

Clinical Preventive Services

- Recommendations for clinical preventive services for persons with HCV infection remain in effect*:
 - Evaluation for alcohol and drug use, intervention if clinically indicated
 - Medical monitoring of disease, advice on treatment options and strategies and monitoring liver health (even if treatment not recommended)
 - Hepatitis A and hepatitis B vaccination
 - HIV risk assessment
 - If BMI ≥ 25 kg/m²: weight management

*Smith B, et al. MMWR 2012.

Policy Questions

PICO question	Does universal screening for HCV infection among <u>adults</u> aged 18 years and older, 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

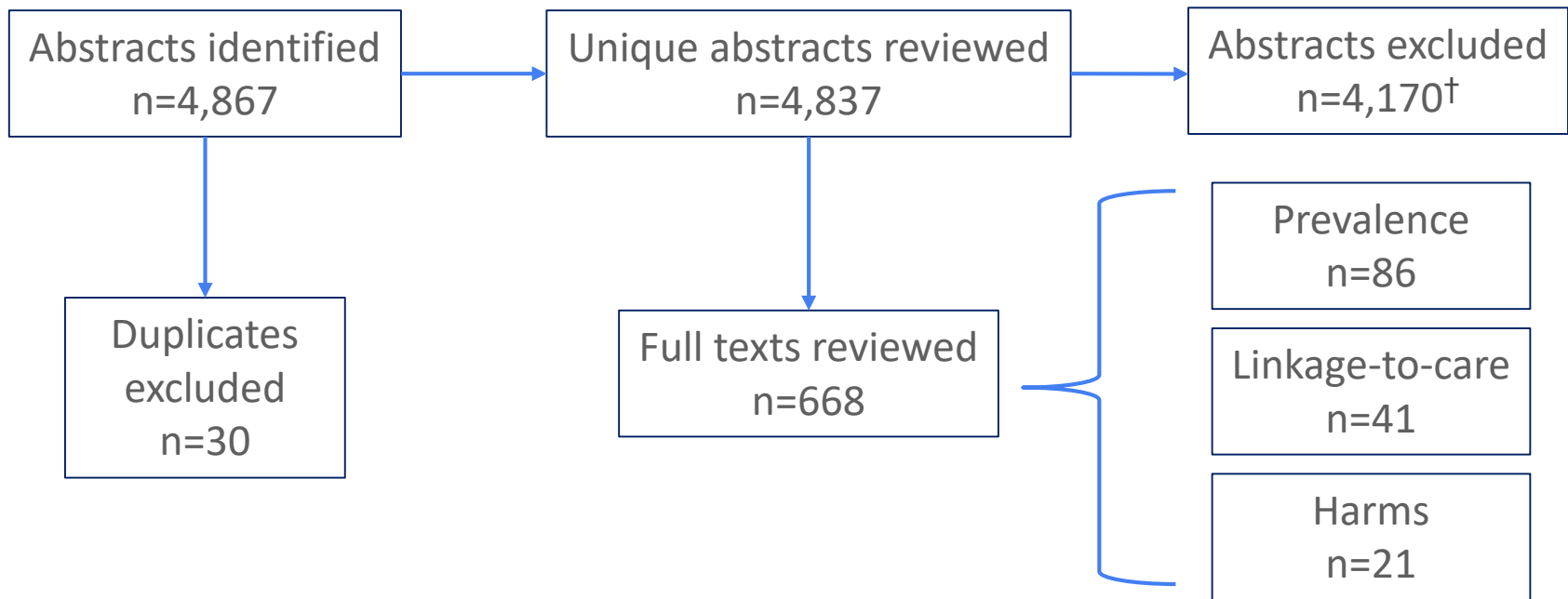
- Systematic review of data informing HCV screening strategy
 - Medline (OVID)
 - Embase (OVID)
 - CINAHL (Ebsco)
 - Scopus
 - Cochrane Library
 - All adults: January 1, 2010-August 6, 2018
 - Pregnant women: January 1, 1998-July 2, 2018
- } Update in progress
- Comparator studies (i.e., controlled trials, cohort studies, and case-control studies) conducted worldwide
 - Limit English language, no age filter
 - Titles and abstracts independently reviewed by 2 reviewers
 - Full article was retrieved and reviewed for titles/abstracts meeting inclusion criteria

