Title of the research project: **Estimating economic burden of HCV treatment strategies in Egypt 2018-2025**

Code: **TDR18.81**

Country: **Egypt**

SECTION A. GENERAL INFORMATION

- **PI name:** **Alaa Osman**
- **Reporting Period:** **From January2019 to December 2019)**
- **Objectives of the study:**
  - **General:**
    - The goal of this study is to assess the economic burden of HCV treatment strategies in Egypt from 2018 to 2025.This will provide policy-maker and public health stakeholders with required evidence for priority setting and planning for HCV treatment programs in Egypt**.**
  - **Specific:**

1-To model economic burden of HCV treatment strategies in Egypt from 2018 to 2025.

2-To estimate Hepatitis C prevalence for Egypt by 2025.

3-To estimate projections of HCV morbidity and mortality based on diagnosis and treatment strategy.

SECTION B. TECHNICAL REPORT:

INTRODUCTION:

Hepatitis C virus (HCV) infection is a stressing public health challenge. It is one of the leading causes of mortality and morbidity worldwide and is the main cause of liver cirrhosis, hepatocellular carcinoma and liver transplantation in developing countries **(Sy and Jamal, 2006).**

About 55%-85% of HCV infected persons become chronic active cases. Of those with chronic HCV infection 15%-30% carry the risk of developing liver cirrhosis within 20 years. Globally, between 130–150 million people have chronic hepatitis C infection **(WHO, 2016)**,with estimated annual HCV related deaths about 700000 **(Lozano *et al.*, 2012).**WHO had estimated that about 8-10 million individuals of the Egyptian population have viral hepatitis **(WHO, 2015).** Egypt has highest prevalence of HCV infection worldwide estimated at 6 % of individuals aged from1 to 59 years old with positive results on HCV antibody test. Four percent out of the same age group (1-59) estimated to be 3.5millions Egyptians with active infection tested by HCV RNA test **(El-Zanaty, 2015).**

Bearing the highest HCV prevalence and its associated epidemiological and economic burden, necessitated Egypt to develop Egyptian national viral hepatitis treatment program at 2006 aiming at disease elimination by 2030.This program is considered as one of the most effective public health programs. Out of one million patients were evaluated , 850000 received treatment by the national treatment program from 2006 to the end of 2016.The Egyptian national viral hepatitis treatment program not concerned only by treating HCV infected patient but also prevention of new infection supporting a comprehensive approach for hepatitis eradication through its “Plan of action for the prevention, care and treatment of viral hepatitis 2014–2018", led by the National Committee of Control for Viral Hepatitis with annual treatment plan of 250000to 300000 patients **(El-Akel *et al*, 2017;**

Esmat, 2015).

Treatment of HCV had witnessed the era of new direct acting antiviral drugs since 2011,rendering the dual therapy with peg interferon and ribavirin no longer the standard treatment of HCV **(Vachon and Dieterich, 2011)**.This previous combination had a result of 40%to 55% Sustained viral Response (SVR) of patients with HCV genotype GT-4 **(Marcellin *et al.*, 2012; Esmat *et al.*, 2013)**. Currently several oral therapy combinations of direct acting antivirals can provide patients with SVR above 90% with fewer adverse effects **(Peter and Nelson, 2015)**.The new HCV direct acting antiviral drug Sofosbuvir has been introduced by the Egyptian Ministry Of Health with more than 90% cure rate of patients who had completed the treatment course since its introduction at 16 October 2014 **(WHO, 2015)**.

Gap of Knowledge:

The rapid change and development of HCV treatment with this high cure rates will change the prevalence and incidence of HCV infection in the following years. So it is very important to catch with this evolution and assess the economic burden of HCV treatment strategies in Egypt in coming years in light of these new treatment regimens.

Although there are few previous studies conducted to assess economic burden of HCV disease, there are limited data regarding the economic burden of different HCV treatment strategies. So, our study will cover this point especially that the Egyptian national viral hepatitis treatment program is about to complete implementation of its “Plan of action for the prevention, care and treatment of viral hepatitis 2014–2018".

METHODOLOGY:

Model was constructed in Microsoft Excel to estimate the economic burden of HCV treatment strategies from 2018-2025 in Egypt and assess the cost

effectiveness of the national HCV screening survey. Input data were gathered through literature review and discussion with experts.

