Cost-effectiveness of Strategies to Identify Children with Perinatally Acquired Hepatitis C Infection

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Abstract

Objectives: We aimed to determine the optimal testing strategy to identify children with perinatally acquired hepatitis C virus (HCV) infection.

Study Design: We used a decision-tree framework with a Markov disease progression model to conduct an economic analysis of four strategies, based on combinations of type and timing of test: Anti-HCV with reflex to HCV RNA at 18 months among children known to be perinatally exposed (ie, baseline comparison strategy); HCV RNA testing at 2–6 months among infants known to be perinatally exposed (Test Strategy 1); universal anti-HCV with reflex to HCV RNA at 18 months among all children (Test Strategy 2); universal HCV RNA testing at 2–6 months among all infants (Test Strategy 3). We estimated total cost, quality-adjusted life years (QALYs), and disease sequalae for each strategy.

Results: Each of the three alternative testing strategies resulted in an increased number of children tested and improved health outcomes. HCV RNA testing at 2–6 months (Test Strategy 1) was cost-saving and resulted in a population-level difference in cost of $469,671. The two universal testing strategies resulted in an increase in QALYs and an increase in total costs.

Conclusions: Testing of perinatally exposed infants at age 2–6 months with a single HCV RNA test will reduce costs and improve health outcomes, preventing morbidity and mortality associated with complications from perinatal HCV infections.

Introduction

The incidence of hepatitis C virus (HCV) infection more than quadrupled during 2010 through 2020 in the United States, with the highest rates and increases among persons 20–39 years of age[1]. Increasing HCV infections among reproductive age adults has resulted in higher numbers of infants with perinatal HCV exposure[1,2]. studies estimate that 5.8% (95% CI, 4.2%–7.8%) of infants born to HCV-infected persons acquire hepatitis C perinatally and approximately 80% of those infants develop chronic HCV infection[3,4]

Curative hepatitis C treatment is approved for use in children beginning at 3 years of age[7,8]. The identification of children with perinatally acquired HCV is the first step. CDC and USPSTF hepatitis C screening recommendations among adults, updated in 2020 and followed with similar recommendations from the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine in 2021, call for hepatitis C screening of all pregnant persons during every pregnancy. Testing recommendations for infants with perinatal exposure to HCV have been developed by medical organizations with variability in timing and type of test recommended[7-10]. Recommendations include HCV antibody testing at age 15 to 18 months, allowing time for passively acquired maternal antibodies to clear, followed by HCV RNA testing for children with reactive antibody results or HCV RNA detection either once or twice in the first year of life starting at 2 months of age[7-12]. Differences in recommendations can contribute to inconsistent implementation by providers.

Recognition of perinatal exposure requires maternal HCV screening and communication of positive results to the child's health provider. Universal pediatric HCV screening could overcome these barriers, but the cost-effectiveness of this approach has not been evaluated. Optimal timing of pediatric evaluation is also unclear. Attendance at recommended well-child visits is highest immediately after birth, including among low-income populations with limited access to care[13]. HCV testing among exposed children at age 18 months or older does not usually exceed 50%, and various assessments have found that only 10–30% receive testing [14-18]. Current testing algorithms call for anti-HCV testing at or after 18 months followed by an HCV RNA test when antibody tests are reactive. Accelerating pediatric HCV evaluation among exposed children from age 18 months or older to age 2–6 months using an HCV RNA test with reliable results, could increase the number of infected children identified by providing testing while more children are engaged in routine care. While HCV RNA testing is more expensive than anti-HCV testing, the cost-effectiveness of an HCV RNA-only testing strategy has not previously been evaluated and must be weighed against high loss to follow-up when testing is delayed.

This modeling study aimed to identify the optimal strategy for identifying children with perinatally acquired HCV infection by assessing the impact and cost-effectiveness of several strategies: a single HCV RNA test during age 2–6 months of age compared with anti-HCV

with reflex to HCV RNA at age 18 months or later; each testing approach among children with known perinatal HCV exposure was compared with universal screening among all children.

Methods

We used a decision analysis framework to compare testing strategies for a cohort of US infants born in 2021. Primary considerations for defining each strategy were timing of testing and type of test used. We defined four testing strategies based on combinations of the type of test, including anti-HCV, HCV RNA, and anti-HCV with reflex to HCV RNA, and timing of test at either age 2–6 months or age 18 months or older. Estimates for sensitivity and specificity of each type of test came from published studies[19,21]. Although some previous recommendations suggest the use of two HCV RNA tests in order to capture transient viremia, we modeled the use of a single HCV RNA test because assays currently used in the United States have greatly improved and now routinely detect HCV viral loads of 15 I.U./ml or less[22]. We modeled these strategies: Anti-HCV with reflex to HCV RNA at 18 months among children known to be perinatally exposed (i.e., baseline comparison strategy); HCV RNA testing at 2–6 months among children known to be perinatally exposed (Test Strategy 1); universal anti-HCV with reflex to HCV RNA at 18 months among all children (Test Strategy 2); universal HCV RNA testing at 2–6 months among all infants (Test Strategy 3).

