Hepatitis C Virus: National Trends and Prevention Recommendations

John W. Ward, M.D.
Division of Viral Hepatitis
Centers for Disease Control and Prevention
Goals

Describe:

- Trends in HCV transmission, disease, and mortality
- Health benefits of HCV testing, care, and treatment
- Strategies to screen and link HCV infected persons to care
Hepatitis C Virus

• Discovered in 1989, RNA virus, family *Flaviviridae*
• 9600 nucleotide genome - single polyprotein
  – Non-structural protein - targets of therapy
  – High genetic diversity – intra-host variants - “quasispecies”
  – 7 major genotypes - varied response to treatment
    • Genotype 1 - ~ 70% of infections in US
    – No vaccine

Global Hepatitis C Burden is Large and Highest in Asia and Africa

- 3-4 million new infections per year
- 130-150 million chronic infections
- 704,000 deaths/ 2010

# Prevalence of Current HCV Infection Among Persons in the United States

<table>
<thead>
<tr>
<th>Prevalence Civilian, Non-Institutionalized Populations (NHANES)</th>
<th>2.7 million (2.2-3.2 million) 1.0% (0.8%-1.2%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated HCV Infection Among Homeless and Incarcerated Persons (Not Included in NHANES)</td>
<td>360,000-840,000 22%-52%</td>
</tr>
</tbody>
</table>

Natural History of HCV Infection

HIV, HBV, alcohol, and steatosis can accelerate disease progression

Modes of HCV Transmission

- Health care exposures- most common cause globally
- Injection drug use – highest risk population
- Other modes
  - Sexual
    - Heterosexual - rare
    - HIV+ MSM have eight fold higher risk than HIV-MSM
  - Perinatal - ~4% transmission risk; ~12% if mother HIV+
- Others reported
  - Non-injecting drug use (e.g., inhaled drugs)
  - Household exposures
  - Unregulated tattooing

MSM: Men who have sex with men.

Healthcare-associated HCV Transmission

• Larger contributor to transmission before viral discovery
• Prevention measures have reduced not eliminated transmission risk
• Total 18 outbreaks reported to CDC 2008-2013
  - 223 outbreak-associated cases
  - >90,550 at-risk persons notified for screening
• Settings
  o Outpatient (e.g., surgical centers), dialysis
  o Hospitals
  o Long term care
• Modes of transmission
  o Syringe reuse
  o Other poor infection control
  o Drug diversion

http://www.cdc.gov/hepatitis/
Outbreaks of HCV in Residential Care Settings

- Investigation of residential care facility - North Dakota
- 35 HCV cases identified; >25% prevalence
- Highly related HCV quasispecies
- Associated with podiatry exposures
HCV Transmission Among People Who Inject Drugs

- Transmission risks
  - Injection duration
  - Frequency of injecting
  - Equipment sharing, not just sharing needles

- Incidence declined in response to harm reduction for HIV (e.g., syringe access programs)

Kwon et al., JAIDS 2009
Role of Public Health in Hepatitis C Prevention, Testing and Cure

US Institute of Medicine, 1988
Discovery of HCV and Impact on HCV Incidence in US

29,000 cases of incident HCV infection reported in 2013

The Growing Burden of Hepatitis C in the United States

- Of 2.7 million HCV-infected persons in primary care
  - 1.47 million will develop decompensated cirrhosis (DCC)
  - 350,000 will develop hepatocellular carcinoma (HCC)
  - 897,000 will die from HCV-related complications

Increases in Hepatitis C Mortality

Rate per 100,000 Persons

Year


19,368
CDC and USPSTF Updated Recommendations for HCV Testing

• **One time screening test for persons born 1945-1965**

• **Major risk**
  – Past or present injection drug use

• **Other risks**
  – Received blood/organs prior to June 1992
  – Received blood products made prior to 1987
  – Ever on chronic hemodialysis
  – Infants born to HCV infected mothers
  – Intranasal drug use
  – Unregulated tattoo
  – History of incarceration

• **Medical**
  – Persistently elevated ALT
  – HIV (annual testing)

The Evolution of HCV Therapy from Interferon to Direct Antiviral Agents

Potential to Avert 320,000 Deaths with Birth Cohort Testing Using Latest Treatments

