AATOD
2019 CONFERENCE

October 19–23 • Walt Disney World, Florida

Out of the Shadows: Managing the Opioid Epidemic through the Continuum of Care
I Have the Following Financial Disclosures:

- Research Support: Abbott, AbbVie, Center for AIDS Research, Conatus Pharmaceuticals, Genfit, Gilead Sciences, Inc., Intercept Pharmaceuticals, Merck, and Patient-Centered Outcomes Research Institute (PCORI)
- Consultant: Abbott Diagnostics, AbbVie, Chronic Liver Disease Foundation, and Merck
- Speakers Bureau: Chronic Liver Disease Foundation
Educational Objectives

• Discuss data on the incidence, prevalence and transmission of HCV in incarcerated individuals
• Describe the detrimental effects of chronic HCV to emphasize the need for diagnosis and treatment in incarcerated individuals
• Discuss updates in screening mandates and treatment guidelines for HCV including the importance of harm reduction and prevention of reinfection
• Propose that HCV elimination is possible now that many prior HCV treatment obstacles have been removed
Transmission, Epidemiology and Natural History of Hepatitis C
I Have the Following Financial Disclosures:

• Speakers Bureau: AbbVie, and Salix Pharmaceuticals
Hepatitis C by the Numbers

- 170 million people worldwide
- #1 blood-borne infection in US
- 5.2 million people in US
- FDA-approved vaccines
- Indication for liver transplantation
- Cause of liver cancer in US

Chak, Talal, Sherman, Schiff, & Saab. 2011.
Transmission and Liver Disease

• **Injection drug use** is the principle risk factor for transmission

• Spontaneous resolution of acute infection occurs in 15 – 25% cases

• **Chronic disease** develops in most patients and can lead to cirrhosis, liver cancer, liver failure, and death

• **Sustained Viral Response (SVR)** can be achieved in the majority of cases = cure!
Populations at Risk

**Baby Boomers (born 1945-1965)**

- **1960s**
  - Up to 300,000 cases of acute HCV per year; risk of exposure via blood transfusion up to 33%

- **1970s**
  - Volunteer donor system reduces risk of exposure via blood transfusion

- **1989**
  - HCV discovered

- **1992**
  - Widespread introduction of HCV antibody testing

**People Who Use Drugs (PWUD)**

- 30-70% prevalence

HIV Transmission:
What Happened Around 1995?

- Large-scale HIV prevention programs
- Syringe exchange
- Pharmacy sales of injection equipment
- Expanded methadone treatment

Such expansion of HIV prevention services resulted in very large reductions in HIV incidence.
Reduction in HCV Transmission Among PWUD Has Been Lower Than HIV

- HCV easier to transmit than HIV
  - Less sharing is needed for transmission
  - Sharing of drug preparation equipment will transmit HCV
- Prevalence of HCV much higher in PWUD than HIV
Transmission via Contact with Contaminated Blood: Needles and Syringes

Fixed

Detachable

Zibbell J. CDC. Presented as part of Hepatitis C Prevention Opportunities Among PWID. April 28, 2015.
Transmission via Contact with Contaminated Blood: Needles and Syringes

Mean Volume of Fluid Retained with Plunger Depressed

- **DETACHABLE Needle**
  - Low dead-space
  - QD syringe
  - Mean Volume: 18μl

- **FIXED Needle**
  - Low dead-space syringe
  - Mean Volume: 2μl

- **HIGH dead-space syringe**
  - Mean Volume: 84μl

Zibbell J. CDC. Presented as part of Hepatitis C Prevention Opportunities Among PWID. April 28, 2015.
Transmission via Contact with Contaminated Blood: Preparation Equipment

Filters

Cookers

Water

Surfaces

Zibbell J. CDC. Presented as part of Hepatitis C Prevention Opportunities Among PWID. April 28, 2015.
HCV Transmission

Bloody fingers

Fingers on cooker and in solution

Zibbell J. CDC. Presented as part of Hepatitis C Prevention Opportunities Among PWID. April 28, 2015.
Hepatitis C and Other Drugs: More Than Just Injecting

- HCV can be spread through straws and pipes!
- HCV in nasal drug users ranges from 2.3% to 35.3%
- HCV has been found on the stems of crack pipes
- USPSTF and AASLD/IDSA Guidance recommend screening for persons with history of intranasal drug use
- Consider HCV in people who smoke crack or crystal meth, especially if linked to sex (“chem-sex”)

How Long Can HCV Survive on Inanimate Objects?

- **Syringe**: 64 days
- **Water container**: 21 days
- **Surface**: 21 days
- **Foil**: 3 days
- **Filter**: 1 day

HCV-contaminated solution needs to be heated for almost 90 seconds and reach temperatures of 144°F for the virus to be at undetectable levels.

Duration of Infection Drives Transmission Among PWUD

• Patients with chronic HCV infection are infectious until they are successfully treated

• To reduce viral transmission
  – Reduce number of contacts & probability of transmission per contact
    • Safe injection equipment
    • Regular testing within networks

• Reduce duration that patient is infectious with HCV treatment
Likelihood of HCV Infection: Initiation and Duration of Injection Drug Use Matters

The Changing Face of Heroin Use in America

948,000¹
Americans reported heroin use in 2016

170,000¹
Americans started using heroin in 2016; nearly double the number of people than in 2006 (90,000)

US Overdose Deaths Involving Heroin: Number Among All Ages, 1999-2017²

New Acute HCV Cases and IDU, 2016

Of the 1,118 acute HCV case reports that contained information about IDU, 68.6% (n = 767) indicated use of injection drugs.

Impact of the US Opioid Epidemic: Opioid Overdose Deaths Increased from 2016 to 2017

Opioids were involved in 70,237 deaths in 2017 and the age-adjusted rate of overdose deaths increased significantly by 9.6% from 2016 to 2017.

Increasing Deaths Due to Opioids


CDC: Reported Number of Acute HCV Cases: United States, 2001 – 2017

Source: CDC, National Notifiable Diseases Surveillance System (NNDSS).
HCV Infection

Acute Infection, 20-30% with symptoms

Clearance of HCV RNA, 15%-25%

Fulminant Hepatitis, Rare

Chronic Infection, 75%-85%

Extrahepatic Manifestations

Chronic Active Hepatitis

Cirrhosis, 10%-20% over 20 years

Decompensated Cirrhosis, 5-year survival rate of 50%

HCC, 1%-4% per year

Chen & Morgan. 2006.
Chronic HCV Infection May Lead to Liver Disease and Liver Cancer

~75% of patients infected with HCV will develop a chronic infection
65% with chronic infection will develop chronic liver disease
The Future of Chronic Hepatitis C

- Burden of HCV liver disease expected to triple in next 10 – 15 years
- Prevalence of cirrhosis 45% by 2030
- HCV deaths doubled 1999 – 2007 to current > 17,000 (projected peak 35,000/yr)
- Economic burden > $10 billion per year

Increasing Deaths Due to HCV

More people are dying of HCV than all 60 other nationally notifiable infectious diseases combined.

