

A Doctor, A Pharmacist and an Activist Talk about HCV

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MISSION STATEMENT

Helping homeless youth and other marginalized people move towards improved health and self-sufficiency.

History



outsidein



outsidein

OUTSIDE IN
TOGETHER ON THE EDGE

Outside In



Hepatitis C is Curable

HCV, which primarily affects people who inject drugs (PWID), bestows a significant and increasing burden.

Current treatment of HCV is simple, safe, and effective.

BUT, there is poor uptake in assessment and treatment of HCV among PWID

HCV and PWID--let's cover:

- HCV is curable
- HCV background
- Treatment history
- Tradition of exclusion of PWID
- Affecting HCV
- Barriers to cure

HCV background

1989-virus is identified/described
(before was “non-A, non-B”)

1992-test is available, blood
products are screened

HCV Background

- “Silent” virus
- Transmitted primarily via sharing injection equipment
- Chronic (lifelong) in 80% of infected
- Sequelae include: liver disease
Huge cost (lives, \$\$)

Running the numbers

Estimated 50% of infected people are unidentified
US - % and (prevalence) of HCV infection:

general population: 1-2% (3-5 million)

homeless/incarcerated: 30-40% (500-800K)

PWID: 75-90% (1-2 million)

20-30% acquire HCV in first 2yrs of injecting

(CDC)

The Numbers

HCV infection progresses to:

Cirrhosis - 20% after 20years of infection

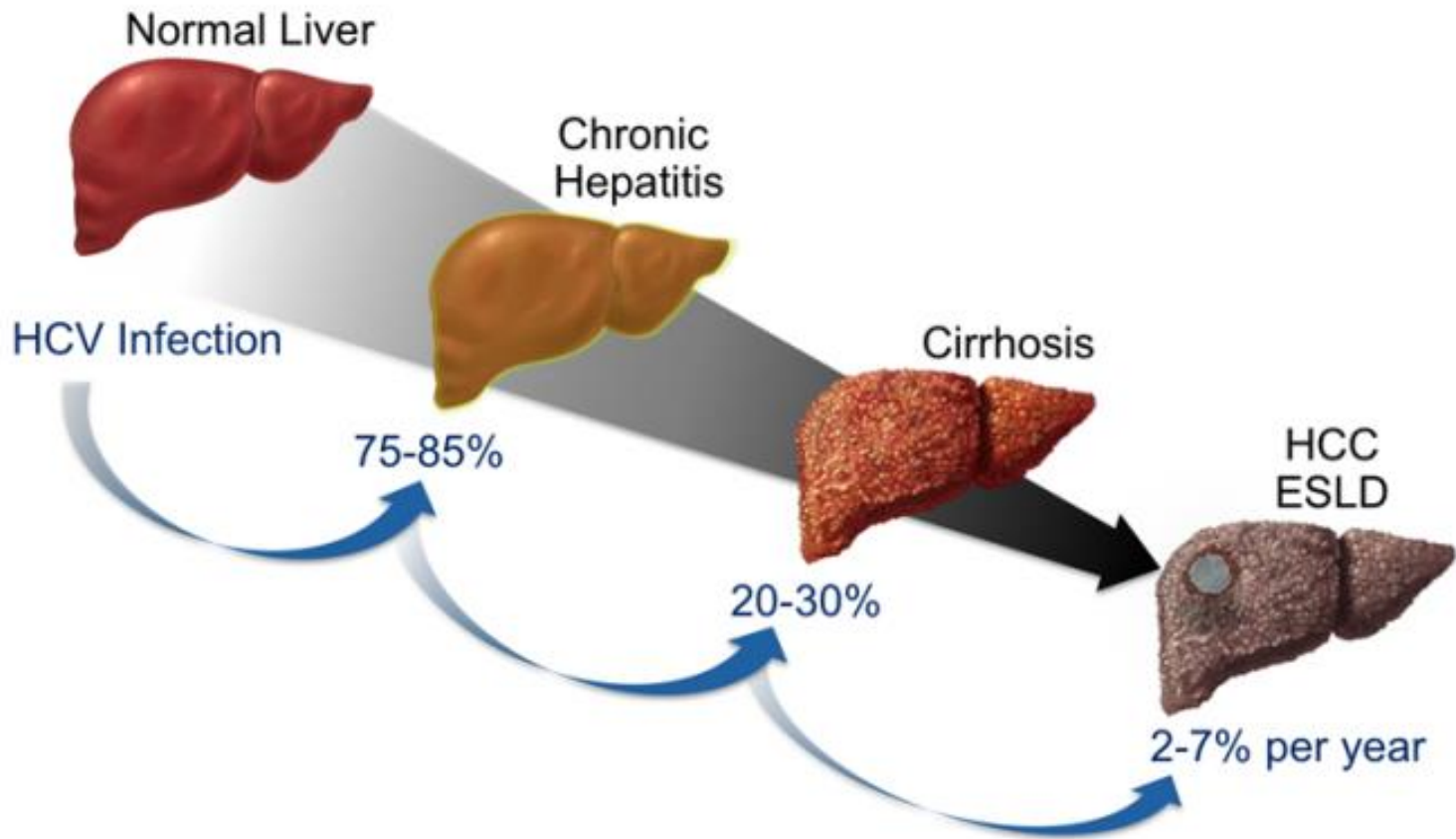
#1 reason for liver transplant

Hepatocellular carcinoma (HCC) - if cirrhosis,

5yr risk is 30%

Mortality - exceeds HIV (since 2007)

