

A decision support simulation study for the elimination of hepatitis C in Egypt

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Abstract—Hepatitis C virus (HCV) is a wide spread disease affecting public health in Egypt. New cases are generated yearly through blood infection; consequently, the prevalence of chronic HCV infection is expected to grow considerably. A new treatment era began after the introduction of direct acting antiviral (DAA) treatment giving hope to all HCV patients to become HCV RNA negative. Ministry of health is establishing a project hoping to eradicate HCV in Egypt. Insufficient statistics about rate of HCV infection and capability of healthcare servers was a planning obstacle. A screening project started in 2017 to provide essential statistical data. This paper proposed the combination between a Mathematical queuing model and inventory control to simulate HCV treatment in Egypt. The simulation model provides decision makers with a set of alternatives plans based on available medical resources and governmental fund to achieve HCV elimination. Different realistic scenarios were applied to this simulation and came up with a set of recommendations based on the most optimal scenario according to available fund.

Index Terms— Queuing theory, Inventory control, Screening of hepatitis C virus, Direct acting antiviral, HCV RNA, HCV infection, statistical data.

1 Introduction

Hepatitis C is a fatal disease that affects public health, giving impact on labor production rates and economy. Egypt has the world's highest prevalence of infection with hepatitis C virus (HCV). A significant number of people with HCV will progress to chronic disease, hepatocellular carcinoma, and death [1]. Queues are created when the demand for service exceeds its supply [2]. Queuing up for services is a common phenomenon; the queue up for services in the bank, restaurants, schools, filling stations, hospital, etc. Queuing has the advantage of producing simple models using less data while including randomness [3] and it also helps managers to determine the optimal supply of fixed resources necessary to concur a variable demand. Health policy formulators and hospital administrators have sought to apply queuing model in all facets of healthcare system [4][5]. The use of queuing network techniques allows us to capture the stochastic nature of arrivals and service time that is typical in healthcare system [6]. Inventory control is a process for managing and locating objects or materials [7]. The inventory control was represented by the Ministry of Health which is responsible of distribution of the available funds to the concerned hospitals and the inventory stock convert to money to estimate the time for each HCV patients. In the study of C. Estes* et al [8] they used a modeling approach to quantify the current HCV-infected population, future disease progression and associated costs in Egypt. They used the direct healthcare costs, that were calculated from a nationally representative hospital and a disability adjusted life year (DALY), a template was used with monetary value assigned to lost life years. For all scenarios in this study [8] the proportion of diagnosed patients under care was assumed to gradually reach 100% by 2030 using the statistical historical. Sincere governmental efforts through the past three decades were carried for the treatment of HCV seeking to control its infection. DAA treatments gave hope to all HCV patients to achieve complete recovery, although it is still crucial to determine the time needed to provide HCV treatment to all patients in Egypt [9]. This research can help the government in deciding the most appropriate strategic health care plan concerning HCV infection. The proposed scheme used a combination of queuing model and inventory control to simulate the HCV treatment process in Egypt. The queuing mathematical model is not only used to determine the time needed to provide medical care to all HCV patients, but also could calculate the waiting time in queues. In this study, we aim to maximize the benefits from the limited medical resources and give recommendation to help eliminate HCV infection. The simulation is used to find the mean and the variance of the time in the system in terms of the busy time to the arrival patients and the delayed time the on queue. The expected number of patients in the system and the expected number in the queue are mathematically estimated. Also, as the probability of the system being busy reduced, the probability of idleness increases. Hence the importance of the mathematical model, and reducing the burden in the wait line. Finally, the complete HCV elimination time and proper scenarios are introduced. The rest of the paper is organized as follows: Section 2 presents HCV treatment scheme mathematical model. In Section 3, describes Proposed System Design. Section 4 presents our Experimental design. Section 5 presents result. Section 6 discusses the result. Section 7 concludes the paper.