Epidemiologic Inputs

Epidemiologic inputs used to define each strategy are in Table 1. The distinction between universal testing strategies and testing strategies among children with known perinatal exposure is the proportion of HCV-infected pregnant persons that are screened during pregnancy. We conducted a systematic review of studies from 2001 to 2021 to identify the prevalence of HCV testing in pregnancy, and rates of testing, transmission, and loss to follow-up among perinatally exposed children. In base case analyses, we utilized data from that review and assumed 0.64% of births occur among persons infected with HCV and that 44.7% of those pregnant persons are screened for HCV infection[23]. Considering this estimate is changing because of a recent recommendation to test all pregnant persons for HCV infection, we conducted several sensitivity analyses to account for expected increases in testing (described below). Additionally, we modeled two points for potential loss to follow-up. First, not all children born to HCV-infected persons receive HCV testing and this differs based on the age of child at which testing is conducted. Second, the opportunity for testing differs between children born to HCV-infected persons and those born to persons without HCV infection because probability of attendance at well childcare visits for the children will vary during age 2–6 months and age 18 months or older. For children with perinatal exposure to HCV, probability of a child being tested was defined as 73.5% for children tested at age 2–6 months and as 43.0% for children tested at age 18 months or older[24]. For children without perinatal exposure to HCV, probability of child testing was defined as 85.0% for children tested at age 2–6 months and as 75.0% for children tested at age 18 months or older[25].

Analytic Model

We analyzed the costs and health outcomes of all strategies using a decision tree model (Figure 2; online) with a Markov model of hepatitis C disease progression in TreeAge Pro 2022. We utilized microsimulation to model trials that represent individual children and each trial resulted in either having a documented HCV infection or healthy life (mutually exclusive) prior to entering the Markov stages. Trials that entered a healthy life process were assumed to never acquire an HCV infection and experienced age-specific annual probability of death as defined by the National Vital Statistics System 2018 US Life Tables[26]. All trials that experienced a documented HCV infection entered a Markov process that was adapted from a previously published model of HCV progression among persons infected as infants[27] which included health states that represent acute and chronic HCV infection, potential treatment and advanced liver disease states (Table 1). We assumed 20% of children with a perinatally acquired infection experienced spontaneous clearance[28] and that all children with infections that were identified in each testing strategy were subsequently linked to treatment at 3 years of age. Trials that had perinatally acquired infections that were not tested and identified in the respective strategy were assumed to not be diagnosed or treated later in life.

The time step for the Markov processes was 1 year and trials accumulated costs and quality-adjusted life years (QALYs) for the lifetime of the cohort. Additionally, we modeled several epidemiologic outcomes among children with perinatally acquired infections, including number of diagnosed HCV infections, treated/cured HCV infections, hepatocellular carcinoma cases, liver transplants and liver-related deaths. We used a limited societal perspective[29,30] that included costs associated with HCV testing and all direct medical costs related to HCV infection and resulting sequelae in 2021 US Dollars (USDs; Table 1). The cost of an anti-HCV test (CPT: 86803) was $14.27 (range: $10.80 to $17.80) and the cost of an HCV RNA test (CPT: 87522) was $42.84 (range: $32.10 to $53.60). All annual health state costs were from a previously published model[31] and converted to 2021 USD using the Medical Care Consumer Price Index (CPI)[32,33]. We estimated cost of treatment to be $70,200 per regimen (range: $7,338 to $94,500), which was the average commercial prices of the three most commonly used treatment regimens (Glecaprevir-pibrentasvir, Sofosbuvir-velpatasvir, and Ledipasvir-sofosbuvir)[34]. Effectiveness was quantified using QALYs, which were estimated by using previously published utility weights[27]. All costs and utilities were discounted at 3% per year and the analytic horizon was the lifetime of the cohort.

Analysis

We estimated average cost and average QALYs per trial for each strategy and compared strategies by calculating incremental cost-effectives ratios (ICERs) and cost per additional diagnosed pediatric infection. Additionally, assuming an annual total of 3.6 million births[35] with 0.64% occurring among pregnant persons with an HCV infection[23], we estimated population-level results for a cohort of 23,040 perinatally exposed children. The base case analysis included the most plausible point estimate for each model input.

sensitivity analyses

we conducted a one -way interval sensitivity analysis on the proportion of pregnant persons that are screened for HCV infection, which is the distinguishing input between the universal

testing strategies and the comparable strategies that test infants with known exposure. Base case value for this input (44.7%) is informed by a systematic review of available data[23], but this value is widely expected to increase as uptake improves for the 2020 recommendation for HCV screening [36]. we conducted a probabilistic sensitivity analysis to evaluate the combined uncertainty of all model inputs. Finally, we conducted a scenario analysis that utilizes recently published data on vertical transmission of HCV infection and timing of clearance among children with perinatally-acquired infection[5,6]. These studies, which were published after our analytic work began, report data from three prospective European cohorts. We conducted a scenario sensitivity analysis that assumed 7.2% of perinatally-exposed infants acquired HCV infection[6] and 20.9% of children with HCV infections that were treated at three years of age would have spontaneously cleared their infection without treatment[5].

