 x ULN
Triglycerides	<1.69 mmol/l	1.69- 2.25 mmol/l	2.26 - 5.63mmol/	5.64- 13.5mmol/ L	>13.56 mmol/L
Cholesterol	-	1.0 - 1.3 x ULN	4.52- 8.48mmol/ L	8.49- 13.56mmol /l	>13.56mmol /L
Lactate	< 2 mmol/l	-	2 – 5 mmol/l	5 – 10 mmol/l	>10mmol/l
Glucose (hyperglycaemia)	4 – 6 mmol/l	-	6 – 8. 9 mmol/l	8.91 - 13.88mmol/l	13.89- 27.76mmol/l
Glucose (hypoglycaemia)	-	4 – 6 mmol/l	3.01- 3.55mmol/l	2.19-3.00 mmol/l	1.67-2.18 mmol/l
Amylase	28 - 100U/L	> 1.0 – 1.5 x ULN	> 1.5 – 2.0 x ULN	> 2.0 – 5.0 x ULN	> 5.0 x ULN
Bilirubin	2 – 21µmol/L	1.1 – 1.5 x ULN	1.6 – 2.5 x ULN	2.6 – 5.0 x ULN	> 5.0 x ULN

Lipase	< 1.5 U/mL	> 1.0 – 1.5 x ULN	> 1.5 – 2.0 x ULN	> 2.0 – 5.0 x ULN	> 5.0 x ULN
Creatinine	0.7 – 1.5mg/dl or 62 - 133µmol/L	> 1.0 -1.5x ULN	> 1.5-3.0 x ULN	> 3.0 -6.0 x ULN	> 6.0 x ULN
Sodium Hyponatraemia	136-145 mmol/l	130 - 135mmol/l	123 -129 mmol/l	116-122mmol/l	<116mmol/l
Potassium (Hyperkalaemia)	3.5 – 5.0 mmol/l	5.1 – 6.0 mmol/l	6.1 – 6.5 mmol/l	6.6 - 7.0 mmol/l	>7.0mmol/l
Potassium (Hypokalaemia)	3.5 - 5.0 mmol/l	3.5 – 3.0 mmol/l	3.0 – 2.5 mmol/l	2.5 – 2.0 mmol/l	<2.0mmol/L
Management	• Continue therapy, and consult expert if grade I or II • Consider stopping therapy and consult expert if grade III or IV				
Lipid imbalances could be managed with exercise, diet and pharmacologically using fibrates and/or statins					

NB: Reference range is based on manufacturer's directives

7.4 Steps to Recognizing and Reporting Adverse Events (AEs)

Healthcare workers should:

- Encourage patients to report any AEs
- Ask and look for any AEs
- Take a detailed history of the patient
- Establish time relationships; as the time from the start of therapy/immunization to the time of onset of the suspected reaction should be logical
- Carry out a thorough physical examination with appropriate laboratory investigations (if necessary)
- Check the known pharmacology of the medicine, intervention, or medication given

7.4.1 Principles of Management of Adverse Drug Reactions (ADR) and Adverse Events (AEs)

Ensure routine screening of all patients receiving medicines for signs/symptoms indicating possible AE using the appropriate forms (see Appendix I and II).

- If there are no new signs and/or symptoms indicating possible adverse reactions, continue case management of patients.
- If there are any new signs and/or symptoms indicating possible adverse reactions:
    - Determine the severity of the adverse event(s) using WHO Severity Grading of ADRs
    - If the suspected adverse event(s) is mild (ADR severity grade 1), counsel patients

on how to manage the adverse event(s), document intervention, and then manage patients as appropriate.

- If the suspected adverse event(s) is moderate, severe, or life-threatening (ADR severity grade II–IV), manage the patients' AEs as appropriate and then document intervention, report the adverse events using the Yellow Form and Adverse Event following Immunization on Reporting Form.

All AEFI during routine immunization within 30 days and up to 42 days for mass campaigns should be reported.

What Should Be Reported About ADRs?

ADRs are of special interest in situations such as drug abuse, misuse, medication error, overdose, occupational exposure, pregnancy, breast feeding mothers, and the aged population. However, the following circumstances should be reported about ADRs:

- All suspected reactions/incidents that occurred after the administration of new medicines
- All serious or unexpected (unusual) AEs that one suspects for established or well-known drugs
- If an increased frequency of a given reaction is observed
- All suspected AEs associated with drug-drug, drug-food or drug-food supplement interactions.
- ADRs related to the failure of contraceptives
- Lack of efficacy of a medication, or when suspected pharmaceutical defects are observed
- Reactions suspected of causing death, danger to life, hospital admissions, prolonged hospitalization, or birth defects. When in doubt whether the suspected adverse event/reaction is an ADR or not, you must report to the National Pharmacovigilance Centre (NPC).
- Only complete Individual Case Safety Reports (ICSRs) and Adverse Event Following Immunization (AEFI) reports should be transmitted to the National Pharmacovigilance Centre (NPC).
- Components of complete ICSR include identifiable patient, identifiable reporter, event, and the drug

All ADRs/AEFIs should be reported on time (refer to guidelines and policy) to the National Pharmacovigilance Centre using the Yellow form approved by the National Agency for Food and Drug Administration and Control (NAFDAC).

Channels for reporting include:

- Health Institutions (primary health care centre, secondary and tertiary health facilities in both public and private sectors)

- NAFDAC State Pharmacovigilance offices
- Zonal Pharmacovigilance offices
- NAFDAC headquarters
- Pharmacovigilance Rapid Alert System for Consumer Reporting (PRASCO)
- Food and Drug Services Department, FMOH

7.5 Drug-Drug Interactions

Drug interaction is the modification of the mechanism of action of one drug by another. Drug interactions can be beneficial, of no consequence, or harmful. Multiple drug use ('polypharmacy') is common in patients being managed for CHB and CHC, so the potential for drug-drug interaction is likely. Adverse drug interactions can be catastrophic but are often avoidable.

It is important to note that antiviral drugs are metabolized by the Cytochrome P450 3A4 isoenzyme in the liver. As a result, other drugs metabolized by this enzyme can either raise or lower the level of antivirals or be increased or decreased themselves by these interactions.

Table 7.6: Drug-Drug Interaction between co-administered HIV and HCV treatment

HIV Antiviral Drugs	Sofosbuvir	Daclatasvir	Ledipasvir /Sofosbuvir	Ribavarin
NRTIs				
Abacavir (ABC)	◆	◆	◆	■
Lamivudine (3TC)	◆	◆	◆	●
Zidovudine (AZT)	◆	◆	◆	●
Tenofovir	◆	■	■	■
NNRTIs				
Efavirenz (EFV)	◆	■	■	◆
Nevirapine (NVP)	◆	■	◆	◆
Protease Inhibitors				
Atazanavir (ATV/r)				■
Lopinavir	◆	◆	◆	◆
Ritonavir	◆	■	◆	◆

◆ Mild Interactions ■ Moderate interactions ● Severe Interactions

*■ ● ***Prescribers should avoid the above drug-drug combinations as much as possible where alternatives are available***

7.6 Prevention of Adverse Drug Reactions

Applying the principles of rational use of medicines can prevent most ADRs and this include;

- Use of few drugs, whenever possible
- Use drugs that you are familiar with
- Do not change therapy from known drugs to unfamiliar ones without good reason
- All patients commencing medicines should be properly counselled on the ADRs related to the medications and what to do when it occurs or is suspected. The healthcare provider should be knowledgeable about this
- Be vigilant (look for) these adverse effects when initiating therapy and during follow-up visits

CHAPTER 8 – MONITORING AND EVALUATION OF THE VIRAL HEPATITIS PROGRAMME

8.1 Introduction

Monitoring and Evaluation (M&E) of the viral hepatitis programme will enable the country to measure the efficacy of interventions put in place for the national response. This will ensure that the country tracks progress towards achieving its programme goals and set targets, provide data for informed decision-making, and effective allocation of resources. The viral hepatitis programme covers the 5 WHO pillars: Infant vaccination, Diagnosis and Treatment, Harm Reduction, Prevention of mother-to-child Transmission (PMTCT), and Blood and injection safety. Objectives of viral hepatitis M&E are:

- To monitor programme performance across the domain of Viral prevention, harm reduction, PMTCT, treatment, and blood and injection safety
- To improve data quality to inform decision-making and programme planning
- To strengthen capacity in data management across all levels of implementation
- To improve data reporting from private, public, and community levels
- To strengthen viral hepatitis surveillance

Routine monitoring should be complemented by periodic systematic evaluations and programme reviews to assess the performance and impact of the viral hepatitis programme. Data triangulation, modelling and other analytic tools will be utilized to improve the accuracy of inferences generated from reported data.

