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UNIVERSITY OF CALIFORNIA SAN DIEGO

Assessing the cost-effectiveness of universal pediatric screening for hepatitis C virus infection

A thesis submitted in partial satisfaction of the requirements for the master's degree

in

Public Health

by

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The Thesis of Melissa Choz is approved, and it is acceptable in quality and form for publication on microfilm and electronically

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TABLE OF CONTENTS

LIST OF ABBREVIATIONS

AASLD	American Association for the Study of Liver Diseases
IDSA	Infectious Diseases Society of America
CDC	Center of Disease Control
DAAs	Direct-Acting Antivirals
HCV	Hepatitis C Virus
HCC	Hepatocellular Carcinoma
HIV	Human Immunodeficiency Virus
HBV	Hepatitis B Virus
ICER	Incremental cost-effectiveness ratio
IDU	Injection Drug Use
PCR	Polymerase Chain Reaction
QALY	Quality-adjusted life years
RNA	Ribonucleic Acid
SVR	Sustained Virus Response
SOC	Standard of Care
WHO	World Health Organization

LIST OF FIGURES

LIST OF TABLES

ABSTRACT OF THE THESIS

Assessing the cost-effectiveness of universal pediatric screening for Hepatitis C Virus

by

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Master of Public Health

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Hepatitis C Virus (HCV) is a flavivirus that can cause both acute and chronic infections which, if untreated, can progressively lead to liver damage, liver cirrhosis, and hepatocellular carcinoma (HCC). With the recent opioid epidemic in the US, there has been an increase in cases

of HCV in both the adult and adolescent populations. This has resulted in an increase in HCV infections in women of childbearing age, and mother-to-child transmission occurs in 2-7% of pregnancies in women who are HCV-infected. Approximately 40% of children with chronic HCV infection are expected to clear the virus, and the remainder will develop a chronic infection that will persist into adulthood if untreated [3]. The American Association for the Study of Liver Diseases (AASLD) currently recommends Direct-Acting Antivirals (DAAs) to treat chronic HCV infection for all children 3 years of age and older, which cures >90% of individuals. However, current risk-based screening strategies (children born to mothers diagnosed with HCV, followed by a 1-time universal screening above age 18) among children born to mothers with HCV are inadequate in identifying the majority of children born with HCV. We conducted a cost-effectiveness analysis of universal HCV screening among children at age 2 compared to the status quo- risk-based screening in the U.S.

Introduction

HCV is a small single-stranded RNA flavivirus that can cause both acute and chronic infections ranging in severity from asymptomatic to life-threatening illnesses such as liver cirrhosis and hepatocellular carcinoma (HCC). It has become one of the main contributors to the global burden of liver-related morbidity and mortality and is responsible for an estimated 27% of cirrhosis and 25% of HCC cases worldwide[4]. The World Health Organization (WHO) recently estimated that 58 million people have chronic HCV infection, and approximately 1.5 million new infections occur annually (World Health Organization, 2022). It is estimated that 3.2 million adolescents and children are currently living with chronic HCV in the world. Additionally, the WHO estimated that in 2019, approximately 290, 000 people died from HCV infection, primarily from cirrhosis and HCC (World Health Organization, 2022).

HCV transmission routes

Parenteral exposure underlies transmission in the United States, with injecting drug use and high-risk sexual practices being the most common method of transmission in adults. With the recent opioid epidemic in the United States, there has been an increase in cases of HCV in both adult and adolescent populations, causing the incidence to triple from 2011 to 2016, and a four-fold increase in cases (or new infections?) among young adults. In children, vertical transmission is responsible for approximately 60% of infections. In the United States, 1-2.5% of pregnant women are estimated to be infected, and this has been increasing over the past decade among those who use opioids[5].. This has resulted in approximately 42,000 pregnancies and 29,000 births among HCV-infected women annually (AASLD, 2022).

HCV natural history

HCV infection is a major cause of chronic liver disease associated with morbidity and mortality globally. Spontaneous clearance of acute HCV infection generally occurs within 6 months of infection in around 30% of cases in adults, when not treated. After vertical transmission of HCV, between 25-40% of infected children will spontaneously clear the infection within the first 4 years of life. The exact mechanism of spontaneous clearance is not fully understood but may be related to viral genotype, host, and immune factors [1].

