Estimating economic and epidemiological burden of hepatitis C in Egypt, 2015-2025

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ESTIMATING ECONOMIC AND EPIDEMIOLOGICAL BURDEN OF HEPATITIS C IN EGYPT, 2015-2025

A Thesis Submitted to the
Public Policy and Administration Department
in partial fulfillment of the requirements for the degree of
Master of Public Policy

By

Wessam Abdelazeem Sadek Mankoula

Fall15
The American University in Cairo
School of Global Affairs and Public Policy

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DEDICATION

I dedicate this thesis to you, my beloved life companion, Eman, for her endless love, support, and encouragement.

I, also, dedicate this thesis to my father who passed away by his body; however the love and the memory of him shall never pass away.
ABSTRACT

Hepatitis C is the most pressing public health challenge in Egypt where Hepatitis C Virus (HCV) prevalence is the highest in the world. In 2015, Egypt Health Issues Survey showed that 10% of Egyptians between 15 – 59 years of age had been infected with HCV infection, while 7% are chronic active hepatitis C patients. This paper aims to estimate the current and future economic and epidemiological burden of HCV between 2015 and 2025. In addition, it compares the impact of different scenarios for management of this huge public health problem to identify the most cost effective strategy capable of reducing the economic and epidemiological burden of this disease at the country level. A Markov model representing hepatitis C progression was established showing the prognosis among HCV infected cohort within different age groups where the members of each group go through predefined states of health over one-year time cycles till 2025. The burden of hepatitis C will be estimated through calculating different transition probabilities and calculating the direct and indirect healthcare cost of the proportion of members who go through each stage of the disease and its complications. Under the current management strategy of 125,000 patients/year, it is estimated that chronic active HCV patients will show minimal decrease to reach about 4.1 million cases, with high economic burden of this strategy is very high where the direct costs are estimated $23.3 billion, and the total costs are $48.3 billion between 2015-2025. While increasing the treatment rate to reach one million patient annually for 5 years in addition to decreasing the annual incidence in the coming 10 years will drop HCV cases to about 636 thousands by 2025, and with only $16.2 billion as a direct costs, and total costs $34.2 billion between 2015-2025 which is 29.2% lower than the current management scenario.
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Abbreviations:

DAA  Direct-Acting Antiviral Agent
DALYs Disability Adjusted Life Years
G Genotype
HCC Hepatocellular Carcinoma
HCV Hepatitis C Virus
HIO Health Insurance Organization
HIV Human Immunodeficiency Virus
IDU Injection Drug Use
MOHP Ministry of Health and Population
PAT Parenteral Anti-schistosomal Therapy
Peg-IFN Pegylated Interferon
PI Protease Inhibitor
QALYs Quality Adjusted Life Years
RBV Ribavirin
SVR Sustained Viral Response
WHO World Health Organization
YLD Years of life Lost to Disability
YLL Years of Life Lost
I. Introduction

Hepatitis C is the most pressing public health challenge in Egypt. According to World Health Organization (WHO), Egypt has the highest prevalence of hepatitis C virus (HCV), where the results of blood screening and testing for the Egyptian blood donors showed 20% positive for HCV (GAR-WHO, n.d.). A recently published Egypt Health Issues Survey (EHIS) in 2015 on a nationally representative sample showed that 10% of Egyptians between 15 – 59 years of age had been infected with HCV infection, while 7% are chronic active hepatitis C patients (Ministry of Health and Population [Egypt], El-Zanaty and Associates [Egypt], & ICF International, 2015). This warrants the need to investigate the current and the future burden of this disease not only from the epidemiological perspective but also from the economic context. This knowledge is highly important for evaluating the different scenarios of interventions in order to manage this huge public health problem. Having this information will make the policy makers in health sectors able to choose the most cost effective strategy that is capable of reducing the economic and epidemiological burden of this disease at the country level.

HCV is a RNA virus responsible for the majority of chronic liver disease, cirrhosis, and Hepatocellular Carcinoma (HCC) cases in Egypt. HCV is transmitted mainly through exposure to infected blood. Historically, the inadequate sterilization and reuse of needles in the mass campaigns for treatment of schistosomiasis in Egypt between 1960s and 1980s were the main risk factors for this huge prevalence of HCV in Egypt (Nafeh et al., 2000; Rao et al., 2002). Recently, about 60% of the cases were infected in hospitals and clinics (Yahia, 2011). Also, it was estimated that 24.3% of patients were infected through blood transfusion, according to EDHS 2008 (Razavi et al., 2014). Also, some social practices, such as sharing common shaving tools at barber shops, sharing of home diabetes testing equipment, or toothbrushes are considerable risk factors outside the health care settings (Yahia, 2011).

HCV is the leading cause of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma (HCC). About 55%-85% of HCV infected cases become chronic active cases and pass through the way of developing fibrosis, cirrhosis, and may progress till
become decompensated cirrhosis and HCC (‘WHO | Hepatitis C’, 2015). There are many risk factors affecting the rate of progression from one stage to the following one in the pathway of the natural history of HCV such as age of the patient, gender, alcohol consumption, degree of inflammation and fibrosis of liver biopsy, co-infection with HIV or HBV, and other comorbidities (Chen & Morgan, 2006).

Globally, hepatitis C is a global public health problem where about 130 to 150 million people suffer from chronic HCV (WHO, 2015). It is estimated that HCV related deaths are 350,000 to 500,000 annually. Mapping the prevalence of HCV all over the world showed that Africa, Central and East Asia have the highest prevalence rate (Hanafiah, 2013).

In Egypt, the high prevalence of HCV is not the only problem, the high incidence of HCV is another important issue which reflects the new HCV infections that occurs annually. Literature showed that the incidence ranges from 2 to 6.9/1000 annually which means 160,000 to 500,000 new HCV infection occurs annually (Breban et al., 2013; Miller & Abu-Raddad, 2010). This huge number of newly infected cases made the problem ongoing and worsen the situation especially with the limited capacities of Egyptian Ministry of Health and Population (MOHP) for treating those patients, preventing new infections, and the high cost and low efficacy of old treatment regimens for HCV.

Although the problem of HCV in Egypt is huge and ongoing, limited data regarding to the economic and in-depth epidemiological burden of disease were found. Even with this limitation, the data available regarding the economic burden of disease in Egypt became outdated especially after the dramatic changes in the key inputs of the previously published models. The main changes were in the baseline data of the prevalence of HCV among the different age groups where the previous two published models used data from DHS 2008, however, a new DHS report was published recently in 2015. Also, new protocols of treatment were approved by MOHP which lead to dramatic changes in drug efficacy rather than that used in the previously published models, in addition to the most recent dramatic decrease in the drugs prices as well.
II. Research objectives:

This thesis aims to cover the following areas:

- **Estimate the current and future economic burden of HCV in Egypt 2015-2025:** This estimation will include the direct burden of HCV represented in the cost of HCV treatment regimen, in addition to other medical expenses for managing different HCV disease progression stages and complications. Also it will estimate the indirect economic burden of the disease such as disability adjusted life years (DALYs) to give an estimation for the productivity loss due to the disease. Also, the monetary value for DALYs will be calculated.

- **Estimate the current and future epidemiological burden of HCV in Egypt 2015–2025:** This part will give an estimation for all HCV viremia cases across the period from 2015 to 2015. It also will follow the trend of patients at cirrhosis stage, hepatocellular carcinoma, and liver related deaths.

- **Compare the impact of implementing different management scenarios on the economic and epidemiological burden of HCV in Egypt 2015 – 2025.** These three scenarios are:
  - Scenario I: is a mimic for the current situation using the same treatment rate, cost of current treatment regimen, efficacy of the used drugs, current incidence rate, and estimate the burden of HCV in the present and in future if this scenario continue as it is.
  - Scenario II: will study the effect of increasing the treatment rate to treat 500,000 cases per year.
  - Scenario III: will discuss the effect of ambitious strategy to treat 1 million cases in the coming five years and decrease the incidence rate by 50% between 2016-2020, then decrease the incidence rate to become 10% of the current rate between 2021-2025.
III. Literature Review

A. Natural History of the disease:

1. Causative organism:
Hepatitis C virus is a RNA virus that replicates in the cytoplasm of liver cells, but is not directly cytotoxic (Chen & Morgan, 2006). The virus has a high ability for replication ranging between 10^{10} and 10^{12} virions per day (Neumann et al., 1998). There are six genotypes of HCV (Boyer et al., 2002), where HCV genotype 4 is the most common one in Egypt, representing more than 90% of the cases (Kamal, 2007), however, no recent data available about HCV genotype in Egypt as genotyping is not routinely done to identify the protocol of management. The virus also has more than fifty subtypes (Chen & Morgan, 2006). HCV genome mutate frequently because of the weak error proofreading by the viral RNA polymerase in addition to rapid viral replication (Bukh, Miller, & Purcell, 1995). Numerous subtypes and frequent mutations have made difficulties in discovering vaccine for HCV till now.

2. Route of transmissions
HCV is a blood borne virus (i.e. the primary mode of transmission is the exposure to infected blood). Risk factors for transmission of HCV include using inadequately sterilized medical equipment in health care facilities especially injection equipment and poorly sterilized surgical instruments, the transfusion of infected blood and blood products (‘WHO | Hepatitis C’, 2015), inadequate commitment to infection control measures in hemodialysis units, and injecting drug use through the sharing of syringes and needles (Chen & Morgan, 2006). Also, some social practices, such as sharing common shaving tools at barber shops, sharing of home diabetes testing equipment, or toothbrushes are considerable risk factors outside the health care settings (Yahia, 2011). A systematic review analysis for the risk of transmission of HCV from infected mother to her baby showed that the rate of infection was 5.8% (95% confidence interval [CI], 4.2%–7.8%) for children of HIV-negative women and 10.8% (95% CI, 7.6%–15.2%) for children of HIV-positive women (Benova et al., 2014). It is rarely transmitted sexually. This vertical transmission increases in Egypt to reach 36% (5/14) according to a study conducted in Alexandria University Hospital in Egypt (Kassem, El-Nawawy, Massoud, El-Nazar, & Sobhi, 2000). HCV does not spread through casual contact such as sharing food or drinks with an infected person,
kissing, and hugging. Also it does not spread through food, water or breast milk (‘WHO | Hepatitis C’, 2015).

3. **Disease Progression:**

HCV can cause acute and chronic hepatitis. When person has infection by HCV it develop acute hepatitis, however, most of these cases, around 80%, are asymptomatic. Only 20% can develop symptoms such as fever, fatigue, nausea, vomiting, decreased appetite, abdominal pain, dark urine, grey-colored feces, pain in joints and jaundice. Among those who get infection, the HCV virus is spontaneously cleared in 15% to 45% of cases. Others who do not able to clear HCV by 6 months become chronic active cases. HCV begin causing fibrosis in the liver which means excessive accumulation of extracellular matrix proteins including collagen (Bataller & Brenner, 2005). On the long term 15% - 30% of them develop cirrhosis within 20 years. In the cirrhotic state, advanced fibrosis occurs and liver loses its normal architecture, however it is still able to do many important functions. Cirrhosis may be developed to decompensated cirrhosis where the liver becomes unable to do its function well leading to variceal hemorrhage, ascites, and hepatic encephalopathy. Also, it could develop hepatocellular carcinoma (HCC) (Figure II).

**Figure III1- Natural history of infection with hepatitis C virus**

(Chen & Morgan, 2006)
There are many variables affect the rate of progression from fibrosis to compensated cirrhosis, decompensated cirrhosis, and HCC such as age of the patient, gender, alcohol consumption, degree of inflammation and fibrosis on liver biopsy, and co-infection with HIV or HBV, and other comorbidities. People who get infected by HCV in the forties have higher chances of developing fibrosis than those infected at a younger age (Poynard, Bedossa, & Opolon, 1997). It was found that males who have daily alcohol consumption 30 g or more are more liable to develop advanced progression of liver fibrosis, in comparable to 20g/ day for females (NIH, 2002). Also, it was found that presence of HIV with low CD4 count (CD4<200), and HBV as well, accelerate the progression of fibrosis in HCV patients (Ragni & Belle, 2001).

