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As part of the EASL Foundation's mission of flanking WHO in the implementation of viral hepatitis elimination programs, which should be terminated by 2030, we are pleased to publish the operational plan drafted by the Kingdom of Saudi Arabia in close collaboration with EILF

Special Report: Hepatitis C Elimination Plan Consensus Recommendations for the Kingdom of Saudi Arabia 2018

I. Policy

- The national HCV elimination plan should include all stakeholders who provide healthcare in the Kingdom and should not be limited to the ministry of health. These stakeholders are listed in Table 1.
- Expand the participants in the HCV Elimination program to include non-medical governmental institutions and bodies with the active participation of civil societies.
- Implementation and monitoring of this plan needs to be undertaken to ensure the adherence to the plan and to make the necessary changes when the need for them arise.
- Specific targets for SVR (90%)
- Number of treated patients annually for the first three years should either be (whichever is more)
  - 4,000-6,000 patients per year
  - 80% of newly diagnosed individuals
- All patients diagnosed with hepatitis C must be treated; both citizens and expats to the Kingdom.
- The recommendations in this document must undergo regular updates - at least every year.

Table 1

Healthcare Providers in Saudi Arabia	
Ministry of Health Hospitals University Affiliated Hospitals and Medical Cities Military Forces Health Services National Guard Health Services Ministry of Interior Health Services King Faisal Specialist Hospital and Research Center Private Medical Services	Saudi Association for the Study of Liver Disease and Transplantation

Other Stakeholders Who Will Contribute to The HCV Elimination Program
Ministry of Education Ministry of the Interior Ministry of Culture and Media Ministry of Labour and Social Development Ministry of Justice

II. Goals

- A better understanding of the epidemiology and natural history of HCV is warranted. However, for the time being, the total number of the infected patients in the Kingdom is estimated at 100,000 Saudi national patients, in addition to expats.
- The main goal is to reach elimination of HCV in the Kingdom of Saudi Arabia by 2030, in accordance with the World Health Organization for elimination of HCV. And these include; diagnosing 90% of the infected people with HCV and treating 80% of them.
- The best available models for hepatitis C suggest that achieving the elimination goals by 2030 will result in the prevention of 3,000 HCV-related deaths, 7,800 HCV-related cirrhosis and 260 related liver cancers.

Goals	Objective	Target by 2021	Activity	Stakeholder
Awareness	Awareness of HCV in society with focus on specific messages: • The Transmission of the virus (how it can and can not be transmitted) • The Natural history of the Virus • Who is at risk • The ease of treatment	75% of University Students understand the messages of the Awareness 75% of the high school teachers understand the messages of the awareness 75% of the social media users know about the HCV elimination programme	Teaching activities for Hepatitis C in schools Media coverage for World Hepatitis Day on July 28th Creating Arabic website for awareness Include HCV information in the education material in high-school	Ministry of Health Ministry of Education Ministry of Culture and Media Activist on social media
	Increase the awareness of HV among healthcare workers	90% of Healthcare workers know about the Hepatitis C Elimination program	Educational website that has CME accredited awareness activities	Ministry of Health Saudi Commission For Health Specialties
	Remove any risk of discrimination against HCV infected individuals	No patients are discriminated against because of HCV diagnosis An official decree that criminalize discrimination against infected individuals	Reporting mechanism for any discrimination against patients	Ministry of Justice Ministry of Labor The National Society for Human Rights

Goals	Objective	Target by 2021	Activity	Stakeholder
Monitoring	Get a better understanding of the epidemiology of HCV in Saudi Arabia, and the burden of the disease	Determine the prevalence of HCV in Saudi Arabia Identify new special high risk group to adjust screening strategy	Establishing the national database for HCV based on the national ID number	Saudi HCV Elimination program
	Monitor the rate of sustained virological response for HCV treated patients	Rate of SVR is accurately determined. The Risk factors for not achieving SVR identified.	National database for HCV that will easily report SVR rates Auditing for patients treated without reporting the outcomes of the treatment	Saudi HCV Elimination program