-Dr. Homie A. Razavi (Managing director at the Center for Disease Analysis (CDA), Louisville CO, USA) helped us in developing the excel model that we are using in the mathematical modeling of this study.

Model Inputs: including the following:

1- Estimated Population of Egypt: population were divided into age groups with 5-year intervals.

2- Prevalence of HCV in Egypt.

3- Incidence of new HCV-infected cases.

4- Baseline health states including:

A) Liver Fibrosis (F0, F1, F2, and F3): This includes data of initial probabilities of different stages of liver disease in each age group.

B) Liver Cirrhosis (compensated and decompensated): regarding to the baseline probabilities of liver cirrhosis.

C) Hepatocellular carcinoma (HCC): concerned with number of HCC patients due to HCV.

5- Disease progression probabilities.

6- Liver related deaths.

7- Sustained viral response.

8- Cost of HCV drugs included in treatment strategy.

Study design:

- Mathematical modeling study of HCV prevalence

Study population and subjects:

- This research is mathematical modeling study that hasn't been conducted on

human subjects; instead we collected the input data from literature review on scientific database and consultation with expert. The included studies are being chosen according the following eligibility criteria:

Inclusion criteria:

- Studies conducted on general populations to assess the HCV prevalence, HCV disease progression probabilities, HCV related deaths, cost of HCV treatment, the sustained viral response (SVR) of treatment regimen and other input data.

Exclusion criteria:

- Studies conducted on HCV high risk groups for example (drug addicts).

Sample size:

- Not applicable in this study

Sampling method:

- Not applicable in this study

Data collection:

- Input data is being gathered through:

1- Literature review of scientific databases e.g. PubMed.

2- Discussion with experts.

Ethical considerations:

- We obtained the approval of the IRB of the National Liver Institute to conduct this study. Attached copy of the ethical approval.

Activity implementation:

Time period	Activities

Jan	- Finalization of the Protocol
Feb	- Literature review
Mar	- Literature review - Preparation of travel for training on how to use the mathematical models (application for US Visa). - Invitation of a speaker preparing for workshop about mathematical modeling of HCV.
Apr	- Literature review - Start of data extraction
June	- Extraction of input data - Preparation for the mathematical modeling workshop; (advertisements and invitation of participants from all over Egypt, preparation of application form, selection of participants, reservation of the ticket and the accommodation for the trainer, preparation of the workshop venue and teaching aids …etc.)
July	- Conduction of workshop entitled "Mathematical modeling in HCV" in the period between 23-27 June 2019. - Model design
Aug	- Model design
Sept	- Communication with experts for quality audit of the data and to get the results for the last national HCV screening survey
Oct	- Data quality audit and data management.
Nov	- Data entry
Dec	- Start of the data analysis - Preparation for travel to CDA (Centre for Disease

	Analysis) Co, USA between the period of 23 Jan- 2 Feb 2020 to finalize the analysis of this study; (e.g. Air ticket and hotel reservations).

Preliminary Results:

- We did a literature search of PubMed between Jan 1, 2000 and Dec 31, 2018, using the following keywords: hepatitis C, prevalence, incidence, epidemiology, mortality, disease burden, DAAs treatment and Egypt. We searched also some conferences e.g. EASL.
- This search resulted in 30 full downloaded studies fulfilling the eligibility criteria of this study.
- Conduction of workshop entitled "Mathematical modeling in HCV" in the period between 23-27 June 2019. We invited participants from all over Egypt and we received wonderful feedback from the participants (attached a sample of the evaluation form and workshop certificates).
- Model constructed on Microsoft excel to quantify the HCV infected population in Egypt and assess the cost-effectiveness of the national HCV screening in Egypt**.**
- Estimation of viremic HCV prevalence for Egypt to be 0.3% by 2025.
- Estimation of projections of HCV morbidity and mortality based on diagnosis and treatment strategy as shown in the figures below.

