CAPACITY STRENGTHENING TOOLKIT

International Hepatitis C in Primary Care and Drug and Alcohol Settings Education Program

Supporting increased hepatitis C screening, linkage-to-care and treatment among people who inject drugs in Egypt

INHSU

Contents

About

This toolkit is provided to participants of the INHSU Hepatitis C in Primary Care and Drug and Alcohol Settings Education Program. The toolkit is intended to provide participants with practical tools with which to implement HCV testing, linkage to care and treatment processes in their setting.

The toolkit is tailored in line with local guidelines and referral pathways for each workshop location.

Although some resources will be applicable only for participants working within the local area of workshop delivery, many, such as DAA treatment regimen quick reference guides, management procedure templates and assessment checklists, will be relevant regardless of practice location.

Resources applicable across all locations within South Africa are available as an enduring education program component as free downloads via the INHSU website:
INHSU - Egypt - HCV education program for health practitioners

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INHSU HCV in Primary Care and Drug and Alcohol Settings

Glossary

Term	Definition
APRI	AST-to-Platelet Ratio Index
Ascites	The accumulation of fluid (usually serous fluid which is a pale yellow and clear fluid) that accumulates in the abdominal cavity
Asymptomatic	Of a condition or a person producing or showing no symptoms
Cessation	The fact or process of ending or being brought to an end
Cerebral infarction	An area of necrotic tissue in the brain resulting from a blockage or narrowing in arteries supplying blood and oxygen to the brain
Cirrhosis	A complication of liver disease which involves loss of liver cells and irreversible scarring of the liver
Enzyme	Macromolecular biological catalysts. They accelerate chemical enzymes
Ethinylestradiol	An orally active estrogen and a synthetic derivative of estradiol, a steroid hormone and the major endogenous estrogen in humans
Etiology	The cause, set of causes, or manner of causation of a disease or condition
Fibrosis	The formation of excess fibrous connective tissue in an organ or tissue in a reparative or reactive process. This can be reactive, benign, or pathological state. In response to injury, this is called scarring, and if it arises from a single cell line this is called a fibroma.
Genotype	The genetic constitution of an individual organism
Hepatocellular carcinoma (HCC)	The most common type of primary liver cancer. It occurs predominantly in patients with underlying chronic liver disease and cirrhosis.
Jaundice	A medical condition with yellowing of the skin or whites of the eyes, arising from excess of the pigment bilirubin and typically caused by obstruction of the bile duct, by liver disease, or by excessive breakdown of red blood cells
Lethargy	A lack of energy
Myalgia	Pain in a muscle or group of muscles
Opioid	An opium-like compound that binds to one or more of the three opioid receptors of the body
Opioid agonist treatment	An effective treatment for addiction to opioid drugs such as heroin and involves taking the opioid agonists methadone or buprenorphine (suboxone)
Palmar erythema	Reddening of the palms
PCR	Polymerase Chain Reaction
Peripheral edema	An accumulation of fluid causing swelling in tissues perfused by the peripheral vascular system, usually in the lower limbs

Portal hypertension	An increase in the blood pressure within a system of veins called the portal venous system
RNA	Ribonucleic acid
Serology	The scientific study or diagnostic examination of blood serum, especially with regard to the response of the immune system to pathogens or introduced substances
Spider nevi	A collection of small, dilated blood vessels that are clustered close to the skin's surface
Thrombocytopenia	A condition in which you have a low blood platelet count
Viremic	A medical condition where viruses enter the blood stream and hence have access to the rest of the body

DECISION MAKING IN HEPATITIS C

HCV

1 When To Test

Clinical Indicators

- Abnormal liver function tests (LFTs) (ALT ≥ 45 IU/L)
- Jaundice

Presence of Risk Factors

- Injecting drug use (current/ever)
- Sharing of drug use equipment
- Born in high prevalence region^
- Receiving treatment for bilharziasis by tatar emetic injections from 1950s to 1980s in Egypt
- Unsterile tattooing/body piercing
- Unsterile medical/dental procedures/blood transfusions in high prevalence countries
- Time in prison
- Needlestick injury
- Mother to child transmission
- Sexual transmission in men who have sex with men (MSM)
- Sexual transmission in those who are HIV positive
- Receiving hemodialysis

^Africa, the Middle East, the Mediterranean, Eastern Europe, and South Asia

Other

- Screening before undergoing surgery
- Screening before employment
- Screening before travelling abroad
- Initiating PrEP
- When someone requests a test

When gaining informed consent before testing, discuss:

- Reason for test
- What a positive antibody result means
- Next steps if antibody positive
- Availability of curative treatment

2 Test/s, Results and Actions

Order HCV Antibody (Ab)*

HCV Ab negative

HCV Ab positive

HCV RNA (qualitative)

HCV RNA negative

HCV RNA positive

Does NOT have HCV

Has CLEARED HCV

Has CURRENT HCV

NO action
However, if possible recent infection re-test (HCV Ab), or if ongoing risk factors repeat screening (HCV Ab) annually

RE-TEST if:
Ongoing risk factors
(repeat RNA test annually)

Further ASSESSMENT and TREATMENT
(see next page)

When conveying a NEGATIVE result, discuss:

- Modes of transmission
- Strategies for reducing risk

When conveying a POSITIVE result, discuss:

- Availability of curative treatment
- Modes of transmission and risk reduction
- Lifestyle factors e.g. alcohol minimization, diet
- Availability of peer support, information and any other support services

***If high level suspicion also consider requesting reflexive HCV RNA**

This resource was originally developed by ASHM. It has been adapted for Egypt by ASHM and the International Network on Health and Hepatitis in Substance Users (INHSU) in collaboration with local partners.

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DECISION MAKING IN HEPATITIS C

HCV

3 Pre-Treatment Assessment

Baseline screening after positive HCV PCR

- ☐ Complete Blood Count (CBC)
- ☐ Urea, electrolytes, creatinine
- ☐ AST, ALT, GGT, ALP, Tbil, Dbil, INR, Alb

Assess liver fibrosis: cirrhotic status

- ☐ Signs of chronic liver disease (spider naevi, palmar erythema, jaundice, encephalopathy, hepatomegaly, splenomegaly, ascites, peripheral oedema)
- ☐ Non-invasive assessment of fibrosis:
  - Serum biomarkers such as APRI (<1.0 means cirrhosis unlikely). Calculator available. hepatitisc.uw.edu/page/clinical-calculators/apri
  - Elastography assessment e.g. FibroScan® (>12.5 kPa consistent with cirrhosis)
  - Ultrasound assessment

Check for other causes of liver disease

- ☐ Check for viral coinfection:
  - HIV Ab
  - Hepatitis A – check hep A IgG; vaccinate if negative
  - Hepatitis B – check HBsAg, anti-HBc and anti-HBs; vaccinate if all negative
- ☐ Heavy alcohol intake
- ☐ Fatty liver disease - check weight, BMI

Check for other major co-morbidities

- ☐ Renal impairment (eGFR < 50)

Review previous HCV treatment

- Choice/length of treatment may be influenced by prior HCV treatment experience/response

Consider pregnancy and contraception

- HCV treatment not recommended for use in pregnant or lactating women

4 Treatment

Is your patient likely to have cirrhosis?
(APRI > 2 or FibroScan® > 12.5)

☐ Yes

Consider discussion with, or referral to experienced HCV treater

☐ No

Has your patient received previous treatment for HCV?

☐ Yes

Consider discussion with, or referral to experienced HCV treater

☐ No

Click HERE to view treatment recommendations for Egypt

Treatment	Dosage	Duration if no cirrhosis present
SOF/DAC~	400/60 mg Once-daily (2 pills, +/- food)	12 weeks

- ☐ Check Egypt Guidelines for further information
- ☐ Check for drug-drug interactions at hep-druginteractions.org

~SOF/DAC = Sofosbuvir/Daclatasvir

Disclaimer: Guidance provided on this resource is based on best-practice at the time of publication. This quick-reference guide is not intended to be a comprehensive list of all available options.

5 Monitoring

Monitoring while on treatment

- Generally not required, but approach should be individualized
- Side effects of HCV treatment are generally minimal
- Consider monitoring adherence

12 weeks post treatment

- ☐ HCV RNA to confirm cure (sustained virological response SVR12 = cure)
- ☐ Liver enzymes

6 Follow Up

If your patient has:

No cirrhosis and normal liver enzyme results (ALT< 45 IU/L)
No clinical follow-up for HCV required

Ongoing risk factors
Annual HCV RNA test. If re-infected offer re-treatment. Offer education on harm reduction strategies

Abnormal liver enzyme results
(ALT ≥ 45 IU/L) Evaluate for other causes of liver disease and refer to specialist for review

Cirrhosis
Refer to specialist. Patients with cirrhosis require long-term monitoring:

- 6-monthly abdominal ultrasound (hepatocellular carcinoma screening)
- Consideration of screening for esophageal varices

CONSULT WITH A SPECIALIST IF:

Pre-treatment

- Cirrhosis is present or likely – APRI ≥2 and elastography score not available; elastography >12.5kPa
- Coinfected with HIV or HBV
- Renal impairment (eGFR < 50)
- Prior treatment failure of HCV treatment
- Complex drug interactions
- Complex co-morbidities
- Not comfortable prescribing HCV treatment

During treatment

- Major medication side effects

Post treatment

- RNA positive 12 weeks post treatment
- Abnormal liver enzymes at SVR12

For more information:
Plan of Action for the Prevention, Care & Treatment of Viral Hepatitis, Egypt 2014 - 2018

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Ministry of Health and Population
National Committee for Control of Viral Hepatitis

وزارة الصحة والسكان
اللجنة القومية لمكافحة الفيروسات الكبدية

Signature for NCCVH Guidelines for the Management of Adult Patients with HCV Infection August 2020

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NCCVH Guidelines for the Management of Adult Patients with HCV Infection August 2020

Inclusion criteria

Positive HCV RNA within the past 6 months. If the patient has received HCV therapy during that period, a new test should be performed.

Exclusion criteria

- Child C cirrhosis.
- Manifest liver decompensation: uncontrolled ascites, history of hepatic encephalopathy, hepatorenal syndrome.
- Serum albumin less than 2.8 g/dl, total bilirubin more than 3 mg/dl and INR 1.7 or more.
- Platelets count less than 50,000/mm^3.
- HCC, except 6 months after concluding an intervention aiming at cure with no evidence of activity by dynamic CT or MRI.
- Extra-hepatic malignancy except after two years of disease-free interval. In lymphomas and chronic lymphatic leukaemia, treatment can be initiated immediately after remission based on the treating oncologist's report.
- Pregnancy or inability to use effective contraception.

Precautions before starting treatment

- Check HCV treatment history.
- Ladies in the childbearing period should have a recent negative pregnancy test and should be counselled for effective contraception especially with the use of ribavirin.
- Check medications received by the patient especially cardiovascular disease therapy (particularly amiodarone), antipsychotic therapy and statins.
- Family counselling for the risk of transmission and prevention of infection.

Management of HCV treatment-naïve patients

Patients are categorized into "easy" or "not easy" to treat groups according to pre-treatment tests:

	Easy to treat group	Not easy to treat group
Criteria	• Total serum bilirubin ≤ 1.2 mg/dl • Serum albumin ≥ 3.5 g/dl • INR ≤ 1.2 • Platelets count ≥ 150,000/mm^3	• Total serum bilirubin > 1.2 mg/dl • Serum albumin < 3.5 g/dl • INR > 1.2 • Platelets count < 150,000/mm^3
Treatment regimen	SOF + DCV for 12 weeks	• SOF + DCV + RBV* for 12 weeks • SOF + DCV for 24 weeks if cases of RBV ineligibility or intolerance

*Ribavirin cannot be given if the patient's hemoglobin is less than 10 g/dl, in case of depression, or cardiac dysfunction. A drop of hemoglobin of 2 g, or less than 10 g/dl necessitates intervention either by dose reduction, possible use of erythropoietin or possible discontinuation. Ribavirin dose starts by 600 mg/day and is raised gradually to 1,000 mg/day according to tolerance.
DCV, daclatasvir; LDV, ledipasvir; RBV, ribavirin; SOF, sofosbuvir.

Management of HCV treatment-experienced patients

Previous Regimen	Child-Pugh class A	Child-Pugh class B
• IFN + RBV • INF+ SOF + RBV • SOF + RBV • SOF + SIM ± RBV • OBV/ PTV/r + RBV	SOF + DCV + RBV for 24 weeks	
• SOF + DCV for 12 weeks	SOF/VEL/VOX for 12 weeks	SOF/VEL + RBV (initial dose 600 mg daily) for 24 weeks ***(Treatment in special centers)***
• OBV/ PTV/r + SOF ± RBV for 12/24 weeks • SOF + SIM +DCV ± RBV for 12 weeks	SOF/VEL/VOX for 12 weeks	
• SOF/VEL/VOX for 12 weeks	SOF/VEL/VOX + RBV for 24 weeks	
• SOF/VEL + RBV for 24 weeks		

DCV, daclatasvir; IFN, interferon; LDV, ledipasvir; OBV, ombitasvir; PTV, paritaprevir; r, ritonavir; RBV, ribavirin; SIM, simeprevir; SOF, sofosbuvir; VEL, velpatasvir; VOX, voxilaprevir.

Patients with chronic kidney disease

- As described above for HCV treatment-naïve and experienced patients.
- Sofosbuvir-containing regimens could be used without dose adjustment in patients with renal disease, including those with an eGFR ≤30 ml/min and those on dialysis.
- RBV dose adjusted according to eGFR and hemoglobin level:
    - eGFR > 50: 600-1,200 mg daily as tolerated
    - eGFR 30-50: 400 mg alternating with 200 mg
    - eGFR < 30, not on dialysis: 200 mg daily to be reduced if not tolerated to 200 mg, 3 times weekly
    - eGFR <30, on dialysis: 200 mg, every other day given on dialysis day, 4 hours before dialysis.
    - Should be discontinued if hemoglobin level declines by more than 2 g/dl despite the use of erythropoietin.

Patients post-liver transplantation ***(Treatment in special centers)***

- As described above for HCV treatment-naïve and experienced patients.
- Voxilaprevir is not recommended in patients receiving cyclosporine.

Dual HBV and HCV infection

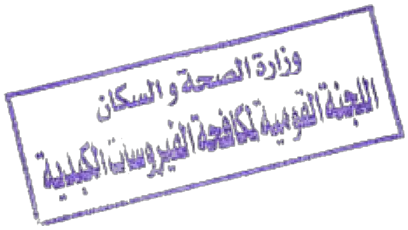
- HCV therapy should be started immediately, following the same rules as in patients with HCV mono-infection.
- HBsAg positive patients are treated if the treatment requirements are present, as in patients with HBV mono-infection. In case these criteria are not met (like an inactive carrier state), the following 2 options are available:
    - Initiate prophylaxis, to be continued until 12 weeks after end of treatment.
    - Monitor HBV DNA levels every 4 weeks, during and immediately after end of treatment for HCV. Nucleos(t)ide therapy is initiated if HBV DNA rises by 10-fold (one log), or if HBV DNA exceeds 1,000 IU/ml if it was previously undetectable.

Combined HCV/HIV Infection and HCV/HBV/HIV **(*Treatment in special centers)***

According to the special protocol for these co-infections.

Precautions after the end of treatment

- Confirmatory PCR test for the sustained virologic response should be performed 12 weeks after the end of treatment.
- Patients with advanced liver fibrosis (FIB4 ≥ 3.25) should be enrolled in the HCC surveillance program using AFP and abdominal ultrasonography every 4 months.
- HBV vaccination should be initiated if not already received.



Plan of Action for the Prevention, Care & Treatment of Viral Hepatitis, Egypt 2014-2018

Ministry of Health & Population

وزارة الصحة والسكان

Viral hepatitis is a global health problem that affects hundreds of millions of people worldwide. Globally, it is estimated that approximately 1.4 million persons die annually from all types of viral hepatitis. Egypt has one of the highest global burdens of hepatitis C virus (HCV) infection, with an estimated 10%, over 6 million people between 15-59 years, being chronically infected. Tragically, an estimated 150,000 new people are being infected annually, and thousands die every year.

In recognition of the enormity of the problem, in 2012, the Ministry of Health and Population (MOHP), in collaboration with stakeholders, developed the "Plan of Action for the Prevention, Care & Treatment of Viral Hepatitis, Egypt" (PoA) which focuses on the seven main components of viral hepatitis prevention and control: surveillance, infection control, blood safety, hepatitis B virus (HBV) vaccination, care & treatment, communication, and research. The PoA highlights the important goals and objectives of the MOHP's viral hepatitis program and reflects the MOHP's commitment to controlling the viral hepatitis epidemic by preventing new infections.

Finalizing the "Plan of Action for the Prevention, Care & Treatment of Viral Hepatitis, Egypt" was a huge step toward achieving MOHP's new vision aimed at National Eradication of Viral Hepatitis. In addition, MOHP has recently introduced new, highly-effective medications to treat HCV infection at an affordable price; these medications have been shown to cure over 90% of those receiving the treatment.

With this vision in mind, MOHP is urging all concerned parties to join forces and turn this plan into action which will not only stop the vicious circle of transmission of infection; but will also increase the effectiveness of new treatment and assist MOHP in translating its vision into reality.

Finally, I wish to express my sincere thanks to all colleagues that participated in the development of this important document and for their commitment to improving the health of the Egyptian people; this document is the product of a collaborative process involving numerous dedicated Egyptian and international partners.

Minister of Health and Population

Professor Adel Adawy

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Plan of Action for the Prevention, Care & Treatment of Viral Hepatitis, Egypt

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LIST OF ABBREVIATIONS

AABB	American Association of Blood Banks
ANRS	Agence Nationale de la Recherche sur le Sida et les Hépatites Virales (French National Agency for Research on AIDS and Viral Hepatitis)
BBP	Blood Borne Pathogens
BD	Birth Dose
CDC	Centers for Disease Control and Prevention
CLIA	Chemiluminescence Immune Assay
CME	Continuous Medical Education
CPHL	Central Public Health Laboratory
DAA	Direct Acting Antiviral
DHS	Demographic and Health Survey
EIA	Enzyme Immune Assay
ELISA	Enzyme-linked Immunosorbent Assay
EMRO	Eastern Mediterranean Regional Office
EPI	Expanded Programme of Immunization
EQAS	External Quality Assessment Schemes
GLP	Good Laboratory Practice
GOTHI	General Organization of Teaching Hospitals and Institutes
HAV	Hepatitis A Virus
HBeAg	Hepatitis B “e” Antigen
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HCW	Healthcare Worker
HDV	Hepatitis D Virus
HEV	Hepatitis E Virus
HIO	Health Insurance Organization
HIV	Human Immunodeficiency Virus
IC	Infection Control
IEC	Information Education Communication
IT	Information Technology
KAP	Knowledge, Attitude and Practice
MMWR	Morbidity and Mortality Weekly Report

MOHP	Ministry of Health and Population
MOU	Memorandum of Understanding
MSBOS	Maximum Surgical Blood Ordering Schedules
NAMRU-3	Naval Medical Research Unit 3
NAAT	Nucleic Acid Testing
NBP	National Blood Policy
NBTS	National Blood Transfusion Services
NCCVH	National Committee for the Control of Viral Hepatitis
NEDSS	National Egyptian Disease Surveillance System
NGO	Non-Governmental Organization
NHTMRI	National Hepatology and Tropical Medicine Research Institute
NITAG	National Immunization Technical Advisory Group
NBRB	National Blood Regulatory Body
NTC	National Treatment Centre
PCR	Polymerase Chain Reaction
Peg-IFN	Pegylated Interferon
PTES	Program of Treatment at the Expense of State
PWID	Person who injects drugs
QC	Quality Control
RBC	Red Blood Cell
REDS	Retrovirus Epidemiology in Donors Study
RHU	Rural Health Unit
RNA	Ribonucleic Acid
SOP	Standard Operating Procedure
STDF	Science and Technology Development Fund
TAG	Technical Advisory Group
USAID	United States Agency for International Development
VCT	Voluntary Counselling and Testing
VHRL	Viral Hepatitis Research Laboratory
WHO	World Health Organization

INTRODUCTION

With an estimated 8-10 million persons living with viral hepatitis in Egypt[1] and millions more at risk for infection, viral hepatitis is among the most significant public health problems facing this country. Most morbidity and mortality result from the chronic form of viral hepatitis caused by hepatitis B virus (HBV) and hepatitis C virus (HCV) infections. Because viral hepatitis can persist for decades without symptoms, many Egyptians remain unaware of their infection status and are not receiving care and treatment. Persons living with viral hepatitis are at increased risk for cirrhosis and liver cancer, and although not all persons infected with viral hepatitis develop these conditions, the medical and economic burden incurred by those who do is significant. Liver disease is a top cause of mortality in Egypt, and mathematical models predict an upsurge in cases of liver cirrhosis and liver cancer in the years to come.[2, 3] Given the high burden of viral hepatitis in Egypt, in 2006 the Ministry of Health and Population (MOHP) established the National Committee for the Control of Viral Hepatitis (NCCVH). By April 2008, this committee had developed a National Control Strategy for Viral Hepatitis, which called for effective surveillance, enhancements in prevention to reduce the incidence of HBV and HCV infection, and expanded access to care and treatment for those with chronic infection.

In recognition of the high prevalence and ongoing transmission of viral hepatitis, in 2011 Egypt's MOHP sought assistance from the World Health Organization (WHO)-Egypt, U.S. Centers for Disease Control and Prevention (CDC), Institut Pasteur, and the Agence Nationale de Recherche sur le SIDA et les Hépatites Virales (ANRS) in reviewing national strategies and identifying interventions to halt transmission. Together with national counterparts, this international team formed a Technical Advisory Group (TAG) to provide advice in the areas of viral hepatitis prevention, treatment, communication, policy, and research. A review by TAG revealed that many activities critical to viral hepatitis control had not been adequately undertaken in Egypt. As a first step to ensuring a more comprehensive approach to this substantial public health problem, TAG recommended that Egypt establish a National Hepatitis Program and create a Viral Hepatitis Plan of Action.

