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Economic Evaluation

Cost-Effectiveness of a Core Antigen–Based Rapid Diagnostic Test for Hepatitis C

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ABSTRACT

Objectives: Hepatitis C virus (HCV) affects 58 million worldwide and > 79% of people remain undiagnosed. Rapid diagnostic tests (RDTs) for HCV can help improve diagnosis and treatment rates. Nevertheless, the high price and infrastructure needed to use current molecular HCV RDT options present a barrier to widespread use—particularly in low- and middle-income countries. We evaluated the performance and cost-effectiveness of a theoretical core antigen (cAg) RDT for HCV viremia confirmation, which requires fewer resources.

Methods: We adapted a previously validated microsimulation model to simulate HCV disease progression and outcomes under different HCV testing algorithms in Georgia and Malaysia. We compared standard of care testing with laboratory-based ribonucleic acid HCV to a cAg-based RDT for HCV confirmation. We simulated a cohort of 10 000 adults in each country, with an HCV-ribonucleic acid prevalence of 5.40% in Georgia and 1.54% in Malaysia. We projected the cumulative healthcare costs, quality-adjusted life-years, and diagnosis coverage rates over a lifetime horizon.

Results: Compared with the standard of care testing, the cAg-based RDT would increase quality-adjusted life-years by 270 in Georgia and 259 in Malaysia per 10 000 people. The high diagnosis rate and treatment rate of the cAg-based RDT result in substantial cost savings because of averted HCV sequelae management costs. Cost savings are $281 000 for Georgia and $781 000 for Malaysia.

Conclusions: We found that a cAg-based RDT for HCV could improve the diagnosis rate and result in cost savings. Such a test could have a substantial impact on the feasibility and cost of HCV elimination.

Keywords: cost-effectiveness analysis, hepatitis C, infectious diseases, lateral flow assay, point-of-care testing, rapid diagnostic test.

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Introduction

Chronic hepatitis C virus (HCV) infection affects approximately 58 million people worldwide.[1] The burden of HCV is particularly high in low- and middle-income countries.[1] The availability of highly effective treatment in the form of direct-acting antivirals (DAAs) offers a hope to reduce the HCV burden. Nevertheless, 79% of the people with HCV remain undiagnosed,[1] and they cannot avail the benefits of treatment unless they become aware of their HCV status.

The World Health Organization (WHO) pledged to eliminate HCV as a public health threat and set a target to diagnose 90% of people with HCV and treat 80% of eligible people by 2030.[2] To meet these targets, HCV testing programs need to reach out to a wider population in each country. At the same time, the number of patients lost to follow-up in the HCV testing process must be reduced. An essential area to focus on for interventions to increase HCV diagnosis is reducing the dropout rate in the current 2-stage testing process. In many situations, after persons are screened for HCV antibodies, they must complete the viremia confirmation testing process at a different location. The drop-off rates are high when patients travel to a different location to get the confirmation test.[3]

Using a rapid diagnostic test (RDT) for confirmation of viremia at the point of care provides an opportunity to improve diagnosis and treatment rates by minimizing loss to follow-up and linking HCV-positive individuals to treatment immediately. Although several molecular tests are available for near point-of-care use, the high price (range $9-$70)[4] and infrastructure needed to use these tests (eg, electricity and trained staff) present a barrier to widespread use. A novel RDT that detects HCV core antigen (cAg) and therefore used for confirmatory testing of HCV viremia could have a substantial impact on the feasibility and cost of HCV elimination. Such a test would be cheaper, easier to use, and therefore more

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accessible than the available point-of-care molecular tests. Early data from test developers suggest that cAg testing at point of care can provide at best 70% to 90% sensitivity (Foundation for Innovative New Diagnostics, 2020). To help address issues with lower sensitivity, these cAg test can be offered in combination with a laboratory-based molecular test for people who test negative with the cAg-based RDT.

Nevertheless, it is not known whether the benefits provided by the accessibility of a cAg-based RDT for HCV diagnosis outweigh the risks associated with its reduced sensitivity compared with molecular testing. Furthermore, the cost-effectiveness of cAg-based RDT is not known. Because the cost of testing can be a substantial contributor to the total cost of HCV elimination programs in low- and middle-income countries,[5] it is important to understand whether cAg-based RDT can reduce the cost of HCV testing, in addition to reducing the loss to follow-up in the HCV testing process.

Our objective was to evaluate the performance and cost-effectiveness of a hypothetical RDT detecting HCV cAg for viremia confirmation compared with standard of care (SOC) testing with laboratory-based confirmation. We selected Georgia and Malaysia as a case study because these countries have national HCV programs and are actively working toward HCV elimination, but with different epidemiological characteristics and healthcare settings. Georgia has one of the highest prevalence of HCV worldwide.[6] Georgia's high HCV prevalence of 5.4% and health system structure could allow for the Georgian findings to be applicable to other eastern European and caucus countries. Malaysia has a relatively lower HCV prevalence, with an estimated 2.5% of the adult population HCV antibody positive. Malaysia has an extensive network of public health services that provide comprehensive care including for HCV.[7] Malaysia's prevalence and national health system mirror that of surround countries, and thus, the Malaysian findings could be applicable to countries in the southeast Asian and western pacific region.