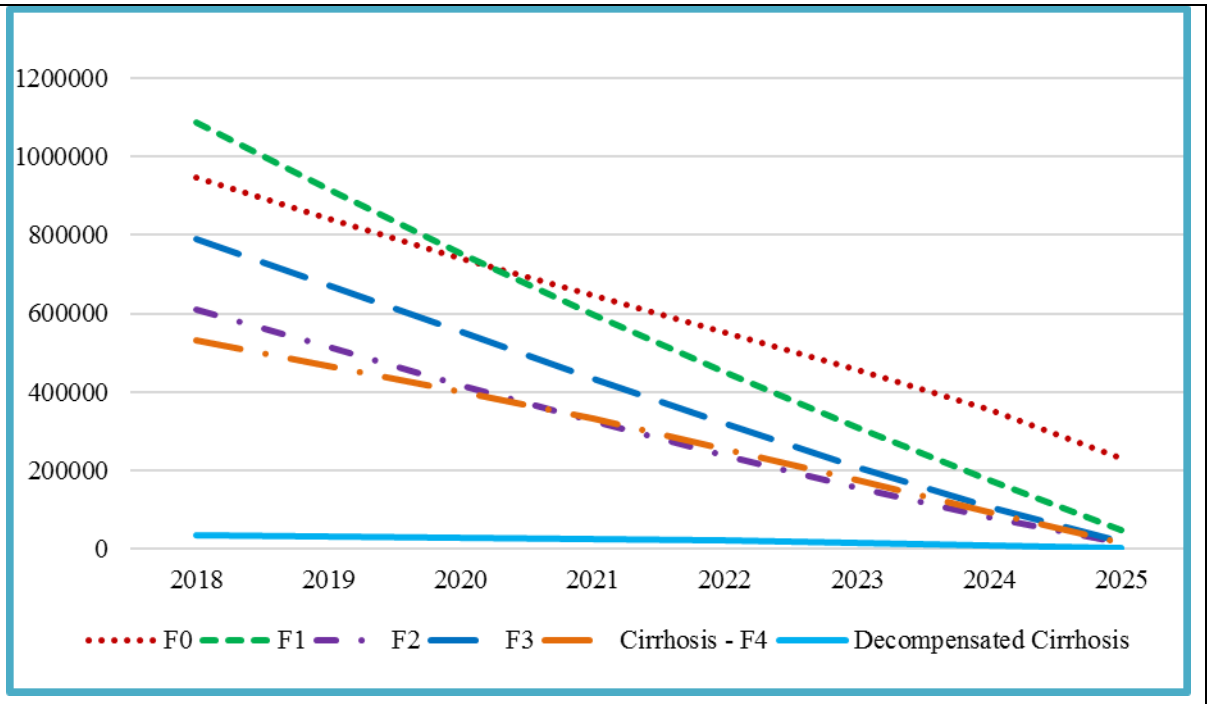

Figure 1: Changes in the numbers of HCV infected patients with different disease stages over time in Egypt.

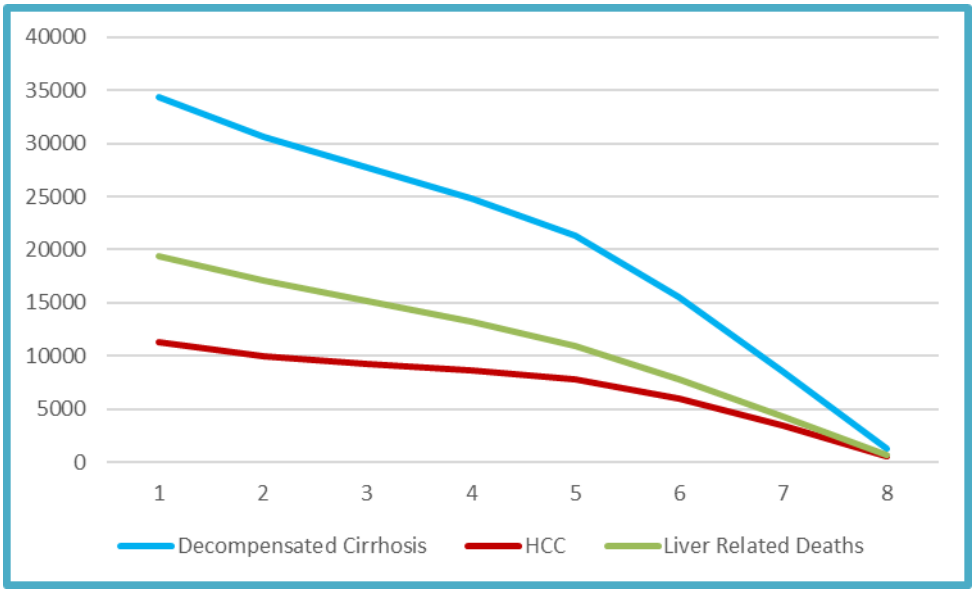

Figure 2: Changes in the numbers of decompensated cirrhosis cases, HCC cases and liver related deaths over time in Egypt.