To prepare the *Plan of Action for the Prevention, Care & Treatment of Viral Hepatitis, Egypt* (referred to in this report as the Viral Hepatitis Plan of Action), during September and October 2012 the MOHP Viral Hepatitis Unit convened expert workgroups from various national and international agencies. Workgroup members were tasked with developing components of the action plan specific to their area of expertise. To engage stakeholders in the planning process, the workgroup solicited input from other agencies, professional societies, and community-based organizations.

(1) Centers for Disease, C. and Prevention, Progress toward prevention and control of hepatitis C virus infection--Egypt, 2001-2012. MMWR Morb Mortal Wkly Rep, 2012. 61 (29): p. 545-9.

(2) Khattab, M.A., et al., Management of hepatitis C virus genotype 4: recommendations of an international expert panel. Journal of hepatology, 2011. 54(6): p. 1250-1262.

(3) Deuffic-Burban, S., et al., Expected increase in hepatitis C-related mortality in Egypt due to pre-2000 infections. Journal of hepatology, 2006. 44(3): p. 455-461.

THE EPIDEMIOLOGY OF VIRAL HEPATITIS

Worldwide, about 1 in every 12 persons (480-520 million people) is living with viral hepatitis. Globally, an estimated 78% of primary liver cancer and 57% of liver cirrhosis cases are caused by viral hepatitis, and 1 million deaths from viral hepatitis occur each year.[4,5,6] Chronic hepatitis B and C are among the leading causes of infectious-disease death worldwide. The proportion of persons living with viral hepatitis is greatest in Asia, Sub-Saharan Africa, and Egypt; however, prevalence of HCV infection is high among subpopulations (e.g., people who inject drugs [PWIDs] and persons living in correctional settings) in almost all parts of the world.

HEPATITIS B

HBV is 50-100 times more infectious than HIV through the parenteral route.[6] WHO estimates that up to 2 billion people worldwide have been infected with HBV; about 240 million people live with chronic HBV infection, and about 780,000 HBV-related deaths occur each year.[6] In Egypt, an estimated 3.3 million persons are infected with hepatitis B. Chronic HBV infection, which occurs when the acute infection is not cleared by the immune system, is associated with a 15-25% risk of premature death from liver cancer or end-stage liver disease.[6,7]

HBV can be found in blood and body fluids of an infected person. Transmission can occur from an HBV-infected mother to child at the time of birth; through incidental community and household exposures; contaminated blood products; medical equipment; syringes; injection-drug use; and sexual contact. Globally, poor infection-control practices in healthcare settings represent a significant mode of viral hepatitis transmission. Mother-to-child transmission of HBV is concerning, because 90% of HBV-infected newborns remain infected throughout their lives. Among persons with chronic HBV infection, 1 in 4 dies from complications of viral hepatitis, primarily cirrhosis and hepatocellular carcinoma (HCC), later in life.

Hepatitis B vaccination, which has been available since the early 1980s, remains an important prevention tool worldwide, as administration of 3 doses of vaccine during childhood is 95% effective in preventing this infection.[6] Globally, for each annual cohort of children born, hepatitis B vaccination has been projected to avert >700,000 future HBV-associated deaths.[8] Hepatitis B vaccines have been part of the routine immunization program in Egypt since 1992.

HEPATITIS C

An estimated 130-150 million people live with chronic HCV infection worldwide, and 350,000-500,000 HCV-related deaths occur each year.[9] Acute HCV progresses to chronic infection in

(4) Perz, J.F., et al., The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. Journal of hepatology, 2006. 45(4): p. 529-538.

(5) Lavanchy, D., Chronic viral hepatitis as a public health issue in the world. Best Practice & Research Clinical Gastroenterology, 2008. 22(6): p. 991-1008.

(6) Organization, W.H., Hepatitis B Fact Sheet WHO/204, Revised July 2014. Geneva: WHO, 2014.

(7) Beasley, R.P., Hepatitis B virus. The major etiology of hepatocellular carcinoma. Cancer, 1988. 61(10): p. 1942-1956.

(8) Centers for Disease Control and Prevention, Ten great public health achievements--worldwide, 2001-2010. MMWR Morb Mortal Wkly Rep, 2011. 60(24): p. 814-8.

(9) Organization, W.H., Hepatitis C Fact Sheet WHO/164, Revised April 2014, Geneva: WHO, 2014.

55-85% of cases; 15-30% of these will develop complications of chronic liver disease, such as liver cirrhosis, and 1-5% will develop liver cancer.[9,10,11] Egypt has the highest prevalence of HCV in the world, with 10% of its population 15-59 years of age being chronically infected.[12] The chronic infection rate increases with age and goes up to more than 25% for 50-60 year-olds. Among 15-19 year-olds, 4% are chronically infected, demonstrating on-going HCV transmission. An estimated 150,000 new HCV infections occur each year in Egypt[1] and HCV morbidity and mortality are predicted to double in the coming 20 years.[13] The HCV epidemic in Egypt is thought to have originated with unsafe injections administered for a mass anti-schistosomiasis campaign conducted in that country during the 1960s and 1970s, representing the world's largest iatrogenic transmission of blood-borne pathogens to date.[14] Currently, contact with infected blood through medical procedures (including unsafe injection practices) is considered the primary mode of HCV transmission in Egypt. In urban areas, illicit drug use also contributes to the epidemic.

A major concern in Egypt is unsafe medical injections, primarily through reuse of disposable syringes. Because of the popular belief among Egyptians that injections are more effective than oral medications without additional risk,[15] the frequency of therapeutic injections is very high in Egypt compared with other low income countries; the estimated average number of injections per person per year is 4.2 in Egypt versus 1.5 in other countries.[15] An estimated 8% of injections are unsafe (i.e., the provider does not use a syringe taken from a closed, sealed packet). Injections are given by a wide variety of providers, including many who have no formal medical education or training.[16] These unsafe practices have been identified as key risk factors in the transmission of HBV and HCV.[15,17] Increasing public awareness of the viral hepatitis epidemic in Egypt, in particular the association between unsafe injections and viral hepatitis infection, could empower people to demand safe medical practices.

Antiviral treatments for HBV and HCV infections effectively reduce the associated morbidity and mortality from liver disease. For HCV in particular, for which no vaccine is available, new treatments can clear HCV from the body and result in virologic cure. Great progress has been made in improving access to care and receipt of these new treatments. Since 2006, a total of 26 treatment centers have been established in Egypt to provide subsidized HCV treatment to more than 200,000 patients. Nevertheless, because these drugs are expensive, they are not widely accessible. Liver transplants can improve health outcomes for persons with advanced viral hepatitis infection, although donated organs are in short supply, and such procedures are costly.

(10) Lavanchy, D., Evolving epidemiology of hepatitis C virus. Clin Microbiol Infect, 2011. 17(2): p. 107-15.

(11) Lavanchy, D., The global burden of hepatitis C. Liver Int, 2009. 29 Suppl 1: p. 74-81.

(12) Egypt. Demographic and Health Survey, 2008. 2008 Available from: http://www.measuredhs.com/pubs/pdf/FR220/FR220.pdf.

(13) Breban, R., et al., Towards realistic estimates of HCV incidence in Egypt. J Viral Hepat, 2012..

(14) Frank, C., et al., The role of parenteral antischistosomal therapy in the spread of hepatitis C virus in Egypt. The Lancet, 2000. 355(9207): p. 887-891.

(15) Specialist Panel on Chronic Hepatitis, B.i.t.M.E., A review of chronic hepatitis B epidemiology and management issues in selected countries in the Middle East. J Viral Hepat, 2012. 19(1): p. 9-22.

(16) Talaat, M., et al., Overview of injection practices in two governorates in Egypt. Tropical Medicine & International Health, 2003. 8(3): p. 234-241.

(17) Mostafa, A., et al., Is the hepatitis C virus epidemic over in Egypt? Incidence and risk factors of new hepatitis C virus infections. Liver Int, 2010. 30(4): p. 560-6.

HEPATITIS TYPES A, D, AND E

In addition to HBV and HCV, at least three other agents cause viral hepatitis: hepatitis A virus (HAV), hepatitis E virus (HEV), and hepatitis D virus (HDV). Both HAV and HEV are responsible for acute infections, whereas HDV acts by coinfection or superinfection of patients with chronic hepatitis B. Spread by the fecal-oral route, HAV is largely transmitted by person-to-person contact and through exposure to contaminated food and food products. Hepatitis A is vaccine preventable; however, the vaccine is not currently part of the immunization program in Egypt. Also spread by the fecal-oral route, most often through exposure to water contaminated by feces, HEV is widely present in south and central Asia, sub-Saharan Africa, and the Middle East. In Egypt, serologic surveys demonstrate considerable circulation of the virus; however, only sporadic acute infections are diagnosed, primarily among those who present to healthcare providers with fever and jaundice. The hepatitis D virus is unique in that it can only replicate in the presence of HBV; therefore, it is only a threat to HBV-infected persons. Hepatitis B vaccination is protective against both HBV and HDV infection.

VIRAL HEPATITIS PLAN OF ACTION OVERVIEW

VISION AND PURPOSE

"VIRAL HEPATITIS TRANSMISSION IS REDUCED THROUGH INCREASED PREVENTION AND EDUCATION, AND ALL EGYPTIANS HAVE ACCESS TO SAFE AND EFFECTIVE CARE AND TREATMENT."

Egypt's MOHP is committed to ensuring that new cases of viral hepatitis are prevented and that persons who are already infected are tested; informed about their infection; and provided with counseling, care, and treatment. The Plan of Action will help the MOHP improve its current efforts to prevent viral hepatitis and related disease by 1) identifying steps that can be taken to reach specific goals; 2) leveraging opportunities to improve coordination of viral hepatitis activities across MOHP sectors; 3) setting priorities for MOHP to develop public-health and primary care infrastructure needed for viral hepatitis prevention across all sectors; and 4) providing a framework for MOHP to engage other governmental agencies and nongovernmental organizations (NGOs) in viral hepatitis prevention and care.

STRUCTURE

The Viral Hepatitis Plan of Action is organized by the following six topic areas:

1. Strengthening Surveillance to Detect Viral Hepatitis Transmission and Disease;
2. Improving Blood Safety to Reduce Transmission of Viral Hepatitis;
3. Promoting Infection Control Practices to Reduce Transmission of Viral Hepatitis;
4. Educating Providers and Communities to Increase Awareness About Viral Hepatitis and its Prevention;
5. Eliminating Transmission of Vaccine-Preventable Viral Hepatitis; and
6. Improving Care and Treatment to Prevent Liver Disease and Cancer.

For each topic area, the Viral Hepatitis Plan of Action offers a dedicated chapter that begins with background information and is followed by recommended goals, objectives, and actions.

IMPLEMENTATION

Successful implementation of the Plan will require leveraging multiple opportunities. Some of the actions can be accomplished through improved coordination and integration of existing activities, whereas others are subject to the availability of funds. Also critical to the overall success of this plan are policy-related support and system changes. The Viral Hepatitis Plan of Action is a multifaceted, comprehensive approach to preventing viral hepatitis and improving the lives of millions of infected persons. The Plan of Action will offer an unprecedented opportunity to provide all Egyptians with improved viral hepatitis prevention, care, and treatment services.

1. STRENGTHENING SURVEILLANCE TO DETECT VIRAL HEPATITIS TRANSMISSION AND DISEASE

GOALS
1.1 Strengthen acute viral hepatitis surveillance to monitor trends of acute disease, assess risk factors, monitor prevention programs, and detect outbreaks.
1.2 Strengthen chronic viral hepatitis surveillance to monitor trends of chronic infection and associated disease and to assess prevention programs.

Public-health surveillance is an essential tool in the prevention and control of infectious and chronic diseases and for medical management. Surveillance data are used to estimate the magnitude of a health problem; describe the natural history of a disease; detect epidemics; document the distribution and spread of a health event or disease; evaluate control and prevention measures; and aid in public health planning.[1] To be valuable, public health surveillance requires standardized, systematic, ongoing collection and management of reliable data. Furthermore, it requires timely analysis and dissemination to facilitate effective public health action.

Egypt's national surveillance system for viral hepatitis is poorly funded and fragmented, resulting in incomplete coverage and inconsistent reporting of cases. The MOHP's Epidemiological Surveillance Unit, established in 1999 with the cooperation of USAID, WHO-Egypt, WHO-Eastern Mediterranean Regional Office (EMRO), and CDC, coordinates surveillance of communicable and non-communicable diseases. Cases of hepatitis A, B, and C are reported monthly from the National Egyptian Disease Surveillance System (NEDSS). Unfortunately, NEDSS capacity is inadequate to fully characterize the reports of viral hepatitis infection throughout the country. As a result, the data collected through this system are limited, resulting in an incomplete picture of the true burden of viral hepatitis. In addition, because diagnostic testing is lacking in Egypt, certain information about the etiology of infection and potential exposures is not routinely collected. All these factors result in inaccurate case counting and erroneous estimation of disease burden.

Adequate laboratory capacity is an important component of any surveillance system. Most laboratories in Egypt are capable of conducting serological tests for viral hepatitis. However, few laboratories in Egypt have the polymerase chain reaction (PCR) capacity necessary to confirm active HCV infection.

GOAL 1.1
Strengthen acute viral hepatitis surveillance system to monitor trends of acute disease, assess risk factors, assess prevention programs, and detect outbreaks.

Acute case surveillance is a key source of information regarding disease outbreaks; changes in transmission patterns; and morbidity and mortality. In Egypt, four surveillance sites (Abbasia, Embaba, Alexandria, Assuit) funded by ANRS in MOHP fever hospitals permitted the identification of current community and iatrogenic risk factors for HBV and HCV transmission. Sentinel surveillance will be transitioned to the MOHP Viral Hepatitis Unit. The MOHP Viral Hepatitis Unit should be equipped to collect and analyze a core set of surveillance data to include a variety of demographic and risk-related information. Expanding sentinel surveillance within the MOHP hospital system would

(1) CDC, Guidelines for viral hepatitis surveillance and case management. 2005, US Department of Health and Human Services: Atlanta, GA.

promote evaluation of methods for collecting surveillance data; identification of best practices for other surveillance sites; and collection of enhanced data regarding transmission patterns, burden of disease, and viral characteristics.

Objective 1.1.1

Continue existing sentinel surveillance systems under the direction of the MOHP viral hepatitis unit.

Five MOHP fever hospitals (Abbasia, Alexandria, Aswan, Helwan, Menof) are currently conducting surveillance and are funded by NAMRU-3 and CDC. Sentinel surveillance will continue in these identified facilities with the potential to extend to another two sites (Asuit and Zakazik fever hospitals).

Actions to Be Initiated:

- Address policy and regulatory requirements of facilities and participating parties, including the development of a Memorandum of Understanding (MOU) between all involved parties.
- Revise/standardize/develop standard operating procedures (SOPs) to allow for future expansion of sentinel surveillance to other sites.
- Recruit MOHP hospital staff for each facility to include epidemiologists and laboratory staff.
- Develop a central data management plan.
- Upgrade surveillance information technology (IT) to improve exchange of surveillance data among reporting sites (e.g., laboratories), MOHP, and supporting partners.
- Revise case investigation forms and case definitions, as needed.
- Develop a standard monthly and annual report format.
- Build laboratory capacity at each sentinel site, including training of personnel and procuring of equipment**.**
- Develop quality assurance program for laboratories supporting sentinel surveillance.
- Train healthcare workers (HCWs) on SOPs.

Objective 1.1.2

Expand sentinel surveillance to other facilities, including MOHP hospitals, university hospitals, military hospitals, private hospitals, and liver institutes in Cairo and Menofia.

Actions to Be Initiated:

- Develop a sentinel site selection plan.
- Explore opportunities to build upon existing surveillance platforms (e.g., acute respiratory illness and acute febrile illness).

- Secure/ensure adequate staffing and equipment.
- Assign and train facility-level teams at selected sites on sentinel surveillance SOPs.
- Link new sites to central sentinel surveillance data management system.

Objective 1.1.3

Increase capacity of the MOHP viral hepatitis unit in the areas of surveillance, epidemiology, data analysis and management, and reporting.

Actions to Be Initiated:

- Identify current gaps in MOHP viral hepatitis unit capacity and identify and implement strategies to address them.
- Ensure adequate number of and appropriately skilled staff to collect, analyze, and disseminate surveillance data.
- Conduct intensive training on viral hepatitis epidemiology; surveillance; laboratory and diagnostics; data management and reporting; and management of research projects.
- Improve the epidemiologic and investigational response capacity of the MOHP viral hepatitis team.
- Ensure sustainability of MOHP viral hepatitis unit (training of new staff, quality assurance reports).

Objective 1.1.4

Increase the capacity of laboratories throughout Egypt to support outbreak investigations and other surveillance activities, and ensure quality of sentinel sites through laboratories at the Central Public Health Laboratory (CPHL) and Viral Hepatitis Research Laboratory (VHRL) within the National Hepatology and Tropical Medicine Research Institute (NHTMRI).

Actions to Be Initiated:

- Review current laboratory system to identify laboratories capable of handling viral hepatitis specimens.
- Identify gaps in laboratory capacity and identify strategies to address them.
- Provide technical assistance to public health laboratories by conducting viral hepatitis workshops and hands-on training for laboratory staff and developing SOPs for laboratory diagnostics.
- Develop a laboratory quality assurance program for the sentinel surveillance sites.

Objective 1.1.5

Strengthen existing routine surveillance (NEDSS) system.

Actions to Be Initiated:

- Review attributes of surveillance systems (*MMWR* Guidelines) through an evaluation of the NEDSS surveillance system.
- Revise the existing system based on results of surveillance evaluation.
- Improve capacity for complete and accurate disease reporting among laboratories and providers.

Objective 1.1.6

Develop supervision, monitoring, and evaluation for the sentinel surveillance system.

Actions to Be Initiated:

- Review current supervisory systems (SOPs), acknowledge gaps, and take measures to strengthen the system.
- Develop indicators for monitoring and evaluation.
- Conduct independent, annual reviews of surveillance systems.

GOAL 1.2
Strengthen chronic viral hepatitis surveillance system to monitor trends of chronic infection and disease and to assess prevention programs.

The MOHP collaborates with USAID to conduct regular surveys of the general population (e.g., the Demographic and Health Survey [DHS]). These surveys, which currently include information on HCV, provide insight into current disease prevalence, demographics, and risk factors at the national level.[2] The 2008 DHS did not include testing for HBV infection. Certain communities and settings (e.g., persons requiring frequent medical procedures, incarcerated individuals, HIV-infected persons, and PWIDs) that may be disproportionately affected by viral hepatitis are underrepresented in the DHS, necessitating specific behavioral and serologic surveys targeting these populations at the community level. Such surveys would provide more accurate estimates of the burden of hepatitis B and C in Egypt.

Objective 1.2.1

Use existing data sources to monitor chronic viral hepatitis infection.

Actions to Be Initiated:

- Identify and assess available data sources (where viral hepatitis testing is currently being conducted) for analysis. Potential data sources include blood donors; hemodialysis groups; patients in intensive care units; HIV surveillance groups-mobile units “voluntary counseling and testing (VCT) sites;” and visa applicants.

(2) Egypt. Demographic and Health Survey, 2008. 2008 Available from: http://www.measuredhs.com/pubs/pdf/FR220/FR220.pdf]

- Improve/ensure quality of data collection and laboratory quality of identified databases.
- Establish policies and procedures for sharing of data between different stakeholders (e.g., visa applicant data from CPHL).
- Establish system for data transferal from identified data sources (e.g., CPHL and blood banks) to viral hepatitis unit at MOHP.
- Establish system for regular analysis and reporting of chronic viral hepatitis surveillance data.
- Integrate viral hepatitis surveillance into the HIV VCT program.
- Revise DHS protocols to include age groups, questionnaires, serology, and storage of samples.

Objective 1.2.2

Establish new surveillance systems for chronic viral hepatitis infections.

Actions to Be Initiated:

- Establish viral hepatitis serologic surveillance among identified groups, including women receiving care at antenatal clinics, military recruits, prisoners, drug users, and patients with medical conditions requiring frequent medical procedures (e.g., blood transfusions, endoscopy, diabetes management, and chemotherapy).
- Improve capacity for complete and accurate disease reporting among laboratories and providers.
- Establish system for regular analysis and reporting of chronic viral hepatitis surveillance data.

Objective 1.2.3

Initiate surveillance programs in hospital dialysis units to measure seroconversion of viral hepatitis (HBV and HCV).

Actions to Be Initiated:

- Develop a standard protocol for Egypt to measure viral hepatitis (HBV, HCV) seroconversion rates in hemodialysis units.
- Establish a system for regular reporting of hemodialysis-related transmissions of viral hepatitis to MOHP viral hepatitis unit.
- Disseminate annual reports on district governorate and national levels of seroconversion in hemodialysis patients.

Objective 1.2.4

Monitor mortality and morbidity related to viral hepatitis.

Actions to Be Initiated:

- Review various institute registries (e.g., health insurance organizations [HIOs], liver treatment centers, and Program of Treatment at the Expense of State [PTES]) to determine suitability as a source of data concerning care and treatment of acute and chronic liver disease.
- Collaborate with liver cancer registries (i.e., Tanta).
- Review available mortality registries (e.g., death certificates).