8.2 Selection of Indicators

The country adapted the WHO 10 core global indicators for M&E reporting of the viral hepatitis programme. The categories of national indicators relate to the following:

1. Prevalence of HBV & HCV
2. Infrastructure for HBV & HCV testing
3. Infant vaccination
    a. Coverage of timely Hepatitis B vaccine birth dose (within 24 hours) and other interventions to prevent mother-to-child transmission of HBV
    b. Coverage of third dose Hepatitis B vaccine among infants
4. Needle-syringe distribution
5. Facility-level injection safety
6. People living with HCV and/or HBV diagnosed
7. Treatment
    a. Treatment coverage for HBV patients
    b. Treatment initiation for HCV patients
8. Viral suppression

    a. Viral suppression for CHB patients treated
    b. Cure for CHC patients treated
9. Incidence
    a. Cumulated incidence of HBV infection in children 5 years of age
    b. Incidence of HCV infection
10. Deaths from HCC, cirrhosis, and liver diseases attributable to HBV and HCV infections

Table 8.1 National Viral Hepatitis Monitoring and Evaluation Framework

NATIONAL VIRAL HEPATITIS MONITORING AND EVALUATION FRAMEWORK						
Domain	**Indicator Type**	**Indicator**	**Indicator definition (Numerator, Denominator) Disaggregation**	**Justification**	**Data Source**	**Frequency of Reporting**
Prevalence of Infections	Impact	1. Prevalence of Chronic HBV infections among children under 5	This indicator measures the HBV prevalence rate among children under 5 years of age	To measure the impact of interventions and assess progress toward elimination among children	Estimates may be modelled from older biomarker surveys	Annually
		2. Number of new infections due to Hepatitis B	This is a measure of the rate of new HBV infections among the general population	To assess progress toward epidemic control of HBV among the general population	Surveys, programme data, studies, and modelling	Annually
		3. Number of new infections due to Hepatitis C	This is a measure of the rate of new HCV infections among the general population	To measure the impact of interventions and progress toward the elimination of HCV infection among the general population	Biomarker survey, regional average, modelled estimates	Annually
		4. Hepatitis C incidence among PWID	This is a measure of the rate of new HCV infections among People who inject drugs	To measure the impact of interventions and the country's progress toward the elimination of HCV infection among PWIDs	Biomarker survey, regional average, modelled estimates	Annually
	Impact	5. Number of Deaths due to Hepatitis B	*Numerator*: Total number of deaths due to HBV related complications *Denominator*: Number of persons diagnosed of HBV	To measure the impact of interventions and progress toward epidemic control	Data from vital registration and cancer registries combined with the fraction of sequelae attributable to HBV/HCV from fixed sentinel centres	Annually
		6. Number of Deaths due to Hepatitis C	*Numerator (N)*: Total number of deaths due to HCV related complications *Denominator (D)*: Number of persons diagnosed with HCV	To measure the impact of interventions and progress toward epidemic control	Data from vital registration and cancer registries combined with the fraction of sequelae attributable to HBV/HCV from fixed sentinel centres	Annually

Prevention	Output and Outcome	7. % coverage of HBV Birth dose (PMTCT)	*N*: Total number of infants that received HBV Birth dose D: Estimated Live births/ Number of Live births	To assess the uptake of prevention services targeted to prevent mother-to-child transmission	DHIS or Recent immunization coverage survey	Monthly
		8. % Coverage of infant HBV vaccination (3-dose vaccine coverage)	*Numerator (N)*: Number of infants that received timely birth-dose coverage; *Denominator (D)*: Estimated Live births	To measure the uptake of prevention services among infants for PMTCT	DHIS or Recent immunization coverage survey	Monthly
		9. Number of Needles and syringes distributed to PWID	This measures the number of needles and syringes given per PWID per annum	To measure the uptake of prevention services among PWIDs	Routine Data from harm reduction programmes, Regional estimates reported by WHO	Annually
		10. Percentage of safe injections given	This measures the percentage of safe health-care injections given within the reporting using new, sterile syringes.	To monitor the usage of sterile syringes for the prevention of viral hepatitis infections	Regional estimates reported by WHO, population surveys, or health facility surveys	Annually
	Output	11. % of Blood screened prior to transfusion	N: Number of blood screened prior to transfusion; D: Number of blood donated	To measure the impact of interventions and progress toward epidemic control	Data from National Blood Transfusion Services	Monthly
Cascade of care and treatment	Outcome	12. % estimated persons infected with HBV that were diagnosed	N: Number of persons diagnosed with HBV infections D: Estimated HBV population; Disaggregation: Age & Sex, Pregnant Women & PWID	To assess screening services uptake and progress towards the 90% target of knowledge of status among estimated HBV population	Routine data from screening centres and facilities	Monthly
	Outcome	13. % of estimated persons infected with Hepatitis C Virus that were diagnosed	N: Number of persons diagnosed with HCV infections D: Estimated HCV population	To assess the uptake of screening services and progress towards the 90% target of knowledge of status among estimated HCV population	Routine data from screening centres and facilities (ART sites)	Monthly

	Outcome	14. % of PLHIV diagnosed for HCV	N: Number of PLHIV diagnosed of HCV infections D Estimated number of PLHIV	To assess the co-infection status of PLHIV and HCV screening services uptake among PLHIV	Routine data from screening centres and facilities (ART sites)	Monthly
		15. % of PLHIV cured of HCV	N: Number of PLHIV cured of HCV infections D: Estimated number of PLHIV coinfected with HCV	PLHIV diagnosed of HCV are cured	Routine Data from Treatment Facilities	Annually
Cascade of care and treatment	Outcome	16. HBV Treatment coverage	N: Number of persons currently on HBV Treatment D: Number of persons eligible for HBV Treatment	To assess the uptake of treatment services among clients eligible for HBV treatment with the aim of achieving viral suppression and subsequent epidemic control	Routine data from treatment facilities	Monthly
Cascade of care and treatment		17. Percentage of Pregnant women initiated on prophylaxis for PMTCT from 28 weeks	N: Number of Pregnant women initiated on prophylaxis for PMTCT from 28 weeks D: Percentage of pregnant women diagnosed with HBV eligible for TDF prophylaxis	This is used to measure coverage of prevention of mother-to-child transmission of HBV (PMTCT) interventions	Routine data from treatment facilities	Monthly
Cascade of care and treatment		18. Percentage of persons treated for HBV that achieved Viral suppression	N: Number of persons treated for HBV that achieved viral suppression D: Number of persons currently on HBV Treatment	To monitor the treatment success of persons on HBV Treatment	Routine data from treatment facilities	Monthly
Cascade of care and treatment		19. Percentage of persons diagnosed with HCV infections	N: Number of persons diagnosed with HCV infections D: Estimated HCV infected population *Disaggregation*: Age & Sex, Pregnant Women & PWIDs	This measures treatment coverage among persons infected with HCV	Routine data from treatment facilities	Monthly

Cascade of care and treatment		20. Percentage of persons initiated on HCV Treatment	N: Number of persons initiated on HCV treatment D: Number of persons diagnosed with HCV infections *Disaggregation*: Age & Sex, PW & PWID	This measures treatment coverage among persons diagnosed with HCV infections	Routine data from treatment facilities HCV MSF	Monthly
Cascade of care and treatment		21. Percentage of persons who achieved sustained Virologic response after completion of Hepatitis C Treatment	N: Number of persons who achieved Sustained Virologic Response (SVR) D: Number of persons tested for Sustained Virologic Response (SVR) after completing HCV treatment. *Disaggregation*: Age & Sex, PW & PWID	To access Hepatitis C treatment effectiveness	Routine data from treatment facilities HCV MSF	Monthly

Domain	**Indicator Type**	**Indicator**	**Indicator definition (Numerator, Denominator) Disaggregation**	**Justification**	**Data Source**	**Frequency of Reporting**
Decentralized VH services	Output	22. Number of Community centres offering and reporting viral hepatitis services	N/A	To monitor the number of community centres and NGOs offering viral hepatitis services	Mapping of community service centres and community engagement	Annually
Advocacy & Community Mobilization		23. Percentage of facilities that received	N: Total number of facilities that received IEC materials & SOPs D: Total number of facilities	To monitor level of awareness creation	State Engagement platforms and facilities offering VH services	Annually

Monitoring		IEC Materials and SOPs on Viral Hepatitis				
		24. Percentage of states that conducted awareness creation on viral hepatitis annually	N: Number of States that conducted awareness creation on Viral hepatitis D: Total Number of States	To monitor level of awareness creation	State Report	Annually
Capacity to Test	Output	25. Percentage of facilities or diagnostic centres offering dual HBV/HCV and HIV RTK test	This measures the Percentage of Facilities offering dual HBV/HCV and HIV RTK test	To monitor the use of dual HBV/HCV and HIV RTK test	Routine data from Facilities and Testing centres	Monthly
Coordination		26. Percentage of states that had community platforms engagement meeting held annually	N: Number of states that had community engagement meeting D: Number of VH states with community platforms	To monitor states that had Community platforms engagement meeting held annually	State Meeting Report	Quarterly

