Is the Hepatitis C Epidemic Over with Curative Therapy?
Not By A Long Shot; How Mental Illness Fuels the Hepatitis C Epidemic and What to do About It

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Learning Objectives
After attending this presentation, participants will be able to:

- Discuss the ways mental illness complicates the treatment of Hepatitis C
- Describe several psychiatric conditions where treatment may improve outcomes
- Discuss the role of integrated care in Hepatitis C treatment

Why is psychiatry interested in Hepatitis C?

- Psychiatric co-morbidity is involved in propagation of the virus through behavior
- Psychiatric co-morbidity is the major barrier to successful treatment
- Models of integrated care
- Models of disease co-morbidity
- Models for understanding major depression
### HIV and Hepatitis C

<table>
<thead>
<tr>
<th></th>
<th>HIV</th>
<th>Hep C</th>
</tr>
</thead>
<tbody>
<tr>
<td>World prevalence</td>
<td>0.8 %</td>
<td>3 %</td>
</tr>
<tr>
<td>World prevalence</td>
<td>38,000,000</td>
<td>200,000,000</td>
</tr>
<tr>
<td>Highest prevalence</td>
<td>Swaziland 26 %</td>
<td>Egypt 18 %</td>
</tr>
<tr>
<td>Highest prevalence</td>
<td>South Africa 5.6 mil</td>
<td>China 42 mil</td>
</tr>
<tr>
<td>New infections/day</td>
<td>7,000</td>
<td>11,000</td>
</tr>
</tbody>
</table>

Source: 7 of 52

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[Slide 8 of 52]


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[Slide 9 of 52]

Pharmacy costs for Rhode Island correctional facilities

<table>
<thead>
<tr>
<th>Treatment regimen</th>
<th>Clinical recommendation*</th>
<th>Total estimated cost$</th>
<th>Estimated cure rate$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir + Interferon + Ribavirin (3D)</td>
<td>GT3, GT4</td>
<td>$93,400</td>
<td>85–90%</td>
</tr>
<tr>
<td>Sofosbuvir + Ribavirin (2D)</td>
<td>GT 4</td>
<td>$75,800</td>
<td>93%</td>
</tr>
<tr>
<td>Sofosbuvir and Maviret (1D)</td>
<td>GT2 non-cirrhotic; GT4</td>
<td>$84,200</td>
<td>85–95%</td>
</tr>
<tr>
<td>Gilead’s Harvoni (2D) (SOF plus OBI)</td>
<td>GT2 cirrhotic</td>
<td>$112,000</td>
<td>90–99%</td>
</tr>
<tr>
<td>Gilead’s Harvoni (2D) (SOF plus OBI)</td>
<td>GT3, GT4</td>
<td>$168,300</td>
<td>90–99%</td>
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<tbody>
<tr>
<td>Sofosbuvir + Ledipasvir (1D)</td>
<td>GT1 non-cirrhotic</td>
<td>$63,000</td>
<td>95–99%</td>
</tr>
<tr>
<td>Sofosbuvir + Ledipasvir (1D)</td>
<td>GT1 treatment naive cirrhotic, treatment experienced non-cirrhotic; GT4</td>
<td>$94,500</td>
<td>95–99%</td>
</tr>
<tr>
<td>Gilead’s Harvoni (2D) (SOF plus OBI)</td>
<td>GT1 treatment experienced cirrhotic</td>
<td>$189,000</td>
<td>95–99%</td>
</tr>
<tr>
<td>Ombitasvir + Paritaprevir + Ritonavir + Dasabuvir</td>
<td>GT1b, GT4</td>
<td>$83,500</td>
<td>90–99%</td>
</tr>
<tr>
<td>Ombitasvir + Paritaprevir + Ritonavir + Dasabuvir</td>
<td>GT1b non-cirrhotic</td>
<td>$162,000</td>
<td>90–99%</td>
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Pharmacy costs for Rhode Island correctional facilities

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<tr>
<td>Estimated drug costs*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total drug costs</td>
<td>$14,170,063</td>
<td>$37,454,139</td>
<td>$15,188,440</td>
</tr>
<tr>
<td>Budget impact*</td>
<td>RODC 2014 pharmacy budget: $2,723,669</td>
<td>125%</td>
<td>115%</td>
</tr>
<tr>
<td>Estimated cost per patient cured: $176,000–190,000</td>
<td>78%</td>
<td>558%</td>
<td></td>
</tr>
</tbody>
</table>

*Total drug costs estimated from interferon-free regimens Sofosbuvir + Ribavirin and Sofosbuvir + Ombitasvir

*Budget impact calculations based on public record of RODC 2014 expenditures

Mood disorder
Executive Disorder
Cognitive Disorder
Addiction
Paraphilia
Personality Disorder
Cognitive limitation
Poverty
Poor coping skills
Social Disenfranchisement

Risk behaviors
Hepatitis C

The web of psychiatric co-morbidity is so dense that it almost defies description

A web of co-morbidity

Drug toxicity
Nerve tissue injury
Immune dysregulation
Neuropathy
Dementia
Depression
Disinhibition
Apathy
Disability
Social isolation
Opiate dependence
Impoverishment
Risk Behavior
Poor adherence
Adherence to Direct-Acting Antivirals

- The high reproductive rate of hepatitis C virus (HCV) makes inadequate suppression lead to resistance-associated mutations and decreases the likelihood of treatment success.
- The increasing use of direct-acting viral inhibitors for HCV that are extremely expensive make a good outcome for treatment imperative.