HCV infection is known to be a slowly developing infection, usually with minimal symptoms. However, when present it is characterized by nonspecific viral symptoms such as fever, myalgia, and fatigue. Those who are not able to clear the infection usually show fluctuating levels of serum aminotransferase levels, and over several decades can result in the gradual progression of liver disease with risks of developing cirrhosis [1]. The time between HCV infection and disease development in children varies and the development of severe disease is most likely to occur about 2 to 3 decades after infection [4]. Overall, if left untreated, the 20-year cumulative incidence of developing cirrhosis is 15–30%, and the risk of developing HCC is 2–4% per year in people with cirrhosis [3]. Some risk factors and comorbidities that are associated with increased severity of the disease include older age at onset, the longevity of the infection, obesity, homelessness or incarceration, history of childhood cancer, anemias requiring chronic transfusions, concomitant alcohol use, IDU, and coinfections with HIV or hepatitis B virus (HBV). HCV infections are usually asymptomatic early on?, making it much more critical to screen and be able to identify individuals who are infected and possibly at high risk for other severe diseases and able to receive adequate treatment [1].

With the rising prevalence and silent transmission of infection, prevention is critical to identify people living with chronic HCV, which can be done through universal screening strategies. The American Academy of Pediatrics recommends that an anti-HCV antibody screening at 18 months of age is done, if positive, then it should be confirmed with a polymerase chain reaction (PCR) test after 3 years of age. Siblings of children with vertically acquired HCV infection, born through the same mother, should also be tested. It is recommended that adults take a one-time anti-HCV antibody test for all adults including pregnant women[5].

HCV Treatment:

Treatment of HCV has improved over the last 3 decades with the creation of direct acting antiviral agents (DAAs). Before DAAs, the only treatments were interferon-based regimens. These treatments required 24-48 weeks of therapy, through subcutaneous administration, and continuous monitoring due to side effects, and most importantly suboptimal sustained virological response rates. DAAs were FDA-approved for adults in 2011 and are now considered the standard care for HCV infection. Currently, multiple versions have improved ease of administration, tolerance, and viral clearance. For children, the safety and efficacy of DAAs were established in 2016. Findings revealed a sustained viral suppression response at 12 weeks posttreatment in 98% of the participants, with no virological failure or serious adverse events reported. In 2019, the first DDA treatment for children ages 3 and up, was FDA-approved. Now there are multiple FDA-approved options available to treat children as young as 3 years of age that cover all genotypes of HCV[2].

The American Association for the Study of Liver Diseases and the Infectious Diseases Society of America (AASLD-IDSA) recommends treating chronic HCV infection with a DAA combination for all children 3 years of age and older. This is based on the longevity of children

who have a lifetime risk for the development of complications of chronic HCV, this accounts for the development of cirrhosis and hepatocellular carcinoma, along with the potential for viral transmission to other people [1]. This amazing advancement in therapeutics for chronic HCV infection has made the eradication of the HCV virus an attainable goal. However, the new challenge globally is finding effective diagnostics to help identify cases efficiently and link them to treatments with affordability and accessibility.

HCV screening in the United States and current gaps

The AASLD and the CDC have recently recommended universal screening during pregnancy [6], a 1-time universal screening for adults aged 18 and older, risk-based screening of children born to mothers with HCV, and routine screening of those with ongoing risk such as people who inject drugs. However, since the change to universal screening during pregnancy, only 45% of women are screened during pregnancy. Additionally, many infants born to mothers with HCV are not screened. For children born to HCV-infected mothers, the CDC recommends that they be tested for HCV via RNA testing as early as 2 months of age, children should not be tested for HCV antibodies before 18 months of age because maternal antibodies can persist until that age [1]. Despite this risk-based screening strategy, only 13.5% of infants born to mothers with HCV are screened, in part because HCV screening is not routine, and most women do not disclose IDU behavior[7].

Improved screening strategies are necessary to effectively diagnose HCV in children, and to further optimize outcomes and minimize disease morbidity. Currently, there is an FDA-approved treatment for children as young as age 3, it is highly important that children born with HCV be diagnosed and treated as soon as possible[8]. HCV screening at age 2 is ideal because existing blood draws already occur between ages 1-2 (for iron testing), and therefore this would

be an ideal time to bundle with HCV testing later on. A one-time universal HCV screening for children would ideally be done when or near the time children can receive the approved HCV treatment, and at a time when other bloods are being drawn, such as lead testing, to increase the probability that a child will be tested. Many children remain undiagnosed with current risk-based screening guidelines, and whether universal screening of children is cost-effective compared to current risk-based approaches is unknown.

