Guidelines for the Prevention and Management of Hepatitis B and C in Malawi

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Tables and Figures

Foreword To The First Edition

Viral hepatitis is an international public health urgency that is comparable to other major communicable diseases such as HIV, tuberculosis, and malaria. According to the World Health Organization's (WHO) *Global Progress Report on HIV, Viral Hepatitis and Sexually Transmitted Infections, 2021*, viral hepatitis contributes to 1.1 million deaths annually. Approximately 800,000 deaths are attributed to hepatitis B and 300,000 to hepatitis C. With the aging of the population and mitigation of other infectious diseases, deaths from viral hepatitis are expected to grow. An estimated 60 million new infections occur annually in the WHO African region, which includes Malawi. To that end, Malawi became a signatory to the global commitment that calls for action towards sustainable development in all sectors. Target 3 in the Sustainable Development Goals calls for efforts to eradicate infectious diseases, including viral hepatitis, by 2030.

This first edition of the *Guidelines for the Prevention and Management of Hepatitis B and C in Malawi* includes all relevant public health policies and clinical protocols. It is written for program managers and health workers. The guideline focuses on hepatitis B and C virus infections as they are estimated to cause the most morbidity and mortality among all known hepatitis viruses (A, B, C, D, E) in Malawi. It covers prevention, screening, diagnosis, linkage to care, and differentiated treatment and support, tailored to patient risk categories.

Malawi aims to integrate the prevention, treatment, and care of viral hepatitis and HIV. Routine, provider-initiated screening for hepatitis B, HIV, and syphilis are integrated in all service delivery points that cater to high-risk populations such as pregnant women, people who inject drugs, and healthcare workers. Program integration will improve the coverage and quality of services, paving the way towards triple elimination of HIV, syphilis, and viral hepatitis. This document covers the implementation aspects of the Viral Hepatitis Strategic and the Health Sector Strategic plans. The protocols and policies are adapted for local health services and follow the public health approach, aiming to reach the maximum number of Malawians in need with the best possible services.

These guidelines will be updated as relevant innovations, new scientific evidence, and normative WHO recommendations become available.

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Secretary for Health
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Abbreviations

ALT	alanine aminotransferase
APRI	aspartate aminotransferase-to-platelet ratio index
ART	antiretroviral therapy
AST	aspartate aminotransferase
AVT	anti-viral treatment
DTP-Hib-HepB	diphtheria-tetanus-pertussis-haemophilus-hepatitis B
HBcAg	hepatitis B core antigen
HbeAg	hepatitis B envelope antigen
HbsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HIV	human immunodeficiency virus
PCR	polymerase chain reaction
PrEP	pre-exposure prophylaxis
RNA	ribonucleic acid
STI	sexually transmitted infection
TB	tuberculosis
TDF	tenofovir disoproxil fumarate
TDF/3TC	tenofovir disoproxil fumarate plus lamivudine
WHO	World Health Organization

Definitions

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST): Intracellular enzymes which are normally present in blood at low levels. Increased levels indicate liver cell injury or death.

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. Do not use the APRI score for patients with very high AST levels (≥350 IU/mL) as this is usually a sign for acute hepatitis and not an indication for starting treatment. In this case, investigate other causes of acute hepatitis. Repeat LFT, FBC after 2 weeks and calculate the APRI score when the AST has dropped below 350 IU/mL.

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

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

Acute HBV infection: Occurs within the first six months of a hepatitis B virus (HBV) infection. It is often asymptomatic but may present with sudden unexplained fever, jaundice, and very raised ALT/AST levels (10 times above normal). It is characterized by the presence of hepatitis B surface antigen (HbsAg) and immunoglobulin M (IgM) antibody to the core antigen. During the initial phase of infection, patients are also seropositive for hepatitis B envelope antigen (HbeAg), which is usually a marker of high levels of replication of the virus signifying highly infectious blood and body fluids of the infected individual.

Chronic HBV infection: The persistence of HbsAg beyond six months of infection. It is officially defined as two specimens six months apart that are HbsAg-positive. In clinical practice the presence of HbsAg without evidence of acute HBV (see above description) usually signifies chronic HBV infection.

Chronic HBV infection, inactive: Inactive chronic HBV infection is defined by these criteria:

- HbsAg present for six months or more.
- HbeAg negative, anti-Hbe positive.
- Serum HBV DNA <2,000 IU/mL.
- Persistently normal ALT and/or AST levels.
- Liver biopsy confirms absence of significant necroinflammation. Biopsy or noninvasive testing show variable levels of fibrosis.

Chronic HCV infection: The presence of hepatitis C virus (HCV) RNA or hepatitis C core antigen (HCVcAg) in association with positive serology for HCV antibody. A positive HCV antibody alone is not sufficient to diagnose chronic HCV infection.

Cirrhosis: An advanced stage of liver disease characterized by extensive hepatic fibrosis, nodularity of the liver, alteration of liver architecture, and disrupted hepatic circulation.

HBV DNA viral load: HBV viral genome that can be detected and quantified in serum by nucleic acid testing. This is a quantitative test.

Hepatocellular carcinoma (HCC): Primary cancer of the liver arising from the hepatocytes (liver calls) and may be a complication of chronic hepatitis B or C infection.

Hepatitis B surface antigen (HbsAg): HBV envelope protein and excess coat particles detectable in the blood in acute and chronic hepatitis B infection. HbsAg in blood is a sign of active HBV infection. However, it may also be detected in HBV uninfected people for up to 14 days after HBV vaccination.

Immune tolerance: A phase in chronic HBV infection characterized by high levels of HBV DNA in serum but no symptoms of liver disease such as normal ALT concentrations, lack of symptoms, and minimal changes on a biopsy.

Immune active: A phase following the immune tolerance phase characterized by high ALT/AST levels and low viral load. This is caused by the immune system attacking virus-infected liver cells.

Integration: The co-location and sharing of services and resources across different disease areas. In the context of hepatitis B or C infection, this may include the provision of testing, prevention, care, and treatment services alongside other health

services, such as HIV/AIDS, tuberculosis, sexually transmitted infections, antenatal care, sexual and reproductive health, and family planning services.

Rapid diagnostic testing: Immunoassays that detect antibodies or antigens and can give a result in less than 30 minutes.

Testing algorithm: Combination and sequence of specific assays used within hepatitis B and C strategies.

1. Introduction

1.1 Background

Viral Hepatitis is a group of highly endemic diseases that are global public health problems and comparable to other major communicable diseases including HIV, tuberculosis, and malaria. Hepatitis B and C are jointly responsible for an estimated 1.1 million deaths per year globally, mostly due to hepatitis-related liver cancer and cirrhosis. Unfortunately, most people in Malawi with chronic viral hepatitis are not aware of their status and do not receive appropriate care.

Despite the significant burden it places on communities, viral hepatitis has been largely ignored as a health and development priority until recently.

In 2010 and 2014, the World Health Assembly called for member states to recognize and address the burden of viral hepatitis through improved prevention and control efforts.

There is limited data about the prevalence of HBV and HCV and the associated morbidity and mortality burden in Malawi. A 2018 systematic review of local studies estimated 8.1% and 7.3% pooled prevalence of HBV and HCV, respectively.[1] The Malawi Directorate of HIV/AIDS, STI and Viral Hepatitis and the US Centers for Disease Control and Prevention are planning a multi-disease serosurvey using stored samples from the Malawi Population-based HIV Impact Assessment.[2]

1.2 Policy context

The government of Malawi has committed to fulfill goals of the WHO *Global Health Sector Strategy on Viral Hepatitis*[3] to eliminate viral hepatitis by 2030. The Directorate of HIV/AIDS, STI and Viral Hepatitis in the Ministry of Health has been mandated to oversee establishment and operations of viral hepatitis in Malawi in line with global standards. This clinical management guideline was developed in line with the National Viral Hepatitis Implementation Framework 2023-2027.

1.3 Guiding documents

These guidelines are informed by international and national frameworks as outlined below:

- WHO *Global Health Sector Strategy on Viral Hepatitis 2016-2021*[4]
- WHO *Global Guidance on Criteria and Processes for Validation: Elimination of Mother-to-Child Transmission of HIV, Syphilis and Hepatitis B*[5]
- WHO *Guidelines for the Prevention, Care and Treatment of Persons with Chronic Hepatitis B Infection*[6]
- United Nations Sustainable Development Goals for 2030[7]
- Malawi Health Sector Strategic Plan III, 2022-2030
- *Malawi National Strategic Plan for HIV and AIDS 2020-2025*[8]
- Viral Hepatitis Implementation Framework, 2023-2027
- National HIV/AIDS policy, 2022-2030

1.4 Goal, purpose, and rationale

1.4.1 Goal

To eliminate viral hepatitis as a public health threat by 2030 in Malawi.

1.4.2 Purpose

This guideline defines the national protocols for simplified, standardized, and quality hepatitis B and C prevention and clinical management. This document will be used for the training of relevant cadres that will provide viral hepatitis services at all service delivery points.

1.4.3 Rationale

Sustainable Development Goal 3 calls for ensuring healthy lives and promoting well-being at all ages. Subsection 3.3 specifically calls for the ending of AIDS, tuberculosis, malaria epidemics, neglected tropical diseases, water-borne diseases, other communicable diseases and to *combat hepatitis*.[9] The substantial disease burden of viral hepatitis has been realized in various countries across the world and Malawi is no exception.

In response to these targets, it is imperative that Malawi establishes a working program for viral hepatitis at both national and district levels. There is a need to develop national data and/or population-based estimates to track national progress and the success of the program in achieving its goals.

1.5 Service delivery approach

Operationalization of the guidelines will be through capacity-building activities, including classroom training and on-the-job mentorship, targeting technical service providers at all service delivery points.

Procurement of diagnostic and treatment commodities has been incorporated into the existing supply chain system.

2. Hepatitis B Virus (HBV) Infection

Key Facts

- HBV is mostly transmitted during childbirth and in early childhood.
- Most people clear acute HBV infection without treatment.
- The risk of developing chronic infection depends on the age when the virus is acquired:[10,11]
  - 90% when infected at birth
  - 30% when infected under five years of age
  - 5% when infected as an older child or adult (if not immunocompromised)
- About 25% of people with chronic HBV infection develop cirrhosis and hepatocellular carcinoma.
- 75% of hepatocellular carcinoma is attributed to chronic HBV infection in Malawi
- HBV is preventable through immunization. The HBV vaccine is routinely given to infants as part of the pentavalent vaccine at 6, 10, and 14 weeks of age (introduced from 2002 in Malawi). However, this infant vaccination schedule does not effectively prevent perinatal transmission from mother to child.
- An additional dose of the HBV vaccine, given within 12 hours after birth, effectively eliminates mother-to-child transmission (birth dose).
- Pregnant women with a positive HbsAg test should be routinely started on HBV treatment (tenofovir/lamivudine) to reduce the risk of transmission. This is particularly necessary until the HBV birth dose vaccination is fully rolled out.
- HBV vaccination should be given to all HbsAg negative high-risk people:
  - Health workers, sex workers, men who have sex with men, prisoners, people who inject drugs, pre-exposure prophylaxis (PrEP) clients, transgender people, and household contacts of people with chronic HBV infection.
- Effective antiviral treatment for chronic HBV infection is available in Malawi.

2.1 HBV disease burden

Hepatitis B is a bloodborne virus that is completely vaccine preventable. The patient's age at the time of infection determines the risk of chronic disease (see Key Facts).

Hepatitis B can be transmitted sexually, parenterally, and vertically from mother to child. The virus is highly contagious and is stable in the environment with a half-life of more than 7 days or more at 37 degrees Celsius. The incubation period of acute HBV is 12 weeks on average (40-150 days).