Source: Center for Disease Control and Prevention

Death certificate data from the National Center for Health Statistics.
Conclusions

• HCV transmission occurs mostly via contact with contaminated blood, but other routes also spread the virus (e.g. pipes, intranasal)

• HIV transmission reduction interventions resulted in decreased incidence of HIV and HCV, but HCV is easier to transmit than HIV

• HCV and opioid injection use are rising in parallel

• HCV incidence is increasing, particularly in white females

• Untreated chronic HCV increases morbidity and mortality

• HCV care in PWUD is a significant issue that requires immediate attention
Screening, Diagnosis and Linkage to Care

Andrew H. Talal, MD, MPH
Professor, Department of Medicine
Director, Center for Research and Clinical Care in Liver Disease
Jacobs School of Medicine and Biomedical Sciences
University at Buffalo
Buffalo, New York
WHO HCV Elimination Efforts
The World Health Organization Visions and Goals to Combat Hepatitis

• WHO’s Vision:
  – A world where viral hepatitis transmission is halted
  – Everyone living with viral hepatitis has access to safe, affordable and effective prevention, care and treatment services

• WHO’s Goal:
  – Eliminate viral hepatitis as a major public health threat by 2030
  – For HCV specifically, the WHO goal is a decrease from 1.75 million new cases and 400,000 deaths in 2015 to approximately 175,000 new cases and 140,000 deaths in 2030

WHO, World Health Organization.
## Progress Toward the WHO Goals

### Number of New Cases

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2020</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>4.7 million</td>
<td>3.3 million</td>
<td>470,000</td>
</tr>
<tr>
<td>HCV</td>
<td>1.75 million</td>
<td>1.23 million</td>
<td>175,000</td>
</tr>
</tbody>
</table>

### Number of Deaths

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2020</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>884,000</td>
<td>796,000</td>
<td>309,000</td>
</tr>
<tr>
<td>HCV</td>
<td>400,000</td>
<td>360,000</td>
<td>140,000</td>
</tr>
</tbody>
</table>

- **30% Reduction**
- **90% Reduction**
- **10% Reduction**

PWUD Require Interventions in Order to Achieve HCV Elimination Goals

- In most high-income regions of the world, IDU is the major source of new HCV infections
- IDU caused approximately 390,000 new cases of HCV in 2015
- Safer injection practices reduce the incidence of HCV infection
  - However, in order to eliminate HCV, the number of sterile needles or syringes distributed to PWUD increase from 27 per person per year to 300 per person per year
- Therefore, HCV elimination efforts require enhanced diagnosis and treatment efforts
  - 90% of all infected persons will need to receive a diagnosis
  - 80% of those diagnosed will need to be treated

Global Care for HCV Declines Along the Continuum

- These data underscore the importance of HCV screening, diagnosis and linkage to care
- Especially since HCV treatments are so highly efficacious

Suburban Evidence of the HCV Cascade of Care in PWUD

- Retrospective chart review conducted in HCV patients, from 2016 to 2018, at Stony Brook Medicine

- HCV care cascade mirrors the national HCV care continuum, largest gaps in care occur:
  - First between HCV RNA confirmatory testing and attendance at first appointment (LTC)
  - Then between LTC and initiation of direct acting antiviral (DAA) therapy

Bottleneck in HCV Cascade to Cure: Screening and Linkage to Care Remain Low

- Only 50% of patients living with HCV are aware
- 5 to 9% of patients living with HCV are cured

HCV Screening and Diagnostic Recommendations
Common EMR for large healthcare system, > 5,000 clinicians and > 1.5 million patients

Beth Israel Deaconess Medical Center, Boston, MA. Quality Outcomes Data.
HCV Screening Is Straightforward: Algorithm for Screening/Diagnosis of Asymptomatic Persons

- Screening Test for Anti-HCV
  - Positive
  - Negative (STOP)
- Test for Quantitative HCV RNA
  - Positive
  - Negative
- Retest in 6 months

Hepatitis C Screening Update

New Draft USPSTF Recommendations

1. HCV screening in persons at high risk of infection

2. 1-time screening for HCV infection in adults ages 18 to 79 years. (B recommendation)

Is Reactive HCV Antibody Test a Diagnosis for Chronic HCV Infection?

• No! It’s a SCREENING test

• Some individuals become infected with HCV and then spontaneously clear the infection

• Approximately 15% – 25% of individuals clear the virus without treatment and do not develop chronic infection

• HCV RNA (viral load) is required to confirm chronic infection

Data on PWUD, Screening and HCV Status
Progress in HCV Testing and Treatment in PWUD: Georgia, 2018

• 40% of HCV infections in the European country of Georgia are attributed to IDU

• An HCV elimination program in PWUD was initiated in 2015

• Following implementation of the elimination program, the number of HCV antibody tests conducted at Needle Sharing Programs increased:
  – From 2006 – 2014: average of 3,638 per year
  – From 2015 – 2018: average of 21,551 per year

• In 2017 – 2018, 482 (97.6% of patients who completed treatment) were cured of HCV infection.

Progress in HCV Testing and Treatment in PWUD: Georgia, 2018 (cont’d)

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of HCV antibody tests</th>
<th>No. of positive HCV antibody test results</th>
<th>Percentage of positive tests</th>
</tr>
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<tbody>
<tr>
<td>2006</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2007</td>
<td>10,000</td>
<td>2,000</td>
<td>20</td>
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<td>2008</td>
<td>15,000</td>
<td>3,000</td>
<td>20</td>
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<tr>
<td>2009</td>
<td>20,000</td>
<td>4,000</td>
<td>20</td>
</tr>
<tr>
<td>2010</td>
<td>25,000</td>
<td>5,000</td>
<td>20</td>
</tr>
<tr>
<td>2011</td>
<td>30,000</td>
<td>6,000</td>
<td>20</td>
</tr>
</tbody>
</table>

Screening Remains Low Amongst Young Adults

- 269,124 adolescents and young adults diagnosed with SUD were evaluated
- Among the participants, 6812 (2.5%) were tested for HCV
  - Only 36% of those with an opioid use diagnosis (just under 300), 37% with a cocaine use diagnosis (just over 300) and 33% with an amphetamine use diagnosis (nearly 600)

Increases in OUD and HCV in Pregnant Women Warrants Additional Screening Efforts

- National Prevalence of Maternal HCV per 1,000 Delivery Hospitalizations, by OUD Status, 2000 – 2015

- Opioid use disorder among pregnant women has increased; the majority of those with HCV infection have opioid use disorder

Available at: https://www.cdc.gov/mmwr/volumes/68/wr/mm6839a1.htm?s_cid=mm6839a1_w. Accessed October 8, 2019.
Linkage to Care in PWUD
Antiviral Therapy Guidelines in PWUD

AASLD/IDSA
Recent/active IDU should *not* be seen as contraindication to HCV therapy\(^1\)

EASL
Treatment should be prioritized in those at risk of transmitting HCV *including* active PWUD\(^2\)

