Chronic Hepatitis C (CHC) is a global problem
- ~ 180 million infected worldwide

CHC is also a domestic problem
- ~ 3-4 million of the US population is chronically infected
- True prevalence of HCV is underestimated
- Most HCV patients are unaware of their infection
- Although HCV incidence in US has decreased, CHC related complications (cirrhosis & HCC) are increasing
- CHC is the most common etiology for HCC and reason for liver transplant in the U.S.
- HCV is associated with extrahepatic manifestations
- HCV has tremendous PRO and economic impact
- Some patient groups present a special challenge
- The risk-based screening was not very successful
- “Baby boomer” screening is now widely recommended
Prevalence of HCV

Consider three important issues related to the prevalence of HCV:
• The baby boomer cohort born between 1945-1965 have higher prevalence of HCV
• The true prevalence of HCV is underestimated
• Most patients with HCV are unaware of their infection

Two-Thirds of Those With Chronic HCV in the U.S. Were Born Between 1946 and 1964

Estimated Prevalence by Age Group

The Impact of HCV

True prevalence of HCV is underestimated

Has the Prevalence of Hepatitis C Infection in the US Been Underestimated?

- An estimated 1,921,748 - 3,821,668 persons living in the USA were unaccounted for in the NHANES survey

<table>
<thead>
<tr>
<th>Population</th>
<th>Reported Prevalence Range</th>
<th>Estimated Number in US</th>
<th>Estimated Range of HCV Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homeless</td>
<td>22.2 - 52.5%</td>
<td>643,067</td>
<td>142,761 - 337,610</td>
</tr>
<tr>
<td>Incarcerated</td>
<td>23.1 - 41.2%</td>
<td>1,613,656</td>
<td>372,754 - 664,826</td>
</tr>
<tr>
<td>Veterans</td>
<td>5.4 - 10.7%</td>
<td>22,915,943</td>
<td>1,237,461 - 2,452,006</td>
</tr>
<tr>
<td>Active Military Duty</td>
<td>0.48%</td>
<td>1,417,747</td>
<td>6,805</td>
</tr>
<tr>
<td>Healthcare Workers</td>
<td>0.9-3.6%</td>
<td>7,200,950</td>
<td>64,809 - 259,234</td>
</tr>
</tbody>
</table>

Chak E et al. Liver Int 2011, 1478-3231
Has the Prevalence of Hepatitis C Infection in the US Been Underestimated? (cont)

<table>
<thead>
<tr>
<th>Population</th>
<th>Reported Prevalence Range</th>
<th>Estimated Number in US</th>
<th>Estimated Range of HCV Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nursing Home Residents</td>
<td>4.5%</td>
<td>1,413,540</td>
<td>63,609</td>
</tr>
<tr>
<td>Chronic Hemodialysis</td>
<td>7.8%</td>
<td>263,820</td>
<td>20,578</td>
</tr>
<tr>
<td>Hemophiliacs with Transfusions before 1992</td>
<td>76.3 - 100%</td>
<td>17,000</td>
<td>12,971 - 17,000</td>
</tr>
</tbody>
</table>

Unaccounted number of HCV positive: 1,921,748 - 3,821,668

NHANES: 3,270,000

Total: 5,191,748 - 7,091,668

Chak E et al. Liver Int 2011, 1478-3231

The Impact of HCV

Most HCV Infected Individuals Unaware of Their Infection
Prevalence of Chronic Hepatitis C Infection

- ~3,300,000 individuals are infected
- Only 825,000 are aware of their infection
- 2,475,000 are unaware of their infection

Hepatitis C is the Most Common Blood-Borne Chronic Viral Infection in U.S.

HCV is Nearly 4 Times as Prevalent as HIV and HBV

The Impact of HCV

Incidence of HCV

Reported number of acute hepatitis C cases — United States, 2000–2010

Source: National Notifiable Diseases Surveillance System (NNDSS)
CDC 2014
The Impact of HCV

Clinical Consequences of HCV
**Natural History of HCV Infection**

- **Acute Infection**: 20%-30% of individuals are symptomatic.
- **Chronic Infection**
  - 75%-85% over 20 years
  - Extrahepatic Manifestations
  - Clearance of HCV RNA 15%-25%
- **Cirrhosis**
  - 10%-20% over 20 years
  - Risk of decompensation increases from 6% (1 year) to 30% (10 years) from the diagnosis of cirrhosis
- **HCC**
  - 1%-4% per year
  - Decompensated Cirrhosis
  - 5-yr survival rate 50%


**The Impact of HCV**

Although HCV incidence in US has largely been decreasing from 2000-2010, CHC related complications (cirrhosis & HCC) are increasing.
HCV-related decompensated cirrhosis and HCC are rising in the aging population.

73.4% of HCV-related deaths occurred among persons 45-64 years of age (Median age was 57 years; ~20 years less than the average lifespan of persons living in the US).


HCV is the leading cause of liver transplants in the US.