Methods

Overview

We adapted our previously validated microsimulation model, Markov-Based Analyses of Treatments for Chronic Hepatitis C (MATCH),[8-10] to simulate HCV disease progression (see Appendix Fig. 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004) and outcomes under different HCV testing algorithms in Georgia and Malaysia—2 middle-income countries. For our base-case analysis, we compared a SOC testing algorithm with laboratory-based ribonucleic acid (RNA) HCV confirmation (Fig. 1A) to the proposed testing algorithm with cAg-based RDT for HCV confirmation (Fig. 1B).

Testing Algorithms

For both the SOC (Fig. 1A) and cAg-based RDT (Fig. 1B) testing algorithms, we assume one-time rapid antibody screening for all 10 000 individuals in the population cohort. For the SOC algorithm, viremia among antibody-positive individuals is confirmed through a laboratory-based RNA test that requires the patient to follow up to receive the test, receive the results, and start treatment (Table 1[11-16]). For the cAg-based RDT algorithm, viremia among antibody-positive individuals is confirmed with a cAg-based RDT test, therefore eliminating loss to follow-up (ie, the follow-up rate is assumed to be 100%). For our base-case analysis, we assumed that all patients who received viremia confirmation through cAg-based RDT testing were started on treatment.

We also conducted a secondary analysis, where we compared 2 alternate testing algorithms, laboratory-based cAg confirmation testing (see Appendix Fig. 2A in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004) and laboratory-based cAg testing plus laboratory-based RNA testing (see Appendix Fig. 2B in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004), with the cAg-based RDT testing algorithm (see Appendix Fig. 2C in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004). The same patient follow-up rates were used for all laboratory-based confirmation testing.

Treatment Regimens and Efficacy

All patients with viremic HCV infection who received their test results were eligible to receive DAA-based treatment. We used individual patient's liver fibrosis stage to determine the appropriate DAA regimen. Data about the efficacy of the DAA regimens in different scenarios were obtained from clinical trials and the real-world effectiveness of DAAs[17-19] (see Appendix Table 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004).

