Strategies for Managing and Treating Hepatitis C Infection in Patients with Behavioral Health Challenges

Camilla S. Graham, M.D., M.P.H.
Division of Infectious Diseases
Beth Israel Deaconess Medical Center
Disclaimer:

The views, opinions, and content expressed in this presentation do not necessarily reflect the views, opinions, or policies of the Center for Mental Health Services (CMHS), the Substance Abuse and Mental Health Services Administration (SAMHSA), or the U.S. Department of Health and Human Services (HHS).

How to ask a question during the webinar

If you dialed in to this webinar on your phone please use the “raise your hand” button and we will open up your lines for you to ask your question to the group. (left)

If you are listening to this webinar from your computer speakers, please type your questions into the question box and we will address your questions. (right)

SESSION IS BEING RECORDED
Slides for today’s CoP are available on the CIHS website at:


Disclosures

Camilla S. Graham, M.D., M.P.H. is a part time employee of TREK Therapeutics, a for-profit company, organized as a public benefit corporation.
Ms. Jones

- 58 y/o woman with bipolar disease, GERD, arthritis
- IDU stopped 20 years ago; never heavy alcohol and none now
- Lives in a structured environment that supervises medications
- Diagnosed with hepatitis C in 2006
- Has seen Hepatology once, told she was not an interferon-alfa candidate, never went back
- Has liver enzymes checked by primary care once a year but no other specific intervention

Recent Exam and Labs

- Seen for routine physical
- Reports mental health provider has recently increased one of her medications
- Complains of fatigue
- No findings concerning for liver disease
- ALT 43, AST 60 (normal less than 40)
- WBC 4,300, Hgb 12.1, Platelets 145,000
What are our concerns?

- She has cirrhosis
- She needs treatment urgently
- Ensure stability of mental health
- Have plan for close monitoring and intervention if she decompensates from a mental health perspective
- Drug-drug interactions with HCV treatment

Barriers to HCV Care

- 50% to 75% of people with HCV infection have not been diagnosed
  - 49% of persons with positive HCV antibodies have not had HCV RNA testing (viral load)\(^1\)
    - 20% - 30% spontaneously clear infection but must have viral load testing to know they do not have active infection
- Many patients never see a hepatitis C specialist
  - HCV specialists may include hepatology, some gastroenterology, some infectious disease, some internal medicine
  - 43% in a CDC-sponsored study; likely higher in certain groups\(^2\)
- If someone is deemed “not a treatment candidate” their candidacy is often not reviewed again
- Non-HCV specialists may not recognize signs of advanced liver disease nor advances in hepatitis C treatment

\(^1\)https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6218a4.htm; \(^2\)Foster; Dig Dis Sci 2016; 61:3469-3477
Barriers to HCV Care, cont’d.

- Patients may harbor beliefs about hepatitis C that make them reluctant to seek care:
  - The treatment is worse than the HCV
    - Interferon almost killed someone I know
  - Everyone has to get a liver biopsy
    - Someone I knew almost died from a biopsy
- Doctors don’t like to treat people like me
  - I feel judged by hepatitis doctors
- Treatment is too expensive

What Doctors Like and Don’t Like

Like:
- Organized
- Neatly dressed
- Attentive
- Pleasant

Don’t like:
- Disorganized
- Distracted
- Disrespectful looking
- Young people?

Neutral:
- Race
- Gender
- Class
- “Tough looking”
Patient Advocacy in Hepatitis C

- Provides services to patients as they navigate the healthcare system
- Works directly with patients to ensure that they have a voice in their care
- Works to make sure that patients have sufficient information to promote informed decision making
- Plays an informational role
- Is committed to helping patients make informed choices and access resources
- Ensures that a patient’s wishes are the guiding force behind decisions affecting medical care and the withholding of care
- Collaborates effectively with other members of the healthcare team

https://pacboard.org/2016/03/09/patient-advocacy-vs-medical-advocacy-view-from-the-pacb/
Working Towards the Elimination of Hepatitis C Virus (HCV)