Coordination		27. Percentage of States with established digital/physical platforms for community engagement	N: Number of States that had a functional digital/physical platform for community engagement D: Number of VH states with established digital/physical platforms for community engagement	To monitor states that had established digital/physical platforms for community engagement ate report & screenshots of digital platforms	State report & screenshots of digital platforms	Quarterly
Generation and Use of data	Output	28. Percentage of facilities trained on the Viral hepatitis data collection tools	N: Number of facilities using VH DCT D: Number of Facilities trained on the VH DCT	To monitor facilities that had been trained on the Viral hepatitis data collection tools	Training Report	Annually
		29. Percentage of facilities reporting Viral hepatitis services	N: Number of facilities reporting VH services; D: Number of facilities offering VH services	To monitor facilities that have been reporting VH services	Routine data from Facilities and Testing centres	Monthly
		30. Percentage of Community reporting Viral hepatitis services	N: Number of communities reporting VH services; D: Number of communities offering VH services	To monitor communities that have been reporting VH services	Community directory	Annually

		31. Percentage of states that had data quality assessment on VH received in the reporting period	N: Number of states had data quality assessment on VH received in the reporting period D: Number of facilities offering VH services	To monitor states that had data quality assessment	Supportive supervisory report	Annually

8.3 Data Management

Data management includes the collection, collation, analysis, dissemination and use of VH data for planning and implementation of VH services. The data are disaggregated by age, sex, location (LGA, state and national), population type, breastfeeding and pregnancy status to improve policy decision-making.

8.3.1 Data Collection

Viral hepatitis (VH) data is routinely collected through paper-based and electronic platforms (where available). The M&E unit continues to strengthen data collection platforms to improve the quality of data collected at various levels. Clients' information is collected using the VH Patient Management and Monitoring (PMM) tools. These tools are used to collect individual level data and help in improving the management of VH.

The tools should be available at every service delivery point (ANC, Laboratory etc.). This information should be monitored routinely to enable healthcare providers assess individuals' journey from screening to treatment response and track the quality of services provided.

The data can also be used to evaluate the effectiveness, efficiency and acceptability of VH service provision at all levels of healthcare.

Healthcare workers (HCWs) at all service delivery points should ensure proper documentation of all VH services provided in appropriate data collection tools. Facility M&E staff are responsible for the collection of data from all service delivery points for monthly reporting.

Generally, the emphasis will be on using the tools to continuously inform qualitative and effective VH programming. Process and outcome evaluations will be periodically conducted to assess programme performance for proper decision making.

8.3.2 Data Collection tools

The following are the current M&E tools used for VH in the National HIV programme (See Annex):

- Viral Hepatitis Enrolment and Follow-Up Card
- Viral Hepatitis Laboratory Register
- Viral Hepatitis Treatment Register
- Viral Hepatitis Monthly Summary Form (MSF)

Viral Hepatitis Enrolment and Follow-Up Card: This is a tool that captures the information of each positive client for either or both hepatitis B and C at diagnosis, management, and outcome of treatment. The front is the enrolment section while the back captures the follow up and is filled by the medical records personnel or data clerk, the attending physician, or other designated personnel.

Viral Hepatitis Treatment Register: This register captures and summarizes the laboratory, treatment and monitoring outcomes for each client HBV/HCV positive and enrolled into care. The register is designed to track the provision of hepatitis services to the clients for as long as they visit the clinic and is filled by the nurse, managing clinician or other designated personnel.

Viral Hepatitis Laboratory Register: This register captures the information of each client screened for and diagnosed with viral hepatitis B and C. It also captures information related to HIV screening. The outcome of the laboratory tests will determine further course of actions necessary and is filled by the designated laboratory personnel.

Viral Hepatitis Monthly Summary Form: This tool captures the information obtained from the source documents (i.e., Hepatitis Treatment and Laboratory Registers) monthly.

The MSF aims to provide valuable data on the client's enrolment into laboratory and treatment services which will provide the basis for determining the burden of Viral Hepatitis (VH) and its sequelae in the country and is filled by the ***designated M&E officer.***

8.3.3 Data Security, Collation and Reporting Flow

Handling of VH tools requires confidentiality and efficiency to give clients a sense of security. A filing system for VH programme records should be developed and followed within each facility. All records should be kept confidential and stored in a secure room with lockable cabinets. Backup records should be secured from damage or loss. At the end of each month, routine VH programme data should be validated for quality and collated into monthly summary forms. Completed monthly summary forms from all sites should be forwarded to the Local Government Area (LGA) and transmitted to the State Ministry of Health (SMOH) through National Data Repository (NDR). At state M&E review meetings VH data should be validated, collated and

analysed by all relevant VH programme stakeholders. States should in turn forward to the NASCP Division of the FMOH for validation, consolidation and global reporting.

The respective health authorities at the various levels will have responsibility for reporting to the viral hepatitis coordinating authorities at the various levels (i.e., health facility to LGA to SMOH to FMOH). Facilities can now upload information on the monthly summary forms directly on the NDR. Validation is conducted by the L.G.A. and the state.

The information can be viewed at the local, state and national level. With the electronic medical record (EMR) system, facilities upload patient-level data into the NDR which can be reviewed for quality at all levels and analysed by stakeholders.

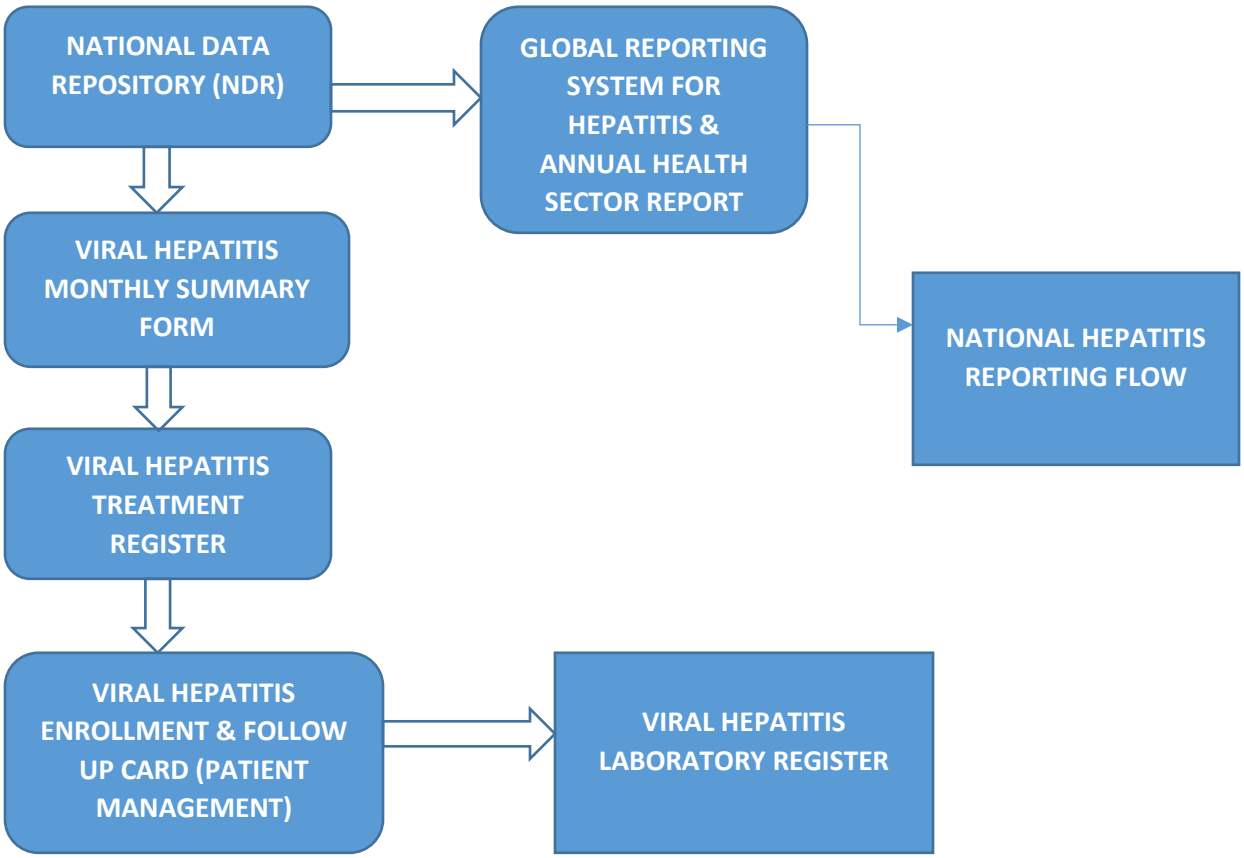


Fig 8.1 Viral Hepatitis Reporting Flow Chart

8.4 Data Quality

M&E unit will ensure that accurate quality data is generated and reported and will be monitored at facility, LGA, state, and national levels. To ensure quality, accuracy and objectiveness of data, responsible personnel should employ proven practices that checks for completeness, validity, reliability and consistency of data. Systematic data quality and verification measures unique to each indicator should be put in place. Mechanisms to ensure data quality such as clear and concise procedures for data collection, use of national and standardized data collection tools, piloting survey tools when necessary, data triangulation, spot checks during data collection and entry should be adopted.

