



# Cost-Effectiveness of Point-of-Care Hepatitis C Virus RNA Testing in the US

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## Abstract

**IMPORTANCE** The standard of care (SOC) laboratory-based hepatitis C virus (HCV) diagnostic algorithm is associated with high rates of undiagnosed cases, patients lost to follow-up, and low rates of treatment initiation, particularly among high-risk populations. Improving diagnostic efficiency is critical for HCV elimination.

**OBJECTIVE** To evaluate the cost-effectiveness of a point-of-care (POC) HCV RNA-first diagnostic strategy compared with SOC across care settings in the US serving people at high-risk of HCV infection.

**DESIGN, SETTING, AND PARTICIPANTS** This economic evaluation used a hybrid decision tree and HCV transmission model using real-world claims data and published literature. The model projected clinical and economic outcomes over 1-year and lifetime horizons. Hypothetical cohorts of individuals eligible for HCV testing were modeled in each of 4 care settings—community health centers, emergency departments, harm reduction clinics, and mobile outreach or street medicine programs in the US—and assumed to be primarily people who inject drugs.

**EXPOSURE** POC HCV RNA-first testing vs SOC laboratory-based HCV antibody and reflex confirmatory RNA testing.

**MAIN OUTCOMES AND MEASURES** The primary outcomes were rates of HCV diagnosis, linkage to care, treatment initiation, sustained virologic response at week 12 after treatment, forward transmission, long-term complications, costs, and incremental cost-effectiveness ratios. One-way and probabilistic sensitivity analyses assessed the impact of uncertainty on results.

**RESULTS** Among modeled cohorts, POC HCV RNA-first testing identified 93.4% of cases vs up to 68.7% with SOC. POC HCV RNA-first testing increased linkage to care (by 37.6%-73.4%), treatment initiation (by 12.1%-48.9%), and sustained virologic response at week 12 after treatment (by 3.6%-26.4%) across care settings. Forward transmission was reduced by 16.3% to 53.3%. Initial costs were higher in some settings, but lifetime costs were lower, with savings of \$3387 per person tested. The POC HCV RNA-first strategy was dominant (lower costs and improved outcomes) over SOC across all settings analyzed.

**CONCLUSIONS AND RELEVANCE** In this economic analysis of HCV testing strategies, a POC HCV RNA-first approach was found to be cost-effective and clinically optimal for high-risk populations, and may represent a critical component of HCV elimination efforts in the US.

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## Key Points

**Question** Is point-of-care (POC) hepatitis C virus (HCV) RNA-first testing cost-effective compared with the standard laboratory-based algorithm in high-prevalence care settings?

**Findings** In this economic evaluation modeling simulated cohorts of individuals eligible for HCV testing, compared with standard of care, the POC HCV RNA-first testing strategy was projected to substantially improve outcomes across all care settings analyzed. Specifically, it was associated with increased HCV diagnosis, linkage to care, and treatment initiation and with reduced forward transmission, incidence of chronic HCV, and related complications.

**Meaning** These findings suggest that POC HCV RNA-first testing was the dominant strategy (more effective and lower costs) across all care settings analyzed; higher short-term treatment costs were offset in the longer-term through reduced incidence of chronic HCV, resulting in long-term cost savings to US payers.

## + Supplemental content

Author affiliations and article information are listed at the end of this article.

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## Introduction

Hepatitis C virus (HCV) is a leading cause of liver disease in the US, with 2.4 to 4.7 million people having active HCV infection; approximately 75% to 85% of cases are asymptomatic and more than 50% of cases are unaware of being infected.<sup>1,2</sup> Acute HCV infections have surged by 492% from 2010 to 2021, mainly in association with injection drug use among young adults.<sup>3</sup> Despite highly effective direct-acting antivirals (DAAs) being introduced in 2013, HCV incidence continues to increase, highlighting the need for improved screening and diagnosis.<sup>4,5</sup>

The standard of care (SOC) for diagnosing HCV infection is a 2-step laboratory-based diagnostic testing algorithm: HCV antibody screening followed by a confirmatory HCV RNA quantitative test for persons with detectable HCV antibodies. This algorithm often requires multiple clinic and/or laboratory visits, resulting in high rates of undiagnosed cases, loss to follow-up, and low treatment initiation, especially in high-risk populations.<sup>6</sup> Linkage to care (LTC) is challenging, relying on successful contact with individuals who test positive for HCV RNA; among people who inject drugs (PWID), LTC rates range from 36% to 65%.<sup>5</sup> Consequently, loss to follow-up can occur at multiple steps beyond diagnosis, including during LTC, treatment initiation, and completion, resulting in low overall rates of successful HCV treatment.<sup>4</sup> In the US, the average time from hepatitis C diagnosis to treatment initiation is approximately 5 months, with substantial variation across geographic locations and care settings.<sup>7-9</sup> These delays are influenced by factors such as insurance approval requirements and linkage to skilled practitioners, although recent policy changes, such as the removal of prior authorization requirements, have helped reduce these barriers.<sup>10,11</sup> Given these systemic delays and attrition points, our model does not incorporate time-to-treatment as a parameter; instead, it focuses on the proportion of patients successfully advancing through each step of the care cascade.

