Treatment of Hepatitis C in People Who Inject Illicit Drugs

Brian R. Edlin, MD
Professor of Medicine
Special Treatment and Research (STAR) Program
SUNY Downstate Medical Center
Adjunct Associate Professor of Medicine and Public Health Center for the Study of Hepatitis C
Weill Cornell Medical College

6th International Workshop on HIV & Hepatitis Co-Infection
June 2, 2010
Global Prevalence of Injection Drug Use

Mathers Lancet 2008;372:1733-45

Presented at the 6th International Workshop on HIV & Hepatitis Co-infection
31 May – 2 June 2010, Tel Aviv Israel
People Who Inject Drugs: the Core of the Hepatitis C Epidemic in Developed Countries

- Largest group of infected persons
- Source of most HCV transmission
- Highest prevalence (50%-90%)
- Highest incidence (10%-30% per year)
- Developing, testing, and implementing prevention and treatment strategies effective with drug users are critical
- Few people who inject drugs are in care; even fewer receive treatment
Treatment of People Who Use Drugs for Hepatitis C

Barriers to Care: Lack of available services

- Comprehensive, continuing primary care
- Integrated, multidisciplinary care
- Subspecialty care: HIV, HCV
- Mental health services
- Substance use services
- Housing
- Social services
- Healthcare coverage
- Science-based drug policy

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Treatment of People Who Use Drugs for Hepatitis C

Barriers to Care: Drug Users

- Poverty
- Homelessness
- Substance Dependence
- Mental health
- Mistrust of the health care system
- Competing priorities
- More pressing needs
Treatment of People Who Use Drugs for Hepatitis C

Barriers to Care: Physicians

- Ignorance
- Inexperience
- Unrealistic expectations
- Frustration
- Negative attitudes
- Moralizing, blaming
Treatment of People Who Use Drugs for Hepatitis C

Physician Concerns

- Poor adherence
- Neuropsychiatric side effects
- Relapse/increase in drug use
- Reinfection after successful treatment
# Studies of Hepatitis C Treatment in Persons Who Inject Drugs

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Location</th>
<th>Setting</th>
<th>IDUs Initiating HCV Rx</th>
<th>Active IDUs initiating HCV Rx</th>
<th>Active IDUs during HCV Rx</th>
<th>SVR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Backmund</td>
<td>2001</td>
<td>Munich</td>
<td>Inpatient detox</td>
<td>50</td>
<td>50</td>
<td>40</td>
<td>36%</td>
</tr>
<tr>
<td>Cournot</td>
<td>2004</td>
<td>France</td>
<td>GI clinic</td>
<td>99</td>
<td>50</td>
<td>Unknown</td>
<td>26%</td>
</tr>
<tr>
<td>Matthews</td>
<td>2005</td>
<td>Australia</td>
<td>Hosp based clinic</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>50%</td>
</tr>
<tr>
<td>Sylvestre</td>
<td>2005</td>
<td>Oakland</td>
<td>Medical clinic</td>
<td>76</td>
<td>23</td>
<td>27</td>
<td>28%</td>
</tr>
<tr>
<td>Sylvestre</td>
<td>2005</td>
<td>Oakland</td>
<td>Medical clinic</td>
<td>28</td>
<td>Unknown</td>
<td>Unknown</td>
<td>52%</td>
</tr>
<tr>
<td>Broers</td>
<td>2005</td>
<td>Switzerland</td>
<td>Multicenter clin trial</td>
<td>11</td>
<td>11</td>
<td>10</td>
<td>56%</td>
</tr>
<tr>
<td>Bargiacchi</td>
<td>2005</td>
<td>Italy</td>
<td>ID &amp; drug rx clinics</td>
<td>12</td>
<td>12</td>
<td>1</td>
<td>75%</td>
</tr>
<tr>
<td>Robaeyens</td>
<td>2006</td>
<td>Belgium</td>
<td>Multicenter clin trial</td>
<td>98</td>
<td>21</td>
<td>21</td>
<td>47%</td>
</tr>
<tr>
<td>Grebely</td>
<td>2007</td>
<td>Vancouver</td>
<td>Comm. clinic</td>
<td>40</td>
<td>14</td>
<td>19</td>
<td>55%</td>
</tr>
<tr>
<td>Jeffrey</td>
<td>2007</td>
<td>Australia</td>
<td>Subst use tx clinic</td>
<td>50</td>
<td>Unknown</td>
<td>18</td>
<td>62%</td>
</tr>
<tr>
<td>Bruggman</td>
<td>2008</td>
<td>Switzerland</td>
<td>Unknown</td>
<td>199</td>
<td>Unknown</td>
<td>Unknown</td>
<td>69%</td>
</tr>
<tr>
<td>John-Baptiste</td>
<td>2009</td>
<td>Ontario</td>
<td>Methadone clinic</td>
<td>109</td>
<td>60</td>
<td>57</td>
<td>56%</td>
</tr>
<tr>
<td>Litwin</td>
<td>2009</td>
<td>New York</td>
<td>Methadone clinic</td>
<td>73</td>
<td>27</td>
<td>22</td>
<td>45%</td>
</tr>
</tbody>
</table>