8.5 Viral Hepatitis Data Dissemination and Use

The importance of data cannot be fully ascertained until it is imparted to all relevant stakeholders for effective planning and decision making. The dissemination of VH data and information products will be through frequent fact sheets, bulletins, reports and official social media platforms. Also validated data are shared with the states quarterly as a way of feedback. Data use should be encouraged at all levels especially at the health facilities where these data are generated, to improve patient management and monitoring.

8.6 Human Resource for M&E

The relevant human resource for monitoring and evaluation should be employed at all levels to boost data management. The FMOH in collaboration with all relevant stakeholders will ensure training and retraining of healthcare workers, local government and state officers on data management and use.

8.7 Viral Hepatitis M&E Logistics

National M&E tools and infrastructure should be made available to all sites delivering VH services for ease and boosting of service documentation and reporting of routine data. Indicator Reference Sheets and User Guides should be made available to end-users to aid understanding of programme indicators and also help in the completion of M&E tools.

8.8 Viral Hepatitis Research

The National VH research policy and agenda seeks to inform VH implementation and formative research that provide evidence-based data to improve the effectiveness and efficiency of VH programme management in Nigeria. Research programmes will be categorized to identify cost-effective mechanisms for VH treatment, care, and support. It should also prioritize research that promotes the reduction of VH among key, vulnerable and general populations, enhance

prevention programmes, strengthen basic and implementation research, clinical trials, social science research and systematic reviews.

8.9 Periodic Monitoring of the Guideline Implementation

Viral hepatitis management is dynamic with emerging evidence and innovations that ameliorate prevention, treatment, and care of persons with viral hepatitis. Hence, this necessitates periodic updates to these guidelines. In addition, there is also a need to monitor and evaluate the level of implementation of these guidelines at service delivery points with the aim of re-strategizing for effective programme implementation. It is recommended that FMOH should take the lead with the support of all stakeholders to ensure regular reviews and update of these guidelines.

CHAPTER 9 - PROGRAMMATIC MANAGEMENT OF VIRAL HEPATITIS

9.1 Preamble

The successful implementation of the recommendations in these guidelines and establishment of affordable prevention, treatment, and care programs for viral hepatitis in the public and private sectors will depend on a well-planned process of adaptation and integration into relevant national strategies to ensure ownership. Essential operational and service delivery issues will be addressed on an ongoing basis to ensure long-term effectiveness and sustainability of the national program. These will be achieved by maximizing available human and financial resources, thereby ensuring patient retention across the continuum of care. Specifically, efforts will be made to promote case-finding, improve laboratory and diagnostic services and accelerate treatment access. The key programmatic components for effective viral hepatitis management include leadership and governance, community awareness, engagement and participation, human resources development, simplified service delivery, procurement and supply chain management, monitoring and evaluation.

9.2 Leadership and Governance

An effective leadership and governance system is paramount to driving the viral hepatitis response. Leadership and governance involve ensuring strategic policy frameworks exist and are combined with effective oversight, coalition-building, regulation, attention to system-design and accountability. In Nigeria, three levels of viral hepatitis leadership and governance exist, namely, National, State and Local Governments. These levels of government should provide leadership directions for effective implementation of the Viral Hepatitis guidelines to the healthcare providers and the citizens.

Within healthcare programme, managers should be adequately trained in order to motivate staff to work at their highest potential to benefit patients, their colleagues, and the organization as a whole. Nurses, doctors and health administrators should supervise teams on daily operations.

9.3 Community Awareness, Engagement and Participation

The burden of viral hepatitis is high in Nigeria. To effectively drive the prevention, control and management efforts, there is need to intensify strategies on social mobilisation, communication, advocacy, community participation and engagement at National, State, Local Government Area (LGA), and Ward levels. Also, it is very necessary to identify key players/leaders, traditional, religious, and community structures at all levels for advocacy and social mobilisation.

9.3.1 Advocacy and Resource mobilisation

The TWG sub-group on advocacy and resource mobilisation should periodically conduct advocacy to legislators, the budget office, and the Federal Ministry of Health. This is to ensure increased budget line for hepatitis programming to cover for funding for management and continuous capacity building and strengthening of healthcare workers and CBOs/NGOs.

9.3.2 Social Mobilisation

- Map and identify available resources for social mobilisation at all levels
- Leverage on available religious, traditional, and social structures to mobilize and sensitize the populace on viral hepatitis preventive and control measures
- Develop and roll out behaviour change communication strategies and advocacy tools for Viral Hepatitis prevention and control
- Promote community ownership of viral hepatitis prevention and control through mobilisation and sensitization of major stakeholders
- Advocate to major stakeholders for resource mobilization for viral hepatitis prevention and control to leverage existing structures like Ward Development Committees (WDC), Community Health Influencers, Promoters and Services (CHIPS), volunteer community mobilizers to sensitize people on viral hepatitis
- Identify and engage key stakeholders to support community mobilization and awareness creation for viral hepatitis interventions.
    - Identify and engage traditional and religious institutions, NGOs, CBOs, CSOs, women and youth associations, and other relevant stakeholders to sensitize populace on viral hepatitis services including prevention and childhood immunization

9.3.3 Communication

- Use conventional media (TV, Radio and Print Media) to sensitize people on viral hepatitis prevention and control
- Use conventional media to promote ANC attendance for pregnant women, health facility deliveries and adherence to timely childhood immunization schedule
- Partner with media organizations to develop and disseminate viral hepatitis prevention and control radio and TV programmes
- Identify and sensitize social media influencers to promote awareness of viral hepatitis prevention and control
- Government should collaborate with CBOs, CSOs and other relevant stakeholders to organize and conduct outreaches (road walk/shows, rallies and community dramas) on viral hepatitis prevention and control
- Increase demand creation for viral hepatitis prevention and control using the existing

public and private structures or facilities

9.4 Human Resources

The limited availability of skilled health workers to deliver quality services is a major setback to the attainment of universal access to viral hepatitis prevention, treatment, and care. There should be adequate human resource to cater for the patient needs at all levels of service provision, whether at health facility or community, in view of the simplified service delivery model for HBV and HCV infections. These include the following:

(a) **Personnel availability and retention**: Governments, agencies, and stakeholders at all levels of care should ensure availability of adequate numbers of HCWs at all facilities providing viral hepatitis services.

(b) **Capacity building for healthcare workers**: All HCWs involved in the provision of viral hepatitis services must have received adequate training prior to offering services and continued medical education for viral hepatitis thereafter. Training of healthcare workers must conform with globally accepted standards using nationally approved viral hepatitis training curriculum and manuals.

(c) **Training of community health service providers**: Persons involved in community health service provision such as Community Health Officers (CHOs), Community Health Extension Workers (CHEWs), community pharmacists, traditional and religious leaders, community volunteers, and CSOs should be trained to provide sensitization, mobilization, vaccination, screening and referral services for viral hepatitis control, using a community directed intervention approach.

9.5 Service Delivery

Viral Hepatitis service delivery comprises prevention, care, and treatment. The earlier medical model of care for viral hepatitis was largely specialist driven. However, with the public health approach, non-specialists can manage uncomplicated cases of the disease through the simplified service delivery model. This could drastically improve access to viral hepatitis service in rural areas and places where there are no medical specialists readily available, hence reducing the viral hepatitis burden and resultant mortality. The FMOH is committed to the WHO recommended simplified service delivery model comprising task sharing allowing non-hepatologist specialists such as family physicians and other cadres of healthcare workers (refer to table 9.1); decentralization of HBV/HCV testing and treatment to PHCs, private clinics, One Stop Shops (OSSs), correctional centres and other closed settings, HIV/ART clinics; and integration of HBV/HCV care with existing services at the peripheral centres.

9.5.1 Simplified Service Delivery Model

9.5.1.1 Task Sharing

Task sharing entails the strategic redistribution of specific tasks among the health workforce and personnel. Specific tasks will be moved, shared, and delegated, usually from higher trained health workers to those with lower training or fewer qualifications. Government and implementing agencies at all levels should adopt task-sharing strategies, which involves the rational redistribution of tasks among teams of healthcare workers. It involves health workers undertaking tasks that are not listed in their professional schedule of duties. Task sharing reduces the burden of work on a particular cadre of health workers and increases the efficiency and productivity in health facilities with large volumes of patients. This improves access to quality healthcare services especially at the community level. Successful task sharing approaches entails continuous mentorship and peer-led learning.