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

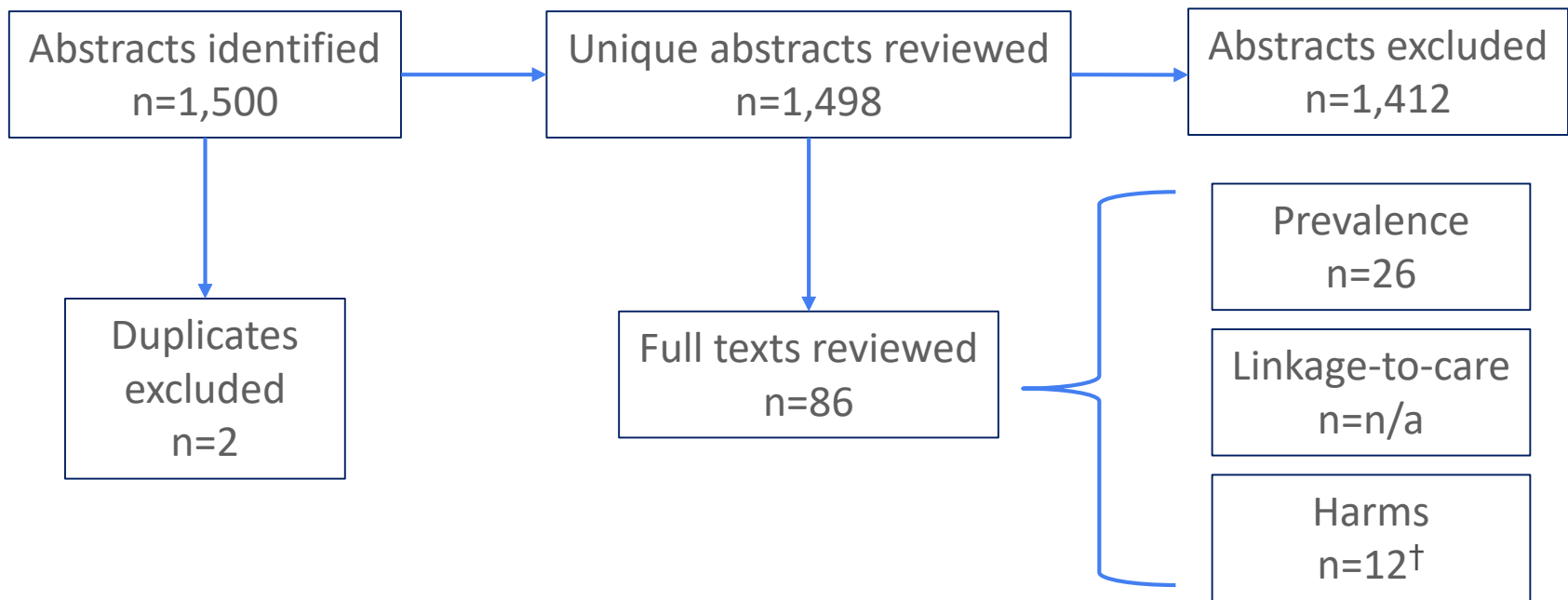
Evidence Retrieval: All Adults*



*Update in progress; final numbers likely to change

†One study uploaded twice into Covidence systematic review software system

Evidence Retrieval: Pregnant Women*



*Update in progress; final numbers likely to change

†3 of 12 studies: harms not specific to pregnant women but identified through pregnancy review

