












ORIGINAL ARTICLE

Impacts of the Egyptian national screening and treatment programme for viral hepatitis C: A cost-effectiveness model

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Abstract

Background & Aims: Egypt used to have one of the highest prevalences of HCV infection worldwide. The Egyptian Ministry of Health launched a national campaign for the detection and management of HCV to reduce its burden. This study aims to carry out a cost-effectiveness analysis to evaluate the costs and benefits of the Egyptian national screening and treatment programme.

Methods: A disease burden and economic impact model was populated with the Egyptian national screening and treatment programme data to assess direct medical costs, health effects measured in disability-adjusted life years and the incremental cost-effectiveness ratio. The scenario was compared to a historical base case, which assumed that no programme had been conducted.

Results: Total number of viremic cases is expected to decrease in 2030 by 86% under the national screening and treatment programme, versus by 41% under the historical base case. Annual discounted direct medical costs are expected to decrease from \$178 million in 2018 to \$81 million by 2030 under the historical base case, while annual direct medical costs are estimated to have peaked in 2019 at \$312 million before declining to \$55 million by 2030 under the national screening and treatment programme. Under the programme, annual disability-adjusted life years are expected to decline to 127 647 by 2030, leading to 883 333 cumulative disability-adjusted life years averted over 2018–2030.

Conclusions: The national screening and treatment programme is highly cost-effective by the year 2021, cost-saving by 2029 and expected to save about \$35 million in direct costs and \$4705 million in indirect costs by 2030.

KEYWORDS

cost-effectiveness analysis, Egypt, HCV, screening, treatment

Abbreviations: CEAC, cost-effectiveness acceptability curve; DAA, direct-acting antiviral; DALY, disability-adjusted life year; DC, decompensated cirrhosis; GDP, gross domestic product; GNI, gross national income; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ICER, incremental cost-effectiveness ratio; LRD, liver-related death; NCCCVH, Egyptian National Committee for Control of Viral Hepatitis; NSTP, national screening and treatment programme; PSA, probabilistic sensitivity analysis; SVR, sustained virologic response; UI, uncertainty interval; USD, United States dollar.

1 | INTRODUCTION

Viral hepatitis is a major global health problem. In 1990, deaths from acute infections, hepatic cirrhosis and hepatocellular carcinoma (HCC) were the tenth leading cause of death worldwide, becoming the seventh leading cause of death in 2013. Nearly half of this mortality is attributed to viral hepatitis C (HCV) infection.¹ In 2015, it was estimated that the annual global mortality due to HCV-related complications was about 400 000.²

In 2015, the global prevalence of viremic HCV infection was 1.0%, with a prevalence of 2.3% in the Eastern Mediterranean Region.² With a population of 104 million,³ Egypt is the most populous country in Middle East and used to be the highest HCV-prevalent country in the region. Previously reported HCV seroprevalence between the ages 15 and 59 was 14.7% in 2009, which had declined to 10.0% by 2015.^{4,5} The Egyptian National Committee for Control of Viral Hepatitis (NCCVH) was established in 2006⁶ to treat patients using the available interferon regimen at that time. In late 2014, the NCCVH succeeded to introduce the first approved effective direct-acting antivirals (DAAs) for the treatment of HCV infection at 1% of their international price, with a reported cure rate up to 90%. The NCCVH started a national HCV DAA treatment programme for patients living with the diagnosis at the expense of the state,⁷ and the Ministry of Health launched a “Plan of Action for the Prevention, Care and Treatment of Viral Hepatitis”.⁸ The NCCVH introduced other approved highly effective DAAs during the subsequent years.

In 2016, the World Health Assembly called for the global elimination of viral hepatitis by 2030 and set global targets of diagnosing at least 30% of all people infected with viral hepatitis by 2020 and 90% by 2030; treating at least 80% of HBV and HCV patients; and achieving 90% reduction in incidence and 65% reduction in mortality from viral hepatitis by 2030.⁹

Four years after the start of the national DAA treatment programme in Egypt, the seroprevalence among untreated adults 18 years and older remained at 4.6%.¹⁰ In a push towards the WHO targets for elimination, between October 2018 and April 2019, Egypt screened approximately 50 million people for HCV in a national screening and treatment programme (NSTP) for the detection and management of the disease, and 92% of the discovered viremic patients started treatment with DAAs to lessen the disease-related morbidity and mortality. The national programme has spent funds on screening, lab tests, treatment, training and a patient registry amounting to nearly \$207 million.¹⁰

The current study aims to carry out a cost-effectiveness analysis¹¹ to estimate the costs and health gains of the national HCV screening and treatment programme in Egypt.