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2 HEPATITIS C VIRUS TREATMENT SCHEME MATHEMATICAL MODEL

HCV healthcare providers in Egypt are all governmental and under the super vision of ministry of health (MOH). The treatment and investigations are offered free of charge for all Egyptian patients. The government funds the complete process including centers run up costs. All of HCV medical treatment centers were represented as one service server for HCV patients on a single Queue, since all Ministry of health hospital and centers as well as universities hospitals have the following common attributes: same treatment schemes (3-6) months with same medication, same fund resources (all are fully funded government treatment programs) and finally no demographic constraints. The most effective method for simulating the medical service provided was using queuing mathematical model.

2.1 The Queuing Mathematical Model

Queuing theory is the theory behind what happens when you have lots of tasks, scarce resources, and subsequently long queues and delays. It aims to estimate if the available resources will suffice in meeting the anticipated demand over a given period. The model adopted in this research is the (M/M/1): (GD/N/N) [10]. The total number of HCV patients (N) in Egypt is assumed to be fixed and the annual HCV healthcare centers maximum service capacity (N). It is assumed that patients' arrivals (λ) follow a Poisson distribution at an average λ number of patients per year. The departure (μ) follows exponential service times; with an average of μ per year. The service discipline (GD) referring to service priority as First Come, First Served (FCFS). The queuing model could be represented mathematically as follow [11].

$$Po = 1/[\sum_{n=0}^{N} \lambda N!/[\mu(N-n)]!] \quad (1)$$

Where Po is the probability that there is no patient in the system, i.e. the servers are idle. The initial counter (n) still increasing until reach to the total number of HCV patients (N). Next are the formulas for performance measures of the queuing system.

$$Lq = N - (\lambda + \mu)(1 - Po)/\lambda \quad (2)$$

The expected number of the patients waiting on the queue (Lq)

$$Ls = N - \mu(1 - Po)\lambda \quad (3)$$

Expected number of the patients in the system (Ls)

$$Wq = Lq/[\lambda(N - Ls)] \quad (4)$$

Expected waiting time of patients in the queue (Wq)

$$Ws = Ls/[\lambda(N - Ls)] \quad (5)$$

Expected time a patient spends in the system (Ws)

$$\rho = {}^{\lambda}/_{\mu} \quad (6)$$

System utilization meaning fraction of time the servers are busy (ρ).The utilization is a measure of how "busy" the system is. It is the ratio λ/μ is called utilization ρ. If this ratio is greater than 1, that says HCV patients are arriving faster than they can be served, and so the line will grow without bound. If the ratio is less than 1, the line will reach some steady state on average.

3 POPULATION AND PREVALENCE (DATA COLLECTION

The data of population and rates of HCV infection came from Egypt Demographic Health Survey (EDHS), Central Agency for Public Mobilization and Statistics (CAPMAS) and Ministry of Health [12] [13]. As regard to HCV prevalence in Egypt, no clear data to a certain infection ratio or rates were found; the government is just establishing a complete screening project to get a clear view of HCV prevalence in Egypt. The research uses the first phase of this screening project covering 5 million of population in rural and urban areas and postulated that the same rates were true for the rest of the population. Table 1 shows prevalence data in different Egyptian provinces. Maximum infection rate found in urban areas was 2.6% while the maximum infection rate in rural was 6.1%. Ratios for each province were measured according to age between (15-65Ys) for the rural and urban. The data was calculated to the rest of unscreened area based on the worst-case scenario. A decision was issued by the government in 2016 for the comprehensive medical survey of the virus, the screening project started in 2017 to provide essential statistical data.

Table 1. Percentages of incidence rates for the screening results in nine Upper Egypt provinces.

