Hepatitis C update: Best practices in screening and treatment

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Philadelphia Fight Community Health Centers
Philadelphia, PA
Disclosures

Grant Support from Gilead Sciences, FOCUS program
Advisory Board, Gilead Sciences (former)
Natural History of HCV Infection

Acute HCV → Chronic HCV
75-85%

15-25%

Spontaneous Resolution → Chronic HCV

Hepatic Inflammation → Hepatic Fibrosis
20% in 20 yrs

Hepatic Fibrosis → Cirrhosis
2 – 4% per yr

Cirrhosis → Hepatocellular Carcinoma
20% in 20 yrs

Cirrhosis → Hepatic Decompensation
2 – 5% per yr

Alcohol, HIV, and hepatitis B may accelerate fibrosis

www.CDC.gov
Extrahepatic manifestations associated with HCV

**Hematologic**
- Mixed cryoglobulinemia
- Aplastic anemia
- Thrombocytopenia
- Non Hodgkin’s b-cell lymphoma

**Dermatologic**
- Porphyria cutanea tarda
- Lichen planus
- Cutaneous necrotizing vasculitis

**Renal**
- Glomerulonephritis
- Nephrotic syndrome

**Neuropsychiatric**
- Depression

**Ocular**
- Corneal Ulcer
- Uveitis

**Vascular**
- Necrotizing Vasculitis
- Polyarteritis Nodosa

**Neuromuscular**
- Weakness/ myalgia
- Peripheral neuropathy
- Arthritis/Arthralgias

**Autoimmune Phenomena**
- CREST syndrome
Sources of Infection for Persons with Newly Diagnosed HCV

- IDU 60%
- Transfusion prior to 1992 10%
- Sexual 15%
- Other 5%
- Unknown 10%

CDC, National Hepatitis C prevention strategy 2001.
Seroprevalence of HCV: 170M to 200M worldwide
Epidemiology of HCV in the US

Most common blood-borne infection in the US
- 3.2 million to 5.2 million persons chronically infected
- Birth cohort 1945-1965: 3.27% antibody positive
  - Non-Hispanic blacks: 6.31%
  - Non-Hispanic whites: 2.92%
  - Mexican American/ other: 2.78%

50% to 75% of individuals chronically infected with HCV are unaware of their infection

Armstrong GL. Annals of Int Med, 2006 144; 705-714
Smith BD. AASLD poster #394, 2011
Chak E. Liver Internat. 2011, 2:1090-1101
Treatment cascade for people with chronic HCV infection

- Chronic HCV-Infected*: 100%
- Diagnosed and Aware‡: 50%
- Access to Outpatient Care‡: 43%
- HCV RNA Confirmed$: 27%
- Underwent Liver Biopsy‖: 17%
- Prescribed HCV Treatment‖: 16%
- Achieved SVR**: 9%

Birth Cohort with high rates of HCV


CDC Recommendations for HCV testing

Birth Cohort based screening

- All individuals born between 1945 and 1965 should be tested at least once for HCV
- All individuals outside of this cohort with a HCV risk factor should be screened
- Cost-effective
- 1-time cohort screening would identify about 86% of undiagnosed cases, compared with 21% with risk-based screening

US Preventive Services Task Force: Grade B recommendation

http://www.uspreventiveservicestaskforce.org/uspstf/uspshepc.htm

CDC. MMWR 2012;61(No. RR-4).
Philadelphia Cascade of Care 2010-2013

Number of Individuals

- HCV infected (estimate): 47%
- HCV Ab: 22%
- HCV RNA: 6%
- HCV in medical care: 3%
A new population of young HCV cases is emerging in Philadelphia 2007-2103

Data provided by Dr. Kendra Viner PhD from the Philadelphia Department of Public Health
### Heroin Use Has INCREASED Among Most Demographic Groups