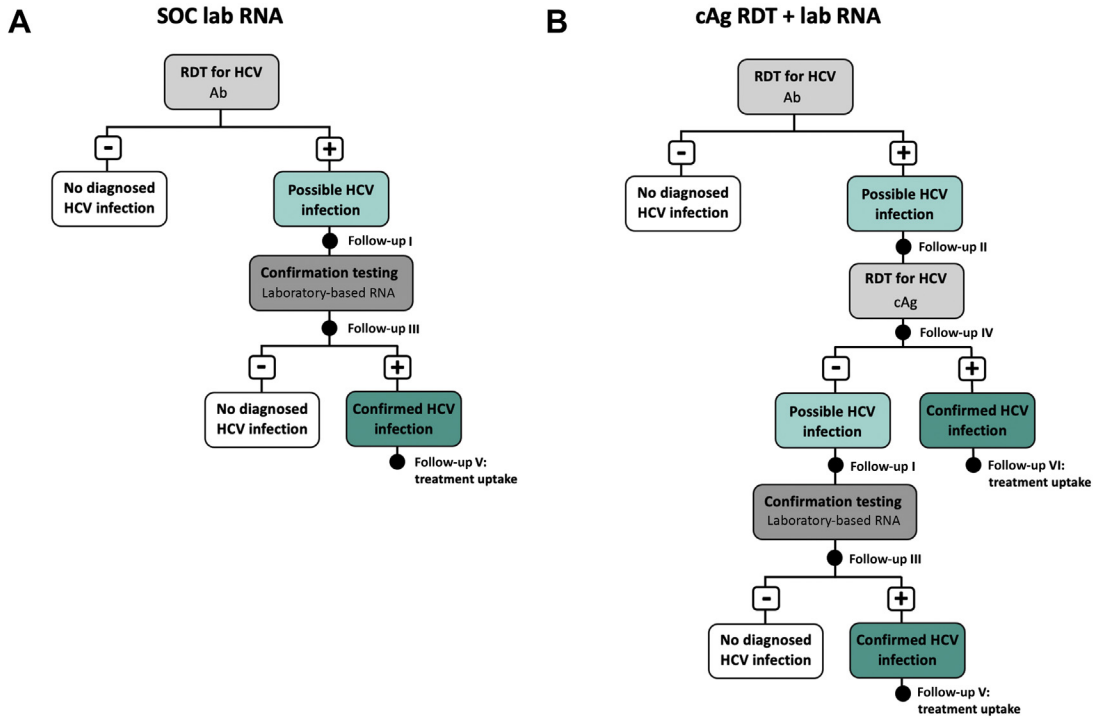
Natural History of HCV

The cohort of 10 000 people in each country is adapted to country-specific demographics, including mean age, age-based mortality, and age-based utility values (see Appendix Table 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004). The HCV-infected population is adapted to the disease burden parameters including prevalence, fibrosis distribution, and genotype distribution (Table 1[11-16]). This cohort then follows the natural history of HCV disease progression, as modeled in our MATCH simulation model, which is shown in Appendix Figure 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004. All simulated patients with HCV start in 1 of 5 METAVIR liver fibrosis states (F0 to F4), and at the end of each 1-week simulation cycle, the patient can remain in the same state or progress into a more severe fibrosis stage, decompensated cirrhosis (DCC), hepatocellular carcinoma (HCC), or liver-related death. Patients can also die of other-cause mortality at the end of each cycle. Patients who are treated in the F0 to F3 states and achieve sustained virologic response are considered cured; nevertheless, patients who are treated in the F4 state and achieve sustained virologic response can still progress to DCC, HCC, and liver-related death states, although at a lower rate than F4 patients who had not achieved sustained virologic response.[20] Treated patients who fail to achieve sustained virologic response were also assumed to continue to progress at rates similar to that of untreated patients with HCV. Progression rates for different fibrosis stages were based on a published metaregression analysis.[21] Progression rates from cirrhosis to DCC and HCC, as well as liver-related mortality rates from DCC and HCC, are from published observational studies.[22-24] The model did not include liver transplantation because of the rarity of this procedure in Georgia and Malaysia.

Medical Costs

All costs were considered from a healthcare payers perspective and are adjusted to 2020 US dollars. Total costs comprised testing costs, DAA-based treatment costs, and HCV sequelae management costs. The HCV testing costs consist of the cost incurred at each step of the diagnostic pathway, which included the costs for conducting laboratory tests and the costs for sample shipment as required. Testing and treatment costs were collected by the Amsterdam Institute for Global Health and Development and the

Figure 1. HCV testing algorithms: (A) SOC with laboratory-based RNA confirmation testing (B) compared with cAg-based RDT confirmation testing followed by laboratory-based RNA confirmation for negative results.



cAg indicates core antigen; HCV, hepatitis C virus; RDT, rapid diagnostic test; SOC, standard of care.

Foundation for Innovative New Diagnostics as part of the HEAD-Start project.[15,16]

Costs associated with HCV sequelae management in the MATCH model were estimated using the WHO's Choosing Interventions That Are Cost-Effective tool[25] (Table 1[11-16]). We extracted inpatient and outpatient primary costs from the WHO's Choosing Interventions That Are Cost-Effective tool, and then we took the weighted average of cost per inpatient visit and cost per outpatient visit for each HCV-associated health state in the United States. Inpatient visits accounted for 38% of healthcare encounters for F0 to F4 patients, 43% for compensated cirrhosis patients, 66% for patients with DCC, and 55% for patients with HCC.[26] We then estimated the ratio of these costs in for Georgia compared with the United States and Malaysia compared with the United States and converted all costs to country-specific estimates by using this ratio.[26]

Quality of Life Weights

Hepatitis C–related quality of life (QOL) weights are assigned to each health state in the model. The QOL weights were derived from published studies.[27-29] For simulated people without HCV, QOL weights were assigned based on age and sex, and patients with HCV who achieved sustained virologic response are assumed to have equivalent QOL weights as the population without HCV.[27] Nevertheless, QOL weights for DCC or HCC were applied for patients who achieved sustained virologic response but then progressed or to DCC or HCC. The adverse effect of anemia on QOL during the treatment period was also considered by applying an anemia multiplier. All QOL weight and multiplier values are summarized in Appendix Table 3 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004.

Model Outcomes

We projected the cumulative healthcare costs and quality-adjusted life-years (QALYs) over a lifetime horizon for the SOC testing algorithm compared with the cAg-based RDT testing algorithm for each country. We also calculated the diagnosis rate of each testing algorithm and the number of people needed to screen to diagnose 1 viremic patient with HCV. In addition, we calculated the cumulative costs of each strategy over varying time horizons from 1 year up to the lifetime horizon. All results are presented for a cohort of 10 000 people in each country.

Sensitivity Analysis

We performed deterministic (1-way and 2-way) and probabilistic sensitivity analyses to evaluate how the cost-effectiveness of the testing pathways would change when model inputs were varied. These inputs included HCV viremia prevalence, cAg test sensitivity rate, state transition probabilities, QOL weights, medical and disease management costs, diagnostic test costs, sample shipping costs, and patient follow-up rates. For 1-way and 2-way sensitivity analyses, we used a range of −50% to +100% from the base values for all cost values. The range for all patient follow-up rates was 50% to 100% (based on expert opinion). We used a range of 0.1% to 10% (based on expert opinion) for HCV viremia prevalence to assess the cost-effectiveness of the testing pathways in different settings. We also conducted a sensitivity analysis on age-specific utility values by varying all age-specific utilities at once by ±15% (see Appendix Table 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004).

For the probabilistic sensitivity analysis, we simultaneously varied all model parameters using the statistical distributions

Table 1. Country-specific model inputs for Georgia and Malaysia.