Results

Compared with the baseline comparison strategy each of the three alternative testing strategies resulted in an increased number of children tested and improved health outcomes (Table 2). Additionally, Test Strategy 1, representing the testing of known HCV perinatally exposed children at age 2–6 months with an HCV RNA test, was cost-saving compared with the baseline comparison strategy, with a population-level difference in cost of $469,671. Compared with the baseline comparison strategy, each of the two universal testing strategies resulted in an increase in QALYs and an increase in total costs. Test Strategy 2, representing universal testing of children at age 18 months or older with anti-HCV and reflex to HCV RNA test, increased population-level costs by over $38 million (ICER=26,105) and Test Strategy 3, representing universal testing of children at age 2–6 months with HCV RNA test, increased population-level costs by over $129 million (ICER=35,887), compared with the baseline comparison strategy.

One-way interval sensitivity analysis on the proportion of pregnant persons screened for HCV infection indicated that Test Strategy 1, testing of known HCV perinatally exposed children at age 2–6 months with an HCV RNA test, was cost-saving and resulted in improved health outcomes in all scenarios. Additionally, as a higher proportion of pregnant persons were screened, the cost per unit of beneficial health outcomes increased in the two universal testing scenarios (Figure). Population-level results for two scenarios that assume 65% and 90% of pregnant persons are screened for HCV infection are presented in Table 4 (online). A comparison of the two universal testing strategies (Test Strategy 2 and Test Strategy 3) against Test Strategy 1 at different assumptions of the percent of persons screened for HCV infection is presented in Table 3. Compared with Test Strategy 1, universal testing of children with anti-HCV tests at 18 months results in higher costs and fewer QALYs in all scenarios in which at least 60% of pregnant persons are screened for HCV infection. Results from the probabilistic sensitivity analysis on all model inputs are presented in Table 5 (online). Notably, across all model runs, Test Strategy 1 was dominant over the baseline comparison strategy, resulting in lower cost and improved health outcomes. Population-level results from the scenario sensitivity analysis assuming higher rates of vertical transmission and clearance are presented in Table 6 (online). In this scenario

analysis, Test Strategy 1 identified 76% more documented HCV infections and had an ICER of $455, compared with the baseline comparison strategy.

Discussion

The objective of this modeling study was to identify the optimal testing strategy that should be used to diagnose perinatally acquired HCV infections. All three comparison strategies resulted in more children tested and better population-level health outcomes including fewer cases of hepatocellular carcinoma, decompensated cirrhosis, liver transplants, and HCV-related deaths, compared with the currently accepted standard of anti-HCV testing at age 18 months or older. Testing of known perinatally exposed children at age 2–6 months with an HCV RNA test compared with the baseline strategy resulted in population-level cost-savings of $469,671. As expected, more testing in each of the universal comparison strategies resulted in increased QALYs, but also over $38 million in increased population-level costs for anti-HCV with reflex to HCV RNA at age 18 months or older and over $129 million in increased population-level costs for testing of all children at age 2–6 months with an HCV RNA test. As uptake of testing recommendations for HCV infection during pregnancy continues to increase, the difference in the number of infections identified between universal testing strategies and testing children with known exposure will continue to decline.

These analyses indicate the optimal timing and most efficient test is a single HCV RNA during age 2–6 months among children perinatally exposed to HCV. Factors driving these results include pediatric loss to follow up, , high attendance at well-child visits in the first 6 months of life, and highly sensitive nucleic acid testing with reliable results starting at age two months. Testing further from birth is associated with loss to follow up and may reduce the likelihood that perinatal exposure will be documented in the child's medical record (e.g., change of providers, loss of custody etc.). This is especially true as HCV-exposed children are disproportionately publicly insured, and infants born to HCV-infected mothers are more likely to be involved with child services and foster care[17,37,38]. One study assessing >150,000 children at two health networks spanning 20 states, determined children rarely missed 2-month, 4-month, and 6-month well-care visits, while 15-month and 18-month visits were attended by less than half of publicly insured children[13]. With advancements in analytical sensitivity allowing detection of low-level viremia, nucleic acid testing for diagnosis of perinatally acquired HCV infection in early infancy provides excellent diagnostic performance[19,22].

. Among exposed children, the increased number of children diagnosed with a single HCV RNA at younger ages with the 2–6 month strategy was cost-saving and had corresponding improved health outcomes, compared with the widely recommended 18 month strategy using anti-HCV with reflex to HCV RNA. The success of these strategies relies heavily on widespread testing during pregnancy and transfer of information to providers caring for infants. Updated CDC hepatitis C screening guidelines call for testing of all pregnant people during each pregnancy but testing currently remains below 50%[39]. At current levels of HCV testing among pregnant persons, a universal approach using anti-HCV testing at 18 months or older costs an additional $142,764 per infection diagnosed, and HCV RNA testing at 2–6 months an additional $187,561 per infection diagnosed, compared with testing known

exposed children with an HCV RNA test at age 2–6 months. As the proportion of pregnant persons tested approaches 90%, universal testing strategies result in diminishing return with costs per additional diagnosed infection increasing to $705,403 for anti-HCV testing, and $273,813 for HCV RNA testing. Cost per additional diagnosed pediatric infection for either universal strategy become prohibitive as the proportion of pregnant persons screened for HCV infection exceeds 70%.