Therefore, we aim to evaluate the potential cost-effectiveness of universal pediatric screening for HCV at age 2 in comparison to the status quo (risk-based screening in childhood and a one-time universal adult screen) in the United States.

Methods and Procedures

A literature review was performed to obtain background information on HCV in children, please refer to the Supplemental Materials for eligibility criteria and search strategy.

Cost-effectiveness evaluation:

Intervention and comparator: We aim to evaluate the cost-effectiveness of universal pediatric screening at age 2 in comparison to status quo screening (risk-based screening among children born to mothers diagnosed with HCV, followed by a 1-time universal screening above age 18). We explore screening at age 2 because existing blood draws occur between ages 1-2 (for iron testing) and therefore this would be an ideal time to bundle with HCV testing.

Perspective and time horizon: We adopt a healthcare provider perspective and a lifetime time horizon.

Model: We developed a state transition, HCV natural history Markov model of HCV disease progression and treatment among children at age 2 at simulation start (Figure 1). All patients in our analysis entered the Markov cycle identified at age 2 and transitioned between health states according to predefined transition probabilities, diagnosis, treatment rate, and loss to follow-up status seen in Table 2. In the Markov model, we assumed that all the patients who entered the model would either be diagnosed, treated, uninfected, or would have achieved spontaneous clearance of the virus at the start of both strategies. For the status quo (risk-based screening) strategy, we assumed that the initial proportion of children with HCV screened by age 2 would be the product of the proportion of mothers screened, the proportion of HCV-infected children

born to diagnosed mothers who are screened and linked to care. For those in the status quo analysis, if children are not screened by the age of 2, they can be diagnosed a) when they are eligible for a 1-time universal screen above age 18 or b) when they develop advanced liver disease (decompensated cirrhosis or HCC). For the universal screening strategy, we assume individuals are diagnosed at age 2. Diagnosed individuals are eligible for treatment. For individuals who are treated and cured (obtain the sustained viral response [SVR]), we assume no disease progression if they have mild-moderate liver disease, and a reduction in disease progression rates if they have METAVIR F4 disease or more severe, consistent with published literature. If not treated within 1 year we assume individuals are lost to follow up. Individuals who are lost to follow-up can be re-engaged with care.

Parameterization: Estimated values of stage-specific transition rates among children and adults were obtained from published studies (Table 2). We found that the HCV treatment rate was 61.2%[9], and background mortality (non-HCV related death) was based on age-specific mortality rates obtained from the World Health Organization life tables [10]. We also incorporated HCV disease-related costs and health utilities from published literature[6].

Analysis: We analyzed the costs and health outcomes of all strategies using a decision tree model with a Markov model of HCV disease progression in TreeAge Pro 2023. We performed a cost-effective analysis to determine what strategy was preferred. We simulated cohorts with the intervention (HCV universal screening) and comparator (status quo risk-based screening) through the disease progression of HCV in children to estimate the total health gain and long-term costs. Costs (in US dollars [USD]) and health utilities (in quality-adjusted life years

[QALYs]) were attached to each health state. Costs and health utilities are discounted at 3% per year. We calculated the mean incremental cost-effectiveness ratio and then calculated the incremental cost-effectiveness ratio (ICER).

$$ICER = \frac{incremental\ costs}{incremental\ QALY'sgained}$$

To make an effective decision and determine how cost-effective a one-time universal pediatric HCV screen would be, compared to the status quo screening, we need to assess the cost-effectiveness by comparing it to a willingness to pay the threshold. The optimal screening scenario will be the one with the most health benefits where the ICER falls under the unofficial willingness-to-pay threshold of $100 000/QALY gained for the US[11].

