Treatment Program Policy Analysis

EGYPT'S VIRAL HEPATITIS PROGRAM

THE WORLD BANK

Egypt's Viral Hepatitis Program
Treatment Program Policy Analysis
2017

This report is developed as part of the World Bank's Technical Assistance on Strengthening Egypt's Response to Viral Hepatitis.

Comments and suggestions concerning the report contents are encouraged and could be sent to emassiah@worldbank.org

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Abbreviations

CAPMAS	Central Agency for Public Mobilization and Statistics
CDC	Centers for Disease Control and Prevention
CHAI	Clinton Health Access Initiative
CHC	Chronic hepatitis C
CS	Caesarean section
DAA	Direct-acting antiviral agent
DOT	Duration of Treatment
EASL	European Association for the Study of the Liver
EDHS	Egypt Demographic and Health Survey
EVR	Early virologic response
GOE	Government of Egypt
HBV	Hepatitis B virus
HCC	Hepatocellular Carcinoma
HCP	Healthcare Professionals
HCV	Hepatitis C virus
HIO	Health Insurance Organization
HIV	Human Immunodeficiency Virus
HRQOL	Health Related Quality of Life
IDU	Intravenous Drug User
IFN	Interferon
MOF	Ministry of Finance
MOHP	Ministry of Health and Population

MOIC	Ministry of International Cooperation
NCCVH	National Committee for the Control of Viral Hepatitis
OOP	Out of Pocket
OR	Odds Ratio
PAT	Parenteral Antischistosomal Therapy
PCR	Polymerase chain reaction
PEG-IFN	Pegylated Interferon
PVT	Private
RBV	Ribavirin
RBV	Ribavirin
RNA	Ribonucleic acid
SOFO	Sofosbuvir
SVR	Sustained virologic response

Definitions

Cirrhosis: progressive scarring of liver tissue that may affect the effectiveness of chronic hepatitis C treatment. Cirrhosis is typically biopsy-proven in clinical trials of chronic hepatitis C therapies.

Decompensated cirrhosis: the presence of cirrhosis plus one or more complications including oesophageal varices, ascites, hepatic encephalopathy, spontaneous bacterial peritonitis, hepato-renal syndrome, or hepatocellular carcinoma.

Genotype: a classification of hepatitis C based on genetic material in the RNA strands of the virus. There are 6 main genotypes, which are further divided into subtypes in some cases.

Interferon-ineligible: patients in whom interferon therapy is contraindicated due to such conditions as anaemia, alcohol abuse, advanced or decompensated cirrhosis, or severe psychiatric disorder.

Interferon-intolerant: patients who discontinue interferon therapy prematurely due to side effects.

Sustained Virologic Response (SVR): absence of detectable HCV RNA, measured 12-24 weeks following the completion of treatment.

Relapse: recurrence of detectable viral RNA at some point after achieving an undetectable HCV viral load during treatment.

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Overview

This report provides a comprehensive landscaping of the viral hepatitis treatment market in Egypt, which in the previous years has been changing dynamically, as more patients are now enrolled on new treatments. With optimistic goals to treat as many patients as possible, the country is preparing itself to walk the path of eliminating Viral Hepatitis.

The report covers the viral hepatitis pharmaceutical and treatment market in Egypt from many different aspects, beginning with the epidemiology data, and then moving with the patient journey from the early phases of infection and presentation till reaching treatment outcomes, moving through the process of different coverage channels whether governmental, private or out of pocket with gap analysis of each step and recommendations towards how to reach a reform plan that we hope will aid in reaching an ultimate goal of complete elimination.

Egypt is currently being perceived as a global leader when it comes to mass treating its population from the disease. From markedly lowering the prices of medicines to initiating mass screening and treatment programs, many firsts have been recorded, and with astonishing results. The report will help to document those experiences and how they were achieved. This, hopefully, will help guide other country programs based on what, and what did not, work well in Egypt.

Executive Summary

As of 2016, more than 5 million Egyptians were estimated to have CHC, making the prevalence of CHC in Egypt the highest in the world. The NCVVH, at the time, identified nearly 1 million patients who were already aware of their condition, while the remaining patients had yet to be diagnosed. Out of that total number, 2.5 percent suffer from decompensated cirrhosis and around 30,000 are on dialysis or have stage 4 CKD. The burden associated with HCV infection in 2013 amounted to $3.19 billion in both direct healthcare costs ($560 million) and indirect costs of loss of life to premature mortality and cost of disability ($2.63 billion).

Around 60 percent of diagnosed CHC cases are males who were discovered while asymptomatic during mandatory screenings under various employment or travel programs. Usually the diagnostic tests requested by HCP are ElISA, PCR, liver function tests, CBC and ultrasound.

During the era of IFN regimens, which used to cost more than 11,000 USD per patient, the public sector was the main player responsible for more than 90 percent of CHC patients on treatment. The NCVVH treated 350,000 patients using IFN, of which 175,000 were non-responders and came back for treatment. Since the arrival of the DAA's era, as of mid-2017, 1.2 million patients have been treated with the new medicines, out of which 900,000 were in the public sector and the rest were either through out of pocket or through private insurance.

Nowadays the market is moving heavily towards getting treatment through the public sector, mainly because treatment at the public facilities is nearly free of charge. Nearly all costs, except for a very minimal user fee of less than 2 USD per patient, are covered by the public facilities. Many treatment combinations are used at these facilities, but since 2016 Egypt has shifted to locally manufactured generic products.

In the private sector, the most common treatment combination is Sofosbuvir + Daclatasvir ± RBV (Generic), representing 60 percent of prescribed combinations. Physicians perceive the success rate of the new regimens to be around 95 percent or more for non-cirrhotic, and around 90 percent for cirrhotic patients. Most

often, the treatment is given for a duration of 3 months, except for some resistant cases where treatment is usually extended to 6 months.

In terms of dollar value, the private sector is expected to cover nearly 45 percent of the total CHC market vs. 55 percent for other sectors (public and other governmental). A retail sales analysis at the end of 2016 projected that 900,000 patients would receive treatment across all sectors that year (with 250,000 paying out of pocket).

For the public sector, patients can seek treatment from either the Ministry of Health and Population (MOHP) or Health Insurance Organization (HIO), depending on their insurance coverage. Both require an online registration by the patient, and usually an appointment is scheduled with a treating doctor on the same week of registration. NCCVH records have shown that 50 percent of the registered patients do not show up for the next step, mainly attributable to the lack of awareness and internet illiteracy. Also, many patients, given the relatively low cost of treatment in the private sector, have opted to pay out-of-pocket in the private sector rather than waiting for the bureaucratic processes of the public sector.

The pharmaceutical industry's perception of the eradication of the CHC is that it is feasible if there is more collaboration between the industry and the NCCVH, in terms of organizing the importation of active pharmaceutical ingredients, pricing of medicines, and ensuring a consistent ordering policy by the public sector, so that they are able to meet the needs of the NCCVH. Yet quality control of locally manufactured generics needs to be of more concern, given the current low sale prices.

Introduction

This report comes among a series of reports undertaken by the World Bank on the request of the Government of Egypt (GOE) for technical assistance to inform policies that would strengthen the country's response to viral Hepatitis C. The President of Egypt has specifically requested the Bank's technical assistance during his bilateral negotiations with the Bank's President at the latter's visit to Egypt in July 2015. Further, the Ministers of Health and Population, International Cooperation, and the Deputy Minister of Finance all reaffirmed this request during a health sector mission to the country in October 2015.

The purpose of these reports is to provide technical assistance to the GOE (Ministry of Health and Population and Ministry of Finance) to strengthen Egypt's response to viral Hepatitis. These include a policy analysis of the treatment program (aim of this work), an assessment of the fiscal impact of needed interventions, input on technical design of the screening program, recommendations for strengthening the M&E capacity of the Egyptian Viral Hepatitis program, and further development of the "Plan of Action for the Prevention, Care and Treatment of Viral Hepatitis, Egypt 2014-2018". At the same time, the work will spearhead and help coordinate efforts undertaken by other development partners, as well as catalyse the transformation of the currently fragmented governmental efforts into becoming a single effective program.

This report is critical given the GOE's prioritization of the issue on its agenda. Government officials have pledged a swift action on the disease with promises of marked reduction of prevalence rates within a few years to less than 1 percent of the population. Further, the President of Egypt has publicly promised to treat at least 1 million patients by the year 2018, a presidential election year.

Chronic Hepatitis C (CHC) is epidemic in Egypt. Elimination through prevention, screening and treatment has become a national priority to policymakers, public health and medical care stakeholders. This report was developed to provide a better understanding of the pharmaceutical market dynamics within that set of priorities. Egypt has made certain strides and has managed to move ahead with an ambitious treatment program, both in the public and private sectors. This report will shed light, in some detail, on this progress, as well as provide a descriptive analysis and recommendations on the program.

Report Methodology and Time-Frame:

The report was developed in 5 phases:

1. Systematic literature review.

2. Thorough analysis of the public system for treating viral hepatitis at both the central NCCVH level and the public hospitals/centres and HIO facilities.

3. Focus group discussions with healthcare professionals (hepatologists) including members of NCCVH. Interviews were done in an audio-recorded qualitative and quantitative setting, using semi-structured questionnaire with transcripts and verbatim analysis. 11 interviews were conducted with Hepatologists for a duration of 60 minutes each.

4. Focus group discussions with pharmaceutical companies producing CHC products, both multinational and local manufacturers.

5. Analysis of retail audit data and secondary reports for private markets.

6. Report timetable: The study was conducted between March and September 2016.

Epidemiology

i) Global Epidemiology of Viral Hepatitis:

Hepatitis C viral infection (HCV) is a major global health problem with a prevalence of about 2.5 percent globally and around 3.5 percent in some regions such as the Middle East. An estimated 130 million people are currently infected worldwide. Without treatment, about 85 percent of the infected cases will advance to chronic infection with HCV, with subsequent cirrhosis, end-stage liver disease or hepatocellular carcinoma. HCV accounts for about 27 percent of the burden of cirrhosis and 25 percent of hepatocellular carcinoma globally, resulting in a major burden of disability and premature death in adults, and significant costs to affected families and society in healthcare expenditures and loss of productivity.

At present, there is no effective vaccine to prevent the infection. Until 2015, the standard treatment protocol in Egypt had been limited to a combination therapy of subcutaneous interferon injection and oral ribavirin, for a regimen of 24 to 72 weeks. This treatment was not only very expensive, especially in a developing country context with a very large burden of disease, but also characterized by low adherence to treatment, poor overall effectiveness at about 50 percent cure rate, and considerable side effects. Recently, the advent of new Direct Antiviral Agents (DAAs) with simple oral administration, high cure rates and better adherence rates have made it possible to treat this subtype of hepatitis, albeit at a costly price initially.

Similarly, Hepatitis B viral infection is the world's silent killer, with nearly 248 million people infected globally, of which 786,000 die each year. Unlike Hepatitis C, Hepatitis B has a preventive vaccine of 3 doses available in the markets, and is increasingly adopted by governments worldwide as a main component of their compulsory vaccination programs for children.