PR = Pegylated Interferon plus Ribavirin for all genotypes, PRPI = PR plus a protease inhibitor for genotype 1, PR for genotypes 2/3; PRS/SR = pegylated interferon, ribaviron, and sofosbuvir for genotype 1, and sofosbuvir plus ribavirin for genotypes 2 and 3; SS/SR = Sofosbuvir and Simeprevir for genotype 1, and sofosbuvir and ribavirin for genotypes 2 and 3.
Testing of Persons Born 1945-1965 is Cost Effective (CE)

- Typical willingness-to-pay thresholds (<$50K-100K/QALY)
  - Treat all -31,828-35,100/QALY at market price (Vikera-Pak-$31,828, Harvoni $35,100)

- Cost/QALY sensitive to stage of liver disease
  - F0- $173K; F2; $37K; F4- $13K; treat all $42K

- Drug costs are now lower than wholesale marker price
  - Payer/Pharma agreements- average ~46% decline
  - Medicaid- mandated 23% discount or to match best price
  - Lawsuits against health plans filed by patients denied treatment

*Quality adjusted life year.
Trends in HCV Ab testing rate, by birth cohort

Rate per 1,000 Quest patients

- CDC birth cohort recommendations
- USPSTF birth cohort recommendations

Q1 2011 - Q1 2015

1945-1965

Pre1945

+41%

+10%
Medicaid Reimbursement Criteria - HCV Therapy

- Minimum fibrosis score
- Prescription by specialist

Some states have few specialists; some states require biopsies for fibrosis scoring

Canary L, Ann Int Med, in press
The Quality of HCV Management Must Improve for Patients to Benefit from HCV Therapy

~ 3 million persons living with HCV

- 50% anti-HCV tested
- 38% HCV care
- 23% HCV RNA
- 11% Treated
- 6% SVR

N.B.: HCV RNA test indicates whether patient’s infection is current or not.

Philadelphia HCV Testing and Care Coordination

- 5 community health centers - Philadelphia
- Underserved, largely Black / Hispanic population
  - ~75% homeless, 37% uninsured, 58% public insurance

Interventions

- Reflex HCV testing
- Patient education
- EMR prompts
- Mid level provider conducting testing
- Linkage to care coordinator
- Uninsured: Referred to social worker
Philadelphia HCV Testing and Care Coordination

16% of 4514 tested

- 65% of anti-HCV+
- 89% informed of HCV RNA+
- 87% specialist referral
- 79% seen by specialist

MMWR, May 2015
Reports of Acute Hepatitis C Cases — United States, 2000–2013

Source: National Notifiable Diseases Surveillance System (NNDSS)
## Recent CDC, State, and Local Public Health Investigations of Young PWID

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>Predominant Race/Ethnicity</th>
<th>Predominant Setting</th>
<th>Virus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northern Plains</td>
<td>2008</td>
<td>American Indian</td>
<td>Rural</td>
<td>HCV</td>
</tr>
<tr>
<td>Erie County, NY</td>
<td>2007</td>
<td>White</td>
<td>Suburban</td>
<td>HCV</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>2011</td>
<td>White</td>
<td>Suburban</td>
<td>HCV</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>2011</td>
<td>White</td>
<td>Rural</td>
<td>HCV</td>
</tr>
<tr>
<td>Indiana</td>
<td>2011</td>
<td>White</td>
<td>Rural</td>
<td>HCV</td>
</tr>
<tr>
<td>Virginia</td>
<td>2012</td>
<td>White</td>
<td>Rural</td>
<td>HBV +/- HCV</td>
</tr>
<tr>
<td>Courtland County, NY</td>
<td>2014</td>
<td>White</td>
<td>Rural</td>
<td>HCV</td>
</tr>
</tbody>
</table>

Common Denominator: Prescription opioid misuse followed by early initiation to injection drug use

---


Surveillance of Acute HCV Infection - 2013

- Estimated 29,000 new HCV infections
- 150% increase since 2010
- 28 of 34 states reported increases
- 66% of cases reported from 12 states
  - (CA, FL, IN, KY, MA, MI, NJ, NY, NC, OH, PA, TN)
  - KY has highest rate
- Case Rates
  - 61% report IDU
  - Equal Male (0.8): Female (0.7)
  - Highest rate
    - by age 20-29 years, 2.01
    - By race American Indian (1.7) and whites (0.82)
Tracking and Intervening to Prevent HCV Social Network of IDU - rural Kentucky - baseline

