What’s New in Viral Hepatitis at the CDC:

Updated HCV Testing Recommendations & Next Steps

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Hepatitis C Virus (HCV): Epidemiology

- Estimated 2.4 million persons (1% of U.S. population) with HCV infection during 2013-16*
- Injection drug use is primary risk factor for infection
- Reported cases of acute HCV infection increased every year from 2009-2017†
  - Highest rates of acute cases among persons aged 20-39
- In 2015, 0.38% of live births delivered by mothers with HCV infection§

Hepatitis C Virus: Natural History and Treatment

- Early studies suggested 75%-85% of persons who become infected with HCV will develop chronic infection,* more recent data suggest ~55% will develop chronic infection†
  - 10%-15% will develop progressive liver fibrosis and cirrhosis*

- Well-tolerated, all oral direct-acting antiviral medication regimens can cease disease progression and result in a virologic cure (sustained virologic response, SVR) in most persons with 8-12 weeks of treatment
  - Not approved for use in pregnant women or children under 3 years of age

U.S. Strategy to End the Hepatitis C Epidemic

- **Anti-HCV assays licensed in U.S.** (1990-1991)
- **U.S. Public Health Service interagency guidelines for screening blood, organs, or tissues** (1998)
- **CDC guidelines for risk-based testing** (1999)
- **U.S. Public Health Service and IDSA guidelines for testing persons with HIV**
- **IDSA/AASLD guidelines for testing during pregnancy** (2018)

IDSA, Infectious Diseases Society of America
AASLD, American Association for the Study of Liver Diseases
Limitations of Existing Strategy

- Awareness of HCV infection suboptimal*
- From 2013-2016, 55.6% of adults with HCV infection reported having ever been told they had hepatitis C
  - 61.5% among Baby Boomers
  - 38.2% among those at risk for significant fibrosis
- Awareness lowest among:
  - Hispanics
  - Asians
  - Foreign-born below federal poverty level
  - Low education level

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%
Updated Recommendations, cont.

- Previously-published recommendations for hepatitis C testing of persons with risk factors remain in effect
- Regardless of age or setting prevalence, all persons with risk factors should be tested for hepatitis C
  - Periodic testing while risk factors persist
Updated Recommendations, cont.

- **Augment (not replace) existing risk-based* and birth cohort† recommendations**
- 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

Updated Recommendations, cont.

- 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

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

# Policy Questions

<table>
<thead>
<tr>
<th>PICO question</th>
<th>Does universal screening for HCV infection among adults aged 18 years and older, compared to risk-based screening, reduce morbidity and mortality?</th>
<th>Does universal screening for HCV infection among pregnant women, compared to risk-based screening, reduce morbidity and mortality for mothers and their children?</th>
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</thead>
<tbody>
<tr>
<td>Population</td>
<td>Adults aged 18 years and older</td>
<td>Pregnant women</td>
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<tr>
<td>Intervention</td>
<td>Universal HCV screening</td>
<td>Universal HCV screening</td>
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<td>Comparison</td>
<td>Risk-based (including birth cohort) screening</td>
<td>Risk-based screening</td>
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<tr>
<td>Outcomes</td>
<td><strong>Benefits:</strong> • Reduction in HCV disease burden • Reduction in HCV-related liver disease <strong>Harms:</strong> • False-positive results (or anti-HCV positive with negative RNA) • Stigma • Harms associated with work-up (e.g., liver biopsy) or treatment</td>
<td><strong>Benefits:</strong> • Reduction in HCV disease burden • Reduction in HCV-related liver disease • Identification of infants for HCV testing <strong>Harms:</strong> • 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</td>
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</table>
# Chain of Indirect Evidence

<table>
<thead>
<tr>
<th>K.Q.1.a. What is the prevalence of HCV infection in the U.S.? By: --general population --risk groups</th>
<th>K.Q.2.a. What is the diagnostic accuracy of HCV antibody testing?*</th>
<th>K.Q.3.a. What is the effect of DAA treatment on HCV viral load?*</th>
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</thead>
<tbody>
<tr>
<td>K.Q.2.b. What are harms of HCV screening?†</td>
<td>K.Q.2.c. What proportion of people who screen positive for HCV are linked to care?§,¶</td>
<td>K.Q.3.b. What is the effect of DAA treatment on morbidity (including cirrhosis, hepatocellular carcinoma)?*</td>
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<td></td>
<td>K.Q.3.c. What is the effect of DAA treatment on mortality (HCV-specific and all-cause)*</td>
<td>K.Q.3.d. What are the adverse effects of DAA treatment?*</td>
</tr>
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</table>

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
- Titles and abstracts independently reviewed by 2 reviewers
- Full article was retrieved and reviewed for titles/abstracts meeting inclusion criteria

Update in progress
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*

- Abstracts identified: n=4,867
- Duplicates excluded: n=30
- Unique abstracts reviewed: n=4,837
- Abstracts excluded: n=4,170†
- Full texts reviewed: n=668
- Prevalence: n=86
- Linkage-to-care: n=41
- Harms: n=21

*Update in progress; final numbers likely to change
†One study uploaded twice into Covidence systematic review software system
Evidence Retrieval: Pregnant Women*

- Abstracts identified: n=1,500
  - Duplicates excluded: n=2
  - Unique abstracts reviewed: n=1,498
    - Abstracts excluded: n=1,412
      - Prevalence: n=26
      - Linkage-to-care: n=n/a
      - Harms: n=12†

*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*

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

*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†)

- **Appointment/ referral made**: 80.2% of RNA-positive patients
- **Appointment attended**: 49.6% of those with appointment
- **Treatment received**: 24.6% of those who attended appointment
- **SVR achieved**: 100.0% of those treated

*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

![Graph showing the ICER of universal screening compared with birth cohort screening by anti-HCV prevalence in non-birth cohort.](image)

Universal Screening dominates Birth Cohort Screening (less expensive and more effective)

ICER, incremental cost-effectiveness ratio


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

![Graph showing the ICER of universal screening compared with risk-based testing by HCV RNA prevalence.](image)

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

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

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.
• 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