Early infections may be missed by the SOC algorithm, as antibody response can take up to 6 months. Many high-risk individuals do not access traditional health care, exacerbating diagnostic and treatment gaps.<sup>6</sup> To address these issues, the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America now recommend point-of-care (POC) HCV RNA testing at the initial visit, enabling faster LTC and treatment, potentially in a single encounter.<sup>1,12</sup>

In June 2024, the US Food and Drug Administration granted marketing authorization with Clinical Laboratory Improvement Amendments waiver for the Xpert HCV test (Cepheid), an in vitro reverse-transcription polymerase chain reaction test for the qualitative detection of HCV RNA in capillary whole blood from adult individuals with or without antibody evidence of HCV infection. The Xpert HCV test may be performed in settings operating under a Clinical Laboratory Improvement Amendments Certificate of Waiver.<sup>13</sup>

Previous cost-effectiveness analyses<sup>14</sup> focused on POC HCV testing in Australia. Our study evaluates a POC HCV RNA-first test-and-treat strategy vs SOC in US care settings, using US-specific data. Key enhancements include modeling HCV transmission, capturing the full care cascade, and assessing both short-term and long-term outcomes.

## Methods

### Cost-Effectiveness Model Structure

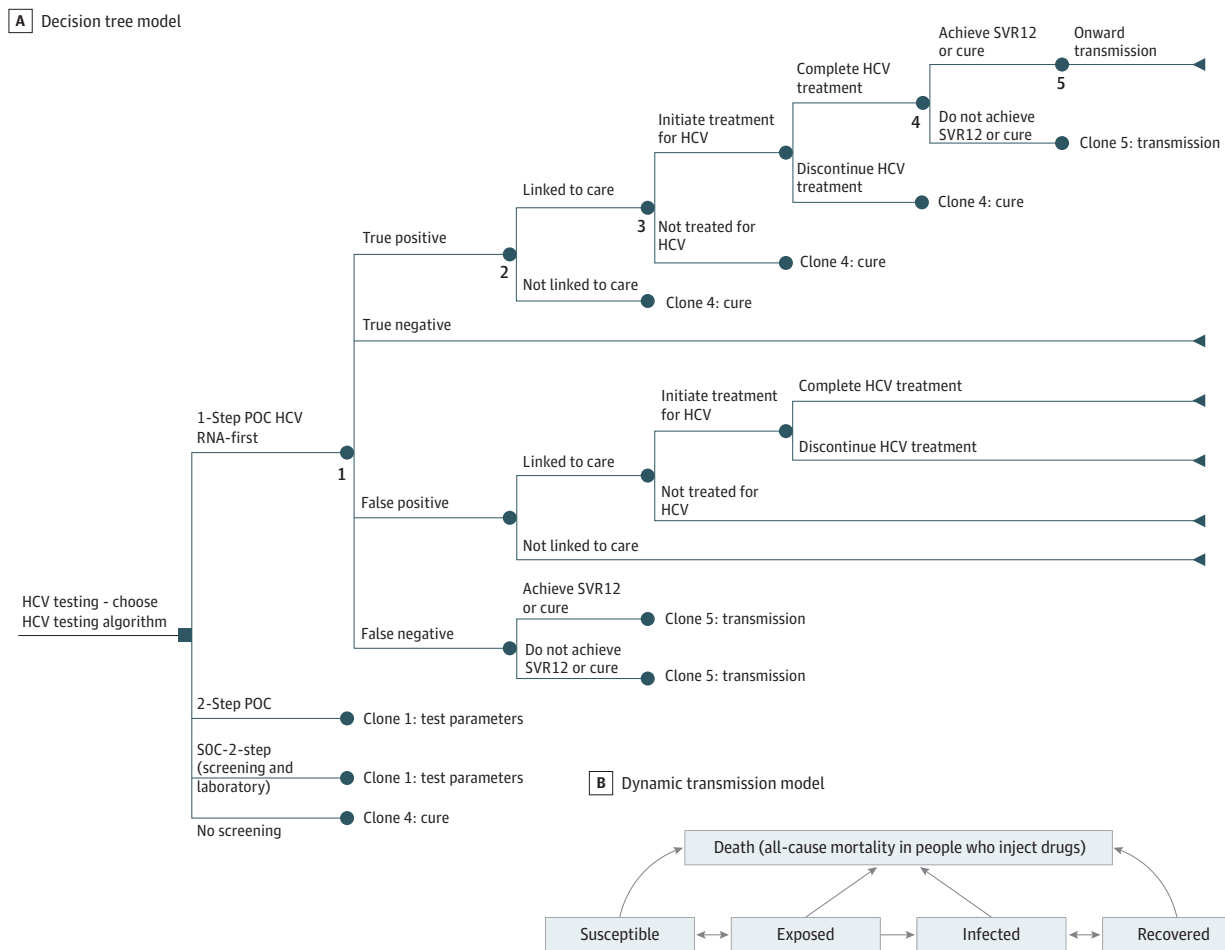
In this economic evaluation study, a hybrid decision tree and HCV transmission model was developed using Excel 365 (Microsoft) to evaluate the clinical and economic outcomes of HCV testing strategies in 4 US settings serving high-risk populations, assumed to be mostly PWID: community health centers (CHCs), emergency departments (EDs), harm reduction centers (HRCs), and mobile outreach/street medicine (MO/SM) programs. Although these settings serve a range of patients, the model accounts for high-risk prevalence documented in these care environments. The model analyzed costs from a third-party payer perspective (weighted average of commercial plans, Medicare, and Medicaid) using a hypothetical cohort of 10 000 people per setting. The decision tree modeled the patient pathway from testing to treatment and cure, whereas the HCV transmission

model projected viral transmission (Figure). This research did not require institutional review board or ethics review, as modeling and analyses with these data do not meet the definition of research involving human participants, as defined within 45 CFR 46.102(f). This analysis was developed in accordance with Consolidated Health Economic Evaluation Reporting Standards (CHEERS) reporting guideline.<sup>15</sup>

