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Cost-effectiveness of Universal Hepatitis C Virus Screening of Pregnant Women in the United States

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Background. Hepatitis C virus' (HCV) chronic prevalence among pregnant women in the United States doubled nationally from 2009–2014 (~0.7%), yet many cases remain undiagnosed. Screening pregnant women is not recommended by the Society of Maternal-Fetal Medicine or the Centers for Disease Control and Prevention, despite new American Association For the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA) guidelines recommending screening for this group. We assessed the cost-effectiveness of HCV screening for pregnant women in the United States.

Methods. An HCV natural history Markov model was used to evaluate the cost-effectiveness of universal HCV screening of pregnant women, followed by treatment after pregnancy, compared to background risk-based screening from a health-care payer perspective. We assumed a HCV chronic prevalence of 0.73% among pregnant women, based on national data. We assumed no Medicaid reimbursement restrictions by fibrosis stage at baseline, but explored differing restrictions in sensitivity analyses. We assessed costs (in US dollars) and health outcomes (in quality-adjusted life-years [QALYs]) over a lifetime horizon, using new HCV drug costs of $25 000/treatment. We assessed mean incremental cost-effectiveness ratios (ICERs) under a willingness-to-pay threshold of $50 000/QALY gained. We additionally evaluated the potential population impact.

Results. Universal antenatal screening was cost-effective in all treatment eligibility scenarios (mean ICER <$3000/QALY gained). Screening remained cost-effective at a prevalence of 0.07%, which is the lowest estimated prevalence in the United States (in Hawaii). Screening the ~5.04 million pregnant women in 2018 could result in the detection and treatment of 33 000 women, based on current fibrosis restrictions.

Conclusions. Universal screening for HCV among pregnant women in the United States is cost-effective and should be recommended nationally.

Keywords. testing; hepatitis C virus; economic; antenatal; pregnancy.

Hepatitis C virus (HCV) infections among pregnant women doubled in the United States from 2009–2014, reaching 8% in rural Tennessee [1]. Roughly 0.7% of pregnant women in the United States have a chronic HCV infection [2], equating to ~42 000 pregnancies and 29 000 births among HCV-infected women annually. Despite the availability of highly-effective (>90% cure) HCV direct-acting antivirals (DAAs) [3], the majority of these women remain undiagnosed and unlinked to care.

Currently, there is disagreement about HCV screening among pregnant women in US clinical guidelines. Recent Society of Maternal-Fetal Medicine and American College of Obstetrics and Gynecology guidelines reaffirmed recommendations for only risk-based testing for HCV among pregnant

women [4]. Similarly, the US Centers for Disease Control and Prevention (CDC) recommends routine screening for human immunodeficiency virus, hepatitis B virus, and syphilis, but not for HCV among pregnant women [5]. By contrast, recent American Association For the Study of Liver Diseases (AASLD)/ Infectious Diseases Society of America (IDSA) guidelines recommend HCV screening for all pregnant women, ideally at the initiation of prenatal care [6]. Additionally, in April 2018, the Kentucky legislature recommended testing pregnant women due to a high HCV burden in that state [7]. For many women, pregnancy is one of their few contact points with health care and health insurance coverage and, as such, pregnancy could provide a critical opportunity for reaching this population. To our knowledge, no study has evaluated the cost-effectiveness of HCV screening in pregnant women in the DAA era in the United States.

To inform HCV screening policies and practices, we assessed the cost-effectiveness of universal HCV screening among pregnant women in the United States, followed by treatment after pregnancy, as determined by state-based Medicaid fibrosis restrictions.

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METHOD

Overview

We performed a cost-effectiveness analysis of universal HCV screening among pregnant women in the United States, compared to background, risk-based screening, from a public sector health-care payer perspective. Our cost-effectiveness analysis includes long-term health benefits among pregnant women only, but we additionally examine the potential impact, in terms of HCV diagnoses among children born to HCV-infected mothers, in the Estimation of Impact section.

Baseline and Comparator

We explored the cost-effectiveness of HCV antenatal screening, followed by treatment after pregnancy, compared to background, risk-based screening. Our main analysis explores the cost-effectiveness in a setting with no treatment restrictions by fibrosis stage, but we additionally explored scenarios with differing treatment eligibilities (see sensitivity analyses).