2 | METHODOLOGY

2.1 | Data

HCV seroprevalence and viremic prevalence data from 2018 were obtained from the NSTP data.¹⁰ Annual cases of HCC in 2018 were

Key points

Egypt conducted a national campaign for detection and management of HCV infection. The intervention was highly cost-effective by 2021 and is expected to be cost-saving by 2029. The results highlight the importance of investment in screening and treatment programmes, especially on the low- and lower-middle-income level.

obtained from GLOBOCAN data.¹² Direct medical costs were analysed for the previous year's outpatients and admitted patients at the National Liver Institute hospital, as described previously.¹³ Egypt's per-capita gross domestic product (GDP) and gross national income (GNI) for 2018 were obtained from the World Bank.^{14,15} Disease severity breakdown, disability weights for different disease stages and monetary value of a disability-adjusted life year (DALY) averted were calculated as previously described in an economic analysis of HCV disease in Egypt¹³ using updated values for 2018. Prices provided in Egyptian pounds were converted to United States dollars (USD) at an exchange rate provided by the U.S. Department of Treasury for the end of 2018.¹⁶ The average monetary value of a DALY averted was set to \$4724.

2.2 | Overview of approach and model

A previously published disease burden¹⁷ model of HCV infection was populated with the Egyptian NSTP data to assess the direct medical costs, health effects measured in DALYs, indirect costs (total monetary value of DALYs averted) and the incremental cost-effectiveness ratio (ICER).

The disease burden model calculates the annual prevalence, incidence and mortality of HCV infection by stage of liver disease, sex and age. The model takes a set of demographic (population, all-cause mortality rate and fertility rate) and epidemiological (genotype distribution, relative size of annual incident cases, HCV-related liver transplantations, new HCV diagnoses and HCV treatment starts) inputs and is calibrated to match reported historical overall and sex- and age-specific HCV prevalence data, as well as the historical HCV diagnosis data. It uses a set of previously published progression rates¹⁸ to forecast the disease burden of HCV infection. Since the last publication, the model was expanded to also calculate disease progression after sustained virologic response (SVR) in patients with compensated cirrhosis or more advanced liver disease to account for the additional incidence of and mortality from end-stage liver disease in the population with a history of SVR.

The economic impact module, which is an add-on on top of the disease burden model, calculates the direct medical costs (for lab tests, follow-up care and antiviral treatment of HCV infection), health effects denominated in DALYs, indirect costs (by applying a

monetary value to DALYs averted) and cost-effectiveness measures associated with an HCV policy. As the disease burden model is run on a given policy scenario, the outputs of the economic impact module change accordingly.

The model outputs under the NSTP were compared to a historical base case, which assumed that the NSTP had not been conducted, considering the entire HCV RNA-positive population in Egypt. Modelled outcomes were measured over 2018–2030.

Future costs and health effects were discounted at an annual rate of 3%. A scenario was considered cost-effective when the ICER (calculated as net cost per DALY averted) was lower than two times the 2018 Egyptian GNI per capita (\$2790) and highly cost-effective when the ICER was lower than the GNI per capita.

Under the comparator – the “historical base case” – approximately 50000 patients were modelled as having been newly diagnosed through 2018–2020, with a built-in decline to reach approximately 44000 annual new diagnoses by 2025.

Under the historical base case, all patients aged 15 years and older with F0 or greater fibrosis (on the METAVIR scale) were eligible for treatment in 2018 and subsequent years (Table 1). Under this scenario, 226152 patients with fibrosis stages \geq F0 were treated in 2018 at a price of \$67 per treatment course for F0–F3 patients and \$109 for patients with cirrhosis. The number of patients treated annually was modelled to decrease to 36000 throughout 2019–2030.

Under the NSTP, 1653293 patients were modelled as having been newly diagnosed in 2018, with 50000 new diagnoses in 2019. Starting in 2020, Egyptian experts expected that the annual number of newly diagnosed patients would decrease to 10000 (Table 1). The number of treated patients in 2018 was kept the same as under the base case. Assuming that patients diagnosed by the NSTP started treatment in 2019, an estimated 1600000 \geq F0 patients were treated in 2019 at a price of \$42 per treatment course at an SVR rate of 99%¹⁰ (Table 1). Starting in 2020, it was assumed that 90% of the newly diagnosed patients would receive treatment.