The model incorporated a 1-year time horizon to capture immediate test-to-treat outcomes: rates of diagnosis, LTC, treatment initiation, sustained virologic response at week 12 after treatment (SVR12), and forward transmission to secondary cases. The model also assessed longer-term impacts of successful test-and-treat on averting chronic hepatitis C and long-term complications (cirrhosis and hepatocellular carcinoma [HCC]), death rates, life-years (LYs), and quality-adjusted life years (QALYs) gained. Total and incremental costs and incremental cost-effectiveness ratios were calculated for each clinical outcome.

We defined (1) LTC as patients attending their first follow-up visit after diagnosis, and (2) treatment initiation as the point when the first prescription for therapy is filled. Initiation of treatment among individuals diagnosed using POC HCV RNA testing was assumed to be 32% higher than those tested with SOC, based on estimates from the literature.<sup>16</sup> Setting-specific treatment completion rates were then applied to those who initiated therapy.

Figure. Decision Tree Model and Hepatitis C Virus (HCV) Transmission Model



A, Decision tree of the cost-effectiveness model illustrates the health states and the health care cascade for individuals tested for HCV. B, Dynamic transmission model depicts interactions between infected individuals and the susceptible population,

along with associated health states. POC indicates point of care; SOC, standard of care; SVR12, sustained virologic response at week 12.

The model assumes that individuals with either false-negative or true-negative HCV antibody or RNA results do not undergo additional HCV testing, leaving them at continued risk of disease progression or future risk of infection. Those who received a diagnosis, but were not linked to care or initiated on treatment, were assigned a 30% probability of spontaneous recovery, with the remaining cohort at risk of developing chronic HCV and transmitting the virus to others.<sup>17</sup> Individuals who have never been infected with HCV or who recovered were placed back into the susceptible compartment in the susceptible-exposed-infectious-recovered model. The model assumes a reproductive number ( $R_0$ ) of 2.99, reflecting transmission potential in this high-risk cohort.<sup>18,19</sup> Our projections focus on the impact of treating the first generation of cases rather than long-term reinfection dynamics.

## Model Inputs

### Clinical Inputs

The prevalence of HCV antibodies and HCV RNA among people with and without HCV antibodies was obtained from published literature. For SOC, overall HCV infection prevalence was calculated as the prevalence of HCV antibodies multiplied by the prevalence of HCV RNA. For the POC HCV RNA-first testing strategy, prevalence was adjusted to include those negative for HCV antibody but positive for RNA (ie, acute infections). Setting-specific HCV RNA prevalence was used to estimate the number of cases detected with each strategy.<sup>5,20-25</sup> Test sensitivity and specificity were applied to estimate true and false-positives and false-negatives among high-risk individuals (Table 1).<sup>26-29</sup>

Persons with positive HCV RNA results, who were linked to care, were assumed to receive oral DAA treatment for 12 weeks. Percentages at each step of the HCV care cascade (linked to care, initiating treatment, completing treatment, and achieving SVR12) were derived using setting-specific estimates.<sup>5,24,30-32</sup> Because of a lack of data for POC HCV RNA-first testing in an ED setting, LTC in ED was assumed to be double that of SOC in the base-case analysis and varied plus or minus 20% in sensitivity analysis (Table 1).

Those with negative antibody or RNA results did not enter the care cascade; false-negatives were at risk for long-term complications and transmission. Rates of chronic hepatitis C, cirrhosis, and HCC were calculated using published incidence rates among untreated PWID with HCV.<sup>31,32</sup> Survival outcomes, including median survival time in the high-risk PWID population and hazard ratios of death for untreated vs successfully treated patients with HCV, were modeled using exponential distributions to estimate LYs, QALYs, and total costs.<sup>32,33</sup> This approach accounts for mortality risks from causes other than HCV, including overdose and other competing risks (Table 1).

### Costs and Utility Inputs

The total cost for each comparator was calculated in each setting on the basis of literature-derived weighted insurance coverage distributions (Medicare, Medicaid, and commercial plans) among the model cohort (Table 1).<sup>21,22,24,34,35</sup> For the 1-year time horizon analysis, direct medical costs of diagnostic testing and treatment in CHC, HRC, and MO/SM were based on reimbursement rates for HCV antibody and RNA tests, a 30-minute outpatient visit, and the average cost of 12 weeks of oral DAA treatment.<sup>36</sup> Annual management costs of long-term complications were added for the lifetime horizon analysis.<sup>37</sup> HCV antibody costs (*Current Procedural Terminology [CPT] code 86803*), HCV RNA (qualitative) (*CPT code 87521*), and HCV RNA (quantitative) (*CPT code 87522*) tests reflect the real-world average paid amounts by Medicare, Medicaid, and commercial payers (November 2022 to October 2023), sourced from IQVIA's claims database. Outpatient visit costs (*CPT code 99203*) were derived from CMS and Congressional Budget Office publications, with all cost inputs adjusted to 2024 US dollars.<sup>38-40</sup>

