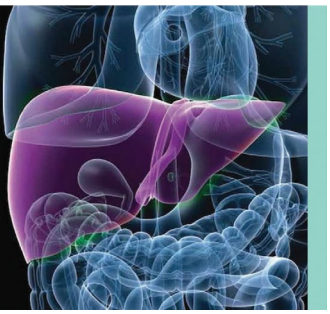

A Tool to Inform Hepatitis C Elimination: A Case for Hepatitis C Elimination in China

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The World Health Organization (WHO) recently launched a global campaign for eliminating hepatitis C virus (HCV) as a public health threat by the year 2030. The campaign aims to reduce HCV incidence by 80% and HCV-related mortality by 65%, primarily through achieving a diagnosis rate of at least 90% and treatment coverage rate of at least 80%.[1] However, most countries do not have a national strategy for HCV screening and treatment that can lead to HCV elimination.

Elimination will require detection of HCV-infected persons who are currently undiagnosed, treatment of a large proportion of those diagnosed, and efforts at prevention of transmission of HCV and occurrence of new cases. For each of these steps, several different approaches are feasible, and we need a better understanding of which approaches will be the most cost-effective and what the effects of different annual screening and treatment rate combinations will be.

The objective of this study was to use mathematical modeling to identify the budget and disease impact of different hepatitis C elimination strategies in China. As part of this analysis, we developed an online HCV elimination budget tool that can identify the most effective strategies (defined by different levels of annual screening and

Abbreviations: DAA, direct-acting antiviral; DC, decompensated cirrhosis; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HEP-SIM, Hepatitis C Disease Burden Simulation; LRD, liver-related death; WHO, World Health Organization; WHO-CHOICE, World Health Organization's CHOosing Interventions that are Cost Effective.

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treatment) to allocate HCV elimination resources using mathematical modeling. The tool provides an investment case for HCV elimination and can be used for discussions with policymakers. We demonstrate the strength of this tool using China as an example, which has more than 9 million people living with HCV[2]—the world's largest HCV-infected population—with the vast majority remaining unaware of their infection status.[3]

METHODOLOGY

We used our previously developed Hepatitis C Disease Burden Simulation (HEP-SIM) model,[4-7] a microsimulation model that simulates the epidemic, disease progression, and elimination strategies of hepatitis C infection in a given country or regional setting. The model incorporates HCV natural history, transmission, diagnosis rate, and treatment access to direct-acting antiviral (DAA) therapies from 2015 to 2040 (see Appendix S1 for details). The previous version of the HEP-SIM model has been expanded for this analysis to also include HCV transmission.

We then used data on the population, HCV epidemic, and health care costs in China (Table 1)[8-13] to project the disease and economic burden under different annual HCV screening and treatment rates. We assumed one-time screening of all adults in the population over a period of years until all adults have been screened. We included a 1-year intervention ramp-up period in 2021, where screening and treatment occur at 50% of the target annual rates. We specifically looked at combinations of screening and treatment that can lead to meeting the WHO elimination targets by the end of 2030. Annual health care costs associated with HCV disease management (Table 1) were estimated using the WHO's CHOosing Interventions that are Cost Effective (WHO-CHOICE) tool.[8] We also conducted a sensitivity analysis on treatments costs by running the same analysis with a 50% reduction in the price for DAAs. We did not include nonmedical costs in this analysis.

Building off of the HEP-SIM model, we also developed an interactive, open-access, online tool for finding HCV elimination strategies in China (available at: http://www.hepcelimtool.org). This tool allows users to change key model parameters, such as HCV prevalence, testing and treatment costs, and elimination targets to be met, and then explore the impact of different screening and treatment rates that can lead to elimination targets being met.