Provinces	incidence rate	urban	Rural
Giza	6.1%	5274876	3357145
Bani Souwaif	3.7%	634925	2519175
Fayoum	2.8%	828625	2768329
Menia	2.4%	989164	4507931
Assiut	2.1%	1135064	3248225
Sohag	2.6%	1054300	3913109
Qena	2.7%	594486	2569795
Aswan	4.5%	605155	868820
Luxor	4.6%	505540	744669

Table 1 was shown the survey report of the screening project established by ministry of health in 2017 in nine Provinces containing urban and rural areas. The government started screening of nine Upper Egypt governorates to have accurate data of HCV patients. The result of the survey will have effect in the wait line of patients annually.

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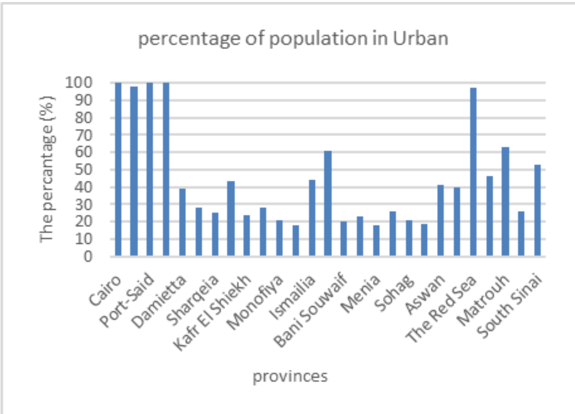

Fig. 1. Number of populations for urban in other provinces.

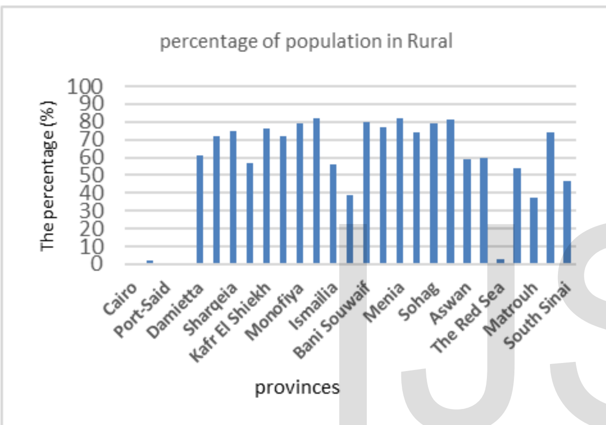

Fig. 2. Number of populations for rural in other provinces.

Fig. 1and Fig.2, described the percentage of the population in urban and rural to the other province. Based on worst case scenario and the screening infection rate obtained in urban and rural in the nine provinces, we forecasted the highest infection rate in the other eighteen provinces. Using statistical analysis, the total arrival annually in the eighteen provinces equivalent to 901 010 in urban l 3 165 508 in rural. According to that prediction of the screening in the rest of the eighteen provinces we proposed 3 scenarios, the first scenario screened five million each year so the probability of total screened arrival annually was five million each year and 225 917 add to the total number of the HCV prevalence annually (λ). The second scenario was changed the screening from five million people to ten million people each year, so the total screened arrival annually was 451 835 add to the total number of the arrival annually (λ). The third scenario was changed from five million screening to fifteen million people each year, so the total screened arrival annually was 677 753 add to the total number of the arrival annually (λ). Under using DAA treatment with 90% SVR and 325 000 doses added to the number of servers annually (μ) according to the state's availability of the balance for the treatment of HCV. In the future, the state emphasizes the importance of raising the doses for treatment to 500000 doses. The production of medicine locally will lead to a decline in price which is expected to raise the available doses annually to 750000 doses. So, table 2 was proposed some scenarios with combination fund treatment annually that added to service rate (μ) and screening rates annually that added to arrival rate annually (λ).

Table 2. The nine scenarios according to the survey and the treatment doses.