Results of this analysis should be interpreted with a few limitations. First, there are limited data on the proportion of infants with perinatal exposure that would be tested at 2-6 months and 18 months. Inputs were based on a single study of infant follow-up at each time period and may not be generalizable to all settings. Second, we only quantified costs and health outcomes among children. We did not quantify any potential costs or benefits that would be gained by the resulting diagnosis and treatment of a birthing parent because of identifying an HCV infection in their child. Additionally, we assumed perinatally-acquired infections undiagnosed in childhood would not be diagnosed and treated later in life, which may result in an overestimate of poor outcomes among persons with undiagnosed perinatal infections. Third, to align with current recommendations[7,10] we assumed treatment occurs at or after age 3 years in all strategies and there was no difference in linkage to treatment or costs associated follow-up testing that providers may recommend prior to 3 years of age. Evaluating approaches in which treatment was initiated at different ages was outside of the scope of this study, which focused on testing strategies. Fourth, the model of HCV disease progression does not include coinfections with HIV, hepatitis B, or other infections, which could alter quality (and length) of life, progression of HCV infection, and associated medical costs. Finally, for universal testing strategies, we did not model program implementation costs that would likely be incurred in such a large scale up of HCV testing, which results in an underestimate of total costs for the universal strategies.

. Identifying optimal strategies for diagnosis of perinatally infected children that are cost-effective are essential for preventing morbidity and mortality associated with complications from perinatal HCV infection, improving individual and population health outcomes, and achieving national hepatitis C elimination goals.

Acknowledgements:

Abbreviations:

HCV	hepatitis C virus (HCV)
RNA	Ribonucleic acid
anti-HCV	hepatitis C virus antibodies

ICER	incremental cost-effectiveness ratio
USD	United States Dollar
QALY	quality-adjusted life years

