



Newly Reported Hepatitis C Infections and Recommendations for Universal Hepatitis C Screening

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Vital Signs: Newly Reported Acute and Chronic Hepatitis C — United States, 2009–2018

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Introduction

- An epidemic of hepatitis C is ongoing in the United States
 - Four-fold increase in acute hepatitis C rates from 2005–2017
 - 2.4M adults living with hepatitis C during 2013–2016 (1% of all adults)
 - Leading cause of death from liver disease (15,713+ deaths in 2018)
- Historically, highest prevalence of chronic hepatitis C among those born 1945–1965 (Baby Boomers)
- New cases occurring among young adults, concurrent with opioid crisis

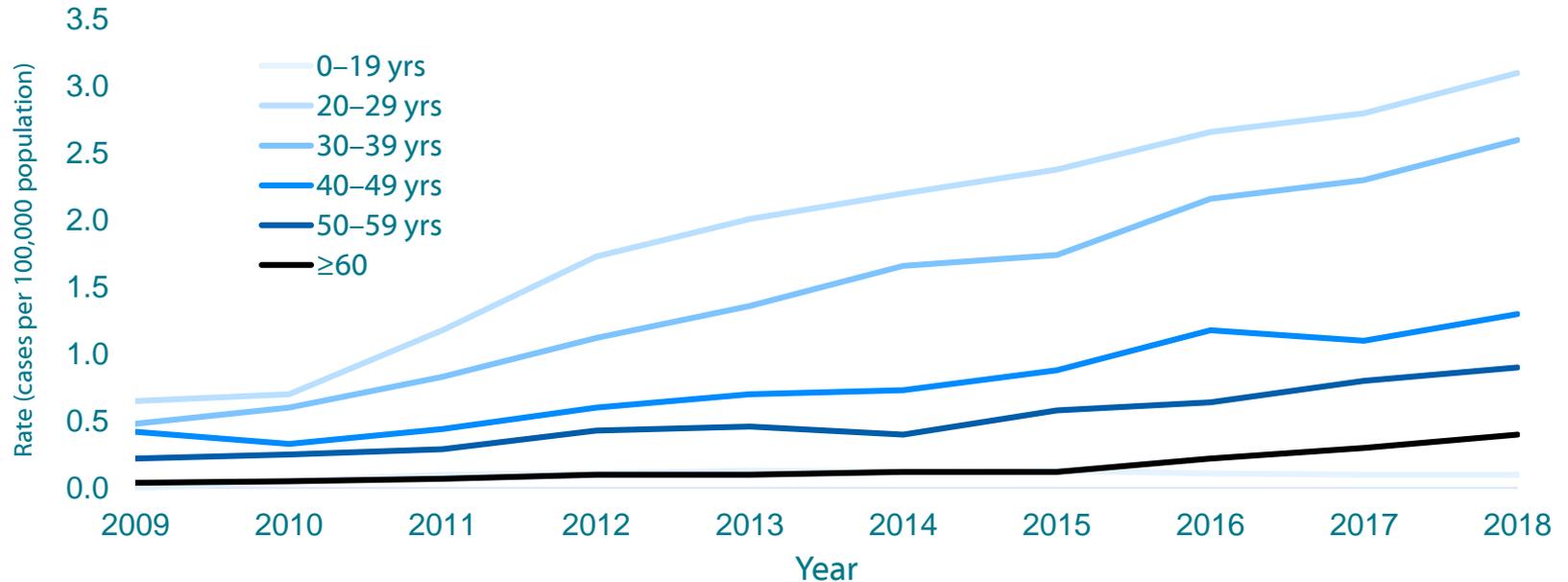
Methods

- National Notifiable Diseases Surveillance System
 - Acute hepatitis C trends, 2009–2018
 - Newly reported chronic hepatitis C, 2018
- National Health and Nutrition Examination Survey, 2015–2018
 - Proportion of HCV RNA+ adults who reported having ever been told they had hepatitis C