The Impact of HCV

Clinical Consequences of HCV: Overall Mortality

By 2007, HCV Deaths Surpassed HIV Deaths

Change in Mortality Rates From 1999 to 2007

By 2007, HCV Deaths Surpassed HIV Deaths

By 2007, HCV Deaths Surpassed HIV Deaths

Clinical Consequences of HCV: Extrahepatic Complications

Chronic HCV Infection Increases Mortality from Both Hepatic and Extrahepatic Diseases

- All Causes
  - (n=2394)
  - Cumulative Mortality (%)
  - Anti-HCV+, HCV RNA detectable
  - Anti-HCV+, HCV RNA undetectable
  - Anti-HCV-

- Liver Cancer
  - (n=115)
  - Cumulative Mortality (%)

- Extrahepatic Diseases
  - (n=2199)
  - Cumulative Mortality (%)

*p<0.001 for comparison among all 3 groups and p<0.001 for HCV RNA detectable versus undetectable.

Chronic HCV infection: A Systemic Disease

- Hepatitis C causes a systemic infection that is associated with both hepatic and non-hepatic manifestations
- Extrahepatic manifestation:
  - Mixed type 2 cryoglobulinemia, PCT, type 2 diabetes, chronic fatigue, lymphoma and cardiovascular diseases

The Impact of HCV

Other Consequences of HCV Infection: PRO and Economic Outcomes
Hepatitis C infection causes impairment of Patient Reported Outcomes (Quality of life, fatigue, and WP)

HCV Causes Impairment of Patient Reported Outcomes and Work Productivity

Modified from Younossi Z et al. Hepatology 2007
Chronic HCV infection

Hepatitis C infection causes significant and growing economic burden

All-Cause and Incremental Per Patient Per Year Cost Associated with Chronic Hepatitis C

Mean All-Cause Health Care Costs for Patients with Hepatitis C Virus Vs. Matched Comparison Enrollees

$113,282

Annual All-Cause Health Care Costs for Patients with Hepatitis C Virus Vs. Matched Comparison Enrollees

∆ = $93,609

$41,943

$58,208

∆ = $5,330

∆ = $5,870

∆ = $27,845

∆ = $43,671

∆ = $9,681

$19,672

$40,000

$60,000

$80,000

$100,000

$0

Mean $ per patient per year (PPPY)

P < 0.001 for all case vs. comparison groups.
All costs were reported in 2009 dollars.
Data Source: National Medical and Pharmacy claims database.

 Costs Associated with the Care of HCV-Infected Patients Increase with Disease Severity

Estimated Mean Annual Costs*

<table>
<thead>
<tr>
<th>Disease Severity</th>
<th>All-Cause Costs (US $) (per-Patient-per-Month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Cirrhotic Liver Disease</td>
<td>$17,777</td>
</tr>
<tr>
<td>Compensated Cirrhosis</td>
<td>$22,732</td>
</tr>
<tr>
<td>End-Stage Liver Disease</td>
<td>$69,686</td>
</tr>
<tr>
<td>Hepatocellular Carcinoma</td>
<td>$112,857</td>
</tr>
<tr>
<td>Orthotopic Liver Transplantation</td>
<td>$145,046</td>
</tr>
</tbody>
</table>


All-Cause Healthcare Costs Rise Significantly with More Severe Disease

Impact of HCV on Resource Utilization for Medicare Beneficiaries

Liver-Related Inpatient Resource Utilization for Medicare Beneficiaries with Hepatitis C

- Patients with HCV who sought liver disease-related inpatient care in 2010: 65.9% male, 73.4% with age<65
- The average annual payment for inpatient services is from $19,800-$24,000 with proportion of Medicare’s responsibility ranging from 86.8% to 89.6%
- The majority of the HCV population in 2010 was still <65 years old; the potential economic impact is not yet fully realized


Impact of HCV on Resource Utilization for Medicare Beneficiaries

Liver-Related Outpatient Resource Utilization for Medicare Beneficiaries with Hepatitis C

- Patients with HCV who sought liver disease-related outpatient care in 2010: 58.3% male, 72.6% with age<65
- There is a trending pattern for outpatient cost. The average annual payment for outpatient is from $2,294-$3,145 with proportion of Medicare’s responsibility ranging from 79.9% to 81.3%

Healthcare Costs Are Climbing Due to the Progression to More Advanced Liver Disease

HCV Population Is Aging
Serious liver disease associated with HCV will have a greater healthcare system impact as the infected population ages


“Special Populations” with CHC

- Increased prevalence of HCV
- Challenges related to access to care
Prevalence of HCV in Select Populations

- Incarcerated: ~330,000 to 860,000 (16–41%)¹
- Injection drug users: ~300,000 (80–90%)²³
- Alcoholics: ~240,000 (11–36%)²
- Homeless: ~175,000 (22%)⁷
- Veterans: ~280,000 (4%)⁸
- Living below poverty level: ~940,000 (3.2%)⁶

HIV-infected: ~300,000 (30%)⁴


Chronic Hepatitis C

HCV Challenges for African Americans and Hispanics
**HCV Infection in Blacks/African Americans**

*High Prevalence of HCV*

![Graph showing prevalence of HCV by age group and race/ethnicity.](image)