Model

We utilized a deterministic, HCV natural history, closed-cohort Markov model of HCV disease progression and treatment among pregnant women attending antenatal clinics (Supplementary Figure S1). The population was stratified by HCV infection stage and by HCV diagnosis and follow-up status. We assumed all individuals were diagnosed and under follow-up upon progression to decompensated cirrhosis or hepatocellular carcinoma due to clinical severity. We incorporated losses to follow-up among diagnosed women; individuals lost to follow-up were eligible for retesting in the community. Individuals who attained a sustained virological response (SVR) with Meta-analysis of Histological Data in Viral Hepatitis (METAVIR) F3 or lower were assumed not to progress further for HCV, whereas those with fibrosis stages F4 or beyond progressed at a lower rate compared to their HCV-infected counterparts. Individuals whose treatment failed were not retreated.

Cost-effectiveness Methods

Cost (in 2018 US dollars [USD]) and health utilities (in quality-adjusted life years [QALYs]) were attached to each health state and discounted by 3%/year. Due to parameter uncertainty, we performed a probabilistic uncertainty analysis where parameters were randomly sampled from probabilistic distributions (Table 1) to generate 10 000 parameter sets. For each parameter set, the model was run and outputs generated. We calculated the mean incremental cost-effectiveness ratios (ICER; $/QALY gained, mean incremental costs divided by the mean incremental QALYs) for the antenatal screening compared to background risk-based screening for each treatment eligibility scenario, assessing cost-effectiveness under a willingness-to-pay threshold of $50 000/QALY gained [8].

Sensitivity Analyses on Cost-effectiveness Results

Due to state differences in Medicaid reimbursement policies by fibrosis stage, we additionally examined scenarios where treatment was restricted until an individual reached METAVIR stage F1 or beyond (F1+), METAVIR stage F2 or beyond (F2+), or METAVIR stage F3 or beyond (F3+), each compared to background screening. In these restriction scenarios, women with chronic HCV infection would be eligible for treatment upon progression to these disease stages if they remain linked to care.

Additionally, for each treatment eligibility scenario, we performed numerous one-way sensitivity analyses. Due to state variability in HCV chronic prevalence among pregnant women [1], we examined the impact of varying HCV prevalences. We additionally performed 1-way sensitivity analyses to examine how the ICER changed with alterations in: SVR (85% and 95% versus 90% at baseline), age at pregnancy (22 or 32 compared to 27 at baseline), HCV treatment costs ($75 000 versus $25 000 at baseline), HCV treatment delivery costs ($625 USD versus $1249 at baseline), proportion previously diagnosed and under follow-up (40% compared to 18% at baseline), discount rate (0% for costs and health utilities or 3% for utilities and 6% for costs, versus 3% for each at baseline), liver transplantation costs (50% or 200% baseline costs), loss to follow-up per year (10/30/50% per year compared to 12% at baseline), background testing rate (10% or 0% per year, compared to 5% at baseline), baseline fibrosis stage distribution (3% cirrhosis versus 10% at baseline), and HCV screening uptake (85% based on hepatitis B virus testing uptake among pregnant women, compared to 100% at baseline) [9]. Additionally, our baseline fibrosis progression rate among US women produced 15% cirrhosis or more advanced liver disease at 20 years, but a recent publication among a German cohort found lower rates of progression (21% cirrhosis or further at 35 years for treatment-naive women [37]), so we evaluated a scenario with lower fibrosis progression rates.

Estimation of US Population Impact

We additionally estimated the national impact of implementing HCV screening of pregnant women in 2018. Due to state heterogeneity in fibrosis restrictions, we first generated state-level estimates of the number of pregnant women in a given year (number of births + number of fetal losses + number of abortions) [38–40]. We estimated births and abortions by multiplying the number of women aged 15–44 in a given state by the state-specific birth rate and abortion rate, respectively. We estimated fetal losses using the national fetal loss rate, based on CDC recommendations, due to state-level differences in fetal loss reporting by gestational age [38]. As 2016 estimates indicated only 1.6% of women did not access any prenatal care during pregnancy, for simplicity, we assumed all women would be eligible for screening [41]. Based on state-level estimates of pregnant women in 2018 and state fibrosis restrictions [42], we multiplied the number of pregnant women by HCV identification and