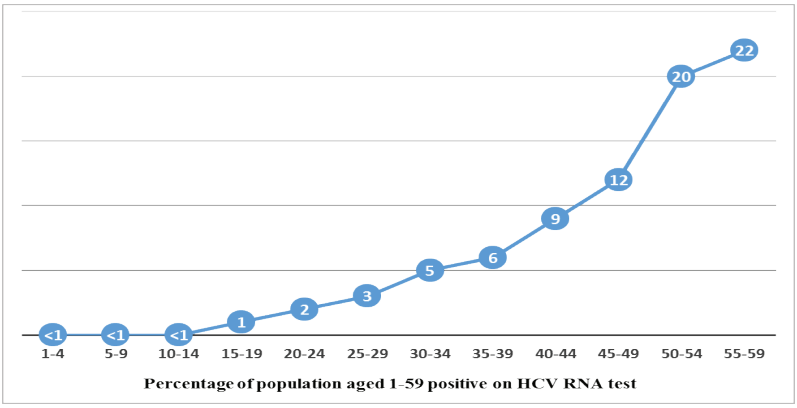
Transmission of both types of viruses has a lot to share with HIV. While vertical and childhood transmissions are the mainstay of new infections in sub-Saharan Africa, iatrogenic causes (unsafe blood transfusion, unsafe injections and improper infection control practices during medical care provision), and unsafe sex (especially among men who have sex with men- MSM) are the predominant

modes of infection in more developed countries. Progression to end-stage liver disease from initial infection of both types is long and asymptomatic. The acute infection, if not resolved, usually progresses to liver cirrhosis, hepatocellular cancer, and may necessitate liver transplantation—putting huge burdens on the healthcare systems, financial resources, and workforce productivity of the affected communities.

ii) Epidemiology in Egypt:

Egypt has the highest HCV infection incidence and prevalence in the world at about 0.2 percent and 7 percent of its adult population (15-59 years), respectively, with the latter near 15 percent in some geographic areas. Close to 70 percent of new infections occur in persons less than 25 years of age. As of 2017, although more than 1 million Egyptians have been treated with DAAs, nearly 4.5 million adults are still chronically infected, with an estimated 150,000 new people infected annually, and about 40,000 dying every year, making Hepatitis C the third-leading cause of death in Egypt after ischemic heart disease and stroke. The main reason behind such high incidence and prevalence rates is iatrogenic, owing to unsafe therapeutic injections of parenteral anti-parasitic drugs with reusable glass syringes to control the schistosomiasis in the 1960s and 1970s (Figure 1), and later on, bad infection control practices in public and private health care facilities, coupled with suboptimal screening for transfused blood.

Figure 1: HCV Prevalence in the Population age 1-59, by Age, Egypt 2015 (EDHS)



Source: EDHS, 2015

As a result of recent scientific advances of HCV virology, a new group of Direct-Acting Antiviral (DAA) drugs has been developed, with significantly shortened treatment period (down to 12 weeks), ease of administration (oral), fewer side effects, and much higher effectiveness resulting up to 97 percent cure rate in some settings, depending on the HCV genotype. The new drugs, such as Sofosbuvir and Daclatasvir, are often given in combination with ribavirin for best results. Many other newer molecules belonging to the same family are currently being licensed around the world, with fewer side-effects, easy administration and less costs.

In 2015, the MOHP started its own program of treating patients. An online self-application registry was initiated, to which nearly 1.8 million people applied as of 2016. Nevertheless, due to availability of funding and availability of locally-manufactured generic medicines, by the end of 2016 the program had treated about 800,000 patients. The program is based on medical criteria for selection, leaving the poor at risk of being crowded out, while those who have health insurance or have access to the Program for the Treatment at the Expense of State, a state-financed program for the uninsured, would have better access for the medicines. Moreover, treatment was being offered at 56 dedicated liver units/centers around the country by 2016.

The GOE has recently showed political leadership by increasing its commitment to prevent, contain and treat the HCV epidemic. The presidency went public with its plan to procure enough medicines to treat 1 million patients with the new generation of drugs at reasonable prices. It has increased procurement of favourable negotiated brands and supported cheaper locally manufactured generics. The MOHP has also allowed various companies to sell their products, at higher prices, at community pharmacies for patients paying out of pocket, albeit with tight controls for medical supervision and registration.

Hepatitis B also remains a large problem. Nearly 800,000 Egyptians aged 1-59 years have an active hepatitis B infection as shown in the latest EDHS data (2014) and CAPMAS (official statistical body) projections. The GOE added Hepatitis B vaccine to the routine national vaccination program 15 years ago. The 3 doses are taken at 2, 4 and 6 months of age. This has remarkably reduced the prevalence rates in the age group 1-14 years to below 0.1 percent. On the other hand, age groups

15-59 show a 1.5 percent infection rate. The GOE of Egypt is also targeting high risk populations with vaccinations, notably the healthcare workers. No national government sponsored treatment program is available in the country.

iii) Epidemiology of Chronic Hepatitis in Chronic Kidney Disease patients:

There are more than 2.6 million reported CKD cases in Egypt, of which 2 percent will suffer ESRD[1] (End Stage Renal Disease), double the global norm (1 percent) (Kramer 2009). Many of those patients undergo regular dialysis at dialysis centres all around the country. The sero-conversion rate (of acquiring infection with Hepatitis C) is high, at 12 percent annually. This is mainly attributed to the lack of safe infection control practices at those centres, especially within the public facilities.

As of 2008, there were more than 52,000 ESRD patients in Egypt (Barsoum 2013), 52 percent of whom had HCV. However, actions have since been taken to reduce this number. According to the latest estimates, the range now has become 30 – 55 percent as a result of:

1. The increasing use of erythropoietin instead of blood transfusions to treat anaemia associated with ESRD.
2. Better Infection control practices at dialysis units.
3. Dedicating dialysis machines for HCV infected patients separate from those used by non-HCV patients.

Thus, the number of patients suffering from both ESRD (also known as Stage 5 CKD) and CHC is between 16,000 and 29,000 patients, while Stage 4 CKD with CHC is calculated to be 2,847 patients ("Chronic Kidney Disease - World Kidney Day", 2017). This has put an emphasis on prioritizing patients with ESRD as among the first cohorts of patients for the National treatment program. It is worth noting that only a few DAAs are licensed for use with HCV patients suffering from ESRD, most of which are imported.

(1) Expert opinion: Dr. Mohamed Hany Hafez.

CHC Patient Characteristics in Egypt

The following section was developed based on inputs of the professional hepatologists interviewed during the study (Expert Opinion). As shown in Figure 2, after acquiring an infection, most patients pass through an acute phase lasting 1-2 months during which he or she may not have any symptoms (asymptomatic) or, in 20-30 percent of cases, may show a transient jaundice. A substantial number of patients will then undergo spontaneous resolution as the body's immune system overcomes the disease. Nevertheless, 50-85 percent of those infected (percentage varying from different study settings) will enter into a chronic infection phase within 6 months. This chronic infection may last years, with 20 percent of the patients developing cirrhosis. Further, hepatocellular carcinoma may develop in nearly 1-4 percent of those infected.

Figure 2: Phases of HCV from incubation to chronic

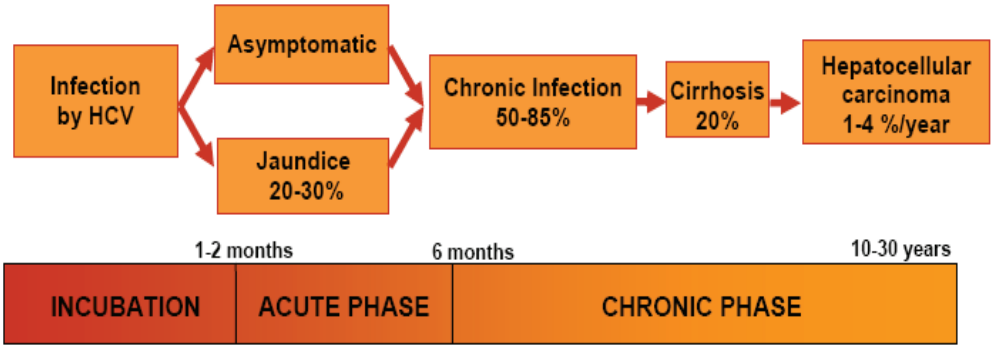
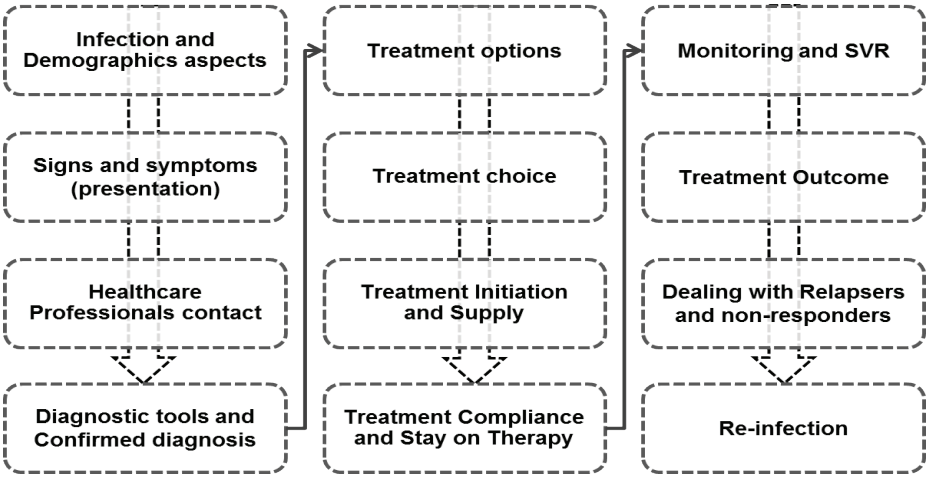


Figure 3 illustrates a typical CHC patient journey through many different diagnostic, treatment and treatment outcome milestones. The latter is usually categorized into either: (i) cure; (ii) no response; (iii) relapse; or (iv) partial response.

Figure 3: CHC patient journey



Demographic Characteristics:

Although the latest national DHS data find no significant differences between male and female prevalence in the country, data collected in this study from patients accessing both public and private entities have shown the following:

- Six out of ten registered HCV patients are male. This is mainly attributed to:
  - Males are more likely to be screened for HCV as a pre-requisite for employment applications in Egypt. Further, the workforce is predominantly male, so males are more likely to undergo on-the-job screening administered by the employer.
  - Applying for a working VISA for the Gulf countries includes a mandatory HCV screening test as one of the requested documents for the VISA issuance.
  - In Upper Egypt, males go to traditional barbershops, a practice that prompts males to screen themselves more frequently than females in fear of acquiring the infection.
- About 88 percent of patients are in the age group of 18-65. (Table 1)
- Almost half of the patients under physician care reside in urban areas.
- The most common HCV patient co-morbidities as reported by treating doctors were diabetes (almost 30 percent) and other non-communicable diseases (Table

2). Patients with a history of having Schistosomiasis constituted almost one third of CHC patients.

Table 1: Percentage of HCV patients' age ranges:

#	Age Ranges	Percent HCV Patients
1	0-17	1%
2	18-45	43%
3	46-65	45%
4	65+	10%

Table 2: Percentage HCV patients having the following co-morbid conditions:

#	Co-morbid Conditions	% of HCV patients with…
1	HIV positive	0%
2	Hepatitis B	7%
3	Cardiovascular Disease	14%
4	ESRD Disease (patients on Dialysis or Stage 4 CKD)	3%
5	Psychiatric Disorders (i.e. Depression, etc.)	6%
6	Diabetes	29%
7	Other co-morbidities (HTN, Obesity, and Anemia)	23%
8	None	42%

Infection:

Physicians have stated that many CHC patients reported a history of exposure to the following: (i) blood transfusion; (ii) attending clinics with suboptimal level of sanitation; and (iii) sharing personal shaving devices. Further, a substantial number of patients were either related to or are members of the same family, suggesting the sharing of unhygienic habits.