Progression of HCV



In Oregon (2008-2012)



Average chronic HCV 5087

Hospitalizations 3917 HCV-infected people
admitted for advanced liver disease

783 (ave) annual hospitalizations

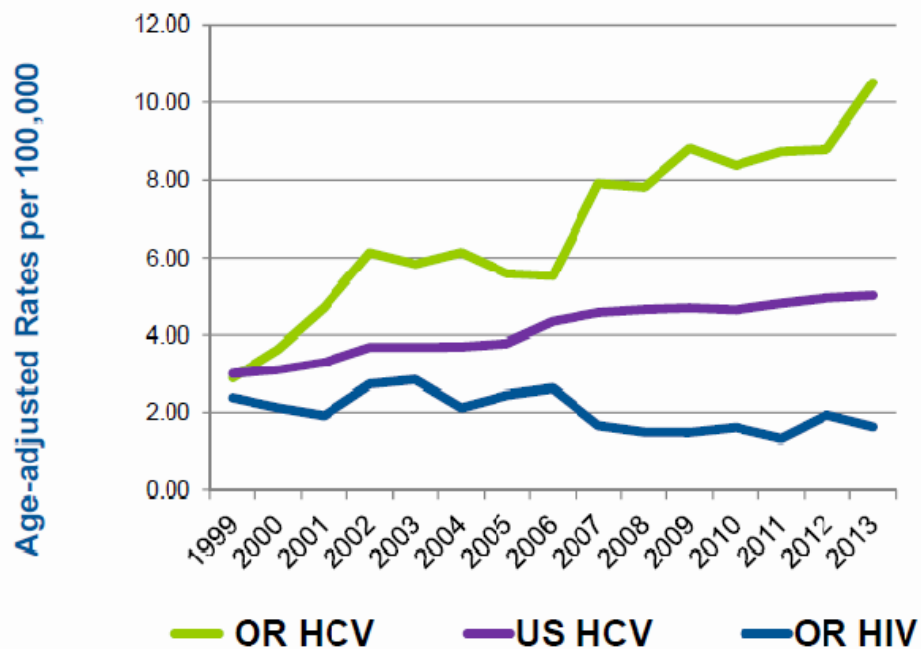
Average stay - 5 days

Average cost - \$27000

Mortality 6x HIV-related mortality

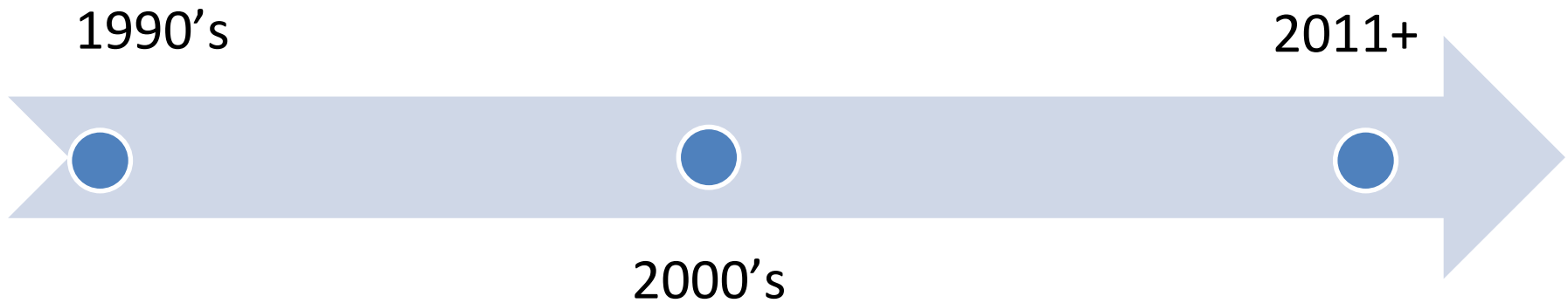
Age-adjusted mortality from HCV and HIV in Oregon and from HCV nationally, 1999-2013

Age-adjusted mortality rates



- 83% of HCV-related deaths were in persons aged 45-64 years
- Only 16% were \geq 65 years

History of Hepatitis C Medications



Progress made each decade.

25 years later- New medications are a game changer!