The proportion of Screening annually	**Scenarios**	**Number of HCV patients discovered annually**	treated annually (tenders)
Five million people screened	1	225917	325 000
	2		500 000
	3		750 000
Ten million people screened	4	451835	325 000
	5		500 000
	6		750 000
Fifteen million people screened	7	677753	325 000
	8		500 000
	9		750 000

3.1 Queuing Model Parameter Computations:

According to the total screening (Y) scenarios that implemented in 2017 in nine Upper Egypt provinces. There must be a method to estimate the problem of the mathematical model parameter. The total financial burden needs to be evaluated as more effective therapies with direct acting antivirals (DAAs) that equivalent to 5825563(N) number of HCV patients in 2015[14], also estimated new Infections cases occur annually (X). The only available historical therapy for HCV in the last three years was pegylated interferon and ribavirin with 50% sustained virologic response (SVR) and the relapse rate (Z) was 50%, and 65 000 patients were treated in 2015 (H). In contrast the new era of DAA in which 325 000 were treated (H) in 2017 and the relapse rate was 10 %(Z). finally, we included the support of the charity (I), equivalent to 60 000 doses to treat HCV patients annually. We represented mathematically equations as follow:

X= New cases annually (incidence annually)
Y= Total screening
Z=Relapses of treated patient annually (not sustained virologic response)
H= number of treated patients annually
I= Charity (contribution Associations)
The number of HCV patients (arrival rate λ) is given as

$$\lambda = X + Y + Z \quad (7)$$

The number of the cured HCV patients (departures rate μ) is given as

$$\mu = H + I \quad (8)$$

The total number of HCV patients (N):
Current N=N previous+ current λ+ current μ (9)

Table 3. Number of patients' arrival annually (λ) and service time (μ) of HCV patients over the year.

International Journal of Scientific & Engineering Research, Volume 9, Issue 12, December-2018
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Year	X	Y	H	μ	λ	N
2015	103113	0	65000	125000	135613	5825563
2016	103301	0	65000	125000	135801	5836176
2017	103492	177246	325000	385000	313238	5846977
2018	102222	225917	440000	500000	372139	5775215
2019	99959	225917	750000	810000	400876	5647354
2020	92717	225917	750000	810000	393634	5238230
2021	85347	225917	750000	810000	386264	4821864
2022	77847	225917	750000	810000	378764	4398128
2023	70214	225917	750000	810000	371131	3966892
2024	62447	225917	750000	810000	363364	3528023
2025	54541	225917	750000	810000	355458	3081387
2026	46496	225917	750000	810000	347413	2626845
2027	38308	225917	750000	810000	339225	2164258
2028	29975	225917	750000	810000	330892	1693483
2029	21495	225917	750000	810000	322412	1214375
2030	12865	225917	750000	810000	313782	726787
2031	4082	225917	750000	810000	304999	230569
2032	0	225917	750000	810000	296060	0

Table 3 illustrates one of the scenarios that were postulated during this study. It showed the incidence rate annually of the HCV, λ, μ and the total number of HCV patients annually with year. The proportion of diagnosed patients under care was assumed to gradually reach 100% by 2031.

3.2 Cost-Effectiveness Analysis

To estimate lifetime costs and human resources loss of productivity, an inventory control simulated by disease stage of patients annually. Three tenders are carried out to provide the Egyptian hospitals with different types of DAA and medical Supplies for HCV medications from local and global market. The balance between the monthly consumption and theses provided from tenders is modulated through an inventory control model. Several methods were employed to reach an average total cost value for the lost production represented by actual per capita annual productivity of the labor force and the lost earnings based on the average national salary. The Lost production (annual productivity) was calculated by dividing the gross domestic product (GDP) by the labor force. GDP in 2012 came from the World Bank [15] and the labor force came from CAPMAS [4]. The lost earning: average annual salary was calculated from CAPMAS. So, we estimated the total cost for HCV patients according to the following set of equations.

$$\text{HR lose Of Productivity Cost} = \text{Income Rate Annually} * \text{HCV Incidience Rate} \quad (10)$$

Ratio of HCV Patients Need 6 months treatment Scheme=Rate of HCV Scheme1* Csix*HCV Incidence Rate (11)