Table 1. Model Parameter Inputs and Sources

State Transitions	HCV Stage	Mean Sampled Value (2.5%–97.5% quantiles)	Sampling Distribution	Source
HCV chronic prevalence among pregnant women	…	0.73% (0.71–0.75%)	Uniform Range: 0.709–0.751	[2]
HCV antibody prevalence among pregnant women	…	1.10% (1.02–1.20%)	…	Calculated based on spontaneous clearance rate
Proportion who spontaneously clear their acute infection	…	34% (30–38%)	Uniform Range: 30–38	[9]
Annual loss to follow-up rates after HCV diagnosis	…	12% (7–17%)	Uniform Range: 7–17	[10]
Proportion of HCV-infected pregnant women previously diagnosed and linked to care	…	18% (10–25%)	Uniform Range: 10–26	[11, 12] See text
Background testing and linkage rate per year	…	5% (2.6–7.4%)	Uniform Range: 2.5–7.5	Assuming an annual testing rate of 10%/year with 50% linked to care [13]
HCV chronic prevalence among PWID (%)	…	52% (44–59%)	Uniform Range: 43–60	[14, 15]
Liver disease stage transition rate per year	F0 to F1	0.1125 (0.996–0.1261)	Beta (251.2107, 1984.813)	[16]
	F1 to F2	0.1125 (0.996–0.1261)	Beta (251.2107, 1984.813)	[16]
	F2 to F3	0.1125 (0.996–0.1261)	Beta (251.2107, 1984.813)	[16]
	F3 to F4	0.1125 (0.996–0.1261)	Beta (251.2107, 1984.813)	[16]
	F4 to DC	0.0406 (0.0312–0.0520)	Beta (58.49116, 1380.788)	[17–19]
	F4 to HCC	0.0212 (0.0163–0.0276)	Beta (52.83443, 2417.472)	[17–19]
	DC to HCC	0.0141 (0.0016–0.0395)	Beta (1.9326, 136.1074)	[17]
	DC/HCC to transplant	0.0313 (0.0014–0.1077)	Beta (1.152814, 36.03474)	[17, 19, 20]
Proportion who achieve SVR	…	0.90	Uniform Range: 0.85–0.95	[3]
Liver-related death rates per year	F4	0.0324 (0.01716–0.05234)	Beta (12.44677, 371.1121)	[21]
	DC	0.2210 (0.1207–0.3414)	Beta (11.61594, 40.93614)	[21]
	HCC	0.2210 (0.1207–0.3414)	Beta (11.61594, 40.93614)	[21, 22]
	Transplant year 1	0.1715 (0.1378–0.2081)	Beta (75.4499, 364.4907)	[23]
	Post-transplant (year 2+)	0. 0353 (0.0288–0.0425)	Beta (97.65551, 2665.93)	[23]
Annual background mortality rate	Varies by age	…	…	[2, 24] WHO lifetable, assuming age 27 at pregnancy
Relative risk of progression if SVR compared to no SVR	F4 to DC	0.07 (0.03–0.2)	Lognormal (5.6356,2.43983)	[25]
	F4 to HCC	0.23 (0.16–0.35)	Lognormal (−3.37754,1.9534)	[25, 26]
	DC to HCC	1	-	…
HCV fibrosis distribution among HCV diagnosed women	F0	0.16	…	[27]
	F1	0.43	…	…
	F2	0.21	…	…
	F3	0.10	…	…
	F4	0.10	…	…
Cost (all costs inflated to USD 2018 [28])				
Annual costs for non-treatment medical expenses among HCV-infected patients	F0–F3	$511 ($304–734)	Uniform ± 50% point estimate	[29–31]
	F4	$2898 ($2009–3786)	Uniform ± 50% point estimate	…
	DC	$34 319 ($32 352–36 330)	Uniform ± 50% point estimate	…
	HCC	$54 741 ($49 302–60 014)	Uniform ± 50% point estimate	…
	Liver transplant Y1	$225 320 ($119 270–330 260)	Uniform ± 50% point estimate	[30]