TABLE 1 Historical base case (comparator) and the national screening and treatment programme, input parameters.

	2018	2019	2020	2021	2022	2023	2024	2025
Historical base case								
Newly diagnosed	50000	50000	50000	48000	48000	46000	46000	44000
Treated	226152	36000	36000	36000	36000	36000	36000	36000
Treatment-eligible	15+	15+	15+	15+	15+	15+	15+	15+
SVR	99%	99%	99%	99%	99%	99%	99%	99%
National screening and treatment programme								
Newly diagnosed	1653293	50000	10000	10000	10000	10000	10000	10000
Treated	226152	1600000	9000	9000	9000	9000	9000	9000
Treatment-eligible	15+	15+	15+	15+	15+	15+	15+	15+
SVR	99%	99%	99%	99%	99%	99%	99%	99%

Abbreviations: NSTP, national screening and treatment programme; SVR, sustained virologic response.

2.3 | Sensitivity analysis

A one-way sensitivity analysis and a probabilistic sensitivity analysis (PSA) were conducted to determine which inputs accounted for the largest variation in the model outputs and to generate 95% uncertainty intervals (UIs) around model outputs. Uncertainty in the following input variables was considered: (1) cost of treatment, for cases with compensated cirrhosis or more advanced liver disease; (2) annual progression rate from compensated cirrhosis to HCC, after SVR; (3) proportion of compensated cirrhosis patients remaining with liver disease after SVR; and (4) annual progression rate from DC (decompensated cirrhosis) to HCV-related mortality, after SVR. All four variables were assumed to be betaPERT-distributed. One-way sensitivity analysis was performed on the 2018–2023 ICER under the NSTP scenario. Since the ICER is defined over a given timeframe, a 6-year period (2018–2023) was chosen as the halfway point between the start (2018) and the end (2030) of the analysis. Similarly, the PSA was conducted on (1) 2018–2023 ICER, (2) year of achieving cost savings and (3) year of achieving cost-effectiveness given the more stringent cost-effectiveness threshold under the NSTP scenario.

A cost-effectiveness acceptability curve (CEAC) was generated for the 2018–2023 ICER under NSTP. The CEAC is a commonly used measure that visualizes the proportion of Monte Carlo simulations that result in a cost-effective model output at a given willingness-to-pay threshold.

3 | RESULTS

3.1 | Disease burden analysis

The impact of the different scenarios on HCV disease burden is reported in terms of total annual numbers of prevalent and incident HCV infections and cases of DC, HCC and liver-related death (LRD) (Figure 1, Table 2).



FIGURE 1 Disease burden outcomes for total viremic infections, incident cases of acute HCV infection, decompensated cirrhosis, hepatocellular carcinoma and liver-related deaths, by scenario, 2018–2030. HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NSTP, national screening and treatment programme.

Under the historical base case, the total number of 2 346 207 viremic cases in 2018 was expected to decrease by 41% by 2030, while the total number of DC, HCC and LRD cases was projected to decline by 30%, 27% and 26%, respectively, by 2030.

In comparison, the NSTP would result in an approximate reduction of 86% in the total viremic cases over 2018–2030, with 61 374, 60 802 and 80 287 averted cases of DC, HCC and LRD, respectively.

3.2 | Economic analysis

Under the historical base case, the annual discounted direct medical costs were expected to decrease from \$178 million in 2018 to

\$81 million by 2030 (Figure 2A), while the cumulative medical costs were projected to reach \$1501 million by 2030 (Figure 2B, Table 3).

Under the NSTP, the annual medical costs were estimated to increase to reach a peak of \$312 million in 2019 before declining to \$55 million by 2030 (Figure 2A). Over 2018–2030, the cumulative direct medical costs of the NSTP were projected to reach \$1466 million (Figure 2B, Table 3).

Under the NSTP, DALYs were projected to decline to reach 127 647 by 2030, leading to 2 591 213 cumulative DALYs incurred over 2018–2030. In comparison, 3 474 545 cumulative DALYs were expected to be incurred under the historical base case by 2030 (Figure 2C).

The cost per DALY averted (relative to the base case) for the national screening and treatment programme was projected to

TABLE 2 Disease burden outcomes over 2018–2030, by scenario.