1990's

Interferon 1991

- Interferes with viral replication
- **Side Effects**
 - Several **Boxed Warnings** for serious disorders
 - Neuropsychiatric- depression, suicidality
 - Autoimmune, infectious, ischemic disorders
 - Fatigue, headache, flu-like symptoms, nausea
- Requires periodic clinical and laboratory monitoring
- Treatment Duration 48 weeks
- SVR 9% (GT1) and 30% (G2-3)

Interferon Boxed Warnings

Boxed Warning

Alpha interferons, including interferon alfa-2b, cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Monitor patients closely with periodic clinical and laboratory evaluations. Withdraw therapy from patients with persistently severe or worsening signs or symptoms of these conditions. In many but not all cases these disorders resolve after stopping interferon alfa-2b therapy.¹



1990's continued...

Ribavirin 1998

- Synthetic nucleoside analogue with broad spectrum antiviral activity.
- Used in combination, not effective by itself.
- Side effects and **Boxed warnings**
 - Anemia
 - Teratogenicity
- Treatment duration 24 to 48 weeks
- SVR 29% (GT1) & 62% GT2-3)

Ribavirin Boxed Warning

Boxed Warning

Ribavirin monotherapy is not effective for the treatment of chronic hepatitis C virus (HCV) infection and should not be used alone for this indication.

The primary clinical toxicity of ribavirin is hemolytic anemia, which may result in worsening of cardiac disease and lead to fatal and nonfatal myocardial infarctions (MIs). Do not treat patients with a history of significant or unstable cardiac disease with ribavirin.

Significant teratogenic and/or embryocidal effects have been demonstrated in all animal species exposed to ribavirin. In addition, ribavirin has a multiple-dose half-life of 12 days, and it may persist in nonplasma compartments for as long as 6 months. Therefore, ribavirin therapy is contraindicated in women who are pregnant and in the male partners of women who are pregnant. Extreme care must be taken to avoid pregnancy during therapy and for 6 months after completion of treatment in women receiving ribavirin therapy and female partners of men who are taking ribavirin therapy. At least 2 reliable forms of effective contraception must be used during treatment and during the 6-month posttreatment follow-up period.^{1 2 3 4 10}



2000's

2001-Enhancements to Interferon and Ribavirin

- Pegylation of Interferon
 - Med stays in the bloodstream longer
 - Move to weekly dosing (from 3 times per week dosing)
- Prefilled syringes
- Co-marketed products
- Treatment duration 24-48 weeks
- SVR 45% (GT1) & 82% (GT2-3)



2011 to present

Protease Inhibitors 2011

- Genotype 1 (some GT4)
- Triple Therapy- Used in combination with interferon and ribavirin.
- Treatment Duration- 24 to 48 weeks
- SVR 66%