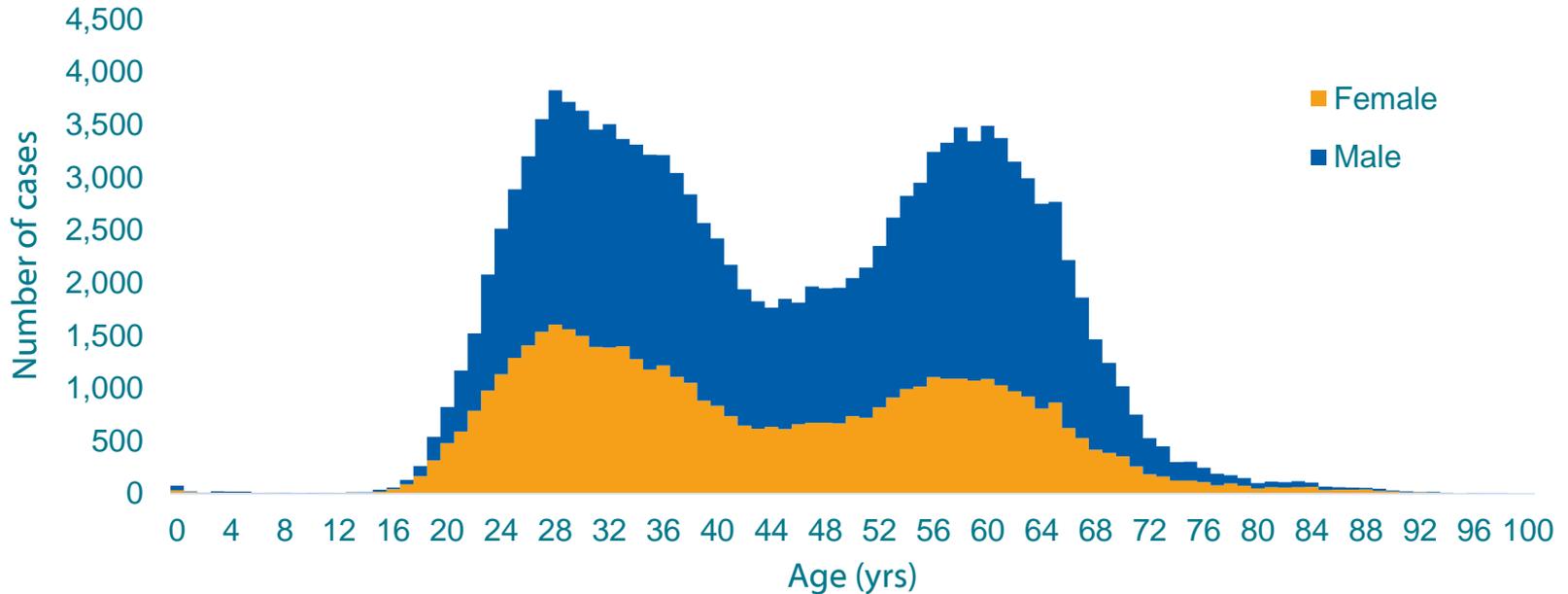
Results

Rate of reported acute hepatitis C cases by year and age group — NNDSS, 2009–2018



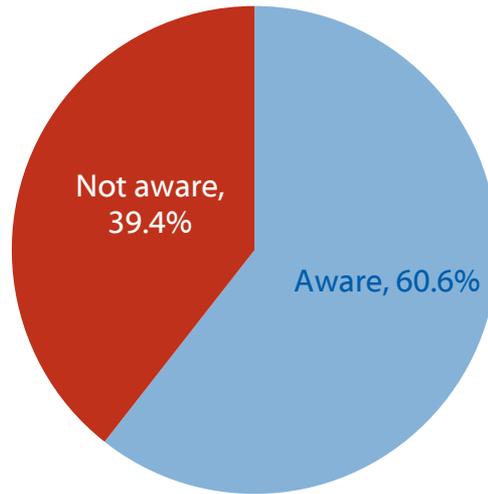
Results

Number of newly reported chronic hepatitis C cases by sex and age — NNDSS, 2018



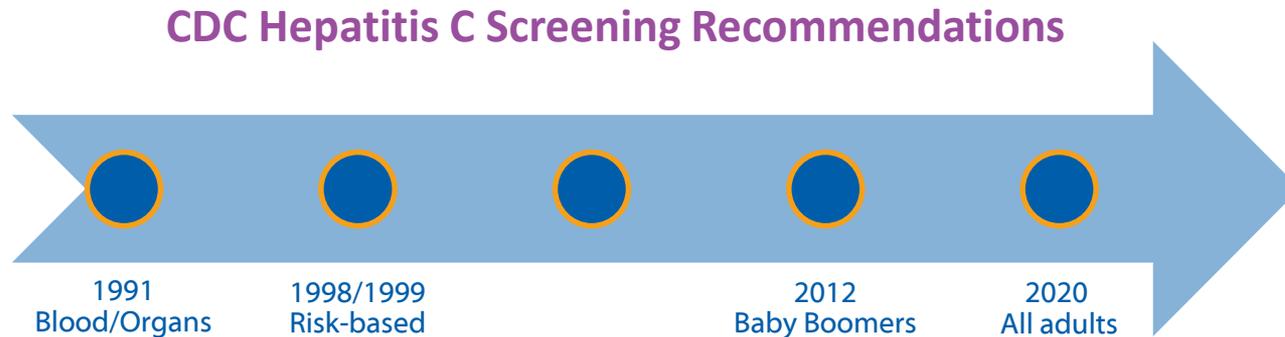
Results

Proportion of HCV RNA+ adults aware of their infection status, NHANES, 2015–2018



Discussion

- Until now, CDC has focused testing efforts on:
 - Those with identified risk factors
 - Born 1945–1965 (Baby Boomers)



Discussion

- Rapid increases in acute infections among young adults, including reproductive-aged persons, have put multiple generations at risk for chronic hepatitis C
- **Concurrent Release of New Screening Recommendation**

CDC Recommendations for Hepatitis C Screening Among Adults — United States, 2020

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Call to Action

Get tested. Get cured.