9.5.1.2 Integration

Integrated service delivery refers to the delivery of different health services in a way that ensures that people receive a continuum of health promotion, disease prevention, diagnosis, and treatment. This results in cost savings and ensures that patients benefit from a robust package of care and eliminate duplication of services, hence improving coordination. Government and health facilities should leverage existing services across the continuum of care to integrate viral hepatitis services.

a. Screening

- Integrate viral hepatitis screening at the different service delivery points and POC service such as the ART clinics, Antenatal clinics, TB clinics, GOPD as well as PHCs, private clinics and OSS
- HCVST is recommended for at-risk and key populations such as PLHIVs, PWIDs, MSMs, SWs, people in correctional centres and other closed settings and vulnerable communities including close contacts of these groups.

b. Diagnostics

- Use of POC services through opportunities of integration of viral load testing (HBV DNA and HCV RNA) on available multi-disease molecular platforms to guide treatment and management of HBV and HCV infections
- Use of laboratory and clinic-based reflex testing for sample collection for HCV RNA testing is meant to improve linkage to care by offering an opportunity to conduct both an antibody and viral load test in a shorter time period. Lab-based approach, reflex viral load testing includes performing confirmation of viremia on a sample already in a lab, while a clinic-based reflex viral load testing includes immediate sample collection to conduct the HCV viral load, following a positive HCV antibody RDT result.

9.5.1.3 Decentralization

This refers to the provision of VH services at the peripheral and community-based facilities in order to bring care nearer to the patients. Effective decentralization approach entails adequate planning of the task sharing and integration model across lower level health facilities to ensure availability of services at the peripheral sites such as the PHCs and secondary healthcare facilities.

Table 9.1 Minimum Package for Viral Hepatitis Services at all Levels of care

Level/Provider	Prevention	Laboratory	Treatment
Community - CHWs	- Provide health education - Provide counselling - Administration of vaccines	- Provide health education - Screening using rapid test kits - Referral for positive patients	- Provide health education - Provide adherence counselling - Administration of antiviral drugs - Referral of positive patients to specialists
Primary Healthcare Centre - Nurse - Counsellor - Laboratory Technician - Medical officers*	- Provide health education - New-born/childhood vaccination - HBV PMTCT - Adult vaccination - Post exposure prophylaxis - Capacity building for CHWs	- Rapid tests for screening - POC HBV DNA and HCV RNA testing - Refer for viral load tests - Liver function tests*, Renal function tests* and Haematology*	- Counselling (adherence, lifestyle) - Administration of antiviral drugs - Refer HBV & HCV positive cases to the next level as appropriate
Secondary Health Facility - General Practitioner /Specialists - Nurse - Laboratory Scientist - Counsellor - Nutritionist	- Provide health education - New-born/Childhood vaccination - HBV PMTCT - Adult vaccination - Post exposure prophylaxis - Supervision and clinical mentorship of Health Centres	- Rapid tests for screening - POC HBV DNA and HCV RNA testing - Liver function tests - Renal function tests - Haematology - Viral Load Monitoring - Ultrasound scan - Liver biopsy	- Clinical assessment for cirrhosis - Counselling (adherence, lifestyle) - Assess eligibility criteria for HBV and HCV using available capacity - Initiate HBV & HCV treatment for non-Cirrhotic cases - Follow up of patients on HBV and HCV treatment - Refer complicated cases to the next level as appropriate
Tertiary Health Facility - Specialist, - General Practitioner - Nurse - Laboratory Scientist - Counsellor - Nutritionist	- Prevention message - New-born vaccination - HBV PMTCT - Adults vaccination - Post exposure prophylaxis - Capacity building of medical at District Hospitals (Training, Mentorship, Supervision)	- Rapid tests for screening - POC HBV DNA and HCV RNA testing - Liver function tests - Renal function tests - Haematology - ELISA Tests - Viral Load Monitoring - Ultrasound scan - Fibroscan - CT scan - Liver biopsy - GIT Endoscopy	- Counselling (adherence, lifestyle) - Advanced clinical assessment for cirrhosis - Assess eligibility criteria for HBV and HCV using available capacity - Initiate HBV treatment complicated cases - Initiate HCV treatment - Follow up of patients on HBV and HCV treatment - Provide guidance on HCV and HBV end of treatment

Capacity building of health care providers should be done at all levels of care

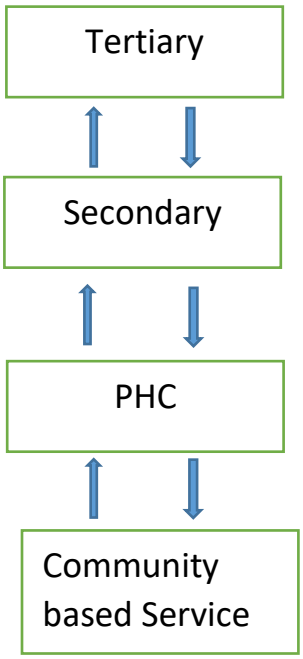


Fig 9.1 Organogram for Level of Service Provision

9.6 Procurement and Supply Chain Management

Procurement and supply chain management systems are required to ensure that quality-assured and sustained access priced viral hepatitis commodities, including antiviral medicines, vaccines and laboratory commodities are available in sufficient quantities at all times when they are needed. This involves adequate financing, forecasting, supply planning, procurement, warehousing, last mile distribution and tracking. The successful administration of this system requires multi-disciplinary and multi-sectoral collaboration including pharmacists, medical officers, medical records personnel, procurement officers, distribution agents, store officers, customs and excise officers, shipping agents, manufacturers of the commodities and administrators of health facilities. The very first step is determining what should be procured and in what quantity.

Drugs and other commodities required for viral hepatitis prevention, treatment and care include:

- Vaccines
- Anti-viral drugs
- Rapid test kits and consumables
- Viral load reagents and/or cartridges, sample collection kits, POC HBV DNA and HCV

RNA and consumables

- Diagnostic equipment - PCR machine, auto-analysers, ultrasound machine, etc.
- Other reagents and consumables for haematology and chemistry laboratory tests

Procurement of viral hepatitis commodities follow strictly the government recommended Procurement Act.

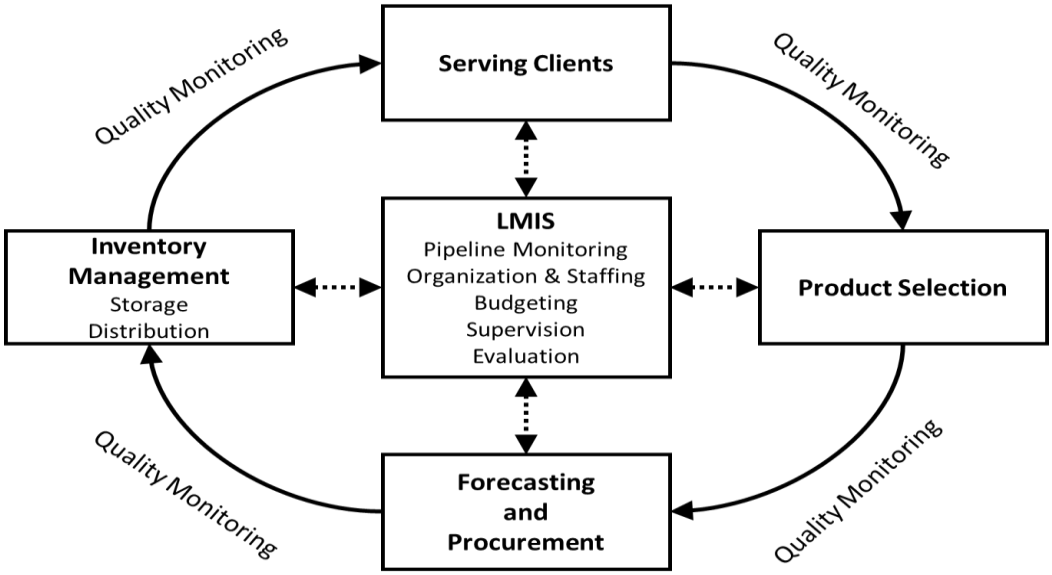


Fig 9.2: The Logistics Cycle

The supply chain management for viral hepatitis is aligned with the existing harmonized Logistics Management Information System. In the absence of government-sponsored (facility) procurement of viral hepatitis commodities, the facility replacement of consumed stock should be done according to the consumption pattern of viral hepatitis commodities at the facility. The logistic team should take into consideration the facility consumption pattern which will aid forecasting and quantification.

However, for government-sponsored/donor procurements (central), facility replacement of consumed stock occurs bi-monthly in response to submission of copies of the ordering Combined Report and Request Forms (CRRF). The reports are directly transmitted to the Central Medical Stores and then to the Logistics Unit in the National Programme where they are analysed for various decisions – ranging from routine re-supply to quantification and forecasting and supply planning. Feedback on reports from the facilities is processed by the Logistics Unit of NASCP and communicated to the facilities. When orders are ready for pick-up, distribution agents are notified and the commodities are transported and delivered directly to the service delivery points.