2. Promoting Infection Control Practices to Reduce Transmission of Viral Hepatitis

GOALS
2.1 Establish government commitment and support of policies that ensure infection control practices in Egypt.
2.2 Reduce transmission of viral hepatitis in secondary and tertiary hospitals.
2.3 Reduce transmission of viral hepatitis in primary government and private healthcare settings.
2.4 Reduce occupational transmission of viral hepatitis.
2.5 Promote safe injection practices.
2.6 Strengthen monitoring and evaluation programs for ensuring implementation of infection control programs.

Lack of infection control (IC) measures is an essential risk factor for both HCV and HBV transmission in Egypt. Consequently, receipt of injections, dental procedures, invasive procedures, blood transfusion, and obstetric procedures, along with being hospitalized, are among the healthcare-related risk factors associated with viral hepatitis transmission.[1, 2,3,4,5] Unsafe injections in particular significantly contribute to ongoing viral hepatitis transmission; of the approximately 280 million injections administered in Egypt during 2001, an estimated 8% (23 million) were unsafe.[6]

In 2002, MOHP, NAMRU-3, and WHO developed a national plan in Egypt to establish an organizational IC program structure, develop IC guidelines, train HCWs, promote occupational safety, and establish a system for monitoring and evaluating IC activities.[6] Implementation of this plan in MOHP facilities and primary care centers resulted in improvements in IC practices; a 2011 International Health Regulations assessment of the plan concluded that the program had substantially reduced iatrogenic transmission of HCV. For instance, annual incidence of HCV infection among dialysis patients has decreased from 28% to 6%. Improvements also were observed in HCWs compliance with standard precautions (e.g., hand hygiene, use of personal protective equipment, safe injection practices, appropriate reprocessing of instruments, and waste management).

Although IC programs were implemented in most MOHP facilities and primary-care health centers, these settings account for only 60% of all inpatient admissions.[7] The remaining

(1) Medhat, A., et al., Hepatitis c in a community in Upper Egypt: risk factors for infection. Am J Trop Med Hyg, 2002. 66(5): p. 633-8.

(2) Mostafa, A., et al., Is the hepatitis C virus epidemic over in Egypt? Incidence and risk factors of new hepatitis C virus infections. Liver Int, 2010. 30(4): p. 560-6.

(3) Talaat, M., et al., Case-control study to evaluate risk factors for acute hepatitis B virus infection in Egypt. East Mediterr Health J, 2010. 16(1): p. 4-9.

(4) Talaat, M., et al., Sentinel surveillance for patients with acute hepatitis in Egypt, 2001-04. East Mediterr Health J, 2010. 16(2): p. 134-40.

(5) Mostafa, A., et al., Seroprevalence of hepatitis B and C in pediatric malignancies. J Egypt Natl Canc Inst, 2003. 15: p. 33-42.

(6) Talaat, M., et al., Overview of injection practices in two governorates in Egypt. Tropical Medicine & International Health, 2003. 8(3): p. 234-241.

(7) Rafeh, N., Julie Williams, and Nagwan Hassan, Egypt Household Health Expenditure and Utilization Survey 2010. Bethesda, MD: Health Systems 20/20 project, Abt Associates Inc., 2011.

portion of Egypt's population receives medical care in University hospitals; the private sector; military and police hospitals; and non-MOHP government hospitals. Therefore, to be effective, any future infection control plan in Egypt must promote the safety of healthcare provided in these alternative healthcare settings.

Outpatient services also must be considered in efforts to improve IC in Egypt. According to Egypt's Household Health Expenditure and Utilization Survey (2009/2010), the private sector (primarily private clinics and pharmacies) remains the primary provider of outpatient services, accounting for 71% of all visits.[7] In light of these data, successful expansion of IC programs to outpatient settings must involve these facilities.

GOAL 2.1
Establish government commitment and support of policies that ensure infection control practices in Egypt.

To ensure expansion of the IC programs to all non-MOHP health facilities in Egypt, regulations must be developed to facilitate IC program coordination and monitoring in these settings. To ensure safe delivery of medical procedures, such policies should be issued and enforced by regulatory bodies, and a mechanism should be established to revise and revive all ministerial decrees, standard protocols, and other regulatory tools. To ensure safe management of medical waste (which can present a substantial risk for viral hepatitis transmission to both HCWs and the community), the environmental sector in MOHP must be involved in all efforts to develop IC regulations. Because community-based, non-licensed professionals (e.g., pharmacists and barbers) serve as "informal" providers of injections in both urban and rural communities, legislation also must address safe injection practices in these settings.

Several factors complicate the regulatory process of healthcare in Egypt. Although the MOHP's Free Treatment Sector is the regulatory body responsible for licensing private-sector hospitals in Egypt, many private-sector and non-MOHP facilities either operate under loose regulatory mechanisms or have not obtained licensing. In addition, licensing typically is not conducted on a regular basis. New legislation and policies must be developed and existing regulation revised to reinforce decisions made by the Free Treatment Sector, including adherence to IC policies as a prerequisite to license issuance and renewal.

Throughout the past decade, several attempts have been made in Egypt to introduce the concept of total quality management for healthcare reform. An independent body for accreditation has taken the lead in this effort; re-introducing this body and assigning it responsibility for IC monitoring would promote viral hepatitis control in Egypt.

Objective 2.1.1

Develop/update policies and legislations to enforce the implementation of IC programs in Egypt.

Actions to Be Initiated:

- Empower the National Infection Control Steering Committee, to include reviewing membership, convening frequent meetings, and creating an exchange forum.

- Introduce IC programs as a strategic element of the High Council of Health.
- Activate the ministerial decree regarding pre-employment training for HCWs on IC measures.
- Develop legislations regarding centralization of all IC regulatory mechanisms through an independent body.
- Ensure implementation of standard IC protocols at all hemodialysis units (e.g., those operated by the government, private sector, and charity organizations).

Objective 2.1.2

Implement and enforce IC legislation in all non-MOHP hospital settings, to include other government (e.g., agriculture, electricity, and industry), private-sector, charity, and military/police hospitals.

Actions to Be Initiated:

- Develop legislation/policies to enforce licensing and renewal of licensing of all hospitals outside MOHP.
- Develop a policy mandating that IC must be an essential element of private hospital licensing.

Objective 2.1.3

Implement/enforce legislation focused on IC in all primary care clinics.

Actions to Be Initiated:

- Implement legislation requiring IC as an essential component of licensing and renewal of primary care clinics.
- Consider policy requiring that clinics cease operations if found to be noncompliant with service-appropriate IC.

Objective 2.1.4

Promote legislation implementing safe injection practices.

Actions to Be Initiated:

- Develop IC legislation intended for informal injection providers (e.g., pharmacists and barbers).

Objective 2.1.5

Ensure establishment of regulations relevant to waste management.

Actions to Be Initiated:

- Activate regulatory mechanisms governing waste management.

Objective 2.1.6

Promote accreditation of healthcare facilities in Egypt.

Actions to Be Initiated:

- Create an independent body responsible for national accreditation.
- Investigate the possibility of assigning the monitoring of IC to this independent body.

GOAL 2.2
Reduce transmission of viral hepatitis in secondary and tertiary hospitals.

Since its creation in 2002, the MOHP IC program has seen both great achievements and persistent challenges. Among the challenges faced is the absence of a comprehensive organizational chart illustrating the coordination of infection control throughout all MOHP hospitals. Furthermore, to realize improvements in IC across MOHP facilities, the human and financial resources of the MOHP's central IC department must be expanded. Another challenge inherent to an expansion of the IC program's coverage to the entire Egyptian healthcare system is the lack of basic, background information of government non-MOHP hospitals; fortunately, this information can be obtained through surveys or available census data.

Equally critical to reductions in healthcare-associated viral hepatitis transmission is engagement of non-MOHP hospitals. Although some university hospitals have already achieved considerable progress in implementing IC programs, many more have yet to undertake this effort. Establishment of a High Committee of IC in university hospitals coordinated by the Supreme Council of Universities would promote the establishment of IC programs in the university hospital setting.

The role of private primary care clinics cannot be overlooked in the context of improving IC practices in Egypt. This sector is known to be run with little to no regulations that ensure the implementation of IC programs. Given the diversity of medical practices carried out in private clinics, each with a unique set of risk factors that require certain IC measures, specific standards and guidelines must be developed and distributed to ensure adequate implementation of IC programs in such settings. Dissemination of these guidelines will establish grounds for requiring these hospitals to have a functional IC program as a prerequisite for HIO contracting.

In both MOHP and private hospital settings, the effectiveness of IC programs hinges on the availability of critical supplies (e.g., soap, protective barriers, and disinfectants), representing a significant challenge for hospitals with limited resources. Regardless of resource capacity, all hospitals are faced with a difficult, erratic, and often unpredictable systems for procurement and distribution of supplies. Occasionally, quality of supplies is marginal and manufacturing specifications to ensure the safety of their performance inadequate (e.g., designation of injection equipment as single-use).

Objective 2.2.1

Enhance/strengthen infection control programs in MOHP hospitals (e.g., General Organization for Teaching Hospital and Institutes [GOTHI] , Health Insurance, and Tropical Institutes) to ensure safe medical care.

Actions to Be Initiated:

- Collaborate with an expert group to create an organizational chart outlining IC organizational structure for Egypt's MOHP hospitals.
- Assess MOHP IC department's financial and human resources to identify needs.
- Collaborate with experts to update National Egyptian IC Guidelines every 2 years.

Objective 2.2.2

Determine current status/presence of IC programs in all hospitals outside MOHP to include non-MOHP government (agriculture, electricity, and industry), private-sector (including charity), and military/police hospitals.

Actions to Be Initiated:

- Through a survey or census, obtain a detailed list of the governmental hospitals not affiliated with MOHP or universities, private health facilities (licensed and non-licensed), and military and police hospitals.

Objective 2.2.3

Strengthen existing and create new IC programs in all university hospitals.

Actions to Be Initiated:

- Establish a High Committee of IC (coordinated by the Supreme Council of Universities) responsible for regulation of IC in university hospitals.
- Identify and develop IC programs in university hospitals lacking an IC program.

Objective 2.2.4

Ensure presence of IC programs in the private sector.

Actions to Be Initiated:

- Empower the "free treatment" sector of the MOHP through collaboration with the central IC department to set IC standards using their expertise.
- Distribute National Egyptian IC guidelines to all private hospitals.
- Establish policies that link payment to quality of care.

Objective 2.2.5

Ensure availability of appropriate, high quality IC supplies and equipment.

Actions to Be Initiated:

- Include IC experts as members of the MOHP committee responsible for purchasing IC supplies.
- Conduct a needs assessment and develop a system for ensuring distribution of IC supplies to those MOHP facilities in need.
- Develop a policy to ban reuse of single-use items.

GOAL 2.3
Reduce transmission of viral hepatitis in primary healthcare settings (governmental and private).

The scope of current National IC guidelines does not address site-specific requirements, such as primary healthcare settings. Thus, guidelines and training curricula specific to primary healthcare should be developed and distributed to both MOHP and non-MOHP primary rural and urban healthcare settings.

Dental procedures continue to be associated with viral hepatitis transmission in Egypt.[8] The IC department could collaborate with the MOHP dentistry sector, ensuring development and dissemination of guidelines specific to dentists' clinics. Furthermore, the IC department could maintain supervision and monitor IC compliance in dental settings to ensure full implementation of IC programs. This cannot be achieved without building the capacity of the dentistry sector, to include development of a database for private clinics and enforcement of licensing procedures.

Objective 2.3.1

Promote IC measures in MOHP primary healthcare settings.

Actions to Be Initiated:

- Develop/distribute national guidelines and training curricula specific to IC measures in primary care to all MOHP primary clinics (e.g., rural health units [RHUs], health centers, and family clinics).

Objective 2.3.2

Ensure implementation of IC in private primary care clinics.

Actions to Be Initiated:

- Create/update standards of IC measures in private clinics linked to the type of health

(8) Arafa N, et al. "Changing pattern of HCV spread in rural areas of Egypt." J Hepatology 2005;43:418-24.

services provided.

- Distribute national guidelines and training curricula specific for IC measures in primary care to all private clinics.

Objective 2.3.3

Develop and implement IC programs for dentistry in Egypt.

Actions to Be Initiated:

- Develop/distribute IC guidelines specific for dentistry.
- Ensure all dentistry hospitals and clinics are implementing IC programs.
- Empower the dentistry department of the MOHP to monitor dentistry private clinics (database for private clinics, renewal of licensing).

GOAL 2.4
Reduce occupational transmission of viral hepatitis.

A critical component of the IC program in Egypt is the promotion of occupational safety and health. The countrywide baseline assessment in 2001 revealed that government and private hospitals had no occupational safety programs in place. Consequently, HCWs were not appropriately trained on how to reduce their risks acquired through occupational exposure. A 2002 survey revealed that Egyptian HCWs engaged in unsafe practices when using and disposing of sharps and experienced frequent needlestick injuries (average of 4.9 needlestick injuries per year); low hepatitis B vaccination coverage (14%) also was documented among those HCWs surveyed.[6]

Educating HCWs on effective IC protocols reduces their risk for blood-borne pathogens (BBPs), including viral hepatitis. Ideally, this education would occur in the school setting, because HCWs are being exposed to BBPs before the start of their professional careers, while still in undergraduate or healthcare training programs. However, most institutes providing education in healthcare do not include an IC component in their curricula. For those that do, existing curricula are outdated.

Several actions can be taken to reduce risks associated with exposure to BBPs, including use of safe injection devices, needlestick programs, and safe disposal of sharps. HCWs who have a potential BBP exposure should be managed according to published guidelines. Such guidelines should be developed and distributed to all healthcare settings and updated on a regular basis. Hospitals must also have an adequate supply of HBV immunoglobulin on site to be administered prophylactically in case of a potential exposure.

Objective 2.4.1

Develop an educational curriculum for IC to be used by multiple disciplines of health professionals to reduce occupational exposure to BBPs, including viral hepatitis.

Actions to Be Initiated:

- Update existing MOHP IC training curriculum every 2 years.
- Require continuous refresher courses for all hospital IC teams every 3 years.
- Introduce a mandatory IC component to be included in undergraduate and postgraduate medical, dentistry, pharmacy, nursing, and physiotherapy institutes.

Objective 2.4.2

Promote the prevention and management of occupational exposure to HBV, HCV, and other BBPs.

Actions to Be Initiated:

- Promote the use of safe devices, needlestick surveillance programs, and safe disposal of sharps.
- Develop and distribute a specific manual for management of occupational exposure of BBPs.
- Ensure hospitals have post-exposure prophylaxis readily available.

GOAL 2.5
Promote safe injection practices in healthcare.

Several studies in Egypt have identified specific actions that can reduce rates of unsafe injections when administered by informal and formal healthcare professionals. For informal injection providers, this research revealed the importance of IC training, whereas for formally trained HCWs, education and monitoring through standardized check-lists were associated with improved compliance with safe injection practices. Use of single-use vials as well as auto-disabled/auto-retracted injection devices has also resulted in considerable reduction of risks associated with injection practices.

Objective 2.5.1

Ensure implementation of safe injection practices.

Actions to Be Initiated:

- Train informal injection providers (e.g., barbers, pharmacists, and housekeepers) on safe injection practices.
- Develop a standardized check-list to monitor injection practices in healthcare settings, including dental clinics.
- Educate HCWs on correct disposal of sharps.
- Expand the use of single-use vials to replace multi-dose vials in hospitals and primary healthcare settings.

- Expand the use of safe injection devices (auto-disabled/auto-retracted) for curative purposes.
- Ensure coordination between MOHP environmental sector and Ministry of Environment to improve, standardize, and regulate sharps disposal methods.

GOAL 2.6
Strengthen monitoring and evaluation programs for ensuring implementation of infection control programs.

The MOHP IC department has been using a scoring system to evaluate ongoing IC programs in different hospitals. Though effective, this system could be revised and validated using current knowledge and evidence-based protocols and guidelines. Also, the development and validation of monitoring tools specific to IC practices would help prevent transmission of BBPs, especially in primary healthcare settings.

Implementing a universal IC program in diverse healthcare settings, to include close monitoring and evaluation, will greatly increase the workload for the MOHP IC department. Delegating monitoring activities to an independent agency could alleviate this burden, along with the availability of updated, standardized monitoring tools and improved coordination with regulatory bodies.

Objective 2.6.1

Develop critical indicators to measure processes of IC (process indicators).

Actions to Be Initiated:

- Develop a multi-disciplinary taskforce to revise and validate current monitoring tools, including the "scoring system" developed by MOHP.
- Develop and validate a monitoring tool specific to viral hepatitis and BBPs in primary healthcare settings.
- Conduct regular supervision and monitoring of all healthcare settings using the updated, revised scoring system.

Objective 2.6.2

Establish an independent body to govern and regulate IC monitoring and evaluation activities using a standardized scoring system.

Actions to Be Initiated:

- Identify an independent agency capable of monitoring IC programs using a standardized monitoring tool and scoring system.
- Disseminate monitoring results using a web-based platform.
- Strengthen collaboration between the independent agency and other regulatory bodies (MOHP free-treatment sector).

3. IMPROVING BLOOD SAFETY TO REDUCE TRANSMISSION OF VIRAL HEPATITIS

GOALS
3.1 Establish government commitment and support of policies that ensure the safety and adequacy of the national blood supply.
3.2 Build a sustainable base of safe blood donors to maintain adequate and safe national blood supplies.
3.3 Apply national standards in all activities related to blood component production and blood testing.
3.4 Ensure the appropriate clinical use of blood and blood products.
3.5 Develop information technology solutions to support safer blood collection and transfusion and to facilitate surveillance, management, and research.

Considering the high prevalence of viral hepatitis in Egypt, ensuring safe, virus-free blood is a priority that requires commitment from all sectors involved in blood transfusion services. The Egyptian blood transfusion system is complex and fragmented, with many stakeholders providing blood products throughout the country. The Egyptian Blood Transfusion Service (BTS) started in 1938 with the formation of an NGO for blood donors. In 1960, a presidential decree (Law No. 178) legalized the Egyptian BTS, creating the Higher Council of Blood. The General Directorate for Blood and Blood Derivatives Affairs was established in 1975 within the MOHP, and since then, MOHP has carried the responsibility of upgrading, organizing, and administrating blood transfusion activities to meet demands for blood and related products across Egypt. In 1997, a project was launched to establish a customized and modern blood transfusion service, and by 2000, the National Blood Transfusion Services (NBTS) had been established. To date, NBTS consists of 24 centers, which provide 30% of blood and blood products in Egypt. The remaining 70% are provided by numerous other organizations (e.g., HIO, public and private hospitals, and Red Crescent). Although reliable statistics are lacking regarding the burden of viral hepatitis attributable to blood transfusions in Egypt, the high prevalence of viral hepatitis among the population, limited standardization, lack of regulations, and limitations of testing techniques suggest the possibility of considerable transfusion-related viral hepatitis cases.[1,2] To prevent viral hepatitis infections acquired through blood transfusions, provision of safe blood should be the priority of every blood bank in Egypt.

(1) Hussein, E. and J. Teruya, Evaluation of blood supply operation and infectious disease markers in blood donors during the Egyptian revolution. Transfusion, 2012. 52(11): p. 2321-8.

(2) Guerra, J., et al., HCV burden of infection in Egypt: results from a nationwide survey. J Viral Hepat, 2012. 19(8): p. 560-7..

GOAL 3.1
Establish government commitment and support of policies that ensure the safety and adequacy of the national blood supply.

The blood transfusion system in Egypt is fragmented and poorly regulated. Currently, more than 15 different organizations provide blood and blood products throughout Egypt, and blood is stored in more than 400 blood banks. Providing safe blood is a complex process with many different layers of security (e.g., blood donor selection, testing of blood units, safe transportation, and transfusion of blood products), requiring well-trained staff and adherence to a strict protocol. The lack of governing bodies and policies for regulating blood banks and monitoring the implementation of standards is a barrier that must be addressed in Egypt's effort to ensure a safe and adequate blood supply.

Objective 3.1.1

Develop an independent National Blood Authority (NBA) with representation by all stakeholders.

Actions to Be Initiated:

- Advocate to appropriate parties for the establishment of an NBA, which will present the Viral Hepatitis Plan of Action during the governance workshop.
- Advocate for the establishment of a National Regulatory Authority (NRA); an independent agency for BTS or within the Central National Regulatory Agency.
- Assign responsibility for regulating and licensing blood banks and conducting compliance inspections to the NRA.
- Ensure that the regulatory body reviews and modifies the National Blood Policy (NBP) to render it applicable to all blood bank sectors.
- Review and update the National Blood Law (NBL).
- Recognize that blood banks will continue to work as a hybrid system but will be subject to the laws passed by the Government/Parliament. (This could be modified in the future if the decision is made to unify blood banks into one national system.)
- Conduct independent assessments of all blood banks to ensure compliance of the NBP; this assessment could be conducted by WHO.
- Re-evaluate current legislation that forbids importation/exportation of human blood products.

Objective 3.1.2

Establish an independent National Regulatory Authority (NRA) for the Egyptian BTS.

Actions to Be Initiated:

- Establish an Expert Advisory Committee with representatives from all service providers (e.g., Ministry of High Education and MOHP) that meet on a regular basis and report to the regulatory body.
- Establish two divisions (one within the Ministry of High Education representing the university hospitals and one within the MOHP representing NBTS, HIOs, and private-sector blood banks). These divisions will assign representatives to be members of the Expert Advisory Committee.
- Blood banks will strive for accreditation by EJAC using the National Technical Standards (NTS) as the accreditation tool.
- Build capacity of blood-bank staff to ensure compliance with NTS.
- Review legislation for licensed blood collection/production facilities and issue penalties for illegal practice.