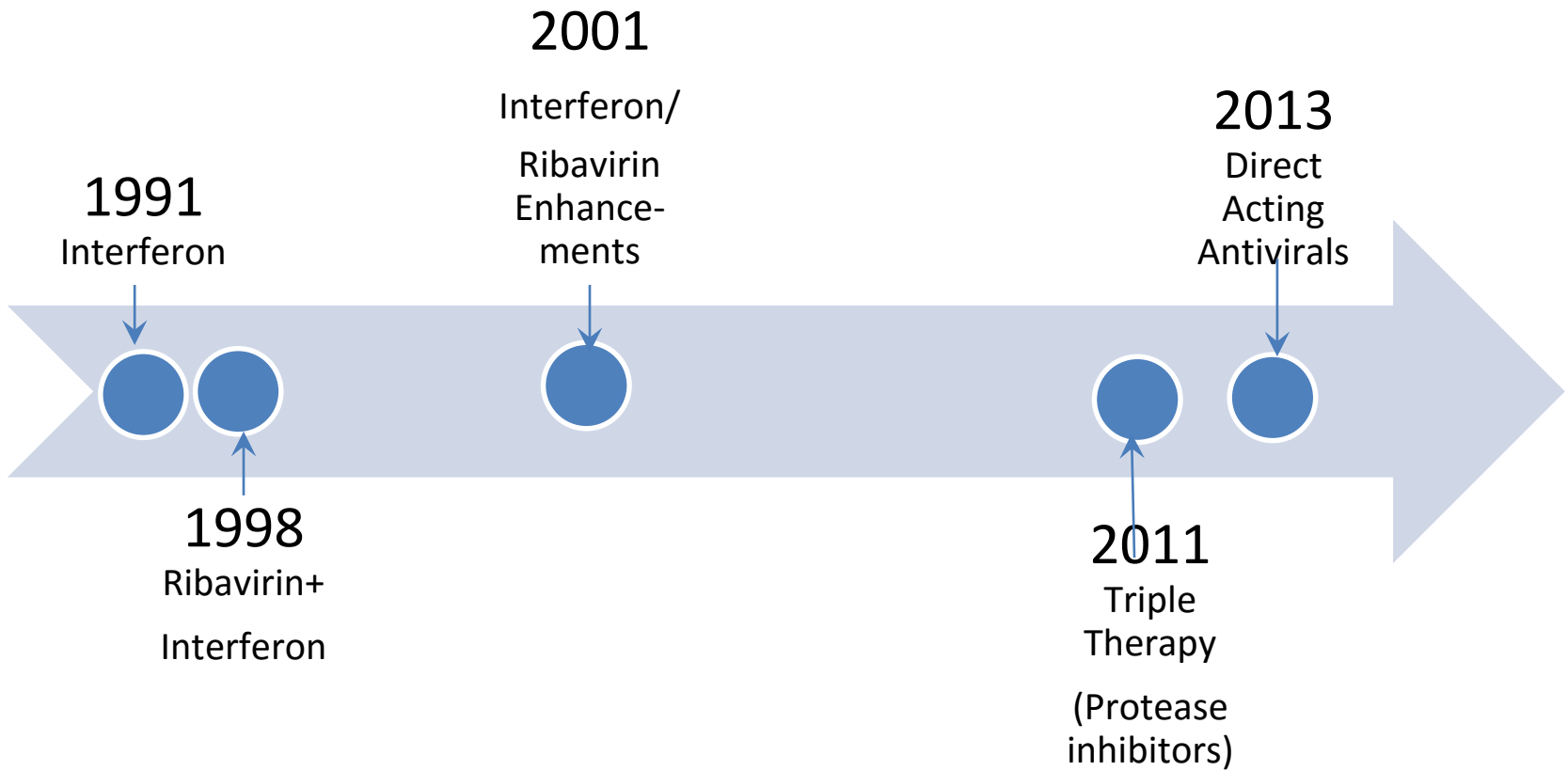


2011 to present

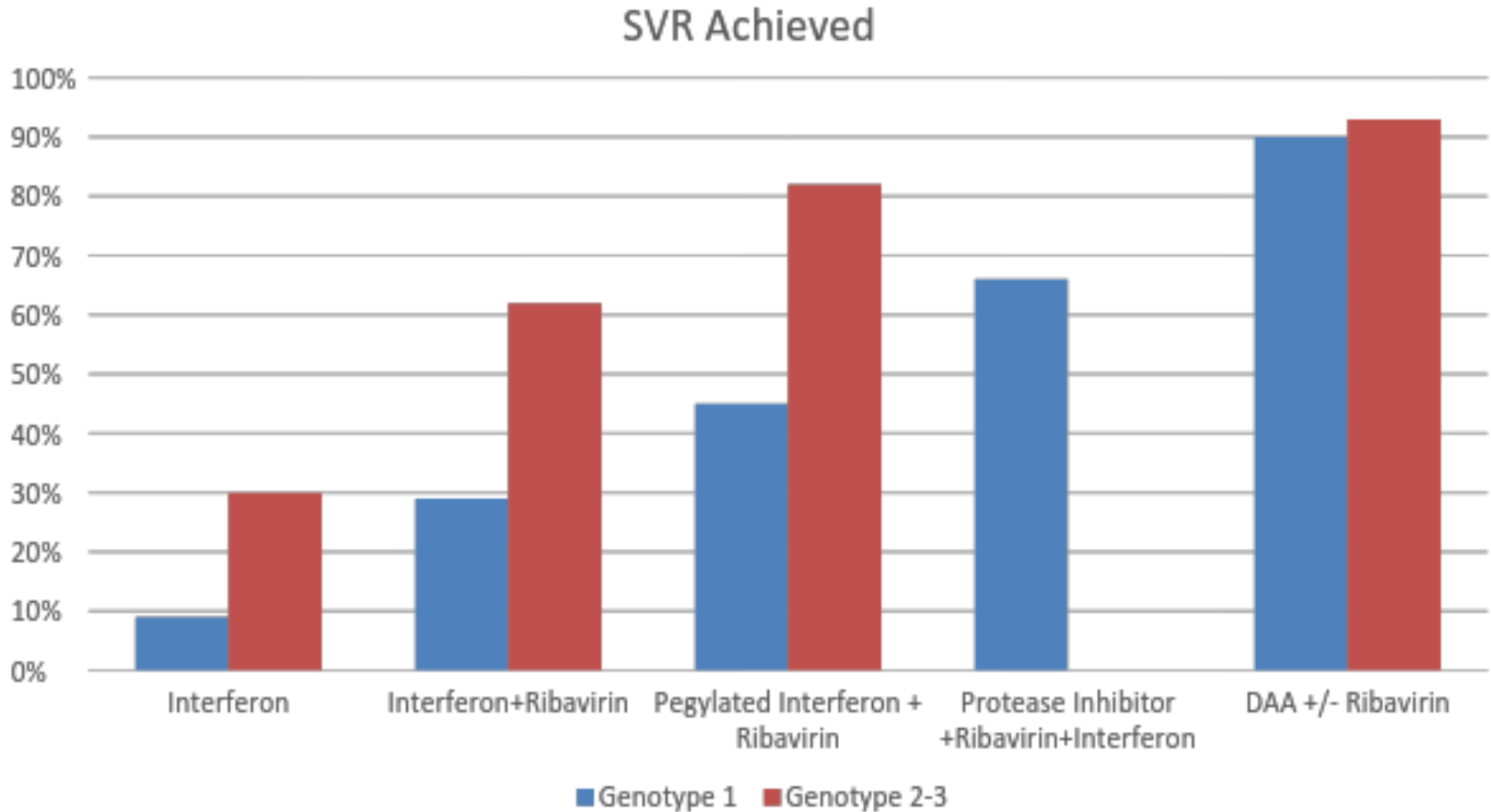
Direct Acting Antivirals 2013

- Target proteins involved in viral replication
- Once Daily Dosing
- Greater tolerability
- No Boxed Warnings
- Treatment Duration- 8 to 24 weeks
- SVR over 90%

Medication Timeline



Sustained Virological Response (SVR)



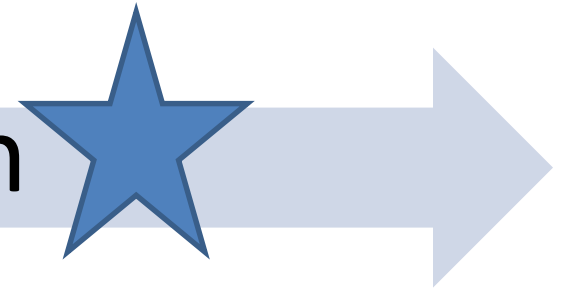
Advantages of Direct Acting Antivirals (DAA)

- Once a day dosing
- Fewer side effects
 - No Neuropsychiatric reactions
 - No Boxed Warnings
- Fewer drug interactions
- Shorter treatment duration
- Less clinical monitoring
 - > Appropriate to treat in primary care

Limitations of DAA

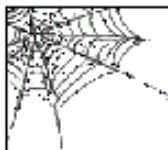
- Expensive
- Insurance coverage restrictions
- Some resistance noted (in NS5A inhibitors)
- Still needs to be used in combination with other agents in certain instances

On the Horizon