Signs and Symptoms (presentation):

Patients usually present asymptomatically due to accidental discovery of the virus when they undergo testing for various reasons as stated earlier. However, some do present with symptoms like fatigue, ascites and/or encephalopathy. Sometimes, the first signs are abnormal lab results such as elevated liver enzymes or ultrasound examination showing fatty liver.

Healthcare Professionals contact:

The first health provider contact for symptomatic cases will usually be a GP doctor, pharmacist or nurse. However once the diagnosis has been confirmed, patients tend to seek hepatologists in their public or private practices via the multiple and fragmented financial coverage mechanisms available in the country. In the private sector, nearly 63 percent of hepatologists report diagnosing patients with CHC for the first time themselves. However 37 percent are referred from other doctors with a diagnosis already (Table 3).

Table 3: Percentage of HCV patients referred to physicians' office from another physician:

#	Source	Percent HCV Patients
1	Referred-in from another physician with an HCV diagnosis	37%
2	Diagnosed with HCV by Physician	63%

Of the Hepatitis C patients who are referred, 79 percent are referred from a private clinic, the rest from the public sector. This indicates that the majority of patients have a tendency to seek multiple consultations regarding their condition (Table 4).

Table 4: Source of referral of HCV patients

#	Source	Percent HCV Patients Referred From…
1	Public sector	21%
2	Private sector	79%
3	Other (Specify) _____	0%

Among patients attending private clinics, the sources of coverage for pharmaceuticals needed for treatment varied. Only 38 percent opted to buy it out of pocket, while more than half obtained them through the public domain, despite the long delay in waiting lists (Table 5).

Table 5: No. of days from indicated as HCV till receiving a treatment

#	Source	Percent of patients	No. of days from indicated as HCV till receiving a treatment
1	Health Insurance	22%	157 Days
2	MOHP state coverage program	32%	205 Days
3	Private Insurance	3%	13 Days
4	Companies / big accounts	2%	1 Day
5	Military / Police	1%	21 Days
6	Out of Pocket / Self-Pay	38%	1 Day
7	OOP (Subsidized value of brand)	2%	1 Day

Diagnostic tools and Diagnosis:

The following diagnostic workups were mainly used for the majority of patients, with variable frequency (Table 6):

- Rapid screening tests (with relatively low sensitivity and even lower specificity rates)
- PCR and viral load
- HCV ElISA (3rd generation)
- Liver Function (ALT – AST)
- Renal Function test
- CBC
- Ultrasound (to estimate cirrhosis level)
- Liver biopsy (very few)

Table 6: The frequency of the prescribed investigations by doctors

#	Test Conducted	Percent of Patients Tested for HCV Using…
1	Liver Function Tests (ALT/AST)	100%
2	Viral load / Quantitative HCV test	90%
3	Qualitative HCV test	0%
4	Genotype Test	1%
5	Liver Biopsy	0%
6	Ultrasound	70%
7	Other (Fibroscan, CBC, ELIZA, PCR)	60%

Laboratory testing is perceived by hepatologists as reliable and relatively cheap in Egypt. The full aforementioned package could cost the equivalent of 56 USD in private sector laboratories but is free for patients seeking care in the public facilities and centres. However, some patients may opt for testing in the private laboratories, provided they can afford it, to avoid long waiting times in the public domain. Some patients may refrain altogether from doing the confirmatory lab tests for one or more of the following reasons:

■ Asymptomatic patients may not believe HCV is a serious disease, as they are not suffering, and they may have friends and relatives who have been diagnosed with CHC for decades with no immediate health concerns.

■ Some patients are afraid to be diagnosed with CHC and begin a treatment journey that might bear serious consequences in terms of side-effects, financial burden or psychological stress.

■ Some patients cannot afford diagnostic tests it the private sector yet are reluctant to seek them in the public facilities owing to the time consuming and bureaucratic procedures.

Table 7 illustrates hepatologists' perceptions of the status of HCV patients visiting to their clinics.

Table 7: relative perception of hepatologists by percent

#	Type of visit	Percent HCV Patients
1	Therapy Naïve (diagnosed patients that have never been treated and may be treated in the future)	**26%**
2	Currently Treated (diagnosed patients that you are currently treating)	**41%**
3	Successfully completed therapy (previously treated with HCV therapy successfully, sustained viral response (SVR))	**30%**
4	Relapsed from therapy (previously treated with HCV therapy successfully, but had un-sustained viral response 24 weeks after completion of therapy and who are not currently receiving treatment)	**3%**
5	IFN Treatment Non-responder (previously treated with HCV therapy unsuccessfully, little or no viral response during therapy and who are not currently receiving treatment)	**0%**
6	Discontinued therapy for reasons other than efficacy	**1%**

Burden of treating CHC patients:

Although the World Bank is completing an assessment of the economic burden of the disease in a separate study, prior evidence has showed mixed economic estimates. In a study by Waked (2014), the total economic burden of HCV in Egypt was calculated in 2013 to be around 80 million USD and projected till 2030 from year 2013 based on 2013 current figures to be 3.2 Billion USD or 1.4 percent of GDP. Direct healthcare costs were calculated to be 560 million USD and indirect costs of loss of life due to premature mortality and cost of disability 2.63 Billion USD (Waked et al., 2014)

In that study, investigators forecasted the future costs based on different scenarios. In one of the scenarios, in which the success rate of treatments reached 90 percent (below the success rates of 97 percent announced by the government and NCVVH in 2016), the result was 32 percent fewer viremic individuals in 2030 compared to the 2013, and total costs declining by 30 percent to 2.42 Billion USD. Direct costs in 2030 were estimated at 363 million USD, a decrease of 35 percent from 2013. Indirect costs were estimated at 1.88 billion USD, a 30 percent decrease compared to 2013, assuming 65,000 patients were treated annually. These numbers are clearly outdated, as treatment numbers in 2015 and 2016 significantly exceeded these predictions.

In a study just completed by the World Bank (Haacker 2016), multiple treatment and screening scenarios were modelled using the most up-to-date information on costs of treatment and screening in Egypt, as well as data on the prevalence and incidence of the disease. These studies, described in more detail in that report, included a demand-driven "treatment scenario," in which patients voluntarily seek out treatment; a "screening scenario," in which the government implements a screening program to screen 10 percent of all Egyptian adults every year and treat those who screen positive; and an "elimination" scenario, in which screening is rapidly scaled up so as to cover essentially the entire population over the next 5-6 years.

Under the "treatment" scenario in that study, deaths from Hepatitis C and the number of new infections are expected to decline by about one-half by 2030. Screening (as modelled under the "screening" and "elimination" scenarios) would significantly augment these effects, averting up to two-thirds of deaths

and reducing new infections by around 90 percent in the elimination scenario. In terms of direct healthcare costs, the "treatment scenario" would be refinanced by savings in costs of within 6 years, whereas screening and elimination would require greater spending in the short-run (elimination even more so than screening), but they are considered cost-effective by conventional norms, and both approaches are much more effective at finding and treating infected patients than the treatment approach alone. For more details on the relative costs and impacts of these policies, please see the full report.

Burden of not treating CHC patients:

Chronic HCV should be analysed as a multifaceted systemic disease leading to heavy direct and indirect costs. The effects of HCV on the liver and the rest of the body significantly increase its potential burden, making treatment crucial from a therapeutic and preventative point of view (Cacoub et al., 2014). Complications include:

1. Liver related complications

a. Cirrhosis: Approximately, 20 percent of people infected with Hepatitis C will develop cirrhosis if not treated (HCV Epidemiology in the United States, 2017). In 2010, 24.8 percent of HCV-infected patients were reported to have already progressed to cirrhosis (Deuffic-Burban, 2010).

b. Hepatocellular Cancer (HCC): Hepatitis C-associated liver disease is the number one cause of HCC, accounting for approximately 50 percent of cases. In a study conducted in Menoufia in 2013, HCV infection was present in 91 percent of the HCC cases (Shaker et al., 2013). The cost paid by the general budget for HCC treatment per patient per year varies from 2,000 to 12,000 EGP, according to the stage of the cancer.

c. Liver Transplantation: Hepatitis C-associated liver disease is the number one indication for liver transplantation and approximately one-third of all people on liver transplantation waiting lists have hepatitis C-associated liver disease. The MOHP contributes 75,000 EGP for transplants; however, the actual overall cost may reach up to 250,000 EGP. An additional 70,000 EGP are also paid for post-transplantation medications.

2. Extra-hepatic complications

Extrahepatic manifestations have been reported in up to 74 percent of HCV patients, including:

a. Autoimmune Disorders: Referred to as extrahepatic manifestations (EHMs), these affect 40 – 70 percent of patients with HCV. Mixed Cryoglobulinemia (MCG) is the most common, affecting up to 50 percent of chronic hepatitis C patients (Al Kafrawy et al., 2014).

b. Peripheral Neuropathy: Patients with chronic HCV infection have a high incidence of developing peripheral neuropathy (from 30 to 45 percent).14

Besides the additional costs of complications from untreated HCV, CKD patients with untreated HCV pose particular concerns. According to expert opinion, these individuals may infect 4-5 new people within their community in their life time (mainly within their own family).

Analysis of Egypt's Pharmaceutical Market for HCV

With the discovery and development of a new category of drugs against Hepatitis C known as Direct Acting Antivirals, or DAAs, treatment has become shorter, better tolerated, and more successful, with cure rates close to 100 percent for patients in the early stages of the disease.

The latest generation of DAAs against Hepatitis C includes molecules such as Sofosbuvir, Ledipasvir, Daclatasvir, Grazoprevir, Elbasvir, Velpatasvir, Ravidasvir, used in combination with each other or with older antivirals such as Ribavirin. According to current data, the combination of Sofosbuvir with Daclatasvir has the best overall spectrum of efficacy against all six genotypes of the Hepatitis C virus. Sofosbuvir plus Ledipasvir is an alternative and may be equally effective against the genotype 4, which is dominant in Egypt.

In contrast to the early years of HIV/AIDS, in which antiretroviral (ARV) drugs were very costly and hard to obtain in low and middle-income countries, originator companies making the DAAs decided early on to provide licenses to generic manufacturers to make and sell these products in developing country markets. Had they not, the high prices charged in developed markets would have blocked access for most Egyptians. This approach has led to a rapid development

of several generic alternatives, led by companies in India and Egypt. There is now growing availability of low price generics in national and international markets, and several of the larger Indian manufacturers and one Egyptian manufacturer have initiated the WHO Prequalification process. The first WHO Prequalified generic Sofosbuvir will soon become available. The same organizations and international experts that helped to make ARVs for HIV/AIDS affordable are now working with producers of the active pharmaceutical ingredient (API) and with generic manufacturers of finished forms. This will ensure a supply of quality, low cost DAAs for Hepatitis C and allow countries with a high disease burden, such as Egypt, to plan and afford mass treatment campaigns at a scale that makes effective control or elimination of the disease a possibility (Dowdle & Cochi, 2011).

The work of international experts at WHO, CDC, CHAI and others has created a transparent market environment in which it is possible to benchmark prices for generic DAAs and develop sourcing strategies. Data from these sources are being used in this analysis. As the market changes constantly with the arrival of new molecules, introduction of additional generics, growing demand, and technical progress that may result in cheaper raw materials, today's data may need to be reviewed and updated at least in yearly intervals.