TABLE 1. CHINA-SPECIFIC MODEL INPUTS: GENERAL POPULATION CHARACTERISTICS, HCV DISEASE BURDEN CHARACTERISTICS, AND MEDICAL COSTS

Parameter	Value
General population parameters	
Total population (billions)[9]	1.38
Annual birth rate (per 1000)[9]	12.43
Sex[10]	
Male	48.1%
Female	51.9%
Age distribution, years[9]	
≤20	21.97%
21-30	15.18%
31-40	14.98%
41-50	16.87%
>50	31.00%
Hepatitis C population parameters	
Initial awareness[3]	30.00%
Prevalence by age[3]	
<20	0.05%
20-34	0.44%
35-44	0.95%
45-54	1.01%
55-64	1.22%
≥65	1.18%
Fibrosis score distribution[11]	
F0	16.20%
F1	32.00%
F2	17.90%
F3	19.00%
F4	14.90%
Virus genotype distribution[2]	
G1	58.20%
G2	15.40%
G3	8.70%
Other	17.70%
Medical costs	
Health state costs (annual in US $)[8,12]*	
F0-F1[†]	$77.51
F2	$78.51
F3	$159.42
F4	$182.06
DC	$1903.42
HCC	$3582.99
Testing and treatment costs (US $)	
Antibody screening test	$17.12
RNA confirmation test	$144.00
Genotyping test	$50.00
DAAs (12-week course)[13‡]	$1383.00

*We estimated annual health care costs associated with HCV disease management using the WHO-CHOICE tool.[8] We first extracted inpatient and outpatient primary costs from WHO-CHOICE and took the weighted average of cost per inpatient visit and cost per outpatient visit for each HCV-associated state in the United States; inpatient visits accounted for 38% of health care encounters for F0-F4 patients, 43% for patients with compensated cirrhosis, 66% for patients with DC, and 55% for patients with HCC.[12] We then estimated the ratio of these costs in China to the United States and, finally, estimated China-specific costs by multiplying this ratio with costs in the United States.[12]

[†]F0–F4, METAVIR fibrosis score.

[‡]DAA cost based on assumed 85% price reduction from current prices based on recent negotiations with Merck and Gilead.[13]

RESULTS

Feasibility of HCV Elimination in China

The WHO HCV elimination goals can be achieved by 2030 in China if universal screening and treatment rates are scaled up. Several strategies, identified by different levels of screening and treatment rates, can meet elimination targets. HCV management costs incurred are different for each strategy, with the most economical strategies typically requiring higher annual screening rates and higher annual treatment rates (Fig. 1). We present results for the HCV elimination strategy with the lowest costs for China, but our online tool (http://www.hepcelimtool.org) allows users to explore other alternative strategies that meet elimination goals.

Screening and Treatment Rates for the Elimination Strategy

In our analysis, the identified least costly HCV elimination strategy in China requires one-time universal screening (all adults screened only once) with an annual screening rate of 22% per year and an annual treatment rate of 80%. This translates to needing to screen 1.57 billion total in China for HCV from 2020 to 2030; this strategy would result in approximately 790,000 cases of HCV diagnosed in 2021 (during the ramp-up period), then approximately 1.5 million every year from 2022 to 2024, with the number of cases diagnosed then declining each year until 2030 (Fig. 2A). A large number of patients with HCV need to be treated early on—1.6 million cases treated in 2021 (during the ramp-up period) and 3.3 million in 2022—but the number of cases treated each year declines to 2.1 million in 2023 and then is gradually reduced, reaching less than 0.2 million in 2026 (Fig. 2B).

HCV Disease Burden Under the Elimination Strategy

In 2020, the number of people with viremic HCV infection was estimated to be 9.3 million in China. The selected elimination strategy would substantially decrease the number of people with viremic HCV infections, decreasing to 5 million at the end 2022 and then down to 550,000 by the end of 2030 (Fig. 3). Incident HCV cases would also be substantially reduced under the selected elimination