The following groups are considered high risk:

- Sexual partners of people with hepatitis B
- Household contacts of people with chronic hepatitis B
- Healthcare workers
- People Living with HIV (PLHIV)
  - PLHIV on non-TDF containing ART regimens
- Patients at heightened iatrogenic risk:
  - Dialysis patients
  - Endoscopy patients
  - Frequently transfused patients (i.e., sickle cell)
- Key populations
  - Sex workers (male, female, and transgender)
  - People who inject drugs or share needles, syringes, and other types of sharp instruments
  - Men who have sex with men
  - Prisoners

2.2 HBV clinical presentation

The virus integrates its DNA into liver cells. Although there is currently no cure for chronic HBV infection, viral activity and disease progression can be fully suppressed with lifelong antiviral treatment. Symptoms of acute HBV infection include:

- Fever
- Anorexia
- Abdominal pain
- Jaundice

Symptoms of chronic and advanced HBV disease (cirrhosis or liver cancer) include:

- Abdominal swelling (ascites)
- Peripheral oedema
- Right upper quadrant abdominal pain
- Jaundice
- Bruising
- Upper gastrointestinal bleeding secondary to varices
- Confusion or coma (hepatic encephalopathy)
- Dilated abdominal veins (caput medusae)

2.3 HBV prevention measures

Hepatitis B vaccination is the most effective prevention method. Specific HBV prevention measures include:

- Pre-exposure vaccination
- Prevention in adult high-risk groups through condom promotion, provision of safe injection equipment, and oral opiate substitution therapy for people who inject drugs
- Prevention of mother-to-child transmission: maternal antiviral treatment and birth dose infant vaccination (as soon as possible, within 24 hours after birth)
- Post-exposure vaccination: in people who have not completed three HBV vaccinations before, vaccination as soon as possible after high-risk exposure*
- Safe handling of sharps and needles
- Blood safety
- Preventing onward transmission by treating people with chronic HBV infection with antiviral drugs

2.3.1 HBV education, counselling, and behaviour change communication

Focus on the following:

- Vaccination for all high-risk groups
- Correct and consistent condom use
- Avoidance of injecting drugs

*Bite, contaminated needlestick, needle-sharing, mucosal exposure to blood or bloody body fluids, sex, rape

- For people who inject drugs, advise them to get into a treatment program. See chapter 3.
- Not sharing personal care items (e.g., razors, toothbrushes)
- Safe tattooing practices

2.3.2 General HBV prevention measures

- Vaccinate targeted populations
  - All adults listed as target populations should receive a three-dose series of vaccinations with their immediate contacts. The second dose is given at week 4 and the third dose is given at week 8.
- Prevent exposure using standard infection precautions amongst healthcare workers
- Screen blood, blood products, and organs for transfusion-transmissible infections
- Implement rigorous infection control procedures for haemodialysis patients
- Introduce needle exchange programs and opiate substitution for people who inject drugs to reduce the spread of HBV, HCV, and HIV
- Advise on lifestyle changes such as reduction and cessation of alcohol intake.

2.3.3 HBV immunization

The hepatitis B vaccine is safe and highly effective. It is available both as a single vaccine (monovalent) or combined with other vaccines (polyvalent). The monovalent HBV vaccine can be used for the birth dose or for adult immunization, but the polyvalent vaccine is not suitable for the birth dose.

The monovalent HBV vaccine is given as soon as possible after birth, within 24 hours. Timely administration provides 90% protection against mother-to-child transmission.

Three follow-up vaccinations must be administered with intervals of four weeks or more to ensure the highest level of protection. The Expanded Programme on Immunization has provided universal vaccination at 6, 10, and 14 weeks after birth against hepatitis B in the combined diphtheria-tetanus-pertussis-haemophilus-hepatitis B (DTP-Hib-HepB) pentavalent vaccine since 2002 in Malawi.[12]

2.3.4 HBV immunization for healthcare workers

Offer all healthcare workers who are involved in direct patient care a full course of hepatitis B vaccination unless they have already completed a full course with three vaccinations in the past. Give the first dose as soon as possible. Give the follow-up doses at months 1 and 6 after the first dose.

Note: This is applicable to healthcare workers who have not received a full course of hepatitis B vaccination before or were vaccinated more than 20 years ago.

2.3.5 Prevention of mother-to-child transmission of HBV

A single positive HbsAg rapid test in pregnancy is an indication to start antiviral treatment to prevent mother-to-child transmission of HBV.[†] HIV-coinfected pregnant women who are taking an ART regimen containing tenofovir disoproxil fumarate (TDF) are fully treated and do not need any additional HBV treatment.

Entecavir is not recommended in pregnancy. Pregnant women who are HIV-HBV coinfected and are not on a TDF-containing regimen will continue on a lamivudine-containing ART regimen.

- Pregnant woman:
  - Initiate tenofovir disoproxil fumarate plus lamivudine (TDF/3TC) as soon as possible. Give 1 tablet of TDF/3TC per day in the morning or in the evening.
  - Continue daily TDF/3TC until six weeks after delivery. The six-week infant immunization visit should be used to stop TDF/3TC to reassess for treatment eligibility.
  - Keep the mother in HBV diagnostic follow-up for at least 6 months to look for HBV flare-ups and to decide if HBV treatment must be re-started. (See flowchart on page 29).
- Baby:
  - Give monovalent HBV birth dose vaccine as soon as possible after birth, within a maximum of 24 hours.
  - Give pentavalent vaccine doses at 6, 10, and 14 weeks to complete the immunization series.

2.3.6 HBV post-exposure vaccination

HBV transmission can be effectively prevented by vaccinating the exposed person as soon as possible after the high-risk event. Giving hepatitis B immunoglobulin also further reduces the infection risk. The first hepatitis B vaccination and immunoglobulin must be given as soon as possible after a high-risk exposure, within 72 hours maximum.

High-risk exposure includes bites, contaminated needle stick injuries, needle-sharing, mucosal exposure to blood or bloody body fluids, sex, and rape. It does not matter if the source person is known to have chronic HBV infection. Offer post-exposure

[†]Universal antiviral prophylaxis with TDF/3TC can be omitted if further HBV lab tests are available that indicate low risk of transmission: HBV DNA below 20,000 IU/mL and/or negative HBeAg. Only when HBV birth dose available.

vaccination to anyone who has experienced a high-risk exposure.

When both the vaccine and immunoglobulin are available and no contraindications exist, give both. However, give either the vaccine or immunoglobulin alone if only one is available.

The following groups do not need post-exposure vaccination:

- Already completed a full course of three hepatitis B vaccinations in the past
- Already on treatment for chronic hepatitis B
- Already on TDF-based ART for HIV

Giving post-exposure vaccination:

- Test for HBV and HIV according to national testing guidelines.
- HbsAg
  1. Negative
     1. Give three doses of the hepatitis B vaccine: give the first dose as soon as possible after exposure, within a maximum of 72 hours. Give the second and third doses at months 1 and 2 after exposure.
     2. Give one dose of 4 ml intramuscular hepatitis B immunoglobulin as soon as possible after exposure, within 72 hours maximum. Inject into a different limb than the hepatitis B vaccine.
  2. Positive:
     1. Do not give post-exposure vaccination when the person already has acute or chronic HBV.
     2. Enroll in viral hepatitis treatment and follow-up. See section **HBV Case Management**
- HIV test
  1. **Negative.** Give post-exposure vaccination for HIV prevention (AVT prophylaxis). Follow the instructions and select the regimen based on the Malawi Guidelines for Clinical Management of HIV in Children and Adults.
  2. **Positive.** Start HIV ART according to the Malawi Guidelines for Clinical Management of HIV in Children and Adults.

2.3.7 Safe handling of sharps and needles

Healthcare workers must follow infection prevention protocols. Refer to the National Infection Prevention and Control Guidelines.

3. HBV Screening And Diagnosis

Follow the Malawi Integrated Rapid Testing Guidelines for HIV, Syphilis, and Hepatitis B.[23]

HBV screening is integrated with HIV and/or syphilis testing in different service delivery points, depending on the risk population.

A single rapid diagnostic test for hepatitis B surface antigen (HbsAg) is used for HBV screening. Any positive HbsAg test confirms current HBV infection, but it cannot distinguish acute from chronic infection. However, a second positive HbsAg test after six months confirms chronic infection.

Further laboratory tests (liver function, full blood count, hepatitis B DNA-PCR), clinical examination, and investigations (e.g., ultrasound scan) are needed for most patient groups to determine the need for HBV treatment.

Offer HBV vaccination to all HbsAg negative persons from high-risk groups.

See Table 2 for routine and focused testing in various groups.

3.1 HBV key serological markers

Hepatitis B has different markers for acute and chronic infection. Table 1 outlines all markers seen that are significant in staging and diagnosis.

Table 1. Key serological markers in determining stage of infection

Short name	Description	Interpretation
HbsAg	Hepatitis B surface antigen, a virus protein	Screening test for current infection First serological marker to appear HbsAg persistence for six months or more confirms chronic infection

Short name	Description	Interpretation
HbeAg	Hepatitis B envelope antigen, a virus protein	Positive HbeAg indicates high active virus replication and high risk of maternal-to-child transmission
HbcAg	Hepatitis B core antigen	Usually not found on serological tests Only antibodies to HBc are detected (i.e., anti-HBc IgG and anti-HBc IgM)
IgG anti-HBc	Immunoglobulin G antibody against HBc protein	Most sensitive lifelong marker of past HBV infection By contrast, anti-HBs may become undetectable after childhood HBV infection
IgM anti-HBc	Immunoglobulin M antibody against HBc protein	Marker of acute infection or reactivation
anti-HBs (HbsAb)	Immunoglobulin antibody against HBs protein	Indicates immunity to HBV, usually after resolution of infection or successful immunization
anti-Hbe (HbeAb)	Immunoglobulin antibody against Hbe protein	HbeAg indicates rapid replication of the virus Usually the immune system has sustained control against the replicating virus

3.2 Whom To Test For HBV

Table 2. Target groups for hbv testing

Population	Recommendation	Routine Testing	Focused Testing in Most Affected Population
Pregnant women	All pregnant women unless previously vaccinated (pentavalent as infant or monovalent later in life) at the first antenatal care visit	✓	
People with sexually transmitted infections	Routine PITC unless previously vaccinated. Offer vaccination if HBV negative”	✓	
Healthcare workers	Routine PITC unless previously vaccinated. Offer vaccination if HBV negative.		✓
Adults, adolescents, and children	Routine PITC unless previously vaccinated. Offer vaccination if HBV negative.		✓
Prisoners	On entry, at 6 months, on discharge unless previously vaccinated. Offer vaccination if HBV negative.	✓	
FSW, TG, MSW, MSM, PWID	12-monthly unless previously vaccinated. Offer vaccination if HBV negative.		✓

Population	Recommendation	Routine Testing	Focused Testing in Most Affected Population
Blood donors[13]	Routine Screening	✓	
Children 0-14 years born to HbsAg positive women	Routine PITC as early as possible from age 9 months up to 14 years, regardless of previous vaccination status. Offer vaccination if HBV negative		✓
Sex partner and household contacts of HBV index client	Routine PITC unless previously vaccinated. Offer vaccination if HBV negative.	✓	
People living with HIV who are not on a regimen containing tenofovir disoproxil fumarate (TDF)	Screen patients who are not on TDF-containing regimen, or have a contraindication to TDF, or develop contraindication to TDF		✓

4. HBV Case Management

Key Facts

- Acute hepatitis B virus (HBV) infection is rarely symptomatic in children under five years of age, but about 40% of older children and adults with acute infection have symptoms. Fulminant acute hepatitis is rare, but more common in adults ages 60 years and older.
- There is no specific treatment for acute hepatitis B.
- Most people with chronic hepatitis B have no symptoms.
- There are two aims for Hepatitis B treatment (AVT):
  - Prevent perinatal mother-to-child transmission
  - Prevent (progression of) fibrosis, cirrhosis, and hepatocellular carcinoma

4.1 Acute hepatitis B

Acute HBV infection is usually asymptomatic but can present with flu-like symptoms. Rarely, acute fulminant hepatitis can develop with signs of liver failure such as confusion and/or bleeding or coagulation problems. Typically, 90% to 95% of immunocompetent adults will spontaneously clear HBV infection[14] within six months. Patients should not be started on treatment if they do not meet the treatment eligibility criteria.

4.1.1 Phases of acute HBV infection

- Early prodromal phase: Ranges from 14-21 days. Characterized by flu-like sickness (fever, malaise), followed by jaundice.
- Pre-icteric phase: Characterized by enlargement of liver and spleen (hepatosplenomegaly), usually mild (2-3 cm below costal margin), vomiting, myalgia, nausea, epigastric pain.
- Icteric phase: After the pre-icteric phase subsides; characterized by the presence of dark urine, pale stools, pruritus, and weight loss.
- Convalescent phase: Jaundice tends to resolve, especially in younger individuals but can last six weeks or more in adults. All symptoms gradually resolve.

Treatment should not be given in the acute phase of illness because it may increase the risk of developing chronic infection.

4.2 Chronic hepatitis B

Chronic HBV is defined as the persistence of HBsAg for six months or more.

HBV infection cannot be eradicated completely with available treatment because of the persistence of the virus in the liver cells, even in individuals with serological markers of resolved infection.

Therefore, therapeutic management of HBV focuses on preventing cirrhosis and hepatocellular carcinoma (HCC). Antiviral drugs reduce the activity of the virus and this halts or decreases harm to the liver and prevents viral transmission to others.

Chronic hepatitis B:

- Is commonly clinically silent
- In advanced stages can present with signs of decompensated liver failure (i.e., ascites, caput medusa, severe splenomegaly).
- Can lead to hepatocellular carcinoma; patients may present with an enlarging and tender nodular liver with or without weight loss.

Antiviral treatment is recommended in selected patients with chronic hepatitis B infection.

4.3 Goal of HBV treatment

The primary goal of treatment is to achieve a functional immunological response with HBV DNA suppression and halting of clinical progression. Even with successful antiviral treatment, seroconversion (loss of HBsAg) is rare.

For most patients, treatment must be continued for life and there is a risk of relapse if treatment is stopped.

Treatment prevents disease progression and long-term complications of chronic HBV such as:

- Cirrhosis
- Liver fibrosis
- Liver failure
- Hepatocellular carcinoma

4.4 HBV treatment eligibility for adults 15+ years

Criteria for starting hepatitis B treatment in HIV negative adults (15+):

Routinely screen all HBsAg positive patients for HIV infection. All HIV co-infected patients need to start TDF-containing ART for HIV and HBV treatment for life.