Shorter treatment durations

Pan-Genotypic treatments



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Management of Hepatitis C

National Institutes Of Health
Consensus Development Conference Statement
March 24-26, 1997



“treatment of patients who are drinking significant amounts of alcohol or who are actively using illicit drugs should be delayed until these habits are discontinued for at least 6 months. Such patients are at risk for the potential toxic effects of alcohol and other drugs”

<https://consensus.nih.gov/1997/1997HepatitisC105html.htm>



From: Restrictions for Medicaid Reimbursement of Sofosbuvir for the Treatment of Hepatitis C Virus Infection in the United States

Ann Intern Med. 2015;163(3):215-223. doi:10.7326/M15-0406

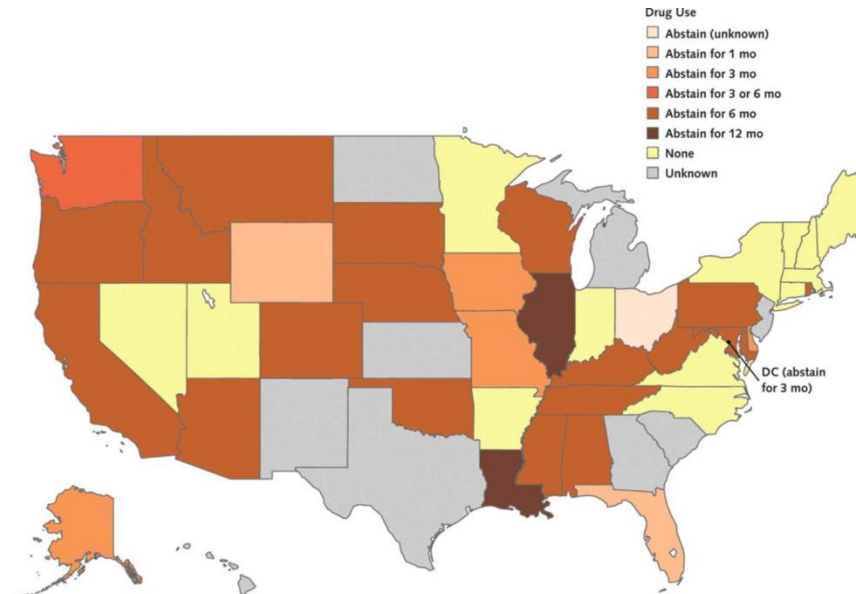


Figure Legend:

Medicaid reimbursement criteria for sofosbuvir based on the required period of abstinence from drug and alcohol use.