WHO SHOULD GET TESTED FOR HEPATITIS C?

| | | |
|---|--|---|
| EVERY ADULT | EVERY PREGNANT WOMAN | EVERYONE WITH RISK FACTORS |
|  |  |  |
| At least once | Every pregnancy | Regularly |

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New Recommendations for Universal Hepatitis C Screening Among Adults

Sarah Schillie, MD, MPH, MBA

Hepatitis C Virus (HCV): Epidemiology

- Estimated 2.4 million persons (1% of U.S. population) with HCV infection during 2013-16*
- Reported cases of acute HCV infection increased every year from 2009-2017[†]
 - Highest rates of acute cases among persons aged 20-39 (e.g., child-bearing age)
 - Injection drug use is primary risk factor for infection
- In 2015, 0.38% of live births delivered by mothers with HCV infection[§]
- Perinatal transmission occurs in 5.8% of infants born to HCV-infected mothers[¶]
 - 10.8% for infants born to mothers co-infected with HIV

*Hofmeister M, et al. Hepatology 2019; [†]2017 CDC surveillance data; [§]Schillie S, et al. Am J Prev Med 2018; [¶]Benova L, et al. CID 2014

HCV: Treatment

- All-oral, well-tolerated, direct acting antiviral agents (DAA) result in virologic cure in >95% of adults with 8-12 weeks of therapy
 - Ledipasvir/sofosbuvir recently approved for children aged 3 years and older
- DAAs not yet approved for use in pregnant women
 - Preliminary data (n=7) demonstrate no adverse fetal effects*

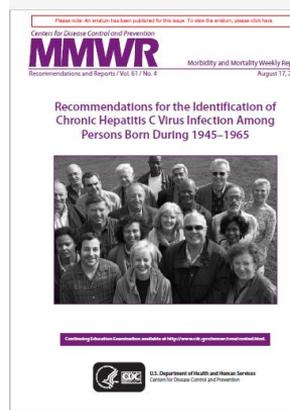
*Chappell C, et al. CROI 2020.

Updated Recommendations

- CDC is augmenting previous guidance to recommend:
 - Hepatitis C screening at least once in a lifetime for all adults aged 18 years and older, except in settings where the prevalence of HCV infection is less than 0.1%
 - Hepatitis C screening for all pregnant women during each pregnancy, except in settings where the prevalence of HCV infection is less than 0.1%

Previously-Published Recommendations

- Previously-published recommendations for hepatitis C testing of persons with risk factors remain in effect



Recommendations for screening 1945-65 birth cohort. Smith B, et al. MMWR 2012.

- Regardless of age or setting prevalence, all persons with risk factors should be tested for hepatitis C
 - Periodic testing while risk factors persist

- One-time hepatitis C testing, regardless of age or setting prevalence, including among persons with recognized exposures:
 - Persons with HIV
 - Persons who ever injected drugs and shared needles, syringes, or other drug preparation equipment, including those who injected once or a few times many years ago
 - Persons with selected medical conditions, including:
 - Ever received maintenance hemodialysis
 - Persistently abnormal ALT levels
 - Health-care, emergency medical, and public safety personnel after needle sticks, sharps, or mucosal exposures to HCV-positive blood
 - Children born to mothers with HCV infection
 - Prior recipients of transfusions or organ transplants:
 - Received clotting factor concentrates produced before 1987
 - Received a transfusion of blood or blood components before July 1992
 - Received an organ transplant before July 1992
 - Notified that they received blood from a donor who later tested positive for HCV infection

- Routine periodic testing for persons with ongoing risk factors, while risk factors persist^{*,†}:
 - Persons who currently inject drugs and share needles, syringes, or other drug preparation equipment
 - Persons with selected medical conditions, including:
 - Ever received maintenance hemodialysis
- Any person who requests hepatitis C testing should receive it, regardless of disclosure or risk, because many persons may be reluctant to disclose stigmatizing risks

*Alter M, et al. MMWR 1998; † Smith B, et al. MMWR 2012.

Overview of Process

- ✓ CHAC recommended CDC issue guidance for universal HCV screening of:
 - ✓ All adults, [December 4, 2017](#)
 - ✓ Pregnant women, [December 4, 2017](#)
- ✓ Systematic review of literature, [July 2018-March 2019](#)
 - ✓ Supplementary review to identify recently-published studies, [November 15, 2019](#)
- ✓ Evidence-to-Recommendations Framework presented to CHAC, [May 15, 2019](#)
- ✓ Recommendation statement entered into CDC clearance, round #1, [June 30, 2019](#)
- ✓ Recommendation statement completed CDC clearance, round #1, [September 30, 2019](#)
- ✓ Peer and public review
 - ✓ Federal Register notice, [October 28, 2019-December 27, 2019](#)
- ✓ Webinar series with targeted stakeholders and partners, [November 2019](#)
- ✓ Recommendation statement entered into CDC clearance, round #2, [December 18, 2019](#)
- ✓ Recommendation statement completed CDC clearance, round #2, [January 24, 2020](#)
- Publication and dissemination, [April 9, 2020](#)
- Evaluation