Treatment eligibility for HIV negative adults is determined by **ONE** of the following categories:

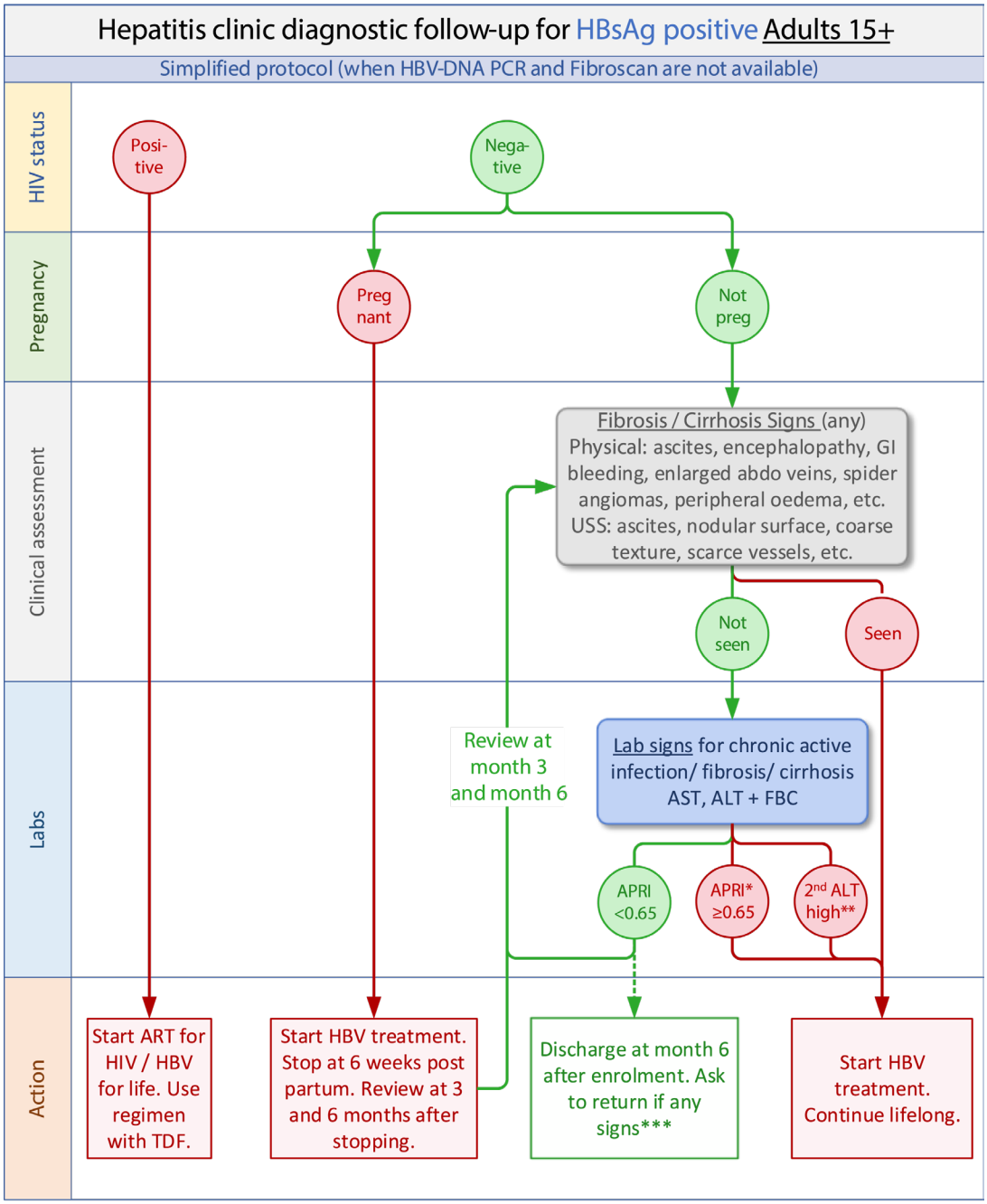
- **Clinical assessment** with any signs of decompensated liver damage such as ascites, caput medusa, and hepatic encephalitis.
- **APRI** score of 0.65 or higher. Do not use the APRI score for patients with very high AST levels (≥300 IU/mL) as this is usually a sign for acute hepatitis and not an indication for starting treatment. In this case, investigate other causes of acute hepatitis. Repeat LFT, FBC after 2 weeks and calculate the APRI score when the AST has dropped below 300 IU/mL.

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

- **Abdominal ultrasound** showing signs suggestive of liver fibrosis and cirrhosis.
- **Persistently elevated ALT** of 40 IU/mL or higher within 6 months and at least 8 weeks apart.

4.4.1 HBV treatment eligibility criteria algorithm for adults

Figure 1. Treatment eligibility algorithm for HBV



* APRI score: Do not use the APRI score for patients with very high AST levels (≥350 IU/mL) as this is usually a sign for acute hepatitis and not an indication for starting treatment. In this case, investigate other causes of acute hepatitis. Repeat LFT, FBC after 2 weeks and calculate the APRI score when the AST has dropped below 350 IU/mL.

** 2nd ALT high: at least 2 ALT results ≥40 IU/mL within 6 months, at least 8 weeks apart

*** Explain the possible signs: tiredness, body pains, stomach discomfort, nausea, appetite loss

4.5 HIV/HBV coinfection in adults

There is usually independent transmission and acquisition of HBV and HIV. HBV is more commonly acquired in childhood under the age of five years through intense contact (horizontal). HIV infection occurs later in life, primarily via sexual intercourse and through mother-to-child transmission.

HIV/HBV coinfection is associated with:

1. Increased HBV replication and rates of HBV reactivation
2. Acute liver failure
3. Increased rates of occult HBV
4. Chronicity of newly acquired HBV infections
5. Accelerated progression to fibrosis and cirrhosis
6. HCC occurs at a younger age and is more aggressive
7. Increased risk of ART hepatotoxicity
8. ART-related immune reconstitution hepatitis

Liver-related mortality is twice as high for HBV/HIV-coinfected individuals compared with HCV/HIV-coinfected individuals, and much more common than in individuals infected with HIV alone.

Patients with a CD4 count of less than 200 cells/mL is associated with a higher risk of liver-related deaths compared to a CD4 count of more than 350 cells/mL[15]

Additionally, a potential association with adverse HIV outcomes in HBV-coinfected individuals was demonstrated in the SMART study where HIV-associated immune deficiency was enhanced by active HBV replication, resulting in increased progression to AIDS-related outcomes and all-cause mortality.[16]

4.5.1 Management of HBV/HIV coinfection in adults

ART initiation takes precedence. When switching a person with HIV/HBV coinfection off their first-line ART, it is important to retain tenofovir in the new regimen.

Treatment of HIV/HBV coinfection:

- HIV status ascertained: Offer ART against HIV.
- Use tenofovir-based regimens as indicated in the *Malawi Guidelines for Clinical Management of HIV in Adults and Children*.[17]
- HIV status not ascertained in the last three months: Offer an HIV test.

4.6 HBV in pregnant and breastfeeding women

4.6.1 Management of the pregnant woman

Screen all pregnant women in antenatal care during the first visit and admission to the labour ward for those with unknown status for hepatitis B in line with the Integrated HIV, Syphilis, and Hepatitis B rapid testing guidelines.[23]

When antiviral treatment during pregnancy is combined with the HBV birth dose vaccine, mother-to-child transmission is effectively eliminated.

In pregnant women who are HBsAg positive, do the following:

- Patient education
  - Explain: transmission risk to infant and sex partner, follow-up tests, prognosis, and treatment choices.
  - Provide family referral slip for family and close contacts for hepatitis testing and vaccine if negative.
- Ascertain HIV status
  - For all women not previously diagnosed with HIV: provide a new HIV test following the standard HIV diagnostic algorithm.
  - For known HIV infected women:
  - Ensure good adherence to ART; initiate or re-initiate women currently not on ART as soon as possible.
  - Ensure the ART regimen includes TDF/3TC. However, 3TC alone is likely to give adequate protection in women with TDF contraindications.
  - HBV / HIV co-infected pregnant women are adequately treated for both conditions with TDF-containing ART. Follow up co-infected patients at the ART clinic.
- HIV negative women
  - Enroll in viral hepatitis care immediately.
  - If HBV DNA viral load and HBe Ag test are not available: offer TDF/3TC immediately until 6 weeks post-partum to reduce the risk of mother-to-child transmission.
  - If HBV DNA viral load is available: defer TDF/3TC treatment if result is <20,000 IU/mL. Start treatment immediately if HBV DNA ≥20,000 IU/mL and continue until 6 weeks post-partum.

- If HBe Ag test is available: defer treatment if HBe is negative. Start treatment immediately if HBe is positive and continue until 6 weeks post-partum.
- Stop treatment at 6 weeks post-partum. Follow up clinically and with LFT, FBC at month 3 and month 6 after discontinuation to decide if treatment needs to be resumed.

4.6.2 Management of an HBV-Exposed infant and breastfeeding[18]

- HBV birth dose vaccine, given within 24 hours of birth, is safe for normal and low birth weight infants.†
- Routine HBV birth dose vaccination is recommended for all infants, regardless of maternal HBV infection. However, prioritize known HBV exposed infants until routine birth dose vaccination is rolled out nationally.
- In addition to the HBV birth dose, the pentavalent vaccine given at 6, 10, and 14 weeks completes the childhood vaccination series.
- The risk of transmitting HBV via breastfeeding is minimal.
- Routinely test all infants born to HBV infected mothers using a regular HbsAg rapid test as soon as possible from age 9 months (align with measles vaccination schedule).
- Test all HBV exposed children who have not previously received a negative HBsAg result up to age 14 years.

1. Negative result: discharge from care. No follow-up HBV testing is needed.
2. Positive result: link to hepatitis care immediately

- Recommend exclusive breastfeeding until age 6 months, followed by mixed feeding until age 18 months, for all infants born to HBsAg-positive mothers, regardless of HBe Ag in the mother or oral mucosal injury in neonates or infants.

4.7 HBV in children (ages 2-14)

Chronic HBV is usually asymptomatic in children, as they are generally in the immune-tolerant phase. Cirrhosis and HCC are very rare in children and adolescents with chronic HBV infection.

Early identification and monitoring of all HBV infected children are key to preventing long-term progression.

Monitor children with chronic hepatitis B annually until age 15 years:

†At 6 weeks post delivery, the child is scheduled to received the Pentavalent vaccine which contains the HBV vaccine

- HBsAg
- Liver function test
- HBV DNA viral load

Start HBV treatment if any signs of cirrhosis or necro-inflammatory disease (biopsy) are detected.

4.7.1 Treatment of HBV in HIV negative children

Most HBV infected children need only clinical and diagnostic follow-up, but no treatment, because most are in the immune-tolerant phase with high viral replication but minimal damage to the hepatocytes.

Enroll in viral hepatitis care and follow-up:

- Conduct full blood count and liver function tests every 3 months for 12 months and annually thereafter.
- Start entecavir **only** when ALT levels are greater than 2.5 times the upper limit of normal on **three or more** visits during the 12-month monitoring period.

Before starting treatment, take a thorough history to rule out other causes of abnormal liver function tests, such as consumption of herbal medications. When a history of herbal medications is present:

- Advise guardian to **stop** the suspected herbal medication for one month and re-conduct liver function tests before considering treatment with entecavir.
- Advise guardians to also disclose **any** medication administered to the patient.

Conduct a biopsy at a tertiary facility to confirm fibrosis and/or necro-inflammatory changes. This finding is an indication to treat.

Alternatively, conduct HbeAg and HBV DNA testing. Start treatment if

- HBeAg is positive and HBV DNA of ≥2000 IU/mL.

4.7.2 Management of HBV/HIV coinfected children

In HBV/HIV coinfected children, management of HIV takes precedence, therefore refer to the current *Malawi Guidelines for Clinical Management of HIV in Children and Adults*.[17]

4.8 Whom Not To Treat For HBV But Continue Monitoring

Antiviral therapy should be **deferred** in persons with:

- No clinical or ultrasound evidence of fibrosis and cirrhosis
- APRI score of less than 0.65 in adults
- Signs of acute hepatitis: AST ≥300 IU/mL

And:

- Persistently normal ALT levels (more than two consecutive normal results)
- Low levels of HBV DNA replication (HBV DNA <2000 IU/mL) (if HBV DNA testing is available)

The higher the HBV viral load, the higher the risk of transmission, disease progression to cirrhosis and HCC. The risk of transmission is low in individuals with a viral load below 2000 IU/mL.

- The client may be discharged from viral hepatitis diagnostic follow-up if all results remain normal.
    - Advise client to return only if they experience:

        I. Jaundice
        II. General Body weakness
        III. Abdominal pain
        IV. Nausea and/or vomiting

- Explain the importance of maintaining a healthy lifestyle:
    - Avoid herbal and other medicines that may cause liver damage
    - Abstain or limiting alcohol
    - Avoid aflatoxin exposure from mouldy maize, groundnuts, etc.