*A mix of active and former users, receiving substance abuse treatment or not, with acute and chronic infection*

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Treatment of People Actively Using Drugs for Hepatitis C

Research Gaps

Data are needed on:

- Successful methods of treating drug users for HCV
- Critical elements of successful programs
- Characteristics of those who can be successfully treated
- Adherence, side effects, effectiveness, reinfection
- Pharmacokinetic interactions between HCV medications and illicit drugs, methadone and buprenorphine
- Cost effectiveness
Objective: To assess the feasibility of treating persons actively using drugs recruited from community-based sites for hepatitis C.

• One million infected persons actively using illicit drugs in U.S. with no access to antiviral treatment for hepatitis C.
Treatment of People Actively Using Drugs for Hepatitis C

Model

- Collaborative
  - Community-based needle exchange programs
  - Tertiary care hepatitis C center

- Multidisciplinary
  - Hepatitis C specialty care
  - Primary care
  - Mental health
  - Substance abuse treatment
  - Intensive case management

- Integrated care
  - Staff cross institutional boundaries
  - Tertiary care provided in community-based locations
Multidisciplinary, Integrated Care Model
**Multidisciplinary, Integrated Care Model: Reducing Barriers and Enhancing Readiness**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Barriers</th>
<th>Readiness Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psycho-education</td>
<td>• Erroneous HCV beliefs</td>
<td>• Enhanced knowledge of HCV and HCV treatment</td>
</tr>
<tr>
<td></td>
<td>• Fear of liver biopsy and treatment side-effects</td>
<td>• Perceived susceptibility/severity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Perceived benefits of antiviral treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Perceived manageability of antiviral treatment</td>
</tr>
</tbody>
</table>

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### Multidisciplinary, Integrated Care Model: Reducing Barriers and Enhancing Readiness

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<tr>
<th>Intervention</th>
<th>Barriers</th>
<th>Readiness Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motivational Enhancement Therapy</td>
<td>• Destabilizing substance use</td>
<td>• Enhanced sense of self-efficacy</td>
</tr>
<tr>
<td></td>
<td>• More urgent/competing priorities</td>
<td>• Increased health-focused behaviors</td>
</tr>
<tr>
<td></td>
<td>• Fear of liver biopsy and treatment side-effects</td>
<td>• Enhanced motivation to undergo HCV antiviral treatment</td>
</tr>
</tbody>
</table>

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## Multidisciplinary, Integrated Care Model: Reducing Barriers and Enhancing Readiness

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<thead>
<tr>
<th>Intervention</th>
<th>Barriers</th>
<th>Readiness Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensive Case Management</td>
<td>• Structural:</td>
<td>• Decreased focus on daily survival needs; freedom to focus on health-related goals</td>
</tr>
<tr>
<td></td>
<td>➢ Homelessness</td>
<td></td>
</tr>
<tr>
<td></td>
<td>➢ Poverty</td>
<td></td>
</tr>
<tr>
<td></td>
<td>➢ Lack of health insurance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• More urgent/competing priorities</td>
<td>• Delivery of coordinated care among multidisciplinary team</td>
</tr>
<tr>
<td></td>
<td>• Fragmented care</td>
<td>• Active partnering in coordinated care plan</td>
</tr>
</tbody>
</table>