Table 1. Contiued

State Transitions	HCV Stage	Mean Sampled Value (2.5%–97.5% quantiles)	Sampling Distribution	Source
	Liver transplant following years	$55 196 ($28 773–81 181)	Uniform ± 50% point estimate	[30]
HCV antibody test (including consultation)	...	$39	...	[22, 32]
HCV RNA test (including consultation)	...	$52	...	[22, 32]
Liver elastography	...	*$130*	...	[22, 32]
HCV antiviral therapy drug cost only, per treatment course	...	$25 000	...	[33] and glecaprevir/ pibrentasvir wholesale acquisition cost
Treatment delivery costs per course	...	$1249 ($676–1853)	Uniform ± 50% point estimate	[3] Supplementary Table S1
Health utilities				
Uninfected	...	1	...	[20]
HCV-infected patients	F0	0.93 (0.83–1)	Beta (59.95413, 4.512676)	[20, 34, 35]
	F1, F2	0.86 (0.78–0.94)	Beta (29.92649, 4.871755)	...
	F3	0.83 (0.78–0.89)	Beta (12.30437, 2.520171)	...
	F4	0.81 (0.68–0.89)	Beta (41.6698, 9.774397)	...
	DC	0.70 (0.56–0.79)	Beta (39.8121, 17.06233)	...
	HCC	0.67 (0.56–0.78)	Beta (35.508, 17.48901)	...
	Posttransplant	0.71 (0.69–0.79)	Beta (7.612184, 3.109202)	...
Incremental increase in health utility upon SVR	...	0.05	...	[36]

Abbreviations: DC, decompensated cirrhosis; F0–F4, fibrosis stages 0–4; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; PWID, people who inject drugs; SVR, sustained viral response; USD, United States dollars; WHO, World Health Organization.

treatment rates generated from the economic model for each fibrosis restriction scenario, assuming the national HCV prevalence among pregnant women. We summed state-level estimates to generate a national estimate of the total and incremental number of pregnant women identified and treated with HCV antenatal screening. We also estimated the total and incremental number of HCV-infected children born who would be identified through follow-up screening, based on a maternal diagnosis during pregnancy. For this analysis, we assumed a vertical HCV transmission rate of 5.8% from a recent meta-analysis [43]. Follow-up testing rates among children born to HCV-infected mothers are uncertain, but a recent study [44] found few (16%) children born to known HCV-infected mothers were tested at 18 months, as recommended by the AASLD and pediatric societies [6], so we assumed 16% for this analysis.

Model Parameterization
All model parameters and sampling distributions are presented in Table 1.

Baseline Population Characteristics
The baseline population included pregnant women, with an average age of 27 years (based on the median age of reproductive-aged women in the United States) [2]. We assumed a chronic HCV prevalence among pregnant women of 0.73% (95% CI 0.71–0.75%), based on national estimates [2], corresponding to an anti-HCV prevalence of 1.11%, given a 34%

spontaneous clearance rate in women [9]. We assumed a chronic HCV prevalence among people who inject drugs of 52% (range 43–60%), based on national estimates [14, 15]. Our HCV fibrosis distribution was based on US national estimates for women [27].

Estimates of the proportion of HCV-infected pregnant women diagnosed and currently under follow-up for HCV are unknown. The 2008 National Health and Nutrition Examination Survey (NHANES) survey estimated 50% of HCV-infected individuals were diagnosed, but this estimated rate was lower among young individuals (29% for age <40) [11]. Updated estimates indicate the overall proportion diagnosed has increased by a relative 10% (from 50% in 2008 to 55% in 2017) [12]. Based on this, we assumed 32% of pregnant women are currently diagnosed, based on estimates among individuals age <40 (29% in 2008, estimated increase by relative 10% in 2017). We note that one study among HCV-infected pregnant women on opiate substitution therapy (OST) found that 70% were previously diagnosed, but it is likely this would overestimate the proportion of all HCV-infected women diagnosed and it is unclear how many were under follow-up [45]. The linkage to HCV care rates similarly vary, with recent estimates of 34% linkage within 6 months among individuals on OST [13] and 55% among patients receiving care in an outpatient clinic [46]. For this analysis, we estimated that 18% of infections among pregnant women were diagnosed and linked (32% diagnosed x 55% linked). We assumed a 12%/year loss to follow-up after diagnosis, based on data from pregnant women on OST [10].

