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Cost-effectiveness analysis of emergency department-based hepatitis C screening and linkage-to-care program

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Abstract

Background In the United States (US), hepatitis C virus (HCV) screening is not covered by payers in settings outside of primary care. A non-traditional, emergency department (ED)-based HCV screening program can be cost-effective and identify infection in vulnerable populations with a high HCV risk. This study examined the long-term cost-effectiveness of routine HCV screening and linkage-to-care for high-risk patients in the ED from the payer's perspective.

Methods The University of Illinois Hospital and Health Sciences System (UIH) implemented Project HEAL (HIV & HCV Screening, Education, Awareness, Linkage-to-Care). Under this initiative, patients who presented to the ED received opt-out HCV screening if they were at high risk for HCV infection (birth cohort between 1945 and 1964, persons who inject drugs, and HIV infection) with subsequent linkage-to-care if infected. Using the summary data from Project HEAL, a hybrid decision-analytic Markov model was developed based on the HCV screening procedure in the ED and the natural history of HCV. A 30-year time horizon and 1-year cycle length were used. All patients who received the ED-based HCV screening were referred for treatment with direct-acting antiviral (DAA) regardless of their fibrosis stage.

Results When unscreened/untreated patients received DAA treatment at F1, F2, F3, and compensated cirrhosis stages, the incremental cost-effectiveness ratio (ICER) ranged from $6,084 to $77,063 per quality-adjusted life year (QALY) gained. When unscreened/untreated patients received DAA treatment at the decompensated cirrhosis stage, no HCV screening was dominated.

Conclusion ED-based HCV screening and linkage-to-care was cost-effective at the willingness-to-pay (WTP) threshold of $100,000/QALY in all scenarios. A reduction in infected persons in the community may provide additional benefits not evaluated in this study.

Keywords Cost-effectiveness, Economic evaluation, Hepatitis C, Emergency department, Direct-acting antiviral

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Introduction

Hepatitis C virus (HCV) is the most common bloodborne infection in the United States (US). Chronic HCV infection can lead to fibrosis, cirrhosis, hepatocellular carcinoma (HCC), and end stage liver disease. Approximately 24% of liver transplantations in the United States (US) are attributed to complications of HCV infection [1].

As of 2020, the Centers for Disease Control and Prevention (CDC) recommends HCV screening for all adults ≥ 18 years old at least once in their lifetime and for all pregnant patients during each pregnancy [2]. The CDC also recommends one-time screening in patients with human immunodeficiency virus (HIV) infection, persons who inject drugs (PWID) or shared drug equipment, patients who received hemodialysis, and children born to a mother with HCV. Despite the HCV screening recommendations, almost half of patients with HCV in the US are unaware of their infection [3].

One significant barrier to HCV screening is the US insurance coverage policy. The national coverage determination (NCD) written by the Centers for Medicare & Medicaid Services (CMS) stated that an annual HCV screening is covered for patients at "high risk" for HCV infection as stated above [4]. A single HCV screening is covered for individuals who were born between 1945 and 1965 only within a primary setting. Coverage is currently not extended to settings outside of primary care, including emergency department (ED), inpatient hospital, ambulatory surgical center, independent testing center, skilled nursing facility, inpatient rehab facility, and hospice care. This limited coverage criteria significantly reduces early detection of HCV infection among patients who do not utilize or have access to primary care, including the uninsured or homeless populations [5, 6]. The ED setting provides care to a high proportion of patients with a history of injection drug use and HIV infection, which are significant co-morbidities of HCV infection [7]. For vulnerable populations, EDs are often the only point of contact with the health care system and a bridge to linkage-to-care.

The University of Illinois Hospital and Health Sciences System (UIH), one of the largest urban medical centers and safety-net providers in Chicago, implemented Project HEAL (HIV & HCV Screening, Education, Awareness, Linkage-to-Care) in 2013. As a part of this initiative, patients who presented to the ED received opt-out HCV screening if they were at high risk for HCV infection between 2015 and 2020. For UIH patients, high risk was defined as birth cohort between 1945 and 1964, PWID (in the past or current), and HIV infection although birth cohort screening is no longer recommended by the CDC [2]. The use of intranasal drugs was not considered, although it is considered a risk factor for HCV.

The goal of Project HEAL was to identify undiagnosed patients with HCV in a non-traditional ED setting and link them to care.

Several studies have demonstrated the feasibility of an ED-based HCV screening program, but the cost-effectiveness of a program is also important for policy-decision makers. Therefore, we assessed the long-term cost-effectiveness of routine HCV screening and linkage-to-care for high-risk patients in the ED from the payer's perspective.