- **Intervention**: Intensive Case Management
- **Barriers**: Structural, Homelessness, Poverty, Lack of health insurance, More urgent/competing priorities, Fragmented care
- **Readiness Goals**: Decreased focus on daily survival needs; freedom to focus on health-related goals.
### Multidisciplinary, Integrated Care Model: Reducing Barriers and Enhancing Readiness

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Barriers</th>
<th>Readiness Goals</th>
</tr>
</thead>
</table>
| Support Groups | • Inadequate social support  
• Fear of liver biopsy and treatment side-effects | • Increased social support  
• Exposure to successful HCV care stories and positive social influence  
• Enhanced self-efficacy |
### Multidisciplinary, Integrated Care Model: Reducing Barriers and Enhancing Readiness

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Barriers</th>
<th>Readiness Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integrated Primary/Subspecialty Medical Care</td>
<td>• Unaddressed medical conditions</td>
<td>• Care for unmet medical needs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Increased knowledge of health status</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Improved health status</td>
</tr>
</tbody>
</table>
# Multidisciplinary, Integrated Care Model: Reducing Barriers and Enhancing Readiness

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Barriers</th>
<th>Readiness Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance Use Treatment</td>
<td>• Unstable substance use</td>
<td>• Reduced levels of substance use</td>
</tr>
<tr>
<td></td>
<td>• More urgent/competing priorities</td>
<td>• Lifestyle stabilization</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Improved levels of functioning</td>
</tr>
</tbody>
</table>
Multidisciplinary, Integrated Care Model: Reducing Barriers and Enhancing Readiness

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Barriers</th>
<th>Readiness Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric Care</td>
<td>• Unstable psychiatric disorders</td>
<td>• Reduction of psychiatric symptoms (depression, anxiety, post traumatic stress, etc.)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Improved levels of functioning</td>
</tr>
</tbody>
</table>
Treatment of People Actively Using Drugs for Hepatitis C

Program Elements

- **Recruitment: S. Bronx, E. Harlem, Lower East Side**
  - Referred from agency staff
  - HCV support groups
  - Outreach

- **Eligibility:**
  - Age $\geq$ 18 yrs
  - Heroin, cocaine, methamphetamine in past 30 days
  - Interested in being assessed for hepatitis C treatment
  - HCV RNA (+)
  - HIV antibody negative
## Treatment of People Actively Using Drugs for Hepatitis C

- Recruited (≥18 yo, heroin, cocaine/30 days) 30
- HCV RNA-negative (ineligible) 8
- Enrolled (N=22) 22

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (IQR)</td>
<td>40 yrs (30-50 yrs)</td>
</tr>
<tr>
<td>Male</td>
<td>64%</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>White: 50%, African American: 32%, Latino: 18%</td>
</tr>
<tr>
<td>Homeless in past 6 months</td>
<td>68%</td>
</tr>
<tr>
<td>Ever Psychiatric Diagnosis</td>
<td>68%</td>
</tr>
<tr>
<td>Jail or prison in past 6 months</td>
<td>46%</td>
</tr>
<tr>
<td>Inpatient drug treatment in past 6 months (incl. detox)</td>
<td>32%</td>
</tr>
</tbody>
</table>
Treatment of Hepatitis C in Persons Actively Using Illicit Drugs

Baseline Characteristics (N=22)

- Median age at first injection (range) 18 years (16, 22 years)
- Median duration of first injection (range) 19 years (10, 31 years)
- Injected heroin in past 30 days 64%
- Injected cocaine in past 30 days 50%
- Smoked crack in past 30 days 36%
- Drank ≥ 5 drinks ≥ 1x in past 30 days 41%
- HCV genotype 1 73%
- HCV RNA ≥ 800,000 IU/mL 68%
Treatment of Hepatitis C in Persons Actively Using Illicit Drugs: Current Outcomes