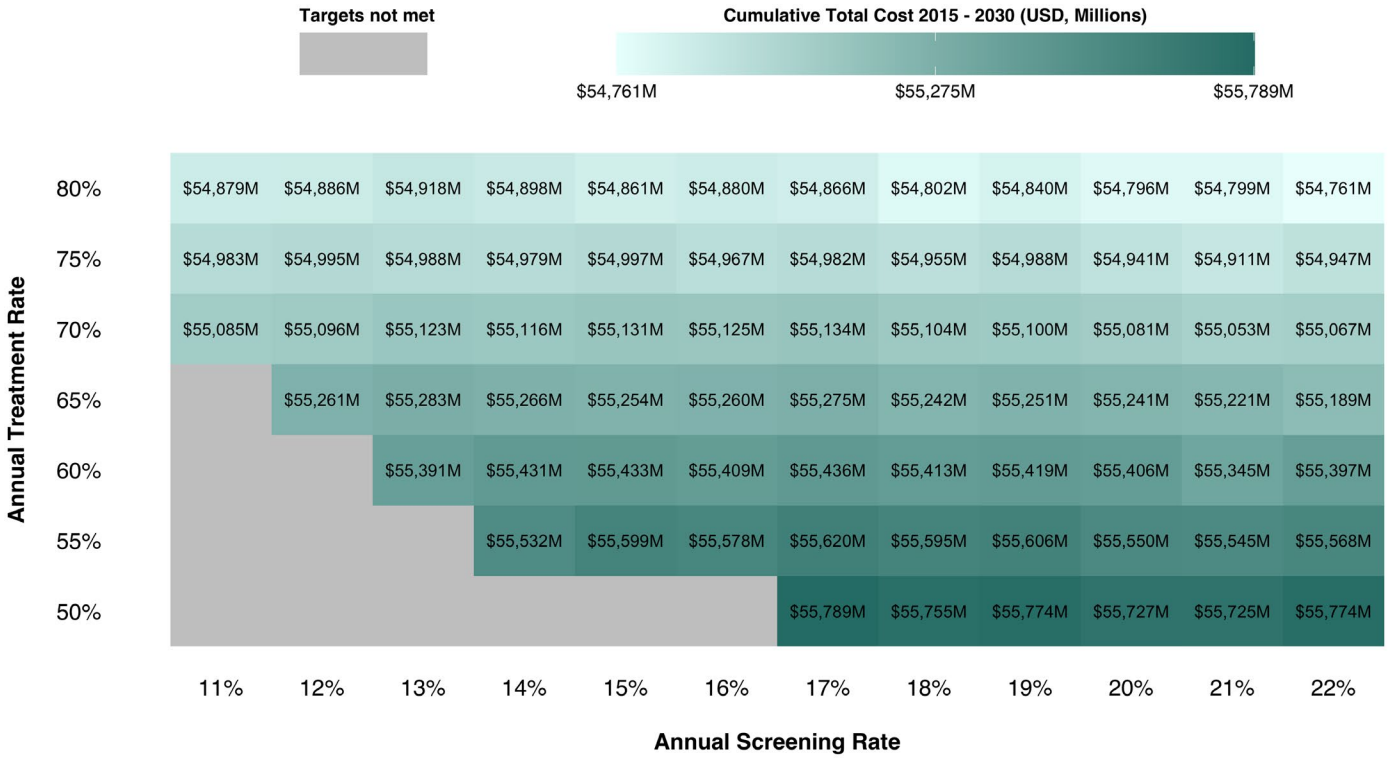

FIG 1 Total HCV-related costs (screening, treatment, and disease management) for different HCV elimination strategies by annual screening and treatment rates in China that meet specified WHO targets by 2030.