<table>
<thead>
<tr>
<th></th>
<th>2002-2004*</th>
<th>2011-2013*</th>
<th>% CHANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SEX</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.4</td>
<td>3.6</td>
<td>50%</td>
</tr>
<tr>
<td>Female</td>
<td>0.8</td>
<td>1.6</td>
<td>100%</td>
</tr>
<tr>
<td><strong>AGE YEARS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-17</td>
<td>1.8</td>
<td>1.6</td>
<td>--</td>
</tr>
<tr>
<td>18-25</td>
<td>3.5</td>
<td>7.3</td>
<td>109%</td>
</tr>
<tr>
<td>26 or older</td>
<td>1.2</td>
<td>1.9</td>
<td>58%</td>
</tr>
<tr>
<td><strong>RACE/ETHNICITY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>1.4</td>
<td>3</td>
<td>114%</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>1.7</td>
<td>--</td>
</tr>
<tr>
<td><strong>ANNUAL HOUSEHOLD INCOME</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than $20,000</td>
<td>3.4</td>
<td>5.5</td>
<td>62%</td>
</tr>
<tr>
<td>$20,000-$49,999</td>
<td>1.3</td>
<td>2.3</td>
<td>77%</td>
</tr>
<tr>
<td>$50,000 or more</td>
<td>1</td>
<td>1.6</td>
<td>60%</td>
</tr>
<tr>
<td><strong>HEALTH INSURANCE COVERAGE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>4.2</td>
<td>6.7</td>
<td>60%</td>
</tr>
<tr>
<td>Medicaid</td>
<td>4.3</td>
<td>4.7</td>
<td>--</td>
</tr>
<tr>
<td>Private or other</td>
<td>0.8</td>
<td>1.3</td>
<td>63%</td>
</tr>
</tbody>
</table>

### Heroin Addiction and Overdose Deaths are Climbing

**Heroin-Related Overdose Deaths**
(per 100,000 people)

**Heroin Addiction**
(per 1,000 people)

**Sources:** National Survey on Drug Use and Health (NSDUH), 2002-2013.

[http://www.cdc.gov/vitalsigns/heroin/](http://www.cdc.gov/vitalsigns/heroin/)
Birth Cohort testing recommendations


Opioid epidemic

CDC. MMWR. August 17, 2012, Vol. 61, No. 4
Recommended testing sequence for identifying HCV infection

- **HCV antibody**
  - **Nonreactive**
    - No HCV antibody detected
      - **STOP***
  - **Reactive**
    - **HCV RNA**
      - **Not Detected**
        - No current HCV infection
          - Additional testing as appropriate†
      - **Detected**
        - Current HCV infection
          - Link to care

* CDC. MMWR 2013; 62(18)
Evolving HCV Treatment

Adapted from Strader DB. Clin Liver Disease 2012, 1:1; 6-11.
Direct Acting Agents
DAA: Direct Acting Antivirals

**Protease**

- **NS3 /4A Inhibitors**
  - High potency
  - Limited genotypic coverage
  - Low barrier to resistance

**NS5B Non Nucleoside Inhibitors (NNI)**
- Intermediate potency
- Limited genotypic coverage
- Low barrier to resistance

**Polymerase**

- **NS5B Nucleos(t)ide Inhibitors (NI)**
  - Intermediate potency
  - Pan genotypic coverage
  - High barrier to resistance

- **NS5A Inhibitors**
  - High potency
  - Multi-genotypic coverage
  - Intermediate barrier to resistance
Mnemonic to remember DAAs

Look at end of the drug’s name

**P**Re**v**ir = **P**rot**E**ase inhibitor
- Telaprevir, boceprevir, simeprevir, grazoprevir, paritaprevir

**U**vir = n**U**cleotide or non-n**U**cleotide polymerase inhibitor
- Sofosbuvir, dasabuvir

**A**svir = NS5A inhibitor
- Ledipasvir, ombitasvir, daclatasvir, elbasvir, velpatasvir
Factors Associated with Treatment Choice and Cure

HCV Genotype
- 1, 2, 3, 4, 5, 6
- Subtype: 1a, 1b

Stage of liver fibrosis
- Cirrhosis versus no cirrhosis
- Metavir score F0-F4

HCV treatment status
- Naïve versus treatment experienced
  - Relapse, partial responder, null responder