Overview of the pharmaceutical sector in Egypt

The pharmaceutical sector in Egypt is regulated by the Egyptian Drug Authority (EDA), which is part of the MOHP. EDA has three sub-units:

■ CAPA – Central Administration of Pharmaceutical Affairs - for core functions such as licensing of pharmaceutical products (also food products and medical devices, but not biologicals), professional licensing, inspection and supervision of the sector.

■ NODCAR – the National Organization for Drug Control and Research, responsible for quality assurance of the CAPA regulated products and home of the drug quality control lab.

■ NORCB – the National Organization for Research and Control of Biologics, which assumes a range of functions for the regulation and quality control of biologics and blood products.

A new law is currently in preparation that foresees a spin-off of the regulatory body to give it a more autonomous status. It also envisions a separation of responsibilities so that the new EDA would only deal with medicines and medical devices. According to the draft, the new EDA would report to the president, thereby eliminating the current potential for conflict of interest if the same ministry that regulates the industry is also the single largest buyer and price regulator.

Another legislative initiative (Decree 425) aims at speeding up the registration process for new medicines by creating parallel pathways in the review process and introducing a Common Technical Document (CTD) format according to international standards. The goal is to shorten the typical time frame from submission to issuance of the marketing license from 4 years or more to 18-24 months.

Egypt has a vibrant pharmaceutical industry. There are about 130 manufacturing plants, some of which make brand name medicines for multinational companies (the industry association). The domestic industry supplies 90 percent of the volume of generic drugs consumed in Egypt (or about 60 percent of the value, as domestic generics are sold at lower prices than international benchmarks).

Fifteen companies so far have obtained a manufacturing license for Sofosbuvir, 10 to 12 are already producing, and 6 are listed as suppliers in the recent public tender. This tender guarantees a minimum volume of 250,000 packs (one month supply per pack). According to MOHP, the volume will be split evenly among the winning companies. The number of manufacturers for Daclatasvir is smaller (so far 6) but growing.

The Egyptian Drug Authority is not yet internationally recognized as a "stringent" regulatory authority. Egypt is not member of the PIC/S scheme ("PIC/S", 2017), meaning certificates for Good Manufacturing Practices issued by EDA would not be recognized in other countries. This points towards a risk of quality variation in the Egyptian market. Companies that are forced to sell at low prices may "cut corners", use lower quality ingredients or find other ways to protect their bottom line unless there is a strong regulator with sufficient enforcement powers and capacity (see above discussion of conflict of interest if the same agency acts as regulator and purchaser).

The size of the pharmaceutical market in Egypt is about 33 billion EGP[2] (2015 data, about 4.3 billion US$) (Egypt Pharmaceuticals & Healthcare Report, 2017). This equals about 29 percent of total health expenditures or US$ 52 per capita consumption of medicines. Egypt is characterized as a country in which pharmacies are widespread and all medicines can be purchased over the counter without prescription, or even delivered to the home of the patient, making self-medication the typical first step in care. The retail sector is large but shows signs of consolidation with the emergence of pharmacy chains offering lower prices and a higher degree of professional standards than individual pharmacy shops. The official retail margin is 20 percent, but pharmacists find ways to buy from informal channels that offer high volume medicines at discounted prices, thereby increasing their profit margin. On the other hand, these informal distribution channels provide an entry point for fake or unlicensed medicines. The MOHP is developing a track-and-trace system that will become mandatory for all pharmaceutical businesses in order to address this challenge. Current plans are to roll this system out over the next three years.

Egypt applies a reference pricing system, controlled by the MOHP, which is currently being revised (Decree 499). Multinational companies are reluctant to offer prices that could impact price levels in other countries; therefore, they sometimes provide hidden rebates in form of free medicines to protect market share. As about 75 percent of the market is in the private sector and paid for out-of-pocket, brand preference plays an important role. Reportedly, there are disputes between physicians and pharmacists professional organizations (syndicates) as to who gets to define which brand is dispensed (prescribing brand name or generic name). The underlying issue may be financial: who gets to benefit from the incentives provided by the industry.

Egypt is planning the introduction of a new social health insurance scheme, which would replace the current Health Insurance Organization and may offer an opportunity to bring more discipline into the market, assuming it has enough resources to be a major purchaser of medicines.

(2) public sector expenditures may not be fully captured in these data.

Current approach to treatment of viral hepatitis and potential future trends

Treatment programs for Hepatitis C have existed for years, but the cost of interferon and the long duration of treatment have been limiting factors for the number of patients benefiting from the program. Since DAAs became available, the country moved quickly to scale up treatment in collaboration with various stakeholders working together in the National Committee for the Control of Viral Hepatitis (established 2006). A new strategy document was developed for the period of 2014 to 2018, covering a comprehensive set of actions to control the epidemic; treatment is but one of several pillars in the new strategy. Preventing new infections is obviously more cost-effective and will accelerate the elimination of the virus reservoir and reduce long term treatment costs.

The roles for defining treatment protocols, setting up treatment centers, procuring medicines and enrolling patients are defined. The number of treatment centers has been scaled up – as of 2016, the National Committee counted 56 centers and had plans to open up to 100 centers. HIO has 37 centers and 90 dispensaries at which patients can refill their prescription.

A web based enrollment tool has been launched and 1.8 million Egyptians registered for treatment. Once registered, they receive a list of lab tests required for their first appointment and instructions for payment (patient copayment is EGP 20, about US$ 2.50, which finances the administration costs and overtime payment for the treatment center staff; physicians and nurses volunteer their time). They also get an appointment at the treatment center and a list of lab tests needed to confirm the diagnosis and status of disease. As this procedure can be challenging for illiterate people or those without internet access, enrollment is also possible at treatment centers. Internet cafes offer assistance to people who otherwise do not have access. Although waiting lists for appointments have largely resolved, temporary drug shortages have delayed treatment for some patients, although the delays are said to be no more than one month (HIO).

According to NCCVH estimates, at least 800,000 patients received treatment in 2016 (after 200,000 in 2015), which is in line with the target number needed to reduce Hepatitis C prevalence to under 1 percent in 2030. Included are about 100,000 patients treated in HIO facilities. The total does not include those

treated in the private sector (estimated at 200,000 for 2016), where there is no mandatory registration or follow up. A system to register patients and refill drug prescriptions only if patients returned the originally dispensed bottle empty[3] was in place when treatment relied on the discounted originator drugs, but has since been abandoned.

Currently, only 50 percent of patients show up for the final lab test scheduled one month after the end of treatment, which is needed to confirm complete clearance of the virus or "sustained response". This lack of follow up is a problem, as calculating the cure rate for the current treatments will be difficult if patients do not get the final test.

Fragmentation of the treatment efforts is an issue. MOHP treatment centers, university hospitals, NGOs and facilities under the HIO each offer treatment centers but not all of them feed into a single monitoring system. The private sector also offers diagnosis and treatment in many facilities, some of which are of low standards and may use substandard lab reagents or medicines. This can negatively impact cure rates and lead to resistance development against the first line medicines that are now available at low cost.

(3) The main purpose was to prevent patients from selling Sofosbuvir (initially provided by Gilead, at a price of about 1% of the official US price) outside the countries in non-discounted markets.

Availability and price of hepatitis treatments in Egypt

Six companies have an agreement as suppliers to the MOHP and all other buying organizations included in the MOHP tender, offering the lowest price for the public sector and a higher, but still competitive, price for the private sector; all companies are supposed to sell at more or less the same price (see table 8).

Table 8: Current negotiated prices for HCV treatment with Direct-Acting Antiviral Drugs (DAA) in US Dollars

Course and Date	Sofosbuvir + Daclatasvir price in EGP
Full treatment costs (3 months) in public sector, 2016	US$200
Full treatment costs in public sector since 2017	US$98

These prices are already at or below the hypothetical lowest price that has been estimated by international experts working for WHO, Clinton Foundation and USAID. The experts used the experience from the HIV antiretroviral market, taking into consideration the costs of raw materials (API from Indian and Chinese sources), costs of manufacturing at scale in a GMP compliant facility and a reasonable profit margin that encourages a sufficient number of companies to enter and stay in the market. They arrived at a current theoretical "best price" of US$ 233 for a full course of combination treatment of WHO Prequalified Sofosbuvir plus Daclatasvir (USAID, Clinton Foundation and WHO AMDS). Estimating manufacturing costs and profitability is not an exact science – there are assumptions to be made and parameters can change rapidly based on scale and costs of inputs. The fact that Egyptian manufacturers offer such low prices to their government can have several potential explanations:

■ Companies may have lower manufacturing costs as they do not have the same sophisticated quality assurance mechanisms that are required for WHO Prequalification (WHO - Prequalification of Medicines Program) (see explanation below). However, this is not likely to be the case for one local company, which is

the current leader in the Egyptian generic DAA market. This company already applied for WHO PQ and is in the review process.

■ Companies accept low profit or even losses in the public sector based on political pressure, some form of material or political compensation in another area of interest not related to Hepatitis drugs, or in an attempt to build market share, hoping that this approach leads to higher private sector sales.

These findings raise the question of whether the low prices in Egypt are sustainable once international quality standards are applied. Current private sector retail prices for Sofosbuvir in India are higher than the prices negotiated for Egypt. As of 2016, they ranged from US$ 160 to 320 for one month supply of Sofosbuvir, compared to approximately US$ 122 for Egypt at the time cost data was collected.

Considering payment delays that need to be financed and exchange rate deterioration versus the US dollar, the current prices charged by Egyptian manufacturers to the MOHP are already below the international benchmark and not likely to go further down in the near term. Of course, over time API prices may change, international competition may drive prices down further and the Egyptian government may want to take steps to take advantage of these possible market developments by re-negotiating or inviting competition from outside the country.

As stated above, the price comparison data do not take into account whether manufacturers have WHO Prequalification (WHO PQ) for their product. WHO PQ is a prerequisite for participation in many international tenders, assuming that there are enough manufacturers meeting this requirement. For the Egyptian government and the local industry, the goal should be to ensure all Egyptian manufacturers go through this process. This would not only reassure the government that the medicines used in Egypt to treat the HCV infected population are of good quality and fully effective, it would also help the Egyptian industry to be competitive in export markets. For companies that are already manufacturing at a high-quality standard (Good Manufacturing Practices), the investment needed for achieving WHO PQ is limited. So far, Pharco has initiated the process, as have several Indian manufacturers.

Not much is known yet about alternative treatment combinations, for example

Sofosbuvir plus Ravidasvir, a new DAA licensed and under development by Pharco. Early clinical data look promising, but to decide which combination(s) to pick for mass treatment campaigns, the MOHP would need to apply a "health technology assessment (HTA)" procedure to identify the cost-benefit ratio and allocate funds based on best value for money. It is likely that parameters such as price and treatment outcome data will change over time, which means the review and decision making process needs to be institutionalized and given sufficient resources to stay on top of the evolving scientific and market data.

One likely unintended consequence of the difference between public and private price is that the industry has an incentive to focus marketing activities on the private sector, potentially pulling ahead of the public sector in screening and identifying patients who then would pay out of pocket for their treatment. At the current price level, many patients would probably prefer the less bureaucratic, pay-as-you-go option over formal enrollment in a public treatment center. If this turns out to be true, these patients would be lost for the monitoring and disease surveillance efforts, as the private sector does not yet have an enrollment and follow-up system.

Developing such a system in collaboration with industry, pharmacists and privately practicing physicians should have high priority. While technically relatively straightforward (a public sector system exists already), it may require monetary incentives to ensure compliance of providers. It should also be easy on the patient and not add any inconvenience, while providing reminders for refills and necessary tests. Such a system should be in the interest of manufacturers, prescribers and pharmacists as it helps ensure patient compliance and thereby secures future sales.