Methods

Study design

This study was approved by the University of Illinois at Chicago Institutional Review Board (IRB). This study also followed the structured reporting of economic evaluations of health interventions according to Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guideline [8]. A hybrid decision-analytic Markov model was developed based on the HCV screening procedure in the ED and the natural history of HCV (Figs. 1 and 2). In the decision-analytic model, patients who did not opt-out of HCV screening were tested for the HCV antibody and positive antibody test automatically reflexed to run an HCV RNA test. Among patients who tested HCV RNA positive and referred for linkage-to-care, some patients attended referral while other patients did not attend referral and were lost to follow-up. Those who attended referral either started DAA treatment or did not start DAA treatment. Therefore, our model included multiple treatment possibilities immediately following screening: (1) HCV infected patients who attended referral and received HCV DAA treatment; (2) HCV infected patients who did not attend referral or did not initially receive HCV DAA treatment; (3) Individuals without HCV infection and were not treated; (4) Individuals who were HCV infected but had false negative antibody or RNA tests and did not receive HCV DAA treatment. In the comparator (no HCV screening), there were only two possible initial outcomes: (1) HCV infected patients who did not initially receive treatment and (2) Individuals without HCV infection and not treated.

At the time of initial presentation to the ED, patients could be in different stages of fibrosis, based upon actual experience from the HEAL project. Patients with untreated infection could progress to several stages of liver complications, starting from no fibrosis (F0), mild to advanced fibrosis (F1-F3), compensated (F4), and decompensated cirrhosis, hepatocellular carcinoma (HCC), and liver transplantation. If patients with F0-F4 or decompensated cirrhosis started DAA treatment and achieved sustained virological response (SVR), they moved to corresponding SVR stages. Patients with HCC did not move

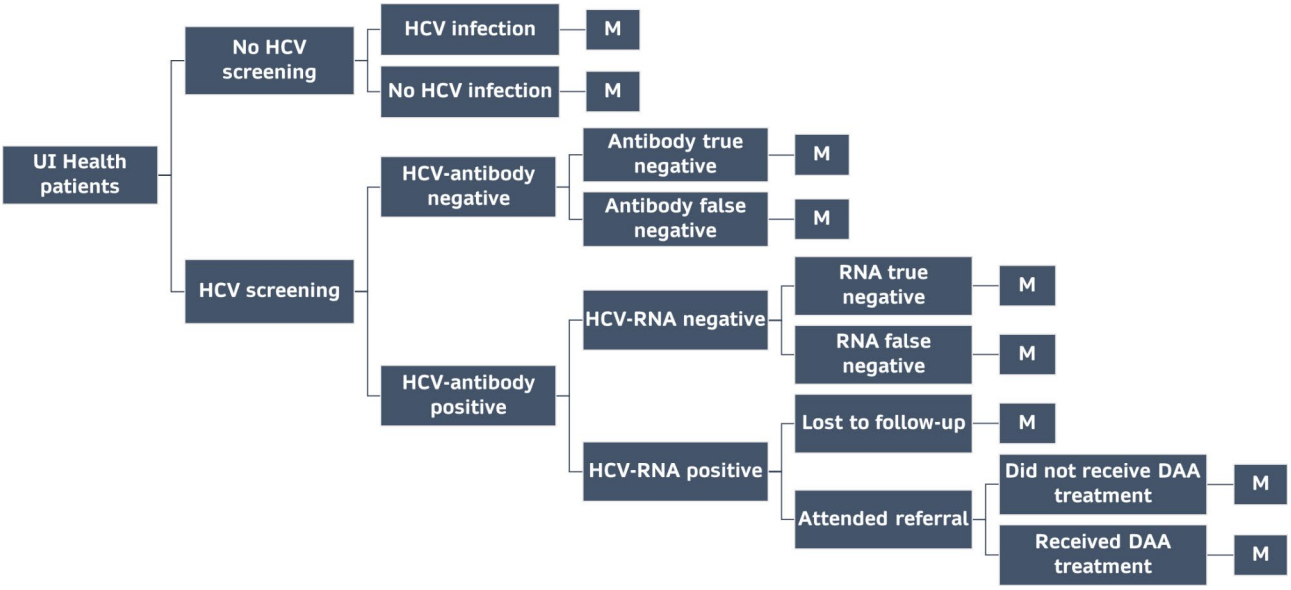

Fig. 1 Decision tree. Abbreviation: UI = University of Illinois; HCV = Hepatitis C; DAA = Direct-Acting Antiviral