Table 2. Cost-effectiveness Results of Hepatitis C Virus Antenatal Versus Background Screening

Scenario	Cost Per Person, in 2018 USD Mean (2.5–97.5% Intervals)	QALYs Per Person Mean (2.5–97.5% Intervals)	Incremental Cost Per Person Mean (2.5–97.5% Intervals)	Incremental QALYs Per Person Mean (2.5–97.5% Intervals)	Mean ICER USD/ QALY Gained
Background screening	921 (443–1397)	25.312 (25.297–25.325)	…	…	…
Universal antenatal screening and treatment after pregnancy, regardless of fibrosis stage	975 (442–1510)	25.331 (25.315–25.343)	53 (−102–175)	0.019 (0.010–0.028)	2826

Abbreviations: ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life-years; USD, United States dollars.

Disease Stage Transition Probabilities and Costs

Estimates of stage-specific transition rates among women were obtained from published studies [16]. Background (non–hepatitis C related) mortality was time-varying, based on age-specific mortality rates obtained from World Health Organization life tables [24]. Individuals with F0–F3 fibrosis stages who achieved SVR were assumed to have no further disease progression, while individuals with cirrhosis or more advanced disease who achieved SVR could progress at a reduced rate (Table 1) [25, 26]. We incorporated HCV disease-related costs from published literature [29–31].

Hepatitis C Virus Testing Costs.— We incorporated the costs of anti-HCV and HCV RNA confirmatory testing based on the 2018 National Fee Schedule [28]. We assumed individuals are screened first for anti-HCV and, if found positive, are then screened for HCV RNA. Outpatient visit consultation costs were included for each testing visit [47]. For individuals who are RNA positive, we incorporated liver elastography costs for disease staging.

Hepatitis C Virus Treatment Efficacy and Costs.— We assumed a baseline DAA treatment efficacy (ie, rate of SVR) of 90% for all genotypes [3]. We assumed drug costs for DAAs of $25 000 per treatment course (based on the wholesale acquisition cost of glecaprevir/pibrentasvir and the price of generic sofosbuvir/ledipasvir and sofosbuvir/velpatasvir available in January 2019) [33]. Cost components of treatment delivery (pre-treatment and on-treatment monitoring) were based upon the IDSA guidelines [3] and the 2018 Clinical Diagnostic Laboratory Fee Schedule [28] (Supplementary Table S1).

Utilities

Health utilities (in QALYs) were obtained from previously published studies [17,18,20]. Consistent with other analyses, we assumed a 0.05 incremental increase in health utility for patients who achieved SVR [48].

RESULTS

Cost-effectiveness

Universal HCV screening for pregnant woman was associated with an incremental cost of $53.2 (2.5-97.5% interval -102 to 174) and

an incremental increase in QALYs of 0.019 (2.5-97.5% interval 0.010–0.028) per pregnant woman screened, compared to background, risk-based screening (Table 2). HCV screening for pregnant women with no treatment reimbursement restrictions was cost-effective compared to risk-based screening, with a mean ICER of $2826 per QALY gained, and fell below the willingness-to-pay threshold of $50 000 per QALY for 100% of the simulations.

Screening remained cost-effective for all the alternative treatment eligibility scenarios by fibrosis stage (mean ICERs of $1934, $2026, and $2632 in the METAVIR stage F3+, F2+, and F1+ scenarios, respectively; Supplementary Tables S2–S5).

Screening remained cost-effective for chronic HCV prevalences among pregnant women at or above 0.03–0.04%, varying by treatment eligibility scenario (Figure 1; Supplementary Figure S2). Results were robust to all sensitivity analyses (Supplementary Tables S2–S5). Screening remained cost-effective in all settings with lower fibrosis progression rates (21% cirrhosis at 35 years), SVRs (85%), higher proportions diagnosed and linked at baseline (40%), lower liver transplantation costs ($112 000 per transplant), higher loss to follow-up rates (50%/year), higher background testing rates (20%/year), and lower proportions of cirrhosis in the baseline cohort (3%).

US Population Impact

Given current state-by-state fibrosis restrictions, we estimate screening of the estimated 5.04 million pregnant women in 2018 would result in the detection and treatment of approximately 33 000 women overall, and an incremental detection and treatment of approximately 7000 women, with the remainder diagnosed and treated later on in their disease. Screening could additionally result in the detection and treatment of an estimated 300 children born to mothers infected by HCV, and potentially many more if the rate of return for 18-month HCV testing of children born to HCV-infected mothers increases from the currently observed 16%.