Ratio of HCV Patients Need 3 months treatment Scheme=Rate of HCV Scheme2* Cthree*Average of HCV Incidence Rate (12)

$$\text{Total Cost} = \text{HR Lose Of Prodictitvity Cost} + \text{Rsix} + \text{Rthree} \quad (13)$$

Next are the formulas for calculation of inventory control equations:
Income Rate Annually= 29 559 by EGP LE
Rate of HCV Scheme1=40%
Rate of HCV Scheme2=60%
Csix= average cost for 6 months treatment scheme.
Cthree= average cost for 3 months treatment scheme.
Rthree = Ratio of HCV patients Need 3 months treatment scheme.
And Rsix=Ratio of HCV patients Need 6 months treatment scheme. So, we represent HR loss of productivity cost according to each scenario.

4 Proposed Algorithms

This algorithm aims to get the best outcome by proposing different data scenarios. The estimation is based on the arrival rate and departure rate of the patients annually (inputs data). It helps for calculating the average wait time in the queue, the waiting time in the system and the expected number of patients in the system (output data). Hence the results of algorithm evaluate the utilization factors for the system and relieve the waiting time in the queue. The probability of the system to be idle will calculate. Then, we detected when the virus will be eradicated. The model illustrated is shown in the following algorithm:

```
Read Input data (year, new cases annually(HCV Incidince Rate), total screening of urban & rural, number of treated annually, served by screening).
Calculate (N), (λ), (μ).
Initialize year=2015 (DAA) and N=5825563 in (2015).
Initialize income rate annually= 29 559 (EGP LE), rate of HCV scheme1=40% and rate of scheme2= 60%.
Inlitize sum=0;
While (N>0)
  If year equal 2015 or 2016
     Calculate λ= new cases annually+ treated Patient
                  Annually*10 %(relapse)
     Calculate μ=number of treated annually+ Contribution
                  Associations
     Calculate N=pervious N+ Current λ+ current μ
  Else
     Calculate λ= new cases annually + treated patient
                  annually*10%+ Screening of urban and rural.
     Calculate μ=number of treated annually+ contribution
                  associations+ Served by screening of urban
                  and rural.
     Calculate N as defined pervious without change.
End if
     Calculate   Po, Ls, Lq, Ws, Wq
     Calculate sum+=new cases annually;
     Calculate   HR loss of productivity cost (as shown in
                 equation 10)
End while
Calculate total New cases annually (sum/the number of year).
Calculate Ratio of HCV Patients Need 6 month's treatment
          Scheme, Ratio of HCV Patients Need 3 month's
          treatment Scheme (as shown in equation 11, 12).
Calculate total cost.
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International Journal of Scientific & Engineering Research, Volume 9, Issue 12, December-2018
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5 Result (Disease burden)

Queuing mathematical model was used to compute the performance measures and total wait time for each HCV patients (N) according to nine different scenarios are that classified based on number of patients screened annually and the amount of HCV treatment doses provided to healthcare servers annually.

Table 4. Performance measures of the Server Queuing Model and optimality solution of HCV for the best scenario.

year	N	Arrival rate(λ)	cured rate(μ)	P0	Ls	Lq	Ws	Wq	Utilization
2015	5825563	135613	125000	1.151043*E -10	5742223	5229583	23549546	21447147	1.084904
2016	5836176	135801	125000	1.151043*E -10	5742225	5229585	23549551	21447150	1.084904
2017	5846977	313238	385000	4.0722237*E -9	5575673	5063033	7622168	6921368	0.813605