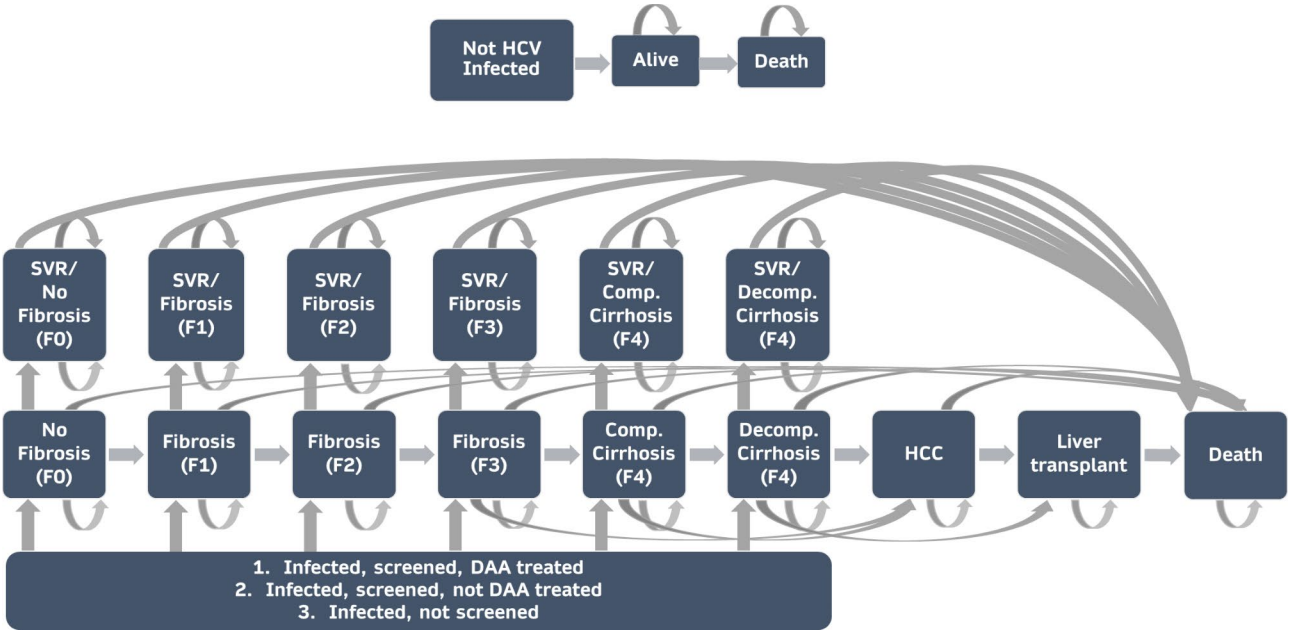

Fig. 2 Markov model diagram. Abbreviation: HCV = Hepatitis C; DAA = Direct-Acting Antiviral; F = Fibrosis Stage

to SVR state because the treatment focus shifts to HCC treatment rather than HCV treatment upon HCC diagnosis, such as surgical, locoregional, or systemic therapy. All patients could progress to the death stage from any Markov health state.

For infected patients who did not undergo ED-based HCV screening or receive DAA treatment, we assumed they would be screened for HCV outside of the ED and receive DAA treatment when they developed symptoms at various stages (i.e., immediately at F1 or at a later stage). We also assumed that DAA treatment would be covered for all patients although some states restrict DAA treatment for early fibrosis stages. A separate Markov model was built for individuals without HCV infection, which consisted of only alive and dead states.

References for the model parameters are summarized in Table 1. Real-world data from Project HEAL was used to develop the decision analytic model. The proportions of patients initially presenting to the ED with F0-F4 were estimated from the study by Lin and colleagues, which investigated the liver fibrosis staging in HCV patients at UIH [9]. Because this study did not report differentiation

Table 1 Model Inputs for Decision Tree and Markov Model Analysis

Parameter	Base Case	Range*	Reference
Population Characteristics			
Mean patient age	64 years	SD: 55.4–72.6	Project HEAL
HIV co-infected patients	2.7%	SD: 0.6-5%	Project HEAL
PWID	27%	SD: 20.9–32.4%	Project HEAL
Patients with F0	12.6%	-	Lin 2021
Patients with F1	9.5%	-	Lin 2021
Patients with F2	30.5%	-	Lin 2021
Patients with F3	16.0%	-	Lin 2021
Patients with F4 compensated Cirrhosis	24.9%	-	Lin 2021/Chirikov 2018
Patients with F4 decompensated Cirrhosis	6.4%	-	Lin 2021/Chirikov 2018
Patients receiving GLE/PIB	50%	-	Assumption
Patients receiving SOF/VEL	50%	-	Assumption
Decision Tree Transition Probabilities			
Probability of positive HCV-antibody among HCV screen eligible patients	0.050	0.041–0.059	Project HEAL
Probability of true negative HCV-antibody test	0.977	0.967–0.984	ARCHITECT® Anti-HCV Assay
Probability of positive HCV-RNA among positive HCV-antibody	0.676	0.586–0.767	Project HEAL
Probability of true negative HCV-RNA test	1.0	0.994-1.0	COBAS® AmpliPrep/COBAS® TaqMan® HCV Test, v2.0
Probability of attend referral/linkage to care among HCV-RNA positive patients	0.232	0.132–0.331	Project HEAL
Probability of taking DAA treatment among patients who attended referral	0.625	0.388–0.862	Project HEAL
Markov Model Annual Transition Probabilities			
F0 to F1	0.047	0.027–0.107	Zeremski 2016/ Erman 2019
F1 to F1	0.072	0.048–0.102	Zeremski 2016
F2 to F3	0.026	0.013–0.117	Zeremski 2016/ Erman 2019
F3 to compensated cirrhosis	0.114	0.058–0.214	Zeremski 2016
F3 to HCC	0.007	0.002–0.013	Xu 2016/ Axley 2018
Compensated cirrhosis to decompensated cirrhosis	0.079	0.045–0.109	Xu 2016/ Konerman 2017/ Park 2019
Compensated cirrhosis to HCC	0.025	0.017–0.034	Xu 2016
Decompensated cirrhosis to transplant	0.013	0.008–0.053	Xu 2016/Konerman 2017/ Dienstag 2011
Decompensated cirrhosis to HCC	0.049	0.035–0.063	Park 2019
HCC to transplant	0.147	0.088–0.206	Dienstag 2011
DAA SVR Rates			
GLE/PIB SVR rate in F0-F2 fibrosis states	0.996	0.987–0.998	Puoti 2018
SOF/VELSVR rate in F0-F2 fibrosis states	0.994	0.992–0.997	Mangia 2020
GLE/PIB SVR rate in F3 fibrosis state	0.964	0.899–0.988	Puoti 2018
SOF/VEL SVR rate in F3 fibrosis state	0.996	0.991-1.0	Mangia 2020
GLE/PIB SVR rate in compensated cirrhosis	0.964	0.937–0.980	Gane 2019
SOF/VEL SVR rate in compensated cirrhosis	0.979	0.970–0.987	Mangia 2019
SOF/VEL SVR rate in decompensated cirrhosis	0.943	0.870–0.980	Curry 2015
SOF/VEL/VOX 12 weeks SVR rate	0.978	0.950–0.990	Bourliere 2017
SOF/VEL + ribavirin 24 weeks SVR rate	0.856	0.770–0.920	Curry 2015
Mortality Rates			
F0-F1 to death	0.014	0.010–0.048	Xu 2016/Kalidindi 2020
F2 to death	0.014	0.010–0.048	Xu 2016/Kalidindi 2020
F3 to Death	0.029	0.020–0.041	Xu 2016
Compensated cirrhosis to death	0.073	0.057–0.142	Xu 2016/Kalidindi 2020
Decompensated cirrhosis to death	0.223	0.192–0.228	Lu 2016/McDonald 2021