Adherence as a model of co-morbidity

Taking medication is a behavior

Environmental exposure

- increase
- positive

Environmental response

Behavior

- decrease
- negative

Depression
Dementia
Delirium
Intellectual endowment
Temperament
Medication taking behavior
Addictions
Life experiences
Social organization and support
Role of Life Story

- Institutional health care may have a negative effect on the way patients view treatment.
- Cultural and personal assumptions strongly influence the way patients behave.
- Behavior profoundly influences the outcome of medical care interventions.

Beliefs about illness
- Immediate life issues
- Health awareness and commitment
- Negative and positive experiences with healthcare and medications
- Cultural attitude toward medical care
- Social organization and support

Interventions for Improved Adherence

- Frequent short visits with positive reinforcement for desired behaviors, and careful avoidance of reinforcing undesirable (non-adherent) behavior.
- Understanding the validity of the influences and previous experiences of the patient.
- Interventions at meaning (insight), assumptions (cognitive), behavior (behavioral), and experience (your response to the behavior) targeted at improved adherence.
The Role of Temperament

- Consequence avoidance vs reward seeking
- Now vs future focus
- Feeling vs function
- Cooperativeness vs disagreeableness
- Distrust (paranoia) vs trust (gullibility)
- Conscientiousness vs spontaneously directed

Simplified model of disposition

Percent of population

Introversion  Extraversion
Punishment avoidant  Reward directed
Future directed  Present directed
Function directed  Feeling directed

"You’re full of moxie - also, gonorrhea."
Cultural factors

- Our patients with vulnerable temperaments and cognitive limitations are particularly affected by cultural factors.

Increased patient satisfaction correlates with increased mortality

**Interventions to Improve Adherence**

- Reframe goals into those that fit the patient's temperament
- Help patients to see the strengths of their endowments
- Rewards that will come from taking medications rather than problems with not taking medications
- Conspiring with the patient to get better despite the system that keeps them ill

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**Role of Substance Abuse**

- Current alcohol abuse and drug use is associated with poorer outcomes and incomplete HCV treatment
- Addiction is associated with viral resistance and increased mortality
- Collaborative treatment improves outcomes
- For opiate addiction, substitution therapy is the best studied intervention and has been shown to have improved outcomes in HCV

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**Interventions to Improve Adherence**

- Ongoing assessment of substance abuse
- In some cases, ongoing toxicology screens
- Collaborative arrangements for substance abuse treatment (if possible within the clinic)
- Opiate substitution therapy (eg, buprenorphine and naloxone) is extremely helpful
- Helping the patient find and initiate 12-step–based treatments (ie, AA, NA) which are free and often effective
Role of Comorbid Mental Illness

- Depression leads to poor adherence
  - Treatment reverses this
  - Treatment of depression models successful treatment to help patients get ready for HCV treatment
- Schizophrenia and bipolar illness are both associated with poor outcomes and poor adherence
  - Collaborative treatment can reverse this

Impoverishment
Disenfranchisement
Demoralization
CNS inflammation
Substance abuse
Cognitive impairment

Depression
Hep C

Impulsivity
Hopelessness
Substance abuse
Cognitive impairment
Disenfranchisement
Pro-inflammatory?

Demoralization
Major Depression
Identifying Major Depression

- **Mood** - the sense of baseline state of happiness that is usually present
- **Vital sense** - the sense of being well, healthy, energetic, alert and able
- **Self Attitude** - the sense of being good, of doing well, of effectiveness and utility to others
- **Anhedonia** - the loss of reward (pleasure, satiation or satisfaction) associated with behaviors

The “neurovegetative” signs of depression

- **Sleep**
  - EARLY MORNING AWAKENING
  - Difficulty falling asleep
  - Disrupted sleep architecture
- **Appetite**
  - Change in food taste
  - Weight loss or gain
- **Poor concentration, decreased interest, fatigue**
- **G.I. function**
- **Motor retardation**
- **Immune dysfunction?**

Factors associated with depression

- CNS inflammation
- Auto-immune disease
- Substance abuse
- Genetic vulnerability
- Subcortical damage
Hepatitis C and Depression

- Depression in 40-50%
  - Probably both as a consequence of depression induced risk as well as depression caused by Hepatitis C
- Antidepressant treatment is effective
- Prophylaxis with antidepressants may be effective

Tavakkoli Nelligan Basseri Lee

<table>
<thead>
<tr>
<th>Rate of depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tavakkoli</td>
</tr>
<tr>
<td>31 %</td>
</tr>
</tbody>
</table>
IL-6 and 5-HIAA correlate with INF administration and depression


LL (long) Serotonin transporter promoter gene is associated with a decreased risk of depression with INF


CC IL-6 genotype ("low IL-6") is associated with a decreased risk of depression with INF
Alleles for decreased Serotonin transporter promoter are associated with increased risk of INF-induced depression


Depression correlates with subcortical deficits in patients receiving INF

Behavior → Reward
### Conclusions

- Hepatitis C is a psychiatric epidemic
- Without collaborative treatment, expense is higher, outcome is poorer, and transmission increases
- The CNS effects of chronic infection are a useful model for understanding pathophysiology
Your insurance company only authorized me to take out one. You pick.

“IT’s the only treatment option he has under his current health plan.”