B. Treatment of HCV (old treatment Vs. new treatment)

1. Obsolete treatment regimen (low efficacy with high side effects):
   Over the past decades, the standard treatment of HCV genotype 4 (HCV- G4) patient was a combination of pegylated interferon (PEG-INF) and ribavirin (RBV) for 48 weeks (Abdel-Razek & Waked, 2015). The efficacy of this combination to treat HCV-G4 patient was small. A worldwide study containing 7163 HCV patient treated by PEG-IFN/RBV showed only 41% sustained virological response (SVR), defined as aviremia 24 weeks after completion of antiviral therapy for chronic hepatitis C virus (Marcellin et al., 2012). Also, between 2007 and 2014 the National program for control of HCV in Egypt has treated about 350,000 patient with this combination (Doss et al., 2008) and the result showed SVR between 45% and 55% (Esmat et al., 2014).

2. Direct acting antivirals (DAAs), the new era for HCV treatment (High efficacy with minimal side effects)
   With discovering DAAs that target specific sites in HCV replication complex, a breakthrough in the efficacy of HCV treatment was introduced. There are two main classes of DAAs, they differ from each other according to the drug target site, and subsequently its efficacy against different genotypes. The first discovered DAAs drugs was S3/S4 protease inhibitors, while the second class of DAAs are inhibitors of viral polymerase. The first wave of the first generation of protease inhibitors is potent against HCV-G1 (Poordad et al., 2011) (Bacon et al., 2011) (Sherman et al., 2011) (Jacobson et al., 2011), but not effective against HCV-G4 (Abdel-Razek & Waked, 2015). That generation included NS3 protease inhibitor and
NS4 protease inhibitor (PIs) such as Boceprevir (BOC) and Telaprevir (TVR). Later on, the second wave of the first generation of PIs was approved for treatment of HCV-G4 such as Simeprevir (SIM). The DAAs drugs targeting HCV polymerase includes NS5B polymerase inhibitors and NS5A inhibitors. NS5B polymerase inhibitors can be divided into two groups: nucleoside inhibitors (NIs) which mimic the natural substrates of the polymerase that cause direct chain termination through its incorporation into the RNA chain (Asselah & Marcellin, 2012), while the other group is non-nucleoside inhibitors (NNIs) which cause conformational protein change through binding to one of the sites on HCV polymerase and inhibit the NS5B (Waked et al., 2014). For example, Sofosbuvir (SOF) was approved as NS5B polymerase inhibitor drug for treatment HCV-G4, while Daclatasvir (DCV) was approved as NS5A polymerase inhibitors for treatment HCV-G4 (Figure III2).

Figure III2- New effective drugs against HCV-G4

![Diagram showing DAAs, NS3/NS4 Protease Inhibitors, and NS5B/NS5A Polymerase Inhibitors]

3. **DAA resistance:**

HCV has a high ability for replication ranging between 10^{10} and 10^{12} virions per day (Neumann et al., 1998). The high error rate of NS%B RNA dependent RNA polymerase leads to the possibility of nucleotide substitution in the HCV genome with every cycle of replication. This nucleotide substitution may lead to resistance to DAA which called resistance associated variant (RAVs) (Abdel-Razek & Waked, 2015).

On one hand, SOF has a high genetic barrier for resistance. In subjects who received SOF in phase III clinical trials, changes in L159F, V321A, and S282T amino
acids were identified. L159F and V321A did not influence the activity of SOF, while S282T caused a reduction in susceptibility to SOF in one patient by 13.5 fold (Han, Mo, & Wong, 2012). On the other hand, NS5A inhibitors have low barrier for resistance. Single mutations at Q30E and Y93N confer high levels of resistance to NS5A inhibitors. These mutations were detected in 4.3% of HCV-4 treatment naive patients (McCormick et al., 2014).

Combining DAAs with different targets of activity limits the effect of these mutations and baseline RAVs. For example, patients who experienced failure of PIs treatment and had a dominant RAV responded to the combination of SOF/DCV in a similar manner as those without baseline RAVs (Sulkowski et al., 2014).

4. Guidelines for management HCV-G4 using DAAs drugs:

- Guidelines of European Association of Study of Liver diseases (EASL):

  The most recent therapeutic guidelines for HCV-G4 published by EASL was released in July, 2015. These guidelines had six treatment options for managing naive and experienced HCV-G4 patients. Two of these options were IFN-containing regimen while the other four options were IFN-Free regimen as shown in table III-1 (‘EASL Recommendations on Treatment of Hepatitis C 2015’, 2015).
Table III-1: Summary of EASL recommendations for treatment of HCV-G4 patients, July, 2015:

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IFN-containing Regimen</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Option 1:</strong></td>
<td>12 wks.</td>
</tr>
<tr>
<td>SOF + PEG-RBV</td>
<td></td>
</tr>
<tr>
<td><strong>Option 2:</strong></td>
<td></td>
</tr>
<tr>
<td>SIM + PEG-RBV</td>
<td>● SIM + PEG-RBV: for 12 wks.</td>
</tr>
<tr>
<td></td>
<td>PEG-RBV: for another 12 wks. in naive and relapse, and for another 36 wks. For prior partial and null responders.</td>
</tr>
<tr>
<td></td>
<td>● Stop treatment: if HCV RNA &gt; 25 IU/ml at treatment week 4, 12 or 24</td>
</tr>
<tr>
<td><strong>IFN-Free Regimen</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Option 1:</strong></td>
<td>12 wks.</td>
</tr>
<tr>
<td>SOF + Ledipasvir</td>
<td></td>
</tr>
<tr>
<td><strong>Option 2:</strong></td>
<td></td>
</tr>
<tr>
<td>Rmbitasvir + Paritaprevir + Ritonavir (± RBV)</td>
<td>● 12 wks.: without cirrhosis</td>
</tr>
<tr>
<td></td>
<td>● 24 wks.: with cirrhosis</td>
</tr>
<tr>
<td><strong>Option 3:</strong></td>
<td>12 wks.</td>
</tr>
<tr>
<td>SOF + SIM (± RBV)</td>
<td></td>
</tr>
<tr>
<td><strong>Option 4</strong></td>
<td></td>
</tr>
<tr>
<td>SOF + DCV (± RBV)</td>
<td>● 12wks.: naive patients</td>
</tr>
<tr>
<td></td>
<td>● 24 wks.: patient with cirrhosis and contraindication for RBV</td>
</tr>
</tbody>
</table>

('EASL Recommendations on Treatment of Hepatitis C 2015', 2015)

- Guidelines of American Association for the study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA)

In August 2015, AASLD and IDSA have recommended three treatment options for the management of HCV-G4 cases. They recommended option 1 and 2 of IFN-Free Regiment in ESAL 2015 guideline, in addition, they also have recommended SOF and weight based RBV for 24 wks. They also mentioned two alternatives, the first one was SOF plus PEG/RBV for 12 wks. And the second
alternative was SOF + SIM (± RBV) for 12 wks. due to limited supportive clinical data about this therapeutic option (AASLD/IDSA HCV Guidance Panel, 2015).

- **Egyptian guidelines**

  The National Committee for Control of Viral Hepatitis (NCCVH) in May 2015 has adopted one IFN-based regimen and two IFN- free regimen for treatment of HCV-G4 patients in Egypt. The IFN- based regimen was composed of SOF+PEG/RBV for 12 wks. For IFN- eligible patient. The second regimen was for patient ineligible for interferon where the first option was SOF + SIM for 12 wks., while the second option was SOF+RBV for 24wks. For patients who have to take amiodarone or cyclosporine drugs (NCCVH, 2015). The inclusion criteria according to May 2015 guideline include all HCV RNA positive patients between 18 and 70 years, either naïve patients or treatment experienced patients without restriction to their fibrosis stage (NCCVH, 2015).

  In November 2015, a new guideline has been published with a significant change in the treatment regimen. There were two treatment regimen, where the first regiment was for patients who are easy to be treated, and the second one for patients who are difficult to be treated. “Easy to Treat” group will get SOF + DCV for 12 wks., while the “Difficult to be Treat” group will get SOF + DCV +RBV for 12 wks. (Saeed, 2015). The inclusion criteria in November 2015 guideline become the same as the previous guideline except for the age which increased to include patients from 18 to 75 years (Saeed, 2015).

5. **Efficacy of oral DAA combinations:**

  Using DAAs for treatment HCV-G4 has showed significant increase in cure rate where SVR has reached nineties in some combinations. For example, in Doss et al. 2015, using SOF + RBV among Egyptian patients with G4 for 24 wks. showed 92% and 89% SVR among naïve and experienced patients respectively; and SVR among cirrhotic and non-cirrhotic were and 78% and 93% respectively, with an average SVR 90% (Doss et al., 2015). In another paper studied the efficacy of triple therapy, SOF+PEG/RBV for 12 wks., on HCV-G4 showed that SVR was 80% among cirrhotic while it was 84% among non-cirrhotic, and the total SVR was 83.3% (Wehmeyer et al., 2015).
6. Cost of the obsolete regimen versus DAAs regimens:
The last price for the treatment course of PEG-INF/RBV for 48 wks. in Egypt was about $ 2000. On the other hand, the price of the new DAAs drugs was very expensive in US and Europe. For example, the initial price of SOF was $84,000 for 12-wk course, and the price of SIM was $ 60,000 for 12-wk course (Fick & Hirschler, 2014), while the Egyptian government succeeded in its negotiation with Gilead Science to get SOF for 12 weeks at $900 only (Wanis, 2014) (Fick & Hirschler, 2014), and this price became the standard for the India and other developing countries (Palmer, 2014). Hence, the cost of the triple therapy (SOF+PEG-IFN/RBV) became $ 1500 (Abdel-Razek & Waked, 2015). Recently, head of NCCVH declared that the cost of the whole course of SOF+DCV that has been approved for treatment of HCV patient in the last treatment protocol in December 2015 will be only $ 319.3 (2500 LE) (Abdelsalam, 2015).
C. Epidemiological Burden

1. Global Burden

Hepatitis C is a huge public health problem facing many countries in the world (Mathurin, 2013). It is estimated that 130 to 150 million people globally suffer from chronic hepatitis C (WHO, 2015) which comprises about 3% of the world population (NIH, 2002). A significant number of those patients will develop complications such as liver cirrhosis and liver cell failure and hepatocellular carcinoma. WHO estimated that 350,000 to 500,000 people die each year from hepatitis C-related liver diseases (WHO, 2015).

Figure III3- Distribution of HCV all over the world

(Hanafiah, 2013)

Figure III3 shows the prevalence of HCV globally where Africa and Asia (Central and East) have reported the highest prevalence rates, while North America, Western Europe, and Australia reported low rates of HCV.

Globally, HCV genotype 1 (HCV-G1) is the most common genotype which represents about 46%, followed by HCV-G4 with 22%, HCV-G2 with 13%, and G4 with 13%. There is variation in dominance of HCV genotypes across the continents where HCV-G1 is dominant in Europe, North America, South America, and Australia.
which represent 53-71% of all cases; however, G3 is the dominant genotype in Asia (40%), on the other hand, in North Africa and Middle East G4 is dominant (71%), however, if Egypt was excluded, G1 will be the dominant (46%) as G1 will decrease to 34% of all infections in the region (Gower et al., 2014).

2. Burden in Egypt

2.1 Incidence of Hepatitis C

Four studies calculating the incidence of hepatitis C in Egypt by prospectively assessing cohort of Egyptian regarding positivity and negativity to HCV antibodies, then follow up the negative people to identify incident cases were reviewed. The first two studies estimated the incidence among population of rural villages. 6,734 Egyptians living in two rural village in lower and upper Egypt were assessed and followed up to calculate the incidence of HCV (Mohamed et al., 2005). The incidence among village resident in Qalubyia, Lower Egypt was 6.8/1,000 person-years, while the incidence among village residents in Assuit, Upper Egypt governorate was 0.8/1,000 person-years (Mohamed et al., 2005). Another 4 years cohort study were conducted in Menoufia governorate, Lower Egypt where the incidence was 2.4/1000 PY (95% CI: 1.6–3.5) (Mostafa et al., 2010). The second two studies calculated the incidence in specific groups such as children and pregnant women. 2852 uninfected infants from three villages with high HCV prevalence were prospectively followed from birth for up to 5.5 years where the incidence rate was 2.7/1000 PY (Doa’a et al., 2008). And for about 2.2 years, 2171 pregnant women in three rural Egyptian village were followed up to calculate the incidence of HCV among pregnant women. The results showed that the estimated HCV incidence was 5.2/1000 PY (Doa’a et al., 2008).