Table 1 (continued)

Parameter	Base Case	Range*	Reference
HCC to death	0.252	0.10-0.354	Gawrieh 2019/Moor 2018/ Turgeon 2021
Transplant to death	0.085	0.034–0.094	Groeschl 2013/Kim 2018/ Groeschl 2013
HR of mortality rate in SVR vs. no SVR	0.48	0.035–0.094	Lu 2016
No HCV infection to death/age-adjusted mortality rate	Mortality rates 64–94		National Vital Statistics Reports 2020
Special Populations			
HCV/HIV co-infection to SVR after GLE/PIB	0.980	0.958-0.1	Rockstroh 2018
HCV/HIV co-infection to SVR after SOF/VEL	0.953	0.890–0.990	Wyles 2017
PWID with HCV to SVR after G/P	0.929	0.860–0.990	Foster 2019
PWID with HCV to SVR after SOF/VEL	0.982	0.970–0.990	Grebely 2016
Re-infection rate in HCV/HIV co-infection	0.023	0.004–0.053	Huang 2021
Re-infection rate in HCV/PWID	0.062	0.043–0.089	Hajarizadeh 2020/ Huang 2021
Re-infection rate in HCV mono-infection	0.001	0.0002–0.002	Huang 2021
Utility Inputs			
Utility of F0-F1	0.83	0.787–0.870	Cossais 2019/ Saeed 2020
Utility of F2	0.82	0.807–0.870	Cossais 2019/ Juanbeltz 2019/ Saeed 2020
Utility of F3	0.76	0.684–0.807	Cossais 2019/ Juanbeltz 2019
Utility of compensated cirrhosis	0.717	0.676–0.758	Saeed 2020
Utility of decompensated cirrhosis	0.595	0.473–0.717	Saeed 2020
Utility of HCC	0.788	0.712–0.864	Saeed 2020
Utility of liver transplant	0.701	0.615–0.787	Saeed 2020
Utility of general US population	0.83	0.787–0.870	Cossais 2019/Saeed 2020
Treatment success utility, SVR	0.029	0.023–0.035	Calculated
Treatment failure disutility	0.011	0.009–0.013	Calculated
Utility of mild to moderate chronic HCV infection (pre-treatment)	0.829	0.788–0.870	Saeed 2020
Utility of SVR	0.858	0.813–0.903	Saeed 2020
Utility of no SVR, post-treatment	0.818	0.767–0.869	Saeed 2020
Cost Inputs[a, b,c]			
Medical costs of F0-F3	$483.85	$0-$7,949.12	Park 2019
Medical costs of compensated cirrhosis	$4,526.66	$0-$30,742.20	Park 2019
Medical costs of decompensated cirrhosis	$39,494.82	$31,183.93-$47,902.83	Rein 2016
Medical costs of HCC	$39,523.05	$29,088.13-$49,532.26	Rein 2016
Medical costs of liver transplant	$207,483.28	$198,271.94-$216,694.61	McAdam-Marx 2011
Medical costs of post-liver transplant	$46,770.26	$42,098.77-$51,441.75	McAdam-Marx 2011
Medical costs of F0-F3 with SVR	$817.88	$0-$5,056.01	Park 2019
Medical costs of compensated cirrhosis and decompensated cirrhosis with SVR	$2,067.46	$0-$11,119.66	Park 2019
Medical costs of no HCV infection	$0	$7,074.99-$19,963.23	Assumption
Drug costs of 12 weeks of generic SOF/VEL treatment[d]	$17,264.35	$13,811.48-$20,717.22	Redbook 2021
Drug costs of 24 weeks of genetic SOF/VEL treatment[c]	$34,528.70	$26,622.96-$41,434.44	Redbook 2021
Drug costs of 8 weeks of GLE/PIB treatment[c]	$17,688.00	$14,150.40-$21,225.60	Redbook 2021
Drug costs of 12 weeks of SOF/VEL/VOX[c]	$54,782.36	$43,825.89-$65,738.83	Redbook 2021
Drug costs of 12 weeks of ribavirin[c]	$421.35	$337.08-$505.62	Redbook 2021
Drug costs of 24 weeks of ribavirin[c]	$674.16	$539.33-$808.99	Redbook 2021
Costs of HCV antibody test	$14.27	-	2021 Clinical Diagnostic Laboratory Fee Schedule
Costs of HCV RNA test	$42.84	-	2021 Clinical Diagnostic Laboratory Fee Schedule