Sample N = 30

RNA Negative n = 8

RNA Positive n = 22

Eligible for Treatment n = 18

Decided Against HCV Treatment n = 9

Started HCV Treatment n = 9

Liver Biopsy n = 15

Relocated n = 2
Incarcerated n = 1
Head Injury n = 1

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### Baseline Characteristics (N=22)

- Injected drugs in past 30 days: 17 (77%)
- Injected heroin in past 30 days: 14 (64%)
- Injected cocaine in past 30 days: 11 (50%)
  - Median # injections in past 30 days (N=17): 30 (IQR, 9 – 123)
  - Median # injections in past 6 months (N=19): 168 (IQR, 42 – 897)
- Smoked crack in past 30 days: 36% (8)
  - Median # days smoked crack in past 30 days (N=8): 10 (IQR, 4 – 19)
- Drank ≥ 5 drinks ≥ 1x in past 30 days: 41% (9)
Treatment of People Actively Using Drugs for Hepatitis C

Liver Biopsy: Fibrosis Stage (N=15)
### Treatment of People Actively Using Drugs for Hepatitis C

#### Treatment (N=22)

- Left NYC: 2 (9%)
- Incarcerated: 1 (5%)
- Traumatic brain injury: 1 (5%)
- Completed evaluation and available for f/u: 18 (82%)

#### (N=18)

- Initiated peginterferon/ribavirin: 9 (50%)
- Opted to defer: 9 (50%)
Treatment of Hepatitis C in Persons Actively Using Drugs

Barriers and Facilitators during Evaluation Phase

- **Facilitators Endorsed**
  - Treated (p=0.28*)
  - Not treated (p=0.38*)
    - (p=0.26**)

- **Barriers Endorsed**
  - Treated (p=0.03*)
  - Untreated (p=0.44*)
    - (p=0.02**)

*Within group difference
**Between-group difference
### Treatment of People Actively Using Drugs for Hepatitis C

#### Participants’ reasons for deferring treatment* (N=9)

<table>
<thead>
<tr>
<th>Reason</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>More urgent needs at present</td>
<td>6</td>
<td>66%</td>
</tr>
<tr>
<td>Homeless/unstable housing</td>
<td>5</td>
<td>56%</td>
</tr>
<tr>
<td>Concerned drug use would interfere w/adherence</td>
<td>3</td>
<td>33%</td>
</tr>
<tr>
<td>Concerned about side effects</td>
<td>3</td>
<td>33%</td>
</tr>
<tr>
<td>Mental health concerns</td>
<td>1</td>
<td>13%</td>
</tr>
<tr>
<td>Mild fibrosis (on biopsy)</td>
<td>1</td>
<td>13%</td>
</tr>
<tr>
<td>Perceived mild fibrosis (no biopsy)</td>
<td>1</td>
<td>13%</td>
</tr>
</tbody>
</table>

*Mean = 2.2 reasons per participant
Treatment of Hepatitis C in Persons Actively Using Illicit Drugs

Tolerability (N=8*)

- **Side effects:**
  - fatigue (n=6)
  - loss of appetite (n=5)
  - difficulty sleeping (n=3)
  - difficulty concentrating (n=3)
  - nausea (n=2)
  - depression (n=3)
  - skin rash (n=3)
  - hair loss (n=2)

- Rx epoetin-alfa (anemia) 5 (63%)
- Rx filgrastim (neutropenia) 5 (63%)
- Rx psych meds before HCV treatment 2 (25%)
- Rx psych meds during HCV treatment 2 (25%)
- Antiviral dose reductions 1 (13%)
- Antiviral drug discontinuations (incl. temporary) 2 (25%)

*Excludes one participant lost to follow-up after 2 weeks
Treatment of Hepatitis C in Persons Actively Using Illicit Drugs

Beck Depression Inventory (BDI) Scores

Mean BDI Score (N=8)