Another two studies built mathematical model to estimate the incidence of HCV in Egypt. In 2010, Miller et al build their model using age-specific prevalence extracted from a population based survey, EDHS 2008. The estimated incidence was 6.9/1,000 (95% CI, 5.5–7.4) PY which means that more than 500,000 new HCV case per year were infected (Miller & Abu-Raddad, 2010). On the other hand, in 2013, another model was conducted to address the assumption of time-independent epidemiology to reach more realistic estimate. This model estimated the incidence of HCV nationwide at around 2.0/1000 PY which means around 150,000 new infections annually (Breban et al., 2013). The difference between the two models may be due to
spatial heterogeneity of HCV prevalence and also present different incidence estimates for young adults.

### 2.2 Prevalence of hepatitis C

#### Prevalence in general population

Several studies investigated the prevalence of HCV among general population in Egypt. In 2008, Egypt Demographic and Health Survey (EDHS) using a national representative sample estimated the prevalence of HCV to be 14.7% among Egyptian aged 15-59 years old using HCV antibody test which means that those people had been exposed to HCV, while the cases with active infection with viremia were 9.8 % using HCV RNA PCR test (El-Zanaty & Way, 2009). Recently in 2015, the newly published Egypt Health Issues Survey (EHIS) showed that the prevalence of anti HCV and HCV RNA among the same age group was 10% and 7%; respectively. By adding a new age group from 1-14 years to the previous estimate, the prevalence of anti-HCV and HCV RNA among age group from 1-59 became 6.3% and 4.4%; respectively due to low prevalence of HCV among young age people (Ministry of Health and Population [Egypt], El-Zanaty and Associates [Egypt], & ICF International, 2015).

According to EHIS 2015, the prevalence of HCV among males are more than females, and there was a marked difference between age 50-54 and 55-59. For example, the prevalence of HCV viremia among male and female in age group 55 to 59 was 27.8% and 17.8% respectively. Also, the prevalence of active hepatitis showed a positive relationship with age where the prevalence among older age groups is much higher than the younger ones. For example, prevalence of active hepatitis in age groups below 20 was less than 1% while it reached 22.1% among age group 55-59 years as presented in figure III4.

It was found that the social determinants of health (SDH) such as place of residence, socioeconomic level and level of education have significant impact on the prevalence of HCV. According to EHIS 2015, the prevalence of active hepatitis cases in rural areas was higher than urban areas where it is 5.1% and 3.1%; respectively. In addition, the prevalence in Lower Egypt governorates is the highest (5.6%), while urban governorates showed the lowest prevalence (3%). Also, it was clear from the results that the prevalence of active hepatitis C cases increase with lower wealth
quintile groups and decrease with the increase of wealth quintile level. For example, HCV-RNA prevalence among lowest wealth quintile was 5.8%, while it was only 2.6% among the highest wealth quintile (Ministry of Health and Population [Egypt], El-Zanaty and Associates [Egypt], & ICF International, 2015). Regarding to the relation between educational level and HCV prevalence, it was found that it is higher in illiterate people (14.5%) while it was much lower among people who have completed secondary education and higher (4.1%) (El-Zanaty & Way, 2009).

Figure III4- Prevalence of active hepatitis by age, Egypt 2015

Prevalence among high-risk groups

There are different high risk group for HCV where the prevalence increases among them. These groups include schistosomiasis patients, patients on hemodialysis multi-transfused patients, thalassemia patients, IDUs, healthcare workers and barbers. Treatment of schistosomiasis patients by using parenteral anti-schistosomal therapy (PAT) campaigns is believed to be the major historic cause for increase the prevalence of HCV in Egypt (Frank et al., 2000). MOH treated millions of Egyptians using intravenous tater emetic drugs in between 1950s and 1980s (Strickland, 2006). During these large scale campaigns, reuse of glass syringe and improper sterilization measures have caused the HCV epidemic in Egypt (Yahia, 2011). Multiple studies were conducted to identify the prevalence of HCV among multi-transfused children.
where the average prevalence was 58%. And the average among children with thalassemia was 58% (Mohamoud et al., 2013). High HCV prevalence rates were observed with averages of about 42% among multi-transfused children and about 58% among children with thalassemia. Multiple studies were also conducted among hemodialysis patients (mostly adults). Very high HCV prevalence was found in both adult populations and children on hemodialysis. Regarding the prevalence among hemodialysis patient, 94.1% of them had HCV according to a study conducted in Mansoura Dakahlia, Lower Egypt (Kassem et al., 2000), while the prevalence decreased to 70% in Cairo (Ibrahim, 2010). The burden of disease among healthcare workers is also high where HCV prevalence was about 17% in average (Mohamoud et al., 2013). Also it was found that the prevalence among barbers reached 12.3% (Shalaby et al., 2010).

2.3 Evidence of ongoing transmission

Although Egypt has the highest HCV prevalence in the world, but the most serious problem is the ongoing transmission of this virus till now. As the capacity of treatment is less than the incidence rate of HCV. In 2013, Mohamoud et al. conducted build multiple regression model to follow the trend of HCV prevalence over time. They built multiple regression analysis which showed no significant decrease in the prevalence of HCV over time (P-value: 0.215) (Mohamoud et al., 2013). Recent studies suggest the iatrogenic (healthcare) exposures is the underlying cause for ongoing transmission of the disease in Egypt (Miller & Abu-Raddad, 2010) (Talaat et al., 2006).

2.4 Published model for estimating the epidemiological burden:

In 2014, Razafi et al. developed a mathematical model to estimate the present and future burden of hepatitis C virus. It was the first trial to give in-depth insight about the epidemiological burden of the hepatitis C in Egypt. A disease progression model was developed using Microsoft Excel where the model start with new acute hepatitis C cases that develop chronicity in addition to chronic viremic HCV case. These cases go through the model and progress from on stage to another according to certain probabilities as in Figure III5. It moves between different stages of fibrosis (F0, F1, F2, and F3) till reach cirrhotic stage, then it develop decompensated cirrhosis which has different forms such as variceal hemorrhage, hepatic encephalopathy, and ascites. It may develop also hepatocellular carcinoma. The chronic HCV cases may end up
with cure after getting suitable treatment, liver transplantation, or death due to liver related mortality (Razavi et al., 2014).

**Figure III-5** The flow of HCV disease progression model of Razavi et al., 2014

(Razavi et al., 2014)

NC= New Cases , TC= Total Cases

This study showed the burden of the disease in 2013 and the estimated future burden by 2030 as shown in table III-2.

**Table III-2 Estimate of HCV disease burden in 2013 and 2030, in Egypt:**

<table>
<thead>
<tr>
<th></th>
<th>2013 Estimate</th>
<th>2030 Estimate</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viremic HCV infection</td>
<td>5,980,000</td>
<td>4,420,000</td>
<td>(20)</td>
</tr>
<tr>
<td>HCC Cases</td>
<td>16,100</td>
<td>18,300</td>
<td>15</td>
</tr>
<tr>
<td>Liver Related Mortality</td>
<td>33,000</td>
<td>36,500</td>
<td>10</td>
</tr>
<tr>
<td>Decompensated Cirrhosis</td>
<td>137,000</td>
<td>136,000</td>
<td>(1)</td>
</tr>
<tr>
<td>Compensated Cirrhosis</td>
<td>626,000</td>
<td>611,000</td>
<td>(2)</td>
</tr>
</tbody>
</table>
One of the main limitations for this model is that it did not take into consideration the progression of disease in cured cases or spontaneously cured cases which may got the infection again with HCV. Also it may progress to advanced stages and develop liver related complications in slower rate despite of viral clearance. This issue may lead to underestimation for cases of decompensated cirrhosis and hepatocellular carcinoma as well. Another important issue is that there are many variables used in this model which have been dramatically changed in the last two years. First, the drugs available at the time of developing this model for treatment HCV were pegylated interferon (Peg-INF) and ribavirin (RBV) which have many side effect and contra indications for this treatment, therefor, only 40% to 60% of HCV patient were eligible for getting Peg-INF/ RBV (Morrill, Shrestha, & Grant, 2005). Second, the Sustained Viral Response (SVR 24) which defined as aviremia 24 weeks after completion of antiviral therapy for chronic HCV infection (Pearlman & Traub, 2011), this SVR for Peg-INF/ RBV was 48% (Razavi et al., 2014), which means that only 48% of people who received this regimen were cured. However, nowadays after discovering Sofosbuvir (SOF) the SVR 12 for the triple therapy containing SOF, Peg-INF/ RBV for 12 weeks is 83.3% (Wehmeyer et al., 2015) and 90% for dual therapy containing SOF and RBV for 24 weeks (Doss et al., 2015) with average 86.65%. Third, the number of annually treated patient in Egypt used in this model was 65,000 patient per year where 77% of them got their treatment in the liver treatment centers affiliated to Ministry of Health and Population (Doss et al., 2008), 15% of them got their treatment from Health Insurance Organization (HIO), and 8% of them got their treatment as out of pocket. However, recently the number of people receiving the treatment annually has increased to 125,000 patients per year (Donald, 2015).

Two recent studies addressed estimation for the current and the future burden of HCV in Egypt when applying different scenarios regarding to treatment rate and treatment efficacy. In 2014, Waked et al used the previously illustrated mathematical model developed by Razavi et al (Razavi et al., 2014). This paper studied three scenarios where the basic one assume fixed number for annually treated patient, eligible patient for treatment, the number of newly diagnosed patient between, and efficacy of the drugs, 2013 till 2030 (Waked et al., 2014). The second scenario assumed increasing efficacy of the drugs to become 90% rather than 48% in the first
scenario, and increasing the percentage of people eligible for getting the treatment to reach 90% compared to 50%, while the third scenario assumed increasing the drug efficacy and treatment eligibility such as previous scenario, in addition to increasing the treatment rate to reach 325,000 patient by 2018 rather than 65,000 in the second scenario (Waked et al., 2014). The impact of each scenario are shown in table III-3

<table>
<thead>
<tr>
<th></th>
<th>2013 Estimate</th>
<th>2030 Estimate</th>
<th>Scenario (1)</th>
<th>Scenario (2)</th>
<th>Scenario (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of total infected</td>
<td>6,000,000</td>
<td>4,420,000</td>
<td>4,045,000</td>
<td>280,000</td>
<td></td>
</tr>
<tr>
<td>% of change from 2013</td>
<td></td>
<td>-26%</td>
<td>-32%</td>
<td>-95%</td>
<td></td>
</tr>
<tr>
<td>No. of compensated cirrhosis</td>
<td>630,000</td>
<td>610,000</td>
<td>507,000</td>
<td>76,000</td>
<td></td>
</tr>
<tr>
<td>% of change from 2013</td>
<td></td>
<td>-2%</td>
<td>-19%</td>
<td>-88%</td>
<td></td>
</tr>
<tr>
<td>No. of decompensated cirrhosis</td>
<td>138,000</td>
<td>136,300</td>
<td>110,000</td>
<td>17,000</td>
<td></td>
</tr>
<tr>
<td>% of change from 2013</td>
<td></td>
<td>-0.6%</td>
<td>-21%</td>
<td>-87%</td>
<td></td>
</tr>
<tr>
<td>No. of HCC</td>
<td>16,000</td>
<td>18,500</td>
<td>16,000</td>
<td>2,400</td>
<td></td>
</tr>
<tr>
<td>% of change from 2013</td>
<td></td>
<td>+15%</td>
<td>0%</td>
<td>-85%</td>
<td></td>
</tr>
<tr>
<td>No. of HCV related Mortality</td>
<td>33,000</td>
<td>36,500</td>
<td>30,700</td>
<td>7,500</td>
<td></td>
</tr>
<tr>
<td>% of change from 2013</td>
<td></td>
<td>+10%</td>
<td>-7%</td>
<td>-77%</td>
<td></td>
</tr>
</tbody>
</table>

(Waked et al., 2014)

Regarding to the design of this model, our previously mentioned criticism is still valid as Waked et al., 2014 used the model of Razavi et al., 2014 as is. Although the authors updated some of data used in the model, these data become now outdated. For example, they added the SVR of the new DAA drugs that have reached phase II and phase III clinical trials and are expected to be in the market soon. They expected...
SVR for this new drugs at that time to be 90%, however the recent studies showed that the SVR for these drugs after using it on large scale to range from 83.3% for triple therapy (Wehmeyer et al., 2015) to 90% for dual therapy (Doss et al., 2015) with average 86.65%. Another issue, the inclusion criteria used in this paper for the persons eligible for treatment were age form 15-59 years old, and the histological state of liver fibrosis was more or equal to F2, however the current inclusion criteria published in May 2015 included wider age group from 18-70 years old, and also include all fibrotic stages including F0 and F1 which will lead to changes in the outcomes of the model (NCCVH, 2015).