Table 1 (continued)

Parameter	Base Case	Range*	Reference
Costs of referral	$113.75	-	2021 Clinical Diagnostic Laboratory Fee Schedule
Other Information			
Rebate rate	33%	-	IQVIA report 2021
Discount rate, costs	3%	-	Assumption
Discount rate, utilities	3%	-	Assumption

Abbreviations: *CMS* Centers for Medicare and Medicaid Services, *HCV* Hepatitis C, *HR* hazard ratio, *PWID* persons who inject drugs

[a] Yearly costs

[b] All costs converted to 2021 US

[c] After Wholesale Acquisition Costs rebate conversion (33%) except for counseling

*In PSA, beta distribution was used for decision tree transition probabilities, Markov model annual transition probabilities, and utility inputs; Gamma distribution was used for cost inputs.

in the proportion of patients with compensated and decompensated cirrhosis, the proportions of patients with compensated (Child–Pugh class A) and decompensated cirrhosis (Child–Pugh class B or C) were estimated from elsewhere [10]. Probabilities of true negative HCV-antibody test and HCV-RNA test were derived from medical device package inserts [11, 12].

Patient characteristics were obtained from Project HEAL, a study involving 5,769 patients eligible for HCV screening between January 2019 and February 2020. The average age of patients was 64 years. The proportions of HCV/HIV co-infected patients and PWID were 2.6% and 26.7%, respectively.

Transition probabilities between fibrosis stages, all-cause mortality rates by each fibrosis stage, and utility inputs were obtained from published retrospective studies [13–34]. SVR rates were obtained from clinical trials [35–43]. All mortality rates were age-adjusted based on the National Vital Statistics Reports 2020 [28]. Hazard ratios (HR) of mortality rates in SVR vs. no SVR were applied to determine the SVR state mortality rates [21]. For patients with F0-F1 (no fibrosis and mild fibrosis) and patients without HCV infection, we assumed the same utility.

Liver-related healthcare costs were derived from burden of illness studies [18, 44, 45]. DAA drug costs were derived from WAC costs listed in Redbook [46]. To estimate a more representative cost for payers, a 33% rebate was applied to DAA treatments [47]. All liver-related healthcare costs and DAA costs were converted to 2021 US dollars using the Personal Consumption Expenditure health component price index (CPI) [48]. Costs of lab tests, including the HCV antibody and RNA tests, were obtained from the 2021 cm Clinical Diagnostic Laboratory Fee Schedule [49].

DAA treatments

At UIH, sofosbuvir/velpatasvir (SOF/VEL) for 12 weeks or glecaprevir/pibrentasvir (GLE/PIB) for 8 weeks is used to treat HCV patients with F0-F3 stage fibrosis and compensated cirrhosis at approximately a 1:1 ratio. This study also assumed that the same DAA treatments were used in patients with F0-F3 stage fibrosis and compensated cirrhosis. Patients with decompensated cirrhosis or more severe liver complications were treated with SOF/VEL plus ribavirin for 12 weeks as recommended by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) HCV guidance [50]. Patients who were re-infected with HCV were treated with the same DAA drug as the initial treatment. Those who did not achieve SVR (treatment failure) were treated with sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX) for 12 weeks if they had F0-F4 stage fibrosis and SOF/VEL plus ribavirin for 24 weeks if they had decompensated cirrhosis or more severe liver complications.

Cost-effectiveness analysis and outcomes

A 30-year time horizon and 1-year model cycle were used in the Markov model to estimate the natural progression of HCV complications. All model inputs were converted to annual rates and a 3% discount rate was applied to cost and utility calculations.

In the analysis, we calculated the total HCV-related healthcare costs, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratio (ICERs) from the payer's perspective when unscreened and untreated patients started DAA treatment at different stages of fibrosis. A willingness-to-pay (WTP) threshold of $100,000/QALY was used to determine the cost-effectiveness of the ED-based HCV screening program [51].