Detection of HCV Infection Should Result in Linkage to Care

*For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended. For persons who are immunocompromised, testing for HCV RNA can be considered.
† To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

Continuum of Care in PWUD

The continuum of care for PWUD in Philadelphia 2013-17

Younger (≤ 35) PWUD (N=1,239)
Older (> 35) PWUD (N=1,151)

Poor linkage to care and very low treatment rates, especially in younger PWUD

*In HCV Care= seeing a specialist or having another RNA > 180 days from 1st RNA result.
**Treatment= report that treatment initiated or the infection resolved.
Liver Center of Western New York

Provider stigma and lack of knowledge are barriers to treatment

Patient discomfort with seeing new providers and issues with travel

In NYS, only 20% of OTPs treat HCV

Off-Site Referral Model

On-Site Telemedicine Model

Methadone Clinic

Liver Center of Western New York

Patient discomfort with seeing new providers and issues with travel

Off-Site Referral Model

On-Site Telemedicine Model
The Model

OTP patient screened for HCV

Patients shown a 7-minute video on telemedicine and what to expect

Initial patient evaluation and discussion on HCV

Provider documents in EHR and works with staff at spoke site

HCV medication dispensed with patients existing methadone dose

Electronic bill submission
Procedures

• All pre-treatment labs (HCV RNA, HCV genotype, Fibrosure [Labcorp]) is performed onsite

• Patients treated for 8 or 12 weeks with 12 week post-treatment follow up to determine SVR status.

• Telemedicine-based visits occur biweekly during HCV therapy

• Social variables obtained from electronic health record.

• Telemedicine Satisfaction Questionnaire (TSQ) administered at first telemedicine evaluation, at initiation of therapy, and at completion of follow up

• Adherence survey is administered biweekly while under HCV therapy
Inflammation and Fibrosis

Fibrosis Stage

- F0: 19%
- F0-F1: 9%
- F1: 4%
- F1-F2: 25%
- F2: 11%
- F2-F3: 16%
- F3-F4: 2%
- F4: 16%

Inflammatory Grade

- A0: 35%
- A0-A1: 14%
- A1: 9%
- A1-A2: 28%
- A2: 5%
- A2-A3: 2%
- A3: 7%
<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Level</th>
<th>Count</th>
<th>Percent</th>
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<tbody>
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<td>M</td>
<td>38</td>
<td>61</td>
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<tr>
<td></td>
<td></td>
<td>F</td>
<td>24</td>
<td>39</td>
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<tr>
<td>Ethnicity</td>
<td>62</td>
<td>AA</td>
<td>38</td>
<td>61</td>
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<tr>
<td></td>
<td></td>
<td>White</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other</td>
<td>18</td>
<td>29</td>
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<tr>
<td>Race</td>
<td>62</td>
<td>Hispanic</td>
<td>16</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Non Hispanic</td>
<td>46</td>
<td>74</td>
</tr>
<tr>
<td>HIV</td>
<td>62</td>
<td>No</td>
<td>47</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td>16</td>
<td>24</td>
</tr>
<tr>
<td>HCV genotype</td>
<td>61</td>
<td>1a</td>
<td>41</td>
<td>67</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1b</td>
<td>16</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2b</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>3</td>
<td>5</td>
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<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>57.53</td>
<td>9.92</td>
<td>58.9</td>
</tr>
<tr>
<td>HCV RNA</td>
<td>6.35</td>
<td>0.58</td>
<td>6.33</td>
</tr>
</tbody>
</table>
Virologic Results

• A total of 62 patients were evaluated and 45 received DAA-based therapy

• 42 (93%) patients achieved SVR

• 1 patient had GI discomfort at week 4 and discontinued treatment prematurely with HCV RNA relapse

• 2 patient likely had reinfection with negative week 4 and positive week 12 HCV RNA values
Adverse Effects
DAA Adherence

The bar chart shows the adherence to DAA therapy over four administrations. The y-axis represents the percentage of patients who missed at least one dose, with categories 'No' and 'Yes'. The chart indicates that a significant number of patients missed at least one dose in each administration, with a notable increase in the second administration.
Convenience for Integrated HCV Care via Telemedicine

Statement: I think the consultation via the computer made it easier and more convenient for me to see the doctor than going to a hospital or clinic for treatment.

Sources: Talal et al. Clin Infect Dis; 2018 Oct 17
Talal et al. Telemed J E Healthl 2018 Oct 16
Preference for Integrated HCV Care via Telemedicine

Statement: I prefer to see the doctor through a computer rather than go to an offsite clinic

Sources: Talal et al. Clin Infect Dis; 2018 Oct 17
Talal et al. Telemed J E Healthl 2018 Oct 16
Social Determinants of Health

• Social, behavioral, and environmental factors that contribute to health inequalities and health outcomes.
Social Variables

- Any category with a positive value could increase the probability of receiving treatment.
- Any category with a negative value could decrease the probability of receiving treatment.
Social Variables Positive and Negative Effects on HCV Care via Telemedicine

• Use of clustering techniques, multiple correspondence analysis and modern statistical learning, can identify factors associated with pursuit of HCV care

• **Positive** factors most influential
  • Married
  • Psychiatric diagnosis other than depression

• **Negative** factors most influential
  • Never married
  • Depression
TEAM-C: Telemedicine Evaluation, Adherence and Medication for Hepatitis C

• Compare effectiveness of telemedicine to usual care among patients on opiate substitution therapy (OST)
  • Patient-Centered Outcomes Research Institute (PCORI) supported 5-year project.

• Secondary aims
  • Compare treatment initiation and completion rates.
  • Assessment of:
    • Satisfaction with health care delivery
    • Satisfaction with telemedicine
    • Sociodemographics
Total Number of methadone clinics in New York State: 126
Telemedicine Summary

• Opioid epidemic continues to increase HCV prevalence and incidence
  • Changing demographics
• HCV care via telemedicine is a feasible, reimbursable model for substance users
  • Excellent patient acceptance that improved over time
  • Excellent treatment efficacy
• Telemedicine is acceptable to substance users
  • Prefer “one stop” shopping and convenience of co-located medical care
  • Privacy is not issue.
• Social determinants of health and drug use characterics
  • Affect linkage to HCV care and completion
  • HCV elimination strategies need to consider these factors
Barriers Persist – Poor Access for Medicaid Patients in the US (Varies by State)

Impact of Care Coordination: Triple E Model

• CLDF designed a self-sustaining, comprehensive HCV education, screening and treatment model

• This program provided 4 important fundamentals to substance abuse centre sites:
  – Staff education
  – Patient education and counselling
  – Antibody (Ab) screening and secondary blood draw (if Ab positive)
  – Linkage to care: links patient directly hepatitis specialist (onsite or via telemedicine in areas where HCV providers are limited) and a CLDF healthcare provider for onsite counselling and management

Impact of Care Coordination: Triple E Model (cont’d)