Table 1. Model Parameter Inputs and Sources

Parameters	**HCV Stage**	**Value: Children**	**Value: Adults**	**Source**
HCV Chronic prevalence among children	---	0.01	---	[11]
HCV Ab Prevalence among children	---	Calculated: prop_Chronic_prevalence/ (1-sponrtaneous clearance)	---	[12]
Proportion who spontaneously clear their acute infection	---	0.397	---	[13]
Proportion of mothers Screened	---	---	0.45	[13]
Proportion treated within 1 year of diagnosis	---	Assume same as adults	0.612	[14]
Proportion of HCV-infected children diagnosed under risk-based screening	---	0.135	---	[4,13] (Assume 45% of mothers are screened under universal antenatal screening, and 30% of children born to HCV-infected mothers are screened. So, proportion screened is 0.45*0.30=0.135)

Table 1. Model Parameter Inputs and Sources continued

Re-engagement rate after loss to follow-up	---	Assume same as adults	0.05	---
Annual screening rate of adults under universal screening	---	---	0.2	Assume all screened within 5 years
Annual Liver Disease Stage Transition Rate without treatment or no SVR				
no SVR	F0 to F1	0.201	0.107	[15,16]
	F1 to F2	0.087	0.082	[15,16]
	F2 to F3	0.096	0.117	[15,16]
	F3 to F4	0.055	0.116	[17,18]
	F4 to DC	Assume same as adults	0.035	[17,18]
	F4 to HCC	Assume same as adults	0.024	[17,18]
	DC to HCC	Assume same as adults	0.0141	[19]
	DC/HCC to Transplant	Assume same as adults	0.0313	[19]
	Liver Transplant to Death 1 year	Assume same as adults	0.169	[6]
	Liver Transplant to Death Year>1	Assume same as adults	0.034	[6]
SVR	F0 to F1	0	0	Assume no progression
	F1 to F2	0	0	Assume no progression
	F2 to F3	0	0	Assume no progression
	F3 to F4	0	0	Assume no progression
	F4 to DC	Assume same as adults	0.002	[17,18]
	F4 to HCC	Assume same as adults	0.005	[17,18]
	DC to HCC	Assume same as adults	Assume same as no SVR	[19]
	DC/ HCC to transplant	Assume same as adults	Assume same as no SVR	[19]
	Liver Transplant to Death 1 year	Assume same as adults	Assume same as no SVR	[19]
	Liver Transplant to Death Year>1	Assume same as adults	Assume same as no SVR	[6]
Proportion who achieves SVR	---	Assume same as adults	0.95	[6]
Liver-Related death rates per year	F4	Assume same as adults	0.0324	[20]
	DC	Assume same as adults	0.216	[21]

Table 1. Model Parameter Inputs and Sources continued

	HCC	Assume same as adults	0.218	[6]
HCV Fibrosis distribution among HCV diagnosed children	F0	1	---	Assume children at age 1 all start in F0
	F1	0	---	---
	F2	0	---	---
	F3	0	---	---
	F4	0	---	---
Costs (USD 2023)				
Annual Costs for Non-Treatment Medical Expenses among HCV-infected Patients	F0-F3	Assume same as adults	$511 ($304-734)	[22]
	F4	Assume same as adults	$2,898 ($2009–3786)	[6]
	DC	Assume same as adults	$34,319 ($32 352–36 330)	[6]
	HCC	Assume same as adults	$54 741 ($49 302–60 014)	[6]
	Liver Transplant Y1	Assume same as adults	$225,320 ($119 270–330 260)	[6]
	Liver Transplant following years	Assume same as adults	$55 196 ($28 773–81 181)	[6]
HCV Antibody test (including consultation)	---	Assume same as adults	39	[6]
HCV RNA test (including consultation)	---	Assume same as adults	52	[6]
Liver elastography	---	Assume same as adults	130	[6]
Treatment delivery costs per course + antiviral therapy costs	---	Assume same as adults	$1249 ($676–1853) + 25000	[6]
Health Utilities				
Uninfected	---	Assume same as adults	1	[6]
Achieve SVR	---	Assume same as adults	0.05	[6]
HCV-Infected patients	F0	Assume same as adults	0.93 (0.83–1)	[6]
	F1, F2	Assume same as adults	0.86 (0.78–0.94)	[6]
	F3	Assume same as adults	0.83 (0.78–0.89)	[6]

Table 1. Model Parameter Inputs and Sources continued

	F4	Assume same as adults	0.81 (0.68–0.89)	[6]
	DC	Assume same as adults	0.70 (0.56–0.79)	[6]
	HCC	Assume same as adults	0.67 (0.56–0.78)	[6]
	Posttransplant	Assume same as adults	0.71 (0.69–0.79)	[6]
Incremental increase in health utility upon SVR	---	Assume same as adults	0.05	[6]