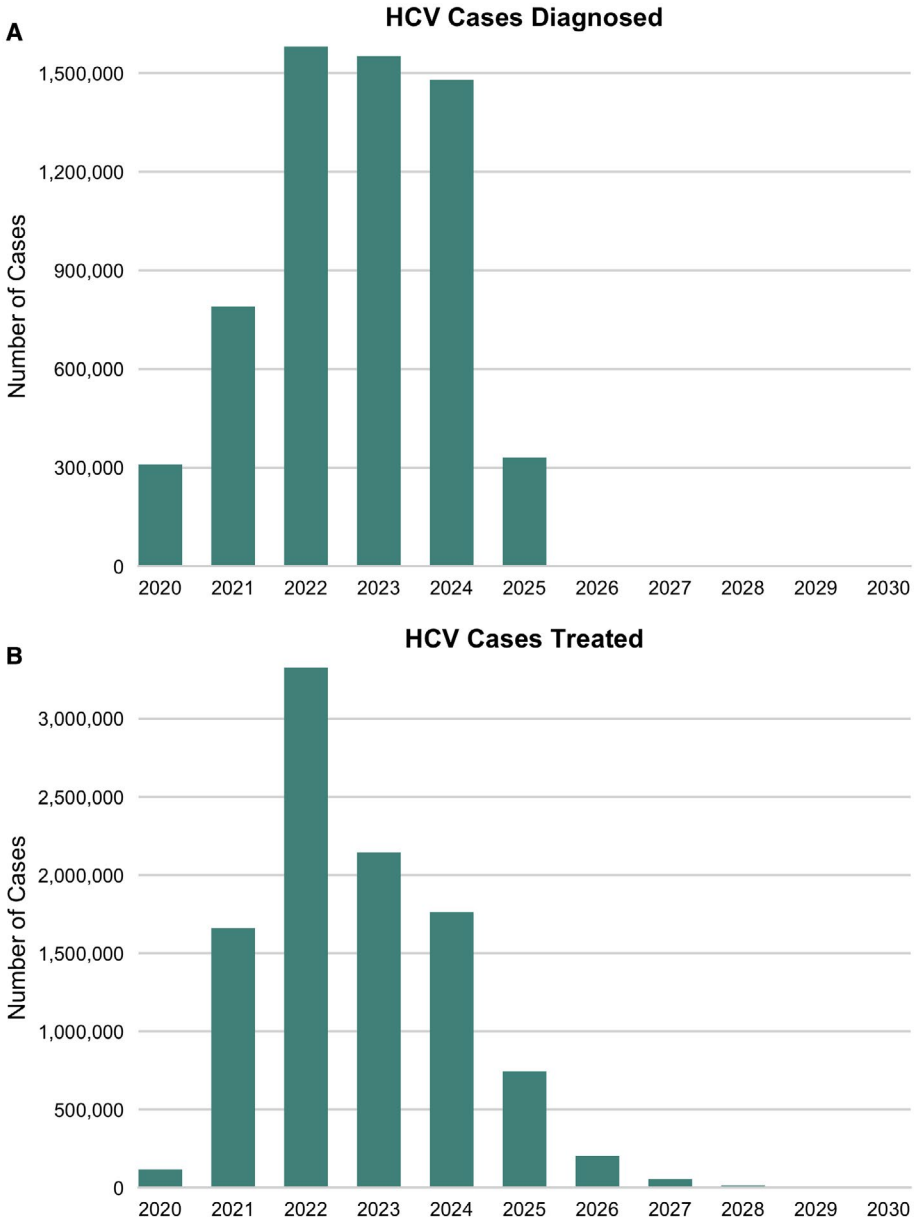

FIG 2 Number of people newly diagnosed with HCV (A) and number of people treated each year (B) under the selected elimination strategy.

strategy, decreasing from 280,000 a year in 2020 to 16,000 in 2030.

Our results also showed that the selected elimination strategy would reduce liver-related deaths (LRDs), decompensated cirrhosis (DC), and hepatocellular carcinoma (HCC) by 2030 (Fig. 4). The number of LRDs would decrease from a peak of 140,000 in 2020 to 30,000 by 2030. Similarly, the number of HCC cases would decrease from 47,000 in 2020 to 15,000 in 2030, and the number of incident DC cases from 59,000 to 10,000.