Factors defining access to treatment and treatment outcomes

Thanks to the internet registration portal, the treatment program has reached literate patients who are aware of—or at least suspicious of—their HCV-positive status. However, this group may be only 10 or 20 percent of all patients in need of treatment. The prevalence of Hepatitis C among the poor and uneducated is moderately higher than among the educated. Screening programs, active outreach and use of community outreach strategies for enrollment will be needed to ensure that the treatment program is "fed" with new patients. Monitoring of patients needs to be improved through a single system rolled out across all providers offering treatment. Such a system could be based on a mobile platform and linked to incentives such as free call phone minutes or data. Currently, the program is offering patients a final "certificate of successful treatment" when they show up for their final test and are confirmed for "sustained response." Having a unified strategy across all treatment platforms (modeled after the "Three Ones Principles" that has been the basis of success for HIV/AIDS treatment campaigns[4]) increases the effectiveness and efficiency of all communications and outreach measures (UNAIDS 2004).

(4) One strategic framework, one coordinating body and one monitoring and evaluation system.

Costing the drug component of a long-term plan to eliminate Hepatitis C in Egypt

Based on current prices and assumptions of patient treatment numbers, the total costs of the drug component for a treatment campaign can be calculated. The calculation is provided here for the next five years only. Two scenarios are shown below: One column reflects the projected drug costs under the "treatment scenario" in the sister report by Haacker 2016, whereas the adjacent column reflects drug costs under the "elimination scenario" in the same report. Note that the drug costs under the elimination scenario are significantly higher as the screening component of that scenario draws significantly more patients into treatment and therefore increases spending on medications, at least in the short-term.

Table 9: Projected Treatment costs (drug costs only) for the next five years of a Hepatitis C elimination campaign*

Year	Treatment Scenario Drug Costs (US$)	Elimination Scenario Drug Costs (US$)
2017	33.9 million	70.5 million
2018	30.3 million	96.4 million
2019	27.2 million	85.5 million
2020	24.4 million	76.7 million
2021	22.0 million	75.6 million

**Prices reflect non-discounted costs*

Depending on the number of patients seeking treatment in the private sector and paying out of pocket, the public expenditure burden may be lower for achieving the target treatment numbers. So far, there are not enough data to calculate how many patients would seek treatment outside the public and HIO centers. The industry will have access to such data and it should be possible over time to come up with a good estimate of the out-of-pocket market, which then can be used to adjust the public expenditure forecast and budget for the treatment provided to patients for free.

Costs for purchasing medicines are only one element of treatment costs, although probably the dominant one. Future treatment costs can be reduced by investing in prevention now – every infection avoided saves not only a future treatment, but also costs for diagnostic tests and evaluations and for lost productivity due to absence, discrimination and illness.

Treatment campaigns require investment into screening and treatment capacity, outreach and patient information, systems for management, monitoring and evaluation and second line interventions for patients that fail to fully respond to first line treatment. These costs will be covered in other components of the Technical Assistance project.

Main Findings for the HCV Pharmaceutical Market in Egypt

With the availability of new, effective treatment options for Hepatitis C, Egypt is in a position to offer treatment on a scale that can reduce the prevalence to a level that equals elimination of the disease. Significant progress has been made in creating a manufacturing base to ensure supply at prices currently below internationally estimated "best price" benchmark. MOHP has made the decision to source medicines for the Hepatitis C treatment campaign exclusively from domestic generic manufacturers. Originator companies importing or manufacturing in Egypt have been lowering their prices to be competitive in the private market, but their volume share will likely remain limited.

One challenge going forward for Egypt is to ensure that low prices do not lead to inferior product quality. The support for a domestic industry is understandable, but it should be complemented with a strict enforcement of quality standards and a push for all manufacturers to achieve WHO Prequalification as a precondition for participation in public tenders. This may require some consolidation and capital investment but will also contribute to the growth of the industry by opening export markets. Many other countries have a high burden of Hepatitis C and Egypt, as a frontrunner, may be able to successfully export medicines as long as they are competitive in price and quality with the Indian generics. Some thoughts on how quality can be further assessed and addressed are summarized in the Annex II.

Another issue that needs to be addressed is the monitoring of patients under treatment across all service delivery platforms. Public sector and HIO share a common tool, but this tool does not automatically follow up with patients who miss their final test to confirm "sustained response." In the private sector, there is no follow-up system in place, therefore there will be no data on how many patients have been successfully treated and how many will relapse. Strengthening the existing monitoring system and developing a (linked) system for the private sector jointly with manufacturers and providers should have a high priority. Otherwise the treatment campaign will become more vulnerable against attacks on its effectiveness.

Treatment Journey in the Public Sector

Patient steps:

There are currently two public payers involved in the treatment program. The first being the NCCVH itself and financed mainly through the general budget and to a lesser extent by donations through large national CSOs. It caters to those who are not eligible for treatment under HIO. The second is the Health Insurance Organization (HIO), which serves those affiliated with its various coverage schemes (mainly civil servants, poor widowed house-wives, farmers and a small part of the formal private sector). Patients have to go to the websites affiliated with the appropriate schemes for self-registration.

1. NCCVH National program of MOHP: (www.nccvh.org.eg/)

The website will request simple basic personal info as: (i) National ID number; (ii) Full Name; (iii) Place of residence; (iv) Governorate of residence; and (v) a mobile phone number. A security verification code must also be entered to prevent spam registrations (Figure A).

Figure A: Screenshot for required personal data at the NCCVH's website

Source: NCCVH

Within one or two business days, and using his/her national ID number as an identifier, the patient must revisit the site to check on his reservation status. Once a unique reservation number detailing the name and address of the assigned center is created, two documents have to be printed. The first document (Figure B) details the reservation time, assigned center, and some general procedural guidelines. The second (Figure C) lists the laboratory test results that the patient must bring with him/her to the appointment. If the patient was not able to do the tests before arriving to his/her appointment, he/she may do them at the same designated center for a very modest user-fee, but ultimately would consume more waiting time. The system will also send a text SMS to the patient's mobile phone listing the main details and requirements for his appointment.

Appointment dates and waiting time do vary according to various criteria: (i) capacity of a specific treatment center; (ii) demand on a specific treatment center; and (iii) availability of testing equipment in the center. At the beginning of the program, the earliest a patient could obtain an appointment was at an average of 3-4 weeks after the registration process. However, in October 2016, the Minister of Health and Population announced that patients could obtain an appointment within 3-4 days.

Figure B: details the reservation time, allocated center and some general procedural guidelines

بيانات الحجز

مكان الكشف مستشفى القاهرة الجديدة

توقيت الكشف من الساعة الثانية عشر ظهراً إلى الساعة السادسة مساءً

تاريخ الحجز: 2016-05-31 رقم الحجز: GIZ-ZPM-0007

الرقم القومي:

الاسم:

عزيزى المواطن الكريم

اتباعك التعليمات يسهل علينا خدمتك ويتيح الفرصة للآخرين للاستفادة من الحملة القومية لعلاج من الالتهاب الكبدي الفيروسي (سي)

نرجو الانتباه للإرشادات الآتية:

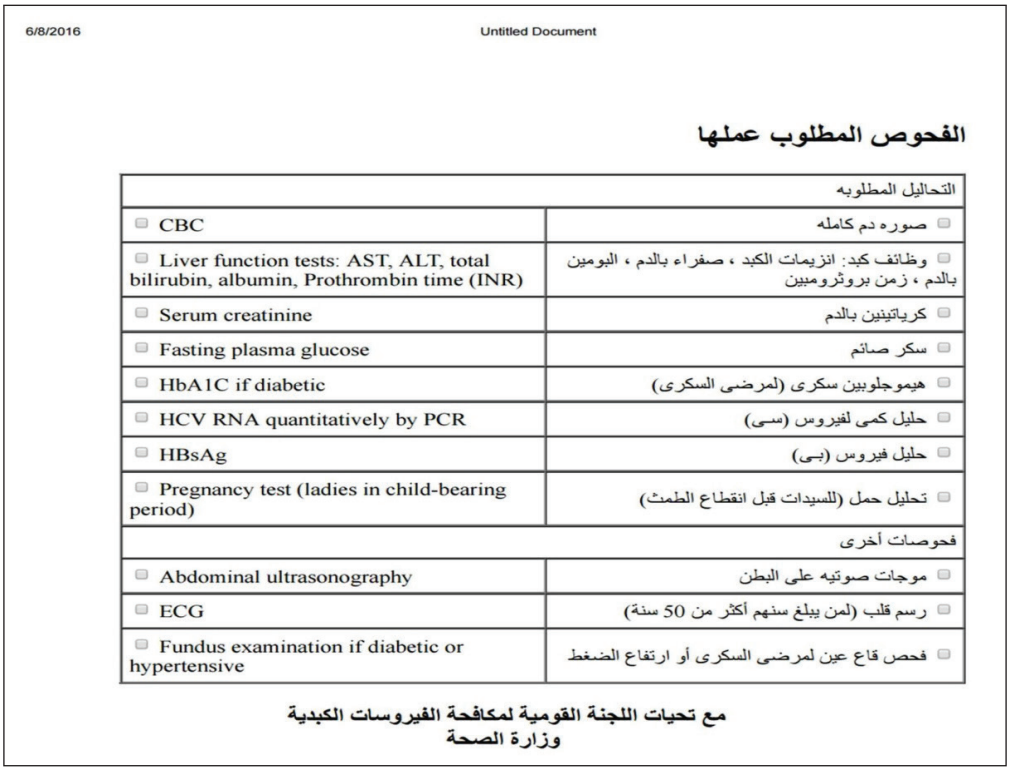
- فور إستعلامك عن مكان المركز العلاجى المحدد لك، إحرص على طبع ورقة حجز موعدك من على البوابة الإلكترونية و اظهرها عند الدخول في اليوم المحدد لمقابلة الطبيب.عدم إبراز ورقة الحجز سيتسبب فى تأخرك عن الدخول للكشف.
- نرجو الإحتفاظ بورقة الحجز لتظهرها مع كل زيارة للوحدة
- نرجو الحضور شخصياً لوحدة العلاج في اليوم المحدد، مع مراعاة عدد المرافقين، وذلك لتجنب إزدحام أماكن الانتظار بغير المرضى الأولى بالرعاية والجلوس.
- الرجاء إحضار المستندات الآتية في أول زيارة:
  - أصل وصورة (وش و ظهر) من بطاقة الرقم القومي سارية الصلاحية
  - إحضار الفحوص المرفقة في الصفحة التالية لموعد الحجز
  - في حالة عدم قدرتك على إجراء الفحوص المطلوبة على نفقتك الخاصة، توجه للمركز في موعدك، وسيقوم الطبيب بمساعدتك في تقديم طلب الفحوص على نفقة الدولة

(1) الموعد المحدد / / ختم الطبيب	(2) الموعد المحدد / / ختم الطبيب	(3) الموعد المحدد / / ختم الطبيب
(4) الموعد المحدد / / ختم الطبيب	(5) الموعد المحدد / / ختم الطبيب	(6) الموعد المحدد / / ختم الطبيب

http://www.nccvh.org.eg/inquiry 1/2

Source: NCCVH

Figure C: Lists the laboratory test results that the patient must bring



6/8/2016 Untitled Document

الفحوص المطلوب عملها

التحاليل المطلوبه	
☐ CBC	☐ صوره دم كامله
☐ Liver function tests: AST, ALT, total bilirubin, albumin, Prothrombin time (INR)	☐ وظائف كبد: انزيمات الكبد ، صفراء بالدم ، البومين بالدم ، زمن بروثرومبين
☐ Serum creatinine	☐ كرياتينين بالدم
☐ Fasting plasma glucose	☐ سكر صائم
☐ HbA1C if diabetic	☐ هيموجلوبين سكرى (لمرضى السكرى)
☐ HCV RNA quantitatively by PCR	☐ حليل كمى لفيروس (سى)
☐ HBsAg	☐ حليل فيروس (بى)
☐ Pregnancy test (ladies in child-bearing period)	☐ تحليل حمل (للسيدات قبل انقطاع الطمث)
فحوصات أخرى	
☐ Abdominal ultrasonography	☐ موجات صوتيه على البطن
☐ ECG	☐ رسم قلب (لمن يبلغ سنهم أكثر من 50 سنة)
☐ Fundus examination if diabetic or hypertensive	☐ فحص قاع عين لمرضى السكرى أو ارتفاع الضغط

مع تحيات اللجنة القومية لمكافحة الفيروسات الكبدية
وزارة الصحة

Source: NCCVH

Advantages of the NCVVH system:

■ A fast process with 1-2 business days to obtain an appointment with a hepatologist.