GOAL 3.2
Build a sustainable base of safe blood donors in order to maintain adequate and safe national blood supplies.

Three types of blood donors are recognized globally: paid donors, family replacement donors (i.e., family members of a patient giving blood before the patient undergoes a procedure), and volunteer donors. The risk of transfusion-transmitted infections depends on the type of donor. [3,4] The collection of blood from paid donors carries the highest risk and has been prohibited in Egypt since 1999. WHO recommends that 100% of blood donations originate from volunteer donors.[5] Efforts have been made to increase the number of volunteer blood donations in Egypt, but the donated supply of blood remains too low to adequately meet national demands. Family replacement donors are still relied upon to meet the blood needs; therefore, better data are needed regarding the prevalence and incidence of transfusion-associated infections resulting from family replacement blood donations.

Objective 3.2.1

Expand the pool of appropriate volunteer blood donors.

Actions to Be Initiated:

- Review current volunteer blood-donor system and recruitment strategies across all sectors.
- Conduct research on donor motivations and deterrents.

(3) Bates, I., G. Manyasi, and A. Medina, Lara, Reducing replacement donors in Sub-Saharan Africa: challenges and affordability. Transfus Med, 2007. 17(6): p. 434-42.

(4) Barker, L.F. and R.G. Westphal, Voluntary, nonremunerated blood donation: still a world health goal? Transfusion, 1998. 38(9): p. 803-6.

(5)WHO. Towards 100% Voluntary Blood Donation. A global framework for action. 2010; Available from: http://www.who.int/bloodsafety/publications/9789241599696/en/index.html.

- Develop marketing approaches for recruitment and retention of safe blood donors (e.g., campaigns at universities, mosques, and factories).
- Increase public awareness regarding need for donated blood (e.g., through development of curricula for university students and secondary students and a national on-going mass media campaign to build awareness).
- Form partnerships between MOHP and the media (to include newspaper, television, and internet) to increase public awareness about blood donation and encourage positive relationships between media and blood services.
- Encourage and engage regular donors in social events.
- Network with NGOs to provide support for donor recruitment.
- Increase access to donation facilities in blood banks across all governorates. (Facilities must meet criteria established in WHO assessment.)

Objective 3.2.2

Improve selection and management of all blood donors (both volunteer and family donors).

Actions to Be Initiated:

- Address deficiencies identified by independent assessment to ensure all blood banks are following the NBP for donor selection.
- Review current blood donor selection criteria at least every 3 years.
- Create a national database of donors with rare blood groups as well as different red blood cell (RBC) phenotype patterns.
- Develop a national database of donors rejected because of HBV/HCV positivity.
- Develop an active surveillance system for detection of adverse reactions among blood donors.
- Establish a counseling and medical referral process for HBV/HCV+ donors.

Objective 3.2.3

Conduct surveillance on the prevalence and incidence of HCV, HBV, and other BBPs in blood donors.

Actions to Be Initiated:

- Develop a standardized format for regular reporting of data by all blood banks to the NBA, Expert Advisory Panel, and the MOHP Viral Hepatitis Unit.
- Establish a national permanent donor deferral list.

GOAL 3.3
Apply national standards in all activities related to blood component production and blood testing.

Egyptian national standards for blood component production and blood testing were developed by the NBTC and updated in 2011, but they were not disseminated to blood banks in other sectors. Because of the fast evolution of technology in this field and the evolving epidemiology of viral hepatitis in Egypt, these guidelines require updating at regular intervals. Every blood bank should be mandated to implement the national technical standards (NTS) which are based on the national standards, ensuring safe blood processing across Egypt. The implementation of NTS in every blood bank is a critical step to ensuring safe blood component production and blood testing.

Objective 3.3.1

Set minimum criteria for infectious disease testing across all blood centers.

Actions to Be Initiated:

- Finalize and adopt NTS as the national standard.
- Train personnel for implementation of the NTS.
- Develop guidelines for evaluation and validation of blood screening assays.
- Conduct external quality assessment schemes (EQAS).
- Ensure all collected blood units are screened for HBV, HCV, and HIV using reliable technology (e.g., Enzyme Immune Assays [EIAs] or chemiluminescence [CLIA]). Use of rapid assays in the blood-bank setting is discouraged due to inferior sensitivity.
- Review screening and confirmatory testing algorithms.
- Conduct research on cost-effectiveness of introduction of nucleic acid amplification testing (NAAT).
- Implement NAAT at additional laboratories if such testing is determined to be cost-effective.

Objective 3.3.2

Establish quality control (QC) systems for blood testing.

Actions to Be Initiated:

- Develop a quality control system using internal/external QC reagents based on the NTS.
- Participate in EQAS.
- Increase number of participating labs with support of MOHP.
- Develop SOPs for blood-group serology (antibody screening) and cross-matching.

- Ensure that blood banks conduct regular audits of procedures and monitoring of equipment to promote compliance with national standards.

Objective 3.3.3

Standardize component preparation throughout all blood banks.

Actions to Be Initiated:

- Ensure all blood banks have the capacity to process products (component preparation) according to criteria set in the NTS; develop an implementation plan to ensure that all blood banks are fully equipped.
- Standardize storage times and cold chain procedures, including maintenance and calibration of equipment and implementation of temperature recording log.
- Establish SOPs for transportation of blood from one facility to another and for sterile processing (including the use of closed systems) to prevent contamination.
- Establish a system for blood-unit identification (e.g., ISBT128 coding and labeling).

GOAL 3.4
Ensure the appropriate clinical use of blood and blood products.

Blood and blood products are valuable resources that should be used sparingly. Appropriate clinical use of these resources is essential to optimize blood utilization and avoid waste; prudent use entails avoiding unnecessary transfusion, which increases the potential for transmission of viral hepatitis and other BBPs.[6,7] Clinicians are key players in this process and should be committed to ordering the right amount of the right blood product for the right patient. In addition, hemovigilance is essential for detecting adverse events and protecting patients; [8, 9] the lack of hemovigilance in current blood transfusion services is a major gap in the protection of transfused patients in Egypt.

Objective 3.4.1

Set national clinical guidelines for blood transfusion criteria.

Actions to Be Initiated:

- Task an expert advisory committee to review existing guidelines by blood product, disease process, and/or complications and diagnostics to determine need for blood products.
- Advocate for establishment of Hospital Transfusion Committees (HTCs) in all hospitals.
- Disseminate guidelines to clinicians and staff working in blood banks (e.g., nurses and technicians).

(6) Carson, J.L., et al., Red blood cell transfusion: a clinical practice guideline from the AABB*. Ann Intern Med, 2012. 157(1): p. 49-58.

(7) WHO. Developing a National Policy and Guidelines on the Clinical Use of Blood. 2001; Available from: http://www.who.int/bloodsafety/clinical_use/en_bct_bhs_01_3.pdf.

(8) Robillard, P., K.I. Nawej, and K. Jochem, The Quebec hemovigilance system: description and results from the first two years. Transfus Apher Sci, 2004. 31(2): p. 111-22.

(9) Andreu, G., et al., Hemovigilance network in France: organization and analysis of immediate transfusion incident reports from 1994 to 1998. Transfusion, 2002. 42(10): p. 1356-64.

- Advocate for using blood substitutes when applicable to decrease the burden on blood utilization.

Objective 3.4.2

Engage and educate clinicians who order or administer blood products.

Actions to Be Initiated:

- Conduct an inventory of the ordering pattern of clinicians, including who is ordering blood and differences in ordering practices; consider maximum surgical blood ordering schedules (MSBOS) and cross-match/transfusion (C/T) ratio.
- Build capacity of blood-bank staff (e.g., nurses, technicians, and physicians) by offering education on appropriate clinical use of blood products and good laboratory practices (GLP).
- Formulate hospital transfusion committees within each facility performing transfusions; committees will meet regularly to monitor transfusion practices.
- Implement appropriate clinical use of blood guidelines.
- Ensure universal availability of blood alternatives (i.e., colloids and crystalloids).

Objective 3.4.3

Measure patient outcomes following transfusion.

Actions to Be Initiated:

- Develop an active surveillance system for detection and investigation of adverse reactions (hemovigilance).
- Monitor outcomes of patients receiving blood products.

GOAL 3.5
Develop IT solutions to support safer blood collection and transfusion and to facilitate surveillance, management, and research.

IT is a vital component of every stage of blood collection, processing, and delivery. IT systems should be instituted in blood banks for surveillance and research purposes, including monitoring trends of infections among blood donors and conducting tailored research projects. Transfusion research projects are essential to understanding a country's blood system and tailoring guidelines appropriately.[10] Currently, blood banks in Egypt are either lacking an IT system or have different systems in place, making the sharing of data problematic. Standardization of these IT systems would not only help ensure safe blood collection and transfusion, but would facilitate surveillance and research.

(10) Edgren, G. and H. Hjalgrim, Epidemiological considerations for the use of databases in transfusion research: a Scandinavian perspective. Curr Opin Hematol, 2010. 17(6): p. 596-601.

Objective 3.5.1

Establish an integrated data warehouse to facilitate surveillance and research.

Actions to Be Initiated:

- Obtain data from all stakeholders.
- Obtain approval from the higher authorities for each group of blood banks (e.g., NBTS, governmental, HIOs, and universities) to establish a nationally integrated data warehouse and establish security rules.
- Organize a workshop for all IT representatives from different sectors.
- Nominate a contact person responsible for integrating data and IT support with needed resources.
- Collect information about currently available blood-bank data (and the data format) in order to resolve data inconsistencies.
- Determine the variables to be collected (e.g., the U.S. Retrovirus Epidemiology in Donors Study [REDS]) and the best format to be used; migrate and reformat data.[11]
- Build capabilities for data analysis.
- Establish a system for dissemination of reports and analyses to research units and stakeholders.

Objective 3.5.2

Develop a national operational IT system for management of blood transfusion services.

Actions to Be Initiated:

- Assess the available hardware infrastructure and software packages available, including networks and communication services.
- Design a new IT system that fulfills user requirements.
- Set cooperation rules between data users (e.g., MOHP, research institutes, and universities).
- Implement the system into centers conducting transfusion services.
- Establish a system for blood unit identification (e.g., ISBT 128 coding and labeling).

(11) Kleinman, S., et al., The National Heart, Lung, and Blood Institute retrovirus epidemiology donor studies (Retrovirus Epidemiology Donor Study and Retrovirus Epidemiology Donor Study-II): twenty years of research to advance blood product safety and availability. Transfus Med Rev, 2012. 26(4): p. 281-304, 304 e1-2.

4. Eliminating Transmission of Vaccine-Preventable Viral Hepatitis

GOALS
4.1 Achieve universal hepatitis B vaccination for populations at high risk for infection or complications.
4.2 Ensure all newborns receive hepatitis B birth dose as soon as possible following birth (<24 hours).
4.3 Assess need for hepatitis A vaccine and implement if needed.

Safe and effective vaccines are available to prevent HAV and HBV, both of which contribute substantially to the burden of viral hepatitis in Egypt. Although hepatitis A vaccine is not widely available in Egypt, hepatitis B vaccination was integrated into Egypt's immunization schedule in late 1992 in response to WHO's recommendation that all countries include hepatitis B vaccine in childhood expanded programme of immunization (EPI) schedules. Three-dose coverage of hepatitis B vaccine among 1-year-olds in Egypt now reaches 97%.[1,2]

GOAL 4.1
Achieve universal hepatitis B vaccination for populations at high risk for infection or complications.

HBV is an easily transmitted blood-borne pathogen, more contagious than HCV or HIV. Despite the introduction of hepatitis B vaccine into Egypt's EPI, HBV continues to be transmitted among unvaccinated older children and adults. Studies of patients with acute HBV in Egypt indicate that more than 90% of patients were born before the vaccine was incorporated into Egypt's childhood vaccination schedule.[3] Certain adults, particularly HCWs, are at increased risk for HBV infection; unvaccinated HCWs who sustain needlestick exposures to HBsAg-positive blood have a 6-30% risk of infection depending on the absence or presence of hepatitis B e-antigen.[4] Although universal hepatitis B vaccination for adults is not recommended, targeted vaccination of some high-risk groups (e.g., HCWs) may be a cost-effective prevention strategy; other countries (e.g., the United States) recommend hepatitis B vaccination for clinical and nonclinical health center staff.[5] Currently, vaccination coverage of HCWs in Egypt is estimated at about 30-40%, with significant variability among different healthcare occupations.[4,5] Beyond HCWs, other persons at risk for HBV infection include those with an HBV-infected household member or sex partner, those with non-healthcare-associated occupational exposure to blood or body fluids, persons who are incarcerated, and those at risk for complications from HBV (e.g., hemodialysis patients and persons who are immunocompromised).

(1) El-Raziky, M.S., et al., Patterns of hepatitis B infection in Egyptian children in the era of obligatory hepatitis B vaccination. Arab J Gastroenterol, 2012. 13(1): p. 1-3.

(2) Organization, W.H. Country data: Hepatitis B (HepB3) immunization coverage among 1-year-olds (%). 2012 [Cited 2012 December 5, 2012]; Available from: http://apps.who.int/gho/data/?vid=80100#.

(3) Talaat, M., et al., Case-control study to evaluate risk factors for acute hepatitis B virus infection in Egypt. East Mediterr Health J, 2010. 16(1): p. 4-9.

(4) Talaat, M., et al., Occupational exposure to needlestick injuries and hepatitis B vaccination coverage among health care workers in Egypt. Am J Infect Control, 2003. 31(8): p. 469-74.

(5) Hanafi, M.I., et al., Needlestick injuries among health care workers of University of Alexandria Hospitals. East Mediterr Health J, 2011. 17(1): p. 26-35.

Objective 4.1.1

Ensure all HCWs are vaccinated against hepatitis B.

Actions to Be Initiated:

- Create a policy paper describing the current status and gaps in hepatitis B vaccination among HCWs and projected resources needed for vaccination.
- Promote legislation requiring completion and documentation of hepatitis B vaccination for all HCWs as a condition for licensing.
- Establish a system to ensure that HCWs have been vaccinated; consider using MOHP database as a prototype and expanding to other sectors as appropriate.
- Develop policies requiring vaccination documentation of students in faculties of medicine, dentistry, pharmacy, nursing, and physiotherapy institutes as a prerequisite for admission to studies.
- Engage the National Immunization Technical Advisory Group (NITAG) to develop recommendations for vaccination of all HCWs.

Objective 4.1.2

Ensure hepatitis B vaccination for persons with chronic medical conditions that place them at high risk for HBV infection or related complications.

Actions to Be Initiated:

- Define persons at high-risk for hepatitis B infection (e.g., hemodialysis patients, persons who are immunocompromised, and those with chronic liver disease).
- Engage NITAG to develop recommendations for hepatitis B vaccination of persons in identified high-risk populations.
- Establish/update standard vaccination protocols to include awareness, education, testing, and vaccination, and consider expanding the MOHP protocol.
- Identify and engage appropriate stakeholders to assist in vaccination of persons in identified high-risk groups.

Objective 4.1.3

Ensure hepatitis B vaccination for persons at high risk for infection from non-medical sources (e.g., commercial sex workers, family members of persons infected with HBV, street children, PWID, incarcerated persons, men who have sex with men [MSM], and patients of sexually transmitted infection [STI] clinics).

Actions to Be Initiated:

- Create a policy paper describing the current status and gaps in hepatitis B vaccination among persons in non-medical high-risk groups and resources needed for vaccination.
- Conduct media campaigns to reach high-risk populations.

- Engage appropriate NGOs and social entrepreneurs providing services to high-risk groups.
- Promote coordination between MOHP programs (viral hepatitis unit, EPI, and HIV).
- Collaborate with NGOs to vaccinate street children, providing NGOs with informational and educational materials.
- Train counselors on how to advise on prevention, screening, and vaccination.
- Conduct research and surveillance to document and identify high risk populations.

GOAL 4.2
Ensure all newborns receive hepatitis B birth dose as soon as possible following birth (<24 hours).

Mother-to-child transmission of HBV takes place primarily at the time of birth, with 10-90% of neonates born to HBsAg-positive mothers becoming infected with hepatitis B. The probability of transmission increases substantially (up to 90%) if the mother is positive for both HBsAg and HBeAg, indicating active viral replication. To prevent perinatal and early childhood infection, WHO recommends that "all infants should receive their first dose of hepatitis B vaccine as soon as possible after birth, preferably within 24 hours," even in countries where the virus is not endemic.[6] Birth dose is effective in preventing 85% of HBV transmission from an infected mother to her child. Despite these recommendations, administration of a birth dose of hepatitis B vaccine is not part of Egypt's routine EPI program. Routine provision of hepatitis B vaccination at birth is feasible in Egypt; a relatively large proportion of births in Egypt occur within health-care facilities under the supervision of workers capable of administering the vaccine. For neonates born at home, community health workers could be trained to administer a birth dose of vaccine immediately following birth. Birth dose delivery of hepatitis B vaccine provides an invaluable opportunity to link immunization delivery systems with maternal healthcare systems; further, it may increase women's access to maternity care from skilled birth attendants.

Objective 4.2.1

Ensure that all hospitals and birthing centers administer a birth dose of hepatitis B vaccine to all newborns as soon as possible following birth (<24 hours).

Actions to Be Initiated:

- Ensure political commitment through development of a policy paper outlining the importance of the birth dose of hepatitis B vaccine and the resources (human and financial) required for implementation.
- Conduct a situation analysis of maternal and neonatal health services.
- Develop a National Implementation Plan.
- Conduct joint planning with maternal health services staff and EPI (and other appropriate parties) to develop SOPs for the introduction of a birth dose of hepatitis B.

(6) Hepatitis B vaccines. Wkly Epidemiol Rec, 2009. 84(40): p. 405-19.

- Update antenatal care protocols and guidelines.
- Include hepatitis vaccination in the essential care package for neonates, and make necessary updates in the infant-care protocol.
- Train all relevant partners on SOPs.
- Establish a system to record and report administration of a birth dose of vaccine, to include modification of the immunization records.
- Ensure birth dose monitoring by the EPI program.
- Through a national media campaign or other education initiatives, inform, educate, and communicate the importance of a birth dose of hepatitis B vaccine to parents and to healthcare providers in both public and private sectors.
- Evaluate the birth dose program on regular basis and modify as needed.

Objective 4.2.2

Ensure that all newborns being delivered outside hospitals receive a birth dose of hepatitis B vaccine within 24 hours of delivery.

Actions to Be Initiated:

- Ensure political commitment through development of a policy paper outlining the importance of birth dose and the resources (human and financial) required for implementation.
- Determine how vaccine will be supplied to skilled professionals attending home births.
- Train skilled attendants on proper administration of the hepatitis B vaccine.
- Educate the community on the importance of timely notification of births.
- Engage community health workers to ensure timely administration of a birth dose.
- Establish a system to record and report administration of a birth dose of hepatitis B vaccine, to include modification of immunization records.
- Coordinate monitoring of birth dose administration through the EPI program.
- Evaluate the birth dose program on a regular basis and modify as needed.

GOAL 4.3
Assess need for hepatitis A vaccine and implement if needed.

HAV is endemic in Egypt, representing a major cause of acute viral hepatitis. Of all acute viral hepatitis cases, 40-50% can be attributed to HAV.[7, 8] Major routes of HAV transmission in Egypt may include person-to-person, contaminated food, infected food handlers, and unsafe

(7) Kamal, S.M., et al., Viral hepatitis a to e in South mediterranean countries. Mediterr J Hematol Infect Dis, 2010. 2(1): p. e2010001.

(8) Talaat, M., et al., Sentinel surveillance for patients with acute hepatitis in Egypt, 2001-04. East Mediterr Health J, 2010. 16(2): p. 134-40.

drinking water. People living in rural areas are at higher risk for hepatitis A infection compared with the urban population because they are more likely to experience poor sanitation and lack a reliable, clean source of water.[7]

Generally, in developing countries with poor water sanitation and hygiene, HAV is acquired early in life, with most infections occurring between 5-15 years of age. In the past 2 decades, sanitation and hygiene have been greatly improved in Egypt, and access to clean drinking water has been extended to a growing percentage of the population. Because of these improvements, children are less likely to be exposed to HAV at a young age, and the mean age at infection is increasing. This epidemiologic shift has caused a decline in herd immunity (especially in large cities and among high social classes); because the severity of clinical disease increases with age of infection, reductions in herd immunity can result paradoxically in an increase in and severity of cases.[8] Although fulminant hepatitis due to HAV has been rarely reported in Egypt, recently, fulminant HAV cases requiring liver transplantation have been reported in adult patients who acquired the infection at an older age.[7] Currently, immunization for HAV is not included in Egypt's EPI schedule. However, due to the shifting epidemiology of HAV in Egypt, surveillance data are needed to determine whether hepatitis A vaccine strategies should be considered for Egypt.

Objective 4.3.1

Determine if routine vaccination against hepatitis A is needed in Egypt.

Actions to Be Initiated:

- Identify gaps in HAV surveillance data.
- MOHP VIRAL HEPATITIS unit will conduct surveillance to determine the burden of HAV in Egypt.
- Conduct an extensive review of available data (literature review/partner outreach) to help assess the burden of HAV in Egypt (i.e., estimate prevalence and incidence, identify current risk factors and high-risk groups, and estimate morbidity and mortality).
- Conduct cost-effectiveness studies focused on implementation of HAV vaccine.

Objective 4.3.2

Develop an implementation plan, if needed.

Actions to Be Initiated:

- Create a policy paper reflecting the need for HAV vaccine and the resources (financial and human) needed to implement into vaccination schedule.
- Create a National Implementation Plan for HAV vaccination, if indicated.
- Design a phase implementation plan based on data from cost-effectiveness studies and surveillance data (high-risk groups).