4.9 HBV Treatment Options

The aim of this treatment is viral suppression (HBV DNA undetectable).

The standard first-line HBV treatment regimen is **TDF/3TC** for patients weighing 30kg+ and **ETV** for children below 30kg. Routinely transition all children on ETV to TDF/3TC once they reach 30kg.

HBV treatment is well tolerated and effective long-term if taken consistently to avoid resistance. Most patients need to continue HBV treatment for life.

The available regimens and dosing are shown in Table 4

Tenofovir (TDF) has a high resistance barrier and is effective as monotherapy or in combination with 3TC or FTC. The standard dose of 300mg can only be given to children and adults from 30kg+.

Lamivudine (3TC) and **emtricitabine** (FTC) are very similar. They are initially effective but have a low resistance barrier. They should not be given as monotherapy unless TDF and ETV are both not tolerated or contraindicated.

Entecavir (ETV) is effective as monotherapy and the standard regimen for children below 30kg. It is also used as an alternative regimen for older children and adults with TDF-contraindications, for example kidney disease.

Table 3. HBV treatment regimens, formulations, indications and contraindications

Paed. Formulation	Adult Fomulation	Used for HBV RX initiation 'Start regimen'	Line	Contraindications	Possible adverse reaction	If confirmed
	TDF 300/ 3TC 300	**Standard for all patients 30 Kg+**	1st	• Renal failure • Uncontrolled diabetes • Epilepsy	• Renal Failure • Headache, Nausea, Diarrhoea • HBV Treatment failure	• **Switch to ETV** • • **Switch to ETV**
	TDF 300/ FTC 300	**Alternative for Standard for all Patients 30 Kg+**	1st	• History of psychosis • Renal failure	• Renal Failure • Headache, Nausea, Diarrhoea • HBV Treatment failure	• **Switch to ETV** • • **Switch to ETV**
EVT (Syrup)	ETV 0.5	**Only**	2nd	• Renal failure • Patient on rifampicin 19 • Pre-existing jaundice or suspected hepatitis 20	• Renal failure • Fatigue, Headache, Dizziness • Hypersensitivity	• **Use with caution** • **Monitor closely** • **Switch TDF/3TC**

Table 4. Dosing of HBV treatment regimens

Drug	Tablets per tin		10 – 13.9 kg		14 – 19.9kg		20 – 24.9kg		25 – 29.9kg		30+ kg	
	Paed.	Adult	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
TDF/3TC	0	30									1	0
TDF/FTC	0	30									1	0
ETV	ml	30	4	0	6	0	8	0	1	0	1	0

Table 5. HCV treatment regimens, formulations, indications, and contraindications

Drug	Tablets per tin		10 – 13.9 kg		14 – 19.9kg		20 – 24.9kg		25 – 29.9kg		30+ kg	
	Paed.	Adult	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
SOF/VEL	pllts	30	1	0	1	0	1	0	1	0	1	0
SOF/DCV	0	30									1	0
GLE/PIB	pllts	30	3	0	3	0	4	0	2	0	3	0

Table 6. Dosing of HCV treatment regimens

Paed. Formulation	Adult Fomulation	Used for HBV RX initiation 'Start regimen'	Line	Contraindications	Possible adverse reaction	If confirmed
SOF 200/ VEL 50	SOF 400/ VEL100	**Standard for all patients 30 Kg+**	1st	HBV infection	HBV reactivation	**Monitor closely for increasing HBV viral load**
	SOF 40/ DCV 60	**Alternative for Standard for all Patients 30 Kg+**	1st	HBV infection	HBV reactivation	**Monitor closely for increasing HBV viral load**
GLE 50/ PIB 20	GLE100/ PIB 40	**Second line for all patients 10kg+**	2nd	Patient with Chronic HBV	HBV reactivation, severe dizziness	**Switch to SOF/VEL**
				Patients on rifampicin	HBV reactivation TB treatment failure	**Switch to SOF/VEL**

§Entecavir can still be used in patients with Renal Failure but with caution i.e., CrCl ≥50 mL/min: No dosage adjustment required, CrCl 30-49 mL/min: Reduce to 0.25 mg/day or 0.5 mg q48hr, CrCl 10-29 mL/min: Reduce to 0.15 mg/day or 0.5 mg q72hr.
**Very rare. But use lower doses return to TDF, and at low doses if renal impairment present.
††Patients on HCV (with HBV co-infection) treatment should have their HBV viral load monitored closely to prevent reactivation. Complete HCV treatment prior to starting HBV treatment.

4.9.1 HBV appointment/dispensing interval

- Give next appointment dates at least two days before the patient will run out of medication (2-day drug buffer).
- Align appointment dates with other scheduled clinic visits such as ANC.
- Patients who start antiviral treatment should be reviewed clinically at months 1, 3, and 6 after initiation.
    - Thereafter, stable and adherent patients can come for appointments every 24 weeks (six months).

4.9.2 When to stop HBV treatment

Clients usually require lifelong antivirals treatment. Treatment interruption can cause HBV reactivation and clinical hepatitis flare-up and liver failure.

Monitor clients who have stopped treatment every 3 months for at least 1 year:

- Clinical signs of liver decompensation
- ALT increase
- HBV DNA viral load (if available)

4.9.3 HBV drug resistance

Explain the importance of daily adherence to antiviral medicines at each clinic visit. Poor adherence leads to virus replication in the presence of low drug levels which can lead to resistance and treatment failure.

TDF and ETV have a high resistance barrier, but resistance can develop quickly on 3TC and FTC monotherapy.

4.9.4 Monitoring for tenofovir and entecavir toxicity

Measurement of baseline renal function and assessment of baseline risk for renal dysfunction are not required but should be considered in all clients with risk factors for renal disease prior to initiation of antiviral therapy.

Risk factors for renal disease include:

- Age 40+ years
- Hypertension
- Diabetes mellitus

- Body mass index <18.5 kg/m^2
- On nephrotoxic medications
- Known creatinine clearance <90 ml/min
- Clinical indications of renal disease

Test urine for proteinuria and blood for **creatinine** before or during treatment, especially in groups at high risk of renal disease and those with symptoms or signs of a possible renal problem.

Creatinine clearance should be calculated using the Cockcroft-Gault formula.

Cockcroft-Gault Formula for Estimating Creatinine Clearance

$$\text{CrCl (mL/min)} = \frac{(140\text{-age}) \times \text{Lean Body Weight (kg)}}{\text{Serum Creatinine (mg/dL)} \times 72} \quad (\times 0.85 \text{ if female})$$

Renal function should be monitored annually in persons with risks or indications of renal disease.

4.9.5 Monitoring for hepatocellular carcinoma

Conduct abdominal ultrasound annually for the following clients:

- Family history of HCC
- Age 40+ years
- Symptoms such as abdominal pain, abdominal swelling

Refer all clients with hepatic masses to tertiary facilities for further investigations.

5. Hepatitis C (HCV) Infection

Key Facts

- HCV is bloodborne, mostly transmitted by:
  - Re-use or poor sterilization of needles and medical equipment
  - Transfusion of unscreened blood products
  - Needle sharing among drug users
  - Mother-to-child during birth
- HCV is sometimes transmitted via sex practices that lead to exposure to blood.
- HCV is not spread through breast milk, food, water, hugging, kissing, and sharing food or drinks with an infected person.
- There is no vaccine for HCV.
- 30% of people clear HCV infection spontaneously, without need for treatment.
- HCV infection can be cured with highly effective direct-acting antivirals.
- Offer treatment to all individuals diagnosed with HCV infection who are 6+ years.
- Most clients with acute HCV infection have no or only mild symptoms.
- HIV/HCV coinfected persons have a higher chance of progression to cirrhosis if not treated.
- The aim treatment for HCV infection is to cure.
  - Treatment of HCV in pregnancy is not recommended.

5.1 Introduction

HCV is caused by an RNA virus that can cause both acute and chronic infection.

Acute HCV is defined by virus clearance from the blood within six months of acquiring the infection.

Chronic HCV infection is the continued presence of HCV six months or more after acquiring infection.

Globally, 58 million people are living with HCV infection.[22,23] About 15% to 25% of infected individuals spontaneously clear the virus within six months of infection. However, the remaining 75% to 85% will develop chronic hepatitis C. Of those chronically infected, the risk of cirrhosis is 15% to 30% within 20 years, with a 1% to 4% annual risk of hepatocellular carcinoma.[24]

Most cases of acute HCV infection are asymptomatic. Although fulminant hepatic failure from acute HCV infection is rare but possible.

- Chronic hepatitis C can cause liver fibrosis, cirrhosis, and finally hepatocellular carcinoma.
- Risk factors such as co-infection with HIV, HBV, alcohol use and immunosuppression accelerate HCV progression to cirrhosis or HCC.
- HIV/HCV coinfected persons with advanced immunodeficiency (CD4 count less than 200 cells/mm^3) are at high risk of progression to cirrhosis and HCC.

5.2 HCV transmission

- Transmission occurs via parenteral and non-parenteral routes through blood, exposure to needles, and rarely through sexual relations (particularly if the immune system is compromised). HCV has an incubation period of approximately eight weeks.

5.3 HCV risk populations

Table 7 Populations at high risk for HCV infection

Population	Comment
People who inject drugs	People who inject drugs experience among the highest burdens of hepatitis C globally. In Tanzania and Kenya, the prevalence of anti-HCV and HCV RNA was 30% and 8.6%, respectively.
Recipients of infected blood products or invasive procedures	Common in healthcare facilities with inadequate infection control practices (e.g., reuse of needles) or insufficient bloodborne pathogen screening of donor blood products.

Population	Comment
Children born to HCV-infected mothers (mother-to-child transmission)	HCV transmission risk is estimated as 4–8% among mothers without HIV infection and 10.8–25% among HIV infected mothers.
Sexual contacts of HCV-infected persons	There is low risk of sexual transmission of HCV among HIV-uninfected heterosexual and homosexual partners.
People with HIV infection	PLHIV are six times more likely to acquire HCV infection.
People who have had tattoos	Tattoo recipients have higher prevalence of HCV compared with persons without tattoos. Use of nonsterile, shared equipment could contribute to HCV transmission. Alternatively, this association might reflect other risk factors among persons with tattoos.
Healthcare workers	Exposure to needle-stick injuries.
Patients on haemodialysis	Patients may be exposed to HCV due to poor infection prevention and control practices, including unsafe injections and infusions, or through receipt or blood products.

5.4 Prevention of HCV

There is no HCV vaccine and prevention depends on reducing exposure.

The primary prevention strategy for HCV infection consists of treatment as prevention, activities that reduce and/or eliminate the risk of transmission, such as increasing awareness through social and behaviour change communications.

5.4.1 Prevention of HCV infection for the public

Harm reduction practices are key for reduction practices among key populations such as people who inject drugs. Key measures are as follows:

- Provide safe injection materials for injecting drug users.
- Avoid unsafe medical and traditional practices such as tattooing, non-medical circumcision and skin cutting in traditional medicine.
- Avoid sharing toothbrushes, razors and intimate contact with carriers.
- Promote correct and consistent condom use.
- Integrated action to include services for vulnerable populations such as victims of gender-based violence
- Routine screening of high-risk groups (annually) and prompt treatment of all eligible clients.

5.4.2 HCV prevention in healthcare settings

It is critical to consider occupational safety measures to prevent transmission of HCV infection to healthcare workers through the following:

- Hand hygiene
- Safe handling and disposal of sharps
- Safe cleaning of equipment
- Testing of donated blood and blood products
- Training of health personnel in general infection prevention and control measures
- Treatment of HCV-infected patients to reduce the risk of transmission

5.4.3 Prevention of mother-to-child transmission of HCV

Mother-to-child transmission occurs in approximately 5% of HCV mono-infected women and 10% of HIV/HCV coinfected women.

Other risk factors history of injecting drugs, prolonged rupture of membranes, and performance of obstetric procedures such as fetal scalp monitoring and forceps delivery.

Prevention of transmission to the infant is paramount.

- Avoid invasive procedures that increase the risk of vertical transmission during labour.

- HCV infection is no indication for routine cesarean section.

Postpartum breastfeeding should commence unless the mother has bleeding or cracked nipples.

5.5 HCV screening and diagnosis

HVC diagnosis requires two steps:

1. Positive HCV antibody test
2. Confirmation with HCV RNA nucleic acid testing (viral load)

Or, if available, use a point-of-care HCV core antigen (cAg) detection test to confirm HCV infection. Individually, this test can confirm HCV infection.

Hepatitis C infection is diagnosed by the detection of HCV RNA or HCV cAg. A positive HCV antibody indicates prior infection but may be negative during acute infection.

	HCV-Ab (+)	HCV-Ab (-)
HCV RNA or cAg (+)	Chronic hepatitis C	Acute hepatitis C
HCV RNA or cAg (-)	Past infection resolved through natural clearance or treatment	Never infected

Patients with ongoing risk of HCV infection (e.g., people who inject drugs) benefit from annual HCV screening.