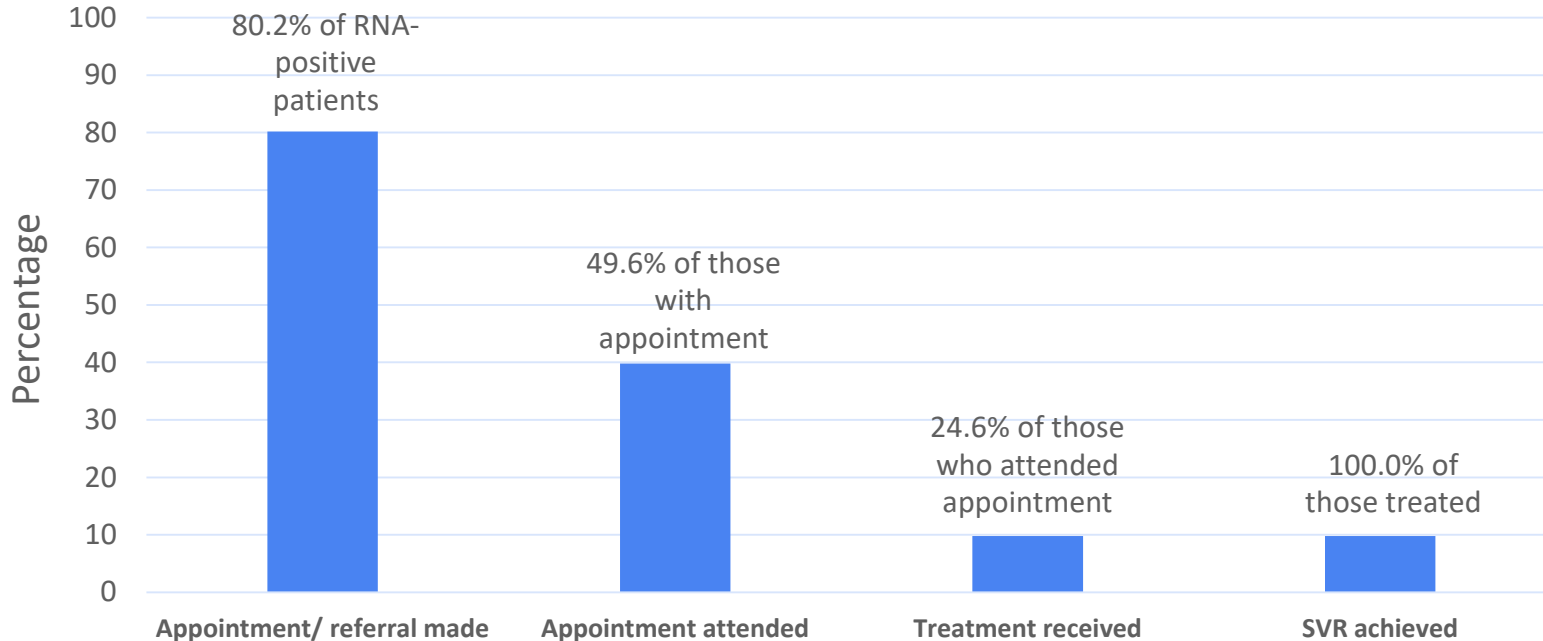
Prevalence of HCV Infection in U.S. Populations*

Sub-Population	Anti-HCV-positivity median, range (number of studies)	HCV RNA-positivity median, range (number of studies)
General population	2.3%, 1.2%-6.2% (6)	65.0%, 46.9%-83.0% (2)
Birth cohort members	3.3%, 0%-19.8% (34)	56.3%, 20.0%-97.6% (15)
ED patients	7.5%, 1.6%-25.8% (3)	57.9% (1)
Immigrant populations	4.7%, 3.4%-7.5% (3)	81.8% (1)
Others at risk†	9.4%, 1.2%-27.4% (24)	72.4%, 45.5%-82.6% (9)
Persons with HIV	15.7%, 8.0%-19.3% (5)	Not reported
Persons who use drugs	43.6%, 1.6%-100% (26)	73.4%, 35.6%-82.6% (6)
Pregnant women	1.2%, 0.1%-67.0% (26)	69.4%, 61.5%-77.2% (2)

