CDC Recommendations for Hepatitis C Testing Among Perinatally Exposed Infants and Children — United States, 2023

SUPPLEMENTARY TABLES

Supplementary Tables:

SUPPLEMENTARY TABLE 1. Chain of indirect evidence

Compared with HCV antibody testing at age 18 months, how would HCV RNA testing at age 2–6 months affect the number of children identified with perinatally acquired HCV infection?	**How many additional children with perinatally acquired HCV infection would be identified?**	**How many additional children with perinatally acquired HCV infection would be linked to care?**	**Do desirable effects (benefits) of testing outweigh undesirable effects (harms)?**	**What is the effect of diagnosis at age 2-6 months with RNA testing on cirrhosis and deaths attributable to hepatitis C?**
K.Q.1.a. What is the prevalence of HCV infection among pregnant people in the United States?	K.Q.2.a. What is the diagnostic accuracy of HCV antibody and HCV RNA testing in perinatally exposed children?	K.Q.3.a. What proportion of children with confirmed HCV infection are linked to care?	K.Q.4.a. What are the benefits of hepatitis C testing among perinatally exposed children?	K.Q.5.a. What is the effect of hepatitis C diagnosis in childhood on related morbidity and mortality (including cirrhosis, hepatocellular carcinoma, and death)?
K.Q.1.b. What proportion of pregnant people are tested for HCV infection in the United States?	K.Q.2.b. What proportion of children perinatally exposed to HCV are tested for HCV infection?		K.Q.4.b. What are the harms of hepatitis C testing among perinatally exposed children?*	K.Q.5.b. What is the effect of DAA treatment in childhood on hepatitis C-related morbidity (including cirrhosis, hepatocellular carcinoma)?
K.Q.1.c. What proportion of children perinatally exposed to HCV become infected?				K.Q.5.c. What is the effect of DAA treatment in childhood on hepatitis C-related mortality?

Abbreviations: DAA = direct acting antiviral; HCV = hepatitis C virus; KQ = key question; RNA = ribonucleic acid.

* Includes U.S. and non-U.S. studies.

SUPPLEMENTARY TABLE 2. Literature search strategy

Search Query: Among children perinatally exposed to HCV, does NAT for HCV RNA at age 2–6 months† compared with HCV antibody testing with reflex RNA testing (i.e., NAT for HCV RNA following a reactive anti-HCV test) at or after age ≥18 months increase the identification of HCV infections, increase linkage to care and treatment, and decrease cirrhosis and deaths attributable to HCV infection?			
Database	**Strategy**	**Run date**	**Records**
Medline (OVID) 1946–	(Hepatitis C OR HCV OR HepC) ADJ5 (test* OR screen* OR assay* OR immunoassay* OR RNA OR antibod* OR serolog* OR polymerase chain reaction OR PCR OR nucleic acid) AND Prenatal* OR mother-to-child OR MTCT OR (vertical* ADJ2 transmi*) OR (vertical* ADJ2 infect*) OR (pregnan* ADJ2 infect*) OR in utero OR perinatal OR antenatal OR neonatal OR neonate* OR infant OR infants OR fetus OR fetal OR foetus OR pediatric OR paediatric OR maternal OR child* Limit 2001–current	06/08/2021	1,790
Embase (OVID) 1988–	(Hepatitis C OR HCV OR HepC) ADJ5 (test* OR screen* OR assay* OR immunoassay* OR RNA OR antibod* OR serolog* OR polymerase chain reaction OR PCR OR nucleic acid) AND Prenatal* OR mother-to-child OR MTCT OR (vertical* ADJ2 transmi*) OR (vertical* ADJ2 infect*) OR (pregnan* ADJ2 infect*) OR in utero OR perinatal OR antenatal OR neonatal OR neonate* OR infant OR infants OR fetus OR fetal OR foetus OR pediatric OR paediatric OR maternal OR child* Limit 2001–current ; NOT Pubmed/Medline	06/08/2021	2,992 – 1,091 duplicates = 1,901 unique items