Policy Questions

| | | |
|----------------------|---|--|
| PICO question | Does universal screening for HCV infection among <u>adults aged 18 years and older</u>, compared to risk-based screening, reduce morbidity and mortality? | Does universal screening for HCV infection among <u>pregnant women</u>, compared to risk-based screening, reduce morbidity and mortality for mothers and their children? |
| Population | Adults aged 18 years and older | Pregnant women |
| Intervention | Universal HCV screening | Universal HCV screening |
| Comparison | Risk-based (including birth cohort) screening | Risk-based screening |
| Outcomes | <p>Benefits:</p> <ul style="list-style-type: none"> • Reduction in HCV disease burden • Reduction in HCV-related liver disease <p>Harms:</p> <ul style="list-style-type: none"> • False-positive results (or anti-HCV positive with negative RNA) • Stigma • Harms associated with work-up (e.g., liver biopsy) or treatment | <p>Benefits:</p> <ul style="list-style-type: none"> • Reduction in HCV disease burden • Reduction in HCV-related liver disease • Identification of infants for HCV testing <p>Harms:</p> <ul style="list-style-type: none"> • False-positive results (or anti-HCV positive with negative RNA) • Stigma; fear of losing custody of infant • Harms associated with work-up (e.g., liver biopsy) or treatment |

Chain of Indirect Evidence

| How would universal screening for HCV affect the number (and composition) of people who screen positive for HCV? | How many additional persons would be linked to care? | Do desirable treatment effects outweigh undesirable effects? |
|--|--|--|
| <p>K.Q.1.a. What is the prevalence of HCV infection in the U.S.? By:</p> <ul style="list-style-type: none"> --general population --risk groups | <p>K.Q.2.a. What is the diagnostic accuracy of HCV antibody testing?*</p> <p>K.Q.2.b. What are harms of HCV screening?†</p> <p>K.Q.2.c. What proportion of people who screen positive for HCV are linked to care?§,¶</p> | <p>K.Q.3.a. What is the effect of DAA treatment on HCV viral load?*</p> <p>K.Q.3.b. What is the effect of DAA treatment on morbidity (including cirrhosis, hepatocellular carcinoma)?*</p> <p>K.Q.3.c. What is the effect of DAA treatment on mortality (HCV-specific and all-cause)?*</p> <p>K.Q.3.d. What are the adverse effects of DAA treatment?*</p> |

KQ, key question

*Previously well-described and therefore not included in this review

†U.S. and non-U.S. studies included

§U.S. studies only included

¶For all adult review only

Evidence Retrieval

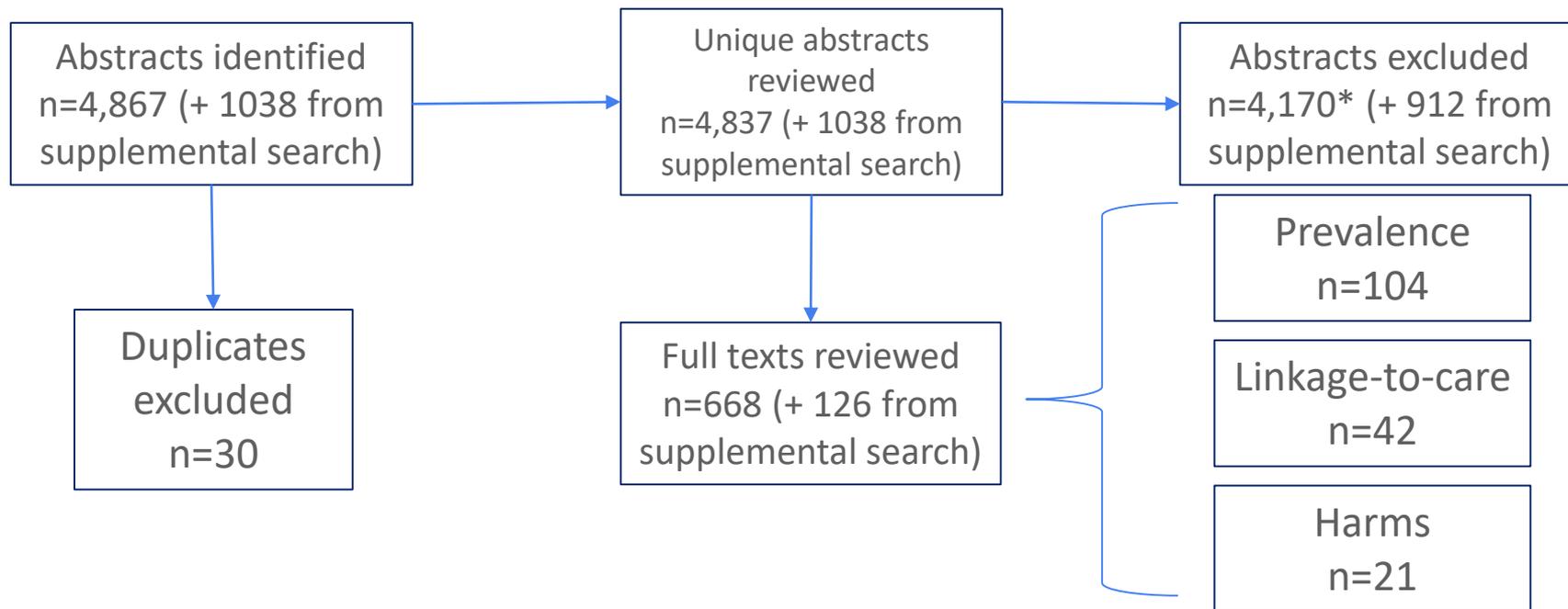
- Systematic review of data informing HCV screening strategy
 - Medline (OVID)
 - Embase (OVID)
 - CINAHL (Ebsco)
 - Scopus
 - Cochrane Library
 - All adults: January 1, 2010-August 6, 2018
 - Pregnant women: January 1, 1998-July 2, 2018
 - Comparator studies (i.e., controlled trials, cohort studies, and case-control studies) conducted worldwide
 - Limit English language, no age filter
 - All titles and abstracts independently reviewed by 2 reviewers
 - For titles/abstracts meeting inclusion criteria, the full article was retrieved and reviewed
- Supplemental search:
11/15/19 (all adults) and
10/29/19 (pregnant women)