Goals	Objective	Target by 2021	Activity	Stakeholder
Micro-elimination	Patients with long term dialysis	Screen 100% of patients in dialysis units Treat 90% of the patients on dialysis	Include nephrologist in the hepatitis C elimination and grant privileges for using DAAs to dialysis patients	Saudi Society Of Nephrology And Transplantation Saudi HCV Elimination Program
	Incarcerated population	Screen 80% of the incarcerated individuals Treat 80% of the incarcerated patients with HCV	Collaboration with the ministry of interior to get a precise census of the incarcerated population and screen them for HCV	Ministry of Interior Saudi HCV Elimination program
	Rehabilitation and addiction treatment centers	Screen 100% of the patients in the rehabilitation center that deal with substance abuse Treat 80% of them	Target the rehabilitation and addiction treatment centers	Saudi HCV Elimination program Ministry of Health

III. Awareness

- In order to ensure successful elimination of HCV, awareness of the public of the natural history, the mode of transmission and the feasibility of cure from the virus must be stressed.
- In order to achieve 'buy-in' from society, the stigma of HCV needs to be corrected. With emphasis on
  - The difficulty of transmission of the virus, and the fact that it is not transmitted through daily contact
  - Sexual transmission is rare
- In order to avoid harm to HCV patients, collaboration with judicial authorities to forbid discrimination against those who are diagnosed with HCV is recommended
- The HCV elimination program will have to stress the meaning of cure from hepatitis C. A short report stating that the patient has achieved SVR and hence is regarded cured from HCV despite the persistence of the HCV antibodies. He has no HCV virus and does not constitute an infection risk.

IV. Screening Diagnosis

- A national database for all the individuals who undergo screening for HCV must be created. This will help to:
  - Monitor screening
  - Help in making the necessary modifications for the screening
  - As per the model developed by CDA (Center For Disease Analysis), Appendix 1), and will lead to great cost saving.
- All the current screenings for hepatitis C at different levels (pre-marital, employment and blood banks) should be linked to the national data base of screening. As we must establish and effective link between such screening programs and the treatment without delay.
- The patients who require screening are those who are known to have high risk for HCV exposure, and those include the patients in the table as targeted population patients and patients who are 40 years of age or older.
- Screening tests:
  - Rapid test for primary-care centers.
  - ELISA for first medical encounter, pre-marital, targeted groups and blood donors
- The technique for screening is summarized in the table below

Table 2

Screening Targets
• All individuals aged between 40 and 75
• First-degree relatives of HCV-positive patients or history of hemodialysis
• Those who received a tattoo/Hijama in an unregulated facility/setting
• History of transfusion with blood or organ transplantation before 1992
• Individuals who were ever in prison
• History of illicit injection drug use (IDU)
• Patients with Hepatitis B or HIV
• Treating physician's assessment that a patient has a risk for HCV.
• Any medical contact with healthcare services

Diagnostic Evaluation

- The first screening tool for HCV is the antibody for hepatitis C virus. This can be achieved by one of two methods
  - A rapid test that has a sensitivity above 98%. This test must have good data indicating its sensitivity. However, American FDA approval is not a prerequisite.
  - Blood sample with ELISA technique for HCV antibodies
- If the Anti-HCV antibody is positive, confirmation is done by establishing the presence of viremia by PCR technique. (the HCV viral load or HCV PCR)
- RIBA test is not indicated or required.
- The negative HCV PCR (no evidence of viremia) excludes the diagnosis of HCV even in the presence of the Anti-HCV antibody.
- Patients with clinical suspicion of HCV and negative antibody may be screened using HCV PCR in the following cases:
  - Immune suppressed patients from any cause, including HIV infection.
  - Patients with recent exposure to HCV (less than 6 months) and suspicion of acute HCV.

V. Evaluation

- Two levels of care will be implemented in the HCV elimination program, the expert and the non-expert
  - An expert is a physician who has the Saudi Commission for Health Care Specialties SCFHS registration as Consultant Gastroenterologist and/or Hepatologist, and has shown interest to managing complex cases for hepatitis C
  - Non-experts are all other physicians who are licenced by the SCFHS to practice in the Kingdom
- Treatment in the HCV elimination program should be based on the non-expert, this will ensure easy link to care and shorten the evaluation treatment cycle.
- All patients can be treated by non-experts except those mentioned in the table
- A full medical history and physical examination are always indicated. Focusing on the risk factors for HCV transmission, the possible physical signs of active HCV infection and the presence of any signs of chronic liver disease
- The basic evaluation steps for patients with established HCV that are prerequisite before treatment and the recommended tests that are preferably available are listed in Table 3