The second study addressed the estimation of the current and the future burden of HCV in Egypt when applying different scenarios regarding to treatment rate and treatment efficacy was conducted by Shelbaya et al., 2015. They developed Markov model to model the transition of HCV infected cohort among different age groups using Egyptian DHS 2008 through following them up over time. In this Markov model, members of the cohort go through predefined states of health over a period of time where the patients move between different health states of the liver disease such as F0, F1, F2, F3, compensated cirrhosis, and complication and liver related death according to specific probabilities. Then the burden of HCV (morbidity and mortality) was estimated for the cohort.

The results of the model showed that the current treatment rate for about 65,000 patient/ year will lead to increase the annual number of HCV related deaths in Egypt from about 15,000 deaths/year in 2015 to about 40,000 deaths/year by 2030 (Shelbaya et al., 2015). Also, all cirrhotic cases is expected to increase from 750,000 cases in 2015 to reach the peak by 2022 where it will be 925,000 cases then slightly decrease to reach 800,000 cases by 2030 (Shelbaya et al., 2015). The paper showed that with the increase the rate of treatment to 8% i.e. treating 300,000 - 450,000 patients the expected total viremic HCV cases will reach 1,000,000 cases by 2030, number of liver related deaths will be lower than 15,000 deaths, and the number of patients with cirrhosis will decline by 87 % to reach about 100,000 cases by 2030 (Shelbaya et al., 2015).

Although this model tried to mimic the natural history of the disease and the possible progression events that could happen, however, there are some issues
regarding the design of the model. First, according to the model, the patient who got the treatment and not cured they either stay in the same health state or progress to the next one, where it is possible to get the treatment another time which may lead to overestimate for the economic burden of the disease. Second, one of transition states in the model for health states F0, F1, F2, F3, F4, compensated cirrhosis, and decompensated cirrhosis health states was “New Incidence” transition state which represents the probability of developing new incident case from the previous health state. However, this probability to develop new incident case should be allocated only to susceptible individuals who are HCV free or cured and should not be allocated to individuals with the disease.

D. Economic burden

Limited literature were found covering the aspect economic burden of HCV in Egypt. The two previously reviewed models in this paper of Razavi et al. 2013 and Shelbaya et al. 2015 were used to estimate the current and future economic burden of HCV in Egypt.

In Estes et al., 2015 model, the direct health care cost and indirect burden of HCV in Egypt was calculated between 2013 and 2030 through using the model established by Razavi et al. 2013, where direct health care cost was calculated based on data collected from the National Liver Institute which is a representative of governmental hospitals. Also, indirect costs were estimated based on calculating disability adjusted life years (DALYs) which includes years of life lost to disability (YLD) and years of life lost due to premature death (YLL); in addition the value of lost productivity was estimated using Egyptian estimates for the value of a statistical life year (VSLY). The same previously used scenarios in Waked et al., 2014 to estimate the economic burden were used by Estes et al., 2015 to calculate the economic burden as well, where the first scenario had the old treatment with 48% SVR and treated cases annually is about 65,000; the second scenario with 90% SVR and 65,000 treated cases annually; while the third scenario had 90% SVR and 325,000 treated cases annually.

The results of the model presented in Table III-4 showed that the old regimen of treatment and number of annually treated burden will result in $ 89.1 billion as a cumulative total cost for HCV, however the new introduced HCV drugs with high
SVR will decrease the burden by 3.7%, while increasing the rate of treatment using this drugs as in scenario no. 3 will cause significant decrease in the burden of HCV by 35.4% to reach $57.6 billion (Estes et al., 2015).

Table III-4 Direct and indirect costs by Scenario – Egypt, 2015–2030

<table>
<thead>
<tr>
<th></th>
<th>Scenario (1)</th>
<th>Scenario (2)</th>
<th>Scenario (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative disability adjusted</td>
<td>7,875,440</td>
<td>7,343,640</td>
<td>4,923,210</td>
</tr>
<tr>
<td>life years 2013–2030</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of change from scenario (1)</td>
<td>-6.8%</td>
<td>-37.5%</td>
<td></td>
</tr>
<tr>
<td>Cumulative direct costs in</td>
<td>23,244,377,860</td>
<td>24,192,586,440</td>
<td>18,632,607,710</td>
</tr>
<tr>
<td>2013–2030 (US $)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of change from scenario (1)</td>
<td>4.1%</td>
<td>-19.8%</td>
<td></td>
</tr>
<tr>
<td>Cumulative indirect costs in</td>
<td>65,822,552,110</td>
<td>61,547,348,360</td>
<td>38,929,874,750</td>
</tr>
<tr>
<td>2013–2030 (US $)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of change from scenario (1)</td>
<td>-6.5%</td>
<td>-40.9%</td>
<td></td>
</tr>
<tr>
<td>Cumulative total costs in</td>
<td>89,066,929,970</td>
<td>85,739,934,800</td>
<td>57,562,482,460</td>
</tr>
<tr>
<td>2013–2030 (US $)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of change from scenario (1)</td>
<td>-3.7%</td>
<td>-35.4%</td>
<td></td>
</tr>
</tbody>
</table>

(Estes et al., 2015)

Shelbaya et al., 2015 model showed that the estimated cost of applying policy of 1% treatment rate will be $600 million in 2015 then decline to $500 million by 2030 where all viremic HCV cases will decline by 15% to reach about 5.5 million cases, while with 5% treatment rate it decline from at $900 million in 2015 to $550 million by 2030 where this policy will lead to decrease the all viremia cases by 61% to reach 2.5 million cases (Shelbaya et al., 2015). However, the cost of treatment of the suggested policy by the paper, 8% treatment rate, was $1.3 billion in the first year of treatment then decrease gradually to reach $ of $580 million by 2030, where all viremia cases will decrease by 84.6% to reach 1 million cases by 2030 (Shelbaya et al., 2015).

On one hand, in Shelbaya et al. 2015, the cost of the treatment was updated to match the new prices of the new drugs available for treatment HCV. On the other hand, all the estimates of the cost data were based on expert opinion from a Delphi panel of local experts. Also, it is not clear if this is the cost of triple regimen or the
dual regimen as the available published model is just poster presentation, therefore did not contain much detailed information. Another comment regarding to the cost estimate is that the cost estimate for liver transplant in first year is very small ($1.197), as the cost of liver transplant surgery is much higher than this cost. According to Khalaf et al., 2005 the cost of living donor liver transplantation (LDLT) in a private based hospital is about $70,000 while it reaches $25,000 in governmental hospital, also a recent estimate in 2015 showed that the cost is about $42,000 according to data collected from the National Liver Institute (NLI), a nationally representative government hospital (Estes et al., 2015). This very low cost estimate for liver transplant may lead to underestimation of the real burden of the diseases.

E. Other types of disease burden:
Lack of awareness about Hepatitis C in the community often leads to misinformation, missing of opportunities for prevention and treatment, and stigmatization of infected populations. Level of support that someone with chronic hepatitis C might receive was less when compared to someone with a chronic illness that does not carry a stigma which might affect self-esteem and cause decrease in the quality of life (Ibrahim & Madian, 2011). This stigma of the disease push 30.9% of the patients to conceal the nature of their illness and 24.4% of them even conceal this information from their families, according to a study conducted in Elghar village, Zagazig governorate (Eassa et al., 2007). Also, HCV patients are not allowed to travel to gulf countries for work. This opportunity lost due to inability of traveling for working in certain countries are not included in our analysis in the thesis.

F. National Strategy for Prevention and Control 2014-2018
As Egypt is the highest country in the world in the prevalence of HCV, World Health Organization (WHO) has called experts from headquarter in Geneva, Center of Disease Control and Prevention (CDC) in U.S, NAMRU-3, and Institut Pasteur/Agence Nationale de Recherches sur le SIDA et les Hépatites Virales (ANRS) to support Egypt in building a comprehensive national strategy for prevention and control of HCV. Multiple mission in different specialties visited Egypt to conduct gap analysis, then began in cooperation with MOH official and Egyptian NGOs to establish “Plan of Action for the Prevention, Care and Treatment of Viral Hepatitis, Egypt, 2014-2018” (MOHP, 2014).
The plan of action is composed of seven pillars to ensure efficient prevention and control of viral hepatitis. The first pillar aimed to strengthen national surveillance system for viral hepatitis to follow the trend of the disease, identify risk factors, and measure the impact of implementation of the prevention and control program. The second pillar is focused on infection control where it aimed to decrease transmission of viral hepatitis through health care facilities, promote safe injection, and strengthen monitoring and evaluation program to ensure proper implementation for infection control measures. The third pillar focused on blood safety through different activities such as establishing national standards for blood transfusion and management, enhance the capacities of blood banks in blood screening and testing, capacity building for staff working in blood banks, and developing IT component to increase safety of collected blood and enhance blood management system. The fourth pillar is focused on vaccination against Hepatitis B where it aimed to achieve universal vaccination among high risk groups, and ensure implementation of zero dose of against HBV for all newborn in the first 24 hours after birth. The fifth pillar is concerned with raising awareness regarding to mode of transmission and methods of prevention among community. The sixth pillar is dedicated to ensuring availability and accessibility of effective drugs for treatment of viral hepatitis. The seventh pillar is concerned with scientific research to fill the gap in knowledge in hepatitis issues, and translate this knowledge into policies and practices (MOHP, 2014).
IV. Methodology:

A. Model Description

A model representing hepatitis C progression was established by using Markov model showing the prognosis among HCV infected cohort within different age groups using Egyptian DHS 2015 results, then following each age group cohort between 2015-2025. In this Markov model, the members of each age group go through predefined states of health over one-year time cycles till the end of the predefined period of time to 2025. The current and future epidemiological burden (morbidity and mortality) and economic burden as well of hepatitis C will be estimated through calculating different transition probabilities and calculating the direct and indirect healthcare cost of the proportion of members who go through each stage of the disease and its complication.

First, all Egyptian population between 1-59 years will be divided according to their age into 5 years interval age groups. Then, each cohort will move through the same health states with different probabilities according to the age. The health states were based on presence or absence of hepatitis C viremia, liver histology, decompensated liver disease, hepatocellular carcinoma, or liver transplantation. The hepatic patient has three histological states based on Metavir classification, F0, F1, F3 and cirrhotic stage. Over a period of time the patient go from a stage to the following or stay at his stage. For example, patient in F0 state after one year could become in F1 stage or stay at F0 stage and so on. The data required for this model such as probability of transmission from stage to another, cost of health care services and utilities of different health states will be gotten from literature and will described in details in “Model Input” section. Annex 1 contains the model structure.