	Estimated number, 2018	Estimated number, 2023	Reduction, 2018–2023 (%)	Estimated number, 2030	Reduction, 2018–2030 (%)
Historical base case					
Total viremic infections	2346207	1838897	22	1386253	41
Incident cases: acute HCV infection	31919	24900	22	18724	41
Total cases: Decompensated cirrhosis	67461	57547	15	47163	30
Total cases: HCC	30394	26445	13	22080	27
Liver-related deaths	28048	24858	11	20772	26
National screening and treatment programme					
Total viremic infections	2346207	439282	81	332027	86
Incident cases: acute HCV infection	31919	5950	81	4587	86
Total cases: Decompensated cirrhosis	67461	45929	32	25947	62
Total cases: HCC	30394	23150	24	14979	51
Liver-related deaths	28048	18165	35	11603	59

Abbreviations: HCC, hepatocellular carcinoma; HCV, hepatitis C virus.

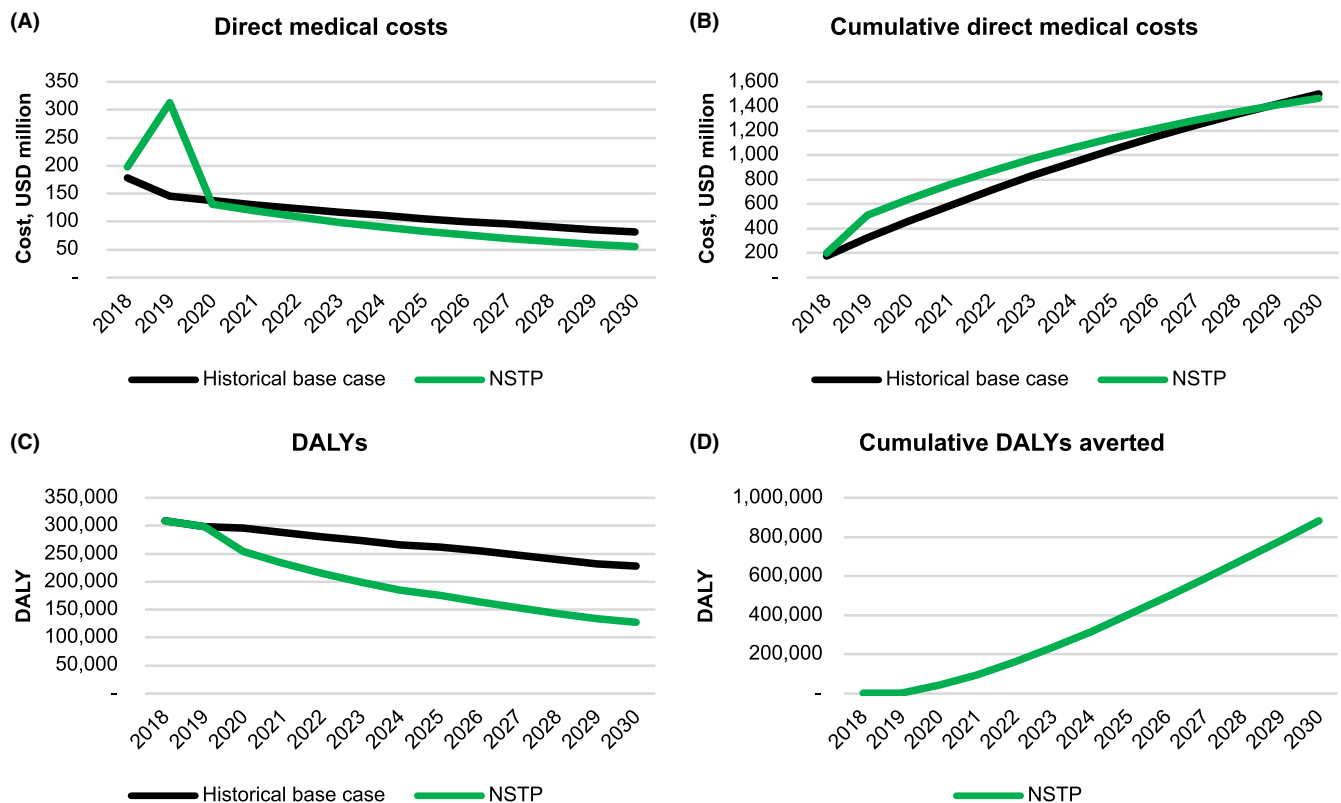


FIGURE 2 Economic burden outcomes for the direct medical costs and disability-adjusted life years, by scenario, 2018–2030. DALY, disability-adjusted life year; NSTP, national screening and treatment programme; USD, United States dollar.

decrease over time to become cost-effective by 2020, highly cost-effective by 2021 (ICER of \$1780 per DALY, 64% of the per-capita GNI), then continue to decline until becoming cost-saving by 2029

(Figure 3), saving about \$8million. Over 2018–2030, the NSTP was projected to save about \$35million in direct medical costs (Figure 2B).