Exclusion Criteria

- Abstracts only
- Non-U.S.* populations (except harms)
- Secondary, modeled, or imputed data
- Self-reported data (except risk factors)
- Linkage-to-care assessed before the availability of direct-acting antiviral agents
 - RNA testing alone not deemed linkage-to-care
- Corrections setting

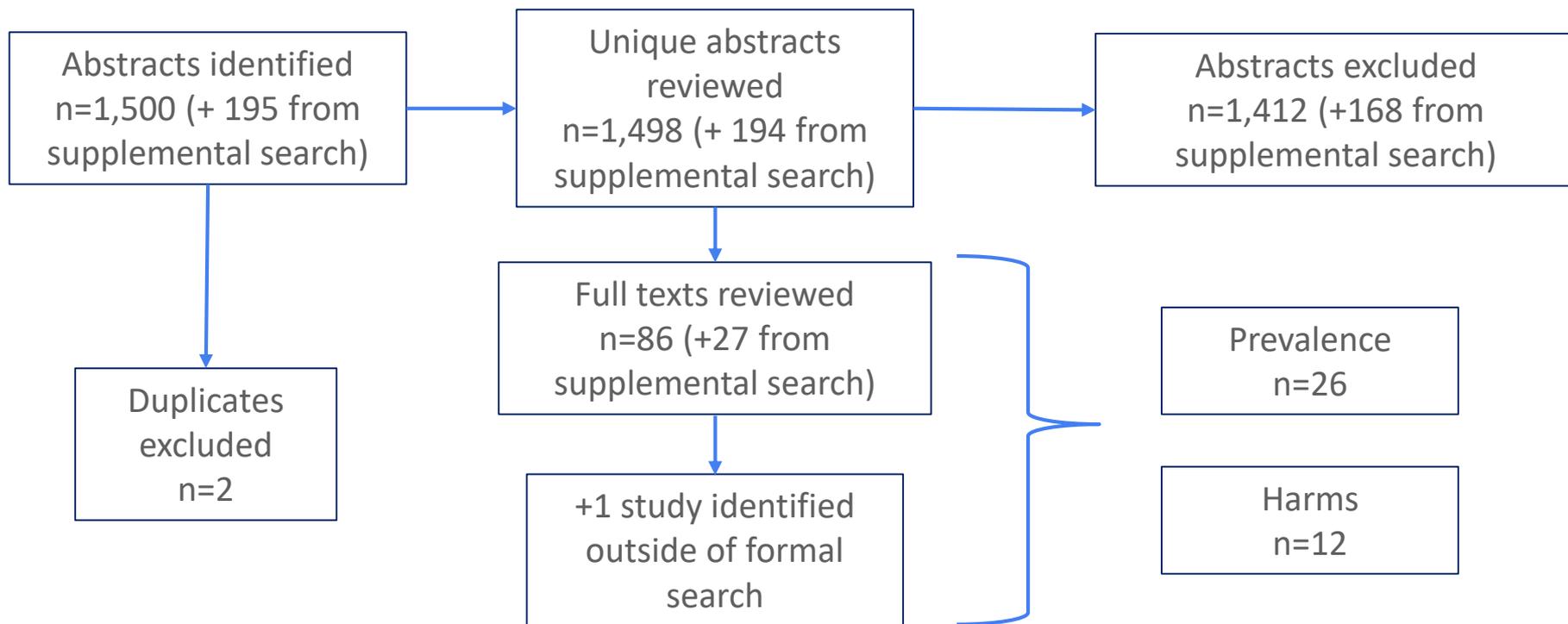
*Prevalence and linkage-to-care among non-U.S. populations deemed less relevant to U.S.-based recommendations