- Patient screening and outcomes data
- 19 substance abuse centre sites involved

Results*

<table>
<thead>
<tr>
<th></th>
<th>Ab Screened</th>
<th>Ab Positive</th>
<th>Blood Draw Completed (on Ab Positive Patients)</th>
<th>Linked to Care (Patients who had Blood Drawn)</th>
<th>HCV RNA Detectable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Pts</td>
<td>1475</td>
<td>658</td>
<td>531</td>
<td>384</td>
<td>369</td>
</tr>
</tbody>
</table>

*Data from March, 2017 - November, 2018.
Impact of Care Coordination: Triple E Model (cont’d)

• HCV education, screening and effective linkage to care are necessary to effectively integrate these treatments into disease management

• Broadening the Triple E model could result in recovery center-focused eradication of HCV

Impact of Care Coordination

- RCT of patients attending ORT clinics in SF and NYC (N = 489)
- Intervention arm received onsite screening, education, counseling, and case management
- 59% HCV seropositive
- Intervention arm
  - ↑ Linkage to care
  - 6 month follow up
  - OR 4.1 (2.35 – 7.17)

OR, odds ratio; RCT, randomized controlled trial.
Accessing the Drug Involved Population Beyond the Conventional Healthcare Setting

• Accessing drug-involved persons at venues where they habitually congregate or receive treatment can potentially overcome the:
  – Stigmatization associated with HCV and
  – Reluctance to seek care within a conventional health care setting

# CDC Guidance for Locating HCV Care Providers and Training Resources

<table>
<thead>
<tr>
<th>Program</th>
<th>Services</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Liver Foundation (ALF)</td>
<td>Online directory of health care providers and treatment facilities,</td>
<td><a href="http://hepc.liverfoundation.org/find-ahealthcare-provider/">http://hepc.liverfoundation.org/find-ahealthcare-provider/</a></td>
</tr>
<tr>
<td></td>
<td>(including substance-use-treatment clinics)</td>
<td></td>
</tr>
<tr>
<td>HRSA Bureau of Primary Health Care’s Health Center Program</td>
<td>Access HCV medical care through an online locator that includes doctors</td>
<td><a href="https://findahealthcenter.hrsa.gov/">https://findahealthcenter.hrsa.gov/</a></td>
</tr>
<tr>
<td></td>
<td>and clinics</td>
<td></td>
</tr>
<tr>
<td>State and local health departments</td>
<td>Local identification of clinics and providers</td>
<td><a href="https://www.cdc.gov/hepatitis/partners/hepatitiscoordslist.htm">https://www.cdc.gov/hepatitis/partners/hepatitiscoordslist.htm</a></td>
</tr>
</tbody>
</table>

Conclusions

• HCV screening and diagnosis is straightforward
• Screening and linkage to care remain low in PWUD
• Even when PWUD test HCV seropositive, nearly half need better linkage to care
• Society guidelines recommend HCV treatment in PWUD
• HCV education, screening and effective linkage are necessary to provide treatment to PWUD
Management and Treatment Update

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Professor of Medicine
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I Have the Following Financial Disclosures:

• Research Support: Assembly, AbbVie, and Gilead
• Consultant: Assembly, AbbVie, and Gilead
• Speakers Bureau: AbbVie and Gilead
HCV Management and Treatment Update
HCV-Related Mortality in US Fell 4% Yearly After Arrival of DAAs

HCV-Related Mortality in US Fell 4% Yearly After Arrival of DAAs (cont’d)

• After (DAA) therapy became available in the United States, HCV-associated mortality fell 4% yearly from 2014 through 2017 [1].

• HCV mortality proved higher in men than women and in blacks than whites or Asians.

• Multiple-Cause-of-Death (MCOD) data indicate that HCV-related mortality rose 6.2% yearly in the United States from 2003 through 2013 [2].

• Analyzing death certificate information, the investigators used ICD-10 codes to determine all-cause mortality. They calculated age-adjusted crude mortality and analyzed overall HCV-associated mortality stratified by race and gender.

• HCV-associated deaths fell from 19,613 in 2014, to 19,566 in 2015, to 18,093 in 2016, and to 17,253 in 2017. The drop in mortality averaged 4% each year.

• Over those 4 years crude HCV mortality waned from 6.2 to 6.1 to 5.6 to 5.3 per 100,000 people.

HCV-Related Mortality in US Fell 4% Yearly After Arrival of DAAs (cont’d)

- Throughout 2014 – 2017, crude HCV-associated death rate per 100,000 people was almost 3-fold higher in the 55-to-64 age group than in the 45-to-54 age group (22.5 versus 7.8 per 100,000).
- HCV-associated mortality was more than twice higher in males than females (8.4 versus 3.3 per 100,000) and higher in blacks (7.8) than in whites (5.7) or Asians (2.0).
- Age-adjusted HCV-related mortality per 100,000 people slipped from 5 in 2014, to 4.9 in 2015, to 4.4 in 2016, and to 4.1 in 2017.
- Over those same 4 years, age-adjusted HBV-associated mortality did not budge from 0.5 per 100,000 people.
- The researchers cautioned that these calculations are limited because half of HCV infections remain undiagnosed in the United States and HCV may not be mentioned in death certificates, which are often written by someone other than the primary care physician.

## Number of Acute Hepatitis Cases Reported/Estimated

**APPENDIX**

<table>
<thead>
<tr>
<th>Year</th>
<th>Hepatitis A Reported</th>
<th>Hepatitis B Reported</th>
<th>Hepatitis C Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2010</td>
<td>1,670</td>
<td>3,350</td>
<td>850</td>
</tr>
<tr>
<td>2011</td>
<td>1,398</td>
<td>2,903</td>
<td>1,232</td>
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<tr>
<td>2012</td>
<td>1,562</td>
<td>2,895</td>
<td>1,778</td>
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<tr>
<td>2013</td>
<td>1,781</td>
<td>3,050</td>
<td>2,138</td>
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<tr>
<td>2014</td>
<td>1,239</td>
<td>2,791</td>
<td>2,194</td>
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<tr>
<td>2015</td>
<td>1,390</td>
<td>3,370</td>
<td>2,436</td>
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<tr>
<td>2016</td>
<td>2,007</td>
<td>3,218</td>
<td>2,967</td>
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<tr>
<td>2017</td>
<td>3,366</td>
<td>3,407</td>
<td>3,186</td>
</tr>
</tbody>
</table>

Source: CDC, National Notifiable Diseases Surveillance System.