Cost of HCV Elimination

Under the least costly HCV elimination strategy, the cumulative total HCV-related costs from 2015 to 2030 were US $54.7 billion–about US $1 billion less than the most costly strategy. The annual cost would first increase to US $6.3 billion in 2021 and peak at US $11.5 billion in 2022 but would then decrease to US $3.2 billion by 2025 and decrease to US $500 million in 2030 (Fig. 5). A high treatment burden in the first few years is due to a substantial number of the currently diagnosed population in China (approximately 61% of viremic individuals) not

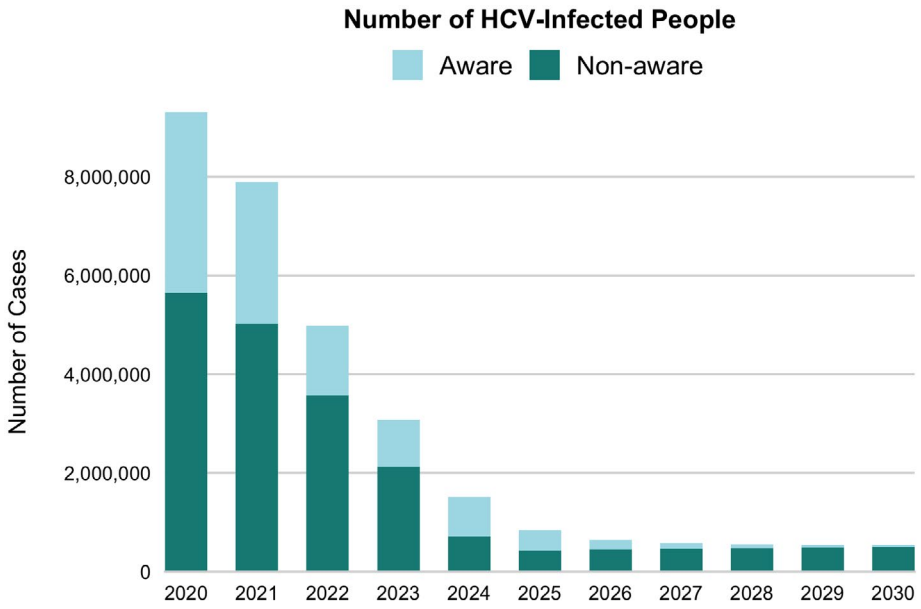

FIG 3 Number of HCV-infected people in China from 2020 to 2030.

having received treatment by the time the new elimination strategy would be implemented in 2021. Treatment costs peak in 2022, accounting for 42% of the total costs in 2022, but this proportion decreases to less than 1% by 2030. In our sensitivity analysis of treatment costs, we found that reducing the price by 50% would result in a cumulative total HCV-related cost of US $47.5 billion (Fig. S3) for the corresponding elimination strategy—a savings of US $7.2 billion. Disease management costs, which account for most of the HCV-related spending in 2020, are less than 1% of the total costs by 2030.

DISCUSSION

Our study highlights the benefit of using mathematical modeling to assist in making policy decisions regarding HCV elimination strategies. The use of an online tool can further engage policymakers and make mathematical modeling more interactive and accessible. Model predictions can be updated based on a changing epidemic and costs. This allows users to make population-level intervention decisions based on total costs and outcomes in a way that they deem most feasible based on available budget and health care capacity and based on their own cost and disease burden inputs. For countries such as China, with a large population of people with HCV, the need for this type of budget optimization in HCV elimination planning is critical.

Our analysis found that eliminating HCV in China by 2030 would require substantial scaling up of HCV screening and treatment. Increasing the annual screening rate creates the biggest financial burden, likely because of the numbers of people eligible for treatment increasing substantially when screening is increased. The cost burden was highest in the second year, once the ramp-up period was over, due to the large number of people diagnosed with HCV in China who have not yet been treated. Total costs at the expenditure peak in 2022 would be US $11.5 billion, which amounts to approximately 2% of China's annual health expenditure for the year 2016.[14]

The annual treatment cost would start declining in the third year of strategy implementation—down from a peak of US $4.7 billion in 2022 to US $2 billion in 2023—and continuously decrease every year until 2030. If the cost of treatment could be further reduced, the implementation of mass treatment could be even more affordable. Reducing the cost of treatment by 50% did not change which HCV elimination strategy was least costly; however, this reduced the total cumulative costs from 2015 to 2030 by US $7.2 billion. Although HCV elimination in China may be ambitious, we believe that strong support from the government and strategic planning can make elimination a reality.