Database	Strategy	Run date	Records
Cochrane Library	(("Hepatitis C" OR HCV OR HepC) NEAR/5 (test* OR screen* OR assay* OR immunoassay* OR RNA OR antibod* OR serolog* OR "polymerase chain reaction" OR PCR OR "nucleic acid")):ti,ab AND (Prenatal* OR mother-to-child OR MTCT OR (vertical* NEAR/2 transmi*) OR (vertical* NEAR/2 infect*) OR (pregnan* NEAR/2 infect*) OR "in utero" OR perinatal OR antenatal OR neonatal OR neonate* OR infant OR infants OR fetus OR fetal OR foetus OR pediatric OR paediatric OR maternal OR child*):ti,ab Limit 2001–current ;	06/08/2021	199 – 59 duplicates = 140 unique items
CINAHL (EbscoHost)	(("Hepatitis C" OR HCV OR HepC) N5 (test* OR screen* OR assay* OR immunoassay* OR RNA OR antibod* OR serolog* OR "polymerase chain reaction" OR PCR OR "nucleic acid")) AND (Prenatal* OR mother-to-child OR MTCT OR (vertical* N2 transmi*) OR (vertical* N2 infect*) OR (pregnan* N2 infect*) OR "in utero" OR perinatal OR antenatal OR neonatal OR neonate* OR infant OR infants OR fetus OR fetal OR foetus OR pediatric OR paediatric OR maternal OR child*) Limit 2001–current ; exclude Medline records	06/08/2021	189 – 66 duplicates = 123 unique items
Scopus	TITLE-ABS-KEY(("Hepatitis C" OR HCV OR HepC) W/5 (test* OR screen* OR assay* OR immunoassay* OR RNA OR antibod* OR serolog* OR "polymerase chain reaction" OR PCR OR "nucleic acid")) AND TITLE-ABS-KEY(Prenatal* OR mother-to-child OR MTCT OR (vertical* W/2 transmi*) OR (vertical* W/2 infect*) OR (pregnan* W/2 infect*) OR "in utero" OR perinatal OR antenatal OR neonatal OR neonate* OR infant OR infants OR fetus OR fetal OR foetus OR pediatric OR paediatric OR maternal OR child*) AND NOT INDEX(Medline)	06/08/2021	601 – 444 duplicates = 157 unique items

Note. Duplicates were identified using the Endnote automated "find duplicates" function with preference set to match on title, author, and year, and removed from Endnote library.

SUPPLEMENTARY TABLE 3. National Institutes of Health (NIH) quality assessment tools*

3a. NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

1. Was the research question or objective in this paper clearly stated?
2. Was the study population clearly specified and defined?
3. Was the participation rate of eligible persons at least 50%?
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?
5. Was a sample size justification, power description, or variance and effect estimates provided?
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
10. Was the exposure(s) assessed more than once over time?
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
12. Were the outcome assessors blinded to the exposure status of participants?
13. Was loss to follow-up after baseline 20% or less?
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

3b. NIH Quality Assessment Tool for Case-Control Studies

1. Was the research question or objective in this paper clearly stated and appropriate?
2. Was the study population clearly specified and defined?
3. Did the authors include a sample size justification?
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?
6. Were the cases clearly defined and differentiated from controls?
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?
8. Was there use of concurrent controls?
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?

11. Were the assessors of exposure/risk blinded to the case or control status of participants?
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?

3c. NIH Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group

1. Was the study question or objective clearly stated?
2. Were eligibility/selection criteria for the study population prespecified and clearly described?
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?
4. Were all eligible participants that met the prespecified entry criteria enrolled?
5. Was the sample size sufficiently large to provide confidence in the findings?
6. Was the test/service/intervention clearly described and delivered consistently across the study population?
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?
12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?

* **Source:** National Institutes of Health. Study quality assessment tools. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health. Accessed March 8, 2022. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools

SUPPLEMENTARY TABLE 4. Supplementary literature search strategy

Search Query: Among children perinatally exposed to HCV, does NAT for HCV RNA at age 2–6 months† compared with HCV antibody testing with reflex RNA testing (i.e., NAT for HCV RNA following a reactive anti-HCV test) at or after age ≥18 months increase the identification of HCV infections, increase linkage to care and treatment, and decrease cirrhosis and deaths attributable to HCV infection?			
Database	**Strategy**	**Records for run date 6/8/21**	**Records for run date 1/17/23**
Medline (OVID) 1946–	(Hepatitis C OR HCV OR HepC) ADJ5 (test* OR screen* OR assay* OR immunoassay* OR RNA OR antibod* OR serolog* OR polymerase chain reaction OR PCR OR nucleic acid) AND Prenatal* OR mother-to-child OR MTCT OR (vertical* ADJ2 transmi*) OR (vertical* ADJ2 infect*) OR (pregnan* ADJ2 infect*) OR in utero OR perinatal OR antenatal OR neonatal OR neonate* OR infant OR infants OR fetus OR fetal OR foetus OR pediatric OR paediatric OR maternal OR child* Limit 2001–current	1,790	160
Embase (OVID) 1988–	(Hepatitis C OR HCV OR HepC) ADJ5 (test* OR screen* OR assay* OR immunoassay* OR RNA OR antibod* OR serolog* OR polymerase chain reaction OR PCR OR nucleic acid) AND Prenatal* OR mother-to-child OR MTCT OR (vertical* ADJ2 transmi*) OR (vertical* ADJ2 infect*) OR (pregnan* ADJ2 infect*) OR in utero OR perinatal OR antenatal OR neonatal OR neonate* OR infant OR infants OR fetus OR fetal OR foetus OR pediatric OR paediatric OR maternal OR child* Limit 2001–current ; NOT Pubmed/Medline	2,992 – 1,091 duplicates = 1,901 unique items	272 – 23 duplicates =249 unique items

Database	Strategy	Records for run date 6/8/21	Records for run date 1/17/23
Cochrane Library	(("Hepatitis C" OR HCV OR HepC) NEAR/5 (test* OR screen* OR assay* OR immunoassay* OR RNA OR antibod* OR serolog* OR "polymerase chain reaction" OR PCR OR "nucleic acid")):ti,ab AND (Prenatal* OR mother-to-child OR MTCT OR (vertical* NEAR/2 transmi*) OR (vertical* NEAR/2 infect*) OR (pregnan* NEAR/2 infect*) OR "in utero" OR perinatal OR antenatal OR neonatal OR neonate* OR infant OR infants OR fetus OR fetal OR foetus OR pediatric OR paediatric OR maternal OR child*):ti,ab Limit 2001–current ;	199 – 59 duplicates = 140 unique items	28 -5 duplicates =23 unique items
CINAHL (EbscoHost)	(("Hepatitis C" OR HCV OR HepC) N5 (test* OR screen* OR assay* OR immunoassay* OR RNA OR antibod* OR serolog* OR "polymerase chain reaction" OR PCR OR "nucleic acid")) AND (Prenatal* OR mother-to-child OR MTCT OR (vertical* N2 transmi*) OR (vertical* N2 infect*) OR (pregnan* N2 infect*) OR "in utero" OR perinatal OR antenatal OR neonatal OR neonate* OR infant OR infants OR fetus OR fetal OR foetus OR pediatric OR paediatric OR maternal OR child*) Limit 2001–current ; exclude Medline records	189 – 66 duplicates = 123 unique items	16 -14 duplicates =2 unique items

Database	Strategy	Records for run date 6/8/21	Records for run date 1/17/23
Scopus	TITLE-ABS-KEY(("Hepatitis C" OR HCV OR HepC) W/5 (test* OR screen* OR assay* OR immunoassay* OR RNA OR antibod* OR serolog* OR "polymerase chain reaction" OR PCR OR "nucleic acid")) AND TITLE-ABS-KEY(Prenatal* OR mother-to-child OR MTCT OR (vertical* W/2 transmi*) OR (vertical* W/2 infect*) OR (pregnan* W/2 infect*) OR "in utero" OR perinatal OR antenatal OR neonatal OR neonate* OR infant OR infants OR fetus OR fetal OR foetus OR pediatric OR paediatric OR maternal OR child*) AND NOT INDEX(Medline)	601 – 444 duplicates = 157 unique items	92 -67 duplicates =25 unique items

Note. Duplicates were identified using the Endnote automated "find duplicates" function with preference set to match on title, author, and year, and removed from Endnote library.