Incidence of HCV Infection Decreased For Over 20 Years but is Now Increasing…

- Decreased Rate of New Infections
  - 1986: Indirect blood screening for HCV/HIV prevention measures
  - 1989: Discovery of HCV
  - 1992: Anti-HCV serologic test licensed
  - 2001: Needlestick Safety and Prevention Act

Estimated Total New Infections

**CDC** Division of Viral Hepatitis, Statistics and Surveillance (NDSS)
Chronic HCV Infection May Lead to Chronic Liver Disease and Liver Cancer

Fibrosis

Cirrhosis

Hepatocellular Carcinoma (with cirrhosis)

Fibrosis1 Chronic HCV infection can lead to the development of fibrous scar tissue within the liver

Cirrhosis1,2 Over time, fibrosis can progress, causing severe scarring of the liver, restricted blood flow, impaired liver function, and eventually liver failure

HCC3 Cancer of the liver can develop after years of chronic HCV infection

Decompensated cirrhosis:
- Ascites
- Bleeding gastroesophageal varices
- Hepatic encephalopathy
- Jaundice

Chronic liver disease includes fibrosis, cirrhosis, and hepatic decompensation; HCC=hepatocellular carcinoma.

Deaths Due to HCV Infections Now Exceed Those Due to HIV Infection

16,600 deaths

Number of HCV-related deaths may be over 60,000 because of under-reporting on death certificates

National Academy of Sciences Consensus Report on Feasibility of HCV Elimination

• It is feasible to eliminate HCV in the US\textsuperscript{1}
  • Approximately 10\% of patients with HCV infection (including those currently undiagnosed) have been treated with DAAs in the US

• Barriers to elimination include:
  • Inadequate surveillance
  • Lack of screening
  • Insufficient linkage and retaining patients in care
  • Ongoing stigma (especially against people who inject drugs) and lack of care in Corrections
  • High price of HCV regimens

\textsuperscript{1} https://www.ncbi.nlm.nih.gov/books/NBK368067/
Fewer than 5% of Patients with HCV Infection Were Treated at Denver Health

Figure 3. HCV Care Continuum for New DH Patients 2008-2015

Retrospective review of HCV care at Kaiser Permanente Colorado and Denver Health found that fewer than 5% of the estimated population with HCV infection who were newly diagnosed from 2008 through 2014 were treated. Indicates lack of necessary testing and linkage to care.

Rowan SE, Durfee J, Tabano DC, et al. The association between HCV and comorbid conditions in 2 large patient cohorts. CROI, February 13-16, 2017, Seattle. #528

Many Gaps in HCV Care Cascade

Screening

Confirm RNA+

Link to Care

Pay for treatment

~4 million people with anti-HCV in US

? cured with ongoing follow up

~3 million with HCV RNA

~0.6 – 0.8M with antiviral treatment

1Tomaszewski Am J Public Health 2012; 102 (11):e101
75% of People with Hepatitis C in the U.S. are Baby Boomers

Baby Boomers (Born in 1945–1965) Account for 76.5% of HCV in the U.S.

An estimated 35% of undiagnosed baby boomers with HCV currently have advanced fibrosis (F3-F4; bridging fibrosis to cirrhosis)³
Who Should Be Tested 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

**USPTF 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


### Beth Israel Deaconess Baby Boomer HCV Testing Program

**Assembled a Core Team**

- Primary Care, Infectious Disease, Hepatology, Information Systems (EHR), and Laboratory Medicine

**Collaboration with Laboratory Medicine**

1. Expand capacity for increased volume: HCV Ab and RNA viral load testing
2. Provided a database report of all positive HCV Ab tests for Nurse Educator
3. Subsequently added report comment indicating “Recommended follow-up for positive HCV Ab results is viral load testing”
Educational Tool for Providers/Patients

(ONE PAGE)

Who Should Be Tested for Hepatitis C?

New: Anyone born between 1945 and 1965 should be tested once, regardless of risk factors

In addition, patients with the following risk factors:
- sibled 50+ (could be intermittent)
- A history of illicit injection drug use or intravenous cocaine use (not recent)
- Needle stick or mucous exposure to blood
- Current sexual partner of an HCV-infected person
- Received blood/organ before 1992
- Received clotting factor products before 1988
- Hemodialysis
- Infections with HIV
- Children born to HCV-infected mothers

Why Test People Born Between 1945-1965?