The health states included in the models are:

- HCV free population: This group includes all the people in this age group who are not suffering from Viremic HCV, while the following health states includes patients who has HCV viremia
- F0_treatment: This group includes the people in this age group who have viremia and their histology according to Metavir criteria showed that they have no fibrosis (F0 stage) (Goodman, 2007). Also, the patient in this age group may get or not get the treatment according to many scenarios such as
probability of diagnosis and availability of drug and eligibility for going through the treatment protocols

- **F0** treatment failure: This group includes the people in this age group who have viremia and their histology according to Metavir criteria showed that they have no fibrosis (F0 stage), and they got HCV treatment previously; however, they did not show SVR (i.e. treatment failure)

- **F1** treatment: This group includes the people in this age group who have viremia and their histology according to Metavir criteria showed that they have portal fibrosis without septa (F1 stage) (Goodman, 2007). Also, the patient in this age group may get or not get the treatment according to many scenarios such as probability of diagnosis and availability of drug and eligibility for going through the treatment protocols

- **F1** treatment failure: This group includes the people in this age group who have viremia and their histology according to Metavir criteria showed that they have portal fibrosis without septa (F1 stage), and they got HCV treatment previously; however, they did not show SVR (i.e. treatment failure)

- **F2** treatment: this group includes the people in this age group who have viremia and their histology according to Metavir criteria showed that they have portal fibrosis with few septa (F2 stage) (Goodman, 2007). Also, the patient in this age group may get or not get the treatment according to many scenarios such as probability of diagnosis and availability of drug and eligibility for going through the treatment protocols

- **F2** treatment failure: This group includes the people in this age group who have viremia and their histology according to Metavir criteria showed that they have portal fibrosis with few septa (F2 stage), and they got HCV treatment previously; however, they did not show SVR (i.e. treatment failure)

- **F3** treatment: This group includes the people in this age group who have viremia and their histology according to Metavir criteria showed that they have portal fibrosis with numerous septa without cirrhosis (F3 stage) (Goodman, 2007). Also, the patient in this age group may get or not get the treatment according to many scenarios such as probability of diagnosis and availability of drug and eligibility for going through the treatment protocols.
• F3_ treatment failure: This group includes the people in this age group who have viremia and their histology according to Metavir criteria showed that they have portal fibrosis with numerous septa without cirrhosis (F3 stage), and they got HCV treatment previously; however, they did not show SVR (i.e. treatment failure)

• Compensated Cirrhosis: This group includes the people in this age group who have viremia and the liver has irreversible diffuse disorganization of its normal structure (El Saadany et al., 2005); however, it is still able to perform many important functions (Franciscus, 2015). Also, the patient in this age group may get or not get the treatment according to many scenarios such as probability of diagnosis and availability of drug and eligibility for going through the treatment protocols

• Compensated Cirrhosis with treatment failure: This group includes the people in this age group who have viremia and the liver has irreversible diffuse disorganization of its normal structure (El Saadany et al., 2005); however, it is still able to perform many important functions (Franciscus, 2015). Also, the patient in this age group may get or not get the treatment according to many scenarios such as probability of diagnosis and availability of drug and eligibility for going through the treatment protocols. The patients in this group got HCV treatment previously; however, they did not show SVR (i.e. treatment failure)

• Diuretic Sensitivity Ascites: This group includes the people in this age group who have viremia and decompensated cirrhosis where the liver is extensively scarred and unable to do its function well (Franciscus, 2015), which leads to a measurable accumulation of intra-abdominal fluid due to the increase in portal venous pressure (El Saadany et al., 2005), and this ascites can be treated with dietary sodium restriction and oral diuretic (Arroyo et al., 1996)

• Diuretic Refractory ascites: This group includes the people in this age group who have viremia and decompensated cirrhosis where the liver is extensively scarred and unable to do its function well (Franciscus, 2015), which leads to a measurable accumulation of intra-abdominal fluid due to the increase in portal venous pressure (El Saadany et al., 2005), however, this ascites cannot be treated with dietary sodium restriction and oral diuretic (Arroyo et al., 1996).
• Variceal Hemorrhage: This group includes the people in this age group who have viremia and decompensated cirrhosis induced portal hypertension (El Saadany et al., 2005)
• Hepatic Encephalopathy: This group includes the people in this age group who have viremia and decompensated cirrhosis that characterized by changes in personality, intellectual impairment, and alteration in level of consciousness (‘Hepatic Encephalopathy’, 2015)
• Hepatocellular Carcinoma: This group includes the people in this age group who have viremia and cirrhosis with a primary malignancy of the liver cells (‘Hepatocellular Carcinoma’, 2015)
• Liver Transplant 1st Year: This group includes the people in this age group who have had conducted liver transplantation operation during this year.
• Liver Transplant Subsequent Year: This group includes the people in this age group who have had conducted liver transplantation operation in the previous year or years
• Cured: This group includes the people in this age group who cured from HCV either spontaneously or by HCV treatment and they do not have cirrhosis
• Cured with Cirrhosis: This group includes the people in this age group who cured from HCV when they got HCV treatment, however, they do developed cirrhosis
• Liver Related Deaths: This group includes the people in this age group who died as a consequence to HCV disease
• Death from Background Mortality: This group includes the people in this age group who died due to any other causes rather than HCV disease.

The current and future burden of HCV with the different policies will be estimated in the form of epidemiological and economic burden. In epidemiological burden we will follow all viremia cases, cirrhosis, HCC, and liver related deaths over the coming 15 years. On the other hand, we will estimate the economic burden in the form of direct expenses that includes cost of treatment, consulting physicians, hospital admissions, and laboratory investigations. In addition to direct heath care cost, the indirect cost will be calculated as well. This indirect cost will be identified by
calculating Disability Adjusted Life Years (DALYs) which includes years of life lost due to disability (YLD), and years of life lost due to premature death (YLL).

This model will be designed and analyzed by using “TreeAge Pro 2015” software application https://www.treeage.com/

B. Different scenarios
After establishing this model we will compare between three scenarios for control of HCV in Egypt where:

- The first scenario: is a mimic for the current situation using the same treatment rate, cost of current treatment regimen for 125,000 cases, efficacy of the used drugs, current incidence rate, and estimate the burden of HCV in the present and in future if this scenario continue as it is. In this scenario, we used the triple and dual therapy for treating HCV cases in 2015 and use the recent treatment protocol published in December 2015 by NCCVH that depend on SOF and DCV for treating cases starting from 2016 (Saeed, 2015).

- The second scenario: will study the effect of increasing the treatment rate to treat 500,000 cases per year starting from 2016 with using the recent treatment protocol published in December 2015 by NCCVH that depend on SOF and DCV±RBV for treating cases starting from 2016 (Saeed, 2015).

- The third scenario: will discuss the effect of ambitious strategy to treat about 1 million cases in the upcoming five years and decrease the incidence rate by 50% between 2016-2020, then decrease the incidence rate to become 10% of the current rate. We also will use the recent treatment protocol published in December 2015 by NCCVH that depend on SOF and DCV±RBV for treating cases starting from 2016 (Saeed, 2015).

C. Model Input:

1. Population:
The data of the population was based on data collected from “Egypt Statistical Year Book,2015” produced by Egyptian Central Agency for Public Mobilization and Statistics (CAPMAS). The population was divided into age groups with 5 year intervals (CAPMAS, 2015). We gathered people who were 60 years or older in one group. Table IV-1 presents the population data used in the model.
2. Prevalence

The data of HCV prevalence was based upon results of the EHIS 2015. The EHIS 2015 had a nationally representative sample of Egypt. Among 842 primary sampling units (PSUs) (shiakhas/villages) from 25 governorates 624 PSUs were selected. Then household list in the sample were prepared and approximately 28,500 individuals between 6 months and 59 years were identified for interviews and testing for HCV (Ministry of Health and Population [Egypt], El-Zanaty and Associates [Egypt], & ICF International, 2015). Two different types of laboratory tests were conducted, HCV antibody and HCV RNA. We used the results of HCV RNA as it represents the chronic active hepatitis cases. Results were presented in five-year age groups for individuals from 1- 59 year (Table IV-1). The prevalence of HCV RNA for individual aged 1- 59 was 4.4%. The prevalence for people aged sixty years and above was assumed to be as equal as those in the age group 55-59 years.

**Table IV-1 Distribution of Egyptian population and HCV RNA positive cases by age, 2015**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Population number *</th>
<th>Probability of Healthy Population</th>
<th>Probability of HCV RNA (+ve) cases **</th>
</tr>
</thead>
<tbody>
<tr>
<td>0- 04</td>
<td>9830000</td>
<td>0.9980</td>
<td>0.0020</td>
</tr>
<tr>
<td>05-09</td>
<td>9126000</td>
<td>0.9995</td>
<td>0.0005</td>
</tr>
<tr>
<td>10-14</td>
<td>8184000</td>
<td>0.9970</td>
<td>0.0030</td>
</tr>
<tr>
<td>15-19</td>
<td>8389000</td>
<td>0.9920</td>
<td>0.0080</td>
</tr>
<tr>
<td>20-24</td>
<td>8929000</td>
<td>0.9780</td>
<td>0.0220</td>
</tr>
<tr>
<td>25-29</td>
<td>8399000</td>
<td>0.9700</td>
<td>0.0300</td>
</tr>
<tr>
<td>30-34</td>
<td>6731000</td>
<td>0.9510</td>
<td>0.0490</td>
</tr>
<tr>
<td>35-39</td>
<td>5281000</td>
<td>0.9400</td>
<td>0.0600</td>
</tr>
<tr>
<td>40-44</td>
<td>4740000</td>
<td>0.9100</td>
<td>0.0900</td>
</tr>
<tr>
<td>45-49</td>
<td>4350000</td>
<td>0.8870</td>
<td>0.1130</td>
</tr>
<tr>
<td>50-54</td>
<td>3777000</td>
<td>0.8010</td>
<td>0.1990</td>
</tr>
<tr>
<td>55-59</td>
<td>3084000</td>
<td>0.7790</td>
<td>0.2210</td>
</tr>
<tr>
<td>&gt;=60</td>
<td>5,993,000</td>
<td>0.7790</td>
<td>0.2210</td>
</tr>
</tbody>
</table>

3. Incidence

We used the most recent estimate for the incidence of HCV in Egypt of Breban et al. 2013, where a nationally represented data were used to give a realistic incidence for HCV. This model estimated the incidence of HCV nationwide around 2.0/1000 PY which means that there are 150,000 new HCV infections annually (Breban et al., 2013).

4. Baseline health states

2.1 Liver Fibrosis (F0, F1, F2, F3)

The data of the baseline or initial probabilities of different stages of liver disease in each age group was based on data from Wong et al. 2000 paper for estimating the burden of HCV in United States (Wong et al., 2000). As we used Metavir classification for the grade of liver fibrosis in our model, we divided the allocated probability of the baseline value of mild hepatitis in Wong paper equally between F0 and F1; while the allocated value for moderate hepatitis was equally divided between F2 and F3 (table IV-2). These baseline probabilities were calculated after taking into consideration the baseline probabilities of HCV related deaths and HCC.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>F0</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-04</td>
<td>0.00100</td>
<td>0.00100</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>05-09</td>
<td>0.00025</td>
<td>0.00025</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>10-14</td>
<td>0.00149</td>
<td>0.00149</td>
<td>0.00001</td>
<td>0.00001</td>
</tr>
<tr>
<td>15-19</td>
<td>0.00396</td>
<td>0.00396</td>
<td>0.00004</td>
<td>0.00004</td>
</tr>
<tr>
<td>20-24</td>
<td>0.00979</td>
<td>0.00979</td>
<td>0.001210</td>
<td>0.001210</td>
</tr>
<tr>
<td>25-29</td>
<td>0.01335</td>
<td>0.01335</td>
<td>0.001640</td>
<td>0.001649</td>
</tr>
<tr>
<td>30-34</td>
<td>0.01737</td>
<td>0.01737</td>
<td>0.00538</td>
<td>0.00538</td>
</tr>
<tr>
<td>35-39</td>
<td>0.02125</td>
<td>0.02125</td>
<td>0.00659</td>
<td>0.00659</td>
</tr>
<tr>
<td>40-44</td>
<td>0.02236</td>
<td>0.02236</td>
<td>0.01431</td>
<td>0.01431</td>
</tr>
<tr>
<td>45-49</td>
<td>0.02790</td>
<td>0.02790</td>
<td>0.01786</td>
<td>0.01786</td>
</tr>
<tr>
<td>50-54</td>
<td>0.02855</td>
<td>0.02855</td>
<td>0.04234</td>
<td>0.04234</td>
</tr>
<tr>
<td>55-59</td>
<td>0.03144</td>
<td>0.03144</td>
<td>0.04662</td>
<td>0.04662</td>
</tr>
<tr>
<td>&gt;=60</td>
<td>0.00254</td>
<td>0.00254</td>
<td>0.05204</td>
<td>0.05204</td>
</tr>
</tbody>
</table>
2.2 Liver Cirrhosis (Compensated and Decompensated):

Regarding the baseline probability of liver cirrhosis, we based also on the value of Wong et al. 2000 paper after dividing it between compensated liver cirrhosis and decompensated states of liver cirrhosis such as, ascites, variceal hemorrhage, and hepatic encephalopathy based on data from Asrani et al. 2014 research. In Asrani et al. 2014, a study conducted in Mayo Clinic for patients with advanced fibrosis undergoing magnetic resonance elastography between 2007–2011. During this period, 430 patients were diagnosed as having advanced fibrosis and/or diagnosed clinically to have cirrhosis (Asrani et al., 2014). The baseline analysis for this cohort showed that 68% are compensated cirrhotic patient while 32% have evidence of decompensated cirrhosis including ascites, variceal hemorrhage, or hepatic encephalopathy (Asrani et al., 2014). Among people who met the criteria of decompensated cirrhosis, 60.44% suffered from ascites, 20.33% of decompensated cirrhotic patient had variceal hemorrhage, and 19.23% had hepatic encephalopathy (Asrani et al., 2014). Hence, the predicted prevalence of cirrhosis in (Wong, 2000) according to age group were divided as follow, 68% of this value allocated for initial probability for compensated cirrhosis state, 19.34% of it for initial probability for ascites patients, 6.51% allocated for variceal hemorrhage state, and 6.15% for the baseline probability for hepatic encephalopathy state (Table IV-3).