Evidence Retrieval: All Adults



*One study uploaded twice into Covidence systematic review software system

Evidence Retrieval: Pregnant Women



Hepatitis C Prevalence by Adult Populations, Summary of Literature Review

| Sub-Population | Anti-HCV-positivity median, range (number of studies) | HCV RNA-positivity among anti-HCV positives median, range (number of studies) |
|--------------------------|--|---|
| Overall | 6.6%, 0.0%-76.1% (104) | 68.7%, 20.0%-100.0% (61) |
| General population | 1.7%, 0.02%-7.9% (9) | 55.2%, 36.8%-83.0% (6) |
| Birth cohort members | 3.3%, 0.0%-43.5% (31) | 62.7%, 20.0%-95.3% (21) |
| ED patients | 7.5%, 1.6%-25.8% (19) | 69.0%, 42.5%-90.5% (12) |
| Immigrant populations | 4.7%, 3.4%-7.5% (3) | 81.8% (1) |
| Others at risk* | 9.3%, 1.6%-76.1% (23) | 74.1%, 47.0%-100.0% (14) |
| Persons with HIV | 5.2%, 1.2%-32.9% (8) | 63.4%, 41.4%-83.6% (4) |
| Persons who use drugs | 54.2%, 12.7%-67.1% (11) | 73.8%, 69.9%-100.0% (3) |
| Pregnant women | 1.2%, 0.1%-70.8% (26) | 66.1%, 61.3%-77.2% (4) |

*Persons experiencing homelessness or who live in communities with high rates of HCV infection

Linkage-to-Care (n=42 studies)

- Follow-up appointments/referrals
 - Made for 76.0% (25.0%-100.0%) of RNA-positive patients
- Attended first follow-up appointment
 - 73.9% (0.0%-100.0%) of those with appointment
- Received treatment
 - 39.0% (21.5%-76.1%) of those who attended appointment
- Achieved SVR
 - 85.2% (66.7%-100.0%) of those treated

Harms

- No study compared harms systematically using comparison groups associated with different screening approaches
- Potential harms reported:
 - All adult studies: 21
 - Pregnant women studies: 12
- Authors concluded identified harms did not outweigh benefits of screening

Harms

All adults

- Physical harms of screening (2 studies)
- Anxiety/stress related to testing or waiting for results (5 studies)
- Expense (1 study)
- Anxiety related to receiving positive results (1 study)
- Interpersonal outcomes (e.g., problems related to family, friends from learning HCV status) (5 studies)
- Attitudes toward people with hepatitis C, including stigma (11 studies)
- Time for screening (2 studies)
- False positive results (6 studies)
 - Including among left ventricular assist device patients, possibly precluding heart transplantation

Pregnant women

- Physical harms of screening (1 study)
- Anxiety/stress related to testing or waiting for results (5 studies)
- Stigma (1 study)
- Psychological issues (2 studies)
- Fears related to sexual relationships (1 study)
- Legal ramifications/potential loss of custody (1 study)
- Decreased quality of life knowing infected (1 study)
- Social repercussions (1 study)
- Reluctance to disclose behaviors (1 study)
- Expense (2 studies)
- False positive results (1 study)

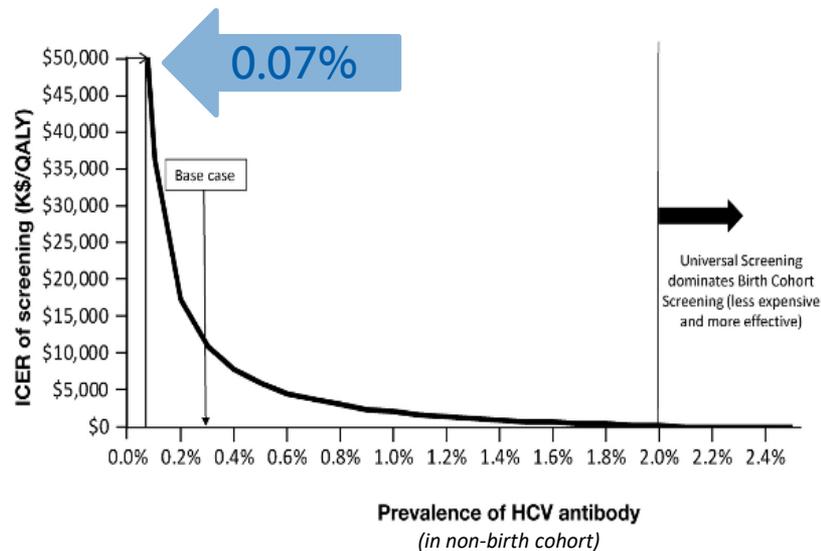
Public and Peer Review Comments

- Peer review: 6 clinicians with expertise in hepatology, gastroenterology, internal medicine, infectious diseases and/or obstetrics and gynecology
 - Structured peer reviews
- Public comment: 69 comments
- Many comments were in support of recommendations
- For comments proposing changes:
 - Against screening during every pregnancy
 - Remove prevalence threshold