DISCUSSION

Our analysis indicates that universal HCV screening among pregnant woman in the United States is highly cost-effective and would be associated with the improved detection of HCV among
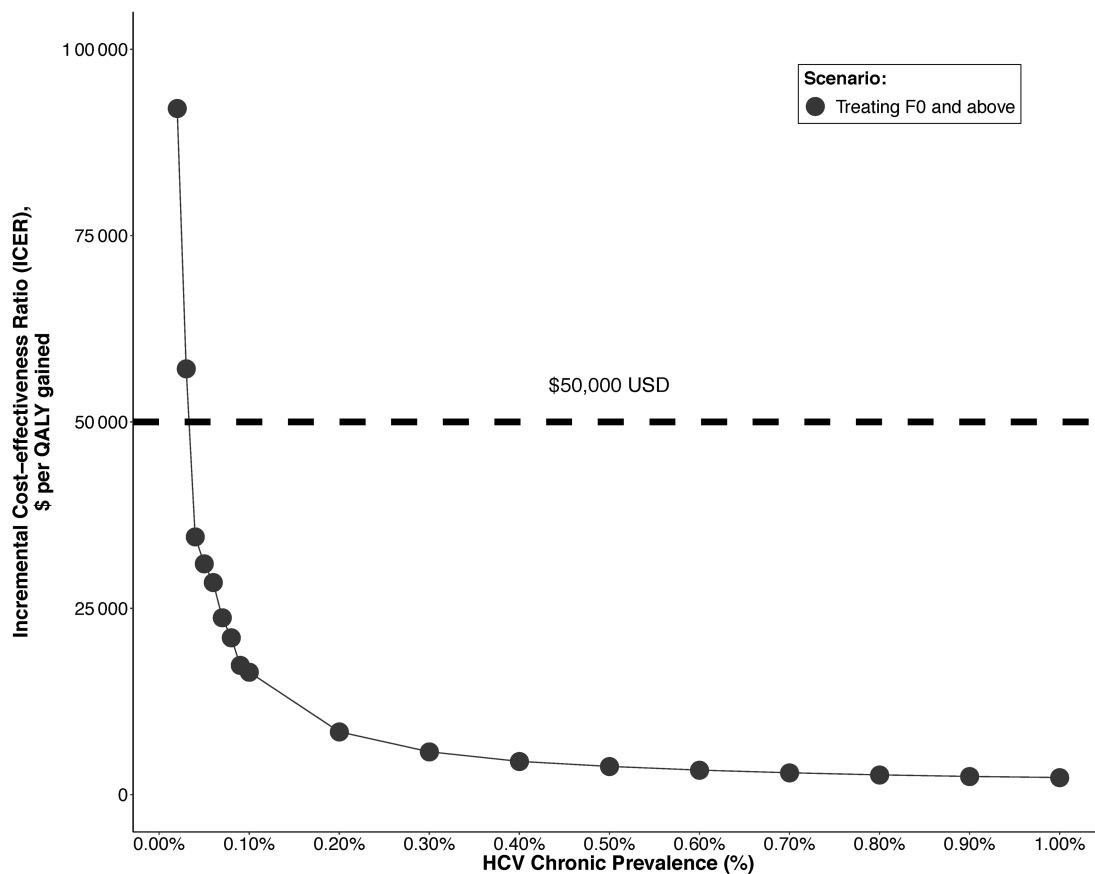
Figure 1. Impact of HCV chronic prevalence among pregnant women (x-axis) on the ICER (y-axis) of universal screening pregnant woman, compared to background risk-based screening. The willingness to pay a threshold of $50 000/QALY is denoted by a horizontal, dashed line. Abbreviations: F0, fibrosis stage 0; HCV, hepatitis C virus; ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life-years; USD, US dollars.

women and their children. Our results were robust to variations in state restrictions on reimbursement for HCV treatment. They were additionally robust to variations in HCV prevalences; screening pregnant women is likely cost-effective in settings with chronic HCV prevalence as low as 0.04%. Comprehensive, state-specific data on HCV prevalences among pregnant women are unavailable, but it appears likely all states are above this threshold. Among the states reporting maternal HCV infections on infant birth certificates, HCV rates vary substantially by state, with the highest at 2.2 per 100 births in Tennessee and the lowest at 0.07 per 100 births in Hawaii in 2014 [1]. If these data are representative of the true HCV prevalence among pregnant women, screening in the lowest prevalence state (Hawaii) would remain cost-effective [1]. As such, our results support calls for a change of the Society of Maternal-Fetal Medicine/American College of Obstetrics and Gynecology and CDC guidelines to recommend the universal HCV screening of pregnant women [49]. Our results also provide additional economic evidence in support of the updated AASLD/IDSA guidelines [6] and the Kentucky legislation [7] recommending screening pregnant women.