5. Role of Care & Treatment in Reducing Transmission of Viral Hepatitis

GOALS
5.1 Provide safe, effective, and affordable treatment to patients with chronic hepatitis B and C.
5.2 Improve care and treatment of patients with advanced forms of liver diseases and those with past treatment failures.
5.3 Increase political commitment to support global pricing for viral hepatitis drugs and increase access to new drugs in Egypt and worldwide.

Providing care and treatment to persons infected with viral hepatitis can greatly improve health outcomes and prevent transmission of infection to others. Since 2006, Egypt has made great progress in the management of viral hepatitis through the establishment of a National Committee for the Control of Viral Hepatitis (NCCVH) with 26 affiliated national viral hepatitis treatment centers (NTCs) distributed across the country. Through these centers, a Viral Hepatitis National Treatment Program (NTP) was launched in 2007. The initial objective of this governmental program was to provide antiviral medications at a reduced cost or even free of charge for individuals not covered by an HIO. The capacity of the NTC was expanded to include provision of integrated care for individuals with viral hepatitis, including screening for hepatocellular carcinoma, and to act as a nuclei for Egypt's network of liver transplantation centers. In some centers, free and subsidized HBV treatment is also provided. Moreover, insured patients (i.e., between 45-50% of the population in Egypt) can obtain free HCV treatment in 26 centers related to HIO. Treatment for viral hepatitis may also be obtained in private facilities, but at a very high cost (six-fold greater than the NTC price).[1] Additionally, Egypt has established a hotline that provides patients with information about viral hepatitis, including treatment options. In collaboration with NGOs and pharmaceutical companies, Egypt has also provided treatment to 700 children chronically infected with viral hepatitis.

The Egyptian NTP is one of the largest treatment programs instituted by a resource-limited country. The estimated cost of this program to the Egyptian government is $80 million annually, which covers 40% of the total costs; the remaining 60% is paid by insurance companies (50%) and patients (10%). Thanks to market competition and availability of a local biosimilar of pegylated interferon (Reiferon Retard®, Minapharm©), the price of a standard 48-week course of HCV treatment has been progressively driven down through negotiations with the pharmaceutical manufacturers, decreasing more than sixfold in the last 7 years. Currently, one full course of HCV treatment costs the Egyptian government <$2,000.[2]

Despite this successful treatment program, only a small fraction of the total number of patients chronically infected with HBV and/or HCV are treated annually. It is therefore crucial to evaluate the program, identify patients most in need of treatment, optimize resource

(1) Rafeh, N., Julie Williams, and Nagwan Hassan, Egypt Household Health Expenditure and Utilization Survey 2010. Bethesda, MD: Health Systems 20/20 project, Abt Associates Inc., 2011.

(2) Ford, N., et al., Expanding access to treatment for hepatitis C in resource-limited settings: lessons from HIV/AIDS. Clin Infect Dis, 2012. 54(10): p. 1465-72.

utilization, and reinforce aspects of the program that will facilitate provision of treatment to an increased number of infected patients.

GOAL 5.1

Provide safe, effective, and affordable treatment to patients with chronic hepatitis B and C.

Standard therapy for HCV genotype 4 (which accounts for >90% of infections in Egypt) consists of 48 weeks of pegylated interferon and ribavirin. From 2007 through 2014, more than 360,000 HCV patients were treated in NTC and HIO centers; approximately half achieved virologic cure.[3] Although these benchmarks represent a remarkable achievement, the treatment program would greatly benefit from evaluation and optimization using data from recent studies. For example, treatment guidelines should be modified to reflect the recent discovery that certain genetic and serological markers (e.g., IP-10, IL-28B) may be reliable predictors of treatment response.[4,5] In addition, recent cost-effectiveness studies suggest that shifting treatment to patients with more advanced forms of disease (i.e., established cirrhosis or stage 4 fibrosis, which was added to the national treatment guidelines in 2012) would be more cost-effective than treating patients in earlier disease stages. In addition, new and highly-effective oral viral hepatitis therapies will soon be available, even in resource-limited countries like Egypt.[6]

In sharp contrast to HCV, subsidized HBV treatment is only delivered in a few NTCs, partly because HBV treatment is usually life-long and requires regular follow-up to monitor virologic breakthrough and drug resistance.[7] Emphasis has instead been directed towards providing HBV vaccination to infants to decrease the number of new infections. Although infant vaccination is an essential component of the national strategy to prevent HBV, treating adolescents and adults who are already infected can prevent and reverse their disease progression. To improve care and treatment of HBV-infected patients and optimize resource utilization, Egypt's HBV treatment program must be scaled-up and MOHP guidelines have been updated to reflect changes in drug availability and pricing that have occurred since new drugs have become available. Such an effort requires regular evidence-based modifications to the current HBV treatment program.

Objective 5.1.1

Optimize treatment management for chronic hepatitis B and C patients in existing treatment facilities in a cost-effective manner.

Actions to Be Initiated:

- Conduct an independent audit of treatment centers to ensure efficiency.

(3) Centers for Disease Control and Prevention, Progress toward prevention and control of hepatitis C virus infection--Egypt, 2001-2012. MMWR Morb Mortal Wkly Rep, 2012. 61(29): p. 545-9

(4) Khattab, M.A., et al., Management of hepatitis C virus genotype 4: recommendations of an international expert panel. Journal of hepatology, 2011. 54(6): p. 1250-1262.

(5) Asselah, T., et al., IL28B polymorphism is associated with treatment response in patients with genotype 4 chronic hepatitis C. J Hepatol, 2012. 56(3): p. 527-32.

(6) Esmat, G., et al., The future for the treatment of genotype 4 chronic hepatitis C. Liver Int, 2012. 32 Suppl 1: p. 146-50.

(7) Mutimer, D.J. and A. Lok, Management of HBV- and HCV-induced end stage liver disease. Gut, 2012. 61 Suppl 1: p. i59-67.

- Revise hepatitis B and C national treatment guidelines, taking into account the latest research (e.g., drug efficacy trials and cost-effectiveness studies); ensure that guidelines address prevention measures for contacts and family members (e.g. screening for HBV and HCV if appropriate).
- Revise MOHP and HIO regulations to ensure consistency with updated and evidence-based guidelines.
- Disseminate national treatment guidelines to the private sector.
- Increase the number of treatment facilities providing subsidized HBV treatment.
- Develop evidence-based treatment guidelines for HBV/HCV co-infected patients.
- Organize regular follow-up visits for patients not eligible for immediate treatment.
- Identify the minimum panel of investigations required for diagnosis and follow-up of infected patients according to revised guidelines (e.g., Fib4, Fibroscan, ultrasound machine, HCV ELISA, and HCV RNA).
- Standardize drug procurement, storage, and distribution practices.
- Establish electronic medical records at each treatment facility and link records to centralized database to improve patient follow-up.
- Establish a partnership with virology laboratories to transfer PCR data to treatment centers (e.g., PCR results during follow-up and at W72 for HCV patients).
- Establish mechanisms to provide subsidized care equitably to the population.
- Establish quality performance indicators for diagnosis and linkage to care.
- Develop evidence-based treatment guidelines for HIV co-infected patients.
- Establish a priority (waiting) list for individuals needing treatment.

Objective 5.1.2

Increase capacity for treatment of chronic hepatitis B and C patients at the national level.

Actions to Be Initiated:

- Expand subsidized treatment facilities (i.e., NTC and HIO) to underserved areas.
- Build capacity of local healthcare staff (e.g., doctors and nurses) to implement revised guidelines.
- Create distance tools for clinicians to obtain advice on patient management from senior hepatologists; conduct pilot testing of distance tools to include monitoring and evaluation.

Objective 5.1.3

Improve counselling and referrals for patients and their families.

Actions to Be Initiated:

- Identify catchment areas (e.g., CPHL, blood banks, NTC, and HIO centers) for counselling and referral.
- Work with multi-disciplinary teams to build culturally appropriate messages and create counseling tools adapted for identified catchment areas.
- Improve counseling for patients receiving treatment to increase compliance and avoid re-infection.
- Train counselors.
- Promote testing among family members of infected patients.
- Refer HBV- and HCV-positive family members for counseling and assessment for treatment and/or vaccination eligibility.

- Establish patient advocacy groups.

GOAL 5.2
Improve care and treatment of patients with advanced forms of liver diseases and those with past treatment failures.

End-stage liver disease represents a major source of morbidity and mortality worldwide. In 2002, cirrhosis and primary liver cancer caused an estimated 783,000 and 619,000 deaths, respectively, with HBV and HCV infections accounting for the majority of this burden.[8] In Egypt, the incidence of HCC is increasing and is now the second most frequent cause of cancer and cancer-related mortality among men. Hospital based studies in Egypt have reported an increase in the proportion of all cancers that are liver-related, from 4.0% in 1993 to 7.3% in 2007.[4] Treatment options for end-stage liver disease are limited. Although liver transplantation can improve outcomes, limited resources, including low donor availability, and high cost of transplantation limit feasibility in Egypt.

Patients with past treatment failure represent another difficult-to-treat population. From 2007-2014, approximately 50% (>180,000) of HCV patients receiving treatment through NTC and HIO centers experienced treatment failure. Upstream efforts, such as improving patient compliance, should be made to prevent HBV and HCV treatment failure. In addition, newly developed antivirals have much higher rates of treatment success, and new highly-effective oral HCV therapies will be available in Egypt soon.

Objective 5.2.1

Provide care for patients with advanced forms of disease (e.g., liver cirrhosis and HCC).

Actions to Be Initiated:

- Consider including F4 compensated cirrhotic patients (Child-Pugh Class A) in the national treatment guidelines.

(8) Perz, J.F., et al., The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. Journal of hepatology, 2006. 45(4): p. 529-538.

- Develop palliative care options and consider subsidizing such care for patients with advanced forms of disease who are not eligible for treatment.
- Revise treatment guidelines for HCV patients who have received liver transplants, taking into account the latest research results.

Objective 5.2.2

Assess the possibility of increasing access to liver transplant.

Actions to Be Initiated:

- Emphasize the need for a well-organized liver transplant registry.
- Conduct a review of the current efficiency and cost of the liver transplant system in Egypt.
- Evaluate the need for subsidizing liver transplantation, taking into account other competing priorities in Egypt.
- Increase the number of facilities able to perform safe liver transplants.

Objective 5.2.3

Increase access to treatment for patients with previous treatment failure.

Actions to Be Initiated:

- Consider including in the national treatment guidelines those persons with advanced fibrosis who have experienced previous treatment failure.
- Advocate to increase clinical trials for HCV genotype 4 patients with past treatment failures.

GOAL 5.3
Increase political commitment to support global pricing for viral hepatitis drugs and increase access to new drugs in Egypt and worldwide.

Ideally, every Egyptian patient with viral hepatitis infection should have access to the most effective antiviral drugs. In the last few years, market competition and the availability of a locally produced pegylated interferon have resulted in dramatic reductions in the cost of HCV treatment (Peg-IFN and ribavirin). Although HCV therapy has been made available to the Egyptian government for <$2,000 standard treatment course, the situation is much different in other countries, where HCV treatment can exceed $15,000.[3] Global efforts should be undertaken to reduce pricing of these drugs, expanding access to resource-limited countries. Moreover, new highly effective antivirals (e.g., the direct-acting antiviral [DAA] agents) will be available for persons with HCV genotype 4 in the coming years. The price of these new therapies will likely be cost-prohibitive initially, and access may be limited in resource constrained settings. A global effort involving advocates from national and international organizations is needed to encourage generic production of these new drugs by established companies (e.g., Cipla in India), set global pricing, and increase access in Egypt and worldwide.

Clinical trials of oral therapies are needed among patients with HCV genotype 4 to evaluate treatment response specifically for Egypt's infected population, especially for those who are treatment naïve or non-responders. Involvement in clinical trials increases access to new, highly effective antiviral therapies. As many resource-limited countries have experienced with HIV, those that become involved in clinical trials are the first to gain access to new drugs. Initiating partnerships with pharmaceutical companies may increase the number of clinical trials performed in Egypt and indirectly increase access to new drugs for Egyptian patients.

Objective 5.3.1

Advocate for global pricing of HCV treatment.

Actions to Be Initiated:

- Encourage WHO to advocate for lower drug prices.
- Create an Egyptian taskforce comprised of diverse sectors (e.g., MOHP, NCCVH, pharmaceutical companies, and civil society) to negotiate drug prices and drive market competition in Egypt.

Objective 5.3.2

Initiate partnerships with pharmaceutical companies to increase access to treatment in Egypt.

Actions to Be Initiated:

- Prepare centers to conduct clinical trials on new drugs for HBV and HCV following international standards.
- Engage in discussions to organize phase 2 to phase 4 clinical trials on genotype 4 patients in Egypt, especially non-responders and patients with past treatment failures.
- Initiate discussions with pharmaceutical companies to introduce HCV drugs, organize technology transfer, and conduct quality control assessments between pharmaceutical companies and generic manufacturers (e.g., Gilead's Access program).
- Initiate discussions with international pharmaceutical companies regarding drug pricing adapted to the country income.
- Garner political support for HBV and HCV treatment programs.
- Involve pharmaceutical companies in prevention campaigns.

Objective 5.3.3

Increase local capacity to produce generic drugs and biosimilar therapies.

Actions to Be Initiated:

- Identify local companies able to produce generics and biosimilar therapies.
- Conduct an independent audit of these companies to evaluate safety, efficacy, production, and capacity.

- Support these companies to increase their production capacities and their skills (e.g., funding, collaboration with pharmaceutical companies for transfer technology, and market share).

Objective 5.3.4

Increase national and international support for viral hepatitis treatment programs in Egypt.

Actions to Be Initiated:

- Link care and treatment activities to prevention activities.
- Develop methodology for identifying Egyptian and international donors with interest in supporting the NTP.
- Advocate to the Global Fund and UNAID to include HBV and HCV patients in their programs.
- Collaborate with national and international civil society representatives (e.g., patients associations and NGOs) to improve access to treatment.
- Educate the media regarding the disease burden in Egypt and the need for treatment to prevent morbidity and mortality.

Objective 5.3.5

Increase political commitment to support research projects and clinical trials in Egypt.

Actions to Be Initiated:

- Develop a research agenda around care and treatment.
- Increase the number of high quality research studies on viral hepatitis conducted in Egypt using local (Science and Technology Development Fund [STDF]) and international funding. Studies could include cost-effectiveness studies, modeling, and pharmacovigilance studies, among others.
- Facilitate the transfer of samples outside of Egypt for research purposes.

6. Educating Providers and Communities to Reduce Transmission of Viral Hepatitis

GOALS
6.1 Increase policymakers' commitment to supporting the policy change necessary to prevent viral hepatitis transmission.
6.2 Educate healthcare workers to prevent transmission of viral hepatitis in Egypt.
6.3 Increase public awareness of viral hepatitis prevention.
6.4 Promote safe injection practices in the community.

Since 2006, great progress has been made in improving access to care and treatment for viral hepatitis patients in Egypt. Nevertheless, because viral hepatitis therapies can be costly and difficult to obtain, many infected persons do not receive these treatments. Every year, there are more new chronic infections (approximately 120,000/year) than patients cured by treatment (approximately 20,000/year), requiring that public health initiatives remain focused on preventing transmission of new viral hepatitis infections.[1]

Better control of viral hepatitis transmission necessitates targeting specific groups, including persons at increased risk for HBV/HCV infection and those who perpetuate transmission of viral hepatitis (e.g., HCWs, HBV/HCV infected patients and their family members, barbers, informal injection providers, dentists, and pharmacists). Because many of these persons lack awareness of the dire viral hepatitis situation in Egypt and are unfamiliar with the modes of transmission, they unknowingly transmit infection to their loved ones, patients, and clients. Knowledge of risk factors and disease processes can be empowering, motivating behavior change and prevention of viral hepatitis transmission in healthcare settings and in the community. A well-informed strategic communication program is key to reducing the burden of these diseases.

Within recent years, IEC efforts have been made to increase awareness of viral hepatitis in Egypt, including World Hepatitis Day celebrations, vaccination campaigns at universities, and establishment of a hotline providing information on viral hepatitis. Although numerous national and international stakeholders (e.g., MOHP, NCCVH, Universities, NGOs, WHO, and USAID) participated in these activities, they were not conducted as part of a cohesive, comprehensive strategy. Reaching groups most affected by viral hepatitis and ensuring sustainable behavior change necessitates a more coordinated, evidence-based approach to communicating prevention messages. As with all public health activities, communication concerning viral hepatitis prevention must be consistent, culturally appropriate and designed to decrease stigmatization of infected patients.

GOAL 6.1
Increase policymakers' commitment to supporting the policy change necessary to prevent viral hepatitis transmission.

Changes in policy are required to efficiently prevent transmission of viral hepatitis in healthcare settings and the community. Such policy changes are possible only through significant political will at high governmental levels. Because any change in viral hepatitis prevention policy will have considerable implications for field workers (who in large part are cognizant of the most pressing

(1) Centers for Disease Control and Prevention, Progress toward prevention and control of hepatitis C virus infection--Egypt, 2001-2012. MMWR Morb Mortal Wkly Rep, 2012. 61(29): p. 545-9.

prevention needs), all knowledgeable stakeholders should be involved in policy discussions to ensure informed decision-making, appropriate prioritization of the most urgent issues, and cohesiveness. Special events, like World Hepatitis Day, should serve as an opportunity to bring all stakeholders together and disseminate consistent messages to the community.

Objective 6.1.1

Advocate for support of policy changes as outlined in the Viral Hepatitis Plan of Action.

Actions to Be Initiated:

- Activation of High Health Council (includes all ministries).
- Include all stakeholders in policy discussions.
- Hold annual workshops to provide professional associations and NGOs with information about viral hepatitis epidemiology.
- Celebrate World Hepatitis Day (July 28).
- Engage professional associations and societies to build support for policy to reduce transmission of viral hepatitis.
- Launch a national campaign for the prevention of viral hepatitis in Egypt (could coincide with World Hepatitis Day).

GOAL 6.2
Educate healthcare workers to prevent transmission of viral hepatitis in Egypt.

In Egypt, most ongoing viral hepatitis transmission occurs within healthcare settings as a result of inadequate infection control, including reuse of syringes and other medical equipment that is not properly sterilized or is intended for one-time use.[2] Improved compliance with IC protocols by HCWs is critical to reducing healthcare-associated infections; understanding existing healthcare-worker knowledge, beliefs, and practices through surveys and focus groups is an important first step to designing effective interventions. Many studies have demonstrated patient-to-patient and HCW-associated transmission of viral hepatitis, but very few studies have surveyed HCWs to understand the determinants of their behavior (e.g., lack of knowledge, proper equipment, time, and willingness to comply with infection-control protocols). Legislative actions are crucial to this endeavor; however, before penalties for noncompliance are instituted, HCWs should be educated about the importance of infection-control compliance.

Objective 6.2.1

Determine HCW's existing beliefs, knowledge, and practices regarding viral hepatitis.

Actions to Be Initiated:

- Conduct extensive review of available data (literature review/partner outreach).
- Identify partners qualified to conduct and support surveys.
- Conduct studies (knowledge, attitude and practices (KAP) studies, focus groups) to help fill any gaps in information.

(2) Talaat, M., et al., Evolution of infection control in Egypt: achievements and challenges. Am J Infect Control, 2006. 34(4): p. 193-200.

Objective 6.2.2

Develop continuous medical education (CME) focused on viral hepatitis infection control.

Actions to Be Initiated:

- Determine how to link training to licensing.
- Meet with relevant professional associations (e.g., dentistry, nursing, and medical) to garner support for CME development.
- Identify any existing infection-control curricula, review for completeness, and collaborate with partners across Egypt to ensure consistency.
- Identify partners capable of developing an electronic and in-person infection-control curriculum for healthcare professionals and those capable of building a database to track completion of learning activities.
- Pilot the curriculum before widespread distribution.
- Expand training campaigns through a "train the trainer" program or volunteer program in facilities that lack internet access.

Objective 6.2.3

Create demand among HCWs for hepatitis B vaccine and infection control practices.

Actions to Be Initiated:

- Launch a proactive education campaign on personal risk of infection and subsequent risk of infecting family members.
- Empower medical and nursing students to observe best practices identified in model hospitals, and to act as patient advocates.

GOAL 6.3
Increase public awareness of viral hepatitis prevention.

Increasing awareness of the viral hepatitis epidemic in Egypt and ways to prevent infection is expected to empower the community and create demand for safe medical practices. People must be educated about ways to avoid becoming infected and prevent transmission to others and the importance of testing and treatment. Ensuring effective and relevant messages and approaches requires identification of target audiences and engagement of the media, social entrepreneurs, and social networks, each of whom are influential in changing social norms. Consistency in messaging is critical, along with ensuring that messages remain accurate as they are disseminated throughout the community.

As more people become aware of viral hepatitis as a health threat, the demand for testing will increase. Currently, persons tested for viral hepatitis in Egypt are not routinely provided with counselling (e.g., how to avoid transmitting infection to others and the importance of testing and treatment), limiting the effectiveness of this important public health measure and compromising health outcomes. Given limited resources, initial counselling efforts in Egypt should be directed to the immediate families of persons who have been diagnosed with viral hepatitis and have entered a liver treatment facility; such counselling will help eliminate on-going transmission of these infections.

A comprehensive, intelligent and well-designed education program can raise awareness of viral hepatitis as a health concern and knowledge regarding the benefits of prevention and care. Further, efforts to raise community awareness can create demand for high quality and safe care, decrease stigmatization and fear, and encourage populations to seek and accept vaccination, testing, care, and treatment.

Objective 6.3.1

Develop scientific materials and messages.