Cost-Effectiveness as a Function of Prevalence

All Adults

ICER of universal screening compared with birth cohort screening by anti-HCV prevalence in non-birth cohort

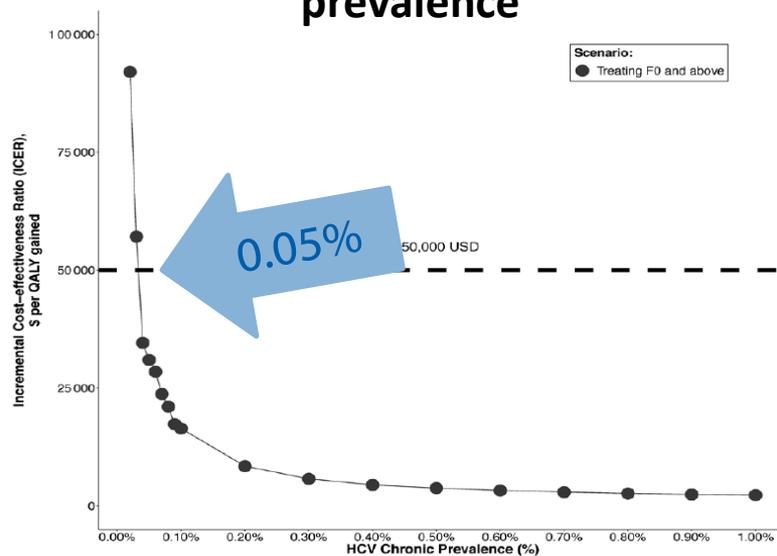


Eckman MH, Ward JW, Sherman KE. Cost effectiveness of universal screening for hepatitis C virus infection in the era of direct-acting, pangenotypic treatment regimens. Clin Gastroenterol Hepatol. 2019 Apr;17(5):930-939.

Slide prepared by Blythe Ryerson.

Pregnant Women

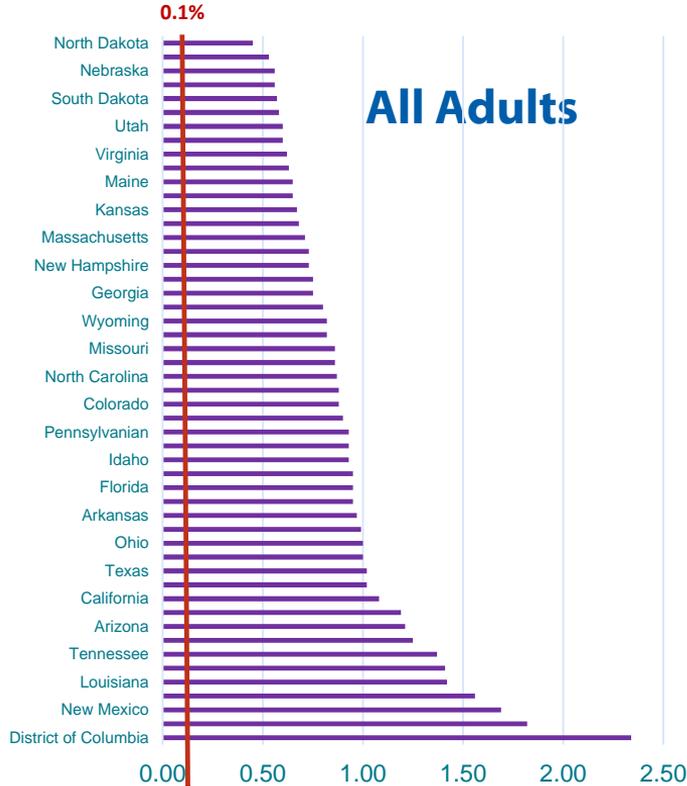
ICER of universal screening compared with risk-based testing by HCV RNA prevalence