In the ED, HCV diagnostic tests are typically included within a single payment (Ambulatory Payment Classifications) for the overall visit. For the 1-year base-case analysis, the total cost (Ambulatory Payment Classifications and physician payments) of an ED visit requiring high-level decision making (*CPT code 99285*) was applied.<sup>38,41</sup> The cost of 12 weeks of oral DAA treatment was applied separately, assuming LTC outside the ED. Annual management costs of long-term

Table 1. Model Inputs

Sources and inputs	Value	Prevalence by setting, %			
		CHC	ED	HRC	MO/SM
Test-related inputs					
Tang et al, <sup>26</sup> 2017					
Laboratory HCV antibody test sensitivity, %	98.0	NA	NA	NA	NA
Laboratory HCV antibody test specificity, %	99.0	NA	NA	NA	NA
Yao et al, <sup>27</sup> 2018					
Laboratory HCV RNA test sensitivity, %	100.0	NA	NA	NA	NA
Laboratory HCV RNA test specificity, %	100.0	NA	NA	NA	NA
Gao et al, <sup>28</sup> 2014					
POC HCV antibody test sensitivity, %	94.1	NA	NA	NA	NA
POC HCV antibody test specificity, %	99.5	NA	NA	NA	NA
Xpert HCV package insert <sup>29</sup>					
POC HCV RNA test sensitivity, %	93.4	NA	NA	NA	NA
POC HCV RNA test specificity, %	99.8	NA	NA	NA	NA
Clinical inputs					
Assoumou et al, <sup>20</sup> 2020, Galbraith et al, <sup>21</sup> 2020, Hernandez-Con et al, <sup>5</sup> 2023, and Rennert et al, <sup>22</sup> 2023					
HCV antibody prevalence	NA	9.8	9.2	34.0	18.3
HCV RNA prevalence (among those with positive HCV antibody)	NA	64.4	62.0	52.0	84.7
Kalita et al, <sup>23</sup> 2022, HCV RNA prevalence (among those who test negative for HCV antibody, acute infections)					
	NA	11.4	11.4	11.4	11.4
Coyle et al, <sup>24</sup> 2016, Hernandez-Con et al, <sup>5</sup> 2023, and Trooskin et al, <sup>25</sup> 2015					
SOC LTC at first appointment	NA	38.7	26.0	73.0	58.3
SOC treatment initiation	NA	19.8	22.0	74.4	57.1
SOC treatment completion	NA	50.0	50.0	77.3	50.0
SOC achieved SVR12	NA	62.5	60.0	69.9	60.0
Maclsaac et al, <sup>30</sup> 2024, Coyle et al, <sup>24</sup> 2016, and Hernandez-Con et al, <sup>5</sup> 2023					
POC RNA LTC at first appointment	NA	94.0	52.0 <sup>a</sup>	94.0	94.0
POC RNA treatment initiation	NA	26.1 <sup>b</sup>	29.0 <sup>b</sup>	98.2 <sup>b</sup>	75.4 <sup>b</sup>
POC RNA treatment completion	NA	50.0	50.0	77.3	50.0
POC RNA achieved SVR12	NA	62.5	60.0	69.9	60.0
Smith et al, <sup>31</sup> 2015					
Incidence of cirrhosis, events/1000 person-years (95% CI)	6.6 (4.8-8.4)	NA	NA	NA	NA
Incidence of decompensated cirrhosis, events/1000 person-years (95% CI)	1.8 (0.3-3.3)	NA	NA	NA	NA
Incidence of HCC, events/1000 person-years (95% CI)	0.3 (0.1-0.6)	NA	NA	NA	NA
Salekšsin et al, <sup>32</sup> 2023, overall survival among high-risk populations, median (95% CI), y					
	23.5 (16.2-27.5)	NA	NA	NA	NA
Gvinjilia et al, <sup>33</sup> 2023					
All-cause mortality for untreated persons with HCV vs treated, HR (95% CI)	5.60 (4.90-6.30)	NA	NA	NA	NA
All-cause mortality for persons with HCV and discontinued treatment vs treated, HR (95% CI)	6.50 (5.80-7.20)	NA	NA	NA	NA
Health insurance mix by care setting					
Klein et al, <sup>34</sup> 2021, Coyle et al, <sup>24</sup> 2016, Galbraith et al, <sup>21</sup> 2020, Thakarar et al, <sup>35</sup> 2021, and Rennert et al, <sup>22</sup> 2023					
Medicaid	NA	47.9	56.8	83.6	39.1
Medicare	NA	18.8	9.1	12.3	19.5
Commercial	NA	33.3	34.1	4.1	41.4
Cost inputs, \$					
IQVIA claims data on file					
ELISA HCV antibody screening test (CPT code 86803)					
Medicaid	NA	12.23	APC bundle	12.23	12.23
Medicare	NA	16.61	APC bundle	16.61	16.61
Commercial	NA	19.16	APC bundle	19.16	19.16

(continued)

Table 1. Model Inputs (continued)