Special populations
- Transplant, chronic kidney dis, age >70, children
## Medications currently FDA approved

<table>
<thead>
<tr>
<th>Medication</th>
<th>Genotype</th>
<th>HCV Type</th>
<th>Others</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Elbasvir/grazoprevir</td>
<td>GT1a</td>
<td>1b</td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/ Sofosbuvir</td>
<td>1a</td>
<td>1b</td>
<td></td>
<td>4</td>
<td>5/6</td>
</tr>
<tr>
<td>Paritaprevir/ritonavir/ ombitasvir/dasabuvir</td>
<td>1a</td>
<td>1b</td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Simeprevir + sofosbuvir</td>
<td>1a</td>
<td>1b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir</td>
<td>1a</td>
<td>1b</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Daclatasvir + sofosbuvir</td>
<td>1a</td>
<td>1b</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>
Critical Resource

AASLD/IDSA treatment guidelines

www.hcvguidelines.org
SVR (Cure) Associated with Decreased All-Cause Mortality

530 patients with advanced fibrosis, treated with interferon-based therapy, and followed for 8.4 (IQR 6.4-1.4) years
Community based testing

A testing and linkage to care campaign that stimulates demand for and provides HIV and HCV testing across an entire zip code.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>49.1</td>
</tr>
<tr>
<td>African American</td>
<td>91.0</td>
</tr>
<tr>
<td>Single</td>
<td>81.1</td>
</tr>
<tr>
<td>Age</td>
<td></td>
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<tr>
<td>&lt;47</td>
<td>71.0</td>
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<tr>
<td>47-67</td>
<td>29.0</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>17.6</td>
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<tr>
<td>High school degree/GED</td>
<td>50.9</td>
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<tr>
<td>At least some college</td>
<td>31.5</td>
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<tr>
<td>Income</td>
<td></td>
</tr>
<tr>
<td>Less than $10,000</td>
<td>46.4</td>
</tr>
<tr>
<td>$10,000 - $14,999</td>
<td>18.7</td>
</tr>
<tr>
<td>$15,000 - $29,999</td>
<td>17.8</td>
</tr>
<tr>
<td>&gt; $30,000</td>
<td>17.1</td>
</tr>
<tr>
<td>Self-identified sexual orientation</td>
<td></td>
</tr>
<tr>
<td>Heterosexual</td>
<td>89.0</td>
</tr>
<tr>
<td>Gay/Lesbian</td>
<td>4.9</td>
</tr>
<tr>
<td>Bisexual</td>
<td>6.1</td>
</tr>
<tr>
<td>Ever incarcerated</td>
<td>36.3</td>
</tr>
</tbody>
</table>

Do One Thing baseline population characteristics n=1,301

Testing and Linkage to Care Protocol

OraQuick® rapid HCV antibody test reactive

- Blood draw for confirmatory HCV PCR
  - HCV RNA Detected
    - Patient Navigator notifies patient and provides counseling + insurance assessment
    - HCV RNA Not Detected
      - Patient Navigator notifies patient and provides counseling

- Uninsured
  - Patient Navigator facilitates appointment with clinical social worker

- Insured with no known primary care provider
  - Patient Navigator facilitates PCP acquisition

- Insured with a primary care provider

PCP Visit
- Obtain Referral to subspecialist
HCV Patients

1,301 participants were tested for HCV
  ◦ 3.9% anti-HCV seroprevalence
  ◦ 2.8% chronically infected

8% of anti-HCV positive participants were already engaged in HCV care

Of those chronically infected individuals:
  ◦ 58% aware of infection but not engaged in care
  ◦ 36% uninsured
  ◦ 58% had an Audit-C score commensurate with alcohol use disorder
  ◦ 80% participants had serious co-morbidities such as mental illness and addiction
Do One Thing Campaign HCV Testing and Linkage to Care Cascade n=1,301