Actions to Be Initiated:

- Build a team with representation from diverse disciplines (e.g., epidemiologists, hepatitis specialists, and communications experts) to review existing materials on hepatitis; revise as needed; and develop scientific materials and messages.

Objective 6.3.2

Determine the impact of stigma associated with viral hepatitis infection.

Actions to Be Initiated:

- Conduct literature review and studies to better understand the magnitude of stigma against people with viral hepatitis.

Objective 6.3.3

Increase awareness among school-aged children (6-17 years).

Actions to Be Initiated:

- In partnership with the Ministry of Education, survey school-age children and teachers to obtain a baseline of viral hepatitis knowledge.
- Review the existing school-based infectious disease curriculum and partner with the Ministry of Education to update materials to include viral hepatitis.
- Provide the Ministry of Education with viral hepatitis prevention tools to facilitate development of effective methods for working with students on a school-by-school basis.

Objective 6.3.4

Empower the youth (ages 15-25) to raise awareness as advocates for viral hepatitis prevention.

Actions to Be Initiated:

- Conduct focus groups of youth and enlist them to help design materials and identify venues for delivering messages.
- Review studies looking at youth awareness of viral hepatitis.
- Identify active and relevant youth groups that have the capacity to act as advocates.
- Work with identified groups to synergize and move forward with common messages.

Objective 6.3.5

Increase awareness of viral hepatitis prevention among persons >25 years of age.

Actions to Be Initiated:

- Work with NGOs to identify social entrepreneurs to disseminate viral hepatitis messages.
- Work with religious leaders to reach target groups.
- Work with community leaders at the local level (Omda).

Objective 6.3.6

Improve counseling services for patients identified with hepatitis, and their families, in order to reduce risk of infection and re-infection.

Actions to Be Initiated:

- Identify catchment areas (e.g., visa applicants, blood banks, liver institutes).
- Coordinate and train viral hepatitis counselors.
- Work with a multidisciplinary team to build messages for counselors.

Objective 6.3.7

Develop partnerships based on social responsibility with media organizations (traditional and social).

Actions to Be Initiated:

- Identify partners (e.g., NGOs, MOHP, media organizations).
- Involve media in all stages of viral hepatitis planning and implementation.

GOAL 6.4
Promote safe injection practices in the community.

A major concern in Egypt is unsafe medical injections, either through reuse of disposable syringes or needles. Injections are mistakenly believed to be more effective than oral medications without posing additional risk;[3] consequently, the frequency of therapeutic injections is very high in Egypt compared with other low income countries (estimated average number of injections per person per year is 4.2 in Egypt *versus* 1.5 in other countries).[4] An estimated 8% of injections administered in Egypt are unsafe (i.e., the provider does not use a syringe taken from a closed sealed packet), and injections are administered by a wide variety of providers, including those with no formal medical education or training.[4] These unsafe practices have been identified as key risk factors in the transmission of HBV and HCV.[3,5] Increasing community awareness of injection risks, including the importance of avoiding reuse of syringes, is crucial to building demand for safe injections from all providers.

(3)Specialist Panel on Chronic Hepatitis, B.i.t.M.E., A review of chronic hepatitis B epidemiology and management issues in selected countries in the Middle East. J Viral Hepat, 2012. 19(1): p. 9-22.

(4) Talaat, M., et al., Overview of injection practices in two governorates in Egypt. Tropical Medicine & International Health, 2003. 8(3): p. 234-241.

(5) Mostafa, A., et al., Is the hepatitis C virus epidemic over in Egypt? Incidence and risk factors of new hepatitis C virus infections. Liver Int, 2010. 30(4): p. 560-6.

More than 40% of injections in Egypt are provided by informal healthcare providers.[4] To protect these providers from viral hepatitis and reduce their patients'/clients' risk for these infections, this group should be targeted with education materials addressing viral hepatitis prevalence, modes of transmission, risk factors and opportunities for testing, and care and treatment. Receipt of well-designed, tailored educational materials could empower the informal healthcare workforce in Egypt to avoid behaviors that could place them at risk for viral hepatitis infection and to provide their patients and clients with counseling about how to avoid infections and where to obtain testing. Building capacity of key community groups can pave the way for positive behavioral changes throughout the entire community.

Objective 6.4.1

Educate informal healthcare providers (e.g., barbers, pharmacists, and housekeepers) to prevent transmission of viral hepatitis.

Actions to Be Initiated:

- Conduct a survey and literature review to understand why healthcare providers are not performing safe injections.
- Revise messaging as needed based on results of survey and literature reviews.
- Create a training program with certification for informal injectors to be managed by NGOs.

Objective 6.4.2

Create public demand for safe injections and non-injectable medications.

Actions to Be Initiated:

- Conduct a survey and literature review to understand why the public prefers receiving medication in injectable form and why they seek care from informal healthcare workers.
- Disseminate results of the survey and literature review to all appropriate parties.
- Revise messaging as needed.

Objective 6.4.3

Reduce unnecessary injections prescribed by the healthcare system.

Actions to Be Initiated:

- Simultaneously educate the public and providers about the importance of reducing the number of unnecessary injections, thereby creating patient demand and increasing prescriptions written for therapeutic alternatives (e.g., oral medications).

7. Research Agenda For Viral Hepatitis

An essential component of any public health program, research enables public health professionals to better understand various aspects of population health specific to a particular country or geographic area. For instance, research can shed light on how well the health-care system is functioning, reveal needs for tailoring interventions, monitor indicators, evaluate actions, develop and assess new drugs, assess the cost-effectiveness of interventions, and evaluate the acceptability of programmes. In Egypt, many gaps exist in understanding the burden of viral hepatitis and the interventions needed to combat these infections. These gaps must be identified, relevant research projects designed, and numerous international and national partners engaged to conduct good quality research. The dissemination of research results to the scientific community is also essential. Although many research studies are performed in Egypt, many are never published. With increased capacity for Egypt's research teams, study results can be published in peer-reviewed journals and made available not only to the scientific community, but to decision makers involved in developing evidence-based policies.

Actions to Be Initiated:

- Identify partners to collaborate on research at national and international level.
- Create a multi-disciplinary, inter-sector technical research task force.
- Conduct a systematic review using Cochrane methodology of available research data and publications.
- Identify gaps in research with partners.
- Include viral hepatitis public health research agenda with Science & Technology Development Fund (STDF).
- Facilitate the dissemination of research results by conducting an annual public health meeting or conference on viral hepatitis prevention, publishing findings in peer-reviewed journals, and presenting results at conferences.
- Translate research results into policy and practices.
- Increase capacity of MOHP hepatitis unit to conduct research projects following ethics guidelines and disseminate and translate research results into public health practice.
- Establish an integrated data warehouse for each component to facilitate research projects.
- Facilitate export of research samples as part of collaborative agreements with international partners.

Potential Areas of Research by Component

Surveillance:

- Determine the incidence and prevalence of HBV and HCV infection in the general popu-

lation and specific groups (e.g., HCWs, dialysis patients, multi-transfused patients, street children, PWIDs, school teachers, and sanitation workers) to assess HBV and HCV burden in Egypt and identify high risk groups.

- Determine the incidence, prevalence, risk factors, and high risk groups associated with HAV infection to assess disease burden in Egypt.
- Conduct research on the risk factors for viral hepatitis to identify current modes of transmission.
- Conduct research on health-seeking behaviors among persons infected with HCV.
- Determine the incidence and prevalence of advanced forms of disease (e.g., severe fibrosis, liver cirrhosis, hepatocellular carcinoma), and their relation to HBV and HCV.

Infection Control:

- Evaluate infection-control practices, behaviors, and attitudes about HCV infection in different settings and groups.
- Conduct qualitative research with HCWs to identify barriers (e.g., nurse/patient ratio, work overflow, and lack of knowledge) to adhere to recommended practices and preventive measures (e.g., HBV vaccination).
- Conduct epidemiologic studies on needle sticks, endoscopy, laparoscopy, cardiac catheterizations, obstetrical procedures and other known risk factors of healthcare-associated viral hepatitis.
- Evaluate purchasing practices of healthcare facilities to understand the patterns of use that contribute to poor compliance.
- Evaluate reuse of single-use items.
- Conduct a cost-effectiveness evaluation of several strategies to implement infection-control programs in different settings.

Blood Safety:

- Determine the prevalence and incidence of HBV and HCV infection in the donor population and in transfused patients.
- Identify risk factors for viral hepatitis infection among blood donors.
- Research blood donor profiles, motivations, and deterrents.
- Identify the most efficient interventions to recruit and retain uninfected blood donors.
- Analyze patient outcomes following transfusion of blood products (e.g., adverse reactions and transfusion-transmitted infections).
- Examine adverse reactions in blood donors.

- Examine the effects of transfusion on the HCV-associated disease process.
- Conduct cost-effectiveness studies on introducing nucleic acid testing in Egypt.

Vaccination:

- Identify the most effective HBV vaccine strategies among HCWs.
- Research non-responders to HBV vaccination.
- Estimate HBV vaccination coverage in infants, children, and persons in high-risk populations.
- Conduct cost-effectiveness studies on HAV vaccination.
- Research need for a booster dose of HBV vaccine in Egypt.

Care and Treatment:

- Prioritize populations in need of viral hepatitis treatment through examination of cost-effectiveness data, markers of treatment response, and other variables.
- Validate new methods for viral hepatitis screening and monitoring (e.g., point-of-care tests and markers of disease severity).
- Estimate treatment response rates in "real-life" conditions, and identify factors associated with treatment response.
- Estimate rates of relapse and re-infection following HCV treatment.
- Identify safe and effective drugs or treatment regimens for persons with chronic viral hepatitis, whether naïve or former relapsers or non-responders.
- Conduct a cost-effectiveness analysis of treatment strategies, including use of newly available antiviral therapies.
- Research access to care and treatment for infected populations.

Information, Education, and Communication:

- Conduct modeling studies to identify the most powerful IEC interventions to decrease viral hepatitis transmission.
- Conduct studies (e.g., KAP/focus groups) to determine a baseline for HCWs beliefs, knowledge, and practices regarding hepatitis.
- Identify indicators that can be measured repeatedly (e.g., during DHS surveys) to monitor behavioural changes (e.g., number of injections in the past year, proportion of re-use of injecting material).
- Conduct studies to better understand the magnitude of stigma against people with viral hepatitis.

- Conduct studies on school-aged children and school teachers to determine gaps in knowledge about viral hepatitis.
- Conduct studies to understand youth (15-25 years of age) awareness of viral hepatitis.
- Administer a survey to informal healthcare providers to better understand factors contributing to unsafe injections.
- Research why the general population prefers injections over oral medications.

CONCLUSION

The Viral Hepatitis Plan of Action presents robust and dynamic steps for improving the prevention of viral hepatitis and the care and treatment provided to infected persons. Some of these life-saving actions already are well underway. Other actions, representing innovations in practice, technology, and therapy, will require new strategic directions and commitment. The success of these actions is contingent on interagency collaboration, stakeholder support, and engagement of the diverse communities being served. Also critical to the success of the plan are policy-related support and system changes. In this unique era of unprecedented opportunity, viral hepatitis activities can be better coordinated between all stakeholders. The Viral Hepatitis Plan of Action will serve as the guide for MOHP and other agencies working together to combat Egypt's viral hepatitis epidemic.

APPENDIX A

PARTICIPATING AGENCY AND PARTNER ABBREVIATIONS

BTC	Blood Transfusion Centre
CAD	Central Administration of Dentistry
CDC	Centers for Disease Control and Prevention
CPHL	Central Public Health Laboratory
EMRO	Eastern Mediterranean Regional Office
EPI	Expanded Programme of Immunization
GIZ	GIZ (German Society for International Cooperation)
GOTHI	General Organization of Teaching Hospitals and Institutes
HIO	Health Insurance Organization
IP	Institut Pasteur
MAO	Misr Alkaher Organization
MHE	Ministry of High Education
MOE	Ministry of Education
MOHP	Ministry of Health and Population
NAMRU-3	Naval Medical Research Unit 3
NBTS	National Blood Transfusion Services
NCA	Nursing Central Administration
NCCVH	National Committee for the Control of Viral Hepatitis
NGO	Non-Governmental Organization
NHTMRI	National Hepatology and Tropical Medicine Research Institute
RBTC	Regional Blood Transfusion Centre
RCRL	Red Cell Reference Laboratory
SAH	School Age Health
SFSD	Sawiris Foundation for Social Development
TM	Terous Misr
TO	Terous Organization
UCSF	University of California San Francisco
UNICEF	United Nations International Children's Emergency Fund
USAID	United States Agency for International Development
VHRL	Viral Hepatitis Research Laboratory
WHO	World Health Organization

EGYPT

CAN ELIMINATE HEPATITIS

NATIONAL HEPATITIS ELIMINATION PROFILE

UPDATED FEBRUARY 21 2022

COALITION FOR GLOBAL HEPATITIS ELIMINATION

Hepatitis B virus (HBV)	Hepatitis C virus (HCV)
NO	**2020**
HBV elimination goal [1]	HCV elimination goal [1]
Action Plan	Action Plan

The National Committee for Control of Viral Hepatitis (NCCVH) set a national strategy in 2014 to make treatment paid for by the Egyptian government available for all and to scale up treatment to millions.

THE HEALTH BURDEN OF VIRAL HEPATITIS

Prevalence

1%

Prevalence of HBsAg, 2019 [2]

0.4%

Prevalence of chronic HCV, 2019 [3]

Estimated prevalence. No recent surveys conducted following the national elimination program.

450,000

Number of persons living with HCV infection, 2021 [4]

Incidence

NO DATA

New HBV infections

6,000

New HCV infections, 2021 [4]

NO DATA

HBV- related deaths

19.4 (11.80 - 28.70)
Deaths per 100,000, 2019 [2]

Mortality

18,000

HCV- related deaths, 2019 [4]

35.9 (24.20-48.90)
Deaths per 100,000, 2019 [2]

PROGRESS TOWARDS 2020 WHO ELIMINATION GOALS

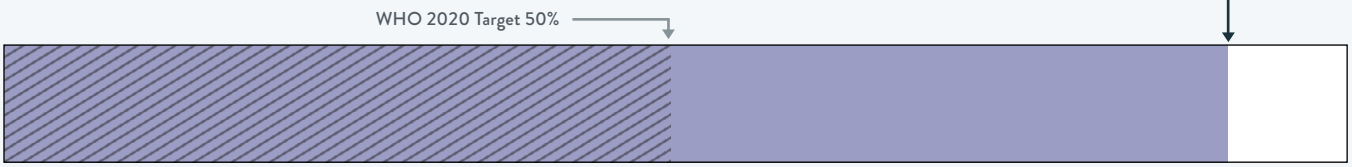
PREVENTION OF NEW INFECTIONS AND MORTALITY

HBV Percentage change in new infections		NO DATA WHO 2020 Target -30% [2]
HBV Percentage change in deaths		NO DATA WHO 2020 Target -10% [2]
HCV Percentage change in new infections, 2015-2020		-40% ↓ WHO 2020 Target -30% [5,6,7]
HCV Percentage change in deaths, 2015-2019		-51% ↓ WHO 2020 Target -10% [2,4]
Prevalence of HBsAg in children < 5 years (%), 2019		0.11% (0.09-0.13%) SDG 2020 Target 1% [2]

- *Goal achieved*
- *Partial progress towards goal*
- *Limited/no progress towards goal*

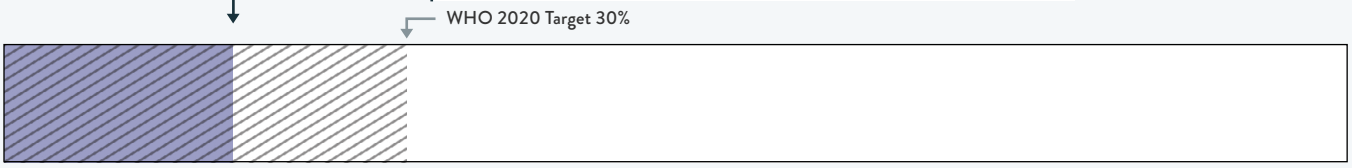
ACCESS TO RECOMMENDED VACCINATION, TESTING AND TREATMENT

92% Hepatitis B timely birth dose vaccination of newborns, 2020 [8] (in first 24 hrs of life)



95% HepB 3 dose vaccine coverage for infants, 2017 [8]

10-15% Proportion of persons living with **HBV** diagnosed, 2021 [4]



25% HBV

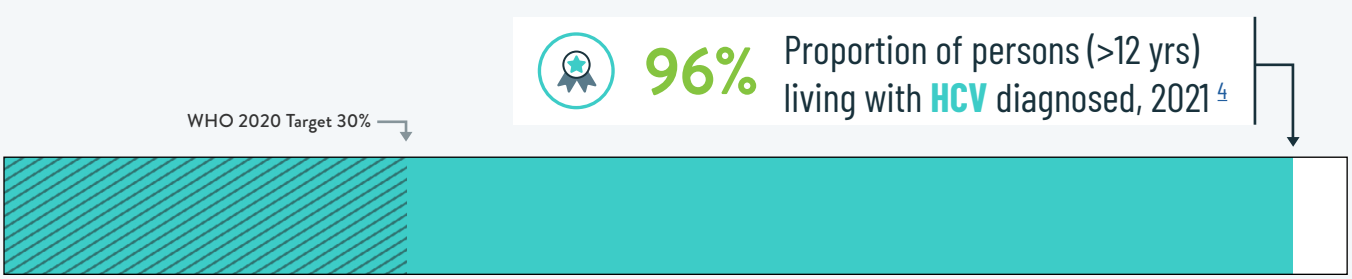
Proportion of diagnosed HBV persons receiving appropriate treatment, 2021 [4]

0

For persons who inject drugs (PWID), number of sterile needles per year [3]

WHO 2020 Target 200

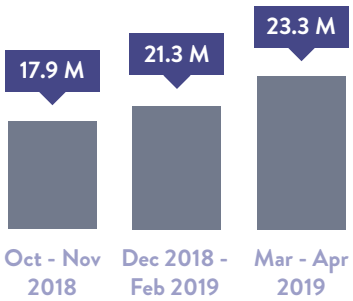
96% Proportion of persons (>12 yrs) living with **HCV** diagnosed, 2021 [4]



92% Proportion of diagnosed persons who have initiated treatment [9]

Number of persons tested for **HCV** [9]

62.5 M adults screened in 7 months



4,000,000

Number of people treated for HCV, 2014-2020 [10]

1.6 Million persons treated for HCV, 2020 [3]

POLICY ENVIRONMENT FOR THE ELIMINATION OF HEPATITIS

ACHIEVEMENT | **INNOVATIONS** | **ROADBLOCKS**

STRATEGIC INFORMATION

Routine official reports to monitor HBV and HCV [1,9]	Mortality ● Incidence ● Prevalence	DHS survey conducted in 2015 and national 2018-2019 screening campaign followed
Estimates of HBV and/or HCV economic burden [11,12]	Partially Adopted	For HCV
Monitoring of HBV and HCV diagnosis and treatment [6]	Adopted	NCCVH database exists that assigns all individuals an electronic national ID number

INNOVATIONS

The Ministry of State for Administrative Development developed a web-based online registration system website (www.nccvh.org.eg) for registration of patients with HCV and scheduling appointments at the treatment centres

A closed virtual private network (VPN), the National Network of Treatment Centers (NNTC), was founded to connect the viral hepatitis treatment centre databases to the head office which improved monitoring and evaluation

ROADBLOCKS

HCV incidence has not been evaluated and is not known after the mass HCV testing and treatment program.

PREVENTION OF MOTHER TO CHILDREN TRANSMISSION

Policy for universal hepatitis B vaccination of newborns [13]	Adopted	HepB birth dose adopted in 2015.
Recommendations for:		
HBV testing of pregnant women [14]	Adopted	TDF treatment of pregnant women with high viral load still not adopted.
HCV testing of pregnant women [14]	Adopted	

ACCESS AND REGISTRATION OF MEDICINES AND TESTS

HCV: Registration of orginator medicines [15]	Adopted
HCV: Eligible for generic medicines [16]	Adopted
HCV: Registration of generic medicines [17]	Adopted
Licensed point-of-care PCR testing to detect HBV and HCV [4]	Adopted

ACHIEVEMENTS

In 2014, the NCCVH negotiated prices of originator direct-acting antivirals (DAA's) to about 10% of prices in the United States at the time.

Local companies began to locally manufacture HCV medicines at low cost. Pharco obtained WHO pre-qualification for its generic DAAs, contributing to public and private partnerships to improve testing and treatment.

Mass procurement through a single negotiating body ensured low prices for HCV diagnostics.

INNOVATIONS

The Egyptian government & Pharco launched initiatives to extend their experience to help global hepatitis elimination (e.g. initiative with goal to provide HCV treatment to 1 million Africans).

TESTING TO DIAGNOSE HBV AND HCV INFECTION

Testing recommendations for:

HBV: Risk-based [18]	Adopted	
HBV: Universal [4]	Partially Adopted	Currently, all patients evaluated or treated for HCV are screened for HBV. In addition, some hospitals screen all admitted patients for HBV
HCV: Risk-based [18]	Adopted	Universal HCV Testing Policy was implemented which aimed at mass screening of adults older than 18 years (61 million) and school-children aged 12 to 18 years, after obtaining consent from their legal guardians (9 million)
HCV: Universal [18]	Adopted	
No patient co-pays for HBsAg and anti-HCV testing [12]	Adopted	HCV screening is free of charge and includes testing for anti-HCV antibody using a WHO prequalified rapid diagnostic test

ACHIEVEMENTS

The Egyptian Presidential Initiative, 100 Million Healthy Lives, was launched in October 2018 with the goal of screening the entire adult population for HCV. This program is the largest HCV screening program in the world. Under the 100 Million Healthy Lives, over 240,000 people were screened per day. There were 77 PCR testing sites around the country with capacity for 36,000 PCR tests daily.