Table 3

Healthcare Providers in Saudi Arabia	
• Cirrhosis (whether compensated or decompensated) • Presence of ascites on U/S • Presence of splenomegaly on U/S • International Normalized Ration of more than 1.3 • Total Bilirubin more than 30 mmol • Platelets Count less than 150	• Patients with chronic kidney disease and creatinine clearance less than 30 • HBV or HIV co-infection • Organ transplant recipients • Interaction with a medication that is considered “High Risk” with no possibility of changing the medication • Relapsers/reinfection of HCV (DAA)

Evaluation of HCV Patients in Primary Health Care Centers	
Mandatory Steps in the Evaluation to Be Done Immediately Once Screening is +ve	
• HCV PCR • Complete blood count • Kidney function test • Liver Enzymes (ALT,AST, Alkaline phosphates and Bilirubin) • Coagulation profile • HBV screening (HBsAg)	Non-invasive assessment of the liver stiffness • FIB-4 should be done for everyone • FIB-4 of < 1.45 has more than 90% sensitivity to exclude advanced fibrosis • If the score is more than 1.45, Fibroscan is mandatory.

VI. Treatment

- All patients diagnosed with hepatitis C must be treated with the oral direct acting antivirals unless there is a clear reason not to treat. Some of these conditions are included in the table.
- The use of Interferon should not be part of the treatment for hepatitis C.
- The use of generic medications in the program is acceptable, provided that these medications have been approved by the Saudi FDA, and the regimen has shown encouraging results in real-world data.
- The ideal regimen for hepatitis C should be; simple, affordable, highly efficient, pangenotypic, addresses special needs and without Ribavirin.
- Until now, no single regimen can cover all different needed for the patients with Hepatitis C. A minority of patients remain in need of special regimens (decompensated cirrhosis, end-stage kidney disease and treatment failure).
- At this point the recommended regimen to treat patients by non-experts on a large scale is limited to Daclatasvir and Sofosbuvir for 12 weeks
- Other more difficult cases will be individualized according to the hepatologist experience with an evidence-based regimen
- Although successful treatment for hepatitis C exceeds 90%, it is estimated that 8,000 to 15,000 will need retreatment due to lack of response/relapse.
- The core concepts for retreatment of hepatitis C are listed in the table

Table 5

Conditions Where Treatment Is Not Approved or Controversial
• Pregnant patients • Children under the age of 12 years • Untreated Hepatocellular carcinoma • Life expectancy of less than 6 months • Advanced decompensated cirrhosis, who are candidate for liver transplantation

Conditions Where Treatment Is Not Approved or Controversial

- One tablet of Sofosbuvir 400mg with one tablet of Daclatasvir 60 mg for 84 days (12 weeks)
- Both medications are taken each as one tablet once daily with or without food
- Prior to starting therapy with these medications, a comprehensive review of the patient medication list is mandatory and evaluation for possible in-teraction is the responsibility of the treating physician

Core Concepts for Retreatment of HCV

- Avoid using the same regimen for retreatment
- Sofosbuvir use is a must, even when it was part of the original regimen
- NS5A exposure should be treated with Sofosbuvir + NS3 regimen or Triple regimen (preferred)
  - This should not be treated with Sofosbuvir + NS5A
- If Sofosbuvir cannot be used, a second generation NS5A with NS3 and ribavirin for a prolonged duration is recommended

VII. Outcomes

- Once the patient finishes his treatment, the HCV viral load should be repeated after 12 weeks from the end of treatment. The objective of this will be to check for the sustained virological response at 12 weeks (SVR-12). SVR-12 is achieved if the virus is not detected at this point.
- SVR-12 is equal to cure from HCV. However, a repeat viral load in 24-48 weeks should be done to confirm cure and to discharge the patient from the program.
- Patients with advanced fibrosis or cirrhosis require special care, as the risk of complications from their advanced liver disease will remain despite curing the virus.
  - This is particularly true for the risk of liver cancer (hepatocellular carcinoma).
  - We recommend the initiation of a national screening program for hepatocellular carcinoma. Such programs when implemented elsewhere results in earlier diagnosis, cost saving and better outcomes overall.
- The patients who are cured from hepatitis C will receive a “document” disclosing that they have been cured. This might play an important role for the patient from a social perspective (marriage and/or employment).