J Havans, NIDA R01-DA024598 and R01-DA033862
Understanding Transmission Among IDU Social Network of IDU - rural Kentucky - 24-Month

J Havans, NIDA R01-DA024598 and R01-DA033862
Regional Drug Injection Trends Among Persons <30 years old in KY, TN, VA, WVA

SAMHSA, Treatment Episode Data Set—Admissions
Heroin Use and Dependence is Increasing

Estimated # of persons 12 years and older reporting abuse/dependence (in thousands)

- Heroin: 214K, 467K, >2 million
- Opioids: 467K, >2 million

Years: 2002 to 2012

SAMHSA NSDUH 2012
HCV prevalence rate*, persons born after 1965 2011

*persons with detectable HCV RNA in q1 2011 per 1,000 persons served by Quest during same period
**data not shown for those states with less than 5% of population served by Quest in 2011.
HCV prevalence rate*, persons born after 1965, 2015

*persons with detectable HCV RNA in q1 2015 per 1,000 persons served by Quest during same period
**data not shown for those states with less than 5% of population served by Quest in 2015
Multi-Component Interventions Appear Most Effective in Preventing HCV Transmission

• In meta-analysis of single interventions, evidence only supports drug treatment

• A combination of readily-available and low threshold OAT (with methadone and/or buprenorphine) and SEPs have been shown to:
  – Reduce syringe sharing
  – Lower injecting risk
  – Reduce incidence of HIV and HCV
    • Up to 80% in UK
    • Three fold - New York

OAT: Opioid Agonist Treatment
SEP: Syringe Exchange Programs

HCV Screening & Testing at Venues Serving PWID

Prevention and Public Health Fund*
January 2013—March 2014

<table>
<thead>
<tr>
<th>Location</th>
<th># of Tests</th>
<th>% anti-HCV+</th>
<th>% RNA Tested</th>
<th>% RNA+</th>
<th>% Referred to Care</th>
<th>% Attended First Appt.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arizona</td>
<td>938</td>
<td>17.3</td>
<td>15.4</td>
<td>76.0</td>
<td>84.2</td>
<td>26.3</td>
</tr>
<tr>
<td>Chicago</td>
<td>672</td>
<td>22.2</td>
<td>40.9</td>
<td>80.3</td>
<td>51.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>2175</td>
<td>8.7</td>
<td>29.6</td>
<td>89.3</td>
<td>100.0</td>
<td>82.0</td>
</tr>
<tr>
<td>Maine</td>
<td>795</td>
<td>28.1</td>
<td>51.1</td>
<td>60.5</td>
<td>98.6</td>
<td>52.2</td>
</tr>
<tr>
<td>New York City</td>
<td>2527</td>
<td>17.6</td>
<td>63.4</td>
<td>71.3</td>
<td>71.1</td>
<td>23.4</td>
</tr>
<tr>
<td>Oakland, CA</td>
<td>579</td>
<td>32.0</td>
<td>18.4</td>
<td>82.4</td>
<td>100.0</td>
<td>21.4</td>
</tr>
<tr>
<td>Seattle, WA</td>
<td>457</td>
<td>56.9</td>
<td>30.0</td>
<td>66.7</td>
<td>86.5</td>
<td>5.8</td>
</tr>
<tr>
<td>Virginia</td>
<td>761</td>
<td>36.8</td>
<td>75.4</td>
<td>78.2</td>
<td>99.4</td>
<td>27.3</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>1127</td>
<td>16.1</td>
<td>107.1</td>
<td>73.3</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10031</strong></td>
<td><strong>20.7%</strong></td>
<td><strong>50.9%</strong></td>
<td><strong>73.5%</strong></td>
<td><strong>87.9%</strong></td>
<td><strong>42.0%</strong></td>
</tr>
</tbody>
</table>

Venues Include: Syringe Exchange Programs; Drug Treatment Centers; Health Departments; Methadone Clinics; Corrections; Shelters

*CDC unpublished data
Antiviral Therapy Might Be Used to Reduce HCV Prevalence Among Injecting Drug Users

- Annually treating 10 HCV infections per 1000 IDU and achieve SVR of 62.5%

- Projected to result in a relative decrease in HCV prevalence over 10 years of 31%, 13%, or 7% for prevalences of 20%, 40%, or 60%, respectively

- Can the HIV model of “Treatment as Prevention” be applied to HCV?