Lessons Learned from *Do One Thing*

The HCV care continuum is complex

Multiple barriers exist
- Referrals
- Obtaining medication for patients/ payer restrictions

Patient navigation is key when patients are tested via outreach

Outreach testing and community engagement is a way to re-engage individuals living with HCV not currently in care

Immediate blood draw for PCR confirmatory testing is necessary
- Local hospital labs can partner to process and test specimens on nights and weekends

These informed our design of C A Difference
Clinical Testing

Community Testing

Patient Navigation

Subspecialty Care for HCV
Integrated Community Based HCV Testing: Lessons Learned

Integrating HCV testing into existing HIV and STI testing programs has advantages
- Sustainability from diversified funding sources
- Reaches individuals at greatest risk
- 1183 tested, anti-HCV seroprevalence 11.5%

Education is required for staff
- Testers should be trained phlebotomists

Communication is key when community testers do not also act as the patient navigator

Maintaining a low patient navigator to patient ratio is critical
Patient needs HCV Screening

To Be Done: hcvscreen

HCV Screening with reflexive Confirmation
Patient needs HCV Confirmatory testing

To Be Done: hcvconfirmatory

HCV RT-PCR, Quant (Non-Graph)
Impact of HCV Testing Prompts on Type of HCV Screening Test Ordered

![Graph showing the impact of HCV testing prompts on the type of HCV screening test ordered. The graph displays the percentage of tests ordered from January to December 2014, with two lines representing preferred tests and other tests. The graph highlights a significant increase in the use of preferred tests from July onwards.](image-url)
Impact of EMR prompts on Percentage of Eligible Baby Boomers Tested for HCV

*EMR prompts added July 2014
Integrating HCV Testing into primary care: Lessons Learned

The prevalence of HCV is high in urban primary care practices
  ◦ 6029 patients tested, anti-hcv seroprevalence 8.23%

PCPs are busy! Testing has to be easy and meaningful
  ◦ Eliminate outdated or less useful tests from testing menus

Educate the providers and their staff & provide feedback

Get to know your IT staff
  ◦ Learn what your EMR can and cannot do
  ◦ The more that testing can be automated, the better
  ◦ QC must be a part of the process

The role of the navigator often differs in a clinical testing model
Next steps

The Jonathan Lax Treatment Center
The Youth Health Empowerment Project
The John Bell Health Center

COMMUNITY BASED TESTING
Syringe Exchange Program
Drug Treatment Programs
Homeless shelters
Opioid substitution programs
Senior Centers

A Program of Philadelphia FIGHT
Philadelphia Cascade of Care 2010-2013

- HCV infected (estimate): 30000
- HCV Ab: 15000 (47%)
- HCV RNA: 6000 (22%)
- HCV in medical care: 600 (6%)
- HCV antiviral treatment: 300 (3%)

Philadelphia Cascade of Care 2010-2013

AASLD/IDSA: Who should be treated?

Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Patients with short life expectancies owing to liver disease should be managed in consultation with an expert.

Rating: Class I, Level A
### Current Challenges in HCV Care: Wholesale Acquisition Costs

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cost</th>
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<tbody>
<tr>
<td>LED/ SOF x 8 weeks</td>
<td>$63,000</td>
</tr>
<tr>
<td>LED/ SOF x 12 weeks</td>
<td>$94,500</td>
</tr>
<tr>
<td>VEL/ SOF x 12 weeks</td>
<td>$74,760</td>
</tr>
<tr>
<td>ELB/ GRA x 12 weeks</td>
<td>$54,600</td>
</tr>
<tr>
<td>PrOD x 12 weeks</td>
<td>$83,319</td>
</tr>
<tr>
<td>SIM/SOF x 12 weeks</td>
<td>$150,360</td>
</tr>
<tr>
<td>DAC/ SOF x 12 weeks</td>
<td>$148,000</td>
</tr>
</tbody>
</table>

- WAC does not include negotiated discounts and rebates

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Arlene Price, Janssen (Personal Communication)
[http://www.hepatitis.uw.edu/page/treatment/drugs/simeprevir-drug](http://www.hepatitis.uw.edu/page/treatment/drugs/simeprevir-drug)