The NSTP resulted in a total of 883 333 cumulative DALYs averted by 2030 compared to the base case (Figure 2D). In 2020, the monetary value of the DALYs averted through the NSTP was equivalent to \$185 million, which was expected to increase annually to reach an estimated \$606 million in 2030 or a total of \$4705 million between 2020 and 2030 (Figure 4).

The cumulative total economic benefit (from direct medical and indirect costs) of the NSTP through 2030 was \$4740 million.

3.3 | Sensitivity analysis

The one-way sensitivity analysis found that three variables accounted for more than 99% of the uncertainty in the 2018–2023 ICER under the NSTP scenario: (1) proportion of compensated cirrhosis patients remaining with liver disease after SVR (accounting for 80% of the uncertainty); (2) annual progression rate from compensated cirrhosis to HCC, after SVR; and (3) annual progression rate from DC to HCV-related mortality, after SVR. The analysis is visualized in Figure 5.

The PSA, varying all uncertain variables, revealed a 2018–2023 ICER of \$584/DALY (95% UI: 296–625) for NSTP, with the scenario

TABLE 3 Economic model outcomes for DALYs averted, cumulative direct medical costs and ICER, by scenario, 2018–2030.

Scenario	DALYs averted	Cumulative direct medical costs (\$ millions)	ICER (\$/DALY)
Historical base case	–	1501	–
National screening and treatment programme	883 333	1466	(40) ^a

Abbreviations: DALY, disability-adjusted life year; ICER, incremental cost-effectiveness ratio.

^aNegative value is represented with parentheses.

becoming highly cost-effective by 2021 (95% UI: 2020–2021) and cost-saving by 2029 (95% UI: 2027–2029).

The CEAC revealed that, at a willingness-to-pay threshold of \$625, the probability of the NSTP being cost-effective was 97% (Figure 6).

4 | DISCUSSION

The primary objective of this analysis was to evaluate the disease burden and economic impact of the NSTP relative to a historical base-case scenario in which the NSTP was not conducted. The NSTP was found to be highly cost-effective by 2021 and cost-saving by 2029.

Additionally, the NSTP scenario was expected to result in an 86% decrease in total viremic patients by 2030, compared with a 41% decrease in the historic base scenario for the same time period. Most of this decline would be expected to occur shortly after implementation of the NSTP, with an 81% reduction expected by 2023. Although Egypt started its efforts to combat viral hepatitis years before the NSTP,^{6–8} the rapid large-scale implementation of the NSTP and the availability of high-efficacy treatment played a significant role in eliminating the public health threat of HCV in Egypt.

Initially (during 2018–2019), the direct medical cost of NSTP was estimated to be higher than that incurred under the historical base case. However, starting from 2020, the direct medical cost would be expected to decline drastically to an even lower level than that incurred under the base case, with a cumulative cost of \$1466 million for the NSTP versus \$1501 million for the base case by 2030. The significant decrease in the total viremic and incident cases is the main cause of this sharp decline in cost, as from 2020 Egyptian experts expected that newly diagnosed cases would not exceed 10 000 annually.

In addition to the direct medical cost savings, the total economic impact of the NSTP would be monumental, with a cumulative total economic return of \$4740 million by 2030.