2018	5775215	372139	500000	1.001108*E -10	5747603	5234963	5892902	5367303	0.744278
2019	5647354	400876	810000	3.7403279*E -8	5436464	4923824	3149095	2852146	0.4949086
2020	5238230	393634	810000	3.7403279*E -8	5436464	4923824	3149095	2852146	0.48596790
2021	4821864	386264	810000	3.2171132*E -7	4923824	4411184	2852147	2555198	0.4768691
2022	4398128	378764	810000	3.1177122*E -7	4813824	4301184	2742147	2445198	0.46760987
2023	3966892	371131	810000	0.0000025	4411186	3898547	2555204	2258255	0.45818641
2024	3528023	363364	810000	0.0000023	4301186	3788547	2445204	2148255	0.44859753
2025	3081387	355458	810000	0.0000181	3898557	3385926	2258296	1961347	0.43883703
2026	2626845	347413	810000	0.0000071	3788557	3275926	2148296	1851347	0.42890493
2027	2164258	339225	810000	0.0636492	1773396	1293385	1097075	800126	0.41879629
2028	1693483	330892	810000	0.1121409	1381304	926152	901186	604237	0.40850864
2029	1214375	322412	810000	0.1823215	1043130	623955	738966	442018	0.39803950
2030	726787	313782	810000	0.1392832	541170	229912	516291	219342	0.3873851
2031	230569	304999	810000	0.1232286	354223	154120	388204	129475	0.3765419
2032	0	296060	810000	1	______	______	______	______	0.3715024

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Table 4 provides the total number of the screened cases in 2015 that was estimated at 5 825 563 cases, had DAAs been adopted, under Scenario 3, the viraemic prevalence of HCV patients would have decreased to 230 569 cases by 2031 that is HCV elimination will be by the end of this year. This scenario is the best one in terms of HCV elimination compared to other scenarios. Similarly, there are eight other tables to calculate the average waiting time in the queue.

5.1 Life Time Cost

The primary endpoint in the cost-effectiveness ratio analysis according to the inventory parameter computation. Several methods were employed to reach an average total cost value for nine scenarios.

Table 5. Total cost for each scenario.

Scenarios	Total cost by EGP LE
1	95 585 million
2	57 820 million
3	37 634 million
4	115 718 million
5	72 272 million
6	48 841 million
7	122 025 million
8	77 293 million
9	53 212 million

Table 5 shows the total cost for the nine scenarios according to equation (13). The least total cost during the period of HCV elimination was found in the third scenario.

Table 6. Recommendation around best scenarios.

Scenarios	Year of elimination HCV	Treated annually	Average wait time
1	2052	325 000	5644746
2	2039	500 000	4957247
3	2031	750 000	4701881
4	2054	325 000	6287203
5	2040	500 000	5061146
6	2033	750 000	4841623
7	2054	325 000	6418696
8	2041	500 000	5984569
9	2033	750 000	5057077

Table 6 illustrates the Ws calculated under each scenario. So, we summarized nine scenarios compared to the treatment doses and the time that HCV eliminations. Hence the third scenario was best, that refer the least interval of complete elimination and least time wait in the lines of treatment.

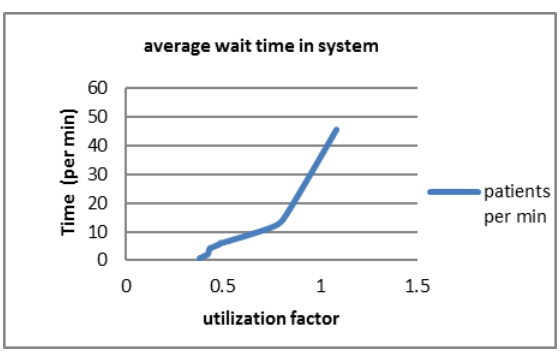

Fig. 3. Utilization Factor (ρ) against Average Waiting Time in the System (Ws) for the third scenario.

Fig 3 illustrates the current HCV treatment model has high wait time in the queues leading to the service as there is high utilization (1.084904). That's why we proposed different scenarios to decrease the wait time. It was found that under the parameters of the 3rd scenario (the best one) the wait time decrease gradually as the utilization decrease until there is no wait time at 30% (0.3715024) utilization.

6 Discussion