*Update in progress; final numbers likely to change

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

Linkage-to-Care* (assessed in 41 studies†)



*Update in progress; final numbers likely to change

†16 (39.0%) only/predominantly among 1945-65 birth cohort members

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

Harm Categories

All adults (number of studies)

- Physical harms of screening (1)
- Anxiety/stress related to testing or waiting for results (4)
- Anxiety related to receiving positive results (1)
- Interpersonal outcomes (e.g., problems related to family, friends from learning HCV status) (5)
- Attitudes toward people with hepatitis C, including stigma (8)
- False positive results (6)
 - Including among left ventricular assist device patients, possibly precluding heart transplantation

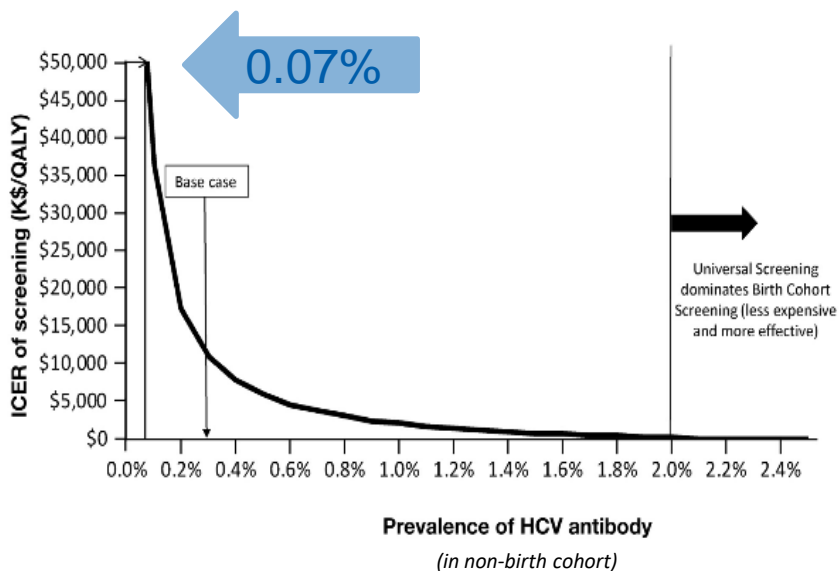
Pregnant women (number of studies)

- Physical harms of screening (1)
- Anxiety/stress related to testing or waiting for results (5)
- Interpersonal outcomes (e.g., problems related to family, friends from learning HCV status) (2)
- Attitudes toward people with hepatitis C, including stigma (1)
- False positive results (1)
- Cost of testing/treatment (4)
- Legal ramifications/potential loss of custody (1)
- Decreased quality of life knowing infected (1)

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

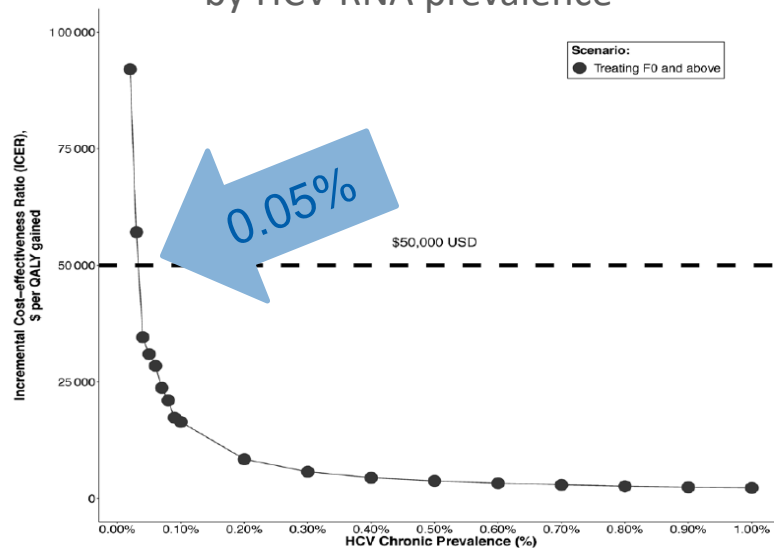


Eckman M, et al. Hepatology 2019.