Table 9.2: National Reporting Schedule

Bimonthly Review Period	Report sent to the central
January – February Report	1st – 7th March
March – April Report	1st – 7th May
May – June Report	1st – 7th July
July – August Report	1st – 7th September
September – October Report	1st – 7th November
November – December Report	1st – 7th January

9.6.1 Viral Hepatitis Commodities' Logistics and Inventory Control System

The forced ordering ("Pull" system) has two-levels (Central and Facility) and is based on maximum-minimum thresholds. Service delivery points are "forced" to order at the end of the review period (2 months in FMOH programme). The quantity of commodities in logistics is tracked as a stock status (i.e., how long stocks will last).

The maximum stock level (4 months of stock in FMOH programme) is set high enough to guarantee adequate supply at all times during the ordering cycle, but low enough to prevent overstock and wastage.

The minimum stock level (2 months of stock in FMOH programme) is set as low as possible but includes a safety margin to prevent stock-outs.

The stock level in the facility has to be assessed frequently as this will alert the storekeeper in case of the need to place emergency order. The emergency order is done when stock levels drop to 2 weeks of stock; it disregards the review period. The quantity to order is calculated to top up the stock on hand to the maximum level.

9.6.3 Logistics Management Information System (LMIS)

One of the primary components of any logistics system is a functional harmonized Logistics Management Information System (LMIS) that ensures availability of timely and accurate data for decision-making. These essential data must always be collected for products at all levels.

The three essential data elements include:

Stock on Hand: This describes the quantities of usable stock of commodities available at a particular point in time. Stock-on-hand information guides us when to place an order and how much of each item is in stock. It also guides redistribution decisions.

Consumption: This describes the quantity of commodities used during the report and order cycle. The rate of consumption is the link between the consumer and the supply chain.

Losses and Adjustments: Losses include the quantity of commodities removed from the distribution system for any reason other than usage (e.g., losses, expiries, and damages). Adjustments may include receipt or issue of supplies to or from one facility to another that is not their usual supplier (e.g., a transfer) or a correction to account for a difference between what was counted during a physical inventory and what was recorded on the inventory control card. Losses/adjustments may therefore be a negative or positive number.

In order to collect and report the above-mentioned data items, a number of forms described below were designed for the management of these commodities.

9.6.4 The LMIS Forms /Tools

Inventory Control Card

This tracks the quantity of health commodities (vaccines, anti-viral drugs, etc.) in a facility's storage area. This record collects two essential data items: stock on hand, and the losses & adjustment data. The Inventory Control Card should always be kept in a facility's storage area.

Daily Consumption Record for Vaccines, Anti-Viral drugs and Daily Usage Record or Register for Test Kits and Reagents

These collect the number of commodities that have been used in the facility daily over a defined period of time. This information is called Consumption data and is one of the essential data items. The Daily Consumption Record for anti-viral drugs should be kept with the person(s) who dispenses at the Pharmacy. The Daily Usage Record for test kits and reagents should be kept with the person(s) who runs the laboratory tests.

Record for Returning/Transferring Commodities

This is a transactional form that is used in the event that commodities may be required to be returned to the CMS or transferred to another facility at the same level for various reasons ranging from expiry, damage, change in the treatment guidelines, or over- stocking.

Combined Report Requisition Form (CRRF)

This form summarizes the information that is collected on the Inventory Control Card, Daily Consumption Record, and Daily Usage Record and is sent to the central store on a regular basis. The CRRF uses this reported data to calculate the facility order quantities and monitor whether stock is maintained according to plan (no overstock, shortages, or stock outs). Information from this report is critical to a well-functioning logistics system.

ANNEXES

Viral Hepatitis M&E Reporting Tools

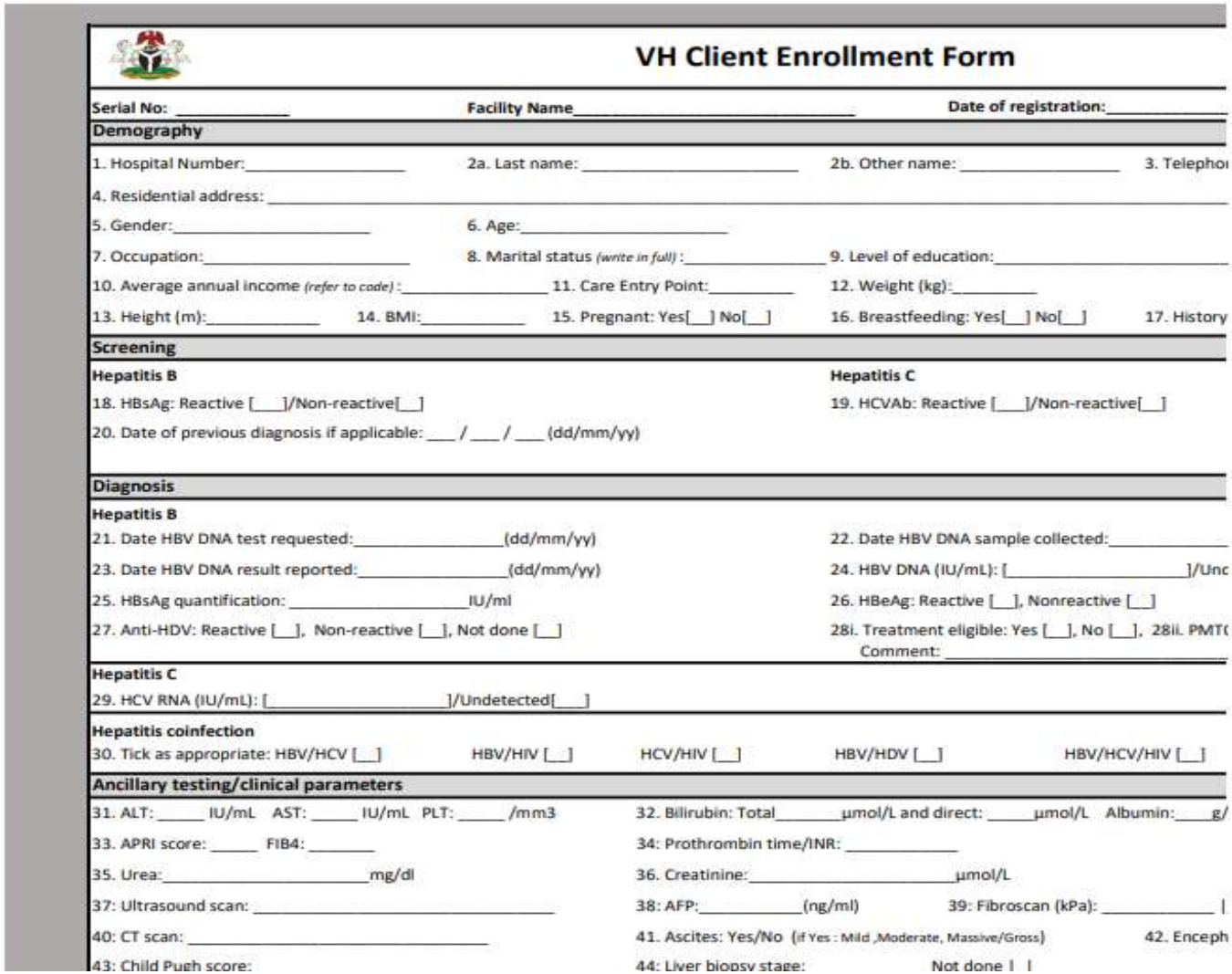
A. Laboratory Register

VIRAL HEPATITIS LABORATORY REGISTER

Facility :_____ State:_____ LGA: _____ Ward: _____ Month/Year: _____

S/N	1. Date	2. Patient Name	3. Hospital Number	4. Residential Address	5. Age in years (Enter absolute Age)	6.Sex (tick as appropriate)		7. Special Group	8. Clinic/Unit where test request was ordered (Write as appropriate e.g ANC*, hepatology* , PMTCT* OPD*, Surgical etc)	9. HBV screening (HbsAg)		10. HBcAb (IgG)		11. HBsAg quantification (IU/ml)	12. HBeAg		13. Anti-HDV		14. HBV DNA Write exact result		15. HCV screening		16. Type of RNA test	17. Hepatitis C Virus RNA Testing		18. HCV RNA Write exact result(IU/ml)	19. HIV screening	
						Female	Male	1. Pregnant Women 2.PWID		Reactive	Non-reactive	Reactive	Non-reactive		Reactive	Non-reactive	Reactive	Non-reactive	<2000 IU/ml	≥2000 IU/ml	Reactive	Non-reactive	1 - Confirmatory 5 - SVR	Detectable	Undetectable		R - Reactive NR - Non reactive	Not Tested
										R			NR						1500 IU/ml									