Currently MOH in Egypt is carrying out HCV screening project in different geographical areas according to nine scenarios. Under scenario 1 reference in table 2 we predicted the screening project of all population would take eighteen years (five million each year) so we would have 225 917 new cases each year in addition to the arrival wait line (λ). Compared to scenario 4 we predicted the screening of all population would take nine years (ten million each years) so we would have 451835 new cases each year in addition to the arrival wait line (λ) and then Scenario 7 we predicted the screening of all population would take six years (fifteen million each years) so we would have 677 753 new case each year in addition to the arrival wait line (λ).Table 4 of group five million screened annually depicts that the third scenarios is better than the other scenarios in terms of the performance criteria used. This analysis shows that while overall HCV prevalence in Egypt is declining in each nine scenarios, but the best three scenarios from them ascending as follow third scenario then sixth scenario and then ninth scenario With regard to lowest expected time for HCV elimination. The third scenario Indicated total number of HCV patients (N) decreased to 230 569 cases by 2031 that the HCV elimination by this year. The sixth scenario Indicated the total number of HCV patients (N) decreased to 220 406 cases by 2033 that the HCV elimination by this year. The ninth scenario Indicated the total number of HCV patients (N) decreased to 346 911 cases by 2033 that the HCV elimination by this year. Three international tenders are made annually to provide DAA medications required to all MOH scenarios. A supply chain starting from MOH stores deliver the medication to all hospital and liver care centers. The inventory control guides the queue demand against supply. The results provide decision makers with many possible alternatives from table 4. The cost wise scenarios 3, 6, 9 are the best ascendingly. With regard to the total cost considerations, third scenario in the system records the lowest cost was 37 634million annually compared to the sixth scenario that records 48 841million annually and the ninth scenario that records 53 212million annually. In table 6 the average time a patient spends in the system nine mints for the third best scenarios. Fig 4 shows the wait time in the different scenarios; it was found that the least wait time in the years leading to elimination of the disease was found in scenario 3 (4701881).

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7 Conclusion

The large national treatment program to treat patients with HCV infection was feasible and manageable. Scaling up of the treatment program was possible with the availability of more medications, with more affordability through both allocating more resources and decreasing costs, with the decision to treat all stages of fibrosis and with removing the requirement of strict fibrosis assessment all with the help of a comprehensive medical screen of the HCV patients. And so, the results of the study showed that average queue length, congestion and waiting time of patients in the system and queue could be cut down, these findings can be used to shape future HCV.

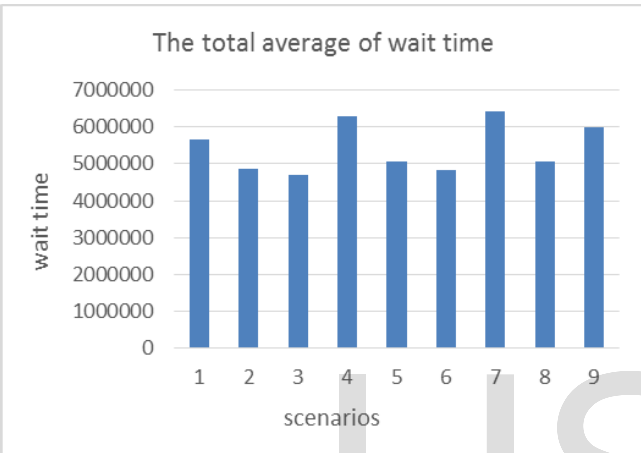

Fig. 4. Average waits time over the nine scenarios.

prevention policies in Egypt and the best scenario was the third from the nine scenarios. We give some of recommendation according to the best scenario that detect HCV elimination in 2031 when we screened five million people annually and the best treatment scheme increased to 750 000 shown in scenario three. How far will successful therapy change the epidemiology of the disease remains to be seen.

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