- 75% of the 100 million people with HCV in the US are baby boomers
- In the 1945-1965 cohort:
  - All 1 out of 10
  - Men 1 out of 10
  - African American men 1 out of 12
- Up to 75% do not know they have HCV
- 72% of HCV-related deaths are in baby boomers

What Can Happen to People with Hepatitis C?

- It is important to identify patients with cirrhosis
- Patients with cirrhosis are at risk for liver cancer (HCC) and liver decompensation (ascites, variceal bleed, hepatic encephalopathy, jaundice)
- Hepatitis C is curable, and cure reduces the risk of severe complications, even with cirrhosis.
- Refer patients to a specialist who has experience treating hepatitis C if they need treatment

Counsel Patients with HCV Infection About Reducing Risk of Transmission

- Do not donate blood, body organs, or tissue, or semen
- Do not share personal items that might have small amounts of blood (toothbrushes, razors, nail or grooming equipment, needles and cuts, and wounds)
- HCV is not spread by hugging, kissing, food or water, sharing utensils, or casual contact
- If in short-term or multiple relationships, use latex condoms. No condoms are recommended for long-term monogamous couples (risk of transmission is very low)

Initial Management

- Evaluate alcohol use (AAT, AUDIT-C) and recommend stopping use
- Vaccinate for hepatitis B and hepatitis A (if not previously exposed)
- Evaluate sources of support social, emotional, financial) needed for HCV treatment

No Simple Answers

- Demographics can be less important than behavior
- To Rx PrEP asking open ended questions is key
- Be cautious of assuming risk profiles
- Heterosexuals and those struggling with IDU are PrEP candidates
- Be flexible with your clients
- Sometimes PrEP is the right choice, sometimes it may not be
Populations Still Being Left Behind

- People born outside the 1945-1965 birth cohort (25%)
- People outside health care system
- Incarcerated
- People who inject drugs (PWID)
- Indian Health Services (IHS) covered patients

We need to test people where they are, such as prisons

Varan, Public Health Rep 2014; 129:187
Treating HCV in PWID

- We have to treat PWID for their own health and to reduce HCV transmission
- People will get re-infected
  - If nobody gets re-infected, we have not been treating the right patients to reduce transmission
- Treating small numbers of patients increases the risk of reinfection
  - Reinfection will increase before it decreases

Negro, CROI 2016.

‘Bring Your Friends’ Approach May Optimize Treatment and Prevention Outcomes

- Treat all members of an individual’s injection network
- Optimize treatment outcomes (Peer support)
- Reduce risk of reinfection (reduce reservoir of HCV in a network)

Courtesy of Shruti Mehta, Johns Hopkins
HCV Treatment

- Seven FDA-approved regimens for genotype 1
  - Three regimens can be used for genotypes 2 and 3
  - A few subgroups require ribavirin (anemia)
- Selection often guided by insurance restrictions
- Most patients receive 12 weeks
- Most receive 1-3 pills once a day
- All patient groups have a >90% SVR (virological cure) rate, including previously difficult-to-cure
  - HIV, post-liver transplant, liver failure, dialysis

www.hcvguidelines.org

African American Patients Have Similar Cure Rates as Caucasians with All-Oral Treatment

Graham, JAMA 2015
**Results: SVR12 by Prior Treatment Experience and Cirrhosis Status HIV-HCV (ION-4)**

<table>
<thead>
<tr>
<th>Overall</th>
<th>Naïve vs Experienced</th>
<th>Cirrhosis Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>96</td>
<td>95</td>
<td>97</td>
</tr>
<tr>
<td>96</td>
<td>94</td>
<td>96</td>
</tr>
</tbody>
</table>