Refer to Figure 2 and Figure 3 in the appendix for testing, diagnosis, and treatment algorithm.

5.5.1 HCV reflex testing

The WHO recommends reflex testing for viraemic confirmation of HCV infection to reduce turnaround time and to improve linkage to care. This method allows patients to get access to treatment without having to wait for a confirmatory HCV RNA nucleic acid test that may take time, requiring them to return to the facility another day.

Two types of reflex testing are:

1. Laboratory reflex testing
    - A venous whole blood sample is taken and tested for HCV antibodies and kept for HCV RNA nucleic acid testing if the result is positive. Results of both tests are sent back to the clinician for treatment commencement.
2. Clinical reflex testing
    - First, a finger prick sample is taken to test for HCV antibodies, and if it is positive, another finger prick sample is taken for point-of-care HCV RNA to confirm viraemic infection.

5.6 HCV counselling

Most patients with HCV infection are asymptomatic at the time of diagnosis. However, the potential sequelae could have important physical and emotional consequences.

Psychosocial counselling is therefore important, especially in high-risk groups such as people who inject drugs.

Offer counselling services and screen for depression at diagnosis and during follow-up in people who inject drugs and are at risk of HCV or diagnosed with HCV. Use the Patient Health Questionnaires [PHQ-9 (see appendix)] to screen for depression according to the Malawi Guidelines for Clinical Management of HIV in Children and Adults.[17]

Counselling should involve discussions about routes of transmission and advice on measures to decrease the risk of transmission from one individual to another. A key prevention measure is needle exchange services.

5.6.1 Needle exchange and opioid substitution therapy programs

A high-risk group for hepatitis C and HIV is people who inject drugs and have substance abuse challenges.

Always offer counselling services for this patient group. Screen for depression and substance abuse where applicable as per the *Malawi Guidelines for Clinical Management of HIV in Children and Adults*.[17]

Needle exchange programs act as a bridge to other healthcare services such as screening, testing, treatment, care, and support against HCV, HIV, and HBV.

Drop-in centres are now accredited ART sites and will offer viral hepatitis services. Other services such as counselling and opioid substitution therapy may be offered by trained cadres in drop-in centres where possible.

Healthcare workers in these sites **should provide** the following:

- Sterile needles in exchange for used needles (for disposal)
- Disinfectant and gauze
- Education and counselling to reduce disease transmission and injection overdose risks
- Condoms to reduce the risk of sexual transmission of HBV, HCV, and STIs.
- HIV, HBV, HCV, and STI testing services (per Integrated testing guidelines)[23]
- Naloxone, if available, to reverse opioid overdoses (if available)
- Referral and linkage to HBV, HIV, HCV, STI, TPT, PrEP, and post-exposure prophylaxis services

6. Hepatitis C Treatment

Key Facts

- The WHO recommends the use of antiviral regimens for the treatment of persons with chronic HCV infection aged 6 years and above.[25]
- Assess the degree of liver damage using the APRI score and clinical signs of compensated or decompensated liver damage.
- Rule out pregnancy because treatment of HCV infection during pregnancy is not recommended
  - The duration of treatment for HCV infection depends on the presence of liver cirrhosis.
  - Decompensated cirrhosis patients may be treated with DAA under specialist care to manage complications.

Treatment should begin for all eligible patients who have active HCV infection (positive HCV antibody test and detectable HCV RNA). All available DAA for HCV treatment are potentially teratogenic. Rule out pregnancy before starting DAA treatment. Women should use effective contraception while on treatment.

Assess whether the patient has compensated or decompensated cirrhosis.

Compensated cirrhosis can be defined as a patient who is asymptomatic or presents with mild symptoms of liver disease such as jaundice. Patients with compensated cirrhosis are **recommended to receive treatment**.

Patients with decompensated cirrhosis present with symptoms of severe liver disease such as ascites, hepatic encephalopathy, variceal hemorrhage (upper gastrointestinal bleeding), or spontaneous bacterial peritonitis. Patients in this group should only be managed with specialist care at central hospitals.

6.1 Patient education for treatment of HCV

It is important to highlight the following issues during interactions with a patient.

Development of cirrhosis and liver damage can take time.

Factors such as excessive alcohol consumption, substance abuse, and obesity can accelerate the progression of liver disease in people living with hepatitis. An alcohol intake assessment is recommended for all persons with HCV infection, followed by a behavioural alcohol reduction intervention for persons with moderate-to-high alcohol intake. See Figure 4 in the appendix for the alcohol consumption assessment tool.

Educate the patient about lifestyle changes and emphasize its importance to the success of treatment and patient management. Patients with chronic hepatitis require a specific diet. Viral hepatitis coordinators should liaise with district dieticians for support.

Ensure the patient knows that the aim of treatment for HCV is to cure it, meaning that the treatment duration is finite.

6.1.1 Treatment for children 6 years+ and adults

Direct-acting antivirals (DAA) are usually well tolerated, with only minor side effects including fatigue, headache, insomnia, and nausea.

Table 8 gives an overview of the standard DAA regimens, including strength of the adult tablet, minimum body weight and duration of treatment course, depending on the presence of cirrhosis. Patients with decompensated cirrhosis may be treated with DAA under specialist care.

Table 8: HCV treatment fixed-dose combination regimens overview

Regimen	Code	Strength (adult tab)	Min. weight	Treatment length	Line
Sofosbuvir/ Velpatasvir	SOF/ VEL	400/100mg	30 kg	12 weeks	Preferred 1st
Sofosbuvir/ Daclatasvir	SOF/ DCA	400/60mg	26 kg	12 weeks (no cirrh.) 24 weeks (cirrhosis)	Alternative 1st
Glecaprevir/ Pibrentavir	G/P	300/120mg	45 kg	12 weeks	Alternative 1st

See **Table 5** and **Table 6** for details on prescribing and dosing.

Assess cure if sustained virological response is seen 12 weeks after treatment completion. Sustained virological response is defined as an undetectable HCV RNA test.

6.2 Treatment of HCV in pregnancy

DAA should not be given in pregnancy. Women should be on effective contraception while on treatment. The safety and efficacy of direct-acting antivirals in pregnancy have not been adequately evaluated.

In addition, women should avoid getting pregnant for six months after completing ribavirin-based therapy. Ribavirin is teratogenic and is contraindicated during pregnancy. It is part of an older treatment regimen and may be used in decompensated liver failure for patients with HCV but only at tertiary care levels.

Interferons are also contraindicated in pregnancy because they have unfavourable neuropsychiatric and systemic effects.

Women with HCV who wish to have children should consider direct-acting antiviral therapy before pregnancy.

There is limited safety data on the HCV direct-acting antiviral use during pregnancy and breastfeeding, although small studies showed no safety concerns. Despite the lack of a recommendation, treatment may be considered on specialist recommendation.

6.3 Treatment of hepatitis C in children (ages 6-11)

Children are mostly infected by their mothers perinatally. Some older children may get infected via unsafe injections and poor infection prevention. Specific HCV symptoms are uncommon in children. Cirrhosis, hepatocellular carcinoma, or extrahepatic manifestations are rare. However, HCV may decrease the general quality of life in adolescents. Perinatal infection leads to cirrhosis at an earlier age. Therefore, early diagnosis and treatment in children is key to preventing long-term morbidity.

Consider DAA treatment from age 6 years, depending on the minimum weight for each regimen and potential availability of paediatric formulations.

Younger children (3-5 years) may be treated with DAA in specialist paediatric care.

6.4 HIV/HCV coinfection

Persons with HIV/HCV coinfection are at a higher risk for progression of fibrosis and must be prioritized for treatment. HIV/HCV-coinfected people have demonstrated more rapid disease progression, compared with those who are HIV mono-infected,

and had an impaired recovery of CD4 cells.

Treatment for HCV infection needs to consider drug interactions between antiviral medications. HIV/HCV coinfection does not affect the choice of HCV direct-acting antiviral regimen or duration of treatment. Refer to Table 9 for drug interactions between antiviral medicines.

The decision about when to initiate treatment for HIV/HCV-coinfected patients depends on their CD4 count.

- For a CD4 count of more than 200 (or ART-experienced persons):
  - Start ART against HIV and direct-acting antiviral therapy as soon as possible.
- For a CD4 count of less than 200 (or ART-naïve persons):
  - Start ART for HIV. Start DAA as soon as the patient is clinically stable and able to take the treatment.

6.5 HBV/HCV coinfection

Persons with HBV/HCV coinfection are at risk for HBV reactivation during and following HCV treatment.

All people with confirmed HCV infection should have an HBsAg test and if positive, start treatment of HBV as soon as possible.

In people with confirmed HCV infection who are HBsAg negative, monitor for onset of jaundice and/or raised or increasing liver function tests during HCV treatment.

Repeat HBsAg test to rule out reactivation.

6.6 TB/HCV coinfection

In persons with TB/HCV coinfection, treatment for active TB takes precedence before treatment of HCV infection. TB/HCV-coinfected persons treated for TB are at an increased risk of hepatotoxicity.

6.7 Retreatment after direct-acting antiviral treatment failure

Currently, there is only one pan-genotypic direct-acting antiviral regimen: sofosbuvir/velpatasvir/voxilaprevir is globally approved for the retreatment of persons whose

previous direct-acting antiviral treatment has failed.

Investigations of a failure to achieve sustained virologic response with direct-acting antiviral therapy includes re-examination of adherence and of potential drug–drug interactions.

6.8 Drug interactions

Commonly prescribed medicines that may lead to drug interactions include proton pump inhibitors, statins, antidepressants, and antiretroviral medicines for HIV.

Table 9 summarizes drug interactions between HCV medicines and antiviral medicines included in the 2022 *Malawi Guidelines for Clinical Management of HIV in Children and Adults*.[17] Where drug interactions are likely, AVT substitutions may be considered before initiating HCV therapy.

Table 9. Drug interaction between antiviral medicines

Green = Combination causes no problems

Yellow = Usually no problems. Monitor for possibly increased side effects or adjust dosage

Red = Do not combine without specialist advice

Drug Name	Treatment	3TC	ABC	ATV/r	AZT	CTX	DRV	DTG	EFV	LPV/r	TDF
Daclatasvir	HCV			1					2		
Glecaprevir/ Pibrentasvir	HCV										
Sofosbuvir	HCV										
Sofosbuvir/ Ledipasvir	HCV			3			3			3	3
Sofosbuvir/ Velpatasvir	HCV										4

1. Reduce Daclatasvir dose to 30mg OD
2. Reduce Daclatasvir dose to 90mg OD
3. Monitor for renal toxicity in TDF-containing protease inhibitor-based regimens and TDF adverse effects
4. Monitor for Renal toxicity

7. Treatment Monitoring

The recommended treatment monitoring schedule is outlined Table 10

Table 10. Monitoring schedule for patients with chronic hepatitis B and C

Test Type	Recommendation	Month 3	Month 6	Annually
HBsAg	Confirms HBV diagnosis		✓	
HBV DNA	Helpful in patients who do not yet meet the treatment criteria for antiviral therapy or those on treatment or following treatment discontinuation		✓	
PLT	Required to calculate the APRI	✓	✓	
ALT	Needed to establish treatment eligibility	✓	✓	
APRI	Non-invasive test for cirrhosis		✓	
Fibroscan	Non-invasive scan for severity of fibrosis		✓	
HBeAg	Provides information on disease stage			✓

8. Quality Assurance For Testing

Rapid diagnostic tests should meet minimum performance standards and be delivered at the point of care to improve access and linkage to care and treatment.

The National Health Reference Laboratory will mandate the quality assurance laboratory technicians to provide on-site quality control and quality assurance for staff performing hepatitis B testing. The emphasis is on supervision, proficiency testing, and quality control testing using known samples from reference laboratories. Feedback on proficiency testing must be provided to the testing services sites in written format and must be kept on file.

8.1 Post-marketing evaluation

For every batch of test kits imported into the country, a sample will be taken for testing with a known panel for quality check. Once a consignment of kits is distributed to the various testing sites, the testing service providers are required to run quality control on every newly opened box of kits, in addition to the routine quality control schedule, and to record results appropriately.

8.1.1 Quality controls

The following quality control checks must be performed for HIV, syphilis, and hepatitis B test kits.

At a minimum, quality control checks must be done once per week and for the following situations:

- A test kit is exposed to conditions outside the range of stability
- A new test kit lot is opened
- A new shipment of test kits is received

Results of quality control checks must be documented in the appropriate section of the testing services register. The testing services supervisor must countersign to verify the results.

8.1.2 Proficiency testing

Proficiency testing is a type of external quality assurance that involves the use of blinded sample panels administered to providers to evaluate their competencies.

The proficiency testing panels are administered by the National HIV Reference Laboratory every six months to all practicing providers through the district laboratories.

- The performance of each provider will be recorded in their individual proficiency testing logbook. Each provider shall receive timely feedback in writing from the National HIV Reference Laboratory.
- For service providers who score less than 100%, district testing services supervisors and zone laboratory supervisors will need to take corrective action.
- Those who score less than 100% in two consecutive proficiency tests must immediately stop testing until they are retrained.
- Laboratory supervision is required at least once every quarter.