Parameters	Georgia	PSA distribution	Malaysia	PSA distribution
Age (mean)[11]	39	Uniform (0,6)	29	Uniform (0,5)
HCV viremia prevalence[12]	5.40%	Beta (12, 210.54)	1.54%	Beta (0.75, 44.98)
Fibrosis score distribution[12]				
F0	37.8%	—	30.9%	—
F1	31.5%	—	33.2%	—
F2	12.9%	—	14.6%	—
F3	10.8%	—	12.9%	—
F4	6.9%	—	8.5%	—
Sex distribution*				
Male	50.0%	—	50.0%	—
Female	50.0%	—	50.0%	—
Virus genotype distribution[12]				
G1	39.5%	—	35.8%	—
G2	24.5%	—	0.7%	—
G3	34.3%	—	62.3%	—
G4	1.7%	—	1.1%	—
Patient follow-up rates				
I: Patient follow-up to get laboratory-based confirmation test†	89.2%	Beta (8, 0.969)	71.6%	Beta (23, 9.123)
II: Patient follow-up to get cAg-based RDT test*	100.0%	Beta (8, 0.008)	100.0%	Beta (8, 0.008)
III: Patient follow-up for laboratory-based confirmation results*	100.0%	Beta (8, 0.008)	100.0%	Beta (8, 0.008)
IV: Patient follow-up for cAg-based RDT confirmation results*	100.0%	Beta (8, 0.008)	100.0%	Beta (8, 0.008)
V: Treatment uptake among positive laboratory-based confirmation test†	89.0%	Beta (7, 0.865)	81.5%	Beta (12, 2.724)
VI: Treatment uptake among positive cAg-based RDT confirmation test†	100.0%	Beta (8, 0.008)	100.0%	Beta (8, 0.008)
Testing and treatment costs†				
Ab RDT test†	$2.66	Gamma (20, 0.133)	$1.04	Gamma (19, 0.055)
cAg-based RDT test*	$5.00	Gamma (2, 2.5)	$5.00	Gamma (2, 2.5)
cAg test at laboratory†	$15.02	Gamma (18, 0.834)	$13.94	Gamma (18, 0.774)
RNA test at treatment center†	$26.53		$49.00	
RNA test at point of service†	$16.85		$49.00	
Cost of sample transport†	$1.00		$0.00	
DAAs (per treatment course)†	$100	Gamma (18, 0.463)	$300	Gamma (19, 1.316)
Test sensitivity and specificity				
Antibody RDT sensitivity[13]	98.0%	Uniform (0.98, 1)	98.0%	Uniform (0.98, 1)
Antibody RDT specificity[13]	100.0%	Uniform (1, 1)	100.0%	Uniform (1, 1)
cAg-based RDT sensitivity*	80.0%	Beta (95, 23.75)	80.0%	Beta (95, 23.75)
cAg-based RDT specificity*	98.0%	Beta (14, 0.286)	98.0%	Beta (14, 0.286)
HCV-RNA (laboratory) test sensitivity	99.8%	Uniform (0.996, 1)	99.8%	Uniform (0.996, 1)
HCV-RNA (laboratory) test specificity	99.7%	Uniform (0.994, 1)	99.7%	Uniform (0.994, 1)
cAg (laboratory) test sensitivity[14]	93.4%	Beta (150, 10.51)	93.4%	Beta (150, 10.51)
cAg (laboratory) test specificity[14]	98.8%	Beta (150, 1.822)	98.8%	Beta (150, 1.822)
HCV sequelae management costs				
F0-F2	$65	Gamma (6, 10.833)	$233	Gamma (6, 37.167)
F3	$133	Gamma (6, 22.167)	$458	Gamma (6, 76.333)
Compensated cirrhosis (F4)	$152	Gamma (6, 25.333)	$530	Gamma (6, 88.333)
Decompensated cirrhosis	$1600	Gamma (17, 94.117)	$5742	Gamma (17, 337.765)
Hepatocellular cancer	$3007	Beta (17.17, 175.131)	$10 658	Gamma (17, 626.941)

Ab indicates antibody; cAg, core antigen; DAAs, direct-acting antiviral; F0-F4, METAVIR fibrosis scores; G1-G4, genotype 1-genotype 4; HCV, hepatitis C virus; PSA, probabilistic sensitivity analysis; RDT, rapid diagnostic test.

*Assumptions made for modeling purposes. Testing cost for the point-of-care cAg test is minimal acceptable price based on multiple discussions with test developers and country stakeholders.

†Patient follow-up rates and testing costs that were collected as part of the HEAD-Start study.[15,16]

Table 2. Costs and outcomes for Georgia per 10 000 people.

Outcomes	Base-case	Intervention
	SOC laboratory RNA	cAg-based RDT + laboratory RNA
Total QALYs	205 152	205 442
Incremental QALYs	—	−270
Total cost (USD)	852 192	570 864
Incremental cost (USD)	—	−281 328
Testing cost (USD)	40 618	34 557
HCV sequelae management cost (USD)	772 815	489 014
Treatment cost (USD)	38 759	47 293
Diagnosis rate, %	77.6	93.9
Number needed to screen to diagnose 1 HCV+ case	27	22

cAg indicates core antigen; HCV, hepatitis C virus; QALY, quality-adjusted life-year; RDT, rapid diagnostic test; SOC, standard of care; USD, US dollar.

defined in Table 1[11-16] and Appendix Table 3 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004. We randomly drew values from the imputed distributions, then passed these inputs to the model, and then repeated this process 1000 times resulting in a distribution of outputs. This analysis provides a global measure of uncertainty in the model outcomes.