From: Restrictions for Medicaid Reimbursement of Sofosbuvir for the Treatment of Hepatitis C Virus Infection in the United States

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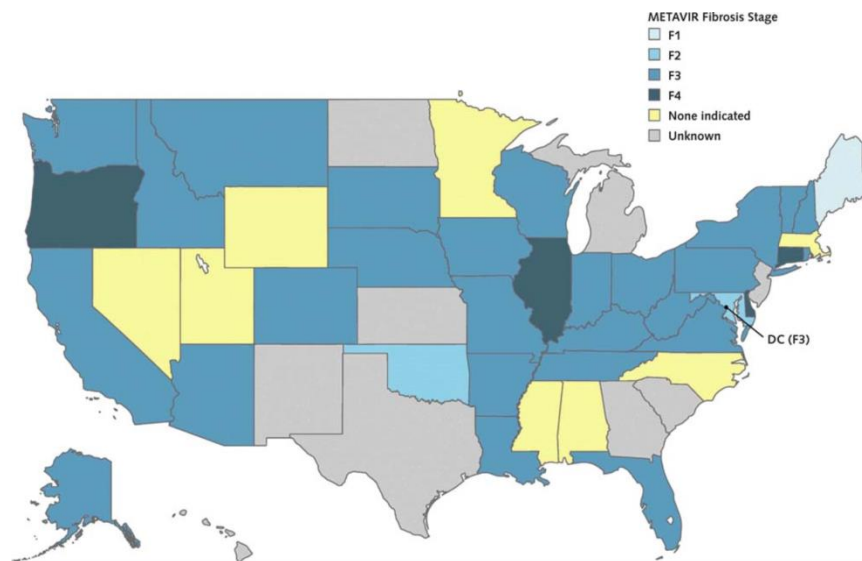


Figure Legend:

Medicaid reimbursement criteria for sofosbuvir based on documented liver fibrosis stage required for reimbursement.
METAVIR = Meta-Analysis of Histologic Data in Viral Hepatitis.

Treatment requirements for insurance to cover it in Oregon

- Fibrosis Criteria- Stage 3 or 4
- Must be abstinent from injection drugs, illicit drugs and marijuana, and alcohol abuse for more than 6 months
- Must be prescribed by or in consultation with a hepatologist or a gastroenterologist with experience with HCV



STIGMA

drug users are more than a label

JOURNAL OF HEALTH PSYCHOLOGY

Health workers' support for hepatitis C treatment uptake among clients with a history of injecting

Loren Brener¹[↑](#)