Note: For consistency, only the National HIV Reference Laboratory is mandated to provide quality control and proficiency testing samples.

9. Supply Chain Management

Key Facts

- The role of logistics and supply chain management is to ensure an uninterrupted supply of commodities including rapid diagnostic tests, antiviral treatment, laboratory reagents, and supplies.
- The logistics section coordinates procurement, supply planning, warehousing, distribution of HIV-related commodities, and offers technical support and system strengthening to all health facilities providing HIV-related services including viral hepatis services. HIV/HCV-coinfected persons have a higher chance of progression to cirrhosis if not treated.
    - Stock levels of program commodities are maintained for 5 to 8 months at central warehouses and 2 to 5 months at health facilities. The national supply plan is used to manage shipments and the national quantification is used to determine annual stock requirements for various commodities.

9.1 Responsibilities

- All healthcare providers must support supply chain management by completing the standard Ministry of Health forms, patient cards, registers, and reporting forms.
- The pharmacy in-charge should manage and account for all commodities received at the various health facilities.
- District Health Management Teams will support coordination and supervision activities for the Viral Hepatitis Program.
- Communication to the HIV/HBV Logistics team for any commodity-related issues can be through either **email** (hivdeptlogistics@gmail.com) OR through the **toll-free lines** for support and authorization codes for: additional supplies from warehouse; inter-facility stock transfer; disposal of expired/spoiled stocks; receipt of damaged or inappropriate stocks; serious (suspected) side effects for any medicines.
    - 5 9 1 9 1 from an Airtel phone
    - 6 8 8 2 from a Telekom Networks Malawi (TNM) phone

9.2 Viral Hepatitis Commodity Supply Cycle

HIV commodities are delivered every four months from the central warehouse in Lilongwe directly to all health facilities. Distribution lists for all health facilities are calculated based on the patient and stock reports collected during quarterly HIV program supervision and reported through the Logistics Management Information System.

Table 11 shows the different commodity groups currently managed by the Viral Hepatitis Program within the Directorate of HIV/AIDS, STI, and Viral Hepatitis.

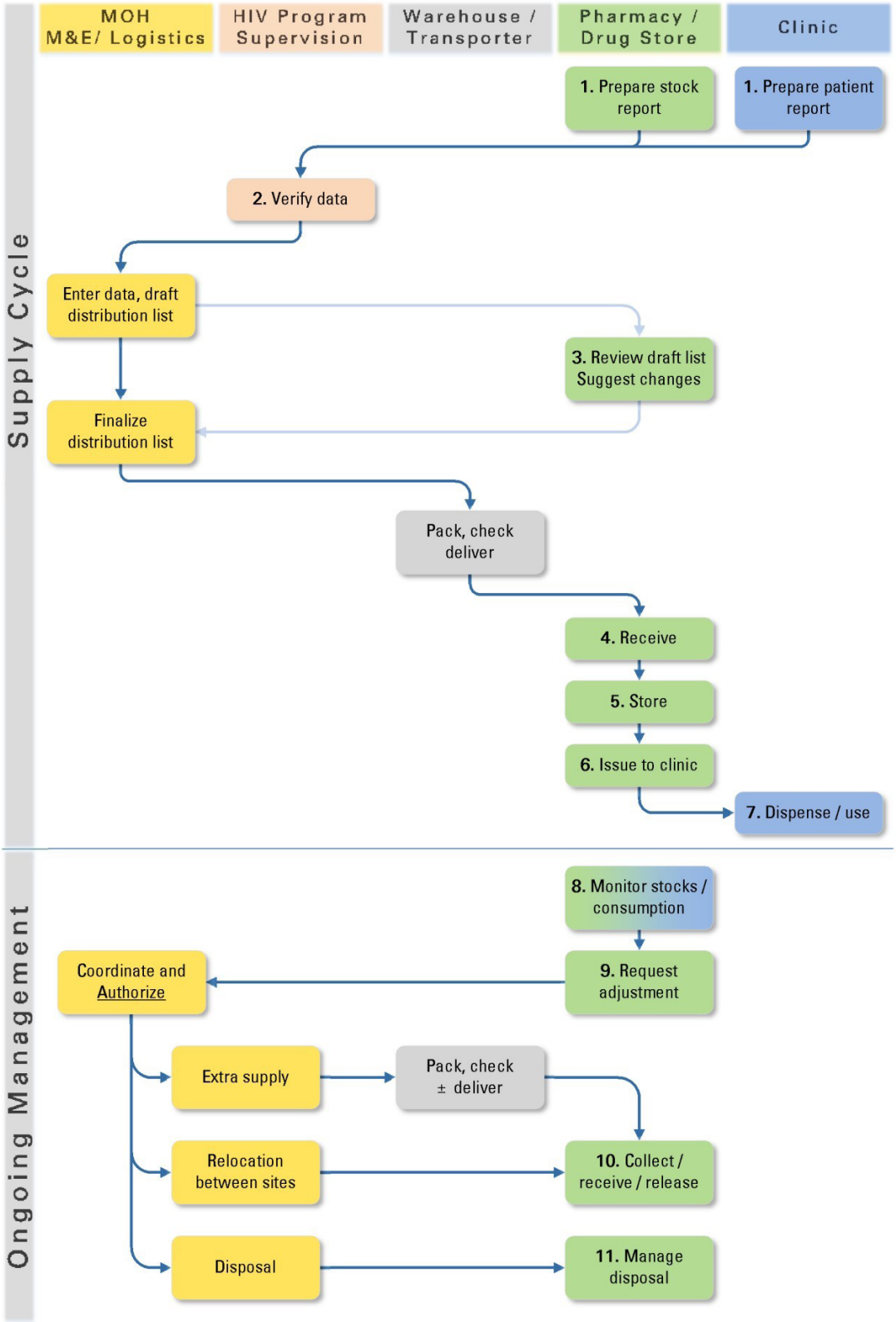
Table 11. Commodities and supplies managed by the viral hepatitis program

#	Commodity group	Examples	Supply*
1	Screening tests (rapid diagnostic tests)	Hepatitis B and C tests	E
2	Antiviral medicines	TDF/3TC 300/300mg, entecavir, etc	E
3	Laboratory reagents and consumables	Complete blood count tests, liver function tests	S

*E = items managed exclusively through the Viral Hepatitis Program. S = items supplemented by the Diagnostics Department for the HIV Program.

The bimonthly supply cycle and ongoing management follow 11 steps as described in the flowchart and narrative below:

Figure 2. Commodity supply chain cycle



9.3 Stock and patient reports

The pharmacy/drug store in-charge and clinician are responsible for preparing stock and patient reports. They are also responsible for the following:

- Confirm each commodity is sorted by expiry date.
- Do a physical count of stock on hand excluding any damaged and/or expired units.
- Ensure all available stock is counted, including in bulk store, at the clinic/testing rooms, etc.

9.3.1 Verify data (integrated HIV/HBV program supervision team)

- Prepare a stock report by doing a physical count. Check for completeness of stock cards, proper use of relocation books, filing of delivery notes and goods received notes, and availability and use of requisition and issue vouchers.
- Prepare a patient report by reviewing patient cards and registers in the clinic.

9.3.2 Review draft distribution list (HIV/HBV logistics, monitoring and evaluation teams, and district health officers)

Bimonthly consignments are calculated by HIV/HBV Logistics from patient numbers and stock reports collected at the last supervision visit. They are scheduled to arrive every four months. Facilities should have about two months of stock remaining when the new consignment arrives, for a total of about five months of stock available.

- Review and confirm items and quantities on the draft distribution list by submitting suggested changes by email (hivdeptlogistics@gmail.com), SMS, or phone, with justification before the deadline shown on the draft list.

9.3.3 Receive consignment (pharmacy-in-charge)

Inspect the entire consignment in the presence of a witness designated by the District Health Management Team/facility in-charge:

- Physically count all re-packed/loose units. Originally sealed boxes do not need to be opened for counting units. Add up the total number of units received for each item. Check batch number and expiry date for all items.
- Write a physical count for each item into the respective box on the delivery note. Write 0 (zero) for any items not received – do not leave any boxes empty. Sign, date, and stamp the delivery note to confirm receipt of the items as indicated.

- The person signing the delivery note is accountable for all items signed for. The facility/pharmacy in-charge will be held responsible for any discrepancies noted later.

9.3.4 Provide storage (pharmacy-in-charge)

- Immediately move all items received to a secure storage area (clean, dry, cool, and off the floor) and record the quantity, date of receipts, and invoice number on stock cards.
- Arrange items by expiry date to make it easy to follow the “first expiry, first out” principle when issuing stock to user units/clinics.

9.3.5 Issue to clinic (pharmacy-in-charge)

- The user units/departments will request commodities from the store using the Requisition and Issue Vouchers (approved by the facility in-charge).
- The pharmacy/stores in-charge assess the stocks and issues accordingly following the “first expiry, first out” principle. The stock card should immediately be updated with the quantity issued and stock on hand.

9.3.6 Dispense/use (laboratory/clinician)

- Test clients following the set algorithm.
- Ensure that all patients enrolled in treatment fully understood how and when to take their drugs and any possible side effects. Document all serious side effects on the yellow pharmacovigilance forms and submit to the Pharmacy and Medicines Regulatory Authority or report using the MEDSAFE-360 USSD platform.
- Account for all commodities dispensed by completing the various registers specifying type and quantity of commodity.

9.3.7 Monitor stocks/consumption (pharmacy-in-charge)

- Do a physical stock count for all items (in store, clinic, laboratory) and update stock cards on the last working day of each month; when handing over pharmacy management to another staff member and whenever discrepancies are noted or any other special scenarios, such as clinic closure, fire, or theft.
- Calculate the average monthly consumption and months of stock for all commodities after doing the monthly physical count to ascertain the stock position of the health facility (understock, overstock, stockout, adequately stocked) and take appropriate action.

9.3.8 Request adjustment (pharmacy-in-charge and HIV/HBV logistics)

Call HIV/HBV Logistics as soon as possible if shortage, excess, or expiry is noted. Before calling, prepare the following information:

- Number of tins, bottles, or tests remaining
- Expiry date
- Number of patients on this regimen or the approximate average monthly consumption
- When additional stocks are needed / to be sent to another site
- If own transport can be organized

- Logistics will review the information and find out the reason for the problem. Coordinate: extra allocation from the warehouse, relocation of stocks between sites, or register disposal of expired commodities.

A unique authorization code for each item will be sent by SMS and the health worker must complete the relocation books with this information regarding all losses and adjustments for commodities.

Caution: Never relocate or dispose of commodities without an authorization code.

Collecting, receiving, or releasing stock from adjustment (pharmacy-in-charge):

- When collecting extra consignments from the warehouse, ensure it can be safely transported in full (e.g., security, sun and rain protection), make an appointment and bring an official ID (e.g., national ID, passport, driving license) and official health facility stamp.
- When relocating stocks between facilities, fill a registration form for relocation and write the authorization code for each item; keep the white copy of the form at the facility releasing the stock and give a pink copy to the facility receiving the relocated commodities. This is mandatory to account for commodities transferred to the health facility.
- All stock transactions (between warehouses and facilities) must be entered on the various stock cards in the pharmacy before issuance to user units.

9.3.9 Manage disposal (pharmacy-in-charge)

- Update the stock cards by subtracting the expired quantities of commodities from the total stock balance. Separate and store expired commodities away from usable stock awaiting destruction. Notify HIV/HBV Logistics of any expiries to receive authorization codes and fill the registration form for relocation and disposal.
- Update the health facility expired commodity list and contact the district pharmacist to arrange for transfer of expired items for controlled destruction.

10. Implementation Considerations

10.1 Health Facility Requirements

The minimum health facility requirements for viral hepatitis services provisions are:

- Minimum of two viral hepatitis trained clinical health workers (nurses/clinicians)
- Functioning laboratory for baseline laboratory tests (full blood count and liver function tests)
- A well-secured pharmacy for commodity storage
- Rooms for service provision (i.e., sexually transmitted infection, antenatal care, antiviral treatment, sexual and reproductive health, family planning, and PrEP services)
- A good monitoring and evaluation system with all relevant viral hepatitis tools

10.2 Service Entry Points and Service Integration

HBV and HCV services will be integrated into specific entry points of the public health system including the following:

- STI clinics
- Antenatal care clinics (especially targeting pregnant women who are 20 years or older)
- HIV ART clinics (targeting clients on non TDF containing ART regimens)
- Drop-in centres as safe spaces for key populations including people who inject drugs
- Prisons scheduled high-throughput screening mass testing
- Outpatient department
- PrEP access points
- Family planning
- Sexual and reproductive health

10.3 Human Resource

The following cadres will be directly involved in viral hepatitis healthcare service provision at the facility level:

- Clinical staff
- Nursing staff
- Pharmacy staff
- Laboratory staff
- HIV diagnostic assistants and health surveillance assistants

11. Monitoring and Evaluation

Quality program data are crucial for planning, implementation monitoring, quality assurance, and supply chain management at the national and facility level.