Table IV-3 Baseline probabilities of compensated cirrhosis and different decompensated cirrhosis states by age

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Compensated Cirrhosis</th>
<th>Variceal Hemorrhage</th>
<th>Diuretic Sensitivity Ascites</th>
<th>Diuretic Refractory Ascites</th>
<th>Hepatic Encephalopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-04</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>05-09</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>10-14</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>15-19</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>20-24</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>25-29</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>30-34</td>
<td>0.00233</td>
<td>0.00022</td>
<td>0.000331</td>
<td>0.000331</td>
<td>0.00021</td>
</tr>
<tr>
<td>35-39</td>
<td>0.00285</td>
<td>0.00027</td>
<td>0.000405</td>
<td>0.000405</td>
<td>0.00026</td>
</tr>
<tr>
<td>40-44</td>
<td>0.01095</td>
<td>0.00105</td>
<td>0.001557</td>
<td>0.001557</td>
<td>0.00099</td>
</tr>
</tbody>
</table>
2.3 HCC:
In 2015, the number of hepatocellular carcinoma (HCC) due to HCV was estimated at 17,000 cases (Waked et al., 2014). Based on a retrospective study that reviewed the data of HCC patients who attended the outpatient clinic of HCC Unit, Ain Shams University Hospitals, Cairo, Egypt between January 2009 and December 2011 (Shaker et al., 2013), and the distribution of HCC patients among the different age groups, the baseline probability of HCC among each age groups was calculated to keep the ratio between age groups as it was in the Ain Shams Study (Table IV-4).

Table IV-4 Baseline probabilities of HCC and Liver related deaths by age

<table>
<thead>
<tr>
<th>Age Group</th>
<th>HCC</th>
<th>Liver Related Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-04</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>05-09</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>10-14</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>15-19</td>
<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>20-24</td>
<td>0.00001</td>
<td>0.00000</td>
</tr>
<tr>
<td>25-29</td>
<td>0.00001</td>
<td>0.00000</td>
</tr>
<tr>
<td>30-34</td>
<td>0.00003</td>
<td>0.00003</td>
</tr>
<tr>
<td>35-39</td>
<td>0.00003</td>
<td>0.00010</td>
</tr>
<tr>
<td>40-44</td>
<td>0.00044</td>
<td>0.00011</td>
</tr>
<tr>
<td>45-49</td>
<td>0.00048</td>
<td>0.00090</td>
</tr>
<tr>
<td>50-54</td>
<td>0.00103</td>
<td>0.00104</td>
</tr>
<tr>
<td>55-59</td>
<td>0.00126</td>
<td>0.00290</td>
</tr>
<tr>
<td>&gt;=60</td>
<td>0.00078</td>
<td>0.00283</td>
</tr>
</tbody>
</table>
5. Disease progression probabilities

Disease progression probabilities were based on back-calculated progression rates conducted by Razavi et al. 2013 for data US and UK data. The fibrosis progression rate between F0 to F1, F1 to F2, F2 to F3, F3 to cirrhosis, F3 to HCC, and cirrhosis to HCC were based on data collected from the US Surveillance, Epidemiology and End Results program between 1999-2009. As the collected data in Razavi et al. 2013 for fibrosis were classified by gender, we calculated the average progression probabilities between male and female. Also, we reduced the progression probability rate from F1 to F2 by 20% due to lower alcohol consumption in Egypt incomparable to US and UK which considered one of the factors that accelerates the progression rate. In addition, the probabilities for the age group 60 years and above were calculated as an average for the probabilities of all age groups from 60 years to more than 85 years mentioned in the same paper (Table IV-5). Other probabilities of spontaneous clearance, progression from diuretic sensitivity ascites to diuretic refractory ascites, different decompensated cirrhotic states to liver related deaths, HCC to death, and from liver transplant to death were collected from literature (Table IV-6).

Table IV-5 HCV Annual disease Progression probability by age

<table>
<thead>
<tr>
<th>Age Group</th>
<th>From F0 to F1</th>
<th>From F1 to F2</th>
<th>From F2 to F3</th>
<th>From F3 to Cirrhosis</th>
<th>From F3 to HCC</th>
<th>From Cirrhosis to HCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-04</td>
<td>0.0485</td>
<td>0.0280</td>
<td>0.0495</td>
<td>0.0000</td>
<td>0.0000</td>
<td>0.0030</td>
</tr>
<tr>
<td>05-09</td>
<td>0.0485</td>
<td>0.0280</td>
<td>0.0495</td>
<td>0.0000</td>
<td>0.0000</td>
<td>0.0030</td>
</tr>
<tr>
<td>10-14</td>
<td>0.0590</td>
<td>0.0344</td>
<td>0.0605</td>
<td>0.0070</td>
<td>0.0000</td>
<td>0.0030</td>
</tr>
<tr>
<td>15-19</td>
<td>0.0590</td>
<td>0.0344</td>
<td>0.0595</td>
<td>0.0070</td>
<td>0.0000</td>
<td>0.0030</td>
</tr>
<tr>
<td>20-24</td>
<td>0.0475</td>
<td>0.0276</td>
<td>0.0485</td>
<td>0.0230</td>
<td>0.0000</td>
<td>0.0030</td>
</tr>
<tr>
<td>25-29</td>
<td>0.0475</td>
<td>0.0276</td>
<td>0.0485</td>
<td>0.0230</td>
<td>0.0000</td>
<td>0.0030</td>
</tr>
<tr>
<td>30-34</td>
<td>0.0345</td>
<td>0.0200</td>
<td>0.0430</td>
<td>0.0520</td>
<td>0.0000</td>
<td>0.0045</td>
</tr>
<tr>
<td>35-39</td>
<td>0.0345</td>
<td>0.0200</td>
<td>0.0430</td>
<td>0.0520</td>
<td>0.0000</td>
<td>0.0045</td>
</tr>
<tr>
<td>40-44</td>
<td>0.1275</td>
<td>0.0740</td>
<td>0.1310</td>
<td>0.0810</td>
<td>0.0005</td>
<td>0.0080</td>
</tr>
<tr>
<td>45-49</td>
<td>0.1275</td>
<td>0.0740</td>
<td>0.1310</td>
<td>0.0810</td>
<td>0.0005</td>
<td>0.0080</td>
</tr>
<tr>
<td>50-54</td>
<td>0.1570</td>
<td>0.0912</td>
<td>0.1605</td>
<td>0.0440</td>
<td>0.0010</td>
<td>0.0130</td>
</tr>
<tr>
<td>55-59</td>
<td>0.1570</td>
<td>0.0912</td>
<td>0.1605</td>
<td>0.0440</td>
<td>0.0010</td>
<td>0.0130</td>
</tr>
<tr>
<td>&gt;=60</td>
<td>0.1840</td>
<td>0.1334</td>
<td>0.1886</td>
<td>0.1414</td>
<td>0.0021</td>
<td>0.0304</td>
</tr>
</tbody>
</table>
### Table IV-6 HCV Annual disease Progression probability

<table>
<thead>
<tr>
<th>From</th>
<th>To</th>
<th>Progression probability</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute HCV</td>
<td>Spontaneous Cure</td>
<td>0.175</td>
<td>(El-Attar et al., 2010)</td>
</tr>
<tr>
<td>Incident case</td>
<td>Fulminant</td>
<td>0.005</td>
<td>(El Saadany et al., 2005)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>Diuretic Sensitive Ascites</td>
<td>0.025</td>
<td>(El Saadany et al., 2005)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>Hepatic encephalopathy</td>
<td>0.004</td>
<td>(El Saadany et al., 2005)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>Liver transplant</td>
<td>0.0015</td>
<td>(Shelbaya et al., 2015)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>Variceal Hemorrhage</td>
<td>0.0011</td>
<td>(El Saadany et al., 2005)</td>
</tr>
<tr>
<td>Diuretic Sensitive Ascites</td>
<td>Diuretic Refractory Ascites</td>
<td>0.067</td>
<td></td>
</tr>
<tr>
<td>Diuretic Sensitive Ascites</td>
<td>Liver related death</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>Diuretic Refractory Ascites</td>
<td>Liver related death</td>
<td>0.33</td>
<td></td>
</tr>
<tr>
<td>Variceal Hemorrhage</td>
<td>Liver related death, year 1</td>
<td>0.4</td>
<td>(Razavi et al., 2014)</td>
</tr>
<tr>
<td>Variceal Hemorrhage</td>
<td>Liver related death, subsequent years</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>Liver related death, year 1</td>
<td>0.68</td>
<td></td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>Liver related death, subsequent years</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>Liver related death, year 1</td>
<td>0.707</td>
<td></td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>Liver related death, subsequent years</td>
<td>0.162</td>
<td></td>
</tr>
<tr>
<td>Liver Transplant</td>
<td>Liver related death, year 1</td>
<td>0.21</td>
<td>(Wong et al., 2000)</td>
</tr>
<tr>
<td>Liver Transplant</td>
<td>Liver related death, subsequent years</td>
<td>0.057</td>
<td></td>
</tr>
<tr>
<td>Decompensated Cirrhosis</td>
<td>Liver Transplant</td>
<td>0.031</td>
<td>(El Saadany et al., 2005)</td>
</tr>
</tbody>
</table>

6. **Liver related Deaths**

It was estimated that the liver related deaths in 2015 was around 35,000 cases.

For estimating the annual rate of liver related deaths by age group, we used the annual rate of liver related deaths collected by US 2013 surveillance of viral hepatitis.
Division of Viral Hepatitis, CDC, 2015); then this rate was adjusted to reach the 35,000 liver related deaths in Egypt keeping the ratio between age groups as it is in US 2013 data of surveillance of viral hepatitis. Table IV-1 show the probability of liver related deaths by age group used in our model.

7. Probability of death from background
This model take into consideration the probability of death from other causes. As this probability is different according to different age groups. We have extracted the mortality rate of each age group of Egypt from Global Health Observatory (GHO) data repository of WHO (GHO-WHO, 2013). Then, probability of background mortality was calculated for each age group through using the following equation:

\[ \text{Probability} = 1 - e^{(-rt)} \]

where \(r\) express for rate and \(t\) express for time. The probability of background mortality, used in this model, are shown in Table IV-10.

8. Direct costs
The data for the direct cost of medical expenses including HCV drugs and other medical care expenses according to different stages of liver disease were collected from different literatures between 2014 and 2015 that based on Egyptian context. The prices of HCV drugs were based on the prices of these drugs for the government (Table IV-7). Regarding to the cost of the IFN- based regimen (SOF +PEG-IFN/RBV) for 12 weeks, it was 9600 LE which is equal $1,226 (Esmat, n.d.), while the cost of IFN- free regimen (DualTherapy) for 24 wks was 12,600 LE which is equal $1,609 (Esmat, n.d.); therefore the average of the cost of this regimen which was used in 2014 for treatment HCV patients was $1417.5.