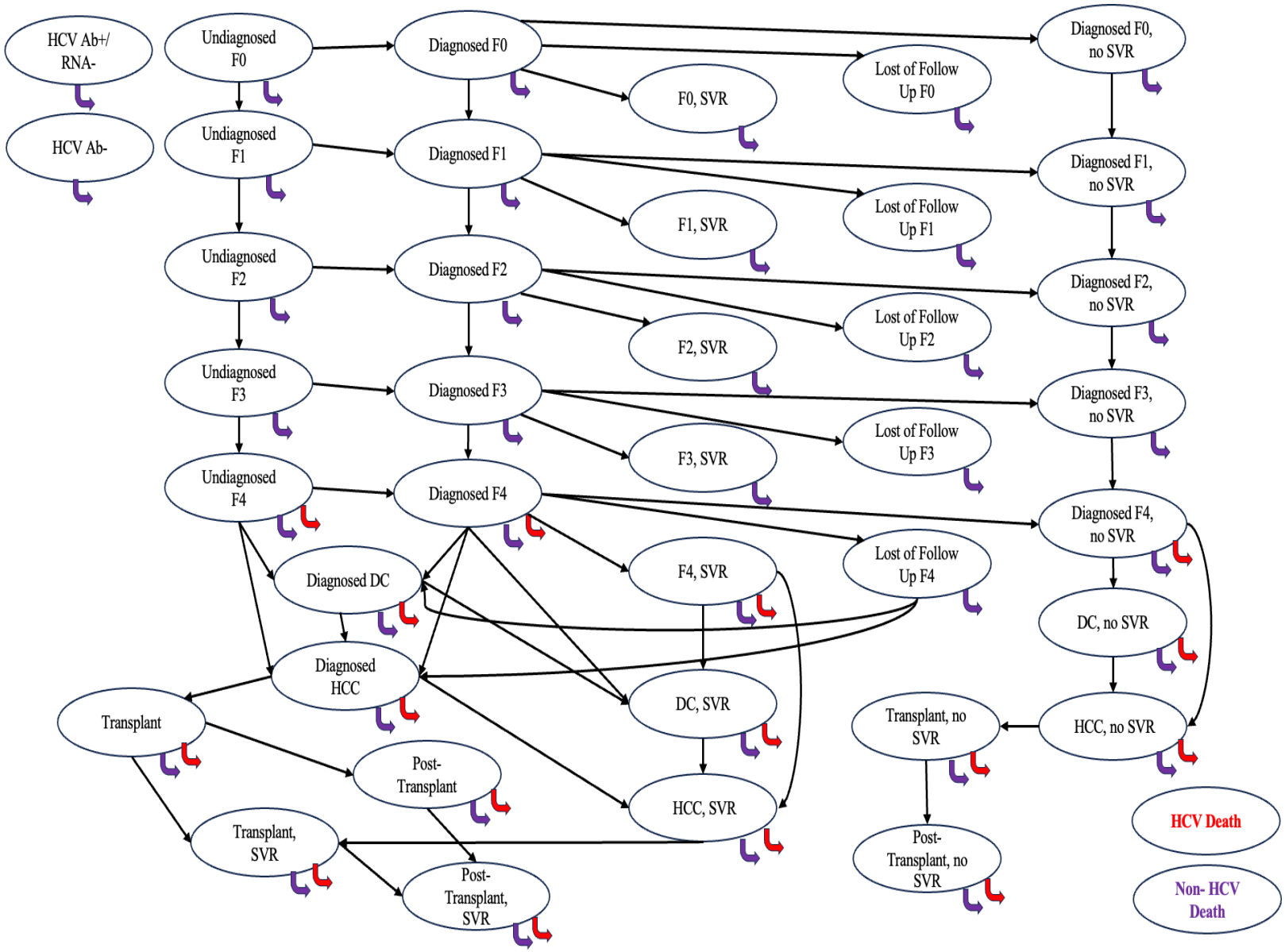

Figure 1. State transition model of HCV disease progression and treatment among children.