Results also showed that most incident HCV cases in China are rooted in the low-risk general population.

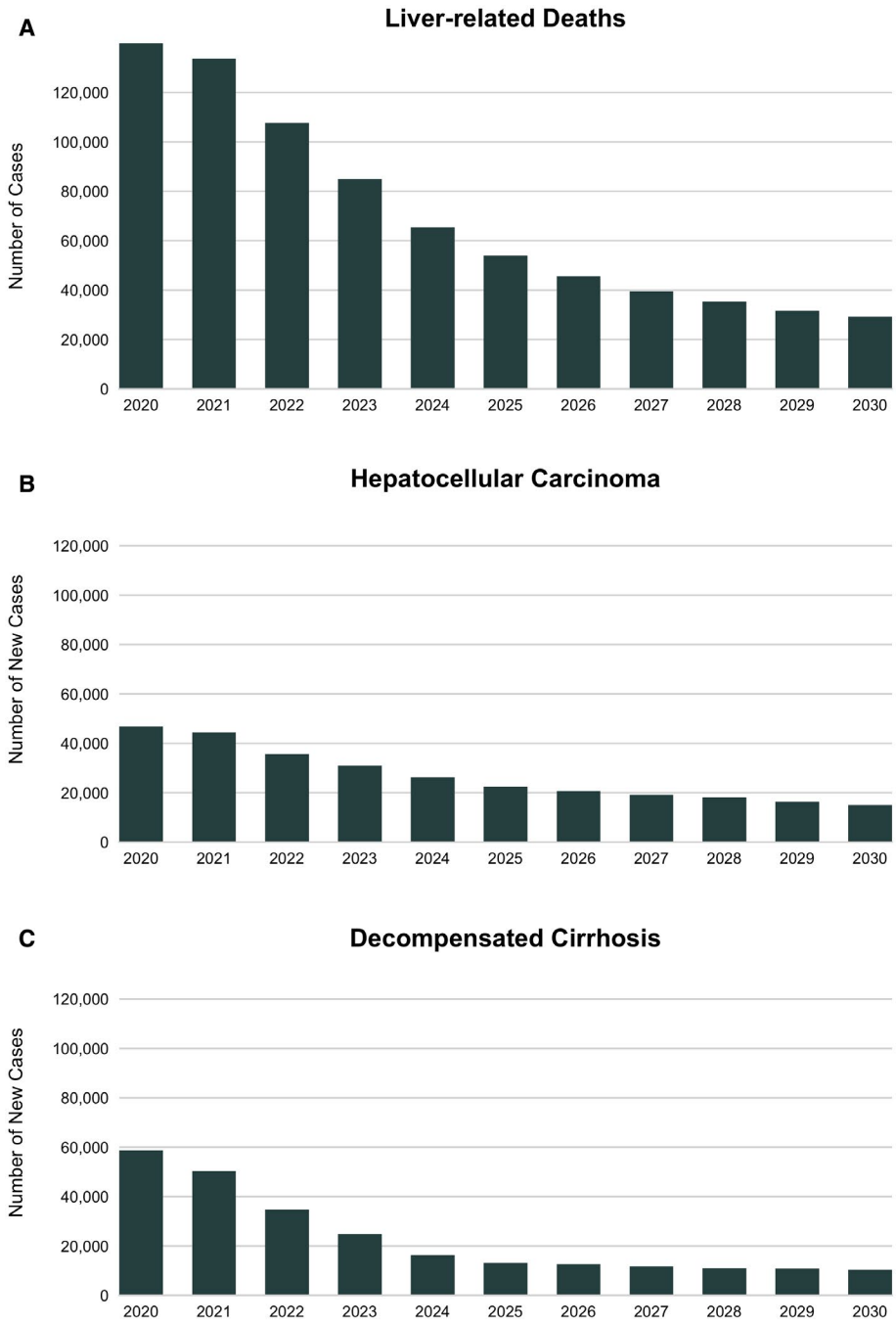

FIG 4 Liver-related deaths (A), hepatocellular carcinoma (B), and decompensated cirrhosis (C) under the selected elimination strategy.

Because of this unique feature of the disease transmission, a two-step approach that addresses the screening in a high-risk population (i.e., people who inject drugs) and then a low-risk population, similar to what is being suggested in Pakistan, might not fit for China. Rather, one-time screening targeting the mass low-risk population should be recommended. Due to the differences in the populations that account for incidence across countries, an expanded online tool could allow policymakers to investigate the screening strategies that are more likely to be effective in their country or region.

Our study had some limitations. First, we consider only adult patients with HCV in China. Second, as with most of the previously published models on HCV treatment, our analysis did not consider the re-treatment of

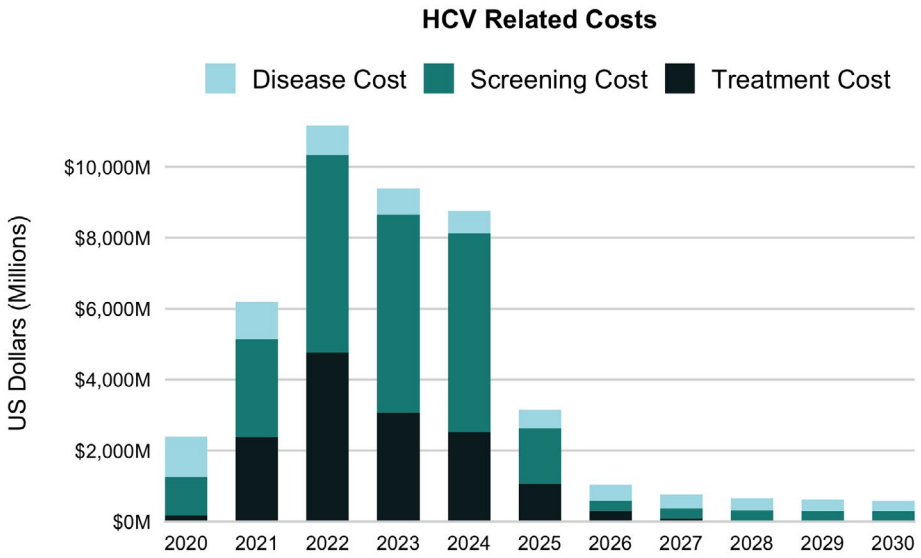

FIG 5 Total HCV-related costs under the selected least costly HCV elimination strategy.

patients with previously unsuccessful DAA therapy. Third, we noted that some unsolicited generic DAA medicines were acquired by a small portion of the Chinese HCV-infected patient population, but such price differentiation was not captured in our model. Fourth, we did not account for population movement in and out of China in our model because international migrants made up only 0.1% of the population in China in 2019.[15] Finally, our model excluded liver transplant as a treatment option for HCV sequelae in China. However, this should not detract from our conclusions because few liver transplants have been performed in China.

In conclusion, our study provides insights into the benefits of making mathematical modeling accessible to policymakers through online tools, to aid in resource allocation decisions for HCV elimination. For China, aggressive universal screening and treatment are needed to achieve HCV elimination, but carefully selecting the strategy used can save more than US $1 billion in elimination costs, compared with the most expensive strategy. Although HCV elimination efforts may require substantial health expenditures up front, the elimination of HCV will lead to substantial decrease in HCV disease and economic burden over time.

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