As the economic burden will be estimated over a long period of time cost adjustment will be applied through applying 3% discounting rate.
### Table IV-7 Annual Cost of different states of HCV in US $

<table>
<thead>
<tr>
<th>Variable</th>
<th>First Year after Diagnosis $</th>
<th>Following Year $</th>
<th>Data Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of medical Care of F0, F1, F2, or F3 *</td>
<td>838</td>
<td>424</td>
<td>(Obach et al., 2014)</td>
</tr>
<tr>
<td>Cost of medical Care of Cirrhosis *</td>
<td>654</td>
<td>602</td>
<td></td>
</tr>
<tr>
<td>Cost of medical Care of Decompensated Cirrhosis (Ascites, Variceal Hemorrhage, or Hepatic Encephalopathy )*</td>
<td>1184</td>
<td>1179</td>
<td></td>
</tr>
<tr>
<td>Cost of medical Care of Hepatocellular Carcinoma</td>
<td>2158</td>
<td>2088</td>
<td></td>
</tr>
<tr>
<td>Cost of liver transplant *</td>
<td>42500</td>
<td>3500</td>
<td>(Estes et al., 2015)</td>
</tr>
<tr>
<td>Triple Therapy (SOF + PEG-INF/RBV)</td>
<td>1226</td>
<td>-----</td>
<td>(Esmat, n.d.)</td>
</tr>
<tr>
<td>Dual Therapy (SOF + RBV)</td>
<td>1609</td>
<td>-----</td>
<td>(Esmat, n.d.)</td>
</tr>
<tr>
<td>Average cost of Triple and Dual therapy</td>
<td>1417.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOF + DCV</td>
<td>319.3</td>
<td>-----</td>
<td>(Abdelsalam, 2015)</td>
</tr>
</tbody>
</table>

* This medical care expenses did not include any of treatment regimen for HCV. Also, it did not include HCV genotyping cost as it was not included as one of the required investigations in the protocol of HCV management in Egypt.

9. **Indirect Burden (DALYs)**

The indirect cost were estimated based on calculating disability adjusted life years (DALYs). DALYs is a metric for measuring the burden of diseases which introduced for the first time in the Global Burden of Disease study measured the burden for about 100 diseases in 1990 (Murray & Lopez, 1996). DALYs include years of life lost to disability (YLDs) and years of life lost due to premature death (YLLs). Disability weights for calculating YLDs were calculated based on data in Table IV-8.

### Table IV-8 Disability weight of different health states of liver disease(YLDs)

<table>
<thead>
<tr>
<th>Health State</th>
<th>Disability weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Undiagnosed Chronic Hepatitis cases</td>
<td>0</td>
</tr>
<tr>
<td>Diagnosed Symptomatic Chronic Hepatitis cases</td>
<td>If &lt;30 Y zero, others 0.1</td>
</tr>
<tr>
<td>weighted average for Diagnosed symptomatic Chronic Hepatitis cases</td>
<td>If &lt;30 Y zero, others 0.015</td>
</tr>
<tr>
<td>Compensated Cirrhosis</td>
<td>If &lt;30 Y zero, others 0.3</td>
</tr>
<tr>
<td>Esophageal Varices</td>
<td>0.4</td>
</tr>
<tr>
<td>Hepatic Encephalopathy</td>
<td>0.8</td>
</tr>
</tbody>
</table>
YLLs will be identified by using WHO life expectancy table of Egypt which show number of years expected to be lived by each age group. The life expectancy in Egypt has increased in the last 20 years. Life expectancy for male has increased from 63.0 years (IHME, n.d.) in 1990 to 68.3 years (GHO-WHO, 2013) in 2013 while the female life expectancy has increased from 67.7 years (IHME, n.d.) to 73.6 years (GHO-WHO, 2013) in the same period. (IHME, n.d.). The life expectancy for Egyptian population by age group was collected from Global Health Observatory data repository of WHO then the average of life expectancy of male and female at the same age group was calculated (Table IV-9).

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Probability of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4 years</td>
<td>0.000758</td>
</tr>
<tr>
<td>5-9 years</td>
<td>0.000478</td>
</tr>
<tr>
<td>10-14 years</td>
<td>0.000392</td>
</tr>
<tr>
<td>15-19 years</td>
<td>0.000563</td>
</tr>
<tr>
<td>20-24 years</td>
<td>0.000835</td>
</tr>
<tr>
<td>25-29 years</td>
<td>0.001029</td>
</tr>
<tr>
<td>30-34 years</td>
<td>0.001343</td>
</tr>
<tr>
<td>35-39 years</td>
<td>0.001597</td>
</tr>
<tr>
<td>40-44 years</td>
<td>0.002358</td>
</tr>
<tr>
<td>45-49 years</td>
<td>0.004887</td>
</tr>
<tr>
<td>50-54 years</td>
<td>0.008921</td>
</tr>
<tr>
<td>55-59 years</td>
<td>0.012259</td>
</tr>
<tr>
<td>60-64 years</td>
<td>0.019302</td>
</tr>
<tr>
<td>65-69 years</td>
<td>0.030268</td>
</tr>
<tr>
<td>70-74 years</td>
<td>0.049122</td>
</tr>
<tr>
<td>75-79 years</td>
<td>0.07991</td>
</tr>
<tr>
<td>80-84 years</td>
<td>0.121357</td>
</tr>
<tr>
<td>85-89 years</td>
<td>0.179102</td>
</tr>
<tr>
<td>90-94 years</td>
<td>0.244894</td>
</tr>
<tr>
<td>95-99 years</td>
<td>0.312166</td>
</tr>
<tr>
<td>100+ years</td>
<td>0.378889</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Life expectancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4 years</td>
<td>71.65</td>
</tr>
<tr>
<td>5-9 years</td>
<td>67.85</td>
</tr>
<tr>
<td>10-14 years</td>
<td>63</td>
</tr>
<tr>
<td>15-19 years</td>
<td>58.1</td>
</tr>
<tr>
<td>20-24 years</td>
<td>53.25</td>
</tr>
<tr>
<td>25-29 years</td>
<td>48.5</td>
</tr>
<tr>
<td>30-34 years</td>
<td>43.7</td>
</tr>
<tr>
<td>35-39 years</td>
<td>39</td>
</tr>
<tr>
<td>40-44 years</td>
<td>34.25</td>
</tr>
<tr>
<td>45-49 years</td>
<td>29.65</td>
</tr>
<tr>
<td>50-54 years</td>
<td>25.25</td>
</tr>
<tr>
<td>55-59 years</td>
<td>21.3</td>
</tr>
<tr>
<td>60-64 years</td>
<td>17.45</td>
</tr>
<tr>
<td>65-69 years</td>
<td>13.95</td>
</tr>
<tr>
<td>70-74 years</td>
<td>10.8</td>
</tr>
<tr>
<td>75-79 years</td>
<td>8.2</td>
</tr>
<tr>
<td>80-84 years</td>
<td>6.1</td>
</tr>
<tr>
<td>85-89 years</td>
<td>4.45</td>
</tr>
<tr>
<td>90-94 years</td>
<td>3.35</td>
</tr>
<tr>
<td>95-99 years</td>
<td>2.65</td>
</tr>
<tr>
<td>100+ years</td>
<td>2.1</td>
</tr>
</tbody>
</table>

(GHO-WHO, 2013)
The monetary value of one DALY was assigned to be $6265 (Estes et al., 2015). This value was based on calculating the mean value of lost productivity, lost earning, and the value of a statistical life year (VSLY) by Estes et al., 2015. Also, it was assumed that there will be 3% annual increase in the value of the DALY between 2015 and 2025.

10. SVR for different treatment regimen

On one hand, SVR 12 for triple therapy (SOF + PEG-INF/RBV) was estimated to be 90% for 12 weeks treatment course (Doss et al., 2015), while it was 83.3% for the dual therapy (SOF +RBV) for 24 weeks treatment course (Wehmeyer et al., 2015). We calculated the average of both regimen (86.65%) and use it in our model to express about the efficacy of HCV treatment protocols in 2015.

On the other hand, SVR 12 for the recent treatment protocol declared by NCCVH which contains SOF and DCV± RBV was applied in our model from 2016 till 2025. Due to limited literature and small sample size in studies estimating the efficacy of this protocol on G4, we calculated the average of SVR 12 of this protocol on available literature for different genotypes which was 95.4% (Asselah, 2014 ; Degasperi & Aghemo, 2014 ; Nelson et al., 2015 ; Wyles et al., 2015). This calculated average was almost similar to the one declared by the head of NCCVH about the efficacy of this new combination which was 95% (Alneweihy, 2015).
V. Results

A. Epidemiological Burden of HCV

1. Scenario I:
Under Scenario I, we studied the impact adopting this scenario on the epidemiological burden of HCV. This scenario represent the current situation where we used the same treatment rate (about 125,000 patients treated annually), the same treatment regimen applied by NCCVH in 2015 which composed of the triple and dual therapy for treating HCV cases (NCCVH, 2015), then the recent treatment protocol published in December 2015 by NCCVH that depend on SOF and DCV for treating cases starting from 2016 (Saeed, 2015), the current cost of these treatment regimens, efficacy of the used drugs, and the current incidence rate. The model calculated the all HCV viremia cases annually, number of cases under different stages of liver fibrosis (F0-F3), annual number of liver cirrhosis cases either compensated or decompensated, hepatocellular carcinoma, and liver related deaths.

The results showed that all HCV viremia cases slightly decreased from 4,664,037 cases by end of 2015 to 4,105,505 cases by 2025 which represent 12% decrease from the viremia in 2015. The number of compensated cirrhosis cases will increase gradually to peak in 2019, at 3.8% above the 1,018,515 compensated cirrhosis cases at 2015, then decline to reach 991,282 cases by 2025 which means 2.7% less than 2015. On the other hand, the decompensated cirrhosis cases decreased by 69.5% from 110,840 patients in 2015 to 33,839 by 2025 (Figure V1).

Figure V1- Number of chronic HCV patients by different disease stages, 2015-2025
The overall number of cases with cirrhosis (compensated and decompensated) showed 9% decrease in comparison to the number of cases in 2015 to reach 1,025,122 cases by 2025.

The number of HCC showed gradual increase over the time to reach the peak 26,682 cases by 2023 then slightly decreased to reach 25,544 cases which is 42.3% higher than the situation at 2015 of 17,953 cases (Figure V3). During this 10 years period the liver related death was expected to decline by 43.6% according to the model to reach 25,907 cases by 2025 (Figure V2).

![Figure V2- Impact of current management scenario on the number of HCC over time](image1)

![Figure V3- Impact of current management scenario on Liver Related deaths over time](image2)

2. Scenario II:
During this scenario we estimated the effect of increasing the treatment rate to treat about 500,000 cases per year starting from 2016 with using the recent treatment protocol published in December 2015 by NCCVH that depend on SOF and DCV± RBV (Saeed, 2015).

The results revealed that the total HCV viremia cases will decline by 56.5% from 4,664,037 cases by end of 2015 to 2,027,717 cases by 2025 (Figure V4). The number of compensated cirrhosis cases will also decreases from 1,018,515 compensated cirrhosis cases at 2015 to 451,262 cases by 2025 which means 55.7% less than the cases in 2015, while the decompensated cirrhosis cases decreased by 84.9% from 110,840 patients at 2015 to 16,756 cases by 2025 (Figure V5); and the overall number
of cases with cirrhosis (compensated and decompensated) showed 58.6% decline between 2015 and 2025 to reach 468,018 cases by 2025.

Figure V4- Impact of adopting different management scenarios on total number of HCV viremia cases, 2015-2025

In addition, the number of HCC showed gradual increase over the time by 19.3% to reach the peak 21,424 cases by 2018, then slightly decreased to become 35.1%

Figure V5- Impact of adopting Scenario II on number of cirrhosis (compensated and decompensated) cases, 2015-2025
below the 2015 base of 17,953 cases to reach 11,650 cases by 2025 (Figure V7).
Also, the liver related death was expected to decline by 69.1% from 45,898 deaths to reach 14,195 cases by 2025 (Figure V6).