B. Client Enrollment Form



VH Client Enrollment Form

Serial No: _____ **Facility Name**_____ **Date of registration:**_____

Demography

1. Hospital Number:_____ 2a. Last name: _____ 2b. Other name: _____ 3. Telephoı

4. Residential address: _____

5. Gender:_____ 6. Age:_____

7. Occupation:_____ 8. Marital status *(write in full)* :_____ 9. Level of education:_____

10. Average annual income *(refer to code)* :_____ 11. Care Entry Point:_____ 12. Weight (kg):_____

13. Height (m):_____ 14. BMI:_____ 15. Pregnant: Yes[__] No[__] 16. Breastfeeding: Yes[__] No[__] 17. History

Screening

Hepatitis B

18. HBsAg: Reactive [___]/Non-reactive[__]

Hepatitis C

19. HCVAb: Reactive [___]/Non-reactive[__]

20. Date of previous diagnosis if applicable: ___ / ___ / ___ (dd/mm/yy)

Diagnosis

Hepatitis B

21. Date HBV DNA test requested:_____(dd/mm/yy)

22. Date HBV DNA sample collected:_____

23. Date HBV DNA result reported:_____(dd/mm/yy)

24. HBV DNA (IU/mL): [_____]/Unc

25. HBsAg quantification:_____IU/ml

26. HBeAg: Reactive [__], Nonreactive [__]

27. Anti-HDV: Reactive [__], Non-reactive [__], Not done [__]

28i. Treatment eligible: Yes [__], No [__], 28ii. PMT(
Comment: _____

Hepatitis C

29. HCV RNA (IU/mL): [_____]/Undetected[___]

Hepatitis coinfection

30. Tick as appropriate: HBV/HCV [__] HBV/HIV [__] HCV/HIV [__] HBV/HDV [__] HBV/HCV/HIV [__]

Ancillary testing/clinical parameters

31. ALT: _____ IU/mL AST: _____ IU/mL PLT: _____ /mm3

32. Bilirubin: Total_____µmol/L and direct: _____µmol/L Albumin:____g/

33. APRI score: _____ FIB4: _____

34: Prothrombin time/INR: _____

35. Urea:_____mg/dl

36. Creatinine:_____µmol/L

37: Ultrasound scan: _____

38: AFP:_____(ng/ml) 39: Fibroscan (kPa): _____ |

40: CT scan: _____

41. Ascites: Yes/No (if Yes : Mild ,Moderate, Massive/Gross) 42. Enceph

43: Child Pugh score:

44: Liver biopsy stage: Not done | |

45. Staging date for Liver Biopsy: ___ / ___ / ___ dd/mm/yyyy

46: Diagnosis: Fibrosis[___] Cirrhosis[___] HCC [___]
Tick as appropriate

Hepatitis B Treatment

47. Treatment experience: Yes [___] No [___]

48: Past treatment regimen: _____

49. New Regimen_____

50. Date started: ___ / ___ / ___(dd/mm/yy)

51. Adverse event Rep

Regimen Switch

52. New Regimen (where applicable):_____

53. Date started: ___ / ___ / ___(dd/mm/yy)

54. Adverse event Rep

55. Reason for switch:_____

56. Date stopped: ___

Reason for treatment

57. Treatment eligible [____] HBV PMTCT [____] Comment: _____

Hepatitis C Treatment

58. Treatment experience: Yes [___] No [___]

59: Past treatment regimen: _____

60. Date started: ___ / ___ / ___

61. Date completed: ___ / ___ / ___

62. Prescribed duratio

63. New regimen: _____

64. Prescribed duration: 12 weeks [___] 24 weeks [___]

65. Date started: ___ / ___ / ___(dd/mm/yy)

66. Date completed: ___ / ___ / ___

67. Adverse event Rep

SVR12 testing

68a. Date tested: ___ / ___ / ___

68b. HCV RNA (IU/mL): [_____]/Undetected[___]

HCV Retreatment

69. HCV genotype: _____

70. New regimen: _____

71. Prescribed duratio

72. Date started: ___ / ___ / ___(dd/mm/yy)

73. Date completed: ___ / ___ / ___

Retreatment SVR12:

74. Date tested: ___ / ___ / ___

75. HCV RNA (IU/mL): [_____]/Undetected[___]

Care Entry Point
TI= Transferred in
WC = Walk in Client
BT = Blood Trasnfusion Service
OPD = Out-patient department
IPD = Inpatient department
C = Community
OO = Others

Marital Status
1. Single
2.Married
3.Divorced
4. Separated
5. Cohabiting
6. Widowed

Educational Level
1. Informal
2. Primary
3. Secondary
4. Tertiary
5. Others (Specify)

Average annual income
1. < N360,000
2. N360,000 - N600,000
3. N600,000 - N1,500,000
4. N1,500,000 - N2,500,000
5. >2,500,000

C. Patient Follow-Up Card

FOLLOW-UP PAGE

Date of Visit (dd/mm/yyyy)	Vital Signs			HBV tests				Liver function test & staging														
	Weight (kg)	**Height** (meter)	Blood pressure (mmHg) (write value)	**HBsAg**	**HBsAg** (quantification)	**HBeAg**	**HBV DNA** (IU/ml)	**ALT** (IU/ml)	**AST** (IU/ml)	**Platelet** (mm3)	**Bilirubin** Total (µmol/L)	**Bilirubin** Direct (µmol/L)	**Albumin** (g/dl)	**APRI score**	**FIB4 score**	**Ultrasound scan result**	**Fibroscan** (kPa)	**CT Scan**	**Ascites**	**Encephalo-pathy (0,1,2,3,4)**	**Child Pugh score**	**Clinical diagnosis (Fibrosis/ Cirrhosis/ HCC)**

Outcome: LT=Lost to follow up, D=Death, C= Cured, R=Referred, U=Undetectable Viral load

D. Viral Hepatitis Treatment Register

Month/Year: _____ VIRAL HEPATITIS TREATMENT REGISTER

Facility: _____ LGA: _____ Ward: _____ Community _____

Demography															Hepatitis Status			Co-morbidities	Diagnosis					
															Mono-infection		Co-infection		HBV					HCV
Serial Number	1. Hospital Number	2. Date of registration (dd/mm/yy)	3. Last name	4. Other names	5. Telephone Number	6. Residential Address	7.Gender (M/F)	8. Age (Enter absolute Age)	9. Marital Status	10. Care Entry Point	11. Pregnant (Yes/No)	12. Breastfeeding (Yes/No)	13. Injection Drug Use (Yes/No)		14. Hepatitis B (Tick if positive)	15. Hepatitis C (Tick if positive)	16. Coinfection status: 1 - HBV/HCV 2 - HBV/HIV 3 - HCV/HIV 4 - HBV/HCV/HIV 5- HBV/HCV/HIV	17. Other Comorbidities (Specify e.g. Hypertension, diabetes)	18. HBV DNA (Write exact result)		19. HbsAg quantification (IU/ml)	20. HBeAg (Positive/ Negative)	21. Eligibility status 1. Treatment 2. PMTCT 3.Not eligible	22. HCV RNA (IU/ml/ Undetected)
																			<2000 IU/ml	≥2000 IU/ml				

Care Entry Point

TI = Transferred in

WC = Walk in Client

BT = Blood Transfusion Service

OPD = Out-patient department

IPD = Inpatient department

C = Community

OD = Others

Ancillary testing			Hepatitis B Management																
			Hepatitis B Treatment						Hepatitis B Treatment Response		Hepatitis B follow up								HBV Final Treatment outcome
24. FIB4 Score	25. Child Pugh Score	26. Diagnosis N - No Fibrosis F - Fibrosis C - Cirrhosis H - HCC	27. HBV Treatment Regimen (TDF/TAF/ Entecavir/ Others)	28. Date HBV regimen commenced (dd/mm/yy)	29. Date of cessation of HBV therapy (If applicable)	30. Regimen Switch (if applicable)	31. Date regimen switch commenced (dd/mm/yy)	32. Date new regimen stopped (dd/mm/yy)	33. HBV DNA <2log drop (Write exact result)	34. HBV DNA >2log drop (Write exact result)	35. HBV DNA U - Undetectable S - Suppressed NS - Not suppressed N - Not done								36. C - Cured (HBsAg loss) L - LTFU DC - Death due to Cirrhosis DHCC - Death due to HCC TO- Transfered Out
											VISIT 1	VISIT 2	VISIT 3	VISIT 4	VISIT 5	VISIT 6	VISIT 7	VISIT 8	

Hepatitis C Management

Hepatitis C Treatment			HCV Treatment	HCV Retreatment (if applicable)				HCV Treatment Final
38. Prescribed Treatment Duration (1: 8/24 weeks)	39. Date HCV regimen commenced (dd/mm/yy)	40. Date HCV regimen completed (dd/mm/yy)	41. SVR testing (IU/ml; Undetected)	42. HCV genotype (1,2,3,4,5,6)	43. HCV retreatment regimen	44. Prescribed Retreatment Duration (1:12; 2:24 weeks)	45. SVR testing (IU/ml / Undetected)	46. C - Cured F - Failed LTFU - Lost to follow up DC - Death due to Cirhosis DHCC - Death due to HCC TO- Transferred Out