Sources and inputs	Value	Prevalence by setting, %			
		CHC	ED	HRC	MO/SM
HCV RNA test (qualitative) (CPT code 87521)					
Medicaid	NA	32.37	APC bundle	32.37	32.37
Medicare	NA	34.80	APC bundle	34.80	34.80
Commercial	NA	72.43	APC bundle	72.43	72.43
HCV RNA test (quantitative) (CPT code 87522)					
Medicaid	NA	38.18	APC bundle	38.18	38.18
Medicare	NA	48.67	APC bundle	48.67	48.67
Commercial	NA	57.65	APC bundle	57.65	57.65
CMS physician fee schedule <sup>38</sup>					
30-Min outpatient clinic visit (CPT code 99203)					
Medicaid	NA	81.22	NA	81.22	81.22
Medicare	NA	81.22	NA	81.22	81.22
Congressional Budget Office <sup>40</sup> 2022					
Commercial 30-min outpatient clinic visit (CPT code 99203)	NA	107.10	NA	107.10	107.10
CMS physician fee schedule, CMS Outpatient Prospective Payment System Addendum B <sup>38,41</sup>					
Emergency Department visit, sum of APC bundle and Physician Fee Schedule rate (CPT code 99285) <sup>c</sup>	NA	NA	785.09	NA	NA
Garrison et al. <sup>36</sup> 2024, cost of 12 wk of DAA treatment, \$ <sup>c</sup>	16 227.00	NA	NA	NA	NA
Nguyen et al. <sup>37</sup> 2019					
Annual cost of treating cirrhosis, \$					
Medicaid	31 520.00	NA	NA	NA	NA
Medicare	86 418.00	NA	NA	NA	NA
Commercial	23 283.00	NA	NA	NA	NA
Annual cost of treating decompensated cirrhosis, \$					
Medicaid	161 357.00	NA	NA	NA	NA
Medicare	230 361.00	NA	NA	NA	NA
Commercial	178 659.00	NA	NA	NA	NA
Annual cost of treating HCC, \$					
Medicaid	79 935.00	NA	NA	NA	NA
Medicare	104 416.00	NA	NA	NA	NA
Commercial	155 216.00	NA	NA	NA	NA
Utilities, Martin et al. <sup>42</sup> 2012					
Baseline without HCV	0.85	NA	NA	NA	NA
HCV infection (asymptomatic)	0.66	NA	NA	NA	NA
HCV infection with cirrhosis	0.55	NA	NA	NA	NA
HCV infection with decompensated cirrhosis	0.45	NA	NA	NA	NA
HCV infection with HCC	0.45	NA	NA	NA	NA

Abbreviations: APC, Ambulatory Payment Classifications; CHC, community health center; CMS, Centers for Medicare & Medicaid Services; CPT, Current Procedural Terminology; DAA, direct-acting antiviral; ED, emergency department; ELISA, enzyme-linked immunosorbent assay; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HR, hazard ratio; HRC, harm reduction center; LTC, linkage to care; MO/SM, mobile outreach/street medicine program; POC, point of care; SOC, standard of care; SVR12, sustained virologic response 12 weeks after treatment.

<sup>a</sup> Owing to lack of data in ED setting, the percentage LTC for the POC HCV RNA-first strategy was assumed as 2 times the percentage in SOC.

<sup>b</sup> Calculated using the relative risk of initiating treatment in the POC vs SOC strategy of 1.32 as published in the systematic literature review and meta-analyses<sup>16</sup> that assessed the treatment uptake rate in patients diagnosed by POC HCV test vs the SOC test strategy

<sup>c</sup> Same cost input applied to Medicaid, Medicare, and Commercial insurers.

complications were added for the lifetime horizon. Baseline health utilities for PWID without HCV, with HCV, and with complications were extracted from literature to calculate total QALYs gained with each strategy.<sup>42</sup> The methods for sensitivity and scenario analyses are described in the eMethods in Supplement 1.

## Results

### Base-Case Analysis Results

In the base-case analysis, the prevalence of active HCV infection was projected to be highest in HRC (25.2%) and MO/SM (24.8%) settings, followed by CHCs (16.6%) and EDs (16.1%). The POC HCV RNA-first testing strategy was projected to identify 93.4% of cases across all settings, whereas SOC identified fewer cases, at best 68.7% in the HRC setting. The POC HCV RNA-first strategy led to increases in LTC (37.6%-73.4%), treatment initiation (12.1%-48.9%), and rates of successful treatment (3.6%-26.4%) across care settings when compared with SOC (**Table 2**). The POC HCV RNA-first strategy lowered forward transmission by 16.3% to 53.3% and resulted in decreased incidence of chronic hepatitis C, cirrhosis and HCC compared with SOC, along with gains of 0.6 to 1.1 LYs and 0.5 to 1.0 QALYs across care settings.

From the payer perspective across CHC, HRC, and MO/SM settings, adopting POC HCV RNA-first testing resulted in increased HCV identification and the percentage of cases in each step of the care cascade. The combined benefits were associated with initial cost increases over a 1-year time horizon of \$361 per person tested in CHCs, \$1736 per person tested in HRCs, and \$1343 per person tested in the MO/SM setting, compared with SOC. The higher up-front costs were mainly attributed to higher treatment costs due to increased rates of treatment initiation with DAAs. The POC HCV RNA-first strategy had smaller increases in testing costs (\$30 per person), which was offset by cost savings with fewer clinic visits (approximately -\$70 per person) compared with SOC. Approximate total costs per person tested were reduced by \$3029 in CHCs, \$3376 in EDs, \$4158 in HRCs, and \$3187 in MO/SM programs.