**HCV Infection in Blacks/African Americans**

*High Prevalence of HCV Genotype 1*

![Bar chart showing weighted percentage of HCV genotypes by race/ethnicity.](image)

HCV Infection in Blacks/African Americans

- Negative prognostic considerations
  - Appear to be unable to clear HCV as efficiently compared with Whites
  - Impaired CD4 cell cytokine response
  - Higher incidence of HCC (histologically documented): 6.1 and 2.8 per 100,000 persons in Blacks/African Americans and Whites, respectively
  - HCC-associated mortality rate is twice that of Whites
  - The response rates are better with newer regimens

African-Americans are Less Likely to Have Hepatitis C Virus (HCV) Infection Cleared

- NHANES (2005-2008) cohort (N=14,750)
  - Of these, 192 (1.32±0.11%) were anti-HCV+ with 76% having detectable HCV RNA
  - HCV Clearance was defined as HCV Ab(+) & HCV RNA (-)
  - The rate of HCV clearance was lowest among African-Americans (9.25±3.47%) as compared to both Caucasians (27.21±6.49%) and Hispanics 31.21±9.09% (p<0.05).
  - In multivariate analysis, the only independent predictor of HCV non-clearance (Active HCV infection) was African American race: OR (95% CI) = 3.80 (1.31-11.06), p = 0.01
HCV Infection in Blacks/African Americans

- Negative prognostic considerations
  - Appear to be unable to clear HCV as efficiently compared with Whites
  - Impaired CD4 cell cytokine response
  - Higher incidence of HCC (histologically documented): 6.1 and 2.8 per 100,000 persons in Blacks/African Americans and Whites, respectively
  - HCC-associated mortality rate is twice that of Whites
  - Lower response to IFN-based treatment
  - The response rates are better with newer regimens

Impact of HCV

Screening for HCV
Risk-Based Screening for Hepatitis C

The CDC and AASLD recommended screening for all patients with 1 or more risk factors for HCV

- Illicit injection or intranasal drug use
- Infection with HIV or HBV
- Recipients of blood products
  - Transfusion or organ transplant before 1992
  - Any blood products before 1987
- Hemodialysis
- Infected mother at birth
- Unexplained ALT/AST elevations
- Multiple sex partners, men who have sex with men or history of STD
- Tattoos and body piercings
- Exposure to HCV-contaminated blood


Screening for Hepatitis C

- Risk-based screening strategy was not very successful accounting for 10% of infected patients
- HCV general population screening not cost-effective
- Because of high prevalence of HCV in the cohort born between 1945-1965, CDC recommended screening for baby boomer cohort (2012)

2012 CDC Recommendations for Birth Cohort (1945–1965) Screening

Recommendation 1
- Adults born from 1945 to 1965 should receive one-time testing for HCV without prior ascertainment of HCV risk
  Grade: strong recommendation
  Evidence: moderate-quality

Recommendation 2
- All persons identified with HCV infection should receive a brief alcohol screening and intervention as clinically indicated, followed by referral to appropriate care and treatment services for HCV infection and related conditions as indicated
  Grade: strong recommendation
  Evidence: moderate-quality

Who Should Be Screened for HCV?

CDC Recommendations
- Everyone born from 1945 through 1965 (one-time)
- Persons who ever injected illegal drugs
- Persons who received clotting factor concentrates produced before 1987
- Chronic (long-term) hemodialysis
- Persons with persistently abnormal ALT levels
- Recipients of transfusions or organ transplants prior to 1992
- Persons with recognized occupational exposures
- Children born to HCV-positive women
- HIV positive persons

USPSTF Grade B Recs*
- Everyone born from 1945 through 1965 (one-time)
- Past or present injection drug use
- Sex with an IDU; other high-risk sex
- Blood transfusion prior to 1992
- Persons with hemophilia
- Long-term hemodialysis
- Born to an HCV-infected mother
- Incarceration
- Intranasal drug use
- Receiving an unregulated tattoo
- Occupational percutaneous exposure
- Surgery before implementation of universal precautions

*Only pertains to persons with normal liver enzymes, if elevated liver enzymes, need HBV and HCV testing

Economic Model of a Birth Cohort Screening (BCS) Program for Hepatitis C Virus

- Cost-effectiveness of BCS compared with current risk-based screening
- Markov model for natural history and the eligible patients were treated
- BCS leads to
  - 84,000 fewer cases of decompensated cirrhosis
  - 46,000 fewer cases of HCC
  - 10,000 fewer OLT
  - 78,000 fewer HCV-related deaths
- BCS led to higher overall costs but lower costs related to advanced liver disease
- ICER: $15,700 to 37,700
- BCS is cost effective

Rein DB et al. Annals of Internal Medicine 2011

Summary

- HCV is common cause of CLD
- The prevalence of HCV is underestimated
- Most patients with HCV are asymptomatic and ~75% have not been diagnosed and are unaware of their infection
- Liver complications of HCV are on the rise
- HCV infection causes both hepatic and extrahepatic manifestation
- HCV has PRO and economic impact
- Screening for HCV has expanded risk-based screening to include birth cohort screening