SUPPLEMENTARY TABLE 5. HCV testing and prevalence in pregnancy

Author, year	Years of study	Study design	Description	Setting	Anti-HCV tested (n/N, %)	Anti-HCV positivity	RNA positivity
Bushman *(22)*, 2021	2014–2018	Retrospective cohort	Comparison of rates of screening in pregnancy	Single urban tertiary care center in the U.S. South (Alabama)	7,033/16,489 (42.7%)	166/16,489 (1.0%)	103/154 (66.9%)
Epstein *(23)*, 2021	2014-2018	Retrospective cohort	Review of pregnant people identified as HCV antibody positive	Safety net hospital in urban city (Boston Medical Center)			255/343 (74.3%)
Kaufman *(24)*, 2022	2011-2021	Retrospective cohort	Review of laboratory data from Quest Diagnostics	United States	1,176,284/5,048,428 (23.3%)		
Kushner *(25)*, 2020	2018–2019	Prospective seroprevalence	Screening among labor and delivery admissions using stored serum tested for syphilis	2 inner city hospitals in New York City, New York (Mount Sinai Health System)		56/7429 (0.8%)	

Author, year	Years of study	Study design	Description	Setting	Anti-HCV tested (n/N, %)	Anti-HCV positivity	RNA positivity
Lopata *(26)*, 2020	2005–2014	Retrospective cohort	Vital statistics-linked administrative data following infants for 2 years	TennCare (TN) Medicaid population		4,072/384,837 (1.1%)*	
Mast *(27)*, 2005	1993–1996 (Texas), 1994–1998 (Hawaii)	Prospective cohort	Maternal serum at enrollment, delivery, infant serum at birth, and 8 well visits - infants followed until age 5	Houston, Texas and Honolulu, Hawaii		567/75,909 (0.8%)	194/242 (80.2%)
Pfeiffer *(28)*, 2022	2015-2020	Retrospective cohort	Review of electronic medical record data among pregnant persons with opioid use disorder	8 delivery hospitals in Maine	582/916 (63.5%)	226/582 (38.8%)	136/210 (64.8%)

Author, year	Years of study	Study design	Description	Setting	Anti-HCV tested (n/N, %)	Anti-HCV positivity	RNA positivity
Prasad *(29)*, 2020	2012–2015	Observational	HCV screening among women presenting for prenatal care	Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network (32 hospitals, 14 states)		254/106,842 (0.2%)	88/129 (68.2%)
Rossi *(30)*, 2020	2009–2017	Population-based, retrospective cohort	Review of live births using National Center for Health Statistics birth records	United States		94,824/31,207,898 (0.3%)[†]	
Smith *(31)*, 2022	2009-2019	Retrospective cohort	Review of mothers living with HIV and their infants for congenital infections	Tertiary care referral center (Children's Hospital Colorado)	251/255 (98.4%)	16/251 (6.4%)	13/16 (81.3%)

Author, year	Years of study	Study design	Description	Setting	Anti-HCV tested (n/N, %)	Anti-HCV positivity	RNA positivity
Watts *(32)*, 2017	2011–2015	Retrospective cohort	Estimate the proportion of women enrolled in Wisconsin Medicaid with HCV infection during pregnancy	Wisconsin Electronic Disease Surveillance System linked to Medicaid data		608/146,267 (0.4%)	180/608 (29.6%)
Watts *(33)*, 2020	2011–2015	Cross-sectional analysis	Pregnant persons with Wisconsin Medicaid coverage	Wisconsin birth certificates and Medicaid enrollment	4,401/78,917 (5.6%)[§]	177/4,490 (3.9%)[§]	

Abbreviations: Anti-HCV = hepatitis C virus antibody; HCV = hepatitis C virus; RNA = ribonucleic acid.

* Diagnosis of HCV based on birth certificates and International Classification of Diseases (ICD) codes from hospitalization.

Diagnosis of HCV based on birth certificates.

HCV testing rates based on Current Procedural Terminology (CPT) and Healthcare Common Procedure Coding System (HCPCS) codes during prenatal period; diagnosis of HCV based on International Classification of Diseases (ICD) codes.