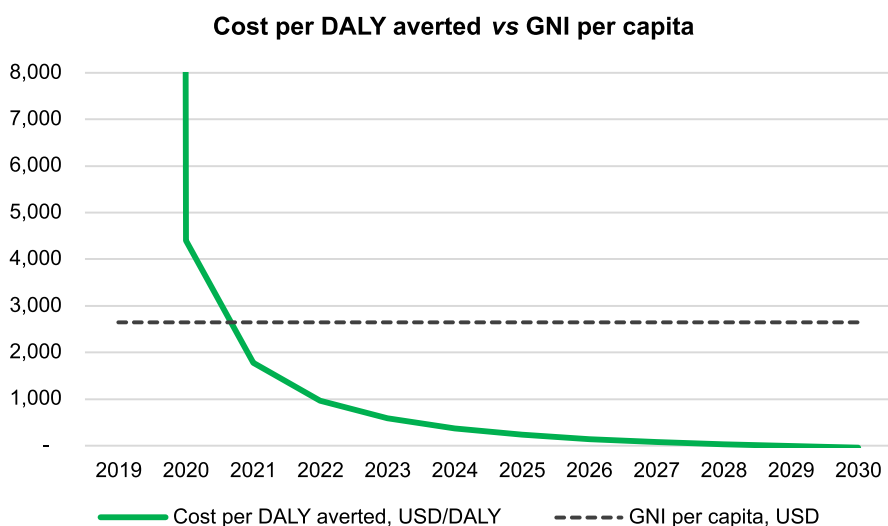


FIGURE 3 Cost per DALY averted for the NSTP. NSTP, national screening and treatment programme; DALY, disability-adjusted life year; GNI, gross national income; USD, United States dollar.

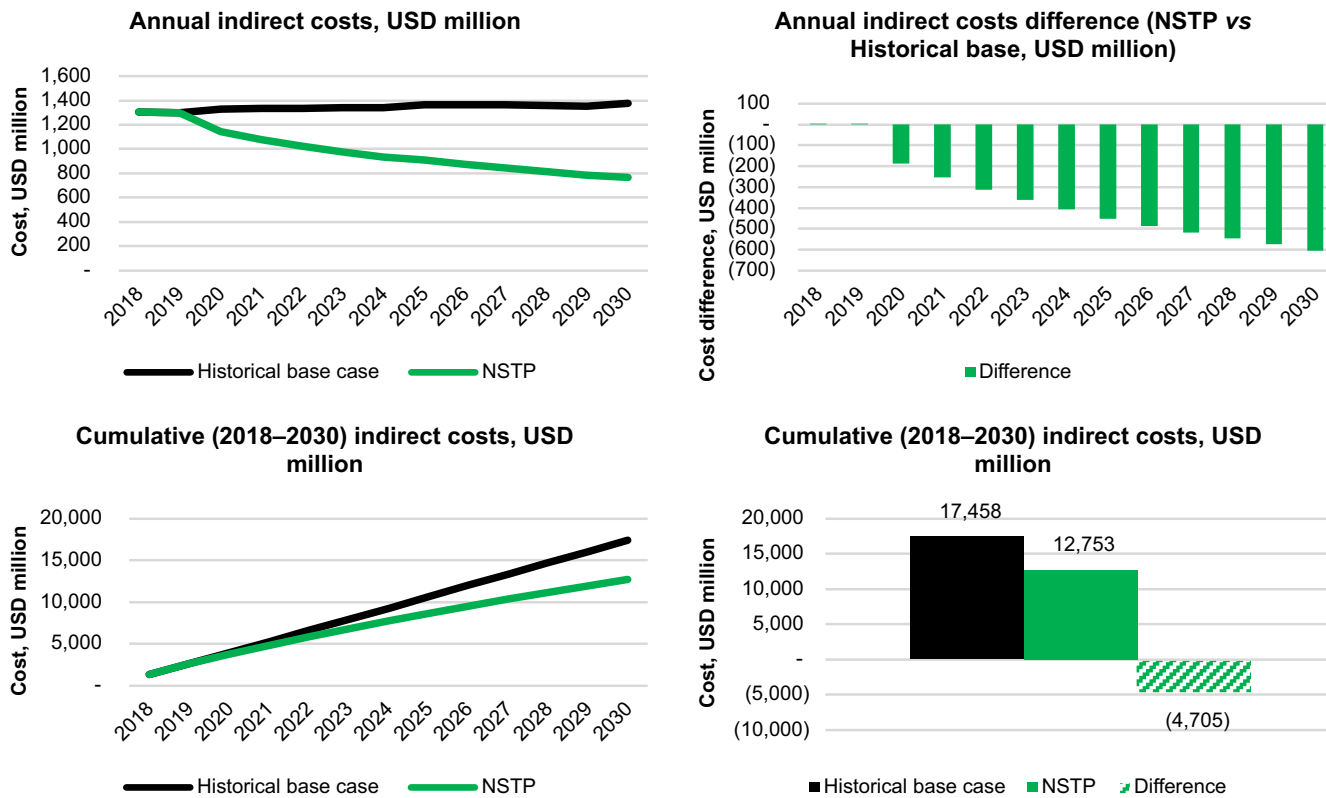
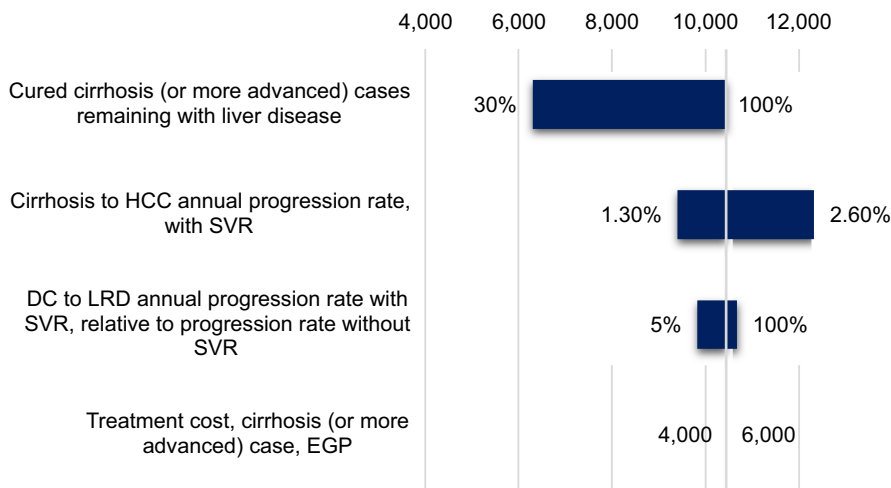