■ Requires very limited personal patient data.

■ Apart from a minimal user-fee for some of the services offered at the facilities, the system and subsequent treatment is free of charge.

■ The system contains a substantial amount of guidelines, FAQ's, etc. that satisfies the majority of concerns on the part of the patients.

■ Directs the patient to a specific clinic/center at a specific date and time, thus avoiding unnecessary waiting times at the facilities with minimal work-life disruptions and/or discomfort to the patients.

Disadvantages of the NCVVH system:

■ A large portion of the general public is computer illiterate, thus preventing access to the system unless they seek the aid of a friend, relative or a computer shop to help them with the registration process.

■ Many patients do not come back within 1-2 business days to check on their appointment status leading to a big number of missed or overdue appointments.

■ The text message is not always received, especially in rural areas where mobile phone coverage is patchy.

■ The designated clinic on the website is not always geographically close to the patient, which may cost the patient substantially in transportation costs on top of the physical exertion associated with commuting.

■ Many patients do not reside on the address shown on their ID cards, which is a major factor in determining which center/facility he/she should go to, creating a huge logistical transportation problem for them with a substantial number of requests to change the facility to another one later on.

■ For some centers, the appointment comes very soon to patients, hence not allowing them to prepare the required documentation in time before their appointment is due.

■ Similarly, HIO affiliated patients would have to register through the HIO main website: http//www.hio.gov.eg/Ar/Pages/sof.aspx

It is worth mentioning that HIO affiliated patients must self-identify their coverage status. This is fairly easy, since most of them are already contributing premiums through their payrolls to HIO and have already obtained an HIO card. The HIO patients would follow more or less the same protocol of the NCVVH. They are requested to follow a general instructions page followed by a registration page as in Figure D and Figure E. Similar to the NCCVH, only basic personal info is required. Further, HIO operates its own network of service providers all around the country. Some of those provision outlets (clinics, hospitals, etc) include dedicated liver disease treatment center to which patients are directed.

Figure D: HIO general instructions

Source: HIO

Figure E: HIO registration page

Source: HIO

Also similar to NCCVH, a page displays the required lab test results for patients to acquire an appointment (Figure F). Notably, the list of required lab tests is more extensive on the HIO than the NCCVH website. However, a larger portion of patients with HIO coverage did go for testing at HIO facilities rather than NCCVH centers owing to their insured status under HIO.

Figure F: HIO required lab tests

Source: HIO

Treatment compliance and stay on therapy:

Once on treatment, more than 96 percent of patients complete the 3 or 6 months regimens, with very few drop outs due to adverse events, no shows, or change of mind. Nonetheless, as dispensing of medicines is done on a monthly basis in an effort to boost compliance, many patients tend to come in late for their monthly rations—as many as 20 percent in some centers. The average delay for these patients is 5-7 days. Another compliance issue reported by hepatologists is that some patients tend to take the pills for only 28 days and drop the remaining 2-3 days at the end of the month, thinking that treatment is only for 4 weeks (28 days) per month.

Hepatologists also noted that because of the seriousness of the disease and increased awareness, the compliance and adherence to treatment were generally high among patients. In some instances at the beginning of the treatment program, stock-outs have led to some patients switching the brands of medicines in the midst of their treatment course or having interruptions of up to weeks in some cases. This has adversely affected their treatment outcomes.

Switching intentionally between different regimens was only permitted under the program if there was no response from treatment or if the patients starts showing intolerable adverse events as: Anemia, gastric pain or skin rashes. Stopping treatment (treatment cessation) is mainly done by hepatologists if the patient becomes advanced cirrhotic.

Monitoring and SVR:

Monitoring is done via the Serologic Viral Response (SVR) test, considered by hepatologists to be the best tool to evaluate successful treatment. It is usually done at month 1 (M1), month 3 (M3) and month 6 (M6). An 'end of treatment SVR" (M3 of initiating treatment) means that the patient is virus free. An SVR at M6 confirms the eradication of virus from the human body (3 months after end of treatment). SVR at M9 and M12 are sometimes also requested.

Treatment Outcomes:

According to experts and drug makers, there is not much difference in outcome among generic or brand medications. However, studies performed under the watch of NCVVH on their own patients indicated a minute difference between branded medicines at 98 percent SVR at six months vs. the locally manufactured products showing SVR rates of 92 – 95 percent at six months for non-cirrhotic patients. For cirrhotic patients, SVR rates at six months hovered between 70 and 85 percent. Those figures are usually higher if treatment is extended longer to 6 months.

Owing to the relatively cheap and affordable PCR test required to check on the final SVR, as many as 50 percent of patients go for testing at local community laboratories and do not come back to the treatment centers for final checks. This pattern subsequently is causing a huge disruption in obtaining data on the outcomes of treatment.

Dealing with Relapsers and Non-responders:

In case of no response or relapse, which affects less than 10 percent of the total patient volume, hepatologists tend to switch to another protocol with a longer duration (six months rather than three), with the addition of RBV.

"Relapsers and non-responders are not a problem anymore, sometimes the Hepatologists fail to treat them and it is time for more experienced Hepatologist to interfere which usually works" – Dr. Gamal Esmat

Re-Infection:

Re-infection is not common. However, due to the young age of the program, not many re-infected cases have been encountered. Viral mutation is not currently an issue and is perceived as falling within very limited occurrences.

Treatment Options in the Private sector

Egypt has a high rate of Dual Practice (medical doctors working in multiple hospitals/clinics simultaneously). There are no official estimates, but some studies estimate the phenomenon to include nearly 85 percent of all practicing doctors (see for example: Rabie 2014; World bank 2013). Patients bypassing the primary healthcare level and/or general practitioners is the mainstay of the private medical provision market in Egypt. Most private clinics offer walk-in or appointment services for secondary and sometimes tertiary treatment (World Bank 2015). Hepatologists offering treatments for viral hepatitis follow the same route. Most prescribed medicines would have to be paid for OOP by the patient through a community pharmacy. For the purpose of this study, interviews were conducted with seven medical doctors specialising in the field (as discussed earlier) to get their perspective on the behaviour and treatment regimens used in the private market. The detailed questionnaire could be found in Annex I.

Hepatologists noted that CHC patients in the private sector fall into one of two categories once they are informed of their condition:

1. Concerned Patients: These patients are generally concerned with their condition, future complications, and the costs associated with therapy. Most of the time, the physician's response is to reassure them that the new regimens are relatively safe, tolerable, of shorter duration and less expensive than previous regimens.

2. Indifferent Patients: These patients are usually indifferent to their diagnosis because serious symptoms have yet to manifest. Physician generally try to educate these patients on the consequences of inaction and raise awareness of how seeking treatment early will minimize the risk of complications, costs of treating those complications, and the possibility of infecting loved ones.

"Once, I have seen father and 3 sons and 1 daughter, all infected with HCV and upon investigating the reason, it turned out that they thought it's because all of them are using the same sanity bathroom tools. What was really strange is that the father was willing to get treatment for himself and his 3 sons but not the daughter!! And he explained that she will cost him treatment fees and she is not productive nor will be working, so there was no need to treat her!! The only way I was able to convince him is by telling him… what if you treat your sons and your daughter re-infects them again? and that was the only way I convinced him," said one of the Hepatologists.

The treatment options that were available at the time of the study for eligible patients were:

1. Sofosbuvir ± RBV (Brand)
2. Sofosbuvir ± RBV (Generic)
3. Sofosbuvir + Daclatasvir ± RBV (Brand)
4. Sofosbuvir + Daclatasvir ± RBV (Generic)
5. Harvoni ± RBV (Brand)
6. Harvoni ± RBV (Generic)
7. Sofosbuvir + Olysio ± RBV (Brand)
8. Paritaprevir/Ritonavir + Ombitasvir (Qurevo) ± RBV (Brand)

Treatment Choice in Private Sector:

The market shares reported in Table 10 reveal a dominance by the generics. At the time of this study, the SOFO+DACLA generic regimen had 59 percent of patient share, followed by Harvoni (generic). Olysio had been relatively popular until December 2015 before declining dramatically due to the announcement of new generic treatments with similar response rates. However physicians still prefer Olysio for non-responders and relapsers as of this writing. Physicians normally prescribe the regimens for 3 months, or six months if the patient is cirrhotic (without RBV). If the patient is on dialysis or has CKD stage 4, physicians tend to prescribe the Paritaprevir/Ritonavir + Ombitasvir (Qurevo) regimen for 3 months. Although the Paritaprevir/Ritonavir + Ombitasvir (Qurevo) regimen is also indicated for all types of patients, physicians tend to reserve it for renal patients owing to the higher cost.

Table 10: perceived treatment combinations in private sector from Hepatologists perspective

#	Regimens	Patient share
1	Sofosbuvir ± RBV (Brand)	0%
2	Sofosbuvir ± RBV (Generic)	0%
3	Sofosbuvir + Daclatasvir ± RBV (Brand)	9%
4	Sofosbuvir + Daclatasvir ± RBV (Generic)	59%
5	Harvoni ± RBV (Brand)	1%
6	Harvoni ± RBV (Generic)	16%
7	Sofosbuvir + Olysio ± RBV (Brand)	2%
8	Paritaprevir/Ritonavir + Ombitasvir (Qurevo) ± RBV (Brand)	5%
9	Others (non-systemic treatment)	7%

Treatment Initiation, Continuation and Supply in the Private Sector:

Physicians report that nearly 80 percent of patients are eligible for therapy with the abovementioned regimens. The remaining 20 percent are ineligible mainly because they have conditions for which treatment with DAAs cannot be initiated. Those conditions usually include severe liver failure, irresponsive ascites, or encephalopathy. Treatment for the second category would usually focus on treating the complications themselves in an effort to stabilize the patient.

Most of the times, hepatologists give patients the choice of getting treatment through the public system (by enrolling through the NCCVH website) or buying it OOP. Due to the declining cost of treatment, patients in 2015 and early 2016 initially bought these medicines from community pharmacies rather than waiting in the public system. However, since July 2016, more and more patients have opted to obtain their medicines from the public system owing to the decreased waiting times.

Physicians were also asked about the main challenges facing patients seeking treatment in the public system. Table 11 lists the main findings.