Error bars represent 95% confidence intervals.
Naggie, CROI 2015

### Drug-Drug Interactions with HIV and HCV Meds (Examples)

<table>
<thead>
<tr>
<th>Drug Interaction</th>
<th>Grazoprevir/Elbasvir</th>
<th>Ledipasvir</th>
<th>Velpatasvir</th>
<th>Paritaprevir/Ombitasvir + Dasabuvir</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ritonavir-boosted atazanavir</strong></td>
<td>GZR ↑, EBR ↑, ATV ↑</td>
<td>LDV ↑; ATV ↑ (avoid TDF)</td>
<td>VEL ↑; ATV ↑ (avoid TDF)</td>
<td>PTV ↑; ATV ↑</td>
</tr>
<tr>
<td><strong>Ritonavir-boosted darunavir</strong></td>
<td>GZR ↑, EBR ↑, DRV ↔</td>
<td>LDV ↑; DRV ↔ (avoid TDF)</td>
<td>VEL ↔; DRV ↔ (avoid TDF)</td>
<td>PTV ↑/↓; DRV ↓</td>
</tr>
<tr>
<td><strong>Cobicistat-boosted elvitegravir</strong></td>
<td>No data</td>
<td>LDV ↑; Cobicistat ↑ (avoid TDF)</td>
<td>VEL ↑; Cobicistat ↑ (avoid TDF)</td>
<td>No data</td>
</tr>
<tr>
<td><strong>Efavirenz</strong></td>
<td>GZR ↓, EBR ↓, EFV ↓</td>
<td>LDV ↓; EFV ↓ (and TDF ↑)</td>
<td>VEL ↓; EFV ↓</td>
<td>No PK data (stopped due to toxicity)</td>
</tr>
<tr>
<td><strong>Rilpivirine</strong></td>
<td>GZR ↔, EBR ↔, RPV ↔</td>
<td>LDV ↔; RIL ↔</td>
<td>VEL ↔; RIL ↔</td>
<td>PTV ↑; RIL ↑ (prolonged QTc)</td>
</tr>
<tr>
<td><strong>Raltegravir</strong></td>
<td>GZR ↔, EBR ↔, RAL ↑</td>
<td>LDV ↔; RAL ↔</td>
<td>VEL ↔; RAL ↔</td>
<td>PrOD ↔; RAL ↑</td>
</tr>
<tr>
<td><strong>Dolutegravir</strong></td>
<td>GZR ↔, EBR ↔, DTG ↑</td>
<td>LDV ↔; DTG ↔</td>
<td>VEL ↔; DTG ↔</td>
<td>PTV ↓; DTG ↑</td>
</tr>
<tr>
<td><strong>Tenofovir disoproxil fumarate</strong></td>
<td>GZR ↔, EBR ↔, TVF ↑</td>
<td>LDV ↔; TVF ↑</td>
<td>VEL ↔; TVF ↑</td>
<td>PrOD ↔; TVF ↔</td>
</tr>
<tr>
<td><strong>Tenofovir alafenamide</strong></td>
<td>No data</td>
<td>LDV ↔; TVF ↑</td>
<td>VEL ↔; TVF ↑</td>
<td>No data</td>
</tr>
</tbody>
</table>

Kiser JJ, [www.HCVguidelines.org](http://www.HCVguidelines.org)
SVR (Cure) Associated with Decreased All-Cause Mortality

- 10-year Cumulative Incidence Rate
- SVR (n=192)
- No-SVR (n=338)

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

FibroScan - Transient Elastography

*Liver biopsies are rarely performed*

- Ultrasound determines velocity of shear wave in m/s, which is proportional to liver stiffness in kilopascal (kPa)
- Entire process requires 15 to 20 minutes, provides immediate results
- Falsely elevated results:
  - High ALT (>100)
  - Eating within 2 hours

Continuum of Fibrosis/Cirrhosis in HCV

<7 kPa = Stage 0-1
7-9.5 kPa = Stage 2
9.5-12.5 kPa = Stage 3
>12.5 kPa = Cirrhosis

>20 kPa = Increased risk liver-related complications


5-year risk of HCV re-infection post-SVR

Low-risk
24 studies
n=6,046
Avg. FU=4.1 years

IVDU / prisoners
16 studies
n=1,203
Avg. FU=5.0 years

HIV co-infected
10 studies
n=1,108
Avg. FU=3.1 years

Hill, AASLD 2014

integration.samhsa.gov
The Price of New Hepatitis C Regimens Has Diminished Willingness to Screen for HCV

Are States Illegally Rationing Hep-C Drugs?