FIGURE 4 Economic burden outcomes including indirect costs, total economic burden, cumulative direct medical costs and indirect costs and cumulative total economic burden, by scenario, 2018–2030. NSTP, national screening and treatment programme; USD, United States dollar.

FIGURE 5 Sensitivity analysis for the 2018–2023 ICER for NSTP, relative to the base case scenario. The middle bar represents the mean 2018–2023 ICER of the NSTP scenario, with all uncertain variables evaluated at their mean value. DC, decompensated cirrhosis; ICER, incremental cost-effectiveness ratio; LRD, liver-related death; NSTP, national screening and treatment programme; SVR, sustained virologic response.

Incremental cost-effectiveness ratio, 2018–2023



Previous studies reported that treating HCV patients with early disease stages was not only more effective but also less expensive than delayed treatment initiation until more advanced disease stages occur.^{19,20} So, the impact of the NSTP was also evident in the health-care costs saved, given an estimated 61 374 and 60 802 averted DC and HCC cases, respectively.

The results of this analysis are aligned with a previous study that found one-time HCV screening and treatment in Egypt to be

cost-saving. However, the intervention used a triple-therapy treatment (sofosbuvir with pegylated interferon and ribavirin), which is no longer used.²¹

Similar findings have been reported by an American study, which aimed to estimate the cost-effectiveness of universal one-time screening for HCV infection in all adults aged 18 and above in the USA compared to the then-current guideline-based strategy of screening adults born from 1945 through 1965. Universal screening

Cost-effectiveness acceptability curve

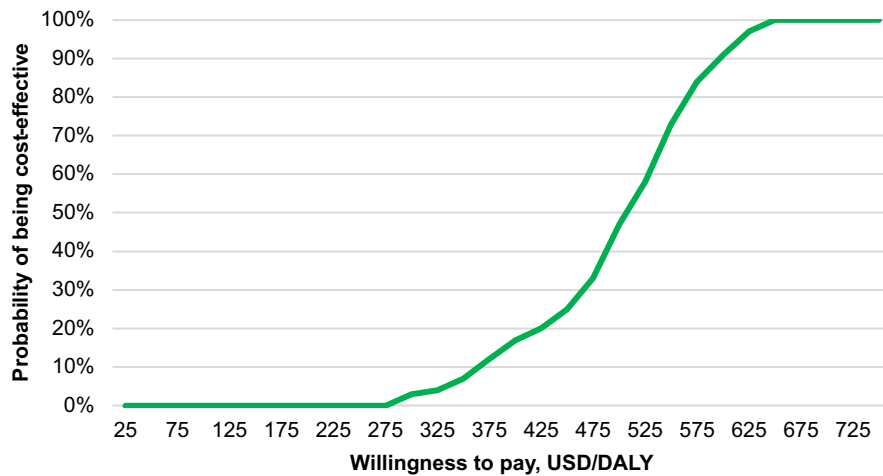


FIGURE 6 Cost-effectiveness acceptability curve of the NSTP scenario. The cost-effectiveness acceptability curve shows the proportion of Monte Carlo realizations of an ICER of a scenario (the y-axis) that is cost-effective at a given willingness-to-pay threshold (the x-axis). DALY, disability-adjusted life year; NSTP, national screening and treatment programme.