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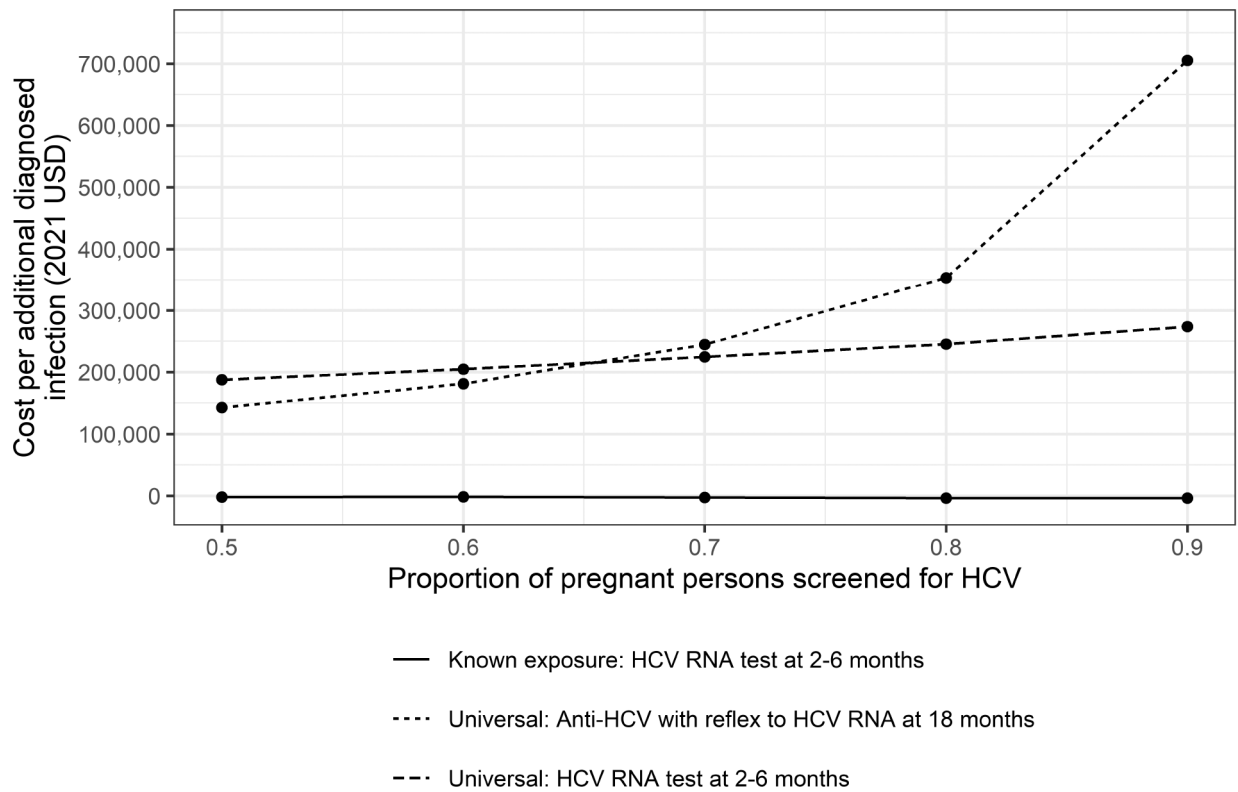
Sensitivity analysis results: Cost (in 2021 USD) per additional diagnosed infection, by strategy and proportion of pregnant persons screened for HCV, compared with anti-HCV with reflex to HCV RNA testing at 18 months among infants with known exposure, United States, 2022. As a higher proportion of pregnant persons were screened, the cost per additional diagnosed infection increased in the two universal testing scenarios.
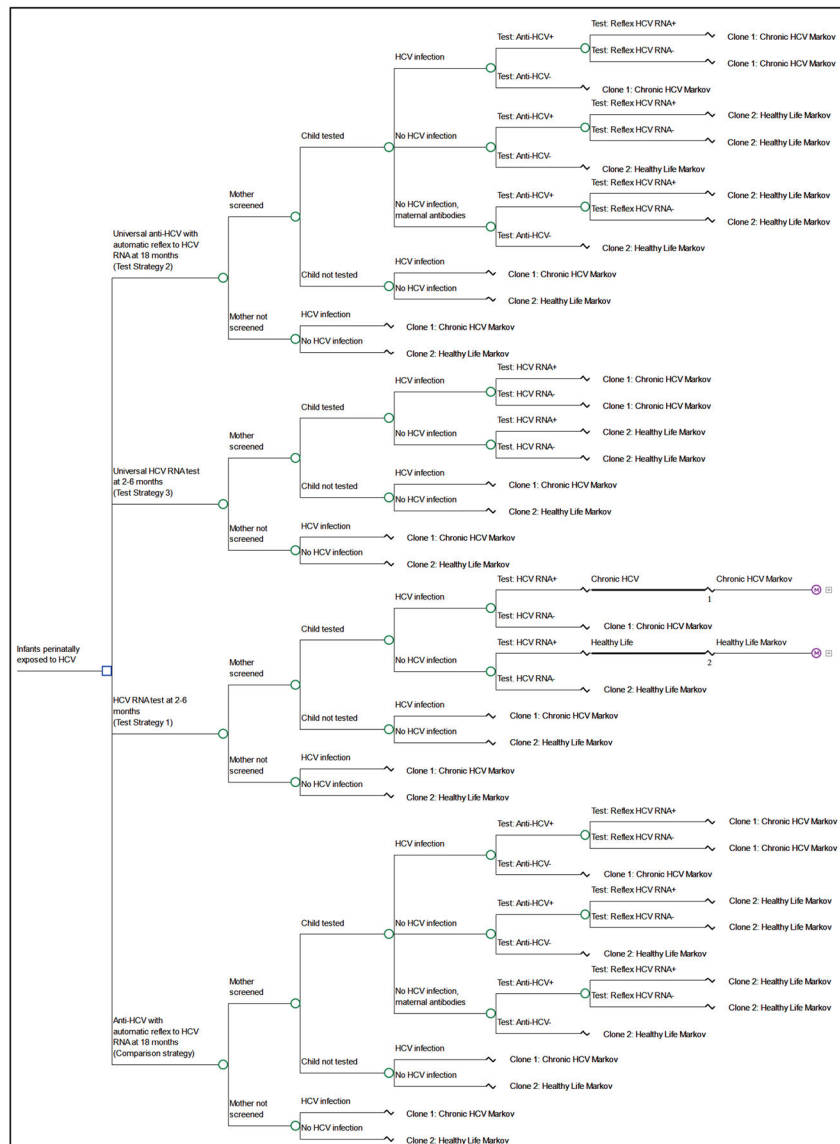
Figure 2.
Decision Tree used in cost-utility analysis of testing approaches for children perinatally exposed to hepatitis C virus, United States, 2022

Table 1.

Epidemiologic inputs, annual transition rates, health state utility values and health state costs used in cost-effectiveness analysis of testing approaches for infants perinatally exposed to hepatitis C virus, United States, 2022

|		Base Case	Lower-Upper	Source
Strategies: Anti-HCV with reflex to HCV RNA at 18				
P HCV RNA+ among pregnant persons (%)		0.64	0.32 – 1.28	22
P of HCV RNA+ pregnant persons screened (%)		44.7	25.0 – 65.0	23
P of infant being tested (no perinatal exposure; %)		75.0	65.0 – 85.0	25
P of infant being tested (perinatal exposure; %)		43.0	35.0 – 52.0	24
P of HCV infection among infants perinatally exposed (%)		5.8	4.2 - 7.8	3
Anti-HCV sensitivity (18 mo; %)		98.1	92.6 – 99.7	21
Anti-HCV specificity (18 mo; %)		99.8	99.2 – 99.9	21
P of maternal antibodies (18 mo; %)		1.6	0.5 – 4.5	12
Reflex HCV RNA sensitivity (18 mo; %)		100	87.5 – 100	19
Reflex HCV RNA specificity (18 mo; %)		100	98.3 –100	19
P of Spontaneous clearance (%)		20.0	15.0 –25.0	28
P of SVR among treated (%)		99	92.4 –100	27
Strategies: HCV RNA test at 2–6 months				
P HCV RNA+ among pregnant persons (%)		0.64	0.32 – 1.28	23
P of HCV RNA+ pregnant persons screened (%)		44.7	25.0 – 65.0	23
P of infant being tested (no perinatal exposure; %)		85.0	75.0 – 95.0	25
P of infant being tested (perinatal exposure; %)		73.5	68.0 - 81.0	24
P of HCV infection among infants perinatally exposed (%)		5.8	4.2 – 7.8	3
RNA test sensitivity (2–6 mo; %)		100	87.5 – 100	19
RNA test specificity (2–6 mo; %)		100	98.3 – 100	19
P of Spontaneous clearance (%)		20.0	15.0 – 25.0	28
P of SVR among treated (%)		99.0	92.4 – 100	27
Testing Cost Inputs (in 2021 USD)				
Anti-HCV test (CPT: 86803)		14.27	10.8 – 17.8	40
HCV RNA quantitative PCR (CPT: 87522)		42.84	32.1 – 53.6	40
Annual Health State Transition Rates				
From:	*To:*			
Chronic HCV (<18 years)	Compensated cirrhosis	0.0018	0.001-0.110	31
Chronic HCV (18+ years)	Compensated cirrhosis	0.110	0.075-0.133	31
Compensated cirrhosis	Decompensated cirrhosis	0.035	0.027-0.043	27
Compensated cirrhosis	HCC	0.024	0.018-0.031	27
Decompensated cirrhosis	HCC	0.068	0.030-0.083	27
Decompensated cirrhosis	Liver transplant	0.033	0.017-0.049	27
Decompensated cirrhosis	Liver-related death	0.216	0.162-0.270	27
HCC	Liver transplant	0.033	0.017-0.049	27
HCC	Liver-related death	0.411	0.310-0.510	27