*The reported number of cases were adjusted for under-ascertainment and under-reporting (5).
Direct-Acting Antivirals (DAA)

**NS3/4a protease:**
- Simeprevir
- Paritaprevir
- Grazoprevir
- Voxilaprevir
- Glecaprevir

**NS5A replication complex:**
- Ledipasvir, Ombitasvir, Daclatasvir, Velpatasvir

**NS5B polymerase:**
- Sofosbuvir (nuc)
- Dasabuvir (nonnuc)
- Elbasvir
- Pibrentasvir

These two are NS5A's
Efficacy of Antiviral Therapy

Sustained Virologic Response (%)

<table>
<thead>
<tr>
<th>Duration</th>
<th>Interferon</th>
<th>IFN + RBV x 48 wks</th>
<th>PegIFN + RBV x 48 wks</th>
<th>BOC/TVR + PegIFN + RBV</th>
<th>DAA 2015 – 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 wks</td>
<td>5 – 19%</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>48 wks</td>
<td>11 – 19%</td>
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</tr>
<tr>
<td>78 wks</td>
<td>10 – 22%</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>33 – 36%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>42 – 52%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>63 – 75%</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>92 – 100%</td>
</tr>
</tbody>
</table>

DAA: Direct Acting Antivirals
Baseline factors associated with all-cause mortality

- Older age
- GT 3 (2-fold increase in mortality and HCC)
- Higher fibrosis score
- Diabetes
- Severe alcohol use

Impact of Antiviral Therapy

*Median follow-up 8.4 years.
Impact of Antiviral Therapy (cont’d)

- Large-scale VA observational cohort studies
- Survival benefit and deceased HCC risk even in patients without advanced liver disease

FIB-4 ≤3.25
No cirrhosis
No decomp
No HCC
No OLT

(n=103,346)

Direct-Acting Antiviral HCV Regimens

• Choice of regimen, treatment duration, and use of ribavirin depends on several factors
  – Presence/absence of cirrhosis
  – Prior treatment experience
  – Genotype (1 – 6)
• All oral, virtually no side effects, no interferon
• Methadone/buprenorphine/naloxone are safe to use during therapy
Effect of Opiates on the Liver

- **Heroin**: No hepatotoxicity. Street heroin may be contaminated with toxic substances (e.g., lead).
- **Methadone**: No hepatotoxicity.
- **Buprenorphine**: Elevated transaminases possible. Anecdotal cases of liver failure.

HCV Treatment in PWUD

• Treatment has no impact on ORT or increased drug use
• Drug use within 6 months of HCV therapy does not affect response
• However, more frequent drug use decreases HCV treatment efficacy

Social functioning and attendance are better indicators of treatment outcome; independently associated with SVR after adjusting for drug use

SLIDE PER Grebely, J.
HCV Treatment in PWUD Is a Priority

• Real-world study results support DAA use in ORT patients
  – Including those with recent drug use
• Adherence and response in these patients is comparable to other HCV-infected populations
• Reducing HCV transmission means treating HCV in patients with recent (previous 6 – 12 months) or ongoing IDU
• Time from HCV infection to the development of cirrhosis among PWUD is 30 – 40 years; delaying treatment may prolong period of infectiousness and potential transmission
• International guidelines support the prioritization of HCV treatment among PWUD

ORT = Opioid Replacement Therapy.
HCV Treatment and Drug Use

- Prospective RCT in patients with high HCV treatment adherence despite drug use
- ~60% of patients had positive urine test for ≥1 of 8 drug classes
  - Amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, opiates, phencyclidine, propoxyphene
- 6/18 (2%) with recurrent viremia had evidence of reinfection

SVR12 Rates Among Patients with High HCV Treatment Adherence

- All GT: 91
- GT1a: 92
- GT1b: 93
- GT4: 94
- GT6: 33

HCV Treatment and ORT

- Patients on stable regimen of ORT
- Methadone vs. buprenorphine: No difference in antiviral efficacy, pharmacokinetics, no dose adjustments
- No difference in efficacy, adherence, adverse events vs. non-ORT

High SVR in PWUD Despite Imperfect Adherence

Anchor Study: Active IDU within 3 m treated with SOF/VEL x 12w

Medication Adherence and SVR

- Total: 52
  - <200 IU/mL: 51 (Adherence generally high)
  - <12 weeks SOF/VEL: 3
  - 12 weeks SOF/VEL: 51
  - Finished on time/early: 14
  - Finished late: 29

Adherence generally high but even missed doses and finishing late had little effect on SVR

HCV Treatment and ORT

• Post-hoc analyses focus on restricted PWUD populations
  – Small sample sizes, recent drug users were excluded
• However, these analyses provide important outcomes data
• Treatment of mild-to-moderate HCV in PWUD is more cost-effective than delaying treatment until cirrhosis develops

HCV Treatment in Patients Not Receiving ORT

• Patients with IDU history might not be receiving ORT, but are receiving HCV care
  – Treatment provided at hospital-based HCV clinics, drug treatment clinics, community health centers, and needle and syringe programs

• Real-world studies of DAA therapy in these patients demonstrate efficacy
  – 93 – 100% treatment completion
  – 80 – 96% SVR

Data on HCV Treatment in Patients Receiving and Not Receiving ORT: The ION Studies

- Stored blood samples tested for illicit drugs
  - 8% ($n = 70$) of samples showed illicit, non-cannabis drug use by participants during therapy

- SVR12 stratified by treatment duration for participants receiving and not receiving ORT

Among people without drug use at the time of therapy initiation, subsequent illicit drug use during therapy did not have a major effect on SVR

Additional Data on HCV Treatment in Patients Not Receiving ORT:

• In a study of 174 participants with a history of IDU in the last year:¹
  – 63% cirrhosis, 37% treatment experienced, 58% genotype 1
  – 95% completed therapy
  – 93% achieved SVR

• Data strongly support DAA treatment in patients not on ORT with recent IDU²
  – More data needed on PWUD who are not on ORT²

Improvements in Patient Reported Outcomes and Quality of Life in HCV-Treatment Patients with or Without ORT

- 8450 patients enrolled in phase 3 clinical trials of sofosbuvir
- PRO instruments completed before, during, and after treatment
  - 4.8% (407) were receiving ORT
- At baseline, ORT recipients had significantly (P < .0001) lower PRO scores (by -3.5 to -15.6 on a 0 – 100 scale)

Clinical Trials on Patient Reported Outcomes During HCV Treatment

A

PROs for the General Population Infected with HCV

- Fatigue: 55% 39% 20%
- Psychiatric Disorders: 45% 28% 12%

B

PROs for Persons with Substance Use Disorders Who Are Receiving ORT

- IFN+/RBV+/DAA+ regimen
  - Fatigue: 71%
  - Psychiatric Disorders: 65%
- IFN-/RBV+/DAA+ regimen
  - Fatigue: 43%
  - Psychiatric Disorders: 27%
- IFN-/RBV-/DAA+ regimen
  - Fatigue: 22%
  - Psychiatric Disorders: 14%

Improvements in Patient Reported Outcomes and Quality of Life in HCV-Treatment Patients with or Without ORT (cont’d)

• SVR results in improved PROs for 12 consecutive weeks after HCV treatment cessation (SVR-12)

• PRO improvements are more dramatic in patients on IFN/RBV-free regimens

• DAAs may have more dramatic positive effects in patients receiving ORT (A) than in those not receiving ORT (B) when compared to older regimens

Reinfection – It Will Happen

• Drug use persisted after cure but remained stable
• Reinfection more common early after SVR

---

<table>
<thead>
<tr>
<th>Reinfection rate among all persons* (N = 199):</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 reinfections</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reinfection rate among persons with reported injection drug use* (n = 80):</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 reinfections</td>
</tr>
</tbody>
</table>

Conclusions

• Promising new direct-acting antiviral drug regimens offer the possibility of eradication of HCV

• International guidelines support the prioritization of HCV treatment among PWUD

• Adherence and response in these patients is comparable to other HCV-infected populations

• Treatment has no impact on ORT or increased drug use

• Drug use within 6 months of HCV therapy does not affect response

• Broadening the treatment of HCV in PWUD will have an invaluable effect on public health
From 2004 – 2014, HCV and Opioid Injection Drug Use Increased Significantly Among People Aged 18 – 39 Years\textsuperscript{1,2}

The national increase in acute HCV infection is associated with the nation’s opioid epidemic.\textsuperscript{1}

Age Distribution of New HCV Infections in the US Skews Toward Adolescents and Young Adults

These data may be indicative of emerging trends in HCV transmission in other regions of the US.