in the era of DAA treatment regimens was found to be cost-effective compared with birth cohort screening when the prevalence of HCV antibody positivity was >0.07% among adults not in the cohort born from 1945 through 1965.²² Results of a similar study also found an expanded age-based testing strategy cost-effective compared with birth cohort-based screening.²³ In fact, the U.S. Preventive Services Task Force recommended screening all American adults 18–79 years of age for HCV, a change from the previous birth cohort-based recommendation.²⁴

In France, after comparing different screening and treatment strategies for HCV, an analysis concluded that universal screening would not only be the most effective strategy but also cost-effective – if followed by treatment of viremic patients regardless of their fibrosis stage.²⁵

In Pakistan, the situation is highly comparable to Egypt as it harbours the second largest HCV burden in the world.²⁶ Instead of a one-time screening and treatment programme as assessed in this analysis, a Pakistani study based on real-life data evaluated the integration of HCV screening and treatment into primary healthcare to be cost-effective.²⁷

Emphasizing the role of investment in scaling up the screening and treatment of HCV, a recent Pakistani study assessed the cost-effectiveness of integrating screening and treatment services and its impact on economic productivity improvement. The analysis concluded that partial integration of HCV testing in the existing health services could be highly cost-effective by 2030 and cost-saving by 2031. Under this HCV elimination strategy, an estimated 5.57 million DALYs and 333 000 HCV-related deaths could be averted over 2018–2023, resulting in a total of \$9.10 billion as a net economic benefit by 2050.²⁸ Screening for other diseases has also been found to be cost-effective, with numerous studies reporting promising findings.^{29–31} For example, in Uganda, an analysis assessed the integration of screening and treatment services for non-communicable diseases (hypertension, diabetes and high cholesterol) among patients living with HIV, providing preliminary evidence of cost-effectiveness of such a programme.²⁹ Moreover, in Malawi, a study found screening

and laser treatment for retinopathy among diabetic patients to be cost-effective.³⁰ Another analysis evaluated the Norwegian Breast Cancer Screening Programme to be highly cost-effective in reducing mortality caused by breast cancer.³¹

Our study has several limitations. Firstly, the analysis used a mathematical model that depends on the data collected from multiple sources. Secondly, there is uncertainty in costs associated with the extrahepatic manifestations that affect up to 74% of chronic HCV-infected individuals.³² Achieving SVR is commonly associated with the remission of some extrahepatic manifestations such as cryoglobulinaemia,³³ though the prevalence of other extrahepatic conditions and their associated costs after SVR has not been studied. The costs and remission rates of the extrahepatic conditions after achieving SVR could subsequently affect the results of this analysis. Furthermore, an overestimation of cost-effectiveness was possible since the analysis only distinguished between vertically and horizontally acquired infections in the entire population and did not explicitly model groups susceptible to reinfection. However, it has been previously shown³⁴ that there was a substantial reduction in incident cases of HCV infection between 2006 and 2018 across Egypt, so the overestimation of cost-effectiveness resulting from this limitation is expected to be small. Lastly, although many studies have been conducted to measure the effectiveness of the new treatment regimens of HCV,^{7,10,35} there is great concern about the cost of expanding the global access to HCV diagnosis and treatment.^{36–38}

In conclusion, the present analysis found the Egyptian national screening and treatment programme to be highly cost-effective by 2021 and cost-saving by 2029. Over 2018–2030, the programme is expected to save about \$35 million in direct medical costs, with a total of 883 333 cumulative DALYs averted equivalent to an economic gain of \$4705 million in indirect costs compared to the base case. The dynamic surrounding the issue of HCV screening has changed since the availability of a new generation of highly effective oral DAAs with few side effects and short treatment course.

Our analysis provides evidence for other countries, especially on the low- and lower-middle-income level, regarding the

cost-effectiveness of conducting nationwide screening and treatment programmes for HCV and even for other diseases. This study further highlights the importance of investment in similar screening and treatment programmes.



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CONFLICT OF INTEREST STATEMENT

SE and AO have received research funding from the World Health Organization. IG, HR and SB are employees of CDA Foundation. CDA Foundation has received research funding from AbbVie, Gilead, Pfizer and Intercept. AG, AR, WA-R and WE-A have no conflicts of interest to declare. GE is speaker, advisory board member and investigator for Gilead Sciences, GSK and AbbVie. He declares no competing interests with respect to this study. IW is speaker/investigator for AbbVie, Arena, AstraZeneca, EVA Pharma, Gilead, Marcyrl, Novartis, Pharco, Roche.

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