		Base Case	Lower-Upper	Source
Liver transplant	Post liver transplant	0.857	0.841-0.876	27
Liver transplant	Liver-related death	0.143	0.124-0.159	27
Post liver transplant	Liver-related death	0.034	0.024-0.043	27
Health State Utility Values				
Chronic HCV		0.806	0.767-0.845	27
Compensated cirrhosis		0.726	0.680-0.772	27
Decompensated cirrhosis		0.657	0.602-0.711	27
Hepatocellular carcinoma		0.717	0.647-0.788	27
Liver transplant		0.500	0.720-0.840	31
Post liver transplant		0.712	0.657-0.767	27
HCV cured (SVR)		0.841	0.801-0.880	27
Annual Health State Costs (2021 USD)				
Chronic HCV		882	682-1,138	31,32
Compensated cirrhosis		1,678	1,299-2,166	31,32
Decompensated cirrhosis		22,619	1,350-39,176	31,32
Hepatocellular carcinoma		47,612	27,488-82,467	31,32
Liver transplant		222,824	128,649-385,940	31,32
Post liver transplant		40,243	23,234-69,702	31,32
Cost of treatment		70,200	7,338-94,500	34

Abbreviations: HCV, hepatitis C virus; anti-HCV, hepatitis c virus antibody; P, probability; SVR, sustained virologic response; USD, United States Dollars; CPT, Current Procedural Terminology; CMS CLFS, Centers for Medicare and Medicaid Services Clinical Laboratory Fee Schedule; mo, months; HCC, hepatocellular carcinoma; SVR, sustained virologic response. Notes: Annual health state costs include all costs associated with HCV-related medical care.

Table 2.

Base case population-level results[1] for HCV testing strategies among a cohort of infants, United States, 2022

Outcome	Testing among known exposed[2]		Universal testing of all infants	
	Anti-HCV with reflex to HCV RNA at 18 months[3] (Comparison)	HCV RNA test at 2–6 months[4] (Test Strategy 1)	Anti-HCV with reflex to HCV RNA at 18 months[3,5] (Test Strategy 2)	HCV RNA test at 2–6 months[4,6] (Test Strategy 3)
Total costs (2021 USD)	77,621,446	77,151,775	116,433,899	207,170,025
Testing outcomes				
Tested infants	4,478	7,588	2,709,916	3,076,918
Anti-HCV tests	4,478	0	2,709,916	0
HCV RNA tests	330	7,588	6,120	3,076,918
Epidemiologic outcomes among perinatally exposed infants				
Diagnosed HCV infections	254	443	553	971
Hepatocellular carcinoma cases	419	342	316	151
Decompensated cirrhosis cases	463	388	334	157
Liver transplants	74	62	58	28
HCV Liver-related deaths	758	626	550	259
Treated/cured HCV infections	196	347	438	775
Total QALYs	693,059	694,026	694,546	696,669
Total Life-years	1,807,109	1,812,187	1,814,939	1,826,061

[1] Assumes 3.6 million births with 0.64% of births occurring among persons who are HCV RNA+.

[2] Assumes 44.7% of all pregnant persons are screened for HCV infection.

[3] Assumes 43.0% of infants born to HCV RNA+ pregnant persons attend an 18-month visit.

[4] Assumes 73.5% of infants born to HCV RNA+ pregnant persons attend a 2–-6 month visit.

[5] Assumes 75.0% of infants born to pregnant persons without HCV attend an 18-month visit.

[6] Assumes 85.0% of infants born to pregnant persons without HCV attend a 2–6 month visit.

Abbreviations: HCV, hepatitis C virus; anti-HCV, hepatitis C virus antibody; USD, United States Dollars; QALYs, quality-adjusted life-years.

Table 3.