---

N=8213

---

N=8717

---

Excludes 915 cases with missing age or sex information.

Excludes 362 cases with missing age or sex information.

Data are current as of Nov 15, 2016 and are subject to change.

Total Hepatitis C by Age, Sex, and Year, New York (Excluding NYC)

Slide courtesy of NYS DOH Bureau of Viral Hepatitis.
A Simplified Algorithm for Management of Hepatitis C Infection

Douglas T. Dieterich, MD, Joseph Ahn, MD, MS, Bruce Bacon, MD, David Bernstein, MD, Marc Bourlière, MD, Steven Flamm, MD, Paul Kwo, MD, Joseph K. Lim, MD, Christian Ramers, MD, MPH, Nancy Reau, MD, Mark Sulkowski, MD, Norman Sussman, MD, Stefan Zeuzem, MD

Background

• WHO has set an objective for elimination of HCV infection as a public health threat by 2030

• Access to treatment is limited in part by lack of screening and the number of available specialists

• Current guidelines are comprehensive and most appropriate for experienced treaters, but non-specialists may consider them too complex

• A simplified treatment algorithm targeting non-traditional HCV treaters to drive HCV elimination is needed

How Simple Can Treatment Become For Most Patients?

Assess for cirrhosis with platelets (>150x10^9/L)

History, Exam, Labs*

Assess for DDI

SOF/VEL 1 tab daily w/ or w/o food for 12 Weeks

GLE/PIB 3 tabs daily w/ food for 8 or 12 Weeks

Universal Screening for HCV almost a year ahead of USPSTF

Simplified Algorithm for Management of Hepatitis C Infection

1. Screening and diagnosis
   - Universal screening optimal
   - Risk factors/age screening
   - HCV antibody test with reflex to PCR

2. Pretreatment assessment and testing
   - Initial assessment
     - Physical exam, stigmata of cirrhosis, clinical and prior treatment history, extrahepatic manifestations
   - Blood tests
     - CBC, AST, ALT, bilirubin, albumin, creatinine; HBV, HIV, HAV; eGFR
   - Platelets > 150x10⁹/L

3. Treatment and monitoring
   - Assess for potential DDI
   - Treatment with pan-genotypic therapy:
     - GLE/PIB or SOF/VEL
   - Assessment of cure (SVR12)
     - HCV RNA, ALT
   - HCV RNA-
   - Cured
   - Platelets < 150 refer to specialist
   - Refer to post-cure management

Positive (+) PCR

Active HCV infection

Platelets > 150x10⁹/L

Platelets < 150 refer to specialist

### Treatment Choice

<table>
<thead>
<tr>
<th>Treatment duration, wk</th>
<th>SOF/VEL†</th>
<th>GLE/PIB‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cirrhosis</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Compensated cirrhosis</td>
<td>12§</td>
<td>12</td>
</tr>
<tr>
<td>Decomp. cirrhosis</td>
<td>12¶</td>
<td>Not indicated</td>
</tr>
</tbody>
</table>

**Dosage**
- **SOF/VEL†**
  - 1 tablet (400 mg SOF + 100 mg VEL)
  - Once daily
  - With or without food
- **GLE/PIB‡**
  - 3 tablets (100 mg GLE + 40 mg PIB per tablet)
  - Once daily
  - Food required

**Common side effects (≥ 5%)**
- **SOF/VEL†**
  - Headache, fatigue, nausea, asthenia, insomnia
- **GLE/PIB‡**
  - Headache, fatigue, nausea

†Treatment duration of SOF/VEL for treatment-experienced patients is 12 weeks.
‡GLE/PIB is also indicated for patients with HCV GT 1 infection with no cirrhosis or compensated cirrhosis (Child-Pugh A) who have been treated with a regimen containing an HCV NS5A inhibitor or NS3/4A protease inhibitor, but not both. Duration of treatment for patients with prior NS5A inhibitor experience or NS3/4A protease inhibitor experience is 16 weeks or 12 weeks, respectively.
§Prescribing information in the EU, but not the US, states that addition of RBV may be considered for patients with HCV GT 3 and compensated cirrhosis.
¶For patients with decompensated cirrhosis, SOF/VEL is indicated in combination with ribavirin.
Monitoring Recommendations

• Advise patients, particularly those with prior HBV infection, to contact their HCP if they experience unexpected or severe symptoms

• At least 12 weeks after treatment completion, confirm cure by assessing HCV RNA by PCR; refer patients with detectable HCV RNA to a specialist

• At least 12 weeks after treatment completion, obtain ALT level; if ALT remains abnormal on repeated measure, refer the patient to a specialist

Postcure Recommendations

• Inform patients who are cured that they are susceptible to reinfection

• Provide patients with appropriate HCV harm-reduction resources to minimize the possibility of reinfection

• Continue HCC surveillance every 6 months in patients who had advanced fibrosis/cirrhosis before HCV treatment or refer to hepatologist
FDA Safety Communication on the Use of PI-Containing DAA Regimens for HCV

• On August 28, 2019, the FDA issued a safety announcement about the rare occurrence of serious liver injury with the use of protease-inhibitor (PI)-containing regimens for hepatitis C (HCV), including Mavyret, Zepatier and Vosevi.

• The announcement states that the use of these drugs to treat chronic hepatitis C in patients with moderate to severe liver impairment has resulted in rare cases of worsening liver function or liver failure. These medicines are not indicated for use in patients with moderate to severe liver impairment.

FDA Safety Communication: Serious Liver Injury with PI-Containing DAA Regimens

- FDA received reports of **63 cases** of worsening liver function, including liver failure and 8 deaths, in HCV patients treated with PI-Containing DAA Regimens:

![Serious liver injury per PI-containing regimen (n)](chart1)

- More than half of the cases with no cirrhosis or compensated cirrhosis (CC) were misclassified and had evidence of advanced liver disease or risk factors for decompensation (low platelets, portal hypertension, alcohol abuse, other liver comorbidities)

![Baseline Liver Function (%)](chart2)

Recommendations Per the FDA Drug Safety Communication

- Perform hepatic laboratory testing at baseline and as clinically indicated or as specified in product labeling, especially in patients with pre-existing significant liver problems or risk factors.
- Monitor for clinical signs and symptoms of hepatic decompensation such as the presence of jaundice, ascites, hepatic encephalopathy, and variceal hemorrhage.
- Encourage patients to read the prescribing information leaflet they receive with their Mavyret, Zepatier or Vosevi prescriptions because there may be new or important additional information about the medicine.
- Discontinue Mavyret, Zepatier or Vosevi in patients who develop evidence of hepatic decompensation or as clinically indicated.
- To help FDA track safety issues with medicines, report adverse events involving Mavyret, Zepatier, Vosevi, or other medicines to the FDA MedWatch program: call 1-800-332-1088 or access https://www.accessdata.fda.gov/scripts/medwatch/
- Other effective FDA approved treatment options are available for patients with cirrhosis who have moderate to severe liver impairment (Child-Pugh B or C).