Results

Compared with the SOC with laboratory-based RNA confirmation testing, the cAg-based RDT testing algorithm would increase QALYs by 270 in Georgia and 259 in Malaysia per 10 000 people.

The cAg-based RDT testing algorithm would be more effective than the SOC for HCV diagnosis. The cAg-based RDT testing algorithm results in a 93.9% diagnosis rate for the cohort for Georgia compared with 77.6% for the SOC with laboratory-based RNA and 89.8% for Malaysia compared with 57.1%. Based on country-specific follow-up rates for confirmation testing, for Georgia 22 people would need to be screened using the cAg-based RDT testing algorithm compared with 27 with the SOC algorithm to diagnose 1 viremic case. For Malaysia, these numbers are 76 for the cAg-based RDT testing algorithm and 119 for the SOC.

The high diagnosis rate and subsequent high treatment rate for the cAg-based RDT testing algorithm result in substantial cost savings because of averted HCV sequelae management costs. Compared with the SOC, the cAg-based RDT testing algorithm would also result in cost savings—$281 000 for Georgia and $781 000 for Malaysia per 10 000 people (Tables 2 and 3). Most cost savings come from averted HCV sequelae management costs (Fig. 2B,D); nevertheless, total testing costs are also lower for the cAg-based RDT testing algorithm. Of note, cost savings begin to accrue for both countries after just the first year, and by 5 years, the costs savings are $29 000 for Georgia and $56 000 for Malaysia. Cumulative cost savings continue to rise steadily and eventually plateau after 46 years for Georgia and 56 years for Malaysia (Fig. 2A,C).

In our scenario analysis, the cAg-based RDT pathway remained the preferred cost-saving option compared with a testing algorithm with laboratory-based cAg confirmation or an algorithm with laboratory-based cAg confirmation plus RNA confirmation for negative cAg tests (see Appendix Tables 4 and 5 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004).

Sensitivity Analysis

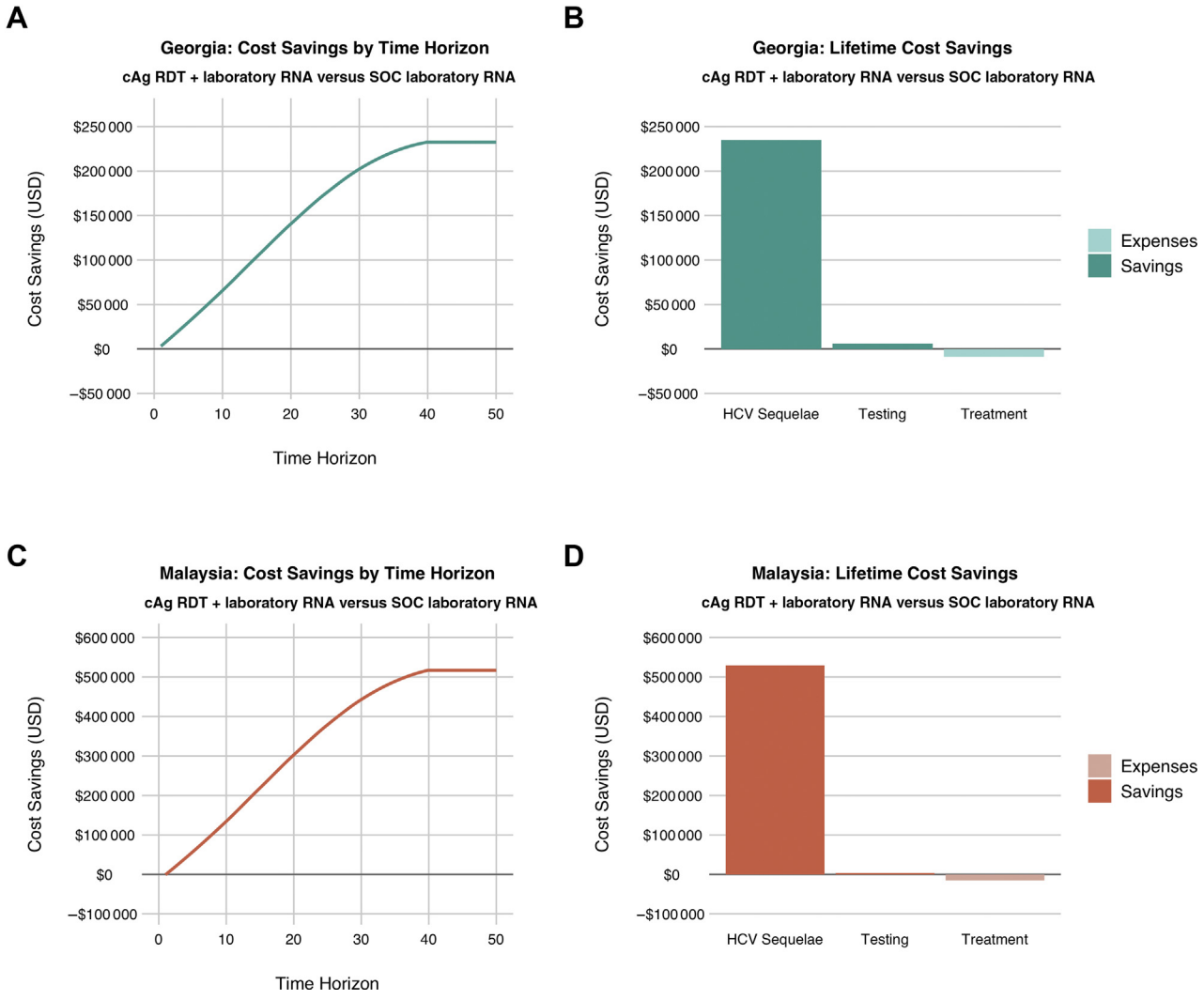
We found that the results were most sensitive to changes in the different patient follow-up rates for the intervention testing algorithm. In general, when the follow-up rate to receive the cAg-based RDT confirmation test drops below the follow-up rate to receive the laboratory-based RNA confirmation test in the SOC algorithm, then the SOC pathway results in higher QALYs and is the preferred option. Appendix Table 6 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004 shows the minimum threshold values of the follow-up rates in the cAg-based