SUPPLEMENTARY TABLE 6. Rates of perinatal HCV testing, transmission, and linkage to care

Author, year	Years of study	Study design	Description	Setting	Proportion of exposed infants referred for HCV testing (n/N%)	Proportion of exposed infants with HCV testing (n/N%)	Rate of perinatal transmission (n/N%)	Definition of perinatal transmission	Proportion of infants with hepatitis C linked to care (n/N%)
Abughali *(34)*, 2014	1993–2011	Pre- and post-intervention comparison	Retrospective medical record review (1993–2005) and prospective follow-up (2006–2011)	Pediatric infectious disease service at an inner-city U.S. hospital		46/193 (23.8%)	5/75 (6.6%)	Positive anti-HCV at age ≥18 months	
Bal *(35)*, 2016	1998–2013	Retrospective cohort	Retrospective review of demographic and clinical data of positive HCV mothers and their infants	Pediatric infectious diseases clinic at Jersey Shore University Medical Center			5/142 (3.5%)	At least 2 positive HCV RNA tests and positive anti-HCV at age ≥18 months	

Author, year	Years of study	Study design	Description	Setting	Proportion of exposed infants referred for HCV testing (n/N%)	Proportion of exposed infants with HCV testing (n/N%)	Rate of perinatal transmission (n/N%)	Definition of perinatal transmission	Proportion of infants with hepatitis C linked to care (n/N%)
Bell *(36)*, 2019	2013–2018	Retrospective cohort	Review of electronic medical records and statewide database of laboratory results	Tertiary care center in southern Maine		94/177 (53.1%)	7/94 (7.4%)	Positive anti-HCV if aged ≥18 months or positive HCV RNA if aged ≥2 months followed by repeat HCV RNA at age ≥12 months	
Berkley *(37)*, 2008	2000–2006	Retrospective medical record review	Medical record review of testing and outcomes of pregnant persons with and without HCV	Large drug dependence program at University of New Mexico Hospital	3/159 (1.9%)				

Author, year	Years of study	Study design	Description	Setting	Proportion of exposed infants referred for HCV testing (n/N%)	Proportion of exposed infants with HCV testing (n/N%)	Rate of perinatal transmission (n/N%)	Definition of perinatal transmission	Proportion of infants with hepatitis C linked to care (n/N%)
Bhardwaj *(38)*, 2021	1993–2016	Retrospective cohort	Medical record review of drug treatment program, testing, and outcomes of pregnant persons with and without HCV	Safety-net hospital; high-risk, urban, inner-city population		108/407 (26.5%)	12/108 (11.1%)	Positive anti-HCV at age ≥18 months or 2 positive HCV RNA tests if aged ≥2 months	
Chappell *(39)*, 2018	2006–2014	Population-based, retrospective cohort	Retrospective chart review	Large, tertiary care maternity hospital (University of Pittsburgh)		73/323 (22.6%)	7/83 (8.4%)		

Author, year	Years of study	Study design	Description	Setting	Proportion of exposed infants referred for HCV testing (n/N%)	Proportion of exposed infants with HCV testing (n/N%)	Rate of perinatal transmission (n/N%)	Definition of perinatal transmission	Proportion of infants with hepatitis C linked to care (n/N%)
Epstein *(40)*, 2018	2006–2015	Retrospective cohort	Review of electronic medical records	Boston Medical Center obstetric clinic for women with substance use disorders		180/404 (44.6%)	5/180 (2.8%)	Two positive HCV RNA at least 1 month apart or positive anti-HCV at age ≥18 months	5/5 (100%)
Gowda *(41)*, 2020	2008–2018	Retrospective cohort	Retrospective review of electronic health record data and laboratory data	Nationwide Children's Hospital, Columbus, Ohio			27/770 (3.5%)	Initial HCV RNA positive at age 2–6 months followed by a second positive RNA or anti-HCV at age ≥24 months	

Author, year	Years of study	Study design	Description	Setting	Proportion of exposed infants referred for HCV testing (n/N%)	Proportion of exposed infants with HCV testing (n/N%)	Rate of perinatal transmission (n/N%)	Definition of perinatal transmission	Proportion of infants with hepatitis C linked to care (n/N%)
Hojat *(42)*, 2020	2011–2018	Retrospective medical review, prospective electronic health records intervention	Control phase: review of records; Intervention phase: automatic alerts indicating need for antibody test in children aged ≥18 months	Urban safety-net hospital system		97/219 (44.3%)	1/97 (1.0%)	Positive anti-HCV at age ≥18 months	
Kuncio *(43)*, 2016	2011–2015	Retrospective cohort	Matched HCV lab data and birth certificate data to identify mothers and screened children	Philadelphia Department of Health		84/537 (15.6%)	4/84 (4.8%)	Positive anti-HCV at age ≥18 months or HCV RNA at age ≥12 months	