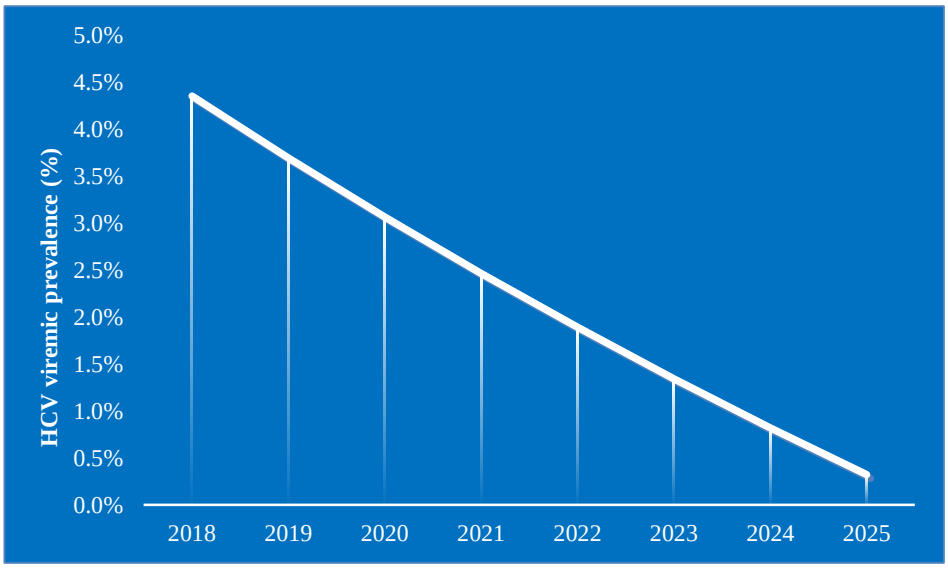

Figure 3: Changes of HCV viremic prevalence in Egypt over time

References:

- Sy, T. and Jamal, M. M. (2006) 'Epidemiology of hepatitis C virus (HCV) infection', International Journal of Medical Sciences, 3(2), pp. 41–46.
- WHO: World Health Organization. (2016) Hepatitis C Fact sheet. Available at: http://www.who.int/mediacentre/factsheets/fs164/en/ (Accessed: 5 March 2017).
- Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V.,et al. (2012) 'Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010.', Lancet (London, England), 380(9859), pp. 2095–128.
- WHO:World Health Organisation. (2015) 'WHO EMRO | Egypt host World Hepatitis Day 2015', pp. 1–2.Available at: http://www.emro.who.int/pdf/egy/programmes/viral-hepatitis.pdf?ua=1

(Accessed: 5 March 2017).

- El-Zanaty (2015) ‘Egypt Demographic Health Survey 2015’ (EDHS 2015). Cairo:Ministry of Health and Population ,National Population Council.
- El-Akel, W., El-Sayed, M. H., El Kassas, M., El-Serafy, M., Khairy, M., Elsaeed, K., et al. (2017) ‘National treatment programme of hepatitis C in Egypt: Hepatitis C virus model of care’, Journal of Viral Hepatitis, (December 2016), pp.
- Vachon, M.-L. and Dieterich, D. T. (2011) ‘The era of direct-acting antivirals has begun: the beginning of the end for HCV?’, Seminars in liver disease, 31(4), pp. 399–409.
- Marcellin, P., Cheinquer, H., Curescu, M., Dusheiko, G. M., Ferenci, P., Horban, A., et al. (2012) ‘High sustained virologic response rates in rapid virologic response patients in the large real-world PROPHESYS cohort confirm results from randomized clinical trials.’, Hepatology (Baltimore, Md.), 56(6), pp. 2039–50.
- Peter, J. and Nelson, D. R. (2015) ‘Optimal interferon-free therapy in treatment-experienced chronic hepatitis C patients.’, Liver international : official journal of the International Association for the Study of the Liver, 35 Suppl 1, pp. 65–70.