We also conducted one-way (OWSA) and probabilistic sensitivity analyses (PSA) to measure the impact of key parameters as well as the level of uncertainty in the base-case results. In OWSA, the minimum and maximum values of key model inputs were obtained from the model input references (e.g., 95% confidence interval or minimum and maximum range) and published literature. If there were no studies reporting minimum or maximum value for input parameters, arbitrary minimum and

maximum ranges were selected, informed by available supporting literature and information. ICERs were calculated accordingly based on these extreme values. In PSA, model inputs were varied based on their distribution using 1,000 Monte Carlo simulations. All analyses were performed in Microsoft Excel 2019 (Microsoft Corporation, Redmond, WA).

Years in HCC and liver transplant states

To evaluate the potential clinical impact of HCV screening and subsequent DAA treatment, we calculated the total life years in HCC and liver transplant states by summing the years that patients spent in these states across the 30-year time horizon for the no HCV screening group vs. the ED-based HCV screening group under different scenarios (DAA intervention in the untreated group at F1-decompensated cirrhosis stages).

Results

When unscreened and untreated patients started DAA treatments as early as F1, F2, F3, compensated cirrhosis, and decompensated cirrhosis, the ICERs were $77,063, $50,870, $25,503, and $6,084 per QALY gained, respectively (Table 2). When unscreened and untreated patients started DAA treatments at decompensated cirrhosis, no HCV screening was dominated, while ED-based HCV screening was cost-saving. Therefore, ED-based HCV screening was cost-effective at the WTP threshold of $100,000/QALY in all scenarios.

When DAA treatment was given at F1 or later fibrosis stage, the OWSA showed that the medical costs of F0-F3 stages, the medical costs of F0-F3 with SVR, and the probability of F0/F1 stages to death had the most impact on the ICERs (Supplementary Tables 1 and Supplementary Fig. 1). The PSA also demonstrated that ED-based HCV screening was 23% and 98% likely to be cost-effective at $50,000/QALY and $100,000/QALY WTP thresholds, respectively (Fig. 3).

In addition to the economic benefits, the ED-based HCV screening program resulted in important clinical benefits, including a reduction in further liver complications such as cirrhosis, HCC, and liver-related mortality. The total number of years an HCV patient suffered from HCC and liver transplant was 0.48 years with no HCV screening and 0.004 years with HCV screening when DAA treatment was given at decompensated cirrhosis (Supplementary Table 2). When DAA treatment was given at F1 or later fibrosis stages, the total number of years in HCC and liver transplant was 0.005 with no HCV screening and 0.004 with HCV screening. Therefore, the total number of years in HCC and liver transplant decreased significantly when DAA treatment was given at an earlier stage.

Table 2 Results

DAA Intervention in Untreated Group[a]	Patient Group	Total Healthcare Costs	QALY(s)	ICER
F1	No HCV Screening	$2,004.54	11.2789	
	ED-Based HCV Screening	$2,036.05	11.2793	$77,062.59/QALY
F2	No HCV Screening	$1,902.41	11.2745	
	ED-Based HCV Screening	$1,942.85	11.2753	$50,869.92/QALY
F3	No HCV Screening	$1,677.60	11.2567	
	ED-Based HCV Screening	$1,737.71	11.2590	$25,502.73/QALY
F4 Comp. Cirrhosis	No HCV Screening	$2,025.93	11.2279	
	ED-Based HCV Screening	$2,055.57	11.2328	$6,084.44/QALY
F4 Decomp. Cirrhosis	No HCV Screening	$2,796.54	11.1763	Dominated
	ED-Based HCV Screening	$2,758.76	11.1857	($4,025.87/QALY)

[a] Stage at which DAA intervention started in unscreened and untreated population

Discussion

This study indicates that non-traditional, ED-based HCV screening was cost-effective compared to no HCV screening. The study results were robust in multiple scenarios using DAA treatment intervention at different stages of HCV infection complications in the unscreened and untreated groups. Furthermore, our study emphasizes the importance of expanding HCV screening efforts beyond traditional primary care settings. Despite the CDC and the U.S. Preventive Services Task Force recommending universal HCV testing in primary care, the screening rate for HCV in these settings remains alarmingly low, ranging from 3 to 19% [52–55]. A significant proportion of individuals, particularly those who are uninsured or experiencing homelessness, lack access to primary care clinicians, thereby missing out on HCV screening opportunities in this setting. Notably, a study has demonstrated that adult patients lacking health insurance had a 22% lower likelihood of undergoing HCV testing compared to those with private health insurance [56].