Results

Universal pediatric HCV screening at age 2 resulted in a total cost of $254.58 per person and yielded 30.13 QALYs per person. The status quo risk-based screening resulted in a total cost of $369.46 per person, yielding 30.11 QALYs per person. Therefore, universal screening at 2 years old was cost-saving, resulting in a net saving of $114.88 per person compared to risk-based screening, and demonstrated an incremental increase of 0.02 QALYs per person (Table 3).

A one-way sensitivity was performed for the HCV chronic prevalence among children. If the chronic HCV prevalence was 0.001% (compared to 0.01%), then universal pediatric HCV screening resulted in an incremental cost of $23.57, and incremental QALYs gained 30.16 compared to the status quo. The incremental cost-effectiveness ratio was $12,884.76/QALY gained, which would be considered cost-effective under a $100,000 willingness-to-pay threshold.

Table 2: Cost Effectiveness Results

Strategy	**Cost Per Person in 2023 USD**	**QALYs Per Person**	**Incremental Cost Per Person ($)**	**Incremental QALYs Per Person**	**Incremental cost-effectiveness ratio**
Status Quo- Risk based screening	369.46	30.11	--	---	---
Universal Pediatric Screening (2 yrs old)	254.58	30.13	-114.88	0.02	Cost-saving

Discussion

The objective of this modeling study was to identify the potential cost-effectiveness of universal pediatric screening for HCV in comparison to the status quo (risk-based screening) in the US. We found that universal pediatric screening for HCV at age 2 was cost-saving compared to the status quo (Risk-based screening in childhood) and resulted in better health outcomes. Our results were robust to lower chronic HCV prevalence.

Changes in HCV epidemiology with increased HCV prevalence among women of childbearing age, and therefore elevated risk of mother-to-child transmission of HCV, highlight the importance of identification and treatment of children at risk of vertical HCV acquisition. Given the availability of HCV treatment for children at age 3 and the known failures of risk-based screening in detecting most HCV-infected children, our work indicates screening guidelines should be reconsidered.

In the last few years, despite the new availability of HCV treatment for age 3, no analyses have examined the cost-effectiveness of HCV screening strategies. Most recent cost-effective analyses of HCV screening have been done among cohorts of pregnant women. In one study, universal antenatal screening proved to be more cost-effective in all treatment eligibility scenarios in comparison with risk-based HCV screening at a low prevalence of 0.07% among pregnant women, which is the lowest estimated prevalence in the US[6]. With the new FDA-approved HCV treatment for infants, further analyses can be done on the pediatric population and help to uncover optimal screening time points.

The results of this analysis should be interpreted with a few limitations. First, there is limited data on HCV disease progression in children available, and although we use data from a systematic review and meta-analysis, this only included data from 3 pediatric cohorts. Second,

there is uncertainty about the prevalence of HCV in pediatric populations in the United States, although our results were robust to changes in prevalence. Nevertheless, additional studies on HCV prevalence would strengthen these results and could highlight important geographical heterogeneity. Third, we only evaluated universal pediatric screening at the age of 2, evaluating different ages of screening is warranted. Lastly, the HCV disease progression model did not examine specific populations such as those coinfected with HIV, HBV, or other infections, which could alter the quality (and length) of life, and other associated medical costs.

In conclusion, our study provides further evidence that universal pediatric HCV screening at 2 years old in the US is cost-effective in comparison to standard risk-based screening and should be recommended to support clinical policies to further improve individual and population health outcomes and achieve national HCV elimination goals.

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Supplemental Material

Eligibility Criteria

Eligible studies were English-language studies that included information on HCV in children within the US and the prevalence, epidemiology, and treatment of HCV among children compared to adults - to demonstrate what is currently being done due to a lack of information about children. Exclusion criteria were studies that were done outside the US, studies with populations that were coinfected with HIV or Hepatitis B Virus (HBV), or studies done among adolescents.

Search Strategy

A systematic review was conducted by performing the following search on PubMed for background information using the following search fields:

1. ((Review[Publication Type]) AND (Hepatitis C Virus in children in the United States)) AND ((Epidemiology))

This literature search resulted in 25 review studies. After the elimination of studies that did not meet the eligibility criteria, 6 reviews were selected to include in the review.