- Baseline: 22
- Start of rx: 17
- During rx: 21

- Severe Depression
- Moderate Depression

Months: 0 1 2 3 4 5 6 7 8 9

On treatment
- Post-treatment

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SUNY Downstate College of Medicine, Brooklyn, NY
Irritability (BSI) During and After Treatment (N=8)

- BSI Anger/Hostility Scale Raw Score
- Months

<table>
<thead>
<tr>
<th>On Treatment</th>
<th>Off Treatment</th>
</tr>
</thead>
</table>

Clinically Significant Irritability

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# Virologic Outcomes of Hepatitis C Antiviral Treatment in People Actively Using Drugs (N=15)

<table>
<thead>
<tr>
<th>Category</th>
<th>First 9 Patients</th>
<th>Next 6 Patients</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained Virologic Response</td>
<td>5</td>
<td>5</td>
<td>10 (67%)</td>
</tr>
<tr>
<td>Nonresponse</td>
<td>1</td>
<td>1</td>
<td>2 (13%)</td>
</tr>
<tr>
<td>Relapse</td>
<td>1</td>
<td>0</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Early discontinuation</td>
<td>1</td>
<td>0</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Loss to follow-up</td>
<td>1</td>
<td>0</td>
<td>1 (7%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>9</td>
<td>6</td>
<td>15 (100%)</td>
</tr>
</tbody>
</table>

**Characteristics:**
- Acute HCV infection: 4/15 (27%)
- Genotype 2/3: 7/15 (47%)
- African American: 4/15 (27%)
# Treatment of Hepatitis C in Persons Actively Using Illicit Drugs

<table>
<thead>
<tr>
<th>Illicit Drug Use after Starting Hepatitis C Rx (N=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stopped using*</td>
</tr>
<tr>
<td>• Stopped using daily*</td>
</tr>
<tr>
<td>• Stopped or reduced*</td>
</tr>
</tbody>
</table>

*On patients’ own initiative
### Treatment of People Actively Using Drugs for Hepatitis C: Drug Use

<table>
<thead>
<tr>
<th>Drug Use: Baseline vs. On Treatment (N=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong> (past 30 days)</td>
</tr>
<tr>
<td>% Days heroin/cocaine</td>
</tr>
<tr>
<td># Injections/day</td>
</tr>
<tr>
<td>% Days heavy alcohol</td>
</tr>
</tbody>
</table>
Conclusions

- A large proportion of persons actively using drugs chose antiviral treatment despite considerable barriers and ongoing active drug use.
- They have tolerated the medications well.
- Responses to treatment have been favorable thus far.
- Treating active drug users for hepatitis C appears to be feasible using a collaborative, multidisciplinary, integrated care model.
- Treating active drug users for hepatitis C may serve as a bridge to healthier behaviors in other domains as well.
Treatment of People Actively Using Drugs for Hepatitis C

Summary

- Barriers to hepatitis C treatment in active illicit drug users are many.
- Experience in an increasing number of centers worldwide suggest that these are not insurmountable.
- Collaboration between those with expertise in viral hepatitis and those with expertise working with substance users is needed.
- Comprehensive, continuing, integrated, multidisciplinary care
- Primary care, expert hepatitis C care from experienced providers, evidence-based substance use treatment, mental health services, social services, case management, motivational enhancement counseling, support groups
- More research on effective hepatitis C treatment methods
Treatment of People Actively Using Drugs for Hepatitis C

Collaborators

Program Participants
Michael Carden, MS, CRC
Citiwide Harm Reduction (George Santana, Raffi Torruella, Nancy Estrada)
Lower East Side Harm Reduction Center (Andrea Lindstrom)
New York Harm Reduction Educators (Donald Davis, Vanilla)
Andrew Talal, MD
Ann B. Beeder, MD
Elizabeth Getter, MD
Steve Ferrando, MD
Jessica Daniels, MD
Colleen A. Flanigan, RN, MS
Susan J. Klein, MS
AIDS Institute, New York State Department of Health
NIH grants R01-DA09532, R01-DA16159 and M01-RR00047
HCV Infection in Injection Drug Users

Research Team

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