ICER, incremental cost-effectiveness ratio

Pregnant Women

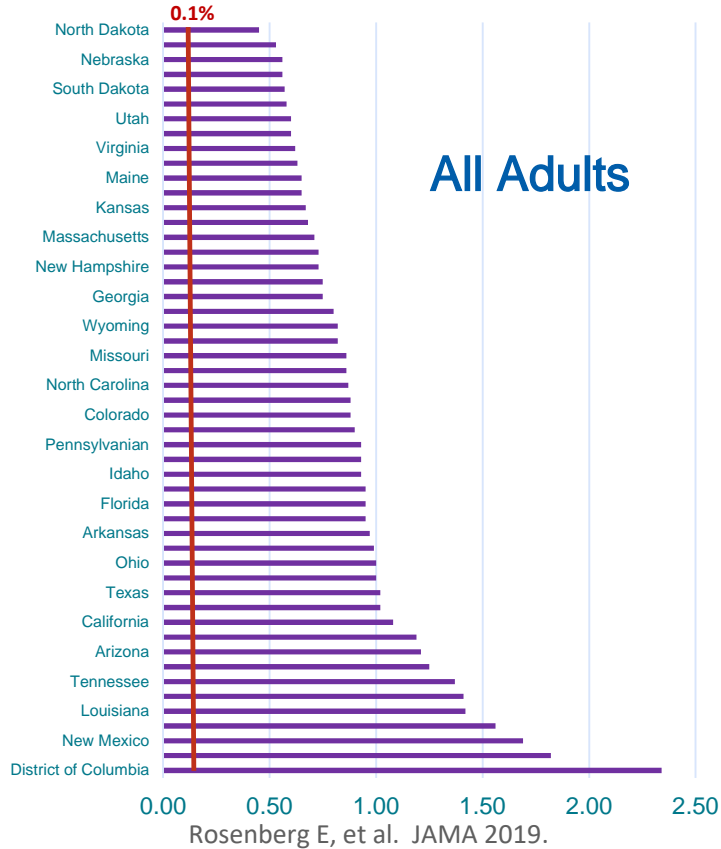
ICER of universal screening compared with risk-based testing by HCV RNA prevalence



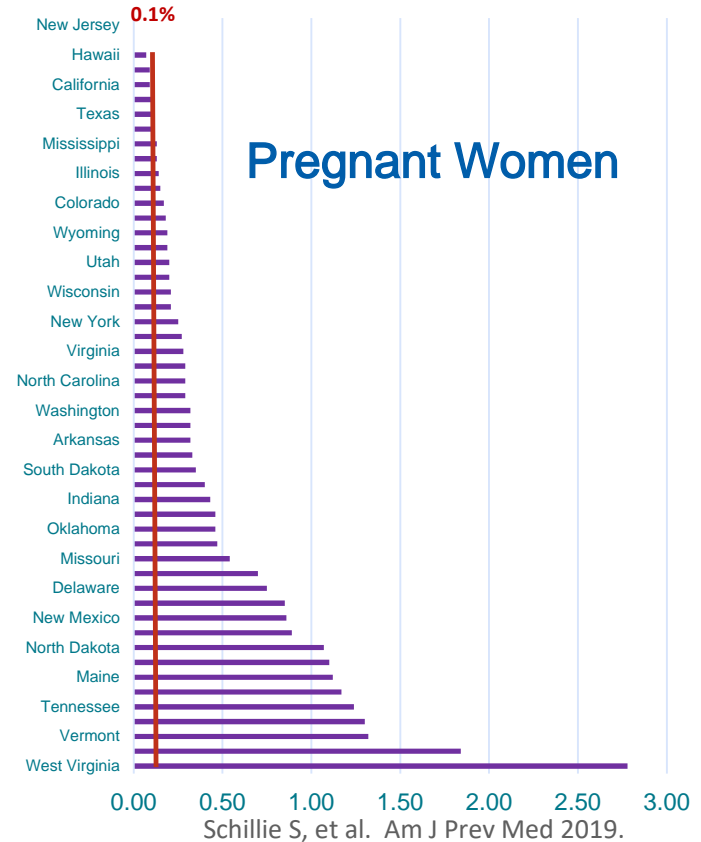
Chaillon A, et al. Clin Infect Dis 2019.