Table 3. Costs and outcomes for Malaysia per 10 000 people.

Outcomes	Base-case	Intervention
	SOC laboratory RNA	cAg-based RDT + laboratory RNA
Total QALYs	253 976	254 245
Incremental QALYs	—	−269
Total cost (USD)	1 579 880	798 657
Incremental cost (USD)	—	−781 223
Testing cost (USD)	15 239	12 001
HCV sequelae management cost (USD)	1 538 110	744 771
Treatment cost (USD)	26 528	41 884
Diagnosis rate, %	57.1	89.8
Number needed to screen to diagnose 1 HCV+ case	119	76

cAg indicates core antigen; HCV, hepatitis C virus; QALY, quality-adjusted life-year; RDT, rapid diagnostic test; SOC, standard of care; USD, US dollar.

Figure 2. The figures on the left show cost savings per 10 000 people over varying time horizons (0-50 years) for Georgia (A) and Malaysia (C), and the figures on the right show cost-savings per 10 000 people by spending category (HCV sequelae management, testing, and treatment) for Georgia (B) and Malaysia (D).



cAg indicates core antigen; HCV, hepatitis C virus; RDT, rapid diagnostic test; SOC, standard of care; USD, US dollar.

RDT testing pathway for it to remain cost-effective or cost saving compared with the SOC.