[www.fairpricingcoalition.org](http://www.fairpricingcoalition.org)
Current Challenges in HCV Care

Restrictive criteria for drug approval for many payers
- Sobriety requirement
- Prescriber requirement
- Disease severity requirement
- HIV may not be a mitigating factor

Arduous prior authorization process for providers
Current Challenges in HCV Care

- Submit Prior Authorization
  - Denial
  - Appeal
    - Denial
  - Appeal
    - Denial
  - Peer to Peer

Grievance

Approximately 8 hrs of staff time per patient
1 to 4 months to go through the process
Comparing 2014 & 2016 Medicaid FFS Liver Disease Requirements

2014 FFS Medicaid Liver Disease Requirements

2016 FFS Medicaid Liver Disease Requirements

Comparing 2014 & 2016 Medicaid FFS Sobriety Requirements

Comparing 2016 Medicaid FFS & MCO Sobriety Requirements

2016 FFS Medicaid Sobriety Requirements

2016 MCO Medicaid Sobriety Requirements

With MCOs, where restrictions varied color denotes low end of the restriction range.
Comparing 2014 & 2016 Medicaid FFS Prescriber Requirements

Incidence of Absolute Denial of DAA Therapy, By Insurance

Figure Legend

- Absolute denial of DAA prescription
- Denial of DAA prescription preceding fill

N=2321
Nov 2014 through April 2015
When insurance will not cover drugs what are the options?

Wait for new drugs to be approved
  ◦ No guarantee that those will be covered/ patient will qualify

Wait until patient qualifies
  ◦ Sobriety
  ◦ Worsening fibrosis

Take legal action

Apply to patient assistance programs to obtain free drug
  ◦ There is only one company that does this currently
  ◦ Financial information to qualify
  ◦ Proof that patient does not qualify for insurance
  ◦ Challenging to navigate
## Changes to State Medicaid Rx Restrictions in Pennsylvania

<table>
<thead>
<tr>
<th>Year</th>
<th>2014</th>
<th>2015/2016</th>
<th>2017</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>F3/F4</td>
<td>F2 for HCV Mono infected patients</td>
<td>F1 for everyone July 1 2017</td>
</tr>
<tr>
<td></td>
<td>No exception for HIV patients</td>
<td>F0 for HIV/HCV Coinfection or anyone with extrahepatic manifestation</td>
<td>F0 for everyone January 1 2018</td>
</tr>
<tr>
<td></td>
<td>No drugs or alcohol for 6 months</td>
<td>No sobriety requirement</td>
<td>Experienced provider</td>
</tr>
<tr>
<td></td>
<td>Specialist Physician</td>
<td>Experienced provider</td>
<td></td>
</tr>
</tbody>
</table>
Welcome to the NVHR Hepatitis C Resources Page

NVHR’s program aims to increase the number of people born 1945-1965 (baby boomers) and other communities at risk tested for hepatitis C. This page has information for providers, patients, and organizations and highlights the work of our community partners.

Program Quicklinks:
- Hepatitis C Baby Boomer Homepage
- Implementing Electronic Medical Record Prompts
- Allscripts EMR
- Epic EMR Prompts
- Provider Training
- Research Articles and Presentations
- Patient Resources
- NVHR Fact Sheets
- Testing Day Events
Thank you!

Do One Thing Team
◦ Amy Nunn ScD, Brown University

C a Difference Team
◦ Lora Magaldi, MA C a Difference Project Coordinator
◦ Carla Coleman, MBA Linkage Coordinator
◦ Ta-Wanda Preston, Outreach specialist
◦ Students, volunteers, patients

Alex Shirreffs MPH, Government Co-Chair of HepCAP
◦ HepCAP members

NVHR & Harvard CHLPI
◦ Ryan Clary
◦ Tina Broder
◦ Robert Greenwald

Gilead FOCUS and Prevent Cancer Foundation