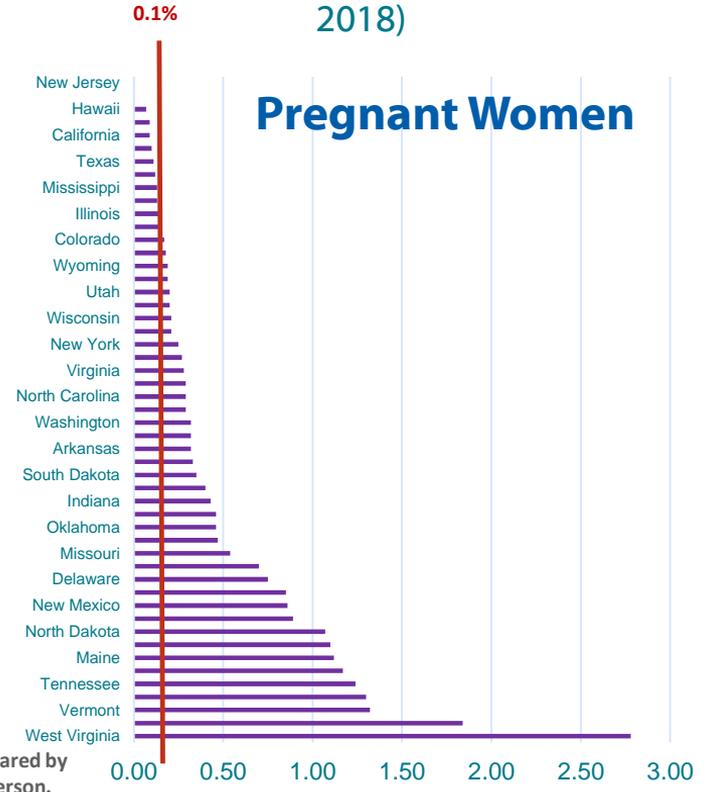
Chaillon A, Rand EB, Reau N, Martin NK. Cost-effectiveness of universal hepatitis C virus Screening of pregnant women in the United States. Clin Infect Dis. 2019 Jan 28 [Epub ahead of print].

Hepatitis C Prevalence

Estimated Prevalence of Persons Positive for HCV RNA, 2013-2016
(Rosenberg et al, 2019)



HCV Infection Among Pregnant Women, NCHS NVSS Birth Certificate Data (Schillie et al, 2018)



Recommendations for Clinical Preventive Services for Persons with HCV Infection Remain in Effect

- Evaluation for alcohol and drug use
 - Intervention if clinically indicated
- HepA and HepB vaccination
- Medical monitoring of disease
- HIV risk assessment
- Weight management
- Avoiding/stopping donating blood, tissue, semen
- Refraining sharing appliances that may come into contact with blood
 - E.g., toothbrushes, razors, glucose meters

Testing Considerations

- Testing should be initiated with an FDA-approved anti-HCV test
- Persons testing anti-HCV positive should undergo follow-up testing with an FDA-approved NAT test for detection of HCV RNA
 - CDC encourages use of reflex HCV RNA testing
- HCV testing should be performed on site, when feasible

Testing Considerations: Pregnant Women

- Data informing the optimal time during pregnancy for which Hepatitis C testing should occur are lacking
 - Testing at an early prenatal visit:
 - Harmonizes Hepatitis C testing with testing for other infectious diseases during pregnancy
 - May miss women who acquire Hepatitis C later during pregnancy
- Pregnant women with ongoing risk factors tested early in pregnancy could undergo repeat testing later in pregnancy

Testing Considerations: Infants*

- RNA testing (1-2 months of life) vs. anti-HCV testing (18 months or older)

Proponents of RNA testing

- Identifies cases earlier
- Infants often lost to follow-up (18.9% never presented to care, 38.7% attended 1 or 2 visits after delivery)†

Proponents of anti-HCV testing

- Definitive testing needed at 18 months of age (spontaneous clearance)
- No treatment prior to age 3 years
- Less expensive

*AASLD/IDSA Guidelines, AAP RedBook; †Towers C, et al. J MF & Neo Med 2018.

Recommendations of Others: Screening for Adults

| Organization | Adults | Pregnant women |
|-------------------------------|--|--|
| USPSTF (2020) | <ul style="list-style-type: none"> 18-79 years (B recommendation) | <ul style="list-style-type: none"> Pregnant adults should be screened (during each pregnancy not specified) Clinicians may want to consider screening pregnant persons under 18 years of age |
| EASL (2018) | <ul style="list-style-type: none"> Screening strategies for HCV infection may include screening of populations at risk of infection, birth cohort testing, and general population testing in areas of intermediate to high seroprevalence ($\geq 2\%$–5%) (B2) | |
| AASLD/IDSA (2018) | <ul style="list-style-type: none"> 18 years and older (I, B) Periodic testing for those with risk factors (IIa, C) Annual testing for PWID and HIV-infected MSM (IIa, C) | <ul style="list-style-type: none"> All pregnant women, ideally at initial prenatal visit (IIb,C) |
| SMFM, endorsed by ACOG (2017) | -- | Risk-based |

Summary

- Hepatitis C is a public health priority
 - Prevalence is high for a curable disease
 - Incidence is increasing
- Desirable anticipated effects from screening outweigh undesirable effects
- Universal screening will be cost-effective and feasible to implement at or above a prevalence of 0.1%
- Although interventions to prevent perinatal transmission are lacking*, Hepatitis C testing of pregnant women allows for:
 - Identification of infants for testing
 - Treatment of women after pregnancy
 - Reduce risk for perinatal transmission in subsequent pregnancies
- DAA treatment for pregnant women may be available in future

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