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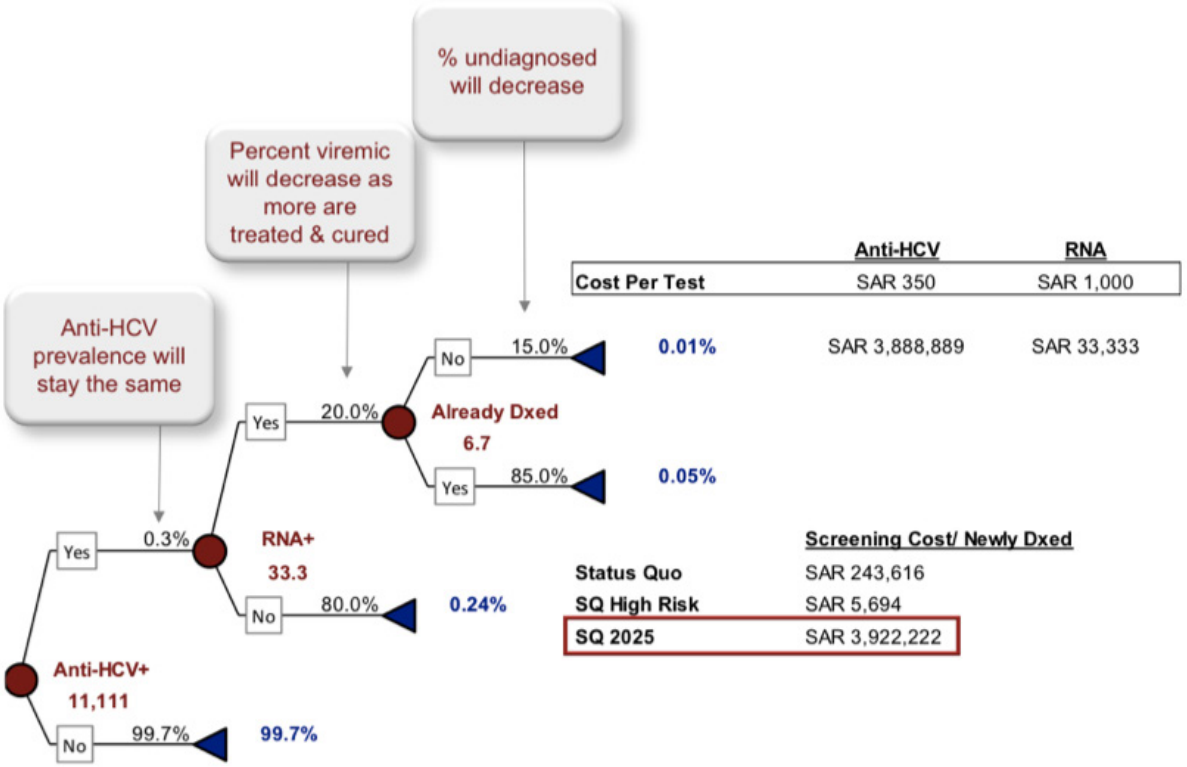
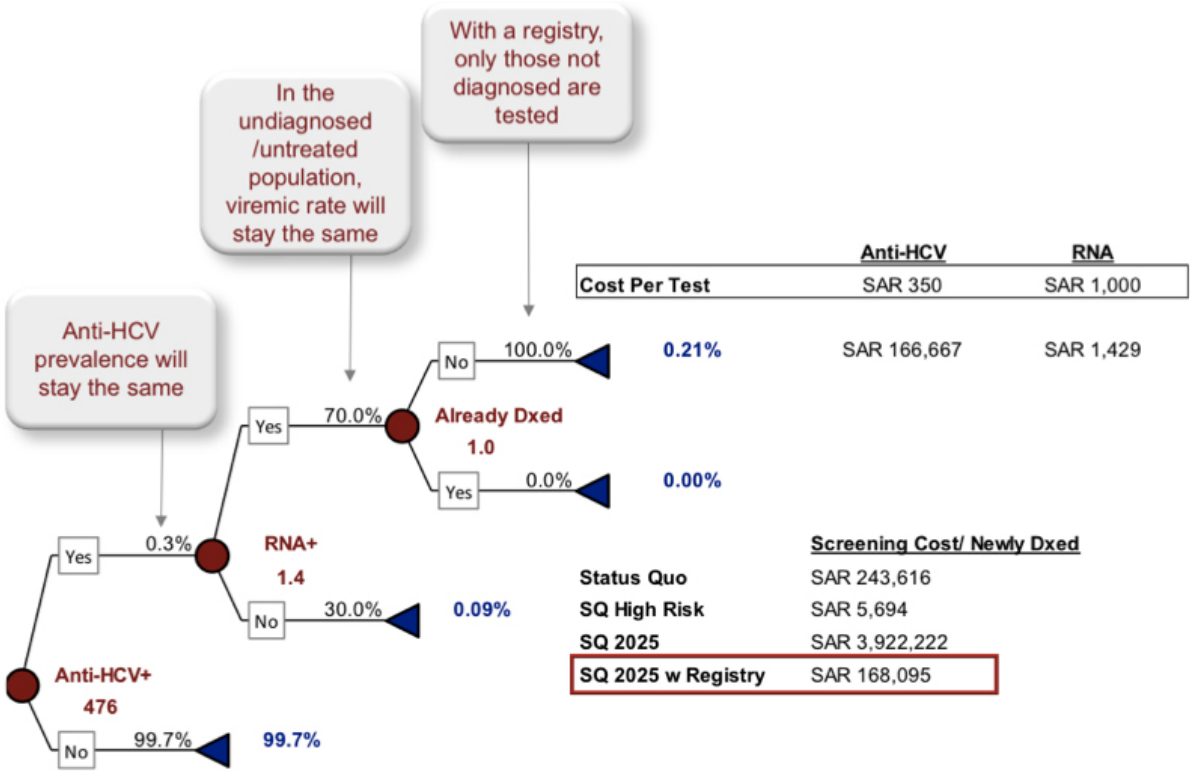
Appendix