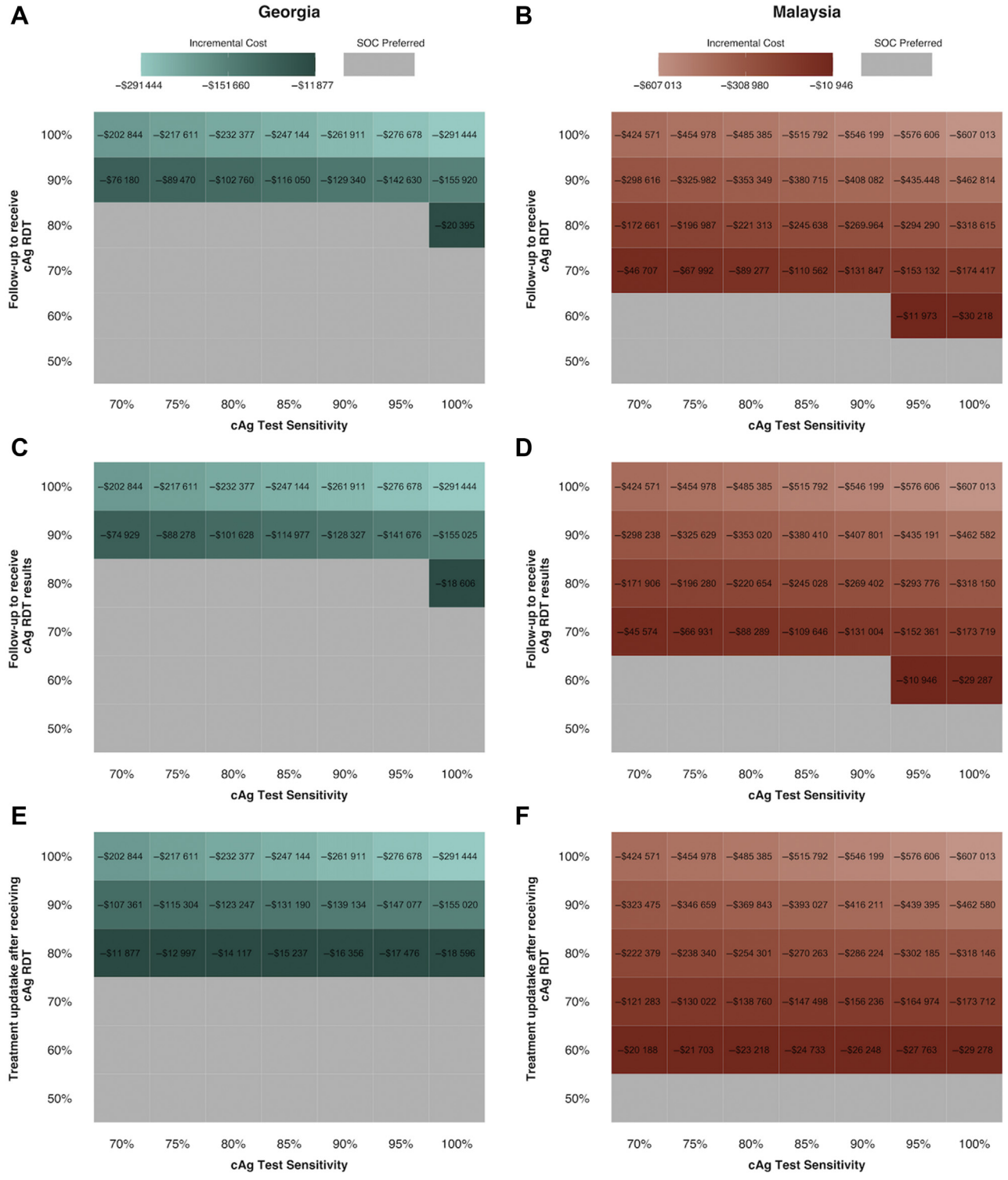
The 2-way sensitivity analysis results for the 3 follow-up rates for the cAg-based RDT confirmation test (receiving the test, receiving test results, and treatment uptake) compared with the cAg-based RDT test sensitivity are shown in Figure 3 A-F. Incremental costs (in this case cost savings) are shown in the heatmap unless the SOC algorithm is preferred because of higher QALYs and lower costs. One-way sensitivity analysis results are shown as tornado diagrams (see Appendix Figs. 3 and 4 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004), and Appendix Figures 5A-C and 6A-C in Supplemental Materials found at https://doi.org/10.1016/j.jval.2022.01.004 show additional 2-way sensitivity analyses; nevertheless, for all additional analyses, the cAg-based RDT algorithm remained cost saving throughout all parameter ranges.

To assess the effect of joint uncertainty in our model inputs, we performed probabilistic sensitivity analysis that varied model parameters of interest. We found that using cAg-based RDT algorithm will not only increase QALYs but also decrease costs compared with the SOC in the vast majority of input scenarios in both Georgia and Malaysia (Fig. 4A and B). This finding further proved the robustness of our conclusion about the advantage of the cAg-based RDT algorithm over the SOC algorithm.

Discussion

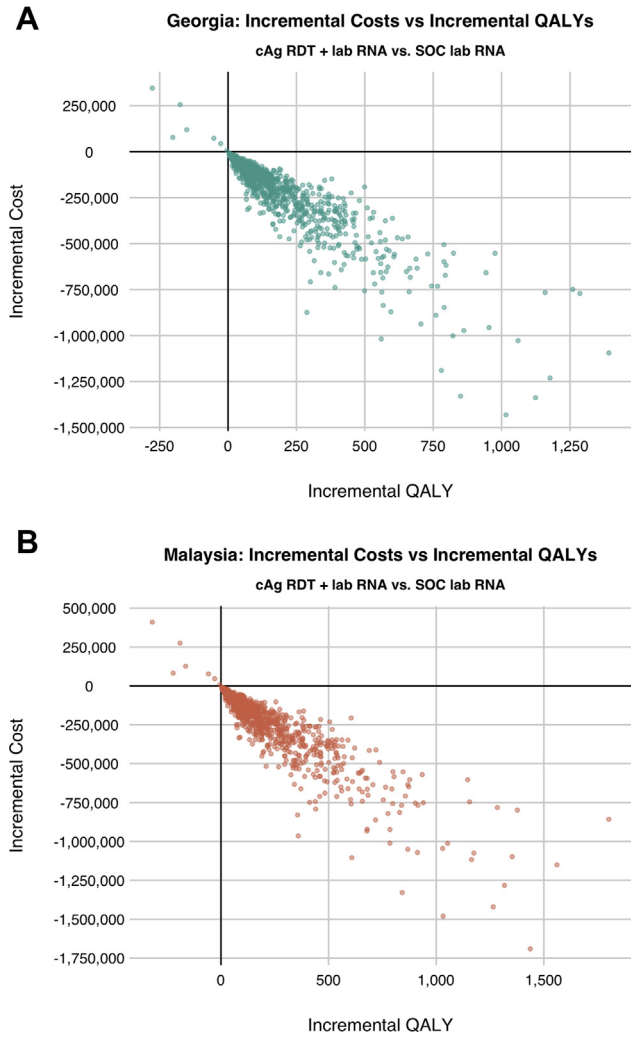
The availability of highly effective antiviral treatment for HCV provides a unique opportunity to eliminate HCV, the stated goal of the WHO. Nevertheless, low diagnosis rates and high cost associated with HCV testing, especially in low- and middle-income countries, remain major barriers to HCV elimination efforts. In this study, we evaluate the effectiveness and cost-effectiveness of a hypothetical novel RDT for HCV. We found that a cAg-based RDT HCV test would improve the diagnosis rates, increase population-level QALYs, and reduce the cost of testing compared with the current SOC of HCV testing. Such a test could be performed without the need for any infrastructure (such as equipment to prepare the sample and electricity) and would make the test less