Author, year	Years of study	Study design	Description	Setting	Proportion of exposed infants referred for HCV testing (n/N%)	Proportion of exposed infants with HCV testing (n/N%)	Rate of perinatal transmission (n/N%)	Definition of perinatal transmission	Proportion of infants with hepatitis C linked to care (n/N%)
Lazenby *(44)*, 2019	2007–2016	Retrospective cohort	Retrospective chart review	Academic obstetrical clinic, Medical University of South Carolina	11/35 (31.4%)	3/35 (8.6%)			
Lopata *(26)*, 2020	2005–2014	Retrospective cohort	Vital statistics-linked administrative data following infants for 2 years	TennCare (Tennessee) Medicaid population		733/4072 (18.0%)			
Mast *(27)*, 2005	1993–1996 (Texas), 1994–1998 (Hawaii)	Prospective cohort	Maternal-infant pairs enrolled during pregnancy; infants followed until age 5	Houston, Texas and Honolulu, Hawaii			9/190 (4.7%)	HCV RNA positive at 2 follow-up visits or anti-HCV at age≥24 months	

Author, year	Years of study	Study design	Description	Setting	Proportion of exposed infants referred for HCV testing (n/N%)	Proportion of exposed infants with HCV testing (n/N%)	Rate of perinatal transmission (n/N%)	Definition of perinatal transmission	Proportion of infants with hepatitis C linked to care (n/N%)
Smith *(31)*, 2022	2009-2019	Retrospective cohort	Review of mothers living with HIV and their infants for congenital infections	Tertiary care referral center (Children's Hospital Colorado)		14/18 (77.8%)	0/14 (0%)	HCV RNA positive at age ≤6 months or anti-HCV positive at age ≥12 months	
Towers *(45)*, 2019	2015–2016	Prospective database	Review of perinatal HCV exposures and follow-up testing	Tennessee; UT Medical Center in Knoxville		55/127 (43.3%)	4/55 (7.3%)	Anti-HCV positive at age ≥18 months	

Author, year	Years of study	Study design	Description	Setting	Proportion of exposed infants referred for HCV testing (n/N%)	Proportion of exposed infants with HCV testing (n/N%)	Rate of perinatal transmission (n/N%)	Definition of perinatal transmission	Proportion of infants with hepatitis C linked to care (n/N%)
Watts*(32)*, 2017	2011–2015	Retrospective cohort	Estimate of the proportion of women enrolled in Wisconsin Medicaid with HCV infection during pregnancy and estimate of frequency of HCV testing and infection in infants born to HCV-infected women	Wisconsin Electronic Disease Surveillance System linked to Medicaid data		31/92 (33.7%)	7/183 (3.8%)	Anti-HCV at age ≥18 months or 2 or more positive HCV RNA at age ≥2 months	

Abbreviations: Anti-HCV = hepatitis C virus antibody; HCV = hepatitis C virus; RNA = ribonucleic acid.

SUPPLEMENTARY TABLE 7. Direct-acting antiviral treatment in children with perinatally acquired hepatitis C virus infection

Author, year	Drugs	Duration of treatment (weeks)	Age group (years)	% perinatally infected*	SVR12 n/N (% [95% CI])	Serious adverse events related to treatment
Jonas *(46)*, 2020	Glecaprevir/Pibrentasvir	8-16	12-17	85%	47/47 (100% [92.4%-100%])	None
Jonas *(47)*, 2021	Glecaprevir/Pibrentasvir	8-16	3-11	Not reported	77/80 (96% [90%-99%])	None
Schwarz *(48)*, 2020	Ledipasvir/ sofosbuvir	12	3–5	100%	33/34 (97% [85%–100%])	None
Rosenthal *(49)*, 2020	Sofosbuvir/ribavirin	12–24	3–11	94%	53/54 (98% [90%–100%])	1 ribavirin overdose†
Murray *(50)*, 2018	Ledipasvir/sofosbuvir +/- ribavirin	12–24	6–11	97%	91/92 (99% [94%–100%])	None
Balistreri *(51)*, 2017	Ledipasvir/ sofosbuvir	12	12–17	84%	98/100 (98% [93%–100%])	None
Wirth *(52)*, 2017	Sofosbuvir/ribavirin	12–24	12–17	73%	51/52 (98% [90%–100%])	None

Abbreviations: SVR12 = sustained virologic response 12 weeks posttreatment (reported among all study participants).