To our knowledge, our study is the first to evaluate the cost-effectiveness of HCV screening among pregnant women

in the United States. Our findings conflict with a previous study, which found HCV screening among pregnant women in the United States was not cost-effective [50], but that study utilized old, interferon-based treatments with low cure rates. Our findings are consistent with a recent study that found antenatal screening in the UK was cost-effective with newer, interferon-based therapies [51]. Our findings are also consistent with studies that found HCV screening in the DAA era is cost-effective among a variety of US populations, such as for adolescents and young adults in primary-care settings [47], in prisons [52], and in methadone programs [13], and for one-time testing strategies in the general population [53]. We note that our results show that screening is highly cost-effective (ICER < $3000), more so than previous analyses, primarily because we used new drug costs of $25 000/treatment. When we used treatment costs similar to previous analyses, we found similar cost-effectiveness results as in a recent study examining general-population screening (around $10 000/QALY gained) [53].

As with all modeling studies, ours was limited by several factors: most notably, uncertainty in the underlying data. First, there is substantial uncertainty in the proportion of pregnant

women previously diagnosed and engaged in care, linkage to care rates, and loss-to-follow-up rates among this population in the DAA era. However, despite this, our sensitivity analyses indicated results were robust to uncertainty in these and other parameters.

Second, we did not simulate changing insurance eligibility over time, but note that in some non–Medicaid expansion states, women can lose their insurance coverage as early as 30 days after giving birth. This restriction could limit the timely uptake of HCV treatment. Clinical studies are underway examining the safety and efficacy of HCV treatment during pregnancy. Treatment during pregnancy could reduce the risks of loss to follow-up or loss of insurance coverage after pregnancy, and potentially prevent vertical transmission. Future analyses should explore the health and economic implications of treatment during pregnancy, and should incorporate women's preferences around treatment. For example, in a recent study, only 21% of HCV-infected women reported a willingness to take DAAs during pregnancy for their individual benefit, but 60% reported a willingness if it reduces perinatal transmission [54].

Third, our cost-effectiveness evaluation incorporated health benefits among pregnant women only, as the outcome of HCV diagnoses during pregnancy on subsequent testing among children is uncertain and the pediatric management of HCV is changing (with studies evaluating treatment among children as young as 2). As such, for the cost-effectiveness analysis, we neglected the additional benefits related to HCV diagnosis and management among babies born to women identified with HCV, although we estimate screening could identify ~300 children born with HCV as a result of pregnancies in 2018. Even more impact and economic benefits could be accrued due to diagnoses of future children born to these mothers. Unfortunately, the data indicate that the subsequent testing and follow-up rates of their babies are low among HCV-diagnosed women [44]: however, this may improve in the DAA era.

Fourth, we neglected the potential risks of reinfection or population treatment as prevention benefits of treatment. It is uncertain, but possible, that a sizeable fraction of HCV-infected pregnant women remain at risk after pregnancy. However, our previous models show that, in settings with 50% chronic prevalence among people who inject drugs, like in the United States, the early treatment of people with ongoing drug-injection use is cost-effective and prevents 0.2–0.8 infections per early treatment, despite the risk of reinfection [55]. As such, including reinfection and prevention benefits would likely increase the cost-effectiveness of screening.

Fifth, our estimates for the population impacts of screening are uncertain, as they are based on state-level estimates of pregnant women and the estimated impact by fibrosis state restrictions, but utilize national estimates of HCV prevalence among pregnant women, due to a lack of state-level data. State fibrosis restrictions are continually changing and will affect the

population impact. Additionally, heterogeneity in the HCV prevalences among pregnant women by state will affect these estimates, and further epidemiological studies are warranted. Nevertheless, we believe our general results indicating the potential, sizeable impact of screening are robust.

In conclusion, our study provides evidence that universal HCV screening of pregnant women in the United States is cost-effective and should be recommended nationally by all clinical societies.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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