Detailed client-level **HBV program data** are recorded on standard patient follow-up cards (see **figure 8 on page 78**). Registration details and outcomes are summarized in a HBV clinic register and reported quarterly. At all facilities, the quality of viral hepatitis services and program data is reviewed during quarterly supportive site supervision.

HBV Clinic registration and cohort outcome data from all facilities are collected during supervision, entered at the Directorate for HIV/AIDS, STI and Viral Hepatitis, and shared via the DHA website and exported to District Health Information System 2.

HBV program scale-up and monitoring tools have been prioritized due to the higher prevalence and current availability of all program commodities. HCV program monitoring tools will be developed later in 2023 and disseminated separately.

11.1 HBV Screening

HBsAg testing details are recorded in the Integrated Rapid Testing and Counseling Register for each client and reported monthly for all testing entry points. This register covers testing for HBsAg alone or in combination with HIV and/or syphilis. It is designed for efficient digitization of (anonymous) client-level data using ScanForm technology. Alternatively, facilities with full electronic medical record systems (EMRS) will be entering data in real-time using point-of-care real-time data capture in the testing rooms. Standard monthly facility reports are auto-generated and available to registered users from the MOH ScanForm data portal and on District Health Information System 2.

11.2 Diagnostic and Treatment Follow-Up of HBsAg positives

The **HBV Patient card** is designed as a standard checklist, job-aid and mentorship tool:

- Relevant baseline characteristics
- Baseline- and follow-up investigations

- Treatment eligibility and drug dispensing details
- Appointment dates and follow-up outcomes.

HBV clinic follow-up outcomes are defined as follows. In every case, write the (approximate) event date in the Outcome Date column:

- **Dis**charged from HBV diagnostic follow-up without ever starting HBV treatment.
- **Def**aulted: More than 2 months overdue after next appointment, unknown survival, and treatment status. This outcome must be actively determined by reviewing all treatment cards at the beginning of each quarter, before report aggregation.
- **Stop**: patient stopped taking HBV treatment (clinician's or patient's own decision)
- **ART**: HIV positive, started ART for HIV. ART referral ends follow-up at the HBV clinic.
- **TO**: Transferred to other HBV clinic (including 'unofficial' transfers)
- **D**: Died. From any cause

All HBsAg positive clients need a new HIV test unless they have already been previously diagnosed with HIV. This is because all co-infected clients need to be on antiviral treatment. TDF-containing ART for HIV that is used for most children 30kg+ and adults is effective for both conditions. Such clients are only registered once at the Viral Hepatitis Clinic, and immediately referred for management and follow-up at the HIV ART clinic.

- Routinely register all HBsAg positive clients in the **HBV clinic register** and fill the **HBV patient card**, regardless of HIV status. Complete case reporting requires universal registration.

11.2.1 HIV negative clients

- Fill in the clinic register, patient card header and first visit.
- Fill in the next appointment data as appropriate and leave Outcome column empty.
- Continue filling in the patient card for each following HBV clinic visit.

11.2.2 HBV / HIV co-infected clients:

- Clients already on, or starting, TDF-containing ART for HIV:
  - Fill the clinic register, the patient card header and the first visit only.

- Circle “on HIV-ART” under Outcome, fill today’s date under Outcome Date
- Update the register with this outcome.

- Clients not currently on HIV-ART, or on ART regimen without TDF:
  - Start or re-start on HIV-ART as soon as possible.
  - Fill in the clinic register, patient card header and first visit.
  - Fill in the next appointment data as appropriate and leave Outcome empty.

Continue filling in the patient card for each following HBV clinic visit.

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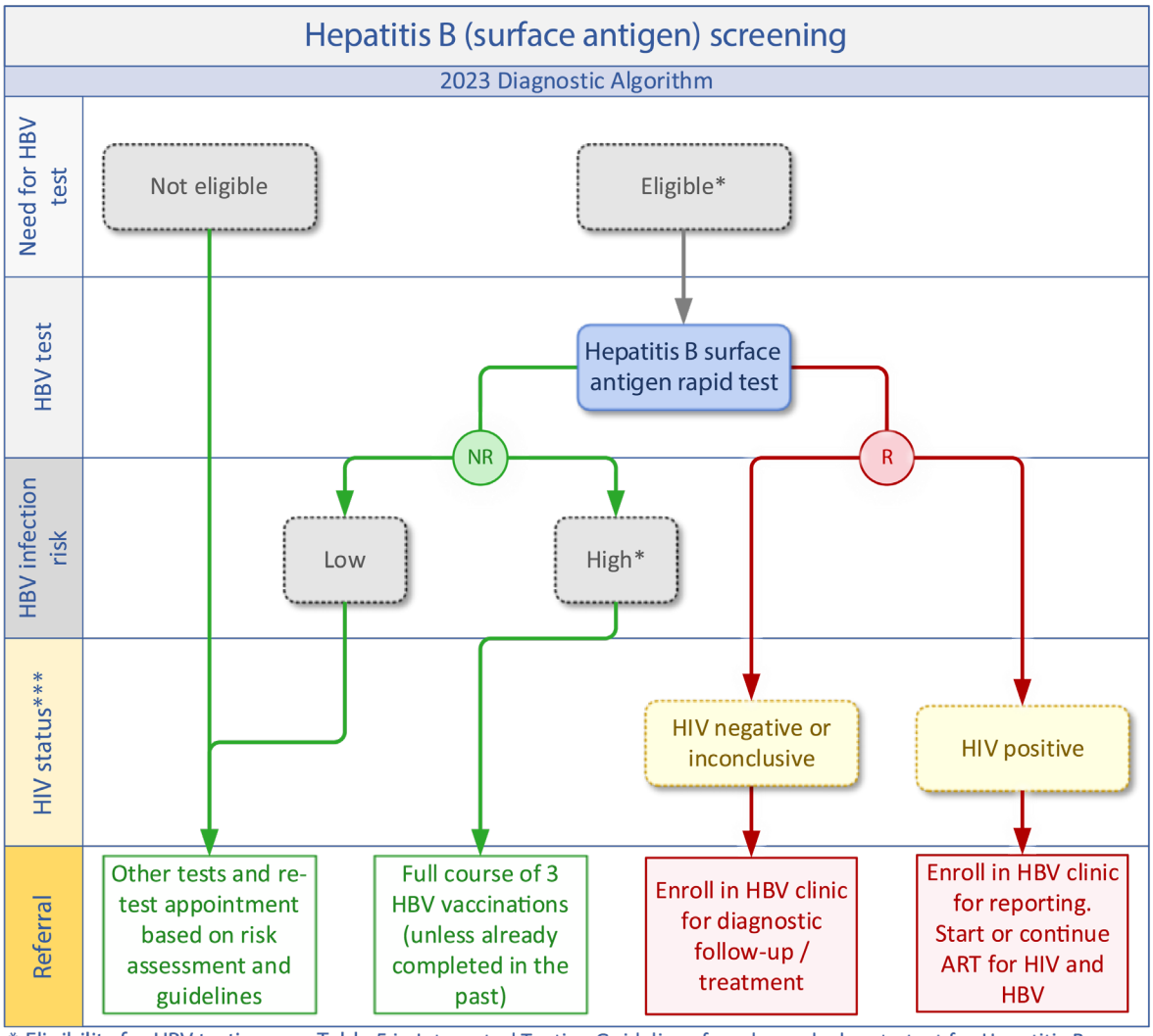
13. Appendix

Figure 3. Hepatitis B surface antigen screening strategy

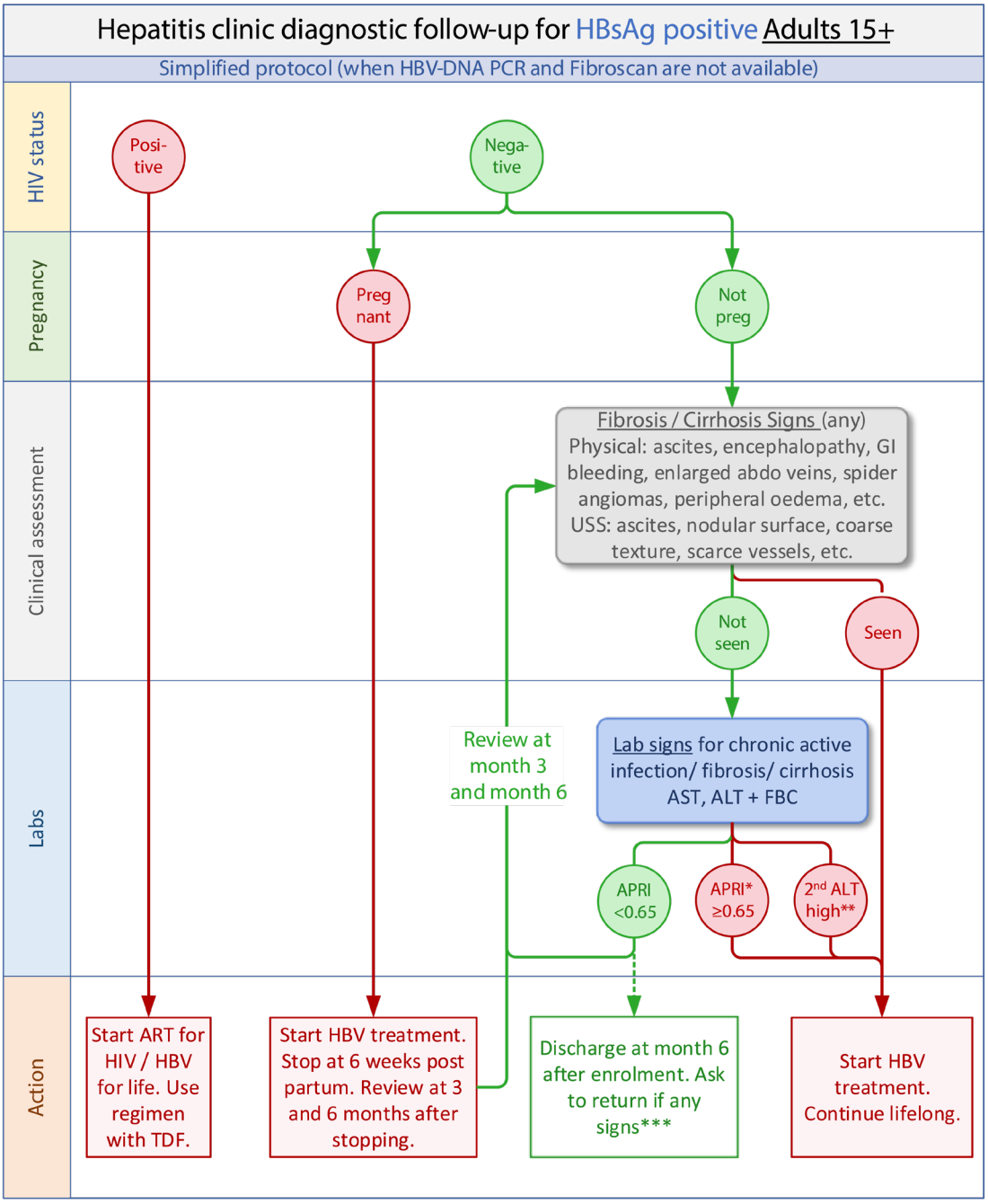


* Eligibility for HBV testing: see Table 5 in Integrated Testing Guidelines for who and when to test for Hepatitis B.

** Table 5 shows high risk groups who should be referred for a course of 3 HBV vaccinations unless they have previously completed 3 HBV vaccinations: FSW, TG, MSW, MSM, PWID, prisoners, PrEP clients, children 0-14 years born to HBV positive women, STI patients, general population at ongoing HIV risk or after high-risk event, health workers, sex partners of HBV index clients, sex partners of STI patients, presumed hepatitis patients, in-patients.

*** HIV status must be ascertained for all HBV positive clients. Perform a new HIV test using the full 3test algorithm unless the client is already known to be HIV positive.