* Non-perinatal modes of transmission included blood product transfusion, contaminated needle or intravenous drug use, contact with infected individual, surgery/operation, and unknown.

† Ribavirin overdose required hospitalization for monitoring; patient completed therapy and achieved SVR12.

SUPPLEMENTARY TABLE 8. Quality assessment results*

Author, year	Type of Assessment	Overall rating
Abughali *(34)*, 2014	Before-after (pre-post) studies with no control group	Fair
Bal *(35)*, 2016	Observational cohort and cross-sectional study	Good
Balistreri *(51)*, 2017	Before-after (pre-post) studies with no control group	Good
Bell *(36)*, 2019	Observational cohort and cross-sectional study	Fair
Berkley *(37)*, 2008	Observational cohort and cross-sectional study	Fair
Bhardwaj *(38)*, 2021	Observational cohort and cross-sectional study	Fair
Bushman *(22)*, 2021	Observational cohort and cross-sectional study	Fair
Chappell *(39)*, 2018	Observational cohort and cross-sectional study	Fair
Epstein *(40)*, 2018	Observational cohort and cross-sectional study	Good
Epstein *(23)*, 2022	Before-after (pre-post) studies with no control group	Good
Hojat *(42)*, 2020	Before-after (pre-post) studies with no control group	Fair
Gowda *(41)*, 2020	Observational cohort and cross-sectional study	Good
Jonas *(46)*, 2020	Before-after (pre-post) studies with no control group	Fair
Jonas *(47)*, 2021	Before-after (pre-post) studies with no control group	Fair
Kaufman *(24)*, 2022	Observational cohort and cross-sectional study	Good
Kuncio *(43)*, 2016	Observational cohort and cross-sectional study	Good
Kushner *(25)*, 2020	Observational cohort and cross-sectional study	Good
Lazenby *(44)*, 2019	Observational cohort and cross-sectional study	Fair
Lopata *(26)*, 2020	Observational cohort and cross-sectional study	Good
Mast *(27)*, 2005	Observational cohort and cross-sectional study	Fair
Murray *(50)*, 2018	Before-after (pre-post) studies with no control group	Fair
Pfeiffer *(28)*, 2022	Observational cohort and cross-sectional study	Good

Author, year	Type of Assessment	Overall rating
Prasad *(29)*, 2020	Case-control study	Good
Rosenthal *(49)*, 2019	Before-after (pre-post) studies with no control group	Fair
Rossi *(30)*, 2020	Observational cohort or cross-sectional study	Good
Schwarz *(48)*, 2020	Before-after (pre-post) studies with no control group	Fair
Smith *(31)*, 2022	Observational cohort and cross-sectional study	Fair
Towers *(45)*, 2019	Observational cohort and cross-sectional study	Fair
Watts *(32)*, 2017	Observational cohort and cross-sectional study	Fair
Watts *(33)*, 2020	Observational cohort and cross-sectional study	Good
Wirth *(52)*, 2017	Before-after (pre-post) studies with no control group	Fair

* Full texts were independently reviewed and scored by two reviewers. All differences in responses were discussed, and agreement was reached on the final rating.

SUPPLEMENTARY TABLE 9. Potential harms of HCV testing among perinatally exposed children identified in evidence review*