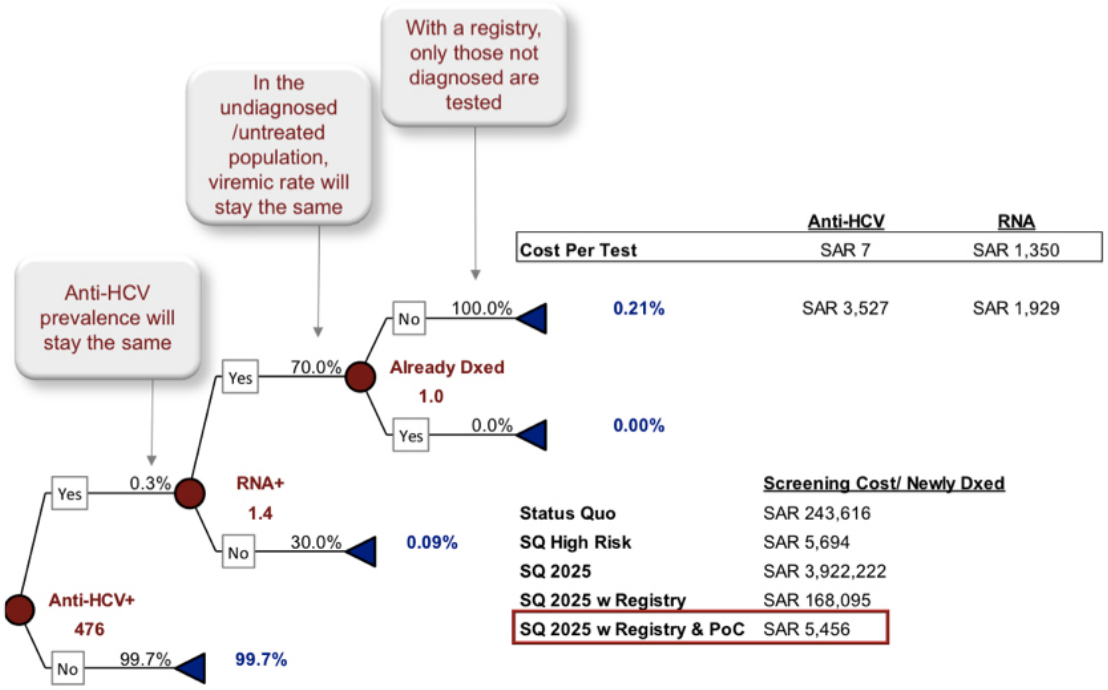


The cost of screening will increase exponentially with treatment of HCV, until the cost of diagnosing one patient reaches almost 4 million SAR. As repeat screening with HCV antibody to individuals who were already screened. In addition to As more patients will be isolated antibody positive, so more patients will require unnecessary HCV PCR.

Please note that the cost of Anti-HCV included the blood extraction, transportation and retrieval of the results.



With the introduction of a registry of the screened and treated individuals. No increase in the number of unnecessary HCV PCR will be done. As the treated individuals and the previously screened



The use of rapid screening at the point of care will further decrease the cost of screening