Table 11: Perceptions of physicians on the challenges facing the patients to receive treatment in the public system

#	Challenges facing patients under the two public insurance systems:	Percentage of Physicians perceiving this as main challenge in the public system
1	The system is too complicated to be understood	43%
2	The insurance protocol doesn't fit the patient condition	86%
3	Not receiving the complete dose	0%
4	Availability of the prescribed drug	29%
5	The prescribed drug is not listed in Hospital drug list	43%
6	The pharmacist switches to a generic or different brand	0%
7	Too much procedures and time to receive the medications	100%
8	Stock outs	71%
9	Limited numbers of qualified physicians at the examination place	57%

"In my private clinic I give the patient the choice, I tell him you can go get the treatment from the Public sector or buy it from the market, either brand or generic, normally they say that they will get the brand, however when I tell them the prices of both brands and generics, they begin to ask about the success rates and when I illustrate that both got exactly the same response rate, they go for the generic"—Dr. Gamal Esmat.

Sales retail analysis in the private sector:

There are no official data on pharmaceutical sales in Egypt. Most data are derived from the IMS, which is a global benchmark for pharmaceutical sales around the world (IMShealth). Nevertheless, the data is self-reported by the pharmaceutical industry and is not verifiable. Initial data for Egypt has shown that the sales of DAAs are almost split between private and public markets, unlike the early years of IFN treatment, where the market was driven by the public sector. As of September 2016, data showed that enough DAAs were sold in both markets enough to treat 850,000 in 2016 alone. It is also worth mentioning that some public centres may offer patients the option to buy medicines OOP from their affiliated pharmacies at a lower price than in the private community pharmacies i.e. not paid for by public funds. No records are kept for those patients, but estimates suggest that nearly 50,000 have used this option. This may explain the markedly higher IMS sales figures at the public facilities than the private sector.

Recently, many tourist agencies, realizing the leadership Egypt has shown in treating CHC, have collaborated with leading private hepatitis clinics/centres to create a medical tourism market for CHC in Egypt. The idea is to target CHC patients from developed countries, where prices of DAAs are extremely costly, to buy tailored tourism-treatment packages in Egypt at a fraction of the costs those patients would incur in their home countries. Many are still debating the legality of such a move, especially when it comes to the manufacturing agreements with international pharmaceutical brand owner companies.

Recommendations

The following section includes the author's recommendations for improving the treatment program to aid in the elimination of CHC in Egypt:

1. Enforce the implementation of the National Plan of Action for Prevention, Care and Treatment of Viral Hepatitis – Egypt. The plan, launched in 2014, enjoys a unanimous support by most stakeholders (Government, Development Partners & CSOs) as the road that Egypt must follow to combat and eliminate the disease. However, the lack of (i) costing of the listed activities, (ii) identification of responsible implementing entities, and (iii) development of relevant monitoring indicators has prevented local and international partners from offering further support. Therefore, it was imperative that such components be included in the plan. The World Bank in collaboration with WHO have undertaken this technical endeavour to support the Egyptian National Plan of Action.

2. Set a realistic target for elimination. Given current strong political support for the program, many ambitious target dates have been proposed to reach elimination. The range is large, with some optimistic views suggesting only 3 to 4 years to reach elimination, while other less optimistic views foresee a need of 10 to 12 years. Accordingly, any forecasts should be based on a set of realistic factors, including but not limited to : (i) a thorough forecast analysis of the capacity to conduct national screening efforts that would ultimately feed patients to the treatment program; (ii) an analysis of the capacity to reduce the number of new infections through scaling-up the quality and quantity of measures to decrease the spread of disease; (iii) a stock-taking of the available and possible future financing resources for the components of the program required for sustainability; and (iv) a detailed, time-based, cost-prioritized version of the national plan of action for the prevention, care and treatment of viral hepatitis in Egypt to reflect the different roles and responsibilities for those involved.

3. Collaborate with the business private sector. The NCCVH should encourage privately owned or parastatal firms, companies and businesses

to initiate screening and treatment programs for their own employees as well as initiate a Community Service Initiative to sustain the same costs for citizens in specific under-developed areas or for disadvantaged population groups. Current Egyptian laws permit a certain number of tax-breaks for firms adopting such initiatives. Notwithstanding, those activities would have to be coordinated with NCCVH to coordinate efforts and prevent any duplications.

4. Widen the screening program campaign: This analysis started in March 2016, during the peak of the influx of already diagnosed CHC patients to treatment centres. This high flow of patients was understandable in the context of previously diagnosed patients seeking cures once DAAs were available. Nevertheless, and as anticipated, by the time these recommendations were drafted, Egypt had managed to treat 800,000 patients and cut the waiting list of patients awaiting treatment. By the end of 2016, the number of patient visits to treatment centres had dropped to 2000 to 3000 patients a day. To maintain the rigor of the treatment program, Egypt needs to actively look for dormant infections among its population. This will have to be achieved through adopting a vigorous screening program.

   The Prime Minister, based on the recommendations of MOH, issued a decree in August 2016 specifying specific population categories as target groups for the first phase of such a screening program. They include: (i) all healthcare workers; (ii) all admitted cases to public hospitals regardless of diagnosis; (iii) all university students; (iv) all males admitted to compulsory military service; (v) all patients on dialysis; and (vi) all persons donating blood. No plan or estimated costs related with the screening efforts were published, nor were future plans for expansion to other groups announced. Therefore, it is imperative that those missing elements be examined. Further, high prevalence (e.g. persons older than 59 years of age) and higher risk groups (e.g. IV drug users) need to be prioritized in the next phases of the screening program. Also, given the modest sensitivity and specificity of the rapid screening tools available in the market, a well informed and researched decision should be made on whether to use those

tools for the national screening program or revert to more sophisticated and costly in-lab testing. The latter raises additional logistical challenges for blood sample collection, transportation, storage and an adequate feedback mechanism of test results to the tested subjects.

5. HCV stakeholders bonding. The Ministry of Health should arrange a quarterly meeting between the NCVVH, the pharmaceutical industry, the pharmaceutical syndicate (representing private community pharmacies) and active NGOs to provide for coordination in terms of: (i) review of pharmaceutical delivery and sales data; (ii) forecasting and estimating the future needs of the program; (iii) resolving pending administrative and financial issues; and (iv) communicating the anticipated changes in treatment protocols early on for early adoption by the industry.

6. Apply high quality standards (GMP) for local manufacturing. With the continuous drop of the prices of locally manufactured DAAs, risks of lower quality generics will increase. The MOH, and through its EDA arm should ensure that the pipeline of products, as the backbone of the program, maintain an acceptable level of efficacy and safety to ensure cure rates remain on par with branded medicines. GMP practices should be encouraged and gradually mandated from local producers. However, the economic viability of the local industry and maintaining a competitive market environment should be considered whenever any regulatory action is being planned. Annex I illustrates in some detail options to verify the quality of Egyptian generics used in publicly financed treatment campaigns.

7. Support the local pharmaceutical Industry. The industry is generally prosperous. However, most pharmaceutical companies in Egypt have to endure dual difficulties. First, the general investment climate in the country affects all kinds of industries, e.g. the lengthy bureaucratic processes as well as a foreign currency crunch issue makes importation of active pharmaceutical ingredients (APIs) a challenging endeavour. Second, the pharmaceutical industry cannot freely price their products, as Egypt imposes a statutory pricing mechanism, yet a prospering counterfeit market hinders its sales and product safety. Therefore, Egypt should support the industry in combating these underlying factors that threaten its business

and patient safety. Further, companies should be encouraged to undergo WHO pre-qualification process to capitalize on growing export markets as other low and middle income countries expand treatment programs. Lastly, approval, registration and pricing processes for newer molecules should be streamlined and fast-tracked for companies to be able to provide the newer medicines in proper quantities to the market.

8. Motivate patients to do End of Treatment SVR (M6). To overcome the problem of patients not returning for SVR (M6) testing, many strategies could be adopted to incentivize patients towards completing their treatment and testing cycle. Global country experiences have provided us with innovative ways of incentivizing patients, including the following:

    a. Offer a free credit to the mobile phone accounts of patients who come back to do the M6 test.

    b. Waive the user fees for another infected person coming for treatment who is referred by any of the patients who do the M6 test.

    c. Offer generous free points to the "Food-subsidy" card of patients completing the M6 tests.

    d. Restrict the issuance of the "Cure Certificate" to those who complete the M6 test.

9. Strengthen the role of the Hepatitis Unit at MOHP. The hepatitis unit was created through a ministerial decree in late 2015 to function as a coordination hub for the various activities that aim to prevent, control and treat viral hepatitis C in Egypt. However, the unit is currently tasked with conducting many operational activities for the program. This unit should focus on its main objective of being a coordination body rather than a direct implementation arm. The monitoring and evaluation task for the various activities under the program should be assigned to the unit. The unit should also be properly staffed with adequate technical capacities that would enable it to perform its duties. The unit staff should be supported in terms of technical capacity building and an enabling governance atmosphere.

10. Enable the NGOs to work where they are most effective. Many large NGOs have been instrumental in supporting the program in terms of (i) providing adequate funding through donation flows; (ii) supporting and implementing awareness campaigns for combating the disease; and (iii) providing logistical and infrastructure support to some elements of the program. Nevertheless, NGOs are persistently asked to offer support in areas outside their sphere of optimal effectiveness. To optimize their contributions, NGOs should have the freedom to support the components of the program that best fit with their strategy and capabilities. The government can support those remaining areas that lay outside the sphere of NGO capabilities.

11. Initiate affordability programs for the private market. Despite treatment becoming progressively more accessible and affordable, many patients will still prefer to obtain their medicines from the private domain. This is based on experience from other health programs where patients insisted on resorting to paying out of pocket for their treatments (e.g. diabetes and oncology treatment, etc.) despite readily accessible and affordable treatment within public facilities. At the same time, the prices of the newer generic classes of DAAs remain elusive to many middle and low income Egyptians. It is therefore prudent to find innovative ways of making those medicines affordable to those groups. International experience brings many successful initiatives in that regards, and Egypt should consider adopting some of them. One simple example, which could be supported by the pharmaceutical industry and local NGOs, is to initiate an installment payment mechanism, where the cost of the medicines is stretched over a range of months with no or highly subsidized interest rates.

12. Do Not Forget HBV. With 800,000 patients with no definitive treatment, HBV infected patients still pose a risk and a burden on the health status and economy of Egypt. Egypt added HBV vaccinations to its EPI program nearly two decades ago. However, vertical transmission (from pregnant mothers to their babies) continues. The zero-dose regimen (given to children right after birth) should be considered, especially since the price of the vaccine is very modest. Further, efforts to vaccinate adult and high risk groups

should be further encouraged. Lastly, chronic treatments for HBV should be also covered by the current financial protection mechanisms (HIO and Payment on the Expense of the State) to minimize complications and their pertinent economic costs.

13. Document the experience. In October 2016, WHO celebrated the cure of 1 million patients worldwide from HCV. Of those, 800,000 were in Egypt alone. This achievement should be celebrated and a source of much joy for those involved in this program. Worldwide, many countries are now looking towards Egypt for experiences and best practices. However, little of Egypt's experience has been documented properly. The national program and development partners should strive to document every step for that purpose. This will further strengthen Egypt's leadership. However, the benefits reaped from this process are not limited to the reputational gains; rather economic gains could be achieved through (i) opening up export markets for locally manufactured DAA generics, (ii) boosting medical tourism revenues; and (iii) providing consultancy expertise to growing programs in other countries.
14. Automate the "Cure Certificate" process. The practice of handing treated patients a "cure certificate" displaying his or her new status has helped alleviate the discrimination some patients face in employment and work visa issuance. This certificate comes in great demand, and hence, is liable for forgery and corruption in a parallel illegal market. Therefore, we recommend developing a online "cure certificate database" with virtual access for entities requiring confirmation of the patient cure status. The national ID number could act as a unique identifier. Proper patient consent to listing his/her name openly should be obtained before the end of the treatment process.