EDs have over 135 million patient-visits annually and a great number of these patients present with a high risk for HCV, such as PWID and HIV infection [57]. A study indicated that HCV antibody seropositivity in patients diagnosed in the ED is twice as high as what the CDC estimates the prevalence is in the 1945–1965 birth cohort [58]. At UIH, 36.2% of eligible patients received HCV screening via Project HEAL between January 2019 and February 2020. This screening rate is higher than the rate in a primary care setting, as mentioned earlier, and demonstrates the potential impact of ED-based HCV

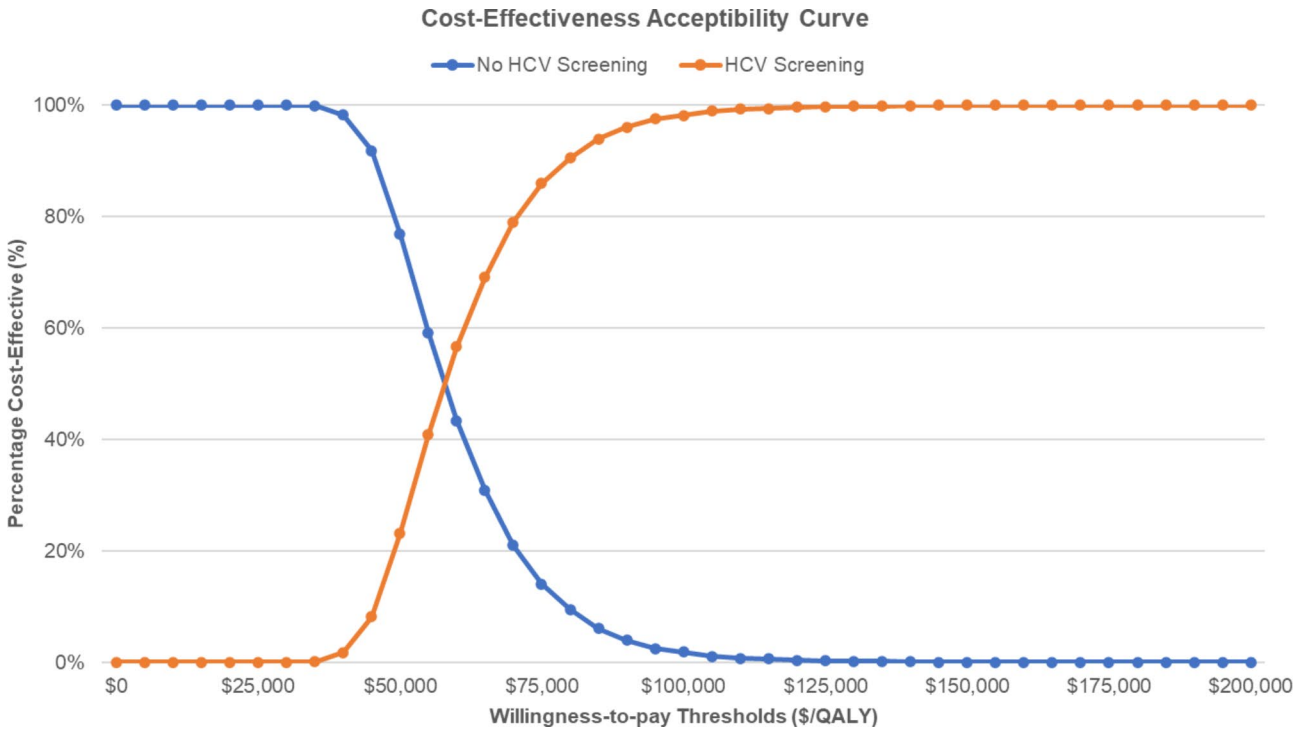

Fig. 3 Cost-effectiveness acceptability curve. *DAA Intervention at F1 or Later Fibrosis Stages

screening initiatives in reaching at-risk populations who may not otherwise access screening and care services.

Several studies showed that ED-based HCV screening programs effectively increased the number of patients screened and diagnosed with HCV. For example, two US studies reported that universal, ED-based, opt-out HCV screening led to a higher volume of new HCV diagnoses, especially among those who did not fall into the CMS coverage criteria for HCV screening [57, 59]. The cost-effectiveness of ED-based HCV screening was also demonstrated in several non-US studies. Opstaele and colleagues investigated the cost-effectiveness of HCV screening and DAA treatment in ED patients in Belgium [60]. Compared to no ED testing, HCV screening resulted in an ICER of €5,967/QALY and was cost-effective at the WTP threshold of €10,000/QALY. Another study evaluated the opt-out ED-based HCV test and linkage-to-care in the UK and showed that the ED-based HCV test was highly cost-effective compared to no test with an ICER of £8,019/QALY (WTP= £20,000/QALY) [61]. In addition, Mendlowitz and colleagues demonstrated that ED-based HCV screening and subsequent DAA treatment were cost-effective among general ED patients and ED patients born between 1945 and 1975 [62]. Although this study was conducted in Canada, it includes the analysis of ED-based HCV screening in the US healthcare setting using US healthcare costs. In the study, general population screening resulted in ICERs of CAN $19,733/QALY and US$32,187/QALY, respectively, and birth cohort screening resulted in ICERs of CAN $25,584/QALY and the US $42,615/QALY, respectively, when compared to no screening. Both screenings were cost-effective at CAN $50,000/QALY WTP threshold. Outside of this study, we are unaware of other published cost-effectiveness studies that evaluate ED-based HCV screening programs in the US, which highlights the importance of this study.

As the Viral Hepatitis National Strategic Plan suggests, one of the strategies to eliminate HCV is to increase the capacity of the public health, healthcare delivery, and healthcare workforce to effectively identify, diagnose, and provide holistic care and treatment for people with viral hepatitis [63]. Thus CMS should support HCV screening efforts and linkage-to-care for patients outside of primary care settings to facilitate efforts toward HCV elimination in the US.