Martin et al. Journal of Hepatology 2011 vol. 54 j 1137–1144
## HIV HCV Outbreak in Scott County, Indiana, 2014-2015

<table>
<thead>
<tr>
<th>Status</th>
<th># Patients</th>
<th>% among persons tested for both HIV and HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-Positive/HCV-Positive</td>
<td>79</td>
<td>26%</td>
</tr>
<tr>
<td>HIV-Positive / HCV-Negative</td>
<td>3</td>
<td>1%</td>
</tr>
<tr>
<td>HIV-Negative / HCV-Positive</td>
<td>106</td>
<td>35%</td>
</tr>
<tr>
<td>HIV-Negative/HCV-Negative</td>
<td>111</td>
<td>37%</td>
</tr>
<tr>
<td>TOTAL SAMPLES</td>
<td>299</td>
<td></td>
</tr>
</tbody>
</table>

### Anti-HCV-positive

<table>
<thead>
<tr>
<th></th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-Risk Patients (reported IDU)</td>
<td>62%</td>
</tr>
<tr>
<td>HIV-Coinfected</td>
<td>96%</td>
</tr>
</tbody>
</table>

HCV antibody results
Activities to Improve Prevention of HCV Transmission in Scott County, IN

- Complete studies of social networks of HCV transmission
- Scale-up drug treatment, harm reduction
- Assess benefits of HCV cure and prevent (CAP)
  - Clinical capacity to treat target number of PWID
  - Ancillary prevention services
  - Drug availability
- Consider a demonstration project
Legal Intervention-Syringe Services Programs

- On March 24, 2015 the Kentucky General Assembly gave municipalities authority to institute a syringe exchange program.

- Indiana passed a law in May allowing counties to seek state approval to run needle exchanges, if they are in the bottom two quartiles among Indiana Counties for average number of newly reported cases of hepatitis C before an exchange can be launched.

https://louisvilleky.gov/government/health-wellness/needle-exchange-program;
http://blogs.law.harvard.edu/billofhealth/2015/05/21/a-needle-in-a-haystack-finding-the-elusive-solution-to-indianas-hiv-outbreak/
Effective Prevention Strategies and Advent of Curative HCV Therapies Have Increased Considerations for HCV Elimination
National HCV Elimination Program- Georgia

- ~4 million persons
- High burden of HCV- 5-7%
- Relatively small in-migration
- Mixed infection risks- healthcare, IDU
- Capacity- modest, good record in HIV prevention
- Motivated government
- First 60 days-
  - 6,177 HCV+ evaluated
  - 1474 started treatment

MMWR July 24, 2015 / 64(28);753-757
HCV Elimination in Georgia

- **Phase I: Immediate introduction of curative treatments (0 – 12 months)**
  - Reduce morbidity and mortality by treating persons with severe HCV associated liver disease
  - Build knowledge base for expanded access program
  - Develop broader elimination plan (Phase II)

- **Phase II: Achieve HCV elimination (7-10 year time frame)**
  - Define measurable/achievable goals
  - Interventions to prevent new infections
  - Expand access to treat all HCV infected persons
Proposals for HCV Elimination - United States

- **Increase priority** - widen public recognition of urgency of action
- **Increase screening** - follow USPSTF recommended screening
- **Improve testing algorithm** - simplify HCV screening and diagnosis
- **Enhance surveillance** - change policies to improve utility of data
- **Expand clinical workforce** - allow for primary care management
- **Increase treatment availability** - modify treatment regimens
- **Reduce payer restrictions** – increase number of therapeutics

Phil Coffin, UCSF, CDc National HCV Summit – 6/2014)
HCV Elimination in Cherokee Nation

- Small population (314,000) in defined 14 county area
- 95% receive care in CN Health Service- hospital, 8 clinics
- High prevalence- anti-HCV 6.0% (2013); 5160 current HCV infections
- Nascent test, care, and cure programs
- Tribal leadership commitment to HCV elimination
- Coalition of public health, clinical care, and academic medicine
Summary