Figure 3. The first row shows two-way sensitivity analysis results for follow up to receive the cAg-based RDT test and the cAg test sensitivity for Georgia (A) and Malaysia (B). The second row show the two-way sensitivity analysis results for follow-up to receive the cAg-based RDT test results and the test sensitivity for Georgia (C) and Malaysia (D). The final row shows the two-way sensitivity analysis results for treatment uptake for people who received cAg-based RDT test and test sensitivity for Georgia (E) and Malaysia (F). Boxes show cost-savings amount for each combination of parameters when the cAg-based RDT testing is more effective, with blank boxes indicating combinations where the standard of care pathway is preferred due to higher effectiveness.



cAg indicates core antigen; RDT, rapid diagnostic test; SOC, standard of care.

Figure 4. Probabilistic sensitivity analysis showing incremental costs versus incremental QALYs of cAg-based RDT algorithm for HCV diagnosis. (A) Georgia. (B) Malaysia.



cAg indicates core antigen; HCV, hepatitis C virus; QALY, quality-adjusted life-year; RDT, rapid diagnostic test; SOC, standard of care.

expensive than its molecular counterparts given that there would not be the need for outlay of equipment and reagents.

Our study provides some of the first data on the effectiveness and cost-effectiveness of a cAg-based RDT test for HCV. Previous modeling work on point-of-care diagnostics for HIV and Malaria found that RDTs provide quick clinical management, reduce loss to follow-up, and are more cost-effective or cost saving than centralized systems.[30,31] Our analysis shows similar findings for the case of HCV testing.

We conducted extensive sensitivity analyses on a range of model inputs including HCV prevalence, cAg-based RDT test sensitivity rates, testing and medical costs, and patient follow-up rates. Throughout most scenarios tested, the cAg-based RDT results in improved outcomes and cost savings, despite the low sensitivity of this test. Even if the cAg-based RDT improves patient follow-up marginally compared with a scenario where laboratory-based testing is required, HCV diagnosis rates are expected to improve, which will result in more patients with HCV receiving antiviral treatment and improvement in population-level outcomes.

The availability of an inexpensive cAg-based RDT for HCV could change the landscape of HCV in low- and middle-income countries. Our study shows that such a test can result in cost savings. With the price of HCV treatment coming down—as low as $100 in several countries—the cost of testing is the major component of the overall cost of HCV elimination program.[30-32] Our results provide important data about the potential of cAg-based RDTs in reducing the cost of an HCV elimination program in a country. Unlike other infectious diseases such as HIV, tuberculosis, and malaria, there is no global funding mechanism for HCV; therefore, most HCV elimination programs are domestically funded. Given that 70% of the burden of HCV is in low- and middle-income countries,[32] in which health programs may have limited funding, it is critical that governments are able to use cost-effective testing approaches.

The cAg-based RDT can be one approach that allows for easier scale-up of HCV testing by potentially by requiring less initial monetary outlay from government compared with a centralized RNA-only testing approach. In addition, this approach would save additional money, beyond testing costs, in the long run. The cAg-based RDT will enable testing and treatment to happen on the same day—a "one-stop shop" strategy where most HCV-infected individuals could initiate HCV treatment on the same visit, thus reducing loss to follow-up and increasing the total number of individuals cured. This type of service delivery model has been shown to improve access to care, decrease loss to follow-up, and improve outcomes and has been called for by many stakeholders including WHO and civil society stakeholders.[3]

Our study has limitations. First, we used data from the Foundation for Innovative New Diagnostics's HEAD-Start studies, which may not be representative of larger country-level testing programs. Nevertheless, we conducted an extensive sensitivity analysis and found that our results remain robust to a wide range of input parameter values. Second, our model did not account for extrahepatic benefits of HCV treatment; inclusion of these benefits would further increase the cost savings associated with cAg-based RDT. Third, as with most of the previously published models on HCV diagnosis, our analysis did not consider the retreatment of patients who failed DAAs. Given that the cure rate of HCV is $>$ 90%, this limitation would not have an impact on our study's findings and conclusions. Finally, our model excluded liver transplant as a treatment option for HCV sequelae in Georgia and Malaysia because liver transplant is not commonly performed in these countries.

Conclusions

We found that a novel cAg-based RDT for HCV could improve the diagnosis rate and result in cost savings. Such a test could be a game changer and have a substantial impact on the feasibility and cost of HCV elimination, especially in low- and middle-income countries.

Supplemental Materials

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2022.01.004.

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