The Egyptian national HCV program demonstrated to the world that population screening of all adults is possible even in resource-limited settings.

The Egypt national HCV testing program's success demonstrated that RDTs can be highly effective as a part of a national HCV diagnostic algorithm.

The screening of school children 12-18 years (this included both Governmental, private schools and technical schools).

INNOVATIONS

HCV screening was integrated with screening for non-communicable diseases, including diabetes, hypertension, and obesity

ROADBLOCKS

Need to scale-up testing and active case finding for key at-risk groups, including people living with HIV (PLHIV), people who inject drugs (PWID), and people who are incarcerated. Regular screening for reinfection among these groups is essential to identify acute infections and treat them early to reduce the risk of transmission.

ACCESS TO HBV AND HCV TREATMENT

HBV:	National treatment guidelines [4]	Adopted	
	Simplified care: Simplified treatment and monitoring algorithm for primary care providers [18]	Not Adopted	HBV care provided through specialized treatment centers
	Simplified care: No patient co-pays [1]	Adopted	HBV treatment free at national treatment centers
HCV:	National treatment guidelines [4]	Adopted	
	Simplified care algorithm: Less than 2 clinic visits during treatment [19]	Adopted	HCV treatment decentralized across the country, including the use of mobile vans to reach rural patients
	Simplifed care algorithm: Non-specialists can prescribe treatment [4]	Adopted	HCV treatment was fully funded by the government irrespective of financial ability or insurance coverage. Those who opted to pay out of pocket paid the reduced wholesale price.
	Simplified care algorithm: No patient treatment co-pays [15]	Adopted	
	No fibrosis restrictions [1]	Adopted	In 2015, Egypt became the first national program in the world to treat all patients irrespective of fibrosis stage.
	No sobriety restrictions [4]	Adopted	
	No genotyping [4]	Adopted	

ACHIEVEMENTS

Over 150 specialized centers for treatment of viral hepatitis were established within Ministry of Health and Population healthcare facilities. Centers were geographically distributed in the most populous areas, so that eventually no patient would have to travel more than 50 km to a center.

INNOVATIONS

To correct low rates of patient follow-up for SVR12 testing, the national program implemented strategies such as phone calls to identify the cause of "no show," issuing "certificates of cure," and initiating hepatitis B vaccination free of charge to encourage return for SVR12 testing

HEALTH EQUITY AND ADDRESSING DISPARITIES

National strategy addresses populations most affected [14]	Adopted	Laws exist to protect people against discrimination on the basis of disability caused by an infectious disease, except where discrimination is necessary to protect public health. However, no hepatitis specific law is in place. Limited instances of discrimination against HBV and HCV patients have been reported.
National anti-discrimination laws against persons living with hepatitis B and/or C [18]	Partially Adopted	
National policy for adult hepatitis B vaccination [20]	Partially Adopted	HBV vaccination was offered at the end of HCV treatment to encourage individuals to return for SVR12 testing. This strategy was not based on reaching populations at highest risk of HBV infection.
National policy for:		
Harm reduction for persons who inject drugs (PWID) [14,21]	Partially Adopted	OST has been recently approved in Egypt and is provided in limited specialized centers. Syringe exchange programs are very limited.
Syringe exchange in federal prisons [21]	Not Adopted	
Decriminalization of possession of syringes & paraphernalia	No Data	The estimated prevalence of HCV among HIV infected Egyptian patients was around 34.8% [22]
Decriminalization of drug use [21]	Not Adopted	The estimated incidence of new HCV infections among PLHIV in a study conducted between 2016 -2019 was 4.06 cases per 100 person-years with 83.3% of new HCV infection cases reported injecting drug use history. In the same study, the incidence among HIV-positive PWID was 7.08 cases per 100 person-years. [23]
		According to the UNODC, the estimated HCV prevalence among PWID in Egypt is 55%. [24]

ROADBLOCKS

Participation in the 100 Million Healthy Lives National Program was lower among men than among women and was lower among those younger than 25 years of age than among older persons.

Need to develop more tailored interventions for key at-risk groups.

About 10.25 million Egyptians live overseas and may have been unable to participate in the 100 Million Healthy Lives National Program.

Patients living with HCV continue to face discrimination within the community, and in some cases within the healthcare settings. Discrimination has declined following national campaign.

INNOVATIONS

Paid public Awareness & media/TV coverage were used to increase awareness and motivate people to seek HCV screening and treatment. Local & global public figures were recruited to be ambassadors for this campaign.

FINANCING

Public budget line for HBV and HCV testing and treatment [14]	Adopted	$310.2 Million - Egypt's Healthcare System Project - (129.6M = HCV screening, 130.6M = HCV treatment 50M = blood transfusions)

ACHIEVEMENTS

Almost 88% of patients treated for HCV were sponsored by the government (29% through the HIO and 56% through governmental support funds) (El-Akel et al)

NEXT STEPS TOWARD ELIMINATION

- Validate elimination of HCV with both internal and external WHO processes
- Document lessons learned in HCV elimination and disseminate to other countries
- Continue to focus on HCV prevention, including improving blood safety, reducing demand for unnecessary injections, scaling up use of auto-disposable syringes, emphasizing infection control, and leveraging mass media campaigns
- Continue to test all pregnant women for HBV and HCV to sustain gains in reduction of incidence, prevalence, and mortality
- Implement HCV and HBV rescreening and treatment for at-risk individuals who missed the national screening program, including persons who inject drugs, persons who are incarcerated, persons who are on dialysis, and the immunesuppressed/ immunecompromised (multiple transfusions, etc).
- Establish harm-reduction program for persons who inject drugs and develop more tailored strategies for delivering enhanced screening, linkage to care, and treatment to persons at increased risk
- Scale-up HBV testing and treatment

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WORKING TOGETHER, WE WILL ACHIEVE ELIMINATION.

COALITION FOR GLOBAL HEPATITIS ELIMINATION

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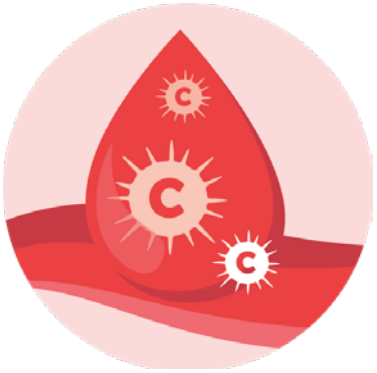
Hepatitis C virus testing and baselining

Has the person ever been exposed to HCV?

Test 1 - The Antibody (Ab) test

A positive HCV Ab result indicates that the person has been exposed to the virus at some point in their life. Note that:

- A positive HCV Ab test result does not distinguish between acute, chronic or cleared infection.
- The presence of HCV antibodies does not provide protection against HCV.



A negative result means that current HCV infection is unlikely. The HCV antibody test has low rates of false negatives or positives. However, this test may need to be repeated if the person has been exposed to risk recently (and possibly tested during the 'window period').

A small number (<5-10%) of immunocompromised hosts, including people living with HIV, may never develop HCV Ab, despite chronic HCV infection. In this case, HCV RNA testing should be performed to diagnose active HCV infection.

Does the person currently have HCV?

Test 2 - The RNA test

This can be determined by ordering a HCV RNA test. This is a test to detect the presence of virus in the blood, by Polymerase Chain Reaction (PCR). The HCV RNA test may be qualitative or quantitative. A positive result confirms the detection of HCV RNA and current viraemic HCV infection.

Ab
Antibody test EVER come into contact with HCV

RNA
Infected with the virus NOW

Ab + + RNA + = **Infected** with HCV **NOW**

Ab + + RNA – = **Infected** with HCV in the **PAST**

Ab – + RNA – = **NEVER** infected with HCV

What HCV genotype do they carry?

AA HCV genotype test is necessary for treatment options that are genotype-specific. HCV genotyping is a routine laboratory test performed during RNA testing.

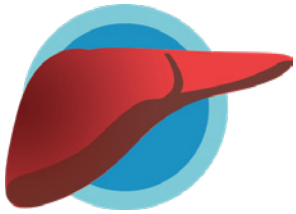
Pan genotypic treatment regimens are also available making all genotypes easier to treat.

Check your local guidelines for what treatment options are available.

What is the HCV RNA level (HCV “viral load”)?

Quantitative HCV RNA at treatment commencement (baseline) may help predict a person’s response to therapy. A low pre-treatment HCV RNA (“viral load”) may allow for a shorter duration of therapy. The length of therapy should be discussed with your local support network who can advise on the most appropriate regimen and its duration.

How is their liver functioning?



Liver Function tests (LFTs) provide a baseline of current liver function and help identify damage to liver cells. The relevant component tests of a routine LFT are bilirubin, ALP, GGT, ALT and AST. Documentation of the presence or absence of cirrhosis influences treatment regimen and duration.

These are the risks…

Blood transfusions (prior to 1992)

Injecting drugs, even once

Unsterile tattoos/piercings

Medical/dental procedures abroad

Other blood to blood contact

Discuss with your GP whether to get tested for hepatitis C

Find out more at **www.hepctrust.org.uk** or call our helpline: **0845 223 4424**

THE HEPATITIS C TRUST

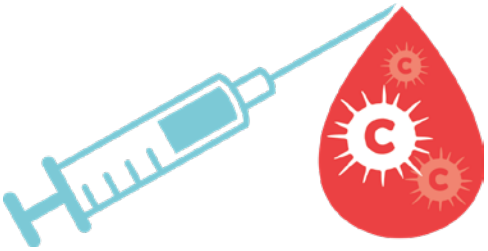
The Hepatitis C Trust is patient-led and is the national UK charity.
All calls are confidential and are charged at the national rate
(but may be more from a mobile).
We are a member of the Helplines Association.

Charity Registration Numbers: England and Wales 1104279, Scotland SCO39914

Introduction to hepatitis C

The word *hepatitis* comes from the Ancient Greek word for liver (*hepar*) and the Latin word for inflammation (*itis*). Chemicals, drugs, excessive alcohol consumption or blood-borne viruses can all cause inflammation to the liver.

What is hepatitis C?



Hepatitis C is an infection caused by the hepatitis C virus that causes inflammation of the liver. Infection can occur through blood-to-blood contact due to unsafe injection and other skin penetration practices, inadequate sterilisation of medical equipment, and the transfusion of unscreened blood and blood products.

Currently, there is no vaccine for hepatitis C virus, as there is for hepatitis A and hepatitis B. A person can be re-infected throughout their life and can live with more than one hepatitis virus at once.

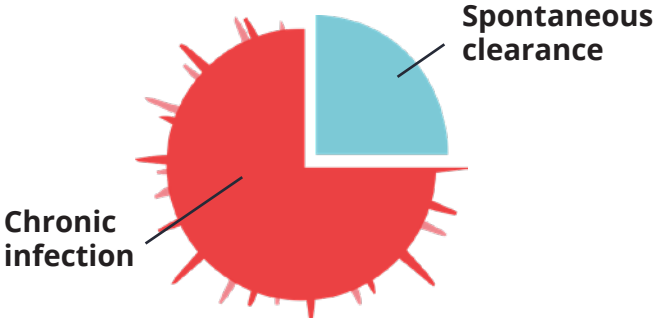
Symptoms and diagnosis

HCV infection can range in severity from a mild illness lasting a few weeks to a serious, lifelong illness.

Common symptoms of acute infection are:

- General aches and pains
- Nausea
- Abdominal pain and discomfort
- Loss of appetite
- Rarely yellowing of the eyes and skin (jaundice)

About 25% of people infected will clear the virus naturally in the first 12 months (**acute infection**).



However, if the infection does not clear up on its own, the virus continues to damage the liver. Of those who are exposed to hepatitis C, up to 75% will go on to develop **chronic infection**.

A person living with chronic hepatitis C may not know they have it because it can take many years for symptoms to appear. Consequently, many people live undiagnosed for years. Some cannot identify how they were infected.

Impact on the liver

Over time Hepatitis C infection can seriously impair liver function, causing fibrosis or cirrhosis (scarring of the liver), and can lead to hepatocellular carcinoma (HCC).

The rate of progression to cirrhosis is variable and depends on several factors, including age of initial infection, male gender, alcohol consumption, co-infections including HIV and hepatitis B virus, and obesity. Around 10-15% of people living with chronic HCV infection will develop cirrhosis within the first 20 years after infection; those who develop cirrhosis are at increased risk of HCC.

Geographical distribution

Globally, there about 70 million people living with hepatitis C, a figure which represents roughly 1% of the population[1] . The regions most affected are Africa and Central and East Asia.

1%

70 million people

Hepatitis C genotypes

There are six main genotypes (viral strains) of HCV worldwide, each with numerous subtypes, and their distribution varies by region. Knowing the genotype is important when making decisions about treatment.

New treatments

Unlike HIV and HBV infection, hepatitis C infection can be cured.

Testing for the virus is simple and the new generation treatments are far more effective, easier to take and have fewer side-effects than the older medications.

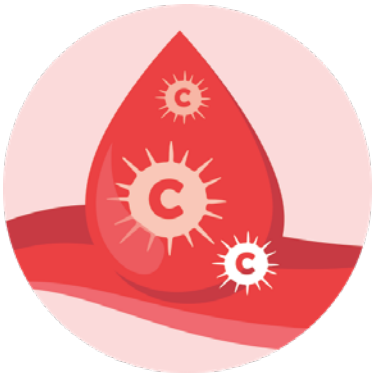
[1] The Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterology and Hepatology 2016 Dec 15. http://dx.doi.org/10.1016/S2468-1253(16)30181-9

How hepatitis C spreads

The hepatitis C virus is a blood-borne virus, meaning it's transmitted when the blood of an infected person enters another person's bloodstream. It only takes a small amount of blood to transmit hepatitis C. The virus can live outside of the body for at least four days. In other conditions, it can survive for much longer (e.g. for many weeks inside a syringe).

Understanding the risks

There are many myths about exactly how hepatitis C is transmitted. It is important to know that the riskiest activities are those with the highest potential and frequency of blood-to-blood contact. Those activities that have no chance of exchanging blood are considered no risk. Based on these distinctions, high-risk, some-risk and no-risk activities are outlined below.



High-risk activities

- Unsterile medical or dental procedures and traditional medical practices where the skin is pierced.
- Re-using someone else's injecting equipment for drugs.
- Unsterile tattooing or body piercing.

Moderate-risk activities

- Needle-stick injuries to healthcare workers.
- Mother-to-child transmission may happen during pregnancy or childbirth if mother has hepatitis C.
- Receiving treatment for bilharziasis by tartar emetic injections from 1950s to 1980s in Egypt.
- Re-using someone else's personal items that may have blood on them, such as razors and toothbrushes.
- Blood-to-blood contact during sex, especially with unprotected anal intercourse.

No-risk activities

If there is no blood-to-blood contact, there is no risk of transmission of hepatitis C. People cannot get or transmit hepatitis C by:

- Sharing toilets, drinking glasses or eating utensils
- Hugging, kissing or touching
- Using swimming pools
- Mosquito or other insect bites
- Coughing or sneezing

Risks for people living with hepatitis C

Understanding how hepatitis C is transmitted is important for people who are living with hepatitis C so they can reduce the chance of:

Being infected with another genotype of hepatitis C.

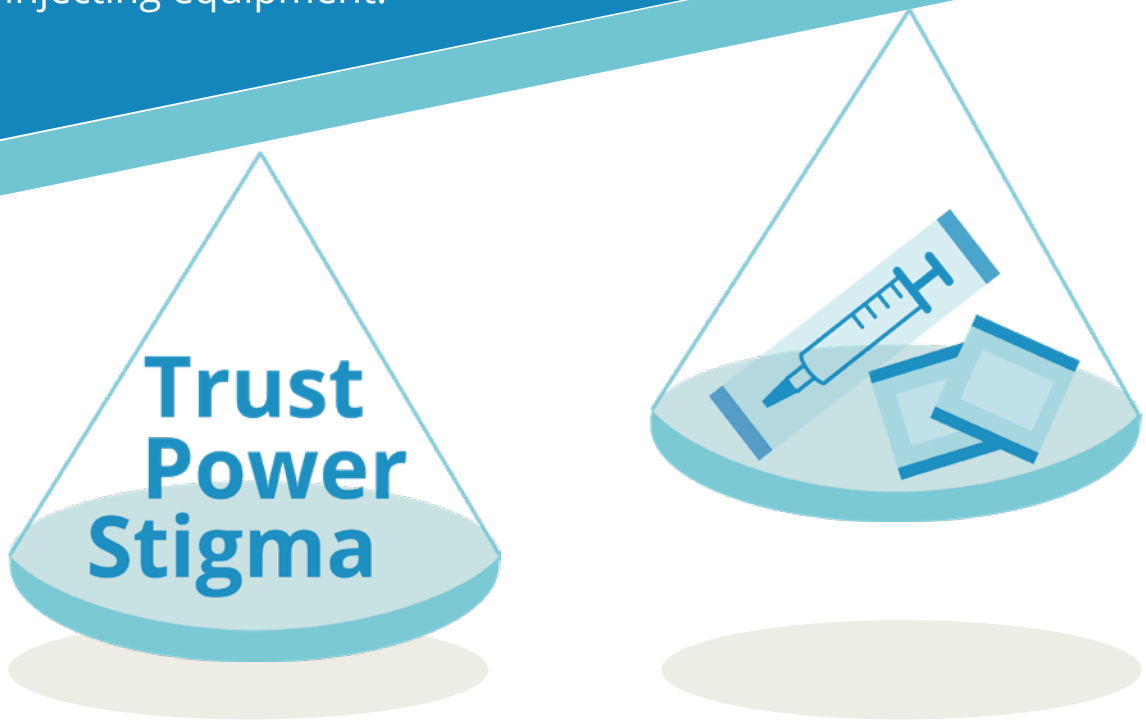
Being re-infected with the same genotype of hepatitis C.

Transmitting hepatitis C to another person.

INHSU

Something to think about: **injecting in the real world**

There are multiple reasons why someone who injects drugs may not feel able to access new, sterile injecting equipment.



Sometimes people who inject drugs may be part of social networks where they are unable to exercise full control over the circumstances in which they inject. For example, in some intimate or familial relationships, voicing an expectation that each person will use their own sterile equipment may be interpreted as implying a lack of trust, making a person uncomfortable or unwilling to jeopardise their relationships in this way.

In other situations, there may be a power imbalance between people who inject together which prevents the person with less power in the relationship from demanding that each person use their own, new equipment. This might be the case, for example, in a relationship between an older man with years of injecting experience and a younger woman who has injected for only a year or two and relies on her partner to purchase and prepare the drugs.

Some people may never have learnt to inject themselves, and rely on others to do it for them. In this case, they are dependent on the person injecting them to be willing to prepare the injections using new equipment, and the experienced injector may be unable or unwilling to do so. In prison, the extremely limited access to injecting equipment means that people who inject drugs in this environment inevitably do so with used equipment.

It is helpful if you acknowledge patients' best intentions while recognising the reality of their lived constraints.

For example, Needle and Syringe Programmes may have uneven distribution. This, combined with stigma and discrimination that some drug users may experience when accessing equipment, and the potential that their confidentiality may be breached and they will be identified as someone who injects drugs, can leave people reluctant to use services.

People may also be reluctant to access NSPs if they feel their eligibility for OST may be threatened, for example if their access points for both OST and sterile equipment are co-located.

If, however, your patient is able to and comfortable accessing their local Needle and Syringe Programme, you could advise them to, where possible, stock up with more injecting equipment than they think they might need ("so there's always some spares, for you or anyone else who might need them"). Patients may also find it useful to make contact with their local peer organisation to access advice and support from people who understand and can relate to their circumstances.

Consent and confidentiality

In your discussions with your patient, you need to ensure they are well informed of the testing process, and you should obtain their verbal informed consent to proceed with testing. You have an opportunity to educate your patient on how to prevent HCV transmission, and assure them of your confidentiality through the discussion.

Gaining informed consent

- Inform the patient of your confidentiality and alleviate any anxiety they have regarding this
- Enquire about their motivation for getting tested
- Provide clear, appropriate information about HCV, including natural history and modes of transmission
- Explain the process of testing, window period and possibility of indeterminate results
- Discuss benefits of early detection
- Assess their ability to cope with positive result and social supports
- Supply written material about HCV (excellent resources for patients are available from www.hepctrust.org.uk)

Conveying test results

- Always give test results in person where possible
- Explain the meaning of the result and discuss immediate implications for the patient
- Avoid overloading the person with information
- Provide emotional support
- Reinforce education about transmission prevention and harm reduction
- Allow adequate time to answer the patient's questions
- Advise on aspects of positive status disclosure
- Arrange any further tests and offer follow-up as required
- Supply written material and contact details for relevant support services and/or peer-based drug users' organisation.

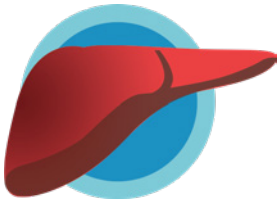
How to test for fibrosis

Once HCV has been diagnosed, the degree of liver fibrosis needs to be determined, as accurate staging will determine appropriate treatment and monitoring.

Non-invasive assessment

Although fibrosis assessment is imperative, liver biopsy is no longer required for most patients with chronic HCV infection. Non-invasive assessment of fibrosis has eliminated the need for biopsy in the majority of patients, and histologic confirmation of clinically evident cirrhosis is not required.

Liver ultrasound



Liver imaging may be used to assess for complications of cirrhosis, including hepatocellular carcinoma and portal hypertension. An ultrasound is preferred over CT scan as the initial investigation to avoid unnecessary radiation.