- HCV incidence is increasing in the US; IDU is major risk
- Prevention Goals
  - Reduce Mortality – Testing Linkage to care and treatment
  - Reduce Transmission – Infection control, harm reduction, drug treatment, cure and prevention strategies
- Timely HCV surveillance to detect and interrupt transmission
  - Excellent continuum of HCV testing, care, and treatment
  - Sustained commitment to HCV prevention
It took us 25 years to bring him to his knees... now let's finish him off...
Contributors

- Dan Church
- Jennifer Havans
- Scott Holmberg
- Saul Karpen
- Anil Suryprasad
- Jon Zibbell
Most don’t know they’re infected
Essential Goals to Eliminate HCV

- **Prevent sequelae of advancing liver disease in those already infected**
  - Baby Boomers, born 1945-1965
  - Many don’t know they are infected

- **Prevent new or “incident” infections**
  - Persons who inject drugs
  - Unsafe healthcare practices
  - Sexual exposures in immunocompromised individuals
HCV Deaths Averted with Birth Cohort Testing Using Different Treatments

PR = Pegylated Interferon plus Ribavirin for all genotypes, PRPI, PR = PR plus a protease inhibitor for genotype 1, PR for genotypes 2/3; PRS/SR = pegylated interferon, ribavirin, and sofosbuvir for genotype 1, and sofosbuvir plus ribavirin for genotypes 2 and 3; SS/SR = Sofosbuvir and Simeprevir for genotype 1, and sofosbuvir and ribavirin for genotypes 2 and 3.
Number of Persons Tested Quarterly for HCV Antibody Conducted by Quest Diagnostics by Year of Birth, United States, Jan 2011 - Sep 2014

- Born after 1965
- Born between 1945 and 1965
- Born before 1945

Screening guidance published
### Staging of HCV-Related Liver Fibrosis Using FIB-4 by Birth Cohort, 2010-2013

<table>
<thead>
<tr>
<th></th>
<th>Born&lt;1945</th>
<th></th>
<th>Born 1945-1965</th>
<th></th>
<th>Born &gt;1965</th>
<th></th>
<th>Total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Percent</td>
<td>Number</td>
<td>Percent</td>
<td>Number</td>
<td>Percent</td>
<td></td>
<td>Percent</td>
</tr>
<tr>
<td>None</td>
<td>79</td>
<td>1</td>
<td>7,315</td>
<td>9</td>
<td>16,587</td>
<td>53</td>
<td>23,981</td>
<td>19</td>
</tr>
<tr>
<td>Moderate</td>
<td>1,543</td>
<td>19</td>
<td>32,996</td>
<td>38</td>
<td>8,949</td>
<td>29</td>
<td>43,488</td>
<td>35</td>
</tr>
<tr>
<td>Severe</td>
<td>2,982</td>
<td>37</td>
<td>22,448</td>
<td>26</td>
<td>2,172</td>
<td>7</td>
<td>27,602</td>
<td>22</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>2,865</td>
<td>36</td>
<td>17,875</td>
<td>21</td>
<td>1,315</td>
<td>4</td>
<td>22,055</td>
<td>18</td>
</tr>
<tr>
<td>Unknown/missing</td>
<td>508</td>
<td>6</td>
<td>5,253</td>
<td>6</td>
<td>2,189</td>
<td>7</td>
<td>8,164</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>7,977</td>
<td></td>
<td>85,887</td>
<td></td>
<td>31,212</td>
<td></td>
<td>125,290</td>
<td></td>
</tr>
</tbody>
</table>

Monina K, CROI 2015
Medicaid Reimbursement Criteria - HCV Therapy

- Illicit drug abstinence before treatment
- Alcohol abstinence before treatment

Some states require blood/urine tests; some states deny payment for patients who test positive for methadone, and marijuana.
HIV Outbreak - Indiana

- Epicenter- Austin, Scott Co.
- 55 confirmed cases to date
- ~80% report HCV+
- IDU predominant risk
- Response
  - HIV testing / PREP
  - HCV testing
  - HA/B vaccination
  - Emergency order for syringe exchange- opened 4/4
Local Hepatitis C Cases Hit All-time High

- Ross County OH- pop 78,000
- 234 cases of acute hepatitis C reported in 2014; 53% increase
- Acute Hepatitis B also increased
- HCV reports exceeded reports of chlamydia