E. HBV Monthly Summary Form

Facility name:_____ **Ward:**_____ **LGA:**_____ **State:**_____

Reporting Month/Year:_____ **Service Delivery Point: Private facility[ ]** **Public facility:** Primary [ ] Secondary [ ] Tetiary [ ] **Commu**

	HEPATITIS B VIRUS DIAGNOSIS	Male		Female		PWID	PW
		<12yrs	≥12yrs	<12yrs	≥12yrs		
1	Number of persons positive for Hepatitis B infection						
2	Number of persons negative for Hepatitis B infection						
	HEPATITIS B, C, D & HIV COINFECTION	**Male**		**Female**		**PWID**	**PW**
		<12yrs	≥12yrs	<12yrs	≥12yrs		
3	Number of persons with HBV & HCV coinfection						
4	Number of persons with HBV & HIV coinfection						
5	Number of persons with HBV & HDV coinfection						
6	Number of persons with HBV, HCV & HIV coinfection						
	HBV RELATED COMPLICATIONS	**Male**		**Female**		**PWID**	**PW**
		<12yrs	≥12yrs	<12yrs	≥12yrs		
7	Number of HBV infected persons diagnosed with complications						
	No fibrosis						
	Fibrosis						
	Cirrhosis						
	Hepatocellular carcinoma						
	HEPATITIS B TREATMENT	**Male**		**Female**		**PWID**	**PW**
		<12yrs	≥12yrs	<12yrs	≥12yrs		
8	Number of persons eligible for HBV treatment						
	HBV DNA <2000 IU/ml						
	HBV DNA ≥2000 IU/ml						
	HBV DNA ≥200,000 IU/ml						
	HBeAg						
9	Number of persons initiated on HBV treatment						
	Tenofovir Diproxil Fumarate						
	Tenofovir Alafenamide						

10	Total number of persons currently on HBV treatment						
	Tenofovir Diproxil Fumarate						
	Tenofovir Alafenamide						
	Entecavir						
	Cirrhotic						
	Non-Cirrhotic						
	HEPATITIS B TREATMENT MONITORING	**Male**		**Female**		**PWID**	**PW**
		<12yrs	≥12yrs	<12yrs	≥12yrs		
11	Number of persons on HBV treatment who received HBV DNA testing						
	Suppressed						
	Unsuppressed						
	HEPATITIS B RELATED MORTALITY	**Male**		**Female**		**PWID**	**PW**
		<12yrs	≥12yrs	<12yrs	≥12yrs		
12	Number of deaths attributable to HBV related liver cirrhosis						
13	Number of deaths attributable to HBV related hepatocellular cancer						
	HUMAN DEVELOPMENT & INFRASTRUCTURE						
14	Number of health workers trained on HBV related services						
15	Write "1" if your facility offers HBV screening services or "0" if not						
16	Write "1" if your facility offers HBV diagnostic services or "0" if not						
17	Write "1" if your facility offers HBV treatment services or "0" if not						

Completed by: **Signature :** **Designation :** **Mobile Phone Number :**

Verified by: **Signature :** **Designation :** **Mobile Phone Number:**

F. HCV Monthly Summary Form

HEPATITIS C MODULE MONTHLY SUMMARY FORM

Facility name:_____ Ward:_____ LGA:_____ State:____

Reporting Month/Year:_____ Service Delivery Point: Private facility[ ] Public facility: Primary [ ] Secondary [ ] Tetiary

	HEPATITIS C VIRUS SCREENING/DIAGNOSIS	Male		Female		PW
		<18yrs	≥18yrs	<18yrs	≥18yrs	
1	Number screened for HCV					
	Reactive					
	Non-reactive					
2	Number of persons tested for HCV RNA					
	Detected					
	Undetected					
	HEPATITIS B, C & HIV CO-INFECTION	**Male**		**Female**		**PW**
		<18yrs	≥18yrs	<18yrs	≥18yrs	
3	Number of persons with HCV & HBV co-infection					
4	Number of persons with HCV & HIV co-infection					
5	Number of persons with HCV, HBV & HIV co-infection					
	HCV RELATED COMPLICATIONS	**Male**		**Female**		**PW**
		<18yrs	≥18yrs	<18yrs	≥18yrs	
6	Number of HCV infected persons diagnosed with complications					
	No fibrosis					
	Fibrosis					
	Cirrhosis					
	Hepatocellular carcinoma					
	HEPATITIS C TREATMENT	**Male**		**Female**		**PW**
		<18yrs	≥18yrs	<18yrs	≥18yrs	
7	Number of persons initiated on HCV treatment within the reporting period					
	Sofosbuvir/Daclatasvir					
	Sofosbuvir/Velpatasvir					
	Sofosbuvir/Ledipasvir					
	IFN based regimen					
	Cirrhotic (24 weeks duration)					

	Non-Cirrhotic (12 weeks duration)					
	HEPATITIS C TREATMENT EFFECTIVENESS	**Male**		**Female**		**PW**
		<18yrs	≥18yrs	<18yrs	≥18yrs	
9	Number of persons tested for Sustained Virologic Response (SVR)					
	Detected					
	Undetected					
	Cirrhotic (24 weeks duration)					
	Non-Cirrhotic (12 weeks duration)					
	HEPATITIS C RETREATMENT	**Male**		**Female**		**PW**
		<18yrs	≥18yrs	<18yrs	≥18yrs	
10	Number of persons initiated on HCV re-treatment therapy					
11	Number of persons tested for Sustained Virologic Response (SVR) post retreatment					
	Detected					
	Undetected					
	HEPATITIS C RELATED MORTALITY	**Male**		**Female**		**PW**
		<18yrs	≥18yrs	<18yrs	≥18yrs	
12	Number of deaths attributable to HCV related liver cirrhosis					
13	Number of deaths attributable to HCV related hepatocellular cancer					
	HUMAN DEVELOPMENT & INFRASTRUCTURE					
14	Number of health workers trained on HCV related services					
15	Write "1" if your facility offers HCV screening services or "0" if not					
16	Write "1" if your facility offers HCV diagnostic services or "0" if not					
17	Write "1" if your facility offers HCV treatment services or "0" if not					

Completed by: **Signature :** **Designation :** **Mobile Phone Numbe**

Verified by: **Signature :** **Designation :** **Mobile Phone Numbe**

Tests for Assessment and Monitoring of Hepatitis B Infection

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST)	Intracellular enzymes which, are released after cell injury or death thereby reflecting liver cell injury
HBV DNA	HBV viral genomes that can be detected and quantified in serum. HBV DNA correlates with levels of circulating viral particles. HBV DNA is measured as IU/mL or copies/mL. 1 IU/mL = 5.3 copies/mL, and so values given as copies/mL can be converted to IU/mL by dividing by a factor of 5. (i.e., 10 000 copies/mL = 2000 IU/mL;100 000 copies/mL = 20 000 IU/mL; 1 million copies/mL = 200 000 IU/mL). All HBV DNA values in the recommendations in these guidelines are reported in IU/mL. An undetectable viral load is an HBV DNA level below the level of sensitivity of the laboratory assay. For sensitive polymerase chain reaction assays, this is generally a concentration below 15 IU/ml.
AFP (alpha-fetoprotein)	A host cellular protein. High levels can occur in persons with hepatocellular carcinoma.
Persistently abnormal or normal ALT level	ALT levels fluctuate in persons with chronic hepatitis B and require longitudinal monitoring to determine the trend. Upper limits for normal ALT have been defined as below 30 U/L for men and 19 U/L for women*, although local laboratory normal ranges should be applied. Persistently abnormal or normal may be defined as three ALT determinations above or below the upper limit of normal, made at

	unspecified intervals during a 6–12-month period or predefined intervals during a 12-month period. *- The upper limit for normal ALT in Nigeria is ----IU/ml for male and ----IU/ml for women

Assessment of Liver Fibrosis by Non-Invasive Tests

APRI	Aspartate aminotransferase (AST)-to-platelet ratio index (APRI) is a simple index for estimating hepatic fibrosis based on a formula derived from AST and platelet concentrations. A formula for calculating the APRI is given: APRI = * (AST/ULN) x 100) / platelet count (10^9/L). An online calculator can be found at: http://www.hepatitisc.uw.edu/page/clinical-calculators/apri
FIB-4	A simple index for estimating hepatic fibrosis based on a calculation derived from AST, ALT and platelet concentrations, and age. Formula for calculating FIB-4: FIB-4 = (age (yr) x AST (IU/L)) / (platelet count (10^9/L x [ALT (IU/L)$^{1/2}$]). An online calculator can be found at: http://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4
Fibro Test (FibroSure)	Commercial biomarker test that uses the results of six blood markers to estimate hepatic fibrosis
Transient elastography (Fibro Scan)	A technique to measure liver stiffness (as a surrogate for fibrosis) and is based on the propagation of a shear wave through the liver

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