5 Biggest Mistakes Addiction Medicine Docs Make in Liver Disease

- Not vaccinating for hepatitis A!
- Not thinking about hepatitis E!
- Not thinking about hepatitis B!
  - Resistance to 3TC monotherapy
  - Stopping 2 drug Rx for HBV
  - NOT SCREENING FOR HCC !!!
- Not thinking about cirrhosis
  - HCV protease inhibitor liver toxicity
  - Not thinking about varices: platelets < 100 requires Endoscopy
  - NOT SCREENING FOR HCC !!!
- Not thinking about NAFLD
  - NOT SCREENING FOR HCC !!!
DON’T LET YOUR FELLOW DO FIBROSCANS!
Addiction and HCV Treatment Acceptance: Barriers and Solutions

Grant Mitchell, MD
Chair, Department of Psychiatry
Mount Sinai Beth Israel
Associate Professor, Icahn School of Medicine
New York, New York
Financial Disclosures

• No relationships to disclose
Mount Sinai Beth Israel
Opioid Treatment Program (OTP)

Largest OTP in the US: 5500 patients, over 1M services/year

<table>
<thead>
<tr>
<th>Male</th>
<th>71%</th>
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</thead>
<tbody>
<tr>
<td>Female</td>
<td>29%</td>
</tr>
<tr>
<td>18 – 35 y/o</td>
<td>10%</td>
</tr>
<tr>
<td>36 – 45</td>
<td>16%</td>
</tr>
<tr>
<td>45 – 55</td>
<td>35%</td>
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<tr>
<td>56+</td>
<td>39%</td>
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<tr>
<td>African-American</td>
<td>23%</td>
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<tr>
<td>Latino</td>
<td>46%</td>
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<tr>
<td>Caucasian</td>
<td>24%</td>
</tr>
<tr>
<td>Other</td>
<td>7%</td>
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</table>
OTP Services

- Medication Management
- Healthcare services and referrals
- Coordination of care
- HCV/HIV testing, education, referral to care
- Individual and group counseling
- Mental health assessment and referral
- Vocational assessment and counseling
- Family services
- Financial assessment and counseling
- Health education including smoking cessation
- Patient Advocacy
OTP – Common Health Issues

- 80% Tobacco use
- 60% Mental health disorders and/or ongoing substance use
- 32% HCV
- 32% Hypertension
- 20% Obesity
- 15% Heart Disease
- 13% Asthma
OTP and HCV Milestones

1990’s – 90% OTP patients were HCV Ab+

HCV incidence began declining due to testing of blood products, needle exchanges

2010 – significant increase in incidence due to surge in young people injecting drugs

2013 – Liver disease-leading cause of death in OTP

2013 – Introduction of new HCV medications (DAA’s)
OTP and HCV Milestones

• HCV elimination is now possible because many prior treatment obstacles to cure have been eliminated (Talal)
• But…overall screening, treatment and cure rates are still unacceptably low
  – All our OTP patients who consent are tested
  – 2016 – 52% were HCV Ab+, 28% of these were RNA+
  – Majority were connected to care in the community, but few initiated/completed treatment
The continuum of care for PWUD in Philadelphia 2013 –17

- Poor linkage to care and very low treatment rates, especially in younger PWUD

*In HCV Care= seeing a specialist or having another RNA > 180 days from 1st RNA result.
**Treatment= report that treatment initiated or the infection resolved.
## MSBI OTP Retention

### 2019

<table>
<thead>
<tr>
<th>Duration</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Days</td>
<td>85%</td>
</tr>
<tr>
<td>90 Days</td>
<td>76%</td>
</tr>
<tr>
<td>180 Days</td>
<td>65%</td>
</tr>
<tr>
<td>1 Year</td>
<td>54%</td>
</tr>
</tbody>
</table>
Why do so many infected and at-risk persons decide not to be evaluated and treated? How do we educate and engage this population?
Patients do not take their medicine as prescribed about half the time.

1/3 prescriptions never filled.
Treatment Refusal: Causes

- Cultural attitudes towards addiction & medication
- Distrust of the healthcare system
- Cognitive impairment is widespread
- No regular daily routine
- Not a priority for the patient
- Failure of Engagement
Engagement Solutions

Critical to establish a trusting relationship, partnership

• Making requests prior to developing trust conveys self-interest or “taking” instead of caring and concern
• Demonstrate interest and understanding
• Offer to address patient’s expressed needs/priorities first
• Focus on caring more than getting a “yes”
• Don’t pressure patients
Engagement Solutions

• Avoid
  – “You should”
  – “You need to”
  – “If you don’t”
  – “I recommend”

• Conclusion – Patients must be seen, heard and feel our sense of compassion and understanding first
Engagement and Education Solutions

• Developed a Peer Engagement Program in OTP
• Responsibilities of peers:
  – Provide “street outreach” to individuals in the community
  – Connect individuals to addictions treatment and other services
  – Educate patients, families, communities about substance use
  – Educate and engage existing patients in the OTP
• Peer Recovery Coaches assist with engagement
• Embedded Patient Navigators to educate and coordinate services
Treatment Refusal: Knowledge Deficits

- Unaware or fearful of new treatments
- Asymptomatic – still at risk
- Concern about others who took the medication
- Web/personal research from unreliable sources
- Fear of addiction/dependency
Treatment Refusal: Other Causes

• Stigma and attitudes from prior contacts with providers
• Cost/Coverage – leads to not filling prescriptions, self-titration, selling the medication
• Simplify medication regimens
• Explore cultural views related to addiction and medication
• Inconvenience
  – Transportation challenges – appointments and the pharmacy
  – Dis-integrated care, multiple treatment locations
Improving Adherence After Treatment Initiation

- Adherence rates are lowest early in treatment and then improve.
- Connection with counselors/staff and regular attendance at OTP are indirect indicators of treatment success.
- Early adherence is a predictor of the future.
- Ask patient about their concerns before initiating and during treatment.
- Partner with the patient to create an individualized adherence solution.
DAA Adherence

- Missed at least one dose
  - No
  - Yes

- Administration

- Percent
  - 0%
  - 25%
  - 50%
  - 75%
  - 100%

- Administration:
  - 1
  - 2
  - 3
  - 4
Improving Adherence After Treatment Initiation