Most EDs currently do not have a HCV test-and-treat infrastructure. The model projected that 12.1% more people receiving a diagnosis would initiate treatment with the POC HCV RNA-first strategy, compared with SOC in EDs. The POC HCV RNA-first strategy was projected to yield cost savings of \$435 per person tested within a 1-year time horizon in the ED setting, making it a dominant (better outcomes and lower cost) strategy over SOC.

Over the lifetime horizon, POC HCV RNA-first testing averted the development of long-term HCV complications and prolonged survival among the model cohort, compared with SOC. The POC HCV RNA-first strategy resulted in lower total costs than the SOC strategy with approximate cost savings of \$3387 per person tested. Therefore, the POC HCV RNA-first testing strategy is the dominant strategy across all settings over a lifetime horizon because the short-term test-and-treat benefits reduced the incidence of chronic HCV infections and complications, which resulted in long-term cost savings to US payers. Results of sensitivity and scenario analyses are presented in eResults, eTables 1 and 2, and eFigures 1, 2, and 3 in [Supplement 1](#).

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## Discussion

Early detection and timely treatment initiation are critical to prevent chronic HCV infection and long-term complications. This economic evaluation found that a POC HCV RNA-first testing strategy offered substantial benefits over SOC by enabling immediate HCV status confirmation and faster LTC, particularly in settings with higher HCV RNA prevalence. POC HCV RNA-first testing was projected to increase diagnosis of HCV cases compared with SOC in all settings of care. Moreover, increasing the rate of early detection was projected to reduce forward HCV transmission by 16.3% to 53.3% across all settings. Rates of chronic hepatitis C, cirrhosis, and HCC were reduced, resulting in improvements in the duration and quality of life.

The POC HCV RNA-first strategy was projected to deliver substantial long-term cost savings for US payers and proved dominant—offering both lower costs and improved outcomes—compared with SOC across the care settings analyzed over a lifetime horizon. Average total costs per person tested were reduced by \$3029 in CHCs, \$3376 in EDs, \$4158 in HRCs, and \$3187 in MO/SM programs. These savings resulted primarily from a higher proportion of individuals successfully receiving a diagnosis

Table 2. Base-Case Analysis Results

Settings and outcomes	Relative % (absolute %)		Difference, relative % (absolute %)	ICER, \$/clinical outcome unit
	POC HCV RNA-first	SOC		
<b>CHC</b>				
CHC 1-y outcomes				
HCV cases identified	93.4 (15.5)	37.3 (6.2)	56.1 (9.3)	3875.90
Cases linked to care	87.8 (14.6)	14.4 (2.4)	73.4 (12.2)	2964.98
Cases initiating treatment	22.9 (3.8)	2.9 (0.5)	20.1 (3.3)	10 828.35
Cases treated successfully	7.2 (1.2)	0.9 (0.1)	6.3 (1.1)	34 650.71
Rate of onward transmission (per 1000 high-risk individuals)	92.8	119.0	-22.0 (-26.2)	13 782.33
Total cost (per person tested), \$	604.42	243.43	360.99	NA
Cost of clinic visits (diagnosis), \$	89.85	167.11	-77.27	NA
Cost of testing, \$	46.18	18.63	27.54	NA
Cost of HCV treatment, \$	468.40	57.68	410.72	NA
CHC long-term outcomes				
Incidence of chronic HCV	47.8 (7.9)	61.8 (10.3)	-14.1 (-2.3)	Dominant
Incidence of cirrhosis including decompensated cirrhosis	15.4 (2.6)	19.9 (3.3)	-4.5 (-0.8)	Dominant
Incidence of HCC	2.4 (0.4)	3.1 (0.5)	-0.7 (-0.1)	Dominant
Mortality rate (per 1000 PYs)	21.2	24.3	-3.0	Dominant
LYs	21.3	20.7	0.6	Dominant
QALYs	18.0	17.5	0.6	Dominant
Total cost (per person tested), \$	12 145.66	15 174.86	-3029.20	NA
<b>ED</b>				
ED 1-y outcomes				
HCV cases identified	93.4 (15.0)	34.8 (5.6)	58.6 (9.4)	Dominant
Cases linked to care	48.6 (7.8)	9.1 (1.5)	39.5 (6.3)	Dominant
Cases initiating treatment	14.1 (2.3)	2.0 (0.3)	12.1 (1.9)	Dominant
Cases treated successfully	4.2 (0.7)	0.6 (0.1)	3.6 (0.6)	Dominant
Rate of onward transmission (per 1000 high-risk individuals)	95.1	113.6	-16.3 (-18.5)	Dominant
Total cost (per person tested), \$	1063.76	1499.18	-435.42	NA
Cost of ED visit (diagnosis), \$	785.09	1460.27	-676.18	NA
Cost of testing, \$	0.00 (APC bundle)	0.00 (APC bundle)	0.00	NA
Cost of HCV treatment, \$	278.67	38.91	239.76	NA
ED long-term outcomes				
Incidence of chronic HCV	48.8 (7.9)	62.5 (10.0)	-13.6 (-2.2)	Dominant
Incidence of cirrhosis including decompensated cirrhosis	15.8 (2.5)	20.1 (3.2)	-4.4 (-0.7)	Dominant
Incidence of HCC	2.5 (0.4)	3.2 (0.5)	-0.7 (-0.1)	Dominant
Mortality rate (per 1000 PYs)	21.1	24.0	-2.9	Dominant
LYs	21.3	20.7	0.6	Dominant
QALYs	18.0	17.5	0.5	Dominant
Total cost (per person tested), \$	11 888.83	15 264.93	-3376.10	NA
<b>HRC</b>				
HRC 1-y outcomes				
HCV cases identified	93.4 (23.5)	68.7 (17.3)	24.7 (6.2)	27 928.66
Cases linked to care	87.8 (22.1)	50.2 (12.6)	37.6 (9.5)	18 307.55
Cases initiating treatment	86.2 (21.7)	37.3 (9.4)	48.9 (12.3)	14 085.62
Cases treated successfully	46.6 (11.7)	20.2 (5.1)	26.4 (6.7)	26 068.70
Rate of onward transmission (per 1000 high-risk individuals)	60.0	128.5	-53.3 (-69.0)	25 323.68
Total cost (per person tested), \$	3262.60	1527.08	1735.52	NA
Cost of clinic visits (diagnosis), \$	82.28	153.05	-70.76	NA
Cost of testing, \$	34.32	20.33	13.98	NA
Cost of HCV treatment, \$	3146.00	1353.70	1792.31	NA