Hepatitis C Prevalence

Estimated Prevalence of Persons
Positive for HCV RNA, 2013-2016



HCV Infection Among Pregnant
Women, Birth Certificate Data, 2015



Summary of Evidence Review

- Although direct evidence informing hepatitis C screening is lacking:
 - Hepatitis C is a public health priority
 - Prevalence is high for a curable disease
 - Incidence is increasing
 - Desirable anticipated effects outweigh undesirable effects
 - Universal testing will be cost-effective and feasible to implement at or above a prevalence of 0.1%

Summary of Evidence Review, cont.

- 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
- Direct-acting antivirals may be available for use in pregnant women and children in the future (treatment and/or prophylaxis)

*Society for Maternal Fetal Medicine (#43, 2017) recommends avoiding internal fetal monitoring, prolonged rupture of membranes, and episiotomy; amniocentesis is recommended over chorionic villus sampling

Testing Considerations

- Hepatitis C screening can be conducted in a variety of settings or programs that serve populations at different risk and with varying hepatitis C prevalence
- Healthcare providers should initiate universal screening for all adults and pregnant women unless the prevalence of HCV infection in their patients has been documented to be $<0.1\%$
- In the absence of existing data for hepatitis C prevalence:
 - Providers should initiate universal hepatitis C screening until they establish that the prevalence of HCV RNA positivity in their population is $<0.1\%$
 - If HCV RNA positivity established at $<0.1\%$: universal screening is no longer explicitly recommended but may occur at the provider's discretion

Testing Considerations, cont.

- Hepatitis C testing should be initiated with an FDA-approved anti-HCV test
 - Immunocompetent persons without hepatitis C risks who test anti-HCV negative require no further testing
- Persons who test anti-HCV positive should have FDA-approved nucleic acid testing for detection of HCV RNA
 - Reflex HCV RNA testing encouraged
- Hepatitis C testing should be provided 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 (although pregnant women tested early in pregnancy with ongoing risk factors could undergo repeat testing later in pregnancy)

Subsequent Steps

- **December 2019** – Complete supplemental literature search to identify recently-published studies
- **December 27, 2019** – End of public comment period for Federal Register Notice ends; link for viewing draft statement and making public comments:
<https://www.regulations.gov/docket?D=CDC-2019-0094> or
<https://www.cdc.gov/hepatitis/policy/ScreeningComments.htm>
- **January, 2020** – CDC response to peer review (six independent reviewers) and public comments
- **January, 2020** – Revised MMWR submitted to CDC clearance, round #2
- **February, 2020** – Submission to MMWR for publication

How is DVH Approaching Viral Hepatitis as a “Winnable Battle”

Current

- Strategic Planning 2025
- Updated HCV testing recs, Vital Signs, communications materials
- New funding opportunity
- FDA down classification hepatitis C diagnostics
- New Strategy & Implementation Unit
 - Focus on accelerating access to prevention, testing & treatment *all* populations

Moving Forward

- **Guidelines and Recommendations**
 - Update guidance for correctional settings (last update 2003)
 - Review of ACIP hepatitis B vaccine recommendations (last update 2018)
 - Update hepatitis B testing guidelines (last update 2008)
- **Conduct analyses (epidemiologic, cost-effectiveness)**
- **Coordinate with other federal agencies**
- **Focus on “Getting Science off the Shelf” (nationally)**
 - Guidance documents, tool kits
 - Simplify, integrate, decentralize

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*At time of work

Discussion