Table 3. Summary of papers that were selected to include in the review

First Author (Publication Year)	Title	Aim(s)	Study Design	Population	Main Findings
Giuseppe Indolfi (2019)	Hepatitis C virus infection in children and adolescents	To provide a comprehensive overview of the epidemiology, natural history, and treatment of HCV infection in children and adolescents, and to highlight key differences and similarities with HCV infection in adults.	Comprehensive narrative literature review.	An adult (18 years or older); an adolescent (12–17 years old); and a child (younger than 12 years).	Research gaps that need to be addressed include age-specific prevalence studies of HCV viremia in priority countries; further validation of non-invasive tests for the staging of liver disease in children; and establishment of pediatric treatment registries and international consortia to promote collaborative research agendas
Sanu R. Yadav, MD (2021)	Hepatitis C: Current State of Treatment in Children	To provide a review of the epidemiology of pediatric HCV infection, its natural history, and the treatments approved by the Food and Drug Administration (FDA) available for children, adolescents and adults with chronic HCV infection,	Retrospective Review Article	An adult (18 years or older); and children (3 to 17 years old).	Hepatitis C in children is on the rise due to perinatal transmission from infected mothers. Prevalence remains underestimated because children at high risk are often not screened. Direct-acting antiviral combinations are safe and effective, with a sustained viral suppression rate of >90% and are FDA approved for children ≥3 years old. Efficient screening and treatment of chronic hepatitis C virus early is cost-effective and reduces burden of disease and its complications.

Table 3. Summary of papers that were selected to include in the review

Sarah Boudova (2018)	Risk-Based Hepatitis C Screening in Pregnancy Is Less Reliable Than Universal Screening: A Retrospective Chart Review	To determine the proportion of women tested for HCV during pregnancy, the prevalence of HCV among women being tested, and the association between testing and risk factors for HCV during pregnancy.	Retrospective Chart Review	Records from outside hospitals and outpatient clinics were not reviewed. Some women had more than 1 pregnancy that began or ended in 2016. Each pregnancy was considered individually.	Found that 7% of pregnant women receiving prenatal care at were tested for HCV and 5% had risk factors for HCV. However, among women with known HCV risk factors, nearly two-thirds were not screened for HCV. We found that 10% of HCV+ pregnancies occurred in women with no reported risk factor. History of IVDU is likely higher than identified. Women may not divulge prior IVDU due to fear of legal retribution or discrimination from health care providers. For these reasons, we believe that the actual number of women with risk factors was likely higher than reported.
Anuli Nwaohiria (2019)	Hepatitis C virus infection in children: How do we prevent it and how do we treat it?	To demonstrate that the new direct-acting antiviral agents that achieve very high rates of sustained virologic response with short regimens has revolutionized the field of HCV treatment and led to the development of global elimination goals for HCV transmission and mortality.	Expert Review of Anti-infective Therapy	Pregnant women, children (under 15 years of age).	Despite the advances in new drug development, critical knowledge gaps remain. Treating HCV infection during pregnancy and preventing HCV infection in children are two such gaps. More clinical trials focusing on the safety and efficacy of DAAs during pregnancy, infancy and early childhood are needed.
Claudia Espinosa, MD (2020)	Management of Hepatitis C in Children	To cover varied topics to familiarize providers with	Comprehensive narrative literature review	An adult (18 years or older); and children (3	Prevalence of chronic HCV infection in children and adolescents is

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	and Adolescents	the current status of pediatric HCV management in light of newly available DAAs medications.		to 17 years old).	increasing in the United States with the opioid epidemic, and a significant number of cases are undiagnosed. Yet, curing HCV is possible because DAA regimens are now available. DAAs are effective, safe, and easy to administer in children. Regimens are convenient, and the incidence of adverse effects is significantly lower compared with interferon-based regimens. Treatment of children and adolescents is recommended, and availability and access to those antivirals should increase to achieve HCV elimination goals.
Claudia Espinosa, MD (2018)	Unique Challenges of Hepatitis C in Infants, Children, and Adolescents	To summarize unique challenges faced by infants, children, and adolescents infected with hepatitis C and their providers. To review the impact of hepatitis C on infants exposed by vertical transmission, and the impact of hepatitis C infection on infected children and adolescents.	Comprehensive Literature Review	Women of child-bearing age, infants, children, and adolescents.	Young people, including women of child- bearing age, infants, children, and adolescents, are being especially affected by hepatitis C infection sec- ondary to the intravenous drug use and opioid epi- demic. Unfortunately, estimates of disease in young populations are all misleading because universal screening has not been implemented.