Limitations

Our study has limitations. First, the economic model was built based on the summary data from Project HEAL, which was implemented in an urban healthcare system. This data includes the probability of linkage-to-care and the proportion of HIV and PWID patients. Therefore, our results may not be generalizable to all US populations. Second, other HCV treatment options (e.g., elbasvir/grazoprevir and ledipasvir/sofosbuvir) were not included in this study because we only considered pan-genotypic HCV treatment regimens that are included in AASLD-IDSA's current simplified HCV guidance [50].

Other healthcare systems may have utilized HCV treatment regimens in different proportions, which may affect total healthcare costs. Third, the cost of hiring the coordinator for ED-based HCV screening, extra time spent asking risk questions, offering and running HCV tests, and delivering results was not included in our model. This cost highly depends on the volume of patients at the ED and therefore would vary significantly across different healthcare systems. Also, our model did not incorporate screening costs for patients who did not undergo HCV screening in the ED due to a lack of available information on the distribution of patients across various HCV screening sites and the associated screening costs at these sites. However, it is worth mentioning that the overall costs associated with HCV screening are relatively minimal. Considering this, ED-based HCV screening would still remain a cost-effective option when compared to delayed screening in primary care settings, hospitals, clinics, or community centers. Finally, there was limited information on the utility of HCV-related conditions from US patients. Thus, utility estimates in our model were derived from European studies, and the actual utilities can be different between the US versus European populations. Further studies are needed to estimate more accurate costs of fibrosis stages and utility estimates for HCV patients in the US.

Conclusion

To our knowledge, our study is the first to evaluate the cost-effectiveness of ED-based HCV screening and linkage-to-care using real-world estimates in the US. The results indicate that ED-based HCV screening can reduce potential hepatic complications and lower the long-term HCV treatment costs. Also, ED-based HCV screening was extremely cost-effective for different scenarios. Opportunities exist as less than half of eligible patients were screened for HCV, and a large proportion of identified HCV-infected patients was lost to follow-up in our study population. If these limitations are addressed, ED-based screening programs could benefit an even greater number of HCV patients.

Abbreviations

AASLD	American Association for the Study of Liver Diseases
CDC	Center for Disease Control and Prevention
CI	Confidence Intervals
CMS	Center for Medicare & Medicaid Service
DAA	Direct-Acting Antiviral
F	Fibrosis Stage
GLE/PIB	Glecaprevir/Pibrentasvir
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
ICER	Incremental Cost-Effectiveness Ratio
IDSA	Infectious Diseases Society of America
NDC	National Coverage Determination
OWSA	One-Way Sensitivity Analysis
PSA	Probabilistic Sensitivity Analysis
PWIDs	People Who Inject Drugs
QALYs	Quality-Adjusted Life Years
SOF/VEL	Sofosbuvir/Velpatasvir
SOF/VEL/VOX	Sofosbuvir/Velpatasvir/Voxilaprevir
SVR	Sustained Virologic Response
UIH	University of Illinois Hospital and Health Science System
US	United States
WTP	Willingness-To-Pay

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12913-024-11793-4.

Supplementary Material 1: Supplementary Table 1. OWSA. Supplementary Table 2. Years in HCC and Liver Transplant States. Supplementary Figure 1. OWSA Tornado Diagram.

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Not applicable.

Authors' contributions

All authors (Sun A Choi, Kandavadivu Umashankar, Anjana Maheswaran, Michelle Martin, Jean Lee, Matt Odishoo, Janet Y Lin, and Daniel R Touchette) contributed to the study conception, design, data collection, and analyses. The first draft of the manuscript was written by Sun A Choi and Kandavadivu Umashankar. All authors reviewed and commented on previous versions of the manuscript. All authors read and provided approval of the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by the University of Illinois at Chicago Institutional Review Board (IRB ID: STUDY2020-0169-MOD002). Authors used the summary data from Project HEAL to build an economic model and did not have access to information that could identify individual participants during or after data collection. Informed consent was waived and not required as approved by the UIC. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

Daniel R Touchette is the Senior Scientific Advisor for Monument Analytics, a consultant for Astra Zeneca, and has received research funding from AbbVie, Inc and Takeda awarded to University of Illinois Chicago for work unrelated to this study. Sun A Choi was the post-doctoral fellow at University of Illinois Chicago, funded by Takeda and currently is a consultant at Cobbs Creek Healthcare. Kandavadivu Umashankar was a post-doctoral fellow at University of Illinois at Chicago, funded by Takeda and currently has a contractor role at AbbVie, Inc. Michelle Martin has served on advisory boards and serves on the speakers' bureaus for AbbVie and Gilead, has received grant funding from Merck and Gilead, and is a minor shareholder for AbbVie, Gilead, and Merck. Janet Y Lin has received funding previously from Gilead to implement routine HCV screening in an emergency department setting at University of Illinois Chicago. Anjana Maheswaran, Jean Lee, and Matt Odishoo do not have competing interests.

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