• Create a blame/shame free culture
  - Why aren’t you taking your medication?
  - It’s important to take the medication
  - What are your concerns about the medication?
  - Many people have a hard time taking medications on a regular basis

• Establish an agreement to be open and direct about medication issues
Improving Adherence After Treatment Initiation

• Most patients report not being asked about adherence
• Discuss all reported concerns and address them
• Inquire about side effects early and often
• Respond positively and express appreciation even if patient reports non-compliance
• Remind patients not to discontinue medication without informing the treatment team
• If e-prescribing, consider verifying fills with pharmacy
Treatment Refusal: Psychiatric Illness

Psychiatric Illness in OTP patients

– OTP patients have 10X higher rates of psychiatric disorders
– Prevalence of depression and anxiety disorders is > 70%
– 75% of patients with psychiatric symptoms were never evaluated or diagnosed
– Awareness of being HCV+ increases risk of depression
– Which has greater effect on quality of life in patients with HCV – extent of liver disease or depression?
Treatment Refusal: Psychiatric Illness

• Depression in HCV patients:
  – Poor occupational/social functioning
  – Lower acceptance of illness and increased stigma
  – Impaired thinking and concentration
  – More physical symptoms

• Most persons with HCV are medically well. Most significant factor threatening the quality of life is the high prevalence of psychiatric disorders (Golden, et al. General Hospital Psychiatry. 27(2005) 431-438).

• Some studies found that achieving SVR is protective against depression
Why is depression so under-recognized and undertreated in the OTP population?

- Stigma
- Staff accept depression as “expected” in the addictions (and HCV) population which leads to a higher threshold for referral
- “Tunnel vision”– Staff are focused on physical health and addiction issues
- Lack of access to mental health care
Any category with a **positive** value could **increase** the probability of receiving treatment.

Any category with a **negative** value could **decrease** the probability of receiving treatment.
Treatment Refusal: Psychiatric Illness Solutions

- Psychiatric history – obtained during initial evaluation
- All patients should be screened at least annually using a simple tool, i.e., PHQ-2 (score 0-6), PHQ-9
- Integrated care
Why Integrated Care?

The PROBLEM

People with mental illness die earlier than the general population and have more co-occurring health conditions.

68% of adults with a mental illness have one or more chronic physical conditions.

1 in 5 adults with mental illness have a co-occurring substance use disorder.

SMI – 53yo
SMI + SUD - 45yo

2/3 deaths are preventable
Integrated Care for Addictions, Psychiatric Illness and HCV

• Services are not just provided, they are integrated and coordinated usually in same setting

• Ideal to integrate services into OTP sites
Levels of Integrated Care

• Coordinated Care – Referral to providers at another site with periodic communication

• Collocated Care – Medical, Psychiatric, and/or Addictions treatment located in same facility, but usually maintain separate cultures, records

• Integrated Care – Close collaboration, shared treatment planning, records
# Traditional vs. Integrated Mental Health Care

<table>
<thead>
<tr>
<th></th>
<th>Traditional MH Care</th>
<th>Integrated MH Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access to MH Care</td>
<td>Usually Wait List</td>
<td>Open Access, no appointment needed</td>
</tr>
<tr>
<td>Focus of Care</td>
<td>Mental Health</td>
<td>Medical and MH issues</td>
</tr>
<tr>
<td>Goal</td>
<td>Diagnose and Treat Psychiatric Conditions</td>
<td>Enhance Overall Health</td>
</tr>
<tr>
<td>Visit Time</td>
<td>Up to 60 min</td>
<td>5 – 10 min</td>
</tr>
<tr>
<td>Number of Visits/Pt</td>
<td>Potentially unlimited</td>
<td>1 – 3 average</td>
</tr>
<tr>
<td>Number of Patients Seen Per Day</td>
<td>10</td>
<td>Unlimited</td>
</tr>
</tbody>
</table>
Why Is the OTP Ideal for Integrated Care?

• Engagement – Trusting relationship already exists with the counselors and other staff
• Most patients are seen frequently – allows for encouragement, close supervision, monitoring
• Patients experience less stigma
• Joint treatment planning
• Convenient, access to care is improved
Integrated Care for Addictions and HCV

- Martin created a pilot program offering collocated addiction/HCV treatment
- Included on-site infectious disease, addictions physician
- 740 patients screened – 22.5% RNA+. All offered treatment – only 43% agreed to take the medication
- 3/4 chose treatment at same site, rest in the community (only 10% completed care)
- Model was successful, but required on-site specialists
Integrated HCV Care: Telemedicine-Based Evaluation and Treatment in OTP’s

Results:

• Staff and patients adapted quickly and easily to telemedicine evaluation and treatment

• No issues with the physician-patient interaction

• Patients appreciated easy access to on-site care and the co-administration of medication

• Staff and patients had an opportunity to participate in research
Integrated HCV Care: Challenges

- Financial – Billing for telemedicine
- Cultural barriers between medicine and addiction services
- Lack of interest/comfort of medical colleagues
- Shortage of practitioners knowledgeable about integration
- Medical Records – Confidentiality, but should be documenting in same EMR
- Space
<table>
<thead>
<tr>
<th>Substance</th>
<th>2019 Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocaine</td>
<td>19.0%</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>21.0%</td>
</tr>
<tr>
<td>Opiates</td>
<td>34.8%</td>
</tr>
<tr>
<td>3+ Drugs</td>
<td>43.7%</td>
</tr>
</tbody>
</table>
Addiction First? HCV First?

• The DAA’s are safe with buprenorphine and methadone
• Abstinence is not necessary for treatment
• Adherence rates and response to HCV treatment are not affected by recent substance abuse
• Some missed doses had little effect on cure rates
Addiction First? HCV First?

- Regular and frequent substance use impacts adherence and efficacy
- Consider detox/rehab prior to HCV treatment if significant, regular use
- Primary impact of concurrent substance use is on adherence with HCV treatment, not the efficacy
- Remember the importance of the relationship to outcomes
- Start as soon as possible to reduce the risk of liver damage and transmission
Conclusions
Specific Challenges Faced by PWUDs

- Stigmatization regarding diagnosis of HCV
- Poor knowledge and inaccurate perceptions about HCV infection, the long-term consequences and associated treatment
- Perceived low need for treatment
  - Absence of noticeable symptoms
  - Belief that HCV is a “benign disease”
- In many states, restrictions on HCV medication provisions still exist
- Variations in reimbursement for HCV therapy create challenges in expanding pool of treating providers

Overall Conclusions: The Need to Prioritize Treatment of PWUD

- Development of tolerable antiviral therapies have revolutionized HCV treatment, but “we are far from having won the war against the virus”
- HCV care among PWUD remains severely restricted, largely because of their inability to access appropriate HCV management
- More effective tools are needed to screen, diagnose and cure HCV-infected PWUDs
  - e.g. telehealth approaches, integrated care models, and point-of-care diagnostics
- The CDC, NIH and other federal and industrial partners have active research programs designed to engage HCV-infected persons with PWUDs into care
- Research gaps need to be addressed to eliminate HCV infection in this population