Annex I

Quantitative perception analysis on CHC treatment Journey (Hepatologists perspective)

The following section displays the actual results obtained from a small survey of seven leading hepatologists. The data are completely based on their professional experiences with patients in their private settings, i.e. private clinics and hospitals. Below are the tabulated grouped answers, averages, based on the quantitative questionnaire that was used:

Average number of patients in total seen by a single Hepatologist in the private sector in a typical month, for any condition across all care settings? (Excluding multiple visits by the same patient. Please provide your best estimate.)

Total number of patients seen in a **typical month**	500

Average number of HCV patients seen in a typical month by Hepatologists', regardless of whether they are treated with active prescription therapy?

Number of HCV patients seen in a **typical month**	150

Percentage of HCV patients' age ranges:

#	Age Ranges	Percent HCV Patients
1	0-17	1%
2	18-45	43%
3	46-65	45%
4	65+	10%

Gender split of HCV patients:

#	Gender	% HCV Patients
1	Male	59%
2	Female	41%

Percentage of HCV patients having the following co-morbid conditions:

#	Co-morbid Conditions	% of HCV patients with…
1	HIV positive	0%
2	Hepatitis B	7%
3	Cardiovascular Disease	14%
4	ESRD Disease (patients on Dialysis or Stage 4 CKD)	3%
5	Psychiatric Disorders (i.e. Depression, etc.)	6%
6	Diabetes	29%
7	Other co-morbidities (HTN, Obesity, and Anemia)	23%
8	None	42%

Percentage of HCV patients referred to physicians' office from another physician for their HCV condition:

#	Source	% HCV Patients
1	Referred-in from another physician with an HCV diagnosis	37%
2	Diagnosed with HCV by you	63%

Of those Hepatitis C patients that are referred to physicians' office, what percentage are referred from each of the following sectors:

#	Source	Percent HCV Patients Referred From…
1	Public sector	21%
2	Private sector	79%
3	Other (Specify) _____	0%

Of patients following up in the physicians' clinic, what are the percentage of patients getting their treatment from the following places on average, and what is the time period required for a referral to your office to be admitted for treatment? (Response is in days, representing the period between a patient's referral to private office until s/he receives a treatment):

#	Source	% of patients	No. of days from being diagnosed with HCV till receiving a treatment
1	Health Insurance Organization	22%	157 Days
2	MOH Insurance	32%	205 Days
3	Private Insurance	3%	13 Days
4	Companies / big accounts	2%	1 Day
5	Military / Police hospitalls	1%	21 Days
6	Out of Pocket / Self-Pay	38%	1 Day
7	OOP (Subsidized value of brand)	2%	1 Day

Patients' treatment type classification at private clinic:

#	Type of visit	% HCV Patients
1	Therapy Naïve (Diagnosed patients that have never been treated and may be treated in the future)	26%
2	Currently Treated (Diagnosed patients that you are currently treating)	41%
3	Successfully completed therapy (Previously treated with HCV therapy successfully, sustained viral response (SVR)	30%
4	Relapsed from therapy (Previously treated with HCV therapy successfully, but had un-sustained viral response 24 weeks after completion of therapy and who are not currently receiving treatment)	3%
5	IFN Treatment Non-responder (Previously treated with HCV therapy unsuccessfully, little or no viral response during therapy and who are not currently receiving treatment)	0%
6	Discontinued therapy for reasons other than efficacy	1%

What are the primary costs that patients sustain in the private sector when undergoing HCV treatment?

#	Cost Items that patients pay in private sector	% of selection of the item from Doctors
1	Cost of medication	100%
2	Cost of managing side-effects of HCV medication	86%
3	Cost of hospital / clinic visits	57%
4	Cost of living / accommodations to be near the hospital / clinic	0%
5	Job-related / source of income costs	29%
6	Cost of travel (for office / hospital / clinic visits)	71%
7	Cost of monitoring the patient's response to treatment / follow-up	57%
8	Cost of tests	100%

What are the perceived principal challenges facing HCV patients under Egypt's insurance systems that make them get treatment through OOP?

#	Challenges facing patients under different insurance systems	% of Doctors selected that item
1	The system is too complicated to be understood	43%
2	The insurance protocol doesn't fit the patient condition	86%
3	Not receiving the complete dose	0%
4	Availability of the prescribed drug	29%
5	The prescribed drug is not listed in Hospital drug list	43%
6	The pharmacist switches to a generic or different brand	0%
7	Too much procedures and time to receive the medications	100%
8	The yearly fund (at the country expense) is not sufficient for the whole year treatment	71%

9	Other (limited numbers of qualified physicians at the examination place)	57%

Are physicians aware of the National Committee for the Control of Viral Hepatitis (NCCVH)?

1	Yes	100%
2	No	0%

What is its role of NCCVH in the treatment of Hepatitis C from physicians' perspective?

#	Item	% of Doctors selecting the item
1	Providing funding for patients' HCV treatment costs	**57%**
2	Providing funding for HCV treatment centers' operating costs	**43%**
3	Providing funding for clinical research	**43%**
4	Establishing treatment guidelines	**100%**
5	Educating health care professionals on HCV	**57%**
6	Educating the public/ raising public awareness of HCV	**57%**
7	Providing HCV screening	**86%**
8	Providing HCV vaccinations	**0%**

What are the various HCV diagnostic tests physicians' conduct to confirm patients HCV diagnosis?

#	Test Conducted	% of Patients Tested for HCV Using…
1	Liver Function Tests (ALT/AST)	**100%**
2	Viral load / Quantitative HCV test	**90%**
3	Qualitative HCV test	**0%**
4	Genotype Test	**1%**
5	Liver Biopsy	**0%**
6	Ultrasound	**70%**
7	Other (Fibroscan, CBC, ELIZA, PCR)	**60%**

What is the patient share of the following regiments and their duration of treatment?

#	Regimens	Patient share
1	Sofosbuvir ± RBV (Brand)	0%
2	Sofosbuvir ± RBV (Generic)	0%
3	Sofosbuvir + Daclatasvir ± RBV (Brand)	9%
4	Sofosbuvir + Daclatasvir ± RBV (Generic)	59%
5	Harvoni ± RBV (Brand)	1%
6	Harvoni ± RBV (Generic)	16%

7	Sofosbuvir + Olysio ± RBV (Brand)	2%
8	Paritaprevir/Ritonavir + Ombitasvir (Qurevo) ± RBV (Brand)	5%
9	Others (non-systemic treatment)	7%

What is the treatment outcome?

#	Treatment outcome	%
1	Successfully completed treatment (SVR)	95%
2	Non responders	1%
3	Relapsers	3%
4	Discontinued therapy due to reasons other than efficacy – mainly due to HCC	1%

Agreement on statements related to HCV from scale of 1 (strongly disagree) to 7 (strongly agree). Results are grouped to show the top two picks for each of the candidates.

#	Statements	% of being in the top 2 picks for candidates
1	There is very low awareness of Hepatitis C among the general population	0%
2	There is very low awareness of Hepatitis C in the broader medical community	0%
3	Hepatitis C is a less serious disease than HIV	43%
4	Hepatitis C is a less serious disease than Hepatitis B	43%
5	I strictly follow the HCV treatment guidelines in my country	57%
6	Clinical trial data for treatment naïve patients can be extrapolated to treatment experienced patients	43%

7	If a drug demonstrated good efficacy in treatment experienced patients during clinical trials, I would expect it to demonstrate even better efficacy in practice on my treatment naïve patients	57%
8	Clinical trial data for G1 patients can be extrapolated to G4 patients	29%

What are the guidelines followed by the physician?

#	Guidelines	% of Doctors
1	AASLD (American Association for Study of Liver Disease)	43%
2	EASL (European Association for Study of the Liver)	86%
3	APASL (Asia Pacific Association for Study of the Liver)	0%
4	WHO guidelines	29%
5	Egyptian National Treatment Guidelines for HCV	71%

The physicians' perception on the results of the reform efforts in 5 year from 2016

#	Reform	% of Doctors believing in that reform
1	Government will increase funding for HCV treatment centers	86%
2	Number of HCV treatment centers will increase	100%
3	Government will expand education efforts around HCV	100%
4	Government will increase payments to HCV patients under MOH/Health Insurance	100%

5	Government will increase patient access to HCV screening	100%
6	Government will establish more aggressive HCV treatment guidelines	71%
7	Government will increase treatment options available under National Health Insurance coverage	100%

How do you as a physician learn of new products to treat HCV?

#	Channel	% of selection
1	Internet	86%
2	Medical Journals	57%
3	Conference presentations/Symposia	86%
4	Product information via PDA/Mobile alerts	0%
5	Pharmaceutical Reps	43%
6	Continuous Medical Education	57%
7	Colleagues	0%
8	Opinion leaders	0%

Do you see local manufacturers or multinational pharmaceutical companies as having a more important role to play in the elimination of HCV from the country?

#	Pharmaceutical	% of mentioning
1	Local	77%
2	Multinational	23%

Annex II

Options to verify the quality of Egyptian generics used in publicly financed treatment campaigns

The following is a list of options, from easy/low impact to more complex, to verify and ensure that the public sector purchases generic drugs from consistent quality, manufactured according to internationally accepted standards:

■ Informal exploration with Egyptian Drug Agency EDA (CAPA, NODCAR) technical experts to understand the level of supervision and the degree to which deviations from Egyptian Good Manufacturing Practices (as they should be defined in by-laws/regulations) lead to regulatory enforcement actions.

■ Informal discussion with quality managers of Egyptian firms that have manufacturing contracts with multinationals, on their experience and assessment of the quality standards that are to be expected in Egypt.

■ If there are doubts that some firms may not be at acceptable levels, one could, on a voluntary basis, invite a technical consultant firm with European credentials to do a gap assessment. This could become a condition for future tender participation. www.tuev-sued.de/plants-buildings-technical-facilities/fields-of-engineering/cleanroom-technology/pharma-life-sciences shows an example of one firm that offers these type of services – of course there are several firms so this is not a recommendation.

■ Define a time frame (example two years) within which manufacturers must be compliant with international GMP, certified by a regulator or a consulting firm with the necessary credentials. This is a condition for WHO Prequalification

(WHO PQ), but WHO PQ has additional requirements specific to the product for which the PQ is granted.

■ Introduce a requirement for bioequivalence studies with originator DAAs for Egyptian generics, done by a contract research firm that has done such studies successfully as part of WHO PQ procedures (may require to go outside Egypt).

■ Specify a time frame (for example three years) within which only WHO PQ drugs will be accepted for public procurement, allowing manufacturers to decide whether they want to make investments into quality or give up this segment of the market.

■ For products that are in the WHO PQ process, there is a procedure called Expert Review Panel (ERP, see http://apps.who.int/prequal/info_press/documents/ERP_article.pdf), which can be used in the interim to define whether the quality risk associated with a specific product is acceptable. Egypt could form its own panel with WHO expert participation and guidance, focused specifically on the DAAs.

■ Hopefully, in the mid-term, the new EDA will build capacity to become a more stringent regulator and join the Pharmaceutical Inspection Cooperation scheme (PIC/S, www.picscheme.org), which would benefit the entire sector and reduce the need to apply specific conditions to DAAs or other lifesaving medicines.

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