(continued)

Table 2. Base-Case Analysis Results (continued)

Settings and outcomes	Relative % (absolute %)		Difference, relative % (absolute %)	ICER, \$/clinical outcome unit
	POC HCV RNA-first	SOC		
<b>HRC long-term outcomes</b>				
Incidence of chronic HCV	31.8 (8.0)	47.5 (12.0)	-15.7 (-4.0)	Dominant
Incidence of cirrhosis including decompensated cirrhosis	10.2 (2.6)	15.3 (3.9)	-5.1 (-1.3)	Dominant
Incidence of HCC	1.6 (0.4)	2.4 (0.6)	-0.8 (-0.2)	Dominant
Mortality rate (per 1000 PYs)	21.5	26.6	-5.1	Dominant
LYs	21.2	20.2	1.1	Dominant
QALYs	18.0	17.0	1.0	Dominant
Total cost (per person tested), \$	14 181.18	18 339.51	-4158.33	NA
<b>MO/SM</b>				
<b>MO/SM 1-y outcomes</b>				
HCV cases identified	93.4 (23.2)	61.2 (15.2)	32.2 (8.0)	16 812.43
Cases linked to care	87.8 (21.8)	35.7 (8.9)	52.1 (12.9)	10 384.20
Cases initiating treatment	66.2 (16.4)	20.4 (5.1)	45.8 (11.4)	11 815.43
Cases treated successfully	19.9 (4.9)	6.1 (1.5)	13.7 (3.4)	39 384.76
Rate of onward transmission (per 1000 high-risk individuals)	140.3	211.2	-33.6 (-70.9)	18 937.69
Total cost (per person tested)	2152.72	810.06	1342.65	NA
Cost of clinic visits (diagnosis)	91.94	171.00	-79.06	NA
Cost of testing	49.43	23.65	25.78	NA
Cost of HCV treatment	2011.35	615.41	1395.94	NA
<b>MO/SM long-term outcomes</b>				
Incidence of chronic HCV	43.4 (10.8)	55.0 (13.6)	-11.6 (-2.9)	Dominant
Incidence of cirrhosis including decompensated cirrhosis	14.0 (3.5)	17.7 (4.4)	-3.7 (-0.9)	Dominant
Incidence of HCC	2.2 (0.5)	2.8 (0.7)	-0.6 (-0.1)	Dominant
Mortality rate (per 1000 PYs)	25.2	28.8	-3.6	Dominant
LYs	20.5	19.7	0.8	Dominant
QALYs	17.3	16.6	0.7	Dominant
Total cost (per person tested), \$	18 139.76	21 326.52	-3186.76	NA

Abbreviations: CHC, community health center; ED, emergency department; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HRC, harm reduction center; ICER, incremental cost-effectiveness ratio; LY, life-years; MO/SM, mobile outreach/street medicine programs; NA, not applicable; POC, point-of-care; PY, person-years; QALY, quality-adjusted life-years; SOC, standard of care.

and being treated, which led to lower incidence of chronic HCV complications and reduced medical resource utilization. The long-term cost reductions offset the higher up-front costs of POC HCV RNA-first testing and increased treatment initiation.

Most EDs do not currently focus on HCV diagnosis or have an effective HCV test-and-treat infrastructure. Manteuffel et al<sup>43</sup> assessed the impact of implementing a reflex testing protocol in a large, urban ED showing that laboratory reflex testing increased the percentage of people with positive antibody tests who received HCV RNA testing from 55% to 84%, but did not significantly affect LTC. Notably, HCV antibody positivity was 11.2% and HCV RNA positivity was 62.6% in that study,<sup>43</sup> supporting the hypothesis that EDs are efficient settings to identify cases. Our study suggests that a POC HCV RNA-first strategy could effectively increase HCV diagnosis, LTC, and treatment initiation, warranting efforts to enable a HCV test-and-treat infrastructure in EDs.

Shih et al<sup>14</sup> conducted a cost-effectiveness analysis from the perspective of the Australian government, evaluating a POC HCV RNA-first strategy, a 2-step strategy of POC antibody test followed by POC RNA test for those with detected antibodies (POC antibody RNA), and SOC among people at risk of HCV infection. Our study results differ from those of Shih et al,<sup>14</sup> who found that, the 2-step POC antibody RNA strategy was more cost-effective than POC HCV RNA-first when HCV antibody prevalence was less than 74%. In contrast, our study found that a POC HCV RNA-first diagnostic strategy was the dominant strategy, even when HCV antibody prevalence was low.