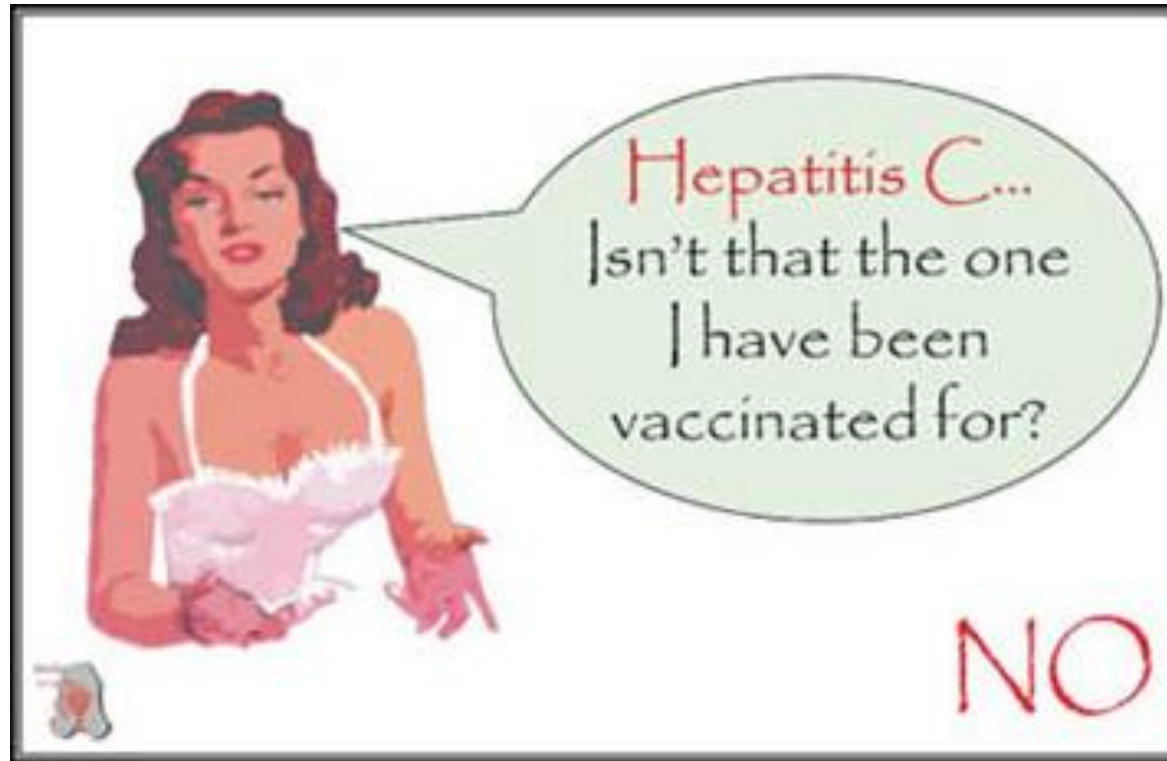
Courtney von Hippel²

Hannah Wilson¹

Max Hopwood¹

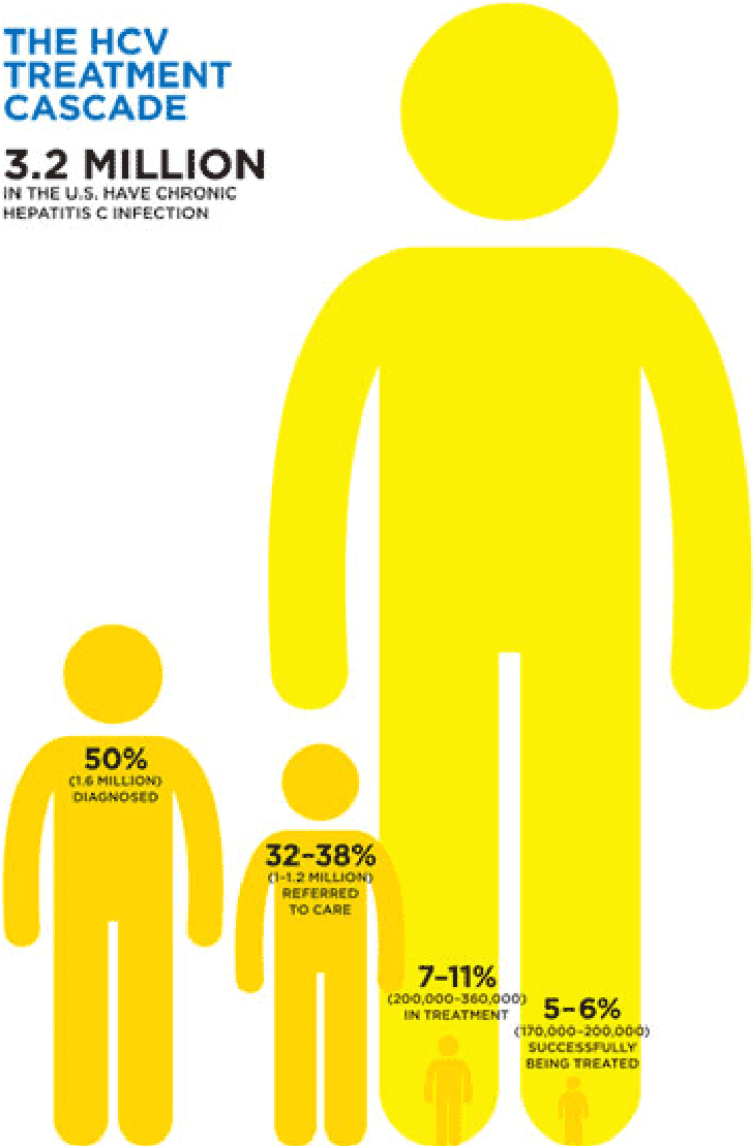
“Participants who showed more negative attitudes towards people who inject drugs were less supportive of clients entering hepatitis C virus treatment, illustrating the influence of health workers' attitudes in determining treatment options offered to clients.”

Lack of Education



THE HCV TREATMENT CASCADE

3.2 MILLION
IN THE U.S. HAVE CHRONIC
HEPATITIS C INFECTION



A photograph of a white sign with black text mounted on a black metal fence. The sign is divided into three horizontal sections. The top section contains the word "RESPECT" in large, bold, sans-serif capital letters. The middle section contains the phrase "BEI AICI" in smaller, bold, sans-serif capital letters, flanked by vertical bars. The bottom section contains the word "OTHER" in large, bold, sans-serif capital letters. The sign is secured to the fence with four metal fasteners, one in each corner. The background shows a clear blue sky and a blurred outdoor setting.

RESPECT
BEI AICI
OTHER

Is treating the PWID population
possible?

Yes!

Using HCV DAA in Vulnerable HIV patients

Retrospective Study looking at HIV/Hep C co-infected individuals with Ongoing Barriers to Care.

- Inclusive HCV treatment protocol
- Connection to syringe exchange
- Adherence aids
- Demonstrated it is possible! SVR 76.5%

Cachay ER, Wyles D, Hill L, et al. The Impact of Direct-Acting Antivirals in the Hepatitis C-Sustained Viral Response in Human Immunodeficiency Virus-Infected Patients With Ongoing Barriers to Care. *Open Forum Infect Dis.* 2015;2(4):ofv168.