Sensitivity analysis results: Incremental cost-effectiveness ratios for HCV infant testing strategies versus HCV RNA testing at 2–6 months for infants with known exposure, by proportion of pregnant persons that are screened for HCV infection, United States, 2022

Proportion of pregnant persons screened for HCV	Strategy (reference=Known exposure: HCV RNA test at 2–6 months)		
	Known exposure: Anti-HCV with reflex to HCV RNA at 18 months (Test Strategy 1)	Universal testing: Anti-HCV with reflex to HCV RNA at 18 months (Test Strategy 2)	Universal testing: HCV RNA test at 2–6 months (Test Strategy 3)
0.50	More expensive, fewer QALYS	129,476	53,665
0.55	More expensive, fewer QALYS	569,548	59,532
0.60	More expensive, fewer QALYS	More expensive, fewer QALYS	67,746
0.65	More expensive, fewer QALYS	More expensive, fewer QALYS	76,727
0.70	More expensive, fewer QALYS	More expensive, fewer QALYS	92,427
0.75	More expensive, fewer QALYS	More expensive, fewer QALYS	113,463
0.80	More expensive, fewer QALYS	More expensive, fewer QALYS	139,075
0.85	More expensive, fewer QALYS	More expensive, fewer QALYS	197,018
0.90	More expensive, fewer QALYS	More expensive, fewer QALYS	292,229
0.95	More expensive, fewer QALYS	More expensive, fewer QALYS	661,659

Notes: The reference strategy is HCV RNA testing at 2–6 months among infants with known exposure. Assumes 43.0% of infants born to HCV RNA+ pregnant persons attend an 18-month visit. Assumes 73.5% of infants born to HCV RNA+ pregnant persons attend a 2–6 month visit. Assumes 75.0% of infants born to pregnant persons without HCV attend an 18-month visit. Assumes 85.0% of infants born to pregnant persons without HCV attend a 2–6 month visit.

Table 4.

Population-level results[1] for HCV testing strategies among a cohort of children, by proportion of pregnant persons screened for HCV infection, United States, 2022.

| Outcome | Universal testing of all infants | | 44.7% of pregnant persons screened (base case) | | Testing known exposed | | | |
| | | | | | 65% of pregnant persons screened | | 90% of pregnant persons screened | |
	Anti-HCV with reflex to HCV RNA at 18 months[2,4] (Comparison)	HCV RNA test at 2-6 months[3,5] (Test Strategy 1)	Anti-HCV with reflex to HCV RNA at 18 months[2] (Test Strategy 2)	HCV RNA test at 2-6 months[3] (Test Strategy 3)	Anti-HCV with reflex to HCV RNA at 18 months[2] (Test Strategy 2)	HCV RNA test at 2-6 months[3] (Test Strategy 3)	Anti-HCV with reflex to HCV RNA at 18 months[2] (Test Strategy 2)	HCV RNA test at 2-6 months[3] (Test Strategy 3)
Total costs (2021 USD)	116,433,899	207,170,025	77,621,446	77,151,775	77,383,912	76,635,250	77,590,443	76,244,415
Testing outcomes								
Tested infants	2,709,916	3,076,918	4,478	7,588	6,466	10,993	8,918	15,221
Anti-HCV tests	2,709,916	0	4,478	0	6,466	0	8,918	0
HCV RNA tests	6,120	3,076,918	330	7,588	470	10,993	649	15,221
Epidemiologic outcomes among perinatally exposed infants								
Diagnosed HCV infections	553	971	254	443	362	632	498	875
HCC cases	316	151	419	342	382	275	334	185
DCC cases	334	157	463	388	416	305	356	197
Liver transplants	58	28	74	62	68	50	62	34
HCV Liver-related deaths	550	259	758	626	684	496	588	327
Treated/cured HCV infections	438	775	196	347	284	501	393	698
Total QALYs	694,546	696,669	693,059	694,026	693,590	694,967	694,319	696,221
Total Life-years	1,814,939	1,826,061	1,807,109	1,812,187	1,809,846	1,817,052	1,813,710	1,823,653

[1] Assumes 3.6 million births with 0.64% of births occurring among pregnant persons who are HCV RNA+.

[2] Assumes 43.0% of children born to HCV RNA+ pregnant persons attend an 18-month visit.

[3] Assumes 73.5% of children born to HCV RNA+ pregnant persons attend a 2-6 month visit.

[4] Assumes 75.0% of children born to pregnant persons without HCV attend an 18-month visit.

[5] Assumes 85.0% of children born to pregnant persons without HCV attend a 2-6 month visit.

Abbreviations: HCV, hepatitis C virus; anti-HCV, hepatitis C virus antibody; USD, United States Dollars; HCC, hepatocellular carcinoma; DCC, decompensated cirrhosis; QALYs, quality-adjusted life-years.

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Table 5.