Differences in findings may be owing to (1) our inclusion of a transmission model to estimate secondary cases; (2) our model capturing more steps of the HCV care cascade, including undiagnosed, untreated, or unsuccessfully treated cases; (3) our analysis including postdiagnosis and posttreatment initiation costs and outcomes from both 1-year and lifetime horizons, incorporating costs and savings related to treatment and averted chronic HCV complications; and (4) differences in health care costs and reimbursement systems between Australia and the US. Although both studies were conducted from third-party payer perspectives (Australian government and US health care payers), Shih et al<sup>14</sup> used an ingredient costing approach that included all resource costs required by a site to conduct testing and clinical assessment (eg, device and consumables, staff, data connectivity, quality assurance, and training). In the US, payers do not fund the resources required by a site to conduct testing and clinical assessment. Our study only includes costs of health care services borne by US payers through reimbursement.

The US Viral Hepatitis National Strategic Plan aims to eliminate viral hepatitis in the US by 2030.<sup>44</sup> Achieving this goal requires expanding HCV testing and treatment and addressing barriers that limit treatment access after HCV-positive results. Although a POC HCV RNA-first strategy can improve case identification and LTC, policy changes, such as reducing prior authorization requirements for DAAs and easing payer or state prescribing and retreatment restrictions, are needed to broaden access. Expanding DAA availability beyond specialty pharmacies would also simplify test-and-treat, particularly in nontraditional care settings. The impact of POC HCV RNA testing may be even greater if these barriers are removed and if infrastructure for sustainable test-and-treat programs and public health reporting are adequately funded.

### Limitations

This study is limited by the accuracy of its assumptions, model structure, and data inputs. Because this model focuses on health care payer costs, it includes only individuals with health insurance; therefore, societal and public health benefits for uninsured populations—who often receive testing and treatment through state and local health programs—are not captured, likely leading to an underestimation of broader population-level impact. We also acknowledge that the up-front costs of adopting POC HCV RNA-first testing, including technology implementation and increased treatment initiation, may be challenging for resource-limited settings or those without insurance billing capabilities.

Although our results favored the POC HCV RNA-first strategy over the lifetime horizon, we also evaluated a 2-step POC antibody RNA approach. Although it may be cost-effective in some contexts, it diagnoses fewer total infections and may miss acute HCV cases. A key assumption in our model was a 32% increase in treatment initiation associated with POC HCV RNA-first testing, derived from a meta-analysis of 11 studies focused largely on high-risk populations and relevant care settings. Limited evidence for this parameter introduces uncertainty, but 1-way sensitivity analysis results showed that varying this value did not alter the overall conclusions (eFigure 1 in Supplement 1).

We also assumed an  $R_0$  of 2.99 on the basis of published modeling among PWID, which aligns with but does not fully represent the populations in our settings. Sensitivity analyses varying  $R_0$ , including to a conservative 1.1, demonstrated that incremental cost-effectiveness ratios remained below \$100 000 per QALY at 1 year and that the POC HCV RNA-first strategy remained dominant long term. Furthermore, the model did not include costs associated with follow-up or treatment-phase visits beyond the diagnostic encounter owing to variability and data limitations; however, varying clinic visit costs in 1-way sensitivity analysis had no meaningful effect on results.

### Conclusions

Future studies are needed in the settings described here, as well as rural, correctional and postcarceral settings, to understand the real-world clinical utility of simplified POC HCV RNA-first testing and the feasibility of expanded test-and-treat protocols. Research in diverse, high-burden care settings can identify barriers that impede long-term outcomes and progress toward national

HCV elimination goals. Priorities include evaluating POC HCV RNA testing's effect on diagnosis rates, the impact of immediate treatment initiation on outcomes and transmission, and logistical challenges of integrating POC test-and-treat protocols into existing practice. Additional research should explore the role of policy changes, such as reducing prior authorization requirements, to enhance access to treatment. Removing barriers could allow POC HCV RNA test-and-treat to substantially reduce the HCV burden, protect against viral transmission, and support national HCV elimination goals.

## ARTICLE INFORMATION

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*Concept and design:* All authors.

*Acquisition, analysis, or interpretation of data:* Al Rawashdh, Ferrufino, Kahn.

*Drafting of the manuscript:* Al Rawashdh, Ferrufino, Kahn.

*Critical review of the manuscript for important intellectual content:* All authors.

*Statistical analysis:* Al Rawashdh, Ferrufino.

*Administrative, technical, or material support:* All authors.

*Supervision:* Ferrufino, Kahn.

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#### SUPPLEMENT 1.

eMethods.

eResults.

eFigure 1. One-way sensitivity analysis on the base-case by setting; ICER (cost / % treated successfully)

eFigure 2. Probabilistic sensitivity analysis by setting (WTP threshold \$100,000/QALY)

eTable 1: Scenario 1 Analysis Results

eTable 2: Scenario 2 Analysis Results

eFigure 3. One-way sensitivity analysis on scenario analysis 2 by setting; ICER (cost / % treated successfully)

#### SUPPLEMENT 2.

Data Sharing Statement