Report Puts Hep C Price Tag as High as $5 Billion for California

White House Is Pressed to Help Widen Access to Hepatitis C Drugs via Medicaid

California Could Spend Nearly $5 Billion on HCV Drugs Over Next Year

Study Shows Medicaid Restrictions for Sofosbuvir Create Barriers for Care

Current Negative Environment Created By High Price of HCV Drugs

- Confusion and doubt among HCV treaters
- Fear from PCPs about testing and treatment
- Fear/outrage among payers (public and private)
- Hesitation in DPH/public outreach programs
  - Difficulty establishing broad baby boomer testing programs
- Declarations by prisons, states’ Medicaid that HCV treatment is not of value
- Rationing of treatment, i.e. F3-F4; substance use
  - Justification for overt discriminatory practices like mandating clean urine samples
- No discussion of cure-as-prevention
- Loss of vision about transformative, curative developments
- Confirmation by patients that they are not “worth” treatment
Price per SVR has Decreased in the U.S.

Limitations on Access to HCV Treatments

- Limits Based on Stage of Fibrosis
- Restrictions Based on Substance Use
- Prescriber Limitations
- Other restrictions
  - HIV Co-Infection limitations
  - “Once per lifetime” limitations
  - Genotype limitations
  - Previous history of treatment adherence requirements
  - Specialty pharmacy restrictions
  - Exclusivity agreements with insurers
MassHealth MCOs Sovaldi Prior Authorization Criteria

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>F3-4</td>
<td>F3-4</td>
<td>F3-4</td>
<td>F4</td>
<td></td>
</tr>
</tbody>
</table>

Requirements Related to Substance Use

- Not abused substances for 6 months
- (For members with past/current issues) abstain from use for 6 months and participation in supportive care
- No substance abuse within past 6 months OR receiving counseling services
- (Known substance abusers) must have been referred to specialist; abstinence from substance abuse for 6 months; ongoing participation in treatment program; adequate psychosocial supports

Prescriber Limitations

- Prescribed by or in consultation with specialist
- Prescribed by or in consultation with specialist
- Prescribed by specialist
- Prescribed by specialist

HIV Co-Infection

- No history of nonadherence
- Individual in composite monitoring program
- No without meeting additional requirements above
- Yes, if compliant with antiretroviral therapy as indicated by undetectable viral load
- No ongoing non-adherence to previously scheduled appointments, meds or treatment; adherence counseling; willing to commit to monitoring

Additional Adherence Requirements

- No history of nonadherence
- Individual in composite monitoring program
- No without meeting additional requirements above
- Yes, if compliant with antiretroviral therapy as indicated by undetectable viral load
- No ongoing non-adherence to previously scheduled appointments, meds or treatment; adherence counseling; willing to commit to monitoring

The National Academies of Sciences recognizes the important of support services for the success of a US viral hepatitis elimination strategy

Conclusions

- Hepatitis C can be eliminated in the U.S.
- Requires increasing education, screening, diagnosis, linking patients to care,
- Increasing resources targeted to prevention, access to antiviral treatment, and follow up
- All steps in the HCV care continuum may be improved with patient support
- Advocacy for increased resources for this curable disease will be important

Q&A and Group Discussion
Resource: A National Strategy for the Elimination of Hepatitis B and C


MAI-COC Community of Practice Session #3: Sharing Integration Innovations

Thursday, April 27
3:00 - 4:30 PM ET

https://attendee.gotowebinar.com/register/5865580454380571138
For More Information & Resources

Visit [www.integration.samhsa.gov](http://www.integration.samhsa.gov) or e-mail [integration@thenationalcouncil.org](mailto:integration@thenationalcouncil.org)

Thank you for joining us today.

Please take a moment to provide your feedback by completing the survey at the end of today’s webinar.