- If the ultrasound shows an abnormality, such as a nodule, more accurate cross-sectional imaging, such as computed tomography scan or magnetic resonance imaging scan, with and without contrast, would be indicated.

FibroScan®

FibroScan® is most accurate in identifying patients:

- Without significant fibrosis (<7.5 kPa)
- With cirrhosis (>11.5 kPa)

It is important to note that:

- Diagnostic accuracy declines when attempting to determine intermediate stages of fibrosis.
- Liver stiffness is increased independently of the degree of fibrosis in inflammatory liver conditions (E.g. acute HCV infection, acute alcoholic hepatitis or non-alcoholic steatohepatitis).
- Hepatic steatosis may increase the liver stiffness measurement obtained by FibroScan®. Abdominal obesity may overestimate the FibroScan® score – make sure the appropriate sized probe is used for each patient.
- FibroScan® does not give a reason for fibrosis or provide info on other liver pathology.

How FibroScan® works

An ultrasonic transducer sends a vibration wave into the liver. The velocity of the wave correlates with tissue stiffness. The stiffer the liver is, the greater the degree of fibrosis.

FibroScan® examination

Ideally, a patient should have fasted for 4 hours before the procedure.

While the patient is lying down, the probe is placed on the skin over the liver area, typically in the right mid-axillary line. Generally 10 measurements are taken to exclude outliers. The patient feels a gentle 'flick' each time a vibration wave is generated by the probe.

The whole procedure takes 5-10 minutes to perform, causes no discomfort, and results are available immediately.

APRI score

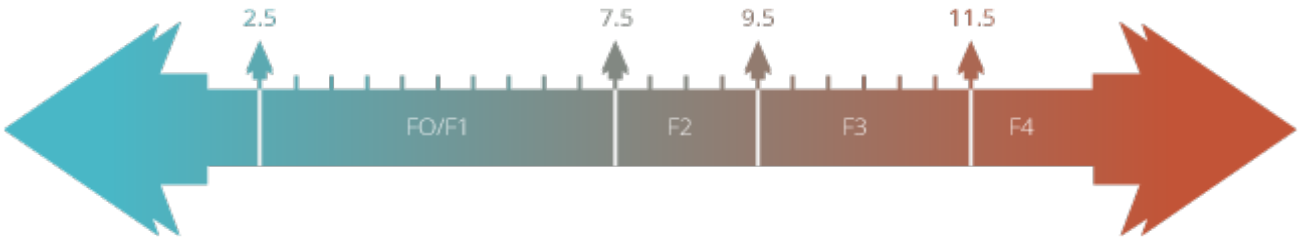
Although serum biomarkers have a role in patient management, they should not be over-interpreted.

In general, FIB-4 or APRI is most accurate for identifying patients at both ends of the spectrum of hepatic fibrosis: those at low risk for early or minimal disease (fibrosis stage 0 to 1) and those at high risk for advanced disease (fibrosis stage 3 to 4).

FibroScan® staging – understanding a FibroScan® result

The FibroScan® provides a numerical score of liver stiffness, which indicates the severity of liver fibrosis.

The diagram below show what FibroScan® scores mean.



Score	2.5 – 7.4	7.5 – 9.4	9.5 – 11.4	> 11.5
Indicates	F0/F1	F2	F3	F4
	No/Mild fibrosis	Moderate fibrosis	Severe fibrosis	Cirrhosis
	Indicates no or minimal liver fibrosis and no evidence of progressive liver disease.	Indicates significant liver fibrosis and evidence of progressive liver disease.	Indicates severe liver fibrosis and high risk progression to cirrhosis.	Indicates extensive liver fibrosis consistent with cirrhosis.

Signs of advanced liver disease

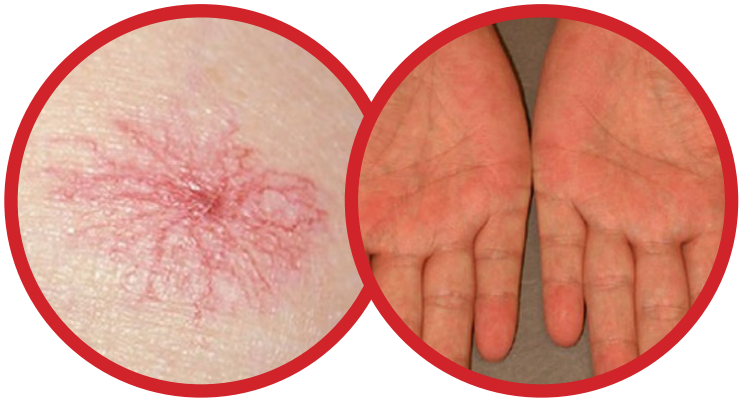
Liver disease, caused by HCV infection, can cause many signs and symptoms. As the disease evolves, signs can appear in many people – but not all, even when cirrhosis is present. Once the disease is well advanced, the features of hepatic decompensation and portal hypertension may appear, including ascites, jaundice, bleeding varices, coagulopathy, encephalopathy and renal failure.

Clinicians need to know what to look for as part of the process for staging liver disease. Cirrhosis severity can be staged by the Child-Pugh, and is based on serum bilirubin, serum albumin, INR, presence of ascites and presence of encephalopathy.

The Fib 4 (Fibrosis 4) score is a non-invasive scoring system based on several laboratory tests that help to estimate the amount of scarring in the liver. A Fib 4 calculator can be found at https://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4.

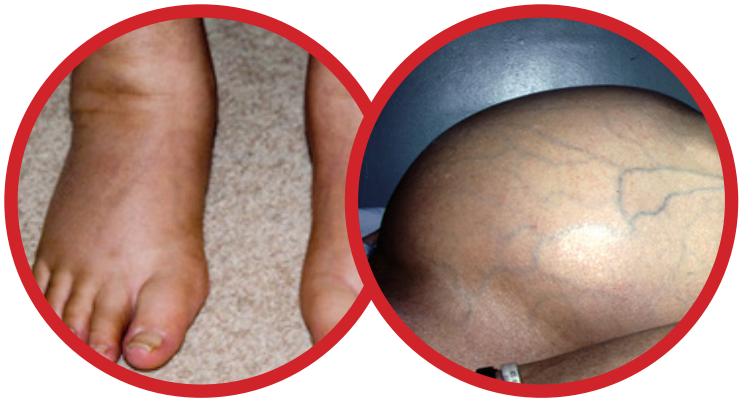
An Enhanced Liver Fibrosis (ELF) score can also be used to help estimate fibrosis. The ELF score combines quantitative serum concentration measurements of three fibrosis markers. Find out more about ELF scores at www.gpnotebook.co.uk/simplepage.cfm?ID=x2016072075237544321

Physical examination findings in chronic liver disease (of any aetiology) may include hepatomegaly and splenomegaly. A wide variety of non-specific signs (e.g. leukonychia, palmer erythema and gynaecomastia) have been associated with liver disease but these signs are of limited value. It is important to determine whether there are any signs of liver decompensation and the physical examination should focus on looking for these features. If there is doubt as to the severity of the liver disease the patient should be discussed with local experts.



Physical examination findings associated with decompensated liver disease

- Signs of hepatic encephalopathy: Drowsiness, asterixis (or 'hepatic flap')
- Jaundice
- Ascites
- Peripheral edema
- Bruising



Complications of chronic liver disease and cirrhosis

- Portal hypertension – varices on endoscopy
- Ascites – may be detected clinically or on ultrasound examination
- Hypersplenism (with or without splenomegaly)
- Synthetic dysfunction
- Hypoalbuminaemia
- Coagulopathy
- Hepatic encephalopathy
- Hepatocellular carcinoma
- Hepatopulmonary and hepatorenal syndromes

Some of the most common extra-hepatic manifestations of HCV infection are described here.

Immune-mediated

Hematologic

- Mixed cryoglobulinemia (10-25% of HCV people have cryoglobulins but this is rarely symptomatic)
- Cryoglobulinaemic vasculitis
- B-cell non-Hodgkins's lymphoma
- Monoclonal gammopathy
- Immune-mediated thrombocytopenia

Rheumatologic

- Sicca syndrome
- Arthralgia/myalgia
- Autoantibody production (ie, cryoglobulin, rheumatoid factor, ANA, anticardiolipin Ab, antithyroid Abs, anti-SM Ab)
- Polyarteritis nodosa

Inflammatory-related

Renal

- Glomerulonephritis
- Nephrotic syndrome

Endocrine

- Type 2 diabetes mellitus
- Insulin resistance

Central and peripheral nervous system

- Depression
- Cognitive impairment
- Peripheral neuropathy

Systemic

- Fatigue

Dermatologic

- Porphyria cutanea tarda
- Lichen planus
- Cutaneous necrotising vasculitis

Other causes of liver damage

When determining how to treat HCV, other causes of liver disease also need to be identified, as these can influence treatment options.

Identifying other causes of liver disease		
Condition	Test	Comment
Non-alcoholic fatty liver disease	Weight BMI Abdominal ultrasound	Very common
Alcoholic liver disease	History CBC LFT	Raised MCV, AST>ALT, raised triglycerides. History of alcohol consumption.
Hepatitis B infection HIV infection	Serology HBsAg anti-HBs anti-HBc HIV Ab	Vaccinate for hepatitis B if non-immune. Check for viral coinfection.
Haemochromatosis	Iron studies Genetic testing	Prevalence 1:400 but gene penetration is low and disease is much less common than the genotype implies.
Autoimmune liver disease	Auto-antibodies	Uncommon, associated with other autoimmune disease
Medication-induced liver disease	Patient history	
Alpha-1-antitrypsin	Alpha 1 antitrypsin	Rare
Wilson's disease	Family history Ceruloplasmin	Very rare Autosomal recessive Symptoms onset usually in adolescence and early 20s.

Understanding cirrhosis

Assessing liver fibrosis helps determine whether the patient could have cirrhosis. Cirrhosis is a histological diagnosis indicating liver disease with necrosis, collapse of architecture, regeneration, and fibrosis surrounding nodules of liver tissue. Cirrhotic status determines treatment regimen and length of treatment, and determines whether the patient needs specialist care.

Assessing severity

Assessing the severity of liver disease is not an exact science, but we can make an excellent attempt if we have:

- A good history to identify risk, likely duration, confounding factors, current symptoms
- A good physical examination to document any evidence of advancing liver disease
- An understanding of liver function tests and consistent use of these for diagnosis and monitoring
- An understanding of other investigations, which may provide insights into disease severity and/or the nature of the factors contributing to the presentation.

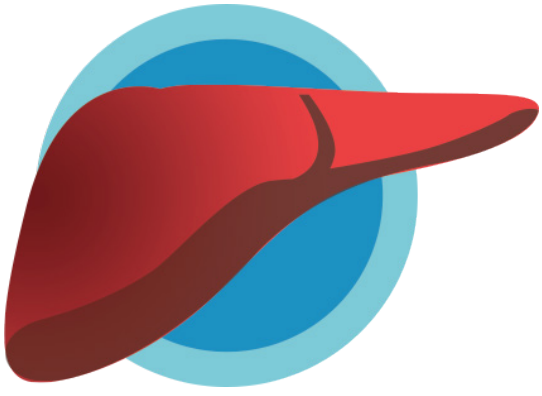
In the presence of cirrhosis and portal hypertension, hypersplenism develops and this leads to reduced haemoglobin, white cell count and platelet count (pancytopaenia). In many, the platelet count falls first and a count of < 100,000 is a surrogate marker of cirrhosis reflecting both the hypersplenism and a reduced production of thrombopoietin by the damaged liver.

Types of cirrhosis

In compensated cirrhosis, no complications have occurred.

Decompensated cirrhosis shows the presence of complications of liver dysfunction and/or portal hypertension. Symptoms include:

- Jaundice
- Hepatic encephalopathy
- Ascites and peripheral oedema
- Variceal haemorrhage



Lab markers of cirrhosis

Blood tests can help identify cirrhosis. Common markers include:

- Reduced platelet count – a count of <100 often indicates cirrhosis
- Lower albumin, total protein
- Lower platelets
- Increased globulin
- Prolonged INR or PT
- Increased bilirubin
- Liver enzymes elevation AST>ALT

Low albumin and platelets <150 are early markers of cirrhosis.

How to assess

Cirrhosis can be assessed through FibroScan® and APRI scores, described in the **HCV Testing** resource.

The Child-Pugh score is a scoring system that can also be used to measure the severity of chronic liver disease inclusive of cirrhosis. A higher score indicates worsening liver function. The score is calculated using several categories:

- total bilirubin, µmol/l (mg/dl)
- serum albumin, g/l
- INR
- presence of ascites
- presence of hepatic encephalopathy

Due to the complexity of managing cirrhosis, it is recommended that patients are managed in conjunction with your local liver unit.

Co-factors in the development of cirrhosis

- Heavy alcohol intake (>4 standard drinks per day)
- Co-infection with HIV or HBV
- Obesity
- Insulin resistance and/or metabolic syndrome
- Autoimmune liver disease – AICAH, PBC, PSC
- Metabolic disorders – haemochromatosis, Wilsons
- a-1 antitrypsin deficiency
- Primary biliary cirrhosis, primary sclerosing cholangitis, biliary atresia
- Chronic inflammatory conditions (e.g. sarcoidosis)

HCV treatment and pregnancy

Administration of PEG-IFN and/or ribavirin in pregnancy is contra-indicated. Animal studies have demonstrated that ribavirin causes birth defects and/or foetal deaths while PEG-IFN is abortifacient.

Ribavirin

Treatment with ribavirin is not recommended during pregnancy or for women who are unable or unwilling to adhere to use of adequate contraception. This includes women who are receiving ribavirin themselves; and/or women who are sexual partners of male patients who are receiving ribavirin.

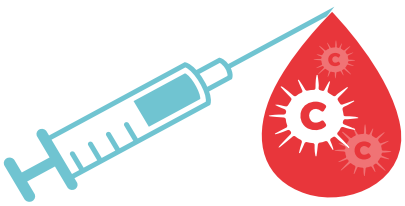
Daclatasvir

Although there is no data regarding daclatasvir for pregnant women, administration is not recommended.

In animal reproduction studies in rats and rabbits, embryo-foetal toxicity was observed in maternally toxic doses that produced exposures of 33 and 98 times the human exposure, respectively, at the recommended human dose of 60 mg.

Other treatments

Other HCV DAA drugs it is recommended that pregnancy is avoided (including sofosbuvir, sofosbuvir/ledipasvir, sofosbuvir/velpatasvir, ombitasvir/paritaprevir/ritonavir, dasabuvir, grazoprevir/elbasvir, glecaprevir/pibrentasvir). They should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.



Given the lack of data, nursing mothers are advised to discontinue breastfeeding prior to commencement of HCV drug therapy.

Patients and pregnancy

Clinicians will need to advise patients who are either planning to become pregnant, or who are already pregnant, about how to manage treatment.

Planning pregnancy

Female patients who have received ribavirin, and female sexual partners of male patients who have received ribavirin should not become pregnant for at least 6 months after stopping ribavirin.

Pregnant

- Treatment with PEG-IFN and/or ribavirin is contra-indicated.
- Given lack of data, HCV DAAs should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Co-morbid conditions

When deciding on the appropriate HCV treatment, other causes of chronic liver disease (or factors which may affect the progression of liver disease) should be excluded as their presence can impact treatment.

Co-morbid conditions to consider include, but are not limited to:

- HIV
- Hepatitis B virus infection
- Alcohol misuse
- Non-alcoholic steatohepatitis (related to the metabolic syndrome, obesity, diabetes mellitus)
- Hemochromatosis
- Autoimmune hepatitis
- Drug-induced liver injury
- Right ventricular failure

Factors which impact on choice and delivery of HCV treatment include:

- Mental health issues
- Drug and alcohol use (as a marker of lifestyle stability)
- Cardiac disease
- Chronic renal disease
- Advanced decompensated liver disease

Specialist referral should be sought for the following:

- Extra-hepatic manifestations of HCV
  1. Mixed cryoglobulinemia
  2. Renal disease (i.e. membrano-proliferative glomerulonephritis)
  3. HCV-associated lymphoma (i.e. diffuse large B cell lymphoma [DLBCL]).
- Transplant recipients
- Hemoglobinopathies
- Bleeding disorders

How to address co-morbid conditions in HCV treatment

HIV

- There is no apparent impact of HIV co-infection on DAA efficacy. There is, however, lower SVR with interferon-based treatment in HIV/HCV co-infection as compared with HCV mono-infection.
- Consider referral to specialist.
- Drug-drug interactions between DAAs and cART require assessment.
- This population should be prioritised for treatment for both individual and population level benefit, given increasing liver-related morbidity and mortality in those with HIV/HCV co-infection and increasing HCV incidence in HIV-positive MSM.

HBV

- Screen all patients for evidence of current, or prior, HBV infection before starting treatment with DAAs (Hep B sAg, anti-Hep B core Ab, anti-Hep B sAb +/- HBV DNA).
- If diagnosis is chronic HBV (HepB sAg positive) or "occult" HBV infection (HepB sAg negative, anti-Hep B core Ab positive, HBV DNA detected), refer to specialist.
    1. Concurrent HBV nucleoside/nucleotide analogue therapy may be indicated.
    2. Monitor patients for HBV flare-ups or reactivation during treatment and post-treatment follow-up.
- Communicate MHRA/CHM advice that Direct-acting antiviral interferon-free regimens to treat chronic hepatitis C have a risk of hepatitis B reactivation (January 2017) to patient.
- Patients with HBV co-infection should be treated with the same DAA regimens, following the same rules as HCV mono-infected patients.

Mental health

- Discuss potential impact on adherence.
- Assess for drug-drug interactions.
- Multidisciplinary care should be considered.
- Assess social and financial situation.

Drug and alcohol use

- Integrated management of substance use, in combination with HCV care, as required.
- Multidisciplinary care should be considered.
- Discuss potential impact on adherence.
- Assess for drug-drug interactions, including illicit drugs.
- Encourage patient to moderate or abstain from alcohol use.
- Assess social and financial situation.
- Discuss harm reduction strategies.
- Advise about risk of reinfection with ongoing injecting following treatment.

Cardiac disease (patients on amiodarone)

Sofosbuvir is contra-indicated in patients receiving amiodarone. Life-threatening bradyarrhythmias have been reported.

Refer to specialist

Chronic renal disease

Mild to moderate renal impairment (CrCl 30 – 80 mL/min)

- Treat according to the general recommendations.
- No dose adjustments of HCV DAAs are needed.
- Monitor carefully.

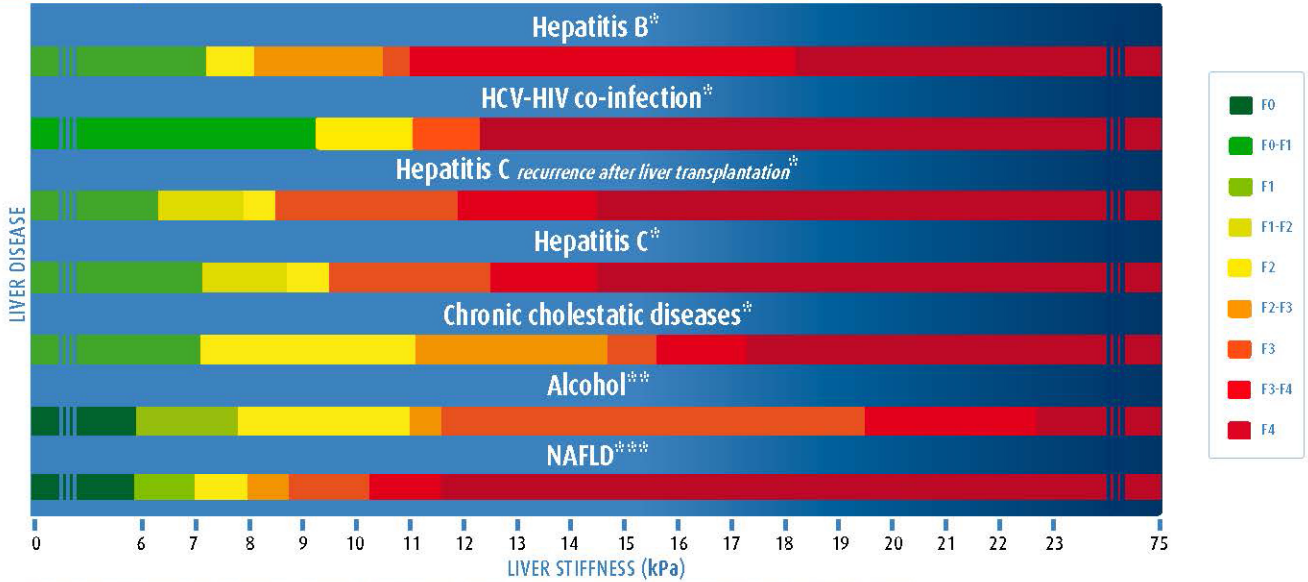
Severe renal impairment or end-stage renal disease, including hemodialysis (CrCl <30 mL/min)

Refer to specialist

- Caution with use of ribavirin given increased risk of hemolytic anemia.

SCORING CARD

CORRELATION BETWEEN LIVER STIFFNESS (kPa) & FIBROSIS STAGE



*According to Metavir score: Transient elastography (FibroScan): V. de Lédinghen, J. Vergniol, Gastroentérologie Clin Bio (2008) 32, 58-67
**According to Brunt score: Nahon et al. J Hepatol (2009) 49, 1062-68, Nguyen-Khac et al. , Aliment Pharmacol Ther (2008), 28, 1188-98
***According to Brunt score: Wong et al. Hepatology (2010) 51, 454-62Transient elastography (FibroScan®): V. de Lédinghen, J. Vergniol, Gastroentérologie Clin Bio (2008) 32, 58-67