3. Scenario III:

During this scenario we estimated will discuss the effect of treatment about 1 million cases in the coming four years and decrease the incidence rate by 50% between 2016-2020, then decrease the incidence rate to become 10% of the current rate. We used the recent treatment protocol published in December 2015 by NCCVH that depend on SOF and DCV±RBV for treating cases starting from 2016 (Saeed, 2015).

The results revealed dramatic decline in all epidemiological burden indicators where the total HCV viremia cases showed great decline by 86.3% from 4,664,037 cases by end of 2015 to 636,652 cases by 2025 (Figure V4). The number of compensated cirrhosis cases will also decreases from 1,018,515 compensated cirrhosis cases at 2015 to 198,817 cases by 2025 which means 80.5% lower than the cases in 2015, while the decompensated cirrhosis cases decreased by 92.5% from 110,840 patients at 2015 to 8,314 cases by 2025 (Figure V8); and the overall number
of cases with cirrhosis (compensated and decompensated) showed 81.7% decline between 2015 and 2025 to reach 207,130 cases by 2025.

**Figure V8- Impact of adopting Scenario III on number of cirrhosis (compensated and decompensated) cases, 2015-2025**

In addition, the implementation of scenario III caused 70.6% decline in HCC cases from 17,953 cases to reach 5,273 cases by 2025 (Figure V10). Also, the liver related death was showed more decline where it became 86.6% less during this 10 years period from 45,898 deaths to reach 6,139 cases by 2025 (Figure V9).

**Figure V9- Impact of adopting scenario III on the number of liver related deaths**

**Figure V10- Impact of adopting scenario III on the number of HCC**
4. Comparison between the three Scenarios:
By comparing the impact of the three scenarios on the epidemiological burden of HCV in Egypt between 2015 and 2025, we found that:

- Adoption of Scenario II will drop the total HCV viremia cases by 50.6% fewer than Scenario I by 2025, while the adoption of Scenario III will go beyond this level to reach 84.5% lower than Scenario I, where it reaches only 636,652 cases instead of 4,105,505 patients in Scenario I (Figure V11)
- Implementing Scenario II will result in having 468,018 cirrhosis cases by 2025 incomparable to 1,025,122 cases in Scenario I, a 54.3% decline lower than Scenario I, while it becomes more lower with Scenario III, a 79.8% reduction compared with Scenario I by 2025 (Figure 11)

**Figure V11- Impact of adopting different management scenarios on total viremia and cirrhosis by 2025**

- The number of HCC in Scenario II will decrease by 54.4% as compared to Scenario I to 11,650 cases, and decrease more with adopting Scenario III to reach 5,273 as compared to 25,544 in Scenario I (Figure V12)
- Also liver related deaths will decrease in Scenario II 45.2% lower than Scenario I to 12,726 deaths, and decline by 76.3% from Scenario I after implementing Scenario III to become only 6,139 (Figure V12)
Figure V12- Impact of adopting different management scenarios on HCC and liver related deaths by 2025

- Scenario I: 25,544 (HCC) vs. 25,907 (Liver related Deaths)
- Scenario II: 11,650 (HCC) vs. 14,195 (Liver related Deaths)
- Scenario III: 5,273 (HCC) vs. 6,139 (Liver related Deaths)
B. Economic Burden

1. Scenario I:
   It was estimated by the model that the direct costs of management HCV under Scenario I (the current management scenario) would be $2,597,875,687 at 2015 and decreased gradually to reach $1,753,385,280 by 2025 which means that the direct costs decreased by 32.5% between 2015-2025 (Figure V13). The cumulative direct cost between 2015-2025 were estimated $23,178,072,617. The DALYs decreased by 78.9%, from 806,756 in 2015 to 170,038 by 2025 (Figure V14), and the cumulative DALYs were 3,794,828. Based on these DALYs, the indirect cost also decreased gradually from 5,344,758,798 to 1,126,502,104 by 2025 (Figure V15). The cumulative indirect cost were calculated $25,140,734,281 from 2015 to 2025. And the total costs associated with chronic active HCV infection in 2025 ($2,879,887,384) were 63.7% less than that in 2015 ($7,942,634,484) (Figure V16), where the cumulative total costs were estimated at $48,318,806,898.

2. Scenario II:
   Under Scenario II, the estimated direct costs of management HCV was decreased 53.2% from 2015 value to $1,216,061,709 at 2025 (Figure V13). The cumulative direct cost were estimated $20,478,601,172 between 2015-2025. The DALYs decreased from 806,756 in 2015 to 93,410 by 2025, an 88.4% decline (Figure V14). Based on these DALYs, the indirect cost also decreased by 2025 to 1,126,502,104 $618,842,604 (Figure V15). The cumulative DALYs were estimated 3,356,612, and the cumulative indirect cost were calculated $22,237,554,464 between 2015 and 2025. And the total costs associated with chronic active HCV infection decreased 76.9% from 2015 value to reach $899,324,519 by 2025 (Figure V16). The cumulative total costs were estimated $42,716,155,636.

3. Scenario III:
   Based on Scenario III, the estimated direct costs of management HCV showed minimal increase in 2016 by 0.2% to reach $2,602,320,222, then it decreased by 53.2% from 2015 value to $1,216,061,709 at 2025 (Figure V13). The cumulative direct cost between 2015-2025 were estimated at $16,202,234,991. The DALYs decreased from 806,756 in 2015 to 93,410 by 2025, an 88.4% decline (Figure V14), and the cumulative DALYs were 2,718,098. Based on the DALYs, the indirect cost also decreased by 2025 to 1,126,502,104 $618,842,604 (Figure V15). The cumulative
indirect cost from 2015 to 2025 were calculated $18,007,401,689. And the total costs associated with chronic active HCV infection decreased 76.9% from 2015 value to reach $899,324,519 by 2025 (Figure V16). The cumulative total costs were estimated $34,209,636,680.

Figure V13- Impact of the different management scenario on the direct cost of HCV management - Egypt, 2015-2025

![Graph showing the direct cost of HCV management from 2015 to 2025 for different scenarios.]

Figure V14- Impact of the different management scenario on Disability adjusted life years due to HCV - Egypt, 2015-2025

![Graph showing the disability adjusted life years due to HCV from 2015 to 2025 for different scenarios.]
Figure V15- Impact of the different management scenario on the indirect cost of HCV - Egypt, 2015-2025

Figure V16- Impact of the different management scenario on the total cost of HCV management - Egypt, 2015-2025

4. Comparison between the three Scenarios:
   By comparing the economic burden of HCV when adopting the Scenario II and Scenario III as compared to the current scenario (Scenario I) in Egypt between 2015 and 2025, we found that:

   - Adoption of Scenario II will decrease the cumulative DALYs by 11.5%, from 3,794,828 in Scenario I to reach 3,356,612 (Figure V17), which will save $2,903,179,817 as indirect costs. Also, the cumulative direct costs will decrease by 11.6% compared with Scenario I to reach $20,478,601,172
Hence, the cumulative total cost will decrease as well and save $5,602,651,262 (Figure V18)

- Adoption of Scenario III will decrease the cumulative DALYs by 28.4% from Scenario I value to become 2,718,098 (Figure V17), which will save $7,133,332,592 as indirect costs. Also, the cumulative direct costs will decrease by 30.1% as compared with Scenario I to reach $16,202,234,991 (Figure V18). Hence, the cumulative total cost will decrease as well by 29.2% and save $14,109,170,218 (Figure V18)

**Figure V17**- The cumulative Disability Adjusted Life Years of the three management Scenario of HCV, Egypt 2015-2025

![Figure V17](image)

**Figure V18**- The cumulative direct, indirect and total cost of the three management scenario of HCV, Egypt 2015-2025

![Figure V18](image)
C. Cost Effectiveness

Cost effectiveness analysis was conducted to identify the most cost effective scenario. The analysis showed that both of Scenario I and Scenario II were absolute dominated by Scenario III as both of them have higher cost and higher DALYs (low effectiveness) than Scenario III. Therefore, Scenario III is the most cost effective scenario.

Adoption of Scenario III instead of Scenario I between 2015 and 2025 will avert 1,076,729 DALYs, and save $6.97 billion as direct costs and $14.11 billion as total costs. Therefore, for direct costs, the ICER for Scenario III was -$6,497 for each DALY averted as compared to Scenario I. In addition, for total costs, the ICER for Scenario III was -$13,104 for each DALY averted as compared to Scenario I.

Adoption of Scenario III instead of Scenario II between 2015 and 2025 will avert 638,514 DALYs, and save $4.28 billion as direct costs and $8.51 billion as total costs. Therefore, for direct costs, the ICER for Scenario III was -$6,697 for each DALY averted as compared to Scenario II. In addition, for total costs, the ICER for Scenario III was -$13,322 for each DALY averted as compared to Scenario II.
VI. Discussion and Recommendations:

With the rapid progress in HCV treatment drugs, not only in their efficacy but also in their prices, in addition to availability of recently published data about the prevalence of HCV in Egypt, this paper presents an updated figure for the current and the future burden of this disease from economic and epidemiological prospective. In addition, it has assessed three different scenarios for management of this huge public health problem facing our beloved country to enable the policy makers to choose the most cost effective strategy that is capable of reducing the economic and epidemiological burden of this disease at the country level.

This paper revealed that the total economic burden of HCV in Egypt according to the current situation is $7.94 billion which is equivalent to 2.7% of Egypt GDP (‘Egypt Home’, 2015). The current direct healthcare costs of HCV in Egypt is about $2.6 billion which consume around 17.4% of the total health expenditure in Egypt (‘WHO | Hepatitis C’, 2015).

Under the current management strategy, Scenario I, small reduction in the prevalence of HCV is expected to be achieved after 10 years where it is estimated that we will have about 4.1 million chronic active HCV patients, 25% of them are in cirrhotic stage, around 25 thousands suffer from HCC, and expected to still have high annual number of deaths, about 25 thousands deaths at 2025. In addition, the economic burden of this strategy is very high where the direct costs are estimated at $23.3 billion, and the total costs are $48.3 billion between 2015-2025.

Adoption of Scenario II which aims to increase the number of treated patients to reach half million annually showed significant decrease in all burdens of the disease, however, adoption of Scenario III which focus aims not only to increase the treatment rate to reach 1 million patient annually in the coming five years but also adopting prevention strategy to decrease the annual incidence by 90% in the coming 10 years will achieve dramatic decrease in the burden of disease. The chronic active HCV cases are estimated to be about 636 thousands cases with a prevalence rate around 0.7%, and with only $16.2 billion as a direct costs, and total costs $34.2 billion between 2015-2025 which is 29.2% lower than the cost of Scenario I. Also, it is the
most cost effective strategy where its adoption will save $13,104 for each DALY averted as compared to the total costs of Scenario I.

It is highly important for success of this strategy to adopt a comprehensive approach for dealing with this huge challenge, where the “Plan of Action for the Prevention, Care and Treatment of Viral Hepatitis, Egypt, 2014-2018” provides the base for this move. We need to focus on availability and accessibility of the new HCV treatment drugs to be able to absorb the huge number of patients required to be treated annually and decrease patients’ waiting list. Also, proper infection control measures, implementing national standards for blood transfusion and testing, increase public awareness regarding to mode of transmission and methods of protection are highly important issues in decreasing the incidence of the disease to ensure proper success of the strategy. The last thing, which is missing in the Egyptian national plan that needs a special focus to ensure the success of Scenario III is the screening pillar. It is highly important to adopt a mass screening policy as it is estimated that the newly diagnosed HCV patients annually are only 110,000 patients (Razavi et al., 2014). This mass screening policy is an important tool for success of scenario III to ensure early detection of patients to provide proper treatment for them and preventing them from spreading the infection.

In brief, adoption of the current scenario for HCV management will have minimal effect on decreasing the epidemiological burden of the disease, and have a high direct and indirect cost. On the other hand, adoption of more rigorous strategy increasing the treatment rate, screening, and decrease the disease transmission as in Scenario III will allow dramatic response in the epidemiological burden of the disease and significantly save direct and indirect costs.
Annex

The model structure for estimating the economic and epidemiological burden of HCV in Egypt, 2015-2025
References

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