Author, year	Potential harm	Level of confidence†	Outcome prioritization§
Ades *(53)*, 2022	Transient viremia¶	High	Not important
Bal *(35)*, 2016	Transient viremia	High	Not important
Bhardwaj *(38)*, 2021	Transient viremia	High	Not important
Biggar *(54)*, 2006	False-positive antibody	Low	Not important
Ceci *(55)*, 2001	Transient viremia	High	Not important
Ceci *(56)*, 2001	Transient viremia	High	Not important
Checa Cabot *(57)*, 2013	Transient viremia	Low	Not important
Di Domenico *(58)*, 2006	False-negative antibody	Moderate	Not important
England *(59)*, 2005	Transient viremia	Moderate	Not important
Ferrero *(60)*, 2003	Cost	High	Important
Fukuoka *(61)*, 2022	Stress and concern about child's health, school, employment, marriage	High	Important
	Guilt	High	Important
Gander *(62)*, 2021	Wait time for screening (to 18 months)	Low	Not important
	Stigma	Low	Important
Greiner *(63)*, 2017	Cost	High	Important
Healy *(64)*, 2001	Delay in clarifying infection status, uncertain prognosis	Low	Important
Hojat *(42)*, 2020	Time to go to lab and wait	Low	Important
	Pressure on clinic staff to order and explain testing	Low	Important
Jhaveri *(65)*, 2015	Transient viremia	Low	Not important
Kushner *(66)*, 2022	Rare misclassification of vertical transmission	Low	Not important
Lopata *(26)*, 2020	Transient viremia	Low	Not important
	Lack of availability of testing and transportation, especially in rural areas	Low	Important
Marjani *(67)*, 2022	Parental refusal	High	Not important
Mast *(27)*, 2005	False-negative antibody	Low	Not important

Author, year	Potential harm	Level of confidence†	Outcome prioritization§
Meskina *(68)*, 2022	Absence of approved treatment	Low	Not important
	Stigma	Low	Important
Mok *(69)*, 2005	Transient viremia	Low	Not important
	Cost	High	Important
Mostafa *(70)*, 2020	Cost	Low	Important
Peixoto *(71)*, 2004	Transient viremia	High	Not important
Pinto *(72)*, 2021	Involvement of social services to follow some children	High	Important
	Stigma	Low	Important
Polywka *(73)*, 2006	Transient viremia	Moderate	Not important
Reid *(74)*, 2018	Stigma	Low	Important
Shebl *(75)*, 2009	Transient viremia	High	Not important
Stinco *(76)*, 2022	Transient viremia	High	Not important
Ziyaeyan *(77)*, 2013	Distance to follow up for families living far away	Moderate	Important

*All assessments were performed individually by two reviewers.

†Level of confidence refers to confidence that the harm was directly measured in the study and was rated as low, moderate, or high.

§ Outcome prioritization determines value of harm to testing recommendations and was rated as critical, important, or not important.

¶ Definition of transient viremia: any mention of transient viremia, intermittent viremia, or spontaneous clearance.

Supplementary Table 10: Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist *(78)* for cost-effectiveness study *(79)*

Section/topic	Item No	Guidance for reporting	Reported on page number	Comments
Title				
Title	1	Identify the study as an economic evaluation and specify the interventions being compared.	1	
Abstract				
Abstract	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	1	
Introduction				
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	1, 2	
Methods				
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.		Not reported
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	1, 2	
Setting and location	6	Provide relevant contextual information that may influence findings.	2	
Comparators	7	Describe the interventions or strategies being compared and why chosen.	2-4	
Perspective	8	State the perspective(s) adopted by the study and why chosen.	3	-
Time horizon	9	State the time horizon for the study and why appropriate.	2-4	
Discount rate	10	Report the discount rate(s) and reason chosen.	4	Discounting rate 3%, reason chosen not reported
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s)	2-4	

Section/topic	Item No	Guidance for reporting	Reported on page number	Comments
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	2-4	
Validation of outcomes	13	Describe the population and methods used to measure and value outcomes	2-4	
Measurement and valuation of resources and costs	14	Describe how costs were valued.	2-4	
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion	2-4, Table 2	
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	2, figure 1,2	
Analytics and assumptions	17	Describe any methods for analyzing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	2-4	
Characterizing heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.		N/A
Characterizing distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.		N/A
Characterizing uncertainty	20	Describe methods to characterize any sources of uncertainty in the analysis.	4, 5	
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study		N/A
Results				
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	4, 5, table 1 & table 2 (footnote)	

Section/topic	Item No	Guidance for reporting	Reported on page number	Comments
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarize them in the most appropriate overall measure.	4, 5	
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	4-7	
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study		N/A
Discussion				
Study findings, limitations, generalizability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	5-7	
Other				
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	1	
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	1	

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