Probabilistic sensitivity analysis[1] population-level results[2] for HCV testing strategies among a cohort of children, United States, 2022

Outcome	Testing known exposed children		Universal testing of all children	
	Anti-HCV with reflex to HCV RNA at 18 months (Comparison)	HCV RNA test at 2-6 months (Test Strategy 1)	Anti-HCV with reflex to HCV RNA at 18 months (Test Strategy 2)	HCV RNA test at 2-6 months (Test Strategy 3)
	median (95% CI)	median (95% CI)	median (95% CI)	median (95% CI)
Total costs (2021 USD)	90,963,369 (66,954,031 – 132,947,567)	87,229,844 (61,499,748 – 126,163,535)	118,280,437 (87,224,385 – 169,656,366)	191,266,412 (130,885,944 – 295,828,495)
Testing outcomes				
Tested infants	4,602 (3,046 – 6,151)	7,787 (5,338 – 10,585)	2,477,119 (1,517,732 – 4,385,218)	2,742,208 (1,672,632 – 5,055,815)
Anti-HCV tests	4,602 (3,046 – 6,151)	0 (0 - 0)	2,477,119 (1,517,732 – 4,385,218)	0 (0 - 0)
HCV RNA tests	358 (222 - 523)	7,851 (5,371 – 10,680)	8,652 (3,775 – 21,498)	2742208 (1,672,632 – 5,055,815)
Epidemiologic Outcomes among infants born to HCV-infected persons				
Diagnosed HCV infections	248 (154 - 340)	439 (289 - 630)	526 (416 - 701)	939 (754 - 1159)
HCC cases	434 (320 - 554)	359 (255 - 500)	330 (250 - 426)	178 (119 - 252)
DCC cases	493 (377 - 635)	408 (290 - 537)	358 (275 - 481)	183 (122 - 260)
Liver transplants	85 (57 - 127)	71 (47 - 110)	63 (41 - 94)	33 (17 - 51)
Liver-related deaths	815 (627 - 992)	668 (486 - 886)	606 (463 - 765)	311 (213 - 423)
Treated/cured HCV infections	196 (120 - 269)	348 (233 - 501)	423 (326 - 557)	758 (598 - 925)
Total QALYs	691,004 (686,437 – 694,672)	692,111 (688,277 – 695,554)	692,862 (689,224 – 696,127)	695,510 (692,364 – 698,273)
Total Life-years	1,799,819 (1,787,793 – 1,811,646)	1,806,173 (1,793,694 – 1,815,681)	1,809,147 (1,800,278 – 1,818,163)	1,821,715 (1,814,756 – 1,827,927)

[1] A triangle distribution was defined for each input, with the base case value set as the distribution mean and the upper and lower limits set as the bounds of the distribution. We sampled 100 input parameter sets and ran 100,000 microsimulation trials with each parameter set. For all outcomes, we report the median and 95% interval (2.5th and 97.5th percentile) from the probabilistic sensitivity analysis results.

[2] Assumes 3.6 million births.

Abbreviations: HCV, hepatitis C virus; anti-HCV, hepatitis C virus antibody; HCC, hepatocellular carcinoma; DCC, decompensated cirrhosis; USD, United States Dollars; QALYs, quality-adjusted life-years.

Table 6.

Population-level results[1] from a scenario sensitivity analysis using data from Ades et al[2] for HCV testing strategies among a cohort of children, United States, 2022.

Outcome	Testing known exposed children[3]		Universal testing of all children	
	Anti-HCV with reflex to HCV RNA at 18 months[4] (Comparison)	HCV RNA test at 2-6 months[5] (Test Strategy 1)	Anti-HCV with reflex to HCV RNA at 18 months[4,6] (Test Strategy 2)	HCV RNA test at 2-6 months[5,7] (Test Strategy 3)
Total costs (2021 USD)	80,058,982	82,265,899	122,475,587	219,378,669
Testing outcomes				
Tested children	4,478	7,588	2,709,916	3,076,918
Anti-HCV tests	4,478	0	2,709,916	0
HCV RNA tests	391	7,588	6,254	3,076,918
Epidemiologic outcomes among perinatally exposed children				
Diagnosed HCV infections	315	555	690	1,214
HCC cases	410	335	306	146
DCC cases	449	375	322	151
Liver transplants	75	62	55	27
HCV Liver-related deaths	736	607	533	251
Treated/cured HCV infections	489	637	724	1,052
Total QALYs	691,536	692,465	692,998	695,033
Total Life-years	1,807,966	1,812,814	1,815,616	1,826,263

[1] Assumes 3.6 million births with 0.64% of births occurring among persons who are HCV RNA+.

[2] Assumes prevalence of HCV infection among children perinatally exposed is 7.2% and 20.9% of children that are treated at age 3 would have spontaneous cleared infection without treatment.

References:

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[3] Assumes 44.7% of all pregnant persons are screened for HCV infection.

[4] Assumes 43.0% of children born to HCV RNA+ pregnant persons attend an 18-month visit.

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[5]Assumes 73.5% of children born to HCV RNA+ pregnant persons attend a 2–6 month visit.

[6]Assumes 75.0% of children born to pregnant persons without HCV attend an 18-month visit.

[7]Assumes 85.0% of children born to pregnant persons without HCV attend a 2–6 month visit.

Abbreviations: HCV, hepatitis C virus; anti-HCV, hepatitis C virus antibody; HCC, hepatocellular carcinoma; DCC, decompensated cirrhosis; USD, United States Dollars; QALYs, quality-adjusted life-years.