Adherence Among PWID

Studies have shown equivalent adherence between PWID and non-PWID (PWARDID)

2008 AIDS and Behavior - 38 studies analyzed = comparable adherence to HAART among PWID vs non-PWID

2013 Aspinall et al - meta-analysis of 10 studies of HCV treatment of PWID = acceptable adherence

2009 Hellard et al - studies of HCV treatment outcomes comparable among PWID vs non-PWID

Systems Can Improve Adherence

Couple treatment with MAT, contingency management, and other novel approaches

Binford et al 2002 - HIV-infected PWID; short-term success

Eliminate System Barriers

HCV treatment does not always require
specialty care

Arora et al 2011 - ECHO model produces good results for underserved populations treated in primary care settings



- #5 Evaluation by a practitioner who is prepared to provide comprehensive management, including consideration of antiviral therapy, is recommended for all persons with current (active) HCV infection. (IIa-C)
- August 2015



- **5. Assessing for HCV treatment**
- All adults and children with chronic HCV infection, including people who inject drugs, should be assessed for antiviral treatment (strong recommendation, moderate quality of evidence).

DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
7500 Security Boulevard, Mail Stop S2-26-12
Baltimore, Maryland 21244-1850



Center for Medicaid and CHIP Services

NOVEMBER 5, 2015

MEDICAID DRUG REBATE PROGRAM NOTICE

Release No. 172

For State Technical Contacts

ASSURING MEDICAID BENEFICIARIES ACCESS TO HEPATITIS C (HCV) DRUGS

The Centers for Medicare & Medicaid Services (CMS) remains committed to Medicaid beneficiaries continuing to have access to needed prescribed medications, a commitment we know that states share. The purpose of this letter is to advise states on the coverage of drugs for Medicaid beneficiaries living with hepatitis C virus (HCV) infections. Specifically, this letter addresses utilization of the direct-acting antiviral (DAA) drugs approved by the Food and Drug Administration (FDA) for the treatment of chronic HCV infected patients.

<https://www.medicare.gov/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/Rx-Releases/State-Releases/state-rel-172.pdf>



Improving Adherence

Studies show SVR is achievable in the PWID population.

These studies:

- Have a prescreening process/Identify candidates
- Offer adherence support

Pharmacist Drug Adherence Work-up Tool (DRAW)

Tool used to identify patient specific adherence issues and offers suggestions for improving adherence rates.

http://millionhearts.hhs.gov/Docs/TUPD/DRAW_Tool.pdf

Medication Adherence



Remembering
to take



Education



Perception of
necessity



Cost/resources



Cognitive
issues



Other barriers

Strategies for Improving Adherence

- Remembering to take meds
 - Incorporating meds into routine (meals, bedtime)
 - Simplifying regimens
 - Daily dosing reminders
 - Pill boxes/Blister packs
 - Calendar
 - Smartphone apps
 - Refill reminders/Med synchronization
- Education
 - What the medication does, what it is for...
 - Side effect management
 - Address health literacy issues

Strategies for Improving Adherence continued...

- Perception of med necessity
 - For HEP C making sure the individual is ready for treatment. Explore commitment to treatment.
 - Employ Motivational Interviewing techniques
- Cost/Resources issues
 - Getting insurance coverage
 - Lost medications
- Cognitive issues

Other Barriers

- Unstable housing or safe place to store meds
- Drug/Alcohol use
- MH issues
- Lack of social support
- Stigma
- Incarceration



How can adherence be improved in people with **Other Barriers**?

- Tying Tx to another service (MAT, HIV tx)
- Access to primary care
- Housing assistance
- Programs with frequent client engagement (BH, syringe exchange, group meetings)
- Balance frequency of medication filling (weekly, every 2 weeks, DOT, pharmacist check ins)
- Contingency/incentives

Affecting HCV

Reservoir: HCV-infected PWID + share equipment

Reach, educate, identify, link to care

Decrease reservoir by:

- Keep using, keep sharing, get treated
- Keep using, stop sharing
 - stop using (eg MAT)

Injection practices and “careers”

Affecting HCV

Mathematical models (Martin et al 2014) estimating 10yr prevalence reductions conclude:

harm reduction (opiate substitution and needle/syringe exchange) cannot substantially reduce prevalence (>45%) among PWID

These measures reduce need to treat medically

TREATMENT

IS

PREVENTION

Affecting HCV

Treatment as prevention

2013 Graham et al: success in HIV treatment has reduced HIV transmission

Target the reservoir, eliminate exclusion

What is being done to combat this



Our Plan

- Integrated care- BH, IDU, Primary Care, Pharmacy etc...
- Treat as many people as possible
- Prevent Reinfection

Questions?

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