Figure 4. Diagnosis and Treatment Algorithm for Chronic HBV

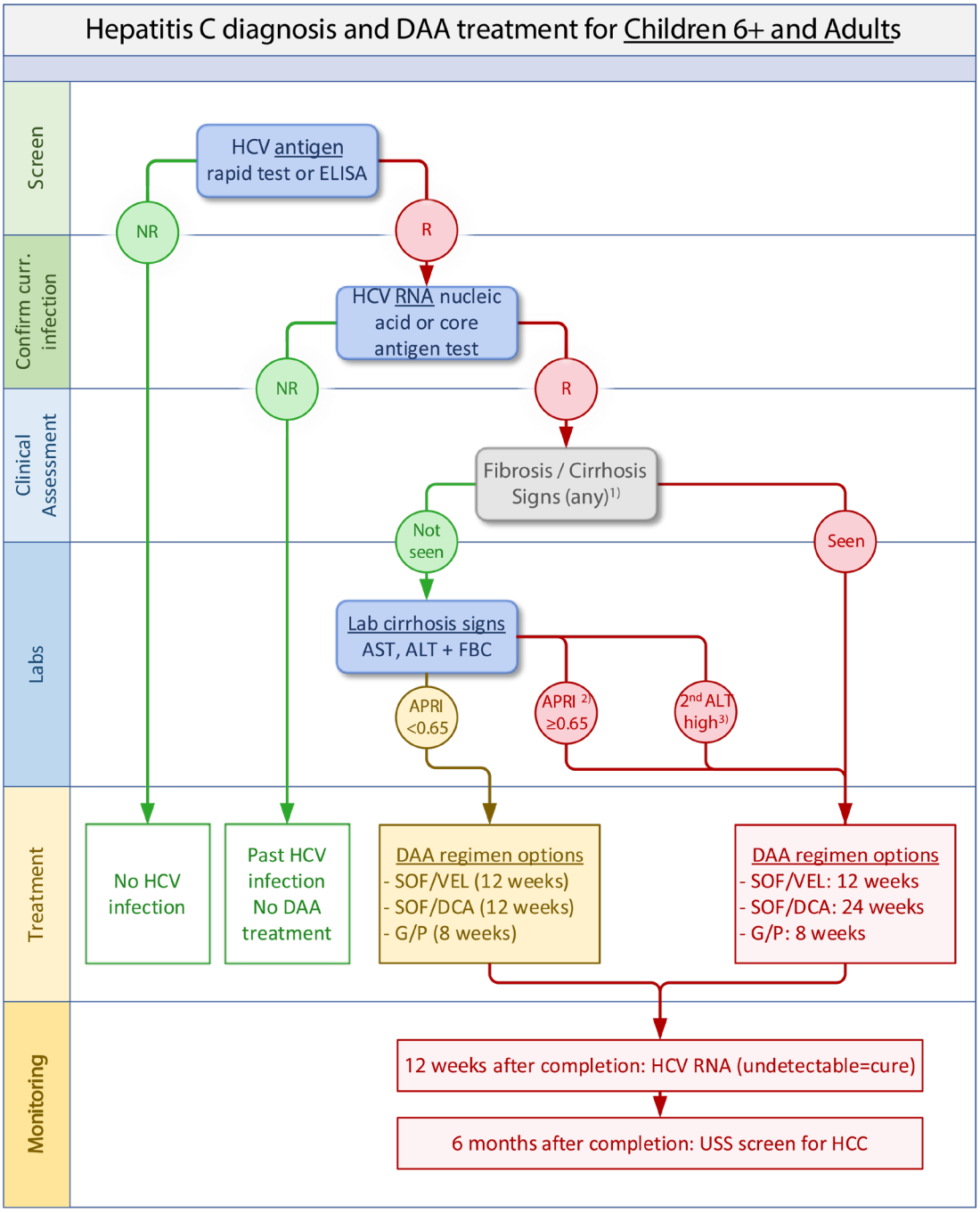


* APRI score: Do not use the APRI score for patients with very high AST levels (≥350 IU/mL) as this is usually a sign for acute hepatitis and not an indication for starting treatment. In this case, investigate other causes of acute hepatitis. Repeat LFT, FBC after 2 weeks and calculate the APRI score when the AST has dropped below 350 IU/mL.

** 2nd ALT high: at least 2 ALT results ≥40 IU/mL within 6 months, at least 8 weeks apart.

*** Explain the possible signs: tiredness, body pains, stomach discomfort, nausea, appetite loss

Figure 5. Diagnosis and Treatment Algorithm for HCV



1) Physical: ascites, encephalopathy, GI bleeding, enlarged abdo veins, spider angiomas, peripheral oedema, etc. USS: ascites, nodular surface, coarse texture, scarce vessels, etc.

2) APRI score: Do not use the APRI score for patients with very high AST levels (≥350 IU/mL) as this is usually a sign for acute hepatitis. In this case, also investigate other causes of acute hepatitis. Repeat LFT, FBC after 2 weeks and calculate the APRI score when the AST has dropped below 350 IU/mL.

3) 2nd ALT high: at least 2 ALT results ≥40 IU/mL within 6 months, at least 8 weeks apart

Alcohol Assessment Tool

One standard drink contains approximately 14 grams of pure alcohol. This is found in:

- About 350ml of 5% beer
- About 150ml of 12% wine
- About 50ml of 40% distilled spirits

Figure 6. Audit C Alcohol Abuse Assessment Tool

Available at https://pcssnow.org/wp-content/uploads/2017/04/AUDIT-C_Measure-and-Scoring.pdf.

AUDIT-C ASSESSMENT TOOL

The AUDIT-C assessment tool[i] can be used to provide a quick assessment of how much and often a woman is drinking alcohol. AUDIT-C is the first three questions of the longer AUDIT tool, which is a more comprehensive assessment of problem drinking. Both tools are internationally recognised and widely used.

Questions	0	1	2	3	4	Score
1. How often do you have a drink containing alcohol?	Never	Monthly or less	2-4 times a month	2-3 times a week	4 or more times a week	
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	1 or 2	3 or 4	5 or 6	7 to 9	10 or more	
3. How often do you have six or more drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
					Total	

Figure 5. Diagnosis and Treatment Algorithm for HCV

AUDIT Total Score	Risk Level	ALCOHOL: Guide for Intervention & Feedback
0		· Provide positive reinforcement and offer relevant literature (may be helpful to others)
1-7	Low risk	Discuss AUDIT score · Discuss benefits of low-risk drinking: – No more than 2 standard drinks per day – No more than 4 standard drinks on a single occasion – Aim for at least 2 alcohol free days per week – If you are pregnant or breastfeeding NO alcohol is the safest option · Offer ' Alcohol & my health' resource
8-12	Risky	Discuss AUDIT score **If client is interested discuss:** · Harms associated with moderate risk alcohol consumption · Tips and benefits for reducing alcohol consumption include: – No more than 2 standards drinks per day – No more than 4 standard drinks on a single occasion – Aim for at least 2 alcohol free days per week – If you are pregnant or breastfeeding NO alcohol is the safest option · Follow-up and referral and or offer alcohol resource
13+	High risk	Discuss AUDIT score **If client is interested discuss:** · Harms associated with high-risk alcohol consumption · Tips and benefits for reducing alcohol consumption (see above) · **Caution**: If the score is 13 or over advise client to seek medical advice before they make any changes to their alcohol consumption. This is due to the risk of medical complications such as seizure and death from alcohol withdrawal in people who are dependent on alcohol. Further medical assessment is recommended (see A Brief Guide to the Assessment and Treatment of Alcohol Dependence, MHC, 2018) · Follow-up and referral and/or offer alcohol resource · Recommended referral to: GP or contact the Alcohol & Drug Support Line for support and services in your area.

Table 12 The Chichewa Patient Health Questionnaire (PHQ-9)

M'masabata awiri apitawa ndi kangati mwakhala ndi chizindikiro chirichonse mwa zizindikiro izi?	Sindinavutikepo/ sindinakhalepo Palibe ndi tsiku limodzi lomwe	Kus aposera sabata imodzi) Masiku 1-7	Kuposera abata imodzi Masiku 8-12	Pafupifupi tsiku lirilonse Masiku 13 kapena 14
1. M'masabata awiri apitawa, ndikangati mwakhala okhumudwa kapena kukhala opanda chiyembekezo (kutaya mtima) kapena nkhawa?	0	1	2	3
2. M'masabata awiri apitawa, ndikangati munavutika kukhala ndi chidwi chochepa kapena chilakolako pa zinthu (kusowa mphamvu, kukhala ndi nthumanzi, mtima wosweka)? Mwachitsanzo: Kusafuna kukhala kapena kucheza ndi anzanu	0	1	2	3
3. M'masabata awiri apitawa, ndikangati mwakhala mukuvutika kupeza tulo (kulephera kugona kapena kukhala m'maso nthawi yogona) kapena kugona mopitilira/moposa nthawi zonse?	0	1	2	3

4. M’masabata awiri apitawa, ndikangati mwakhala mukumva kutopa, kukhala ndi ulesi, kufooka kapena kupelewera/ kuchepa mphamvu? Mwachitsazo: Kulephera kupanga ntchito za tsiku ndi tsiku	0	1	2	3
5. M’masabata awiri apitawa, ndikangati mwakhala mukusowa chilakolako cha chakudya kapena kudya kwambiri/ mowonjeza?	0	1	2	3
6. M’masabata awiri apitawa, ndikangati munaziona ngati opanda pake (osazikhulupilira kapena wolephera kapena kuziona osafunikila/ onyozeka) komanso kuti mwanyozetsa banja lanu?	0	1	2	3

7. M’masabata awiri apitawa, ndikangati munavutika Kulephera kukhazikika pazochita, mwachitsanzo: kulephera kuwerenga kapena kulephera kukhazikika kumvera wailesi kapenanso kuwonera zowonera wonera, kucheza ndi anzanu, kulephera kuchita nawo zokambirana mumsonkhano?	0	1	2	3
8. M’masabata awiri apitawa, ndikangati mwakhala mukuyenda kapena kuyankhula pang’onopang’ono kwambiri mpakana anthu ena nkudabwa, kusakhazikika nkumangoyenda yenda moposera muyeso?	0	1	2	3
9. M’masabata awiri apitawa, ndikangati mwakhala ndi maganizo akuti kuli bwino kungofa kapena maganizo ofuna kuzivulaza nokha mwanjira ina iliyonse?	0	1	2	3

Figure 7. English Patient Health Questionnaire (PHQ-9) available at https://www.apa.org/depression-guideline/patient-health-questionnaire.pdf

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✔" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING 0 + _____ + _____ + _____

=Total Score: _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

Figure 8. Standard hepatitis B diagnostic and follow-up and treatment patient card, version 1

Hepatitis B Diagnostic Follow-up and Treatment Patient Card White Card — *Version 1* May 2023 — Transfer-In Date [ ] — **HepB Reg no** [ ] — Year [ ]

Patient / Guardian Details			
Patient Name			
Sex, Birth Date	M F	DOB	Height (CM)
Physical Address			
Guardian Name			
Phone	Patient	Guardian	
Agrees to FUP	N Y	Guardian Relation	

Status at Treatment Initiation	Serology	Date	Cirrhosis Signs	
HBsAg	Pos Neg Nd		Caput medusae	– + ++ +++
HBeAg	Pos Neg Nd		Ascites	– + ++ +++
HBV DNA (IU/mL)	Nd		USS	Nd – + ++ +++
HIV	Pos Neg Nd		Fibroscan	Nd 0 1 2 3 4
	Alcohol Assessment		**Liver Function Test / Platelet**	
Range	ND 1-7 8-12 13+		Aminotransferases (IU/mL)	ALT / AST
Risk level	ND Low Risky High		Platelets (count/mm³)	

Visit Date	Weight	Pregnant or Breast-Feeding	Cirrhosis signs *specify in Notes*	ALT		AST	PLT	APRI		HBsAg	HBV DNA VL result	HBV Treatment Status		No. of tabs given	Next Appointment or Outcome Date	Outcomes
				Value	Category							None	Yes			
D M Y	*kg*			*IU/mL*		*IU/mL*	*count/ mm³*	Score	Category	Negative Positive Not done	*IU/mL*		TDF/3TC TDF/FTC TAF ETV			Discharged Defaulted Stopped On HIV-ART Transfer out Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non	TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non	TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non	TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non	TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non	TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non	TL TE TAF ETV			Dis Def Stop ART To Died

Notes

Hepatitis B Diagnostic Follow-up and Treatment Patient Card *Version 1* May 2023

White Card

Transfer-In Date ______ **HepB Reg no** ______ Year ______

Visit Date (D M Y)	Weight (kg)	Pregnant or Breast-Feeding	Cirrhosis signs *specify in Notes*	ALT Value (IU/mL)	ALT Category	AST (IU/mL)	PLT (count/mm³)	APRI Score	APRI Category	HBsAg (Negative / Positive / Not done)	HBV DNA VL result (IU/mL)	HBV Treatment Status: None / Yes (TDF/3TC, TDF/FTC, TAF, ETV)	No. of tabs given	Next Appointment or Outcome Date	Outcomes (Discharged / Defaulted / Stopped / On HIV-ART / Transfer out / Died)
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non TL TE TAF ETV			Dis Def Stop ART To Died
		Preg Bf	N Y		Norm Hi				Ok Hi	– + Nd		Non TL TE TAF ETV			Dis Def Stop ART To Died

Notes

HBV Treatment
- TDF Tenofovir Disoproxil Fumarate
- TAF Tenofovir Alafenamide Fumarate
- ETV Entecavir
- 3TC Lamivudine
- FTC Emtricitabine

HBsAg hepatitis B surface antigen test
- – Negative
- + Positive
- Nd Not done

Outcomes
- Dis Discharged from HBV diagnostic follow-up without ever starting HBV treatment.
- Def Defaulted: More than 2 months overdue after next appointment, unknown survival, and treatment status
- Stop Patient stopped taking HBV treatment (clinician's or patient's own decision)
- ART HIV positive patient started ART for HIV. ART referral concludes HBV follow-up on this card.
- TO Transferred to